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A Review of *JACC* Journal Articles on the Topic of Interventional Cardiology: 2011–2012

The Editors

The Worldwide Environment of Cardiovascular Disease: Prevalence, Diagnosis, Therapy, and Policy Issues: A Report From the American College of Cardiology

The environment in which the field of cardiology finds itself has been rapidly changing. This supplement, an expansion of a report created for the Board of Trustees, is intended to provide a timely snapshot of the socioeconomic, political, and scientific aspects of this environment as it applies to practice both in the United States and internationally. This publication should assist healthcare professionals looking for the most recent statistics on cardiovascular disease and the risk factors that contribute to it, drug and device trends affecting the industry, and how the practice of cardiology is changing in the United States. The environment in which the field of cardiology finds itself has been rapidly changing. This supplement, an expansion of a report created for the Board of Trustees, is intended to provide a timely snapshot of the socioeconomic, political, and scientific aspects of this environment as it applies to practice both in the United States and internationally. This publication should assist healthcare professionals looking for the most recent statistics on cardiovascular disease and the risk factors that contribute to it, drug and device trends affecting the industry, and how the practice of cardiology is changing in the United States (1).

Cost-Effectiveness of Transcatheter Aortic Valve Replacement Compared With Surgical Aortic Valve Replacement in High-Risk Patients With Severe Aortic Stenosis: Results of the PARTNER (Placement of Aortic Transcatheter Valves) Trial (Cohort A)

Objectives The aim of this study was to evaluate the cost-effectiveness of transcatheter aortic valve replacement (TAVR) compared with surgical aortic valve replacement (AVR) for patients with severe aortic stenosis and high surgical risk.

Background TAVR is an alternative to AVR for patients with severe aortic stenosis and high surgical risk.

Methods We performed a formal economic analysis based on cost, quality of life, and survival data collected in the PARTNER A (Placement of Aortic Transcatheter Valves) trial in which patients with severe aortic stenosis and high surgical risk were randomized to TAVR or AVR. Cumulative 12-month costs (assessed from a U.S. societal perspective) and quality-adjusted life-years (QALYs) were compared separately for the transfemoral (TF) and transapical (TA) cohorts.

Results Although 12-month costs and QALYs were similar for TAVR and AVR in the overall population, there were important differences when results were stratified by access site. In the TF cohort, total 12-month costs were slightly lower with TAVR and QALYs were slightly higher such that TF-TAVR was economically dominant compared with AVR in the base case and economically attractive (incremental cost-effectiveness ratio <$50,000/QALY) in 70.9% of bootstrap replicates. In the TA cohort, 12-month costs remained substantially higher with TAVR, whereas QALYs tended to be lower such that TA-TAVR was economically dominated by AVR in the base case and economically attractive in only 7.1% of replicates.

Conclusions In the PARTNER trial, TAVR was an economically attractive strategy compared with AVR for patients suitable for TF access. Future studies are necessary to determine whether improved experience and outcomes with TA-TAVR can improve its cost-effectiveness relative to AVR. (THE PARTNER TRIAL: Placement of AoRTic TraNscathetER Valve Trial; NCT00530894) (2).

Zotarolimus-Eluting Peripheral Stents for the Treatment of Erectile Dysfunction in Subjects With Suboptimal Response to Phosphodiesterase-5 Inhibitors

Objectives This study sought to evaluate the safety and feasibility of zotarolimus-eluting stent implantation in focal atherosclerotic lesions of the internal pudendal arteries among men with erectile dysfunction (ED) and a suboptimal response to phosphodiesterase-5 inhibitors.

Background ED, a common condition, is often mediated by atherosclerosis. Current treatment options are limited.

Methods Male subjects with atherosclerotic ED and a suboptimal response to phosphodiesterase-5 inhibitors

As a service to our readers, we have compiled all the relevant manuscripts in individual subject areas of cardiology. These collections should provide a single repository of *JACC* publications in the specific areas. In addition, these compilations should put in perspective the recent advancements and future directions in the important disciplines of cardiovascular medicine.

were enrolled in this prospective, multicenter, single-armed safety and feasibility trial. A novel combination of clinical, duplex ultrasound, and invasive angiographic factors were used to determine eligibility for stent therapy. The primary safety endpoint was any major adverse event 30 days after the procedure. The primary feasibility end point was improvement in the International Index of Erectile Function (Erectile Dysfunction Domain) score ≥4 points in ≥50% of subjects at 3 months. We report 6-month follow-up results, including duplex ultrasound and angiography.

Results Forty-five lesions were treated with stents in 30 subjects. Procedural success was 100% with no major adverse events through follow-up. The primary feasibility endpoint at 6 months was achieved by 59.3% of intention-to-treat subjects (95% confidence interval: 38.8% to 77.6%) and 69.6% of per-protocol subjects (95% confidence interval: 47.1% to 86.8%). Duplex ultrasound peak systolic velocity of the cavernosal arteries increased from baseline by 14.4 ± 10.7 cm/s at 30 days and 22.5 ± 23.7 cm/s at 6 months. Angiographic binary restenosis (≥50% lumen diameter stenosis) was reported in 11 (34.4%) of 32 lesions.

Conclusions Among patients with ED and limited response with pharmacologic therapy, percutaneous stent revascularization of the internal pudendal artery is feasible and is associated with clinically meaningful improvement in both subjective and objective measures of erectile function. (Safety and Feasibility of the Zotarolimus Stent in Treating Males With Erectile Dysfunction (ED) (ZEN); NCT01643200) (3).

A Randomized Multicenter Study Comparing a Paclitaxel Drug-Eluting Balloon With a Paclitaxel-Eluting Stent in Small Coronary Vessels: The BELLO (Balloon Elution and Late Loss Optimization) Study

Objectives The aim of this study was to evaluate the efficacy of drug-eluting balloons (DEB) compared with paclitaxel-eluting stents (PES) for the reduction of restenosis in small vessels.

Background DEB have been shown to be effective in the treatment of coronary in-stent restenosis, but data are limited regarding their efficacy in de novo disease.

Methods BELLO (Balloon Elution and Late Loss Optimization) is a prospective, multicenter trial that randomized 182 patients with lesions located in small vessels (reference diameter <2.8 mm) to treatment with paclitaxel DEB and provisional bare-metal stenting (n = 90) or PES implantation (n = 92). The primary endpoint was noninferiority of angiographic in-stent (in-balloon) late loss with a delta of 0.25 mm. Secondary endpoints were angiographic restenosis, target lesion revascularization, and major adverse cardiac events (MACE; death, myocardial infarction, target vessel revascularization) at 6 months.

Results Baseline characteristics were well matched, except for a smaller vessel size in the DEB group (2.15 ± 0.27 mm vs. 2.25 ± 0.24 mm; p = 0.003). The majority (89%) of lesions involved vessels with a diameter <2.5 mm. Bailout stenting was required in 20% of lesions in the DEB group. The primary endpoint of in-stent (in-balloon) late loss was significantly less with DEB compared with PES (0.08 ± 0.38 mm vs. 0.29 ± 0.44 mm; difference −0.21; 95% CI: −0.34 to −0.09; pnoninferiority < 0.001; psuperiority = 0.001). At 6 months, DEB and PES were associated with similar rates of angiographic restenosis (8.9% vs. 14.1%; p = 0.25), target lesion revascularization (4.4% vs. 7.6%; p = 0.37), and MACE (7.8% vs. 13.2%; p = 0.77).

Conclusions Treatment of small-vessel disease with a paclitaxel DEB was associated with less angiographic late loss and similar rates of restenosis and revascularization as a PES. (Balloon Elution and Late Loss Optimization [BELLO]; Study NCT01086579) (4).

A New Drug Delivery System for Intravenous Coronary Thrombolysis With Thrombus Targeting and Stealth Activity Recoverable by Ultrasound

Objectives The purpose of this study was to develop a new intelligent drug delivery system for intracoronary thrombolysis with a strong thrombolytic effect without increasing bleeding risk.

Background Rapid recanalization of an occluded coronary artery is essential for better outcomes in acute myocardial infarction. Catheter-based recanalization is widely accepted, but it takes time to transport patients. Although the current fibrinolytic therapy can be started quickly, it cannot achieve a high reperfusion rate. Recently, we generated nanoparticles comprising tissue-type plasminogen activator (tPA), basic gelatin, and zinc ions, which suppress tPA activity by 50% with 100% recovery by ultrasound (US) in vitro.

Methods The thrombus-targeting property of nanoparticles was examined by an in vitro binding assay with von Wilbrand factor and with a mouse arterial thrombosis model in vivo. The thrombolytic efficacy of nanoparticles was evaluated with a swine acute myocardial infarction model.

Results Nanoparticles bound to von Wilbrand factor in vitro and preferentially accumulated at the site of thrombus in a mouse model. In a swine acute myocardial infarction model, plasma tPA activity after intravenous injection of nanoparticles was approximately 25% of tPA alone and was recovered completely by transthoracic US (1.0 MHz, 1.0 W/cm^2). During US application, plasma tPA activity near the affected coronary artery was recovered and was higher than that near the femoral artery. Although treatment with tPA alone (55,000 IU/kg) recanalized the occluded coronary artery in only 1 of 10 swine, nanoparticles containing the same dose of tPA with US achieved recanalization in 9 of 10 swine within 30 min.

Conclusions We developed an intelligent drug delivery system with promising potential for better intravenous coronary thrombolysis (5).

Effects of Radial Versus Femoral Artery Access in Patients With Acute Coronary Syndromes With or Without ST-Segment Elevation

Objectives The purpose of this study was to determine the consistency of the effects of radial artery access in patients with ST-segment elevation myocardial infarction (STEMI) and in those with non–ST-segment elevation acute coronary syndrome (NSTEACS).

Background The safety associated with radial access may translate into mortality benefit in higher-risk patients, such as those with STEMI.

Methods We compared efficacy and bleeding outcomes in patients randomized to radial versus femoral access in RIVAL (RadIal Vs femorAL access for coronary intervention trial) (N = 7,021) separately in those with STEMI (n = 1,958) and NSTEACS (n = 5,063). Interaction tests between access site and acute coronary syndrome type were performed.

Results Baseline characteristics were well matched between radial and femoral groups. There were significant interactions for the primary outcome of death/myocardial infarction/stroke/non–coronary artery bypass graft–related major bleeding (p = 0.025), the secondary outcome of death/myocardial infarction/stroke (p = 0.011) and mortality (p = 0.001). In STEMI patients, radial access reduced the primary outcome compared with femoral access (3.1% vs. 5.2%; hazard ratio [HR]: 0.60; p = 0.026). For NSTEACS, the rates were 3.8% and 3.5%, respectively (p = 0.49). In STEMI patients, death/myocardial infarction/stroke were also reduced with radial access (2.7% vs. 4.6%; HR 0.59; p = 0.031), as was all-cause mortality (1.3% vs. 3.2%; HR: 0.39; p = 0.006), with no difference in NSTEACS patients. Operator radial experience was greater in STEMI versus NSTEACS patients (400 vs. 326 cases/year, p < 0.0001). In primary PCI, mortality was reduced with radial access (1.4% vs. 3.1%; HR: 0.46; p = 0.041).

Conclusions In patients with STEMI, radial artery access reduced the primary outcome and mortality. No such benefit was observed in patients with NSTEACS. The radial approach may be preferred in STEMI patients when the operator has considerable radial experience. (A Trial of Trans-radial Versus Trans-femoral Percutaneous Coronary Intervention (PCI) Access Site Approach in Patients With Unstable Angina or Myocardial Infarction Managed With an Invasive Strategy [RIVAL]; NCT01014273) (6).

Radial Versus Femoral Randomized Investigation in ST-Segment Elevation Acute Coronary Syndrome: The RIFLE-STEACS (Radial Versus Femoral Randomized Investigation in ST-Elevation Acute Coronary Syndrome) Study

Objectives The purpose of this study was to assess whether transradial access for ST-segment elevation acute coronary syndrome undergoing early invasive treatment is associated with better outcome compared with conventional transfemoral access.

Background In patients with acute coronary syndrome, bleeding is a significant predictor of worse outcome. Access site complications represent a significant source of bleeding for those patients undergoing revascularization, especially when femoral access is used.

Methods The RIFLE-STEACS (Radial Versus Femoral Randomized Investigation in ST-Elevation Acute Coronary Syndrome) was a multicenter, randomized, parallel-group study. Between January 2009 and July 2011, 1,001 acute ST-segment elevation acute coronary syndrome patients undergoing primary/rescue percutaneous coronary intervention were randomized to the radial (500) or femoral (501) approach at 4 high-volume centers. The primary endpoint was the 30-day rate of net adverse clinical events (NACEs), defined as a composite of cardiac death, stroke, myocardial infarction, target lesion revascularization, and bleeding). Individual components of NACEs and length of hospital stay were secondary endpoints.

Results The primary endpoint of 30-day NACEs occurred in 68 patients (13.6%) in the radial arm and 105 patients (21.0%) in the femoral arm (p = 0.003). In particular, compared with femoral, radial access was associated with significantly lower rates of cardiac mortality (5.2% vs. 9.2%, p = 0.020), bleeding (7.8% vs. 12.2%, p = 0.026), and shorter hospital stay (5 days first to third quartile range, 4 to 7 days] vs. 6 [range, 5 to 8 days]; p = 0.03).

Conclusions Radial access in patients with ST-segment elevation acute coronary syndrome is associated with significant clinical benefits, in terms of both lower morbidity and cardiac mortality. Thus, it should become the recommended approach in these patients, provided adequate operator and center expertise is present. (Radial Versus Femoral Investigation in ST Elevation Acute Coronary Syndrome [RIFLE-STEACS]; NCT01420614) (7).

Discontinuation of Long-Term Clopidogrel Therapy Is Associated With Death and Myocardial Infarction After Saphenous Vein Graft Percutaneous Coronary Intervention

Objectives This study sought to examine the pattern of death and myocardial infarction (MI) after clopidogrel cessation in patients undergoing percutaneous coronary intervention (PCI) of the saphenous vein graft (SVG).

Background The timing and incidence of adverse events by different durations of clopidogrel therapy after SVG PCI remain unknown.

Methods This is a cohort study of patients undergoing SVG PCI between 2000 and 2009, followed for all-cause mortality or MI after stopping clopidogrel. Incidence rates were calculated across different time periods after clopidogrel cessation. Adjusted incidence rate ratios (IRR) were calculated with multivariable regression (piecewise exponential and Poisson).

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Results There were 603 patients who underwent SVG PCI, of which 411 were event-free at the time of clopidogrel cessation. The incidence rate (95% confidence interval: [CI])/1,000 person-days of death or MI after stopping clopidogrel in the time intervals of 0 to 90 days, 91 to 365 days, and 1 to 2 years were 1.26 (95% CI: 0.93 to 1.70), 0.41 (95% CI: 0.30 to 0.56), and 0.41 (95% CI: 0.30 to 0.55), respectively. In multivariable analyses, the overall IRR (95% CI) for death or MI in the 0- to 90-day interval after stopping clopidogrel compared with the 91- to 365-day interval was 2.58 (95% CI: 1.64 to 4.07). Similar results were observed over a broad range of clopidogrel treatment durations (<6 months, 6 months to 1 year, 1 to 2 years, or >2 years). The results were also consistent across subgroups, including sex, stent type, stent diameter, PCI period, and diabetes status. When death alone was evaluated, there remained a significant increase in the event rate in the 0- to 90-day interval compared with the 91- to 365-day interval (IRR: 2.33; 95% CI: 1.32 to 4.11).

Conclusions A clustering of events was observed in the initial 0 to 90 days after clopidogrel cessation in all treatment durations of clopidogrel investigated after SVG PCI. These results might have important implications in high-risk cohorts undergoing PCI. Additional studies are needed to elucidate the mechanisms underlying the early clustering of events after clopidogrel cessation (8).

A Prospective Randomized Multicenter Comparison of Balloon Angioplasty and Infrapopliteal Stenting With the Sirolimus-Eluting Stent in Patients With Ischemic Peripheral Arterial Disease: 1-Year Results From the ACHILLES Trial

Objectives The study investigated the efficacy and safety of a balloon expandable, sirolimus-eluting stent (SES) in patients with symptomatic infrapopliteal arterial disease.

Background Results of infrapopliteal interventions using balloon angioplasty and/or bare stents are limited by a relatively high restenosis rate, which could be potentially improved by stabilizing the lesion with a SES.

Methods Two hundred patients (total lesion length 27 ± 21 mm) were randomized to infrapopliteal SES stenting or percutaneous transluminal balloon angioplasty (PTA). The primary endpoint was 1-year in-segment binary restenosis by quantitative angiography.

Results Ninety-nine and 101 patients (mean age 73.4 years; 64% diabetics) were randomized to SES and PTA, respectively (8 crossover bailout cases to SES). At 1 year, there were lower angiographic restenosis rates (22.4% vs. 41.9%, p = 0.019), greater vessel patency (75.0% vs. 57.1%, p = 0.025), and similar death, repeat revascularization, index-limb amputation rates, and proportions of patients with improved Rutherford class for SES versus PTA.

Conclusions SES implantation may offer a promising therapeutic alternative to PTA for treatment of infrapopliteal peripheral arterial disease (9).

Long-Term Outcomes of Older Diabetic Patients After Percutaneous Coronary Stenting in the United States: A Report From the National Cardiovascular Data Registry, 2004 to 2008

Objectives The purpose of this study was to characterize long-term outcomes of percutaneous coronary intervention (PCI) in elderly diabetic patients in routine practice.

Background Although drug-eluting stent (DES) implantation in diabetic patients is common practice, pivotal randomized trials enrolled <2,500 diabetic patients, most of whom were <65 years of age.

Methods Data from 405,679 patients ≥65 years old (33% had diabetes mellitus, of whom 9.8% had insulin-treated diabetes mellitus [ITDM], and 23.3% had noninsulin-treated diabetes mellitus [NITDM]) undergoing PCI from 2004 to 2008 at 946 U.S. hospitals were linked with Medicare inpatient claims data.

Results Over 18.4 months median follow-up (25th to 75th percentile: 8.0 to 30.8 months), ITDM/NITDM were associated with significantly increased adjusted hazards of death (hazard ratio [HR]: 1.91 [95% confidence interval (CI): 1.86 to 1.96], p < 0.001/HR: 1.32 [95% CI: 1.29 to 1.35], p < 0.001) and myocardial infarction (HR: 1.87 [95% CI: 1.79 to 1.95], p < 0.001/HR: 1.29 [95% CI: 1.25 to 1.34], p < 0.001) compared with nondiabetic patients. The adjusted hazard of undergoing additional revascularization procedures (HR: 1.14 [95% CI: 1.10 to 1.18, p < 0.001/HR: 1.08 [95% CI: 1.05 to 1.10], p < 0.001) and subsequent hospitalization for bleeding (HR: 1.40 [95% CI: 1.31 to 1.50], p < 0.001/HR: 1.18 [95% CI: 1.13 to 1.24], p < 0.001) were also significantly increased. Compared with nondiabetic patients, there were similar excess risks associated with ITDM/NITDM in patients selected for DES and BMS use; selection for use of DES was associated with reductions in death in ITDM/NITDM and myocardial infarction in ITDM, but not NITDM. There were no significant interactions between diabetes status and stent type for revascularization or bleeding.

Conclusions One-third of older patients undergoing PCI have diabetes. After adjustment for other comorbidities, diabetes, particularly ITDM, remains independently and strongly associated with increased long-term adverse events after both DES and BMS implantation (10).

Comparison of the Prognosis of Spontaneous and Percutaneous Coronary Intervention–Related Myocardial Infarction

Objectives This study compared prognoses of myocardial infarction related to percutaneous coronary intervention (PCI, procedural MI) using increasing creatine kinase-myocardial band (CK-MB) thresholds with spontaneous MI.

Background Procedural MI usually is defined by a CK-MB elevation of more than 3 times the upper limit of normal (ULN), but higher thresholds have been proposed.

Methods Patients from the EARLY-ACS (Early Glycoprotein IIb/IIIa Inhibition in Non–ST-Segment Elevation Acute Coronary Syndrome) study and the SYNERGY (Superior Yield of the New strategy of Enoxaparin, Revascularization and GlYcoprotein IIb/IIIa inhibitors) study treated with PCI were included. The primary end point was 1-year all-cause mortality from 24 h after PCI. To determine an enzymatic threshold for procedural MI with a prognosis similar to that of spontaneous MI, we redefined procedural MI using increasing CK-MB thresholds and compared corresponding hazard ratios with those of spontaneous MI (CK-MB more than twice the ULN). Hazard ratios for mortality for procedural and spontaneous MI were calculated using Cox proportional hazards regression and Global Registry of Acute Cardiac Events covariates for risk adjustment.

Results Nine thousand eighty-seven patients who underwent PCI (46.8%) were included; 773 procedural MI and 239 spontaneous MI occurred within 30 days. Adjusted hazard ratios for 1-year death were 1.39 (95% confidence interval [CI]: 1.01 to 1.89) for procedural MI and 5.37 (95% CI: 3.90 to 7.38) for spontaneous MI. The CK-MB threshold for procedural MI that achieved the same prognosis as spontaneous MI was 27.7 times the ULN (95% CI: 13.9 to 58.4), but this differed between the SYNERGY study (57.9 times the ULN, 95% CI: 17.9 to 63.6) and the EARLY-ACS study (20.4 times the ULN, 95% CI: 5.16 to 24.2). Of all procedural MI, 49 (6%) had CK-MB elevations of 27.7 or more times the ULN.

Conclusions The current enzymatic definition of procedural MI (CK-MB more than 3 times the ULN) used in clinical trials is less strongly associated with death than that of spontaneous MI. Procedural MI achieves similar prognosis for 1-year mortality when much higher CK-MB thresholds are applied (11).

Retrograde Coronary Chronic Total Occlusion Revascularization: Procedural and In-Hospital Outcomes From a Multicenter Registry in the United States

Objectives This study sought to examine the contemporary outcomes of retrograde chronic total occlusion (CTO) interventions among 3 experienced U.S. centers.

Background The retrograde approach, pioneered and developed in Japan, has revolutionized the treatment of coronary CTO, yet limited information exists on procedural efficacy, safety, and reproducibility of outcomes in other settings.

Methods Between 2006 and 2011, 462 consecutive retrograde CTO interventions were performed at 3 U.S. institutions. Patient characteristics, procedural outcomes, and in-hospital clinical events were ascertained.

Results Mean patient age was 65 ± 9.7 years, 84% were men, and 50% had prior coronary artery bypass surgery. The CTO target vessel was the right coronary artery (66%), circumflex (18%), left anterior descending artery (15.5%), and left main artery or bypass graft (0.5%). The retrograde approach was used as the primary method in 46% of cases and after failed antegrade recanalization in 54%. Retrograde collateral vessels were septal (68%), epicardial (24%), and bypass grafts (8%). Technical and procedural success was 81.4% (n = 376) and 79.4% (n = 367), respectively. The mean contrast volume and fluoroscopy time were 345 ± 177 ml and 61 ± 40 min, respectively. A major complication occurred in 12 patients (2.6%). In multivariable analysis, years since initiation of retrograde CTO percutaneous coronary intervention (PCI) at each center, female sex, and ejection fraction ≥40% were associated with higher technical success.

Conclusions Among selected U.S. programs, retrograde CTO PCI is often performed in patients with prior coronary bypass graft surgery and is associated with favorably high success and low complication rates (12).

Improved Survival Associated With Pre-Hospital Triage Strategy in a Large Regional ST-Segment Elevation Myocardial Infarction Program

Objectives This study sought to compare the 1-year survival of patients diagnosed with ST-segment elevation myocardial infarction (STEMI) and transferred via pre-hospital triage strategy for primary percutaneous coronary intervention (PCI) with those transferred via inter-hospital transfer within a large suburban region in Canada.

Background Primary angioplasty is the preferred therapy for STEMI if it is done within 90 min of door-to-balloon time by an experienced team in a high-volume center.

Methods Patients identified to have STEMI on the ambulances equipped with electrocardiography bypassed the local hospitals and were sent directly to the PCI center, whereas other patients that were picked up by ambulances without electrocardiographic equipment were transported to the local hospitals where the diagnosis of STEMI was made and were re-routed to the PCI center. Patient demographic data, clinical presentation, procedural data, in-hospital course, and vital statistics were prospectively recorded in a provincial cardiac registry.

Results A total of 167 patients were brought into the PCI center via pre-hospital triage strategy, and 427 patients were brought in via inter-hospital transfer during a 2-year study period. Baseline demographic data, infarct location, cardiovascular history, and hemodynamic status were similar between the 2 groups. When compared with the inter-hospital transfer group, a significantly higher proportion of pre-hospital triaged patients achieved the 90-min door-to-balloon time benchmark (80.4% vs. 8.7%, $p < 0.001$) and post-procedural Thrombolysis In Myocardial Infarction flow grade 3 after the emergency procedure (97.6% vs. 91.4%, $p = 0.02$). In addition, the pre-hospital triage strategy was associated with a significantly lower 30-day (5.4% vs. 13.3%, $p = 0.006$) and 1-year (6.6% vs. 17.5%, $p = 0.019$)

mortality. Pre-hospital triage was an independent predictor for survival at 1 year (hazard ratio: 0.37, 95% confidence interval: 0.18 to 0.75, p = 0.006).
Conclusions Pre-hospital triage strategy was associated with improved survival rate in patients undergoing primary PCI in a regional STEMI program (13).

*CYP2C19*2 and *17* Alleles Have a Significant Impact on Platelet Response and Bleeding Risk in Patients Treated With Prasugrel After Acute Coronary Syndrome

Objectives The present study was designed to assess the effect of genetic variants on chronic biological response to prasugrel and bleeding complications.
Background CYP2C19*2 loss-of-function allele and CYP2C19*17 gain-of-function allele have been linked with response to clopidogrel, but preliminary data did not show any significant influence of these alleles on prasugrel effect.
Methods A total of 213 patients undergoing successful coronary stenting for acute coronary syndrome and discharged with prasugrel 10 mg daily were included. Prasugrel response was assessed at 1 month with the platelet reactivity index (PRI) vasodilator-stimulated phosphoprotein (VASP) and high on-treatment platelet reactivity (HTPR) defined as PRI VASP > 50% and hyper-response as PRI VASP <75th percentile (PRI VASP < 17%). CYP2C19*2 and CYP2C19*17 genotyping were performed.
Results Carriers of loss-of-function *2 allele had significantly higher PRI VASP than noncarriers (33 ± 15% vs. 27 ± 14%, p = 0.03) and higher rate of HTPR (16% vs. 4%, p = 0.01). Conversely, carriers of *17 gain-of-function allele had significantly lower PRI VASP than noncarriers (25 ± 13% vs. 31 ± 15%, p = 0.03, p = 0.03), lower rate of HTPR (1% vs. 10%, p = 0.02), higher rate of hyper-response (34% vs. 21%, p = 0.02), and higher rate of bleeding complications than noncarriers: 23% versus 11%, (odds ratio [95% confidence interval]: 2.5 [1.2 to 5.4]; p = 0.02). No significant influence of genotypes on platelet reactivity assessed by adenosine diphosphate–induced platelet aggregation was observed.
Conclusions The present study shows a significant influence of CYP2C19*2 and *17 alleles on response to chronic treatment by prasugrel 10 mg daily and occurrence of bleeding complications (14).

Safety and Efficacy of High- Versus Low-Dose Aspirin After Primary Percutaneous Coronary Intervention in ST-Segment Elevation Myocardial Infarction: The HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) Trial

Objectives This study sought to examine the relationship between the aspirin dose prescribed at hospital discharge and long-term outcomes after ST-segment elevation myocardial infarction in patients treated with primary percutaneous coronary intervention (PCI).
Background Patients with ST-segment elevation myocardial infarction who undergo primary PCI are prescribed maintenance aspirin doses that vary between 75 and 325 mg daily. Whether the dose of aspirin affects long-term patient outcomes is unknown.
Methods We compared 3-year outcomes in patients who were prescribed high-dose (>200 mg daily) versus low-dose (≤200 mg daily) aspirin from the large-scale HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trial.
Results Among 2,851 patients, 2,289 patients (80.3%) were discharged on low-dose aspirin and 562 patients (19.7%) were discharged on high-dose aspirin. Patients discharged on high-dose rather than low-dose aspirin were more likely to have a history of hypertension, hyperlipidemia, family history of premature coronary disease, prior treatment with PCI or coronary artery bypass surgery, and to be enrolled in the United States. Patients discharged on high-dose aspirin had higher 3-year rates of major adverse cardiovascular events, reinfarction, ischemic target vessel revascularization, major bleeding, and stent thrombosis. After multivariable analysis, discharge on high-dose aspirin was an independent predictor of major bleeding (hazard ratio: 2.80; 95% confidence interval: 1.31 to 5.99; p = 0.008), but not of adverse ischemic events.
Conclusions In patients with ST-segment elevation myocardial infarction undergoing primary PCI, discharge on high-dose rather than low-dose aspirin may increase the rate of major bleeding without providing additional ischemic benefit (15).

Impact of a New Conduction Defect After Transcatheter Aortic Valve Implantation on Left Ventricular Function

Objectives This study sought to evaluate the impact of new conduction defects after transcatheter aortic valve implantation (TAVI) on the evolution of left ventricular (LV) function during 1-year follow-up.
Background New left bundle branch block (LBBB) or need for permanent pacing due to atrioventricular (AV) block are frequent after TAVI.
Methods A total of 90 consecutive patients treated with TAVI and who had 12-month echocardiographic follow-up were included in the study. In 39 patients, a new conduction defect (new LBBB or need for permanent pacemaker activity.) persisted 1 month after TAVI. In 51 patients, no persistent new conduction defect was observed. Two-dimensional echocardiography using parasternal short-axis, apical 4-chamber, and apical 2-chamber views was performed before TAVI and at 1-year follow-up to determine LV volumes and ejection fraction based on Simpson's rule. Speckle-tracking echocardiography was applied using standard LV short-axis images to assess the effect of new

conduction defects on time-to-peak radial strain of different LV segments as a parameter of LV dyssynchrony.

Results New conduction defects resulted in marked heterogeneity in time-to-peak strain between the 6 analyzed short-axis segments. During 1-year follow-up after TAVI, there was a significant increase in left ventricular ejection fraction (LVEF) in patients without new LBBB (53 ± 11% pre TAVI to 59 ± 10% at follow-up; $p < 0.001$), whereas there was no change in LVEF in patients with a new conduction defect (52 ± 11% pre TAVI to 51 ± 12% at follow-up, $p = 0.740$). Change in LV end-systolic volume was also significantly different between patient groups (−1.0 ± 14.2 vs. −11.2 ± 15.7 ml, $p = 0.042$). New conduction defect and LVEF at baseline were independent predictors of reduced LVEF at 12-month follow-up after TAVI.

Conclusions LVEF improves after TAVI for treatment of severe aortic stenosis in patients without new conduction defects. In patients with a new conduction defect after TAVI, there is no improvement in LVEF at follow-up (16).

Incidence, Management, and Outcomes of Cardiac Tamponade During Transcatheter Aortic Valve Implantation: A Single-Center Study

Objectives The aim of this study was to explore the incidence, causes, and outcomes of cardiac tamponade in patients undergoing transcatheter aortic valve implantation (TAVI).

Background Use of TAVI is increasing, but the procedure is vulnerable to complications, given the cohort of patients. Cardiac tamponade is a possible complication, and there is a scarcity of data on the incidence and outcomes of cardiac tamponade during TAVI.

Methods All patients who sustained cardiac tamponade during or post-TAVI between 2007 and 2012 were included in the study.

Results Of 389 patients who underwent TAVI, 17 (4.3%) had cardiac tamponade. The mean age was 82.3 ± 3.7 years, and most were women (n = 12, 70.6%). Causes of cardiac tamponade were right ventricular perforation by temporary pacemaker (9 patients, 52.9%), annular rupture or aortic dissection (4 patients, 23.5%), and tear in the left ventricular free wall caused by Amplatz stiff wire or catheters (4 patients, 23.5%). Mortality occurred in 4 patients (23.5%), and all had tamponade caused by injury to the high-pressured left-sided circulation (left ventricle and aorta). Most patients (n = 14, 82.4%) sustained cardiac tamponade during the procedure—2 patients (11.7%) within 24 h, and 1 patient after 24 h.

Conclusions Cardiac tamponade during TAVI is not frequent but is associated with high mortality rates especially when left-sided structures are involved. Meticulous handling of the equipment and improvements in the safety of currently used devices could further reduce the occurrence of this complication (17).

A Prospective Randomized Trial of Thrombectomy Versus No Thrombectomy in Patients With ST-Segment Elevation Myocardial Infarction and Thrombus-Rich Lesions: MUSTELA (MUltidevice Thrombectomy in Acute ST-Segment ELevation Acute Myocardial Infarction) Trial

Objectives The aim of this study was to evaluate whether thrombectomy during primary percutaneous coronary intervention (pPCI) in patients with high thrombus burden improves myocardial reperfusion and reduces infarct size.

Background Thrombectomy aims at reducing distal thrombotic embolization during pPCI, improving myocardial reperfusion and clinical outcome.

Methods We randomized 208 patients with high thrombus burden in a 1:1 ratio to either pPCI with thrombectomy (Group T) or standard pPCI (Group S). Thrombectomy was performed with either rheolytic or manual aspiration catheters. Three-month magnetic resonance imaging was performed to assess infarct size and transmurality and microvascular obstruction (MVO). The primary endpoints were ST-segment elevation resolution (STR) >70% at 60 min and 3-month infarct size.

Results The baseline profile was similar between groups, except for a higher rate of initial Thrombolysis In Myocardial Infarction flow grade 3 in Group S ($p = 0.002$). Group T showed a significantly higher rate of STR (57.4% vs. 37.3%; $p = 0.004$) and of final myocardial blush 3 (68.3% vs. 52.9%; $p = 0.03$). Group T and Group S did not differ with regard to infarct size (20.4 ± 10.5% vs. 19.3 ± 10.6%; $p = 0.54$) and transmurality (11.9 ± 12.0% vs. 11.6 ± 12.7%; $p = 0.92$), but Group T showed significantly less MVO (11.4% vs. 26.7%; $p = 0.02$) and a higher prevalence of inhomogeneous scar ($p < 0.0001$). One-year freedom from major adverse cardiac events was similar between groups.

Conclusions Thrombectomy as an adjunct to pPCI in patients with high thrombus load yielded better post-procedural STR and reduced MVO at 3 months but was not associated with a reduction in infarct size and transmurality. Thromboaspiration in Patients With High Thrombotic Burden Undergoing Primary Percutaneous (Coronary Intervention; NCT01472718) (18).

Self-Expanding Versus Balloon-Expandable Stents in Acute Myocardial Infarction: Results From the APPOSITION II Study: Self-Expanding Stents in ST-Segment Elevation Myocardial Infarction

Objectives This study sought to investigate whether self-expanding stents are more effective than balloon-expandable stents for reducing stent malapposition at 3 days after implantation in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention.

Background Acute myocardial infarction is associated with vasoconstriction and large thrombus burden. Resolution of vasoconstriction and thrombus load during the first hours to

days after primary percutaneous coronary intervention may lead to stent undersizing and malapposition, which may subsequently lead to stent thrombosis or restenosis. In addition, aggressive stent deployment may cause distal embolization.

Methods Eighty patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention were randomized to receive a self-expanding stent (STENTYS, STENTYS SA, Paris, France) (n = 43) or a balloon-expandable stent (VISION, Abbott Vascular, Santa Clara, California; or Driver, Medtronic, Minneapolis, Minnesota) (n = 37) at 9 European centers. The primary endpoint was the proportion of stent strut malapposition at 3 days after implantation measured by optical coherence tomography. Secondary endpoints included major adverse cardiac events (cardiac death, recurrent myocardial infarction, emergent bypass surgery, or clinically driven target lesion revascularization).

Results At 3 days after implantation, on a per-strut basis, a lower rate of malapposed stent struts was observed by optical coherence tomography in the self-expanding stent group than in the balloon-expandable group (0.58% vs. 5.46%, $p < 0.001$). On a per-patient basis, none of the patients in the self-expanding stent group versus 28% in the balloon-expandable group presented ≥5% malapposed struts ($p < 0.001$). At 6 months, major adverse cardiac events were 2.3% versus 0% in the self-expanding and balloon-expandable groups, respectively (p = NS).

Conclusions Strut malapposition at 3 days is significantly lower in ST-segment elevation myocardial infarction patients allocated to self-expanding stents when than in those allocated to balloon-expandable stents. The impact of this difference on clinical outcome and the risk of late stent thrombosis need to be evaluated further. (Randomized Comparison Between the STENTYS Self-expanding Coronary Stent and a Balloon-expandable Stent in Acute Myocardial Infarction [APPOSITION II]; NCT01008085) (19).

Impact of Post-Procedural Aortic Regurgitation on Mortality After Transcatheter Aortic Valve Implantation

Objectives The goal of the study was to clarify the impact of post-procedural aortic regurgitation (post-AR) grade 2/4 on clinical outcomes.

Background Post-AR >2/4 is known to be associated with poor short- to midterm outcome after transcatheter aortic valve implantation (TAVI).

Methods We compared clinical outcomes in 400 consecutive TAVI recipients according to post-AR grade: grade 0 or 1 (group 1 = 74.8%), grade 2 (group 2 = 22.2%), or grade 3 or 4 (group 3 = 3.0%).

Results The mean age was similar in the 3 groups (83.4 ± 6.1 years) as was the logistic EuroSCORE (22.5 ± 11.4%, 24.5 ± 11.6%, and 21.5 ± 9.4%, p = 0.28) and annulus size (22.0 ± 1.8, 22.2 ± 2.1, and 22.5 ± 2.1 mm, p = 0.53). The Edwards valve was most frequently used in group 1 compared with groups 2 and 3 (89.3%, 78.7%, and 83.3%, p = 0.03), and the implanted valve size was similar in all groups (25.6 ± 2.0, 25.4 ± 2.2, and 25.5 ± 2.2 mm, respectively, p = 0.69). Post-dilation was required more frequently in group 3 (4.7%, 24.1%, and 50.0%, respectively, $p < 0.01$). Post-procedural increase in mitral regurgitation was in line with the post-AR grade (0.78 ± 0.73, 1.22 ± 0.80, and 1.89 ± 0.78, respectively, $p < 0.01$). Despite the absence of difference in 30-day mortality, longer-term outcome was significantly poorer in patients with AR grade 2 than in those with AR grade 0 or 1 (log-rank $p < 0.01$), albeit better than in patients with AR grade 3 or 4 (p = 0.04), regardless of TAVI type and left ventricular function. Post-AR ≥2/4 was also identified as an independent predictor of mid- to long-term mortality (hazard ratio: 1.68, 95% confidence interval: 1.21 to 1.44, $p < 0.01$).

Conclusions Post-AR grade 2/4 after TAVI is associated with worse outcome compared with grade 0 or 1. Careful valve selection and post-dilation when required to avoid post-AR grade 2 may contribute to improved clinical outcome after TAVI (20).

Drug–Drug Interactions in Cardiovascular Catheterizations and Interventions CME

Patients presenting for invasive cardiovascular procedures are frequently taking a variety of medications aimed to treat risk factors related to heart and vascular disease. During the procedure, antithrombotic, sedative, and analgesic medications are commonly needed, and after interventional procedures, new medications are often added for primary and secondary prevention of ischemic events. In addition to these prescribed medications, the use of over-the-counter drugs and supplements continues to rise. Most elderly patients, for example, are taking 5 or more prescribed medications and 1 or more supplements, and they often have some degree of renal insufficiency. This polypharmacy might result in drug–drug interactions that affect the balance of thrombotic and bleeding events during the procedure and during long-term treatment. Mixing of anticoagulants, for instance, might lead to periprocedural bleeding, and this is associated with an increase in long-term adverse events. Furthermore, the range of possible interactions with thienopyridine antiplatelets is of concern, because these drugs are essential to immediate and extended interventional success. The practical challenges in the field are great—some drug–drug interactions are likely present yet not well understood due to limited assays, whereas other interactions have well-described biological effects but seem to be more theoretical, because there is little to no clinical impact. Interventional providers need to be attentive to the potential for drug–drug interaction, the associated harm, and the appropriate action, if any, to minimize the potential for medication-related adverse events. This review will focus on drug–drug interactions that have the potential to affect

procedural success, either through increases in immediate complications or compromising longer-term outcome (21).

The Effect of Age on Outcomes of Coronary Artery Bypass Surgery Compared With Balloon Angioplasty or Bare-Metal Stent Implantation Among Patients With Multivessel Coronary Disease: A Collaborative Analysis of Individual Patient Data From 10 Randomized Trials

Objectives This study sought to assess whether patient age modifies the comparative effectiveness of coronary artery bypass graft (CABG) surgery and percutaneous coronary intervention (PCI).

Background Increasingly, CABG and PCI are performed in older patients to treat multivessel disease, but their comparative effectiveness is uncertain.

Methods Individual data from 7,812 patients randomized in 1 of 10 clinical trials of CABG or PCI were pooled. Age was analyzed as a continuous variable in the primary analysis and was divided into tertiles for descriptive purposes ($\leq$56.2 years, 56.3 to 65.1 years, $\geq$65.2 years). The outcomes assessed were death, myocardial infarction and repeat revascularization over complete follow-up, and angina at 1 year.

Results Older patients were more likely to have hypertension, diabetes, and 3-vessel disease compared with younger patients ($p < 0.001$ for trend). Over a median follow-up of 5.9 years, the effect of CABG versus PCI on mortality varied according to age (interaction $p < 0.01$), with adjusted CABG-to-PCI hazard ratios and 95% confidence intervals (CI) of 1.23 (95% CI: 0.95 to 1.59) in the youngest tertile; 0.89 (95% CI: 0.73 to 1.10) in the middle tertile; and 0.79 (95% CI: 0.67 to 0.94) in the oldest tertile. The CABG-to-PCI hazard ratio of less than 1 for patients 59 years of age and older. A similar interaction of age with treatment was present for the composite outcome of death or myocardial infarction. In contrast, patient age did not alter the comparative effectiveness of CABG and PCI on the outcomes of repeat revascularization or angina.

Conclusions Patient age modifies the comparative effectiveness of CABG and PCI on hard cardiac events, with CABG favored at older ages and PCI favored at younger ages (22).

The Risk of Adverse Cardiac and Bleeding Events Following Noncardiac Surgery Relative to Antiplatelet Therapy in Patients With Prior Percutaneous Coronary Intervention

Noncardiac surgery (NCS) may be required within the first year after percutaneous coronary intervention (PCI) in approximately 4% of patients and is the second most common reason for premature discontinuation of antiplatelet therapy (APT), which may, in turn, increase the risk of perioperative ischemic events, particularly stent thrombosis. Its continuation may increase the risk of perioperative bleeding. We review current information on the incidence of these events, particularly related to APT, describe potentially useful strategies to minimize the risks of adverse outcomes, and provide recommendations on APT use. Percutaneous coronary intervention (PCI) is the most common strategy for myocardial revascularization, with more than a million procedures performed annually in the United States alone (1). Enthusiasm has been tempered by the potentially lethal complication of stent thrombosis (ST) (2). The most important ST predictor is premature discontinuation of dual antiplatelet therapy (DAPT) (3,4). Apart from noncompliance, the second most common reason for early discontinuation of either DAPT or single antiplatelet therapy (APT) is the need for noncardiac surgery (NCS), accounting for one-third of cases (4).

In both retrospective (5) and prospective (6) studies, approximately 4% of patients undergo NCS within the first year after index PCI (approximately 40,000 patients in the United States by current PCI usage). This large cohort presents a challenge for the treating surgeon, anesthesiologist, and cardiologist in managing APT in the perioperative period. On the basis of current American College of Cardiology/American Heart Association guidelines, approximately two-thirds of all NCS procedures in the first year after index PCI are classified as moderate to high risk for major adverse cardiac events (MACE) (5,6,7). Surgical stress creates a prothrombotic state due to increased platelet activation and decreased fibrinolysis, explaining in part the well-described MACE increase in the perioperative period (8,9,10).

The small, but persistent, ST risk long after PCI raises the important issue of perioperative management. On the one hand, MACE, particularly ST, is a concern after APT discontinuation; with its continuation, bleeding looms as a persistent danger. In this paper, we review studies of NCS outcomes following PCI with either bare-metal stents (BMS) or drug-eluting stents (DES), particularly in relation to APT, and potential strategies to decrease these risks (23).

A Contemporary View of Diagnostic Cardiac Catheterization and Percutaneous Coronary Intervention in the United States: A Report From the CathPCI Registry of the National Cardiovascular Data Registry, 2010 Through June 2011

Objectives This study sought to provide a report to the public of data from the CathPCI Registry of the National Cardiovascular Data Registry.

Background The CathPCI Registry collects data from approximately 85% of the cardiac catheterization laboratories in the United States.

Methods Data were summarized for 6 consecutive calendar quarters beginning January 1, 2010, and ending June 30, 2011. This report includes 1,110,150 patients undergoing only diagnostic cardiac catheterization and 941,248 undergoing percutaneous coronary intervention (PCI).

Results Some notable findings include, for example, that on-site cardiac surgery was not available in 83% of facilities performing fewer than 200 PCIs annually, with these facilities representing 32.6% of the facilities reporting, but performing only 12.4% of the PCIs in this data sample. Patients 65 years of age or older represented 38.7% of those undergoing PCI, with 12.3% being 80 years of age or older. Almost 80% of PCI patients were overweight (body mass index $\geq$25 kg/m^2), 80% had dyslipidemia, and 27.6% were current or recent smokers. Among patients undergoing elective PCI, 52% underwent a stress study before the procedure, with stress myocardial perfusion being used most frequently. Calcium scores and coronary computed tomography angiography were used very infrequently (<3%) before diagnostic or PCI procedures. Radial artery access was used in 8.3% of diagnostic and 6.9% of PCI procedures. Primary PCI was performed with a median door-to-balloon time of 64.5 min for nontransfer patients and 121 min for transfer patients. In-hospital risk-adjusted mortality in ST-segment elevation myocardial infarction patients was 5.2% in this sample.
Conclusions Data from the CathPCI Registry provide a contemporary view of the current practice of invasive cardiology in the United States (24).

Assessing the Association of Appropriateness of Coronary Revascularization and Clinical Outcomes for Patients With Stable Coronary Artery Disease

Objectives The study assessed the appropriateness of coronary revascularization in Ontario, Canada, and examined its association with longer-term outcomes.
Background Although appropriate use criteria for coronary revascularization have been developed to improve the rational use of cardiac invasive procedures, it is unknown whether greater adherence to appropriateness guidelines is associated with improved clinical outcomes in stable coronary artery disease.
Methods A population-based cohort of stable patients undergoing cardiac catheterization was assembled from April 1, 2006, to March 31, 2007. The appropriateness for coronary revascularization at the time of coronary angiography was retrospectively adjudicated using the appropriate use criteria. Clinical outcomes between coronary revascularization and medical treatment without revascularization, stratified by appropriateness categories, were compared.
Results In 1,625 patients with stable coronary artery disease, percutaneous coronary intervention or coronary artery bypass grafting was only performed in 69% who had an appropriate indication for coronary revascularization. Coronary revascularization was associated with a lower adjusted hazard of death or acute coronary syndrome (hazard ratio [HR]: 0.61; 95% confidence interval [CI]: 0.42 to 0.88) at 3 years compared with medical therapy in appropriate patients. The rate of coronary revascularization was 54% in the uncertain category and 45% in the inappropriate category. No significant difference in death or acute coronary syndrome between coronary revascularization and no revascularization in the uncertain category (HR: 0.57; 95% CI: 0.28 to 1.16) and the inappropriate category (HR: 0.99; 95% CI: 0.48 to 2.02) was observed.
Conclusions Using the appropriateness use criteria, we identified substantial underutilization and overutilization of coronary revascularization in contemporary clinical practice. Underutilization of coronary revascularization is associated with significantly increased risks of adverse outcomes in patients with appropriate indications (25).

Effects of Renal Sympathetic Denervation on Arterial Stiffness and Central Hemodynamics in Patients With Resistant Hypertension

Objectives This study investigated the effect of catheter-based renal sympathetic denervation (RD) on central hemodynamics in patients with resistant hypertension.
Background High central blood pressure (BP) increases cardiovascular events and mortality independently of peripheral BP. The effect of RD on central BP is unclear.
Methods A total of 110 patients underwent bilateral RD. Radial artery applanation tonometry and pulse wave analysis were used to derive central aortic pressure and hemodynamic indices at baseline and 1, 3, and 6 months after ablation. Ten patients with resistant hypertension not undergoing RD served as controls.
Results RD significantly reduced mean central aortic BP from 167/92 mm Hg to 149/88 mm Hg, 147/85 mm Hg, and 141/85 mm Hg at 1, 3, and 6 months ($p < 0.001$), respectively. Aortic pulse pressure decreased from 76.2 $\pm$ 23.3 mm Hg to 61.5 $\pm$ 17.5 mm Hg, 62.7 $\pm$ 18.1 mm Hg, and 54.5 $\pm$ 15.7 mm Hg 1, 3, and 6 months after RD ($p < 0.001$), respectively. Six months after RD aortic augmentation and augmentation index were significantly reduced by -11 mm Hg ($p < 0.001$) and -5.3% ($p < 0.001$), respectively. Carotid to femoral pulse wave velocity showed a significant reduction from 11.6 $\pm$ 3.2 m/s to 9.6 $\pm$ 3.1 m/s at 6 months ($p < 0.001$). Consistently, ejection duration and aortic systolic pressure load were significantly diminished, indicating improvement of cardiac work load by RD. No significant changes were obtained in control patients.
Conclusions Besides the known effect of RD on brachial blood pressure, the study showed for the first time that this novel approach significantly improves arterial stiffness and central hemodynamics, which might have important prognostic implications in patients with resistant hypertension at high cardiovascular risk (26).

Long-Term Outcomes After Transcatheter Aortic Valve Implantation: Insights on Prognostic Factors and Valve Durability From the Canadian Multicenter Experience

Objectives This study sought to evaluate the long-term outcomes after transcatheter aortic valve implantation (TAVI) in the Multicenter Canadian Experience study, with

special focus on the causes and predictors of late mortality and valve durability.

Background Very few data exist on the long-term outcomes associated with TAVI.

Methods This was a multicenter study including 339 patients considered to be nonoperable or at very high surgical risk (mean age: 81 ± 8 years; Society of Thoracic Surgeons score: 9.8 ± 6.4%) who underwent TAVI with a balloon-expandable Edwards valve (transfemoral: 48%, transapical: 52%). Follow-up was available in 99% of the patients, and serial echocardiographic exams were evaluated in a central echocardiography core laboratory.

Results At a mean follow-up of 42 ± 15 months 188 patients (55.5%) had died. The causes of late death (152 patients) were noncardiac (59.2%), cardiac (23.0%), and unknown (17.8%). The predictors of late mortality were chronic obstructive pulmonary disease (hazard ratio [HR]: 2.18, 95% confidence interval [CI]: 1.53 to 3.11), chronic kidney disease (HR: 1.08 for each decrease of 10 ml/min in estimated glomerular filtration rate, 95% CI: 1.01 to 1.19), chronic atrial fibrillation (HR: 1.44, 95% CI: 1.02 to 2.03), and frailty (HR: 1.52, 95% CI: 1.07 to 2.17). A mild nonclinically significant decrease in valve area occurred at 2-year follow-up ($p < 0.01$), but no further reduction in valve area was observed up to 4-year follow-up. No changes in residual aortic regurgitation and no cases of structural valve failure were observed during the follow-up period.

Conclusions Approximately one-half of the patients who underwent TAVI because of a high or prohibitive surgical risk profile had died at a mean follow-up of 3.5 years. Late mortality was due to noncardiac comorbidities in more than one-half of patients. No clinically significant deterioration in valve function was observed throughout the follow-up period (27).

Prospective, Randomized, Multicenter Evaluation of a Polyethylene Terephthalate Micronet Mesh–Covered Stent (MGuard) in ST-Segment Elevation Myocardial Infarction: The MASTER Trial

Objectives This study sought to evaluate the potential utility of a novel polyethylene terephthalate micronet mesh–covered stent (MGuard) in patients with acute ST-segment elevation myocardial infarction (STEMI) undergoing percutaneous coronary intervention (PCI).

Background Suboptimal myocardial reperfusion after PCI in STEMI is common and results in increased infarct size and mortality. The MGuard is a novel thin-strut metal stent with a polyethylene terephthalate micronet covering designed to trap and exclude thrombus and friable atheromatous debris to prevent distal embolization.

Methods A total of 433 patients with STEMI presenting within 12 h of symptom onset undergoing PCI were randomized at 50 sites in 9 countries to the MGuard ($n = 217$) or commercially available bare metal or drug-eluting stents ($n = 216$). The primary endpoint was the rate of complete (≥70%) ST-segment resolution measured 60 to 90 min post-procedure.

Results Baseline characteristics were well matched between the groups. The primary endpoint of post-procedure complete ST-segment resolution was significantly improved in patients randomized to the MGuard stent compared with control patients (57.8% vs. 44.7%; difference: 13.2%; 95% confidence interval: 3.1% to 23.3%; $p = 0.008$). By core laboratory analysis, the MGuard stent compared with control stents also resulted in superior rates of Thrombolysis In Myocardial Infarction 3 flow (91.7% vs. 82.9%, $p = 0.006$) with comparable rates of myocardial blush grade 2 or 3 (83.9% vs. 84.7%, $p = 0.81$). Mortality (0% vs. 1.9%, $p = 0.06$) and major adverse cardiac events (1.8% vs. 2.3%, $p = 0.75$) at 30 days were not significantly different between patients randomized to the MGuard stent and control stent, respectively.

Conclusions Among patients with acute STEMI undergoing emergent PCI, the MGuard micronet mesh–covered stent compared with conventional metal stents resulted in superior rates of epicardial coronary flow and complete ST-segment resolution. A larger randomized trial is warranted to determine whether these benefits result in reduced infarct size and/or improved clinical outcomes. (Safety and Efficacy Study of MGuard Stent After a Heart Attack [MASTER]; NCT01368471) (28).

Catheter Ablation of Long-Standing Persistent Atrial Fibrillation: 5-Year Outcomes of the Hamburg Sequential Ablation Strategy

Objectives This study describes the 5-year efficacy of catheter ablation for long-standing persistent atrial fibrillation (LS-AF).

Background Long-term outcome data after catheter ablation for LS-AF are limited.

Methods Long-term follow-up of 56 months (range 49 to 67 months) was performed in 202 patients (age 61 ± 9 years) who underwent the sequential ablation strategy for symptomatic LS-AF. Initial ablation strategy was circumferential pulmonary vein isolation (PVI). Additional ablation was performed only in acute PVI nonresponder, if direct current cardioversion failed after PVI.

Results After the first ablation procedure, sinus rhythm was documented in 41 of 202 (20.3%) patients. After multiple procedures, sinus rhythm was maintained in 91 of 202 (45.0%) patients, including 24 patients receiving antiarrhythmic drugs. In 105 patients, PVI was the sole ablative therapy, 49 (46.7%) of those patients remained in sinus rhythm during follow-up. Patients with a total AF duration of <2 years had a significantly higher ablation success rate than patients whose AF duration was >2 years (76.5% vs. 42.2%, respectively; $p = 0.033$). Persistent AF duration (hazard ratio: 1.09 [95% confidence interval: 1.04 to 1.13]; $p < 0.001$) independently predicted arrhythmia recurrences, and acute PVI responders had a reduced risk of relapse

(hazard ratio: 0.57 [95% confidence interval: 0.41 to 0.78]; $p < 0.001$) after the first ablation.
Conclusions During 5-year follow-up, single- and multiple ablation procedure success was 20% and 45%, respectively, for patients with LS-AF. For patients with a total AF duration of <2 years, the outcomes were favorable (29).

Assessment of Clinical, Electrocardiographic, and Physiological Relevance of Diagonal Branch in Left Anterior Descending Coronary Artery Bifurcation Lesions

Objectives This study sought to investigate the clinical, electrocardiographic, and physiological relevance of main and side branches in coronary bifurcation lesions.
Background Discrepancy exists between stenosis severity and clinical outcomes in bifurcation lesions. However, its mechanism has not been fully evaluated yet.
Methods Sixty-five patients with left anterior descending coronary artery (LAD) bifurcation lesions were prospectively enrolled. Chest pain and 12-lead electrocardiogram were assessed after 1-min occlusion of coronary flow and coronary wedge pressure (Pw) was measured using a pressure wire.
Results ST-segment elevation was more frequent during LAD occlusion (92%) than during diagonal branch occlusion (37%) ($p < 0.001$). Pain score was also higher with the occlusion of LAD than with the diagonal branch ($p < 0.001$). However, both Pw and Pw/aortic pressure (Pa) were lower in the LAD than in diagonal branches (Pw: 21.0 ± 6.5 vs. 26.7 ± 9.4, $p < 0.0001$; Pw/Pa: 0.22 ± 0.07 vs. 0.27 ± 0.08, $p = 0.001$). The corrected QT interval was prolonged with LAD occlusion (435.0 ± 39.6 ms to 454.0 ± 45.4 ms, $p < 0.0001$) but not with diagonal branch occlusion. There was no difference in vessel size between the diagonal branches with and without ST-segment elevation during occlusion. Positive and negative predictive values of vessel size (≥2.5 mm) to determine the presence of ST-segment elevation were 48% and 72%, respectively.
Conclusions Diagonal branch occlusion caused fewer anginas, less electrocardiogram change, less arrhythmogenic potential, and higher Pw than did a LAD occlusion. These differences seem to be the main mechanism explaining why aggressive treatment for side branches has not translated into clinical benefit in coronary bifurcation lesions. (Comparison Between Main Branch and Side Branch Vessels; NCT01046409) (30).

Comparison of Nonculprit Coronary Plaque Characteristics Between Patients With and Without Diabetes: A 3-Vessel Optical Coherence Tomography Study

Objectives The aim of the present study was to compare the characteristics of nonculprit coronary plaques between diabetes mellitus (DM) and non-DM patients using 3-vessel optical coherence tomography (OCT) imaging.
Background DM patients have a higher recurrent cardiovascular event rate.
Methods Patients who had undergone 3-vessel OCT imaging were identified from the Massachusetts General Hospital OCT Registry. Characteristics of nonculprit plaques were compared between DM and non-DM patients.
Results A total of 230 nonculprit plaques were identified in 98 patients. Compared with non-DM patients, DM patients had a larger lipid index (LI) (averaged lipid arc × lipid length; 778.6 ± 596.1 vs. 1358.3 ± 939.2, $p < 0.001$) and higher prevalence of calcification (48.4% vs. 72.2%, $p = 0.034$) and thrombus (0% vs. 8.3%, $p = 0.047$). DM patients were divided into 2 groups based on glycated hemoglobin (A1C) levels of ≤7.9% and ≥8.0%. LI was significantly correlated with diabetic status (778.6 ± 596.1 [non-DM] vs. 1,171.5 ± 708.1 [A1C ≤7.9%] vs. 1,638.5 ± 1,173.8 [A1C ≥8%], p value for linear trend = 0.005), and fibrous cap thickness was inversely correlated with the A1C level (99.4 ± 46.7 μm [non-DM] vs. 91.7 ± 29.6 μm [A1C ≤7.9%] vs. 72.9 ± 22.7 μm [A1C ≥8%], p value for linear trend = 0.014). Patients with A1C ≥8% also had the highest prevalence of thin-cap fibroatheroma (TCFA) and macrophage infiltration.
Conclusions Compared with non-DM patients, DM patients have a larger LI and a higher prevalence of calcification and thrombus. The LI was larger and TCFA and macrophage infiltration were frequent in patients with A1C ≥8% (31).

Clinical Impact of Second-Generation Everolimus-Eluting Stent Compared With First-Generation Drug-Eluting Stents in Diabetes Mellitus Patients: Insights From a Nationwide Coronary Intervention Register

Objectives This study sought to study the second-generation everolimus-eluting stent (EES) as compared with first-generation sirolimus-eluting (SES) and paclitaxel-eluting stents (PES) in diabetes mellitus (DM) patients.
Background There are limited data available comparing clinical outcomes in this setting with EES and SES, whereas studies comparing EES with PES are not powered for low-frequency endpoints.
Methods All DM patients treated with EES, PES, or SES from January 18, 2007, to July 29, 2011, from the SCAAR (Swedish Coronary Angiography and Angioplasty Registery) were included. The EES was compared with SES or PES for the primary composite endpoint of clinically driven detected restenosis, definite stent thrombosis (ST), and all-cause mortality.
Results In 4,751 percutaneous coronary intervention-treated DM patients, 8,134 stents were implanted (EES = 3,928, PES = 2,836, SES = 1,370). The EES was associated with significantly lower event rates compared with SES (SES vs. EES hazard ratio [HR]:

1.99; 95% confidence interval (CI): 1.19 to 3.08). The same was observed when compared with PES (PES vs. EES HR: 1.33; 95% CI: 0.93 to 1.91) but did not reach statistical significance. These results were mainly driven by lower incidence of ST (SES vs. EES HR: 2.87; 95% CI: 1.08 to 7.61; PES vs. EES HR: 1.74, 95% CI: 0.82 to 3.71) and mortality (SES vs. EES HR: 2.02; 95% CI: 1.03 to 3.98; PES vs. EES HR: 1.69; 95% CI: 1.06 to 2.72). No significant differences in restenosis rates were observed between EES and SES or PES (SES vs. EES HR: 1.26; 95% CI: 0.77 to 2.08; PES vs. EES HR: 1.05; 95% CI: 0.71 to 1.55).

Conclusions In all-comer DM patients the use of EES was associated with improved outcomes compared with SES and PES mainly driven by lower rates of ST and mortality. These results suggest better safety rather than efficacy with EES when compared with SES or PES (32).

Time-Dependent Detrimental Effects of Distal Embolization on Myocardium and Microvasculature During Primary Percutaneous Coronary Intervention

Objectives The authors sought to investigate the impact of distal embolization (DE) on myocardial damage and microvascular reperfusion, according to time-to-treatment, using contrast-enhanced cardiac magnetic resonance (CE-CMR).

Background DE, occurring during primary percutaneous coronary intervention (p-PCI), appears to increase myocardial necrosis and to worsen microvascular perfusion, as shown by surrogate markers. However, data regarding the behavior of DE on jeopardized myocardium, and in particular on necrosis extent and distribution, are still lacking.

Methods In 288 patients who underwent p-PCI within 6 h from symptom onset, the authors prospectively assessed the impact of DE on infarct size and microvascular damage, using CE-CMR. The impact of DE was assessed according to time-to-treatment: for group 1, <3 h; for group 2, ≥3 and ≤6 h.

Results DE occurred in 41 (14.3%) patients. Baseline clinical characteristics were not different between the 2 groups. At CE-CMR, patients with DE showed larger infarct size ($p = 0.038$) and more often transmural necrosis compared with patients without DE ($p = 0.008$) when time-to-treatment was <3 h, but no impact was proven after this time (p = NS). Patients with DE showed more often microvascular obstruction, as evaluated at first-pass enhancement, than patients without DE (100% vs. 66.5%, $p = 0.001$) up to 6 h from symptom onset.

Conclusions These findings suggest that the detrimental impact of DE occurring during p-PCI on myocardial damage is largely influenced by ischemic time, increasing the extent of necrosis in patients presenting within the first hours after symptom onset, and having limited or no impact after this time window (33).

Walking Beyond the GRACE (Global Registry of Acute Coronary Events) Model in the Death Risk Stratification During Hospitalization in Patients With Acute Coronary Syndrome: What Do the AR-G (ACTION [Acute Coronary Treatment and Intervention Outcomes Network] Registry and GWTG [Get With the Guidelines] Database), NCDR (National Cardiovascular Data Registry), and EuroHeart Risk Scores Provide?

Objectives This study sought to compare the in-hospital prognostic values of the original and updated GRACE (Global Registry of Acute Coronary Events) risk score (RS) and the AR-G (ACTION [Acute Coronary Treatment and Intervention Outcomes Network] Registry and the GWTG [Get With the Guidelines] Database) RS in acute coronary syndromes (ACS). To evaluate the utility of recalculating risk after percutaneous coronary intervention (PCI) with newer RS models (NCDR [National Cardiovascular Data Registry] and EHS [EuroHeart Score] RS).

Background Defined in 2003, GRACE is among the most popular systems of risk stratification in ACS. An updated version of GRACE has since appeared and new RS have been developed, aiming to improve risk prediction.

Methods From 2004 to 2010, 4,497 consecutive patients admitted to a single center in Spain with an ACS were included (32.1% ST-segment elevation myocardial infarction, 19.2% unstable angina). Discrimination (C-statistic) and calibration (Hosmer-Lemeshow [HL]) indexes were used to assess performance of each RS. A comparative analysis of RS designed to predict post-PCI mortality NCDR and EHS RS versus the GRACE and AR-G RS was performed in a subgroup of 1,113 consecutive patients included in the study.

Results There were 265 in-hospital deaths (5.9%). Original and updated GRACE RS and the AR-G RS all demonstrated good discrimination for in-hospital death (C-statistics: 0.91, 0.90 and 0.90, respectively) with optimal calibration (HL p: 0.42, 0.50, and 0.47, respectively) in all spectra of ACS, according to different managements (PCI vs. conservative) and without significant differences between the 3 different RS. In patients undergoing PCI, EHS and NCDR RS (C-statistic = 0.80 and 0.84, respectively) were not superior to GRACE RS (C-statistic = 0.91), albeit in the subgroup of patients undergoing PCI who were categorized as high risk using the GRACE RS, both EHS and NCDR have contributed to decrease the false positive rate generated by using the GRACE RS.

Conclusions Despite having been developed over 8 years ago, the GRACE RS still maintains its excellent performance for predicting in-hospital risk of death among ACS patients (34).

Impact of Insulin Resistance on Post-Procedural Myocardial Injury and Clinical Outcomes in Patients Who Underwent Elective Coronary Interventions With Drug-Eluting Stents

Objectives This study sought to evaluate the associations between homeostatic indexes of insulin resistance (HOMA-IR) and post-procedural myocardial injury and clinical outcome after a percutaneous coronary intervention (PCI) with a drug-eluting stent.

Background Insulin resistance increases the risk of cardiovascular events. However, the association between insulin resistance and clinical outcome after coronary intervention is unclear.

Methods We evaluated 516 consecutive patients who underwent elective PCI with drug-eluting stents. Blood samples were collected from venous blood after overnight fasting, and fasting plasma glucose and insulin levels were measured. HOMA-IR was calculated according to the homeostasis model assessment. Post-procedural myocardial injury was evaluated by analysis of troponin T and creatine kinase-myocardial band isozyme levels hours after PCI. Cardiac event was defined as the composite endpoint of cardiovascular death, myocardial infarction, and any revascularization.

Results With increasing tertiles of HOMA-IR, post-procedural troponin T and creatine kinase-myocardial band levels increased. In the multiple regression analysis, HOMA-IR was independently associated with troponin T elevation. During a median follow-up of 623 days, patients with the highest tertiles of HOMA-IR had the highest risk of cardiovascular events. The Cox proportional hazard models identified HOMA-IR as independently associated with worse clinical outcome after adjustment for clinical and procedural factors.

Conclusions These results indicated the impact of insulin resistance on post-procedural myocardial injury and clinical outcome after elective PCI with drug-eluting stent deployment. Evaluation of insulin resistance may provide useful information for predicting clinical outcomes after elective PCI (35).

Device Closure of Secundum Atrial Septal Defects in Children <15 kg: Complication Rates and Indications for Referral

Objectives This study sought to determine institutional complication rates in a previously underreported patient population and discuss referral indications.

Background There has been a trend over the years for referral of younger and smaller patients for "elective" closure of atrial septal defects (ASD). In general, the risks associated with ASD device closure are believed and reported to be relatively low. Complication rates in this group of smaller patients are not well described in the literature for either percutaneous or surgical approaches.

Methods Retrospective review of all patients who underwent elective transcatheter closure of secundum ASD between March 2000 and April 2010. We excluded all children >15 kg, as well as those with complex congenital heart defects. Major and minor complications were predefined and indications for referral were evaluated.

Results We identified 128 patients meeting criteria with a median procedural age of 1.92 years (3 months to 4.92 years), and median weight of 10.8 kg (4.3 to 14.9 kb). There were 7 major (5.5%) and 12 minor (9.4%) complications. Nearly two-thirds of referrals were for right heart enlargement or poor growth. Rate of resolution of residual shunt was 99%. When compared with age, there was no difference in the rate of resolution of right heart enlargement. No clinically significant improvement in growth was observed.

Conclusions Transcatheter ASD closure in small children is highly successful, but with an increase in previously perceived complication rates. In small, asymptomatic patients, deferral of closure until the historically established timeline of around 4 to 5 years of age should be strongly considered (36).

Randomized Comparison of Conservative Versus Aggressive Strategy for Provisional Side Branch Intervention in Coronary Bifurcation Lesions: Results From the SMART-STRATEGY (SMart Angioplasty Research Team–Optimal STRATEGY for Side Branch Intervention in Coronary Bifurcation Lesions) Randomized Trial

Objectives The authors sought to compare conservative and aggressive strategies for provisional side branch (SB) intervention in coronary bifurcation lesions.

Background The optimal provisional approach for coronary bifurcation lesions has not been established.

Methods In this prospective randomized trial, 258 patients with a coronary bifurcation lesion treated with drug-eluting stents were randomized to a conservative (n = 128) or aggressive (n = 130) SB intervention strategy. The criteria for SB intervention after main vessel stenting differed between the conservative and aggressive groups; Thrombolysis In Myocardial Infarction flow grade <3 versus diameter stenosis >75% for non–left main bifurcations and diameter stenosis >75% versus diameter stenosis >50% for left main bifurcations. The primary endpoint was target vessel failure (cardiac death, myocardial infarction, or target vessel revascularization) at 12 months.

Results Left main bifurcation lesions were noted in 114 patients (44%) and true bifurcation lesions in 171 patients (66%). SB ballooning after main vessel stenting and SB stenting after SB ballooning were performed less frequently in the conservative group than in the aggressive group (25.8% vs. 68.5%, $p < 0.001$; and 7.0% vs. 30.0%, $p < 0.001$, respectively). The conservative strategy was associated with a lower incidence of procedure-related myocardial necrosis compared with the aggressive strategy (5.5% vs.

17.7%, p = 0.002). At 12 months, the incidence of target vessel failure was similar in both groups (9.4% in the conservative group vs. 9.2% in the aggressive group, p = 0.97).
Conclusions Compared with the aggressive strategy, the conservative strategy for provisional SB intervention was associated with similar long-term clinical outcomes and a lower incidence of procedure-related myocardial necrosis. (Optimal Strategy for Side Branch Stenting in Coronary Bifurcation Lesions [SMART-STRATEGY]; NCT00794014) (37).

A New Score for Risk Stratification of Patients With Acute Coronary Syndromes Undergoing Percutaneous Coronary Intervention: The ACUITY-PCI (Acute Catheterization and Urgent Intervention Triage Strategy–Percutaneous Coronary Intervention) Risk Score

Objectives This study sought to develop a new score specific for patients with non–ST-segment elevation acute coronary syndromes (NSTEACS) undergoing percutaneous coronary intervention (PCI) (the ACUITY-PCI [Acute Catheterization and Urgent Intervention Triage Strategy–Percutaneous Coronary Intervention] risk score).
Background The TIMI (Thrombolysis In Myocardial Infarction) and GRACE (Global Registry for Acute Coronary Events) risk scores are recommended for risk stratification of patients with NSTEACS. However, these scores were not optimized for patients undergoing an early invasive strategy with PCI.
Methods The ACUITY-PCI risk score was created from data for 1,692 patients enrolled in the formal angiographic substudy of the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial by integrating clinical, angiographic, laboratory, and electrocardiographic variables selected by multivariable analysis. The score was subsequently validated in a different population of 846 patients and compared with the GRACE and TIMI risk scores, and the SYNTAX (Synergy Between PCI with Taxus and Cardiac Surgery) and Clinical SYNTAX scores.
Results Six variables (2 clinical, 1 laboratory/electrocardiographic, and 3 angiographic) were included in the ACUITY-PCI score: insulin-treated diabetes; renal insufficiency; baseline cardiac biomarker elevation or ST-segment deviation; bifurcation lesion; small vessel/diffuse coronary artery disease; and the extent of coronary artery disease. Event rates increased significantly across tertiles of ACUITY-PCI score. Compared with the other scores, the ACUITY-PCI score had the best discrimination (C-statistic), calibration (Hosmer-Lemeshow statistic), and index of separation. Moreover, the net reclassification improvement varied from 9% to 38% and the integrated discrimination index from 1.9% to 2.7%.
Conclusions The ACUITY-PCI risk score is a new tool integrating clinical, angiographic, and laboratory/electrocardiographic variables specifically developed for patients with NSTEACS undergoing PCI. This score displayed better prognostic accuracy in terms of discrimination and calibration than other currently available scores for risk stratification of patients with NSTEACS. (Comparison of Angiomax Versus Heparin in Acute Coronary Syndromes [ACS]; NCT00093158) (38).

Development and Validation of a Stent Thrombosis Risk Score in Patients With Acute Coronary Syndromes

Objectives This study sought to develop a practical risk score to predict the risk of stent thrombosis (ST) after percutaneous coronary intervention (PCI) for acute coronary syndromes (ACS).
Background ST is a rare, yet feared complication after PCI with stent implantation. A risk score for ST after PCI in ACS can be a helpful tool to personalize risk assessment.
Methods This study represents a patient-level pooled analysis of 6,139 patients undergoing PCI with stent implantation for ACS in the HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) and ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trials who were randomized to treatment with bivalirudin versus heparin plus a glycoprotein IIb/IIIa inhibitor. The cohort was randomly divided into a risk score development cohort (n = 4,093) and a validation cohort (n = 2,046). Cox regression methods were used to identify clinical, angiographic, and procedural characteristics associated with Academic Research Consortium–defined definite/probable ST at 1 year. Each covariate in this model was assigned an integer score based on the regression coefficients.
Results Variables included in the risk score were type of ACS (ST-segment elevation myocardial infarction, non-ST-segment elevation ACS with ST deviation, or non–ST-segment elevation ACS without ST changes), current smoking, insulin-dependent diabetes mellitus, prior PCI, baseline platelet count, absence of early (pre-PCI) anticoagulant therapy, aneurysmal/ulcerated lesion, baseline TIMI (Thrombolysis In Myocardial Infarction) flow grade 0/1, final TIMI flow grade <3, and number of treated vessels. Risk scores 1 to 6 were considered low risk, 7 to 9 intermediate risk, and 10 or greater high risk for ST. Rates of ST at 1 year in low-, intermediate-, and high-risk categories were 1.36%, 3.06%, and 9.18%, respectively, in the development cohort (p for trend <0.001), and 1.65%, 2.77%, and 6.45% in the validation cohort (p for trend = 0.006). The C-statistic for this risk score was over 0.65 in both cohorts.
Conclusions The individual risk of ST can be predicted using a simple risk score based on clinical, angiographic, and procedural variables. (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction [HORIZONS-AMI]; NCT00433966) (Comparison of Angiomax Versus Heparin in Acute Coronary Syndromes [ACUITY]; NCT00093158) (39).

Coronary Flow Reserve During Dipyridamole Stress Echocardiography Predicts Mortality

Objectives The goal of this study was to evaluate the ability of coronary flow reserve (CFR) over regional wall motion to predict mortality in patients with known or suspected coronary artery disease (CAD).

Background CFR evaluated using pulsed Doppler echocardiography testing on left anterior descending artery is the state-of-the-art method during vasodilatory stress echocardiography.

Methods In a prospective, multicenter, observational study, we evaluated 4,313 patients (2,532 men; mean age 65 ± 11 years) with known (n = 1,547) or suspected (n = 2,766) CAD who underwent high-dose dipyridamole (0.84 mg/kg over 6 min) stress echocardiography with CFR evaluation of left coronary descending artery (LAD) by Doppler. Overall mortality was the only endpoint analyzed.

Results Stress echocardiography was positive for ischemia in 765 (18%) patients. Mean CFR was 2.35 ± 0.68. At individual patient analysis, 1,419 (33%) individuals had CFR ≤2. During a median follow-up of 19 months (1st quartile 8; 3rd quartile 36), 146 patients died. The 4-year mortality was markedly higher in subjects with CFR ≤2 than in those with CFR >2, both considering the group with ischemia (39% vs. 7%; $p < 0.0001$) and the group without ischemia at stress echocardiography (12% vs. 3%; $p < 0.0001$). At multivariable analysis, CFR on LAD ≤2 (hazard ratio [HR]: 3.31; 95% confidence interval [CI]: 2.29 to 4.78; $p < 0.0001$), ischemia at stress echocardiography (HR: 2.40, 95% CI: 1.65 to 3.48, $p < 0.0001$), left bundle branch block (HR: 2.26, 95% CI: 1.50 to 3.41; $p < 0.0001$), age (HR: 1.08, 95% CI: 1.06–1.10; $p < 0.0001$), resting wall motion score index (HR: 3.52, 95% CI: 2.38 to 5.21; $p < 0.0001$), male sex (HR: 1.74, 95% CI: 1.12 to 2.52; $p = 0.003$), and diabetes mellitus (HR: 1.47, 95% CI: 1.03 to 2.08; $p = 0.03$) were independent predictors of mortality.

Conclusions CFR on LAD is a strong and independent indicator of mortality, conferring additional prognostic value over wall motion analysis in patients with known or suspected CAD. A negative result on stress echocardiography with a normal CFR confers an annual risk of death <1% in both patient groups (40).

Colchicine for Prevention of Early Atrial Fibrillation Recurrence After Pulmonary Vein Isolation: A Randomized Controlled Study

Objectives The purpose of the present study was to test the potential of colchicine, an agent with potent anti-inflammatory action, to reduce atrial fibrillation (AF) recurrence after pulmonary vein isolation in patients with paroxysmal AF.

Background Proinflammatory processes induced by AF ablation therapy have been implicated in postablation arrhythmia recurrence.

Methods Patients with paroxysmal AF who received radiofrequency ablation treatment were randomized to a 3-month course of colchicine 0.5 mg twice daily or placebo. C-reactive protein (CRP) and interleukin (IL)-6 levels were measured on day 1 and on day 4 of treatment.

Results In the 3-month follow-up, recurrence of AF was observed in 27 (33.5%) of 80 patients of the placebo group versus 13 (16%) of 81 patients who received colchicine (odds ratio: 0.38, 95% confidence interval: 0.18 to 0.80). Gastrointestinal side-effects were the most common symptom among patients receiving active treatment. Diarrhea was reported in 7 patients in the colchicine group (8.6%) versus 1 in the placebo group (1.3%, $p = 0.03$). Colchicine led to higher reductions in CRP and IL-6 levels: the median difference of CRP and IL-6 levels between days 4 and 1 was −0.46 mg/l (interquartile range: −0.78 to 0.08 mg/l) and −0.10 mg/l (−0.30 to 0.10 pg/ml), respectively, in the placebo group versus −1.18 mg/l (−2.35 to −0.46 mg/l) and −0.50 pg/ml (−1.15 to −0.10 pg/ml) in the colchicine group ($p < 0.01$ for both comparisons).

Conclusions Colchicine is an effective and safe treatment for prevention of early AF recurrences after pulmonary vein isolation in the absence of antiarrhythmic drug treatment. This effect seems to be associated strongly with a significant decrease in inflammatory mediators, including IL-6 and CRP (41).

Drug-Eluting Balloon for Treatment of Superficial Femoral Artery In-Stent Restenosis

Objectives The purpose of this prospective registry was to evaluate the safety and efficacy, at 1 year, of the use of drug-eluting balloons (DEB) for the treatment of superficial femoral artery (SFA) in-stent restenosis (ISR).

Background The use of the self-expanding nitinol stent has improved the patency rate of SFA after percutaneous transluminal angioplasty (PTA). As the population with SFA stenting continues to increase, occurrence of ISR has become a serious problem. The use of DEB has showed promising results in reducing restenosis recurrence in coronary stents.

Methods From December 2009 to December 2010, 39 consecutive patients underwent PTA of SFA-ISR in our institution. All patients underwent conventional SFA PTA and final post-dilation with paclitaxel-eluting balloons (IN.PACT, Medtronic, Minneapolis, Minnesota). Patients were evaluated up to 12 months.

Results Technical and procedural success was achieved in every patient. No in-hospital major adverse cardiac and cerebrovascular events occurred. At 1 year, 1 patient died due to heart failure. Primary endpoint, primary patency rate at 12 months, was obtained in 92.1% (35 patients). At 1 year, patients were asymptomatic for claudication, and duplex assessment demonstrated lack of recurrent restenosis (100% rate of Secondary patency). The presence of an occlusive restenosis at the time of treatment was not

associated with an increased restenosis rate, when compared with non-occlusive restenosis, at 1 year.

Conclusions The data suggest that adjunctive use of DEB for the treatment of SFA-ISR represents a potentially safe and effective therapeutic strategy. These data should be considered hypothesis-generating to design a randomized trial (42).

Predictive Factors and Long-Term Clinical Consequences of Persistent Left Bundle Branch Block Following Transcatheter Aortic Valve Implantation With a Balloon-Expandable Valve

Objectives This study evaluated the predictive factors and prognostic value of new-onset persistent left bundle branch block (LBBB) in patients undergoing transcatheter aortic valve implantation (TAVI) with a balloon-expandable valve.

Background The predictors of persistent (vs. transient or absent) LBBB after TAVI with a balloon-expandable valve and its clinical consequences are unknown.

Methods A total of 202 consecutive patients with no baseline ventricular conduction disturbances or previous permanent pacemaker implantation (PPI) who underwent TAVI with a balloon-expandable valve were included. Patients were on continuous electrocardiographic (ECG) monitoring during hospitalization and 12-lead ECG was performed daily until hospital discharge. No patient was lost at a median follow-up of 12 (range: 6 to 24) months, and ECG tracing was available in 97% of patients. The criteria for PPI were limited to the occurrence of high-degree atrioventricular block (AVB) or severe symptomatic bradycardia.

Results New-onset LBBB was observed in 61 patients (30.2%) after TAVI, and had resolved in 37.7% and 57.3% at hospital discharge and 6- to 12-month follow-up, respectively. Baseline QRS duration ($p = 0.037$) and ventricular depth of the prosthesis ($p = 0.017$) were independent predictors of persistent LBBB. Persistent LBBB at hospital discharge was associated with a decrease in left ventricular ejection fraction ($p = 0.001$) and poorer functional status ($p = 0.034$) at 1-year follow-up. Patients with persistent LBBB and no PPI at hospital discharge had a higher incidence of syncope (16.0% vs. 0.7%; $p = 0.001$) and complete AVB requiring PPI (20.0% vs. 0.7%; $p < 0.001$), but not of global mortality or cardiac mortality during the follow-up period (all, $p > 0.20$). New-onset LBBB was the only factor associated with PPI following TAVI ($p < 0.001$).

Conclusions Up to 30% of patients with no prior conduction disturbances developed new LBBB following TAVI with a balloon-expandable valve, although it was transient in more than one third. Longer baseline QRS duration and a more ventricular positioning of the prosthesis were associated with a higher rate of persistent LBBB, which in turn determined higher risks for complete AVB and PPI, but not mortality, at 1-year follow-up (43).

SeQuent Please World Wide Registry: Clinical Results of SeQuent Please Paclitaxel-Coated Balloon Angioplasty in a Large-Scale, Prospective Registry Study

Objectives This study sought to assess the safety and efficacy of paclitaxel-coated balloon (PCB) angioplasty in an international, multicenter, prospective, large-scale registry study.

Background In small randomized trials, PCB angioplasty was superior to uncoated balloon angioplasty for treatment of bare-metal stent (BMS) and drug-eluting stent (DES) restenosis.

Methods Patients treated with SeQuent Please PCBs were included. The primary outcome measure was the clinically driven target lesion revascularization (TLR) rate at 9 months.

Results At 75 centers, 2,095 patients with 2,234 lesions were included. The TLR rate was 5.2% after 9.4 months. Definite vessel thrombosis occurred in 0.1%. PCB angioplasty was performed in 1,523 patients (72.7%) with DES or BMS restenosis and 572 patients (27.3%) with de novo lesions. The TLR rate was significantly lower in patients with PCB angioplasty for BMS restenosis compared with DES restenosis (3.8% vs. 9.6%, $p < 0.001$). The TLR rate did not differ for PCB angioplasty of paclitaxel-eluting stent and non–paclitaxel-eluting stent restenosis (8.3% vs. 10.8%, $p = 0.46$). In de novo lesions (small vessels), the TLR rate was low and did not differ between PCB angioplasty with and without additional BMS implantation ($p = 0.31$).

Conclusions PCB angioplasty in an all-comers, prospective, multicenter registry was safe and confirmed in a large population the low TLR rates seen in randomized clinical trials. PCB angioplasty was more effective in BMS restenosis compared with DES restenosis, with no difference regarding the type of DES (44).

Percutaneous Treatment of Patent Foramen Ovale and Atrial Septal Defects

Percutaneous treatment of inter-atrial septal defects has undergone exponential growth in the past 2 decades. Improved percutaneous devices and interventional techniques with low complication rates make this procedure an attractive therapeutic option for congenital atrial septal defects (ASD). Although indications for catheter-based ASD closure are well-documented, those for catheter-based patent foramen ovale (PFO) closure are still evolving. Results from 2 randomized clinical trials question the benefit of percutaneous PFO closure, but concern has also been raised about the efficacy of the device used in those trials. This review will focus on the anatomy, associated syndromes, detection, and data for percutaneous closure of both PFOs and ASDs. Percutaneous treatment of inter-atrial septal defects has opened new areas of research, because unexpected associations have been uncovered.

Improved devices, interventional techniques, and low complication rates make this procedure an attractive therapeutic option for congenital atrial septal defects (ASD). In the United States, the rates of annual percutaneous patent foramen ovale (PFO) and ASD closures have increased nearly 50-fold over the past decade. Although indications for catheter-based ASD closures are well-documented by many society guidelines, those for catheter-based PFO closure are still evolving. The results of 2 recent randomized clinical trials raise questions about the utility of percutaneous PFO closure. This review will focus on the anatomy, physiology, associated syndromes, detection, and data for percutaneous closure of both PFOs and ASDs (45).

Effect of Cardiac Resynchronization Therapy on the Risk of First and Recurrent Ventricular Tachyarrhythmic Events in MADIT-CRT

Objectives This study aimed to evaluate the effect of cardiac resynchronization therapy with a defibrillator (CRT-D) on the risks of first and recurrent ventricular tachyarrhythmic events (VTEs) in the MADIT-CRT.

Background Reverse remodeling associated with CRT-D therapy was suggested to reduce arrhythmic risk. However, the effect of the device on the risk of recurrent VTEs among patients who experience a first arrhythmic event has not been investigated.

Methods The CRT-D versus defibrillator-only risks for first and subsequent fast VTEs (>180 beats/min) were assessed by Cox proportional hazards and Andersen-Gill proportional intensity regression modeling, respectively, in efficacy analyses recognizing active device-type during follow-up.

Results Multivariate analysis showed that CRT-D was associated with a significant 29% ($p = 0.003$) reduction in the risk of a first VTE, with a pronounced effect among patients with left bundle branch block (LBBB) (hazard ratio [HR]: 0.58; $p < 0.001$) and no significant effect among non-LBBB patients (HR: 1.05; $p = 0.82$, p for the difference $= 0.02$). Patients with LBBB who experienced a first VTE had no change in the risk of subsequent VTEs with CRT-D (HR: 0.98; $p = 0.85$). In contrast, the risk of recurrent VTEs with CRT-D was significantly increased among non-LBBB patients (HR: 3.62; $p = 0.002$, p for the difference $= 0.009$). Recurrent VTEs increased the risk of subsequent heart failure or death.

Conclusions In MADIT-CRT, active treatment with CRT-D was associated with a significant reduction in the risk of life-threatening VTEs. However, our findings suggest that CRT-D does not reduce the risk of subsequent VTEs in patients who experience a first arrhythmic event and may increase subsequent arrhythmic risk in non-LBBB patients. (Multicenter Automatic Defibrillator Implantation With Cardiac Resynchronization Therapy [MADIT-CRT]; NCT00180271) (46).

Left Main Percutaneous Coronary Intervention

The introduction of drug-eluting stents and advances in catheter techniques have led to increasing acceptance of percutaneous coronary intervention (PCI) as a viable alternative to coronary artery bypass graft (CABG) for unprotected left main disease. Current guidelines state that it is reasonable to consider unprotected left main PCI in patients with low to intermediate anatomic complexity who are at increased surgical risk. Data from randomized trials involving patients who are candidates for either treatment strategy provide novel insight into the relative safety and efficacy of PCI for this lesion subset. Herein, we review the current data comparing PCI with CABG for left main disease, summarize recent guideline recommendations, and provide an update on technical considerations that may optimize clinical outcomes in left main PCI. More than 30 years have passed since the first—and failed—attempt at left main percutaneous coronary intervention (PCI) by Andreas Gruentzig. Given the low prevalence of this lesion subset, robust data from dedicated randomized controlled trials (RCTs) comparing PCI with coronary artery bypass graft (CABG) are lacking, and CABG remains the traditional standard for the treatment of left main obstruction according to society guidelines (1). The introduction of drug-eluting stents (DES), combined with a culture within interventional cardiology that promotes shared experience through prompt dissemination of new techniques and outcomes, has led to a rapid evolution in the percutaneous approach to left main disease and broad clinical adoption of PCI that outpaces current guidelines. Herein, we summarize these guidelines, review the current state of observational and RCT data that pertain to left main intervention, and provide an update on technical considerations that may optimize clinical outcomes in left main PCI (47).

Factors Contributing to the Lower Mortality With Ticagrelor Compared With Clopidogrel in Patients Undergoing Coronary Artery Bypass Surgery

Objectives This study investigated the differences in specific causes of post–coronary artery bypass graft surgery (CABG) deaths in the PLATO (Platelet Inhibition and Patient Outcomes) trial.

Background In the PLATO trial, patients assigned to ticagrelor compared with clopidogrel and who underwent CABG had significantly lower total and cardiovascular mortality.

Methods In the 1,261 patients with CABG performed within 7 days after stopping study drug, reviewers blinded to treatment assignment classified causes of death into subcategories of vascular and nonvascular, and specifically identified bleeding or infection events that either caused or subsequently contributed to death.

Results Numerically more vascular deaths occurred in the clopidogrel versus the ticagrelor group related to myocardial

infarction (14 vs. 10), heart failure (9 vs. 6), arrhythmia or sudden death (9 vs. 3), and bleeding, including hemorrhagic stroke (7 vs. 2). Clopidogrel was also associated with an excess of nonvascular deaths related to infection (8 vs. 2). Among factors directly causing or contributing to death, bleeding and infections were more common in the clopidogrel group compared with the ticagrelor group (infections: 16 vs. 6, $p < 0.05$, and bleeding: 27 vs. 9, $p < 0.01$, for clopidogrel and ticagrelor, respectively).

Conclusions The mortality reduction with ticagrelor versus clopidogrel following CABG in the PLATO trial was associated with fewer deaths from cardiovascular, bleeding, and infection complications. (Platelet Inhibition and Patient Outcomes [PLATO]; NCT00391872) (48).

The Problem With Asymptomatic Cerebral Embolic Complications in Vascular Procedures: What If They Are Not Asymptomatic?

Cerebral embolic events related to carotid and cardiac disease have been known for decades. Recently, cerebral embolic events have become a focus of clinical importance as complications of vascular procedures. Further, the development of new technologies and procedures has increased the overall clinical significance. Although the relative safety of these procedures is usually defined by acute stroke risk, it is also becoming clear that far more subclinical events are occurring. Recent reports provided substantial evidence of memory loss, cognitive decline, and dementia related to these so-called silent infarcts. Literature reports of magnetic resonance imaging events lead to an estimate of as many as 600,000 patients with new brain injury each year in the United States alone. Given the magnitude of the numbers involved, the impact of accelerated cognitive loss and premature senescence in a vulnerable at-risk population could well be significant.

Cerebral embolic events related to carotid and cardiac disease have been known for decades and have formed a central part of clinical stroke research and management. More recently, cerebral embolic events have become a focus of clinical importance as complications of vascular procedures. Surgical and endovascular procedures, both neurointerventional and cardiac, are associated with embolic risks, and the development of new technologies and procedures has increased the overall clinical significance. Although the relative safety of these procedures is usually defined by the acute stroke risk, it is also becoming clear that far more subclinical events are occurring. Although the fundamental issues of the nature of the embolic particles, precise mechanisms of cerebral injury, and effective prevention remain debated and unclear, recent reports have provided substantial evidence of memory loss, cognitive decline, and dementia related to these so-called silent infarcts (49).

Pre-procedural Risk Quantification for Carotid Stenting Using the CAS Score: A Report From the NCDR CARE Registry

Objectives We developed and internally validated a risk score to predict in-hospital stroke or death after carotid artery stenting (CAS).

Background A tool that accurately assesses CAS risk could aid clinical decision making and improve patient selection.

Methods Patients undergoing CAS without acute evolving stroke from April 2005 through June 2011 as part of the NCDR Carotid Artery Revascularization and Endarterectomy (CARE) Registry were included. In-hospital stroke or death was modeled using logistic regression with 35 candidate variables. Internal validation was achieved with bootstrapping, and model discrimination and calibration were assessed.

Results A total of 271 (2.4%) primary endpoint events occurred during 11,122 procedures. Independent predictors of stroke or death included impending major surgery, previous stroke, age, symptomatic lesion, atrial fibrillation, and absence of previous ipsilateral carotid endarterectomy. The model was well calibrated with moderate discriminatory ability (C-statistic: 0.71) overall, and within symptomatic (C-statistic: 0.68) and asymptomatic (C-statistic: 0.72) subgroups. The inclusion of available angiographic variables did not improve model performance (C-statistic: 0.72, integrated discrimination improvement 0.001; $p = 0.21$). The NCDR CAS score was developed to support prospective risk quantification.

Conclusions The NCDR CAS score, comprising 6 clinical variables, predicts in-hospital S/D after CAS. This tool may be useful to assist clinicians in evaluating optimal management, share more accurate pre-procedural risks with patients, and improve patient selection for CAS (50).

Trends in Permanent Pacemaker Implantation in the United States From 1993 to 2009: Increasing Complexity of Patients and Procedures

Objectives This study sought to define contemporary trends in permanent pacemaker use by analyzing a large national database.

Background The Medicare National Coverage Determination for permanent pacemaker, which emphasized single-chamber pacing, has not changed significantly since 1985. We sought to define contemporary trends in permanent pacemaker use by analyzing a large national database.

Methods We queried the Nationwide Inpatient Sample to identify permanent pacemaker implants between 1993 and 2009 using the International Classification of Diseases-Ninth Revision-Clinical Modification procedure codes for dual-chamber (DDD), single-ventricular (VVI), single-atrial (AAI), or biventricular (BiV) devices. Annual permanent pacemaker implantation rates and patient demographics were analyzed.

Results Between 1993 and 2009, 2.9 million patients received permanent pacemakers in the United States. Overall use increased by 55.6%. By 2009, DDD use increased from 62% to 82% ($p < 0.001$), whereas single-chamber ventricular pacemaker use fell from 36% to 14% ($p = 0.01$). Use of DDD devices was higher in urban, nonteaching hospitals (79%) compared with urban teaching hospitals (76%) and rural hospitals (72%). Patients with private insurance (83%) more commonly received DDD devices than Medicaid (79%) or Medicare (75%) recipients ($p < 0.001$). Patient age and Charlson comorbidity index increased over time. Hospital charges ($2011) increased 45.3%, driven by the increased cost of DDD devices.
Conclusions There is a steady growth in the use of permanent pacemakers in the United States. Although DDD device use is increasing, whereas single-chamber ventricular pacemaker use is decreasing. Patients are becoming older and have more medical comorbidities. These trends have important health care policy implications (51).

Pilot Trial of Cryoplasty or Conventional Balloon Post-Dilation of Nitinol Stents for Revascularization of Peripheral Arterial Segments: The COBRA Trial

Objectives The purpose of this study is to compare post-dilation strategies of nitinol self-expanding stents implanted in the superficial femoral artery of diabetic patients with peripheral arterial disease.
Background Endovascular treatment of superficial femoral artery disease with nitinol self-expanding stents is associated with high rates of in-stent restenosis in patients with diabetes mellitus.
Methods We conducted a prospective, multicenter, randomized, controlled clinical trial of diabetic patients to investigate whether post-dilation of superficial femoral artery nitinol self-expanding stents using a cryoplasty balloon reduces restenosis compared to a conventional balloon. Inclusion criteria included diabetes mellitus, symptomatic peripheral arterial disease, and superficial femoral artery lesions requiring implantation of stents >5 mm in diameter and >60 mm in length. Primary endpoint was binary restenosis at 12 months, defined as ≥2.5-fold increase in peak systolic velocity by duplex ultrasonography.
Results Seventy-four patients, with 90 stented superficial femoral artery lesions, were randomly assigned to post-dilation using cryoplasty ($n = 45$ lesions) or conventional balloons ($n = 45$ lesions). Mean lesion length was 148 ± 98 mm, mean stented length was 190 ± 116 mm, mean stent diameter was 6.1 ± 0.4 mm, and 50% of the lesions were total occlusions. Post-dilation balloon diameters were 5.23 ± 0.51 mm versus 5.51 ± 0.72 mm in the cryoplasty and conventional balloon angioplasty groups, respectively ($p = 0.02$). At 12 months, binary restenosis was significantly lower in the cryoplasty group (29.3% vs. 55.8%, $p = 0.01$; odds ratio: 0.36, 95% confidence interval: 0.15 to 0.89).
Conclusions Among diabetic patients undergoing implantation of nitinol self-expanding stents in the superficial femoral artery, post-dilation with cryoplasty balloon reduced binary restenosis compared to conventional balloon angioplasty. (Study Comparing Two Methods of Expanding Stents Placed in Legs of Diabetics With Peripheral Vascular Disease [COBRA]; NCT00827853) (52).

Double Antiplatelet Therapy After Drug-Eluting Stent Implantation: Risk Associated With Discontinuation Within the First Year

Objectives The goal of this study was to assess the risk associated with double antiplatelet therapy (DAT) discontinuation, and specifically, temporary discontinuation, during the first year after drug-eluting stent (DES) implantation.
Background Doubts remain about the risk of temporary DAT discontinuation within 1 year after DES implantation.
Methods A total of 1,622 consecutive patients undergoing DES implantation at 29 hospitals were followed up at 3, 6, 9, and 12 months to record the 1-year antiplatelet therapy discontinuation (ATD) rate, the number of days without DAT, and the rate of 1-year major cardiac events. Cox regression was used to analyze the association between ATD considered as a time-dependent covariate and 1-year cardiac events.
Results One hundred seventy-two (10.6%) patients interrupted at least 1 antiplatelet drug during the first year after DES implantation, although only 1 during the first month. Most ($n = 111$, 64.5%) interrupted DAT temporarily (median: 7 days; range: 5 to 8.5): 79 clopidogrel (31 temporarily), 38 aspirin (27 temporarily), and 55 both drugs (53 temporarily). Discontinuation was followed by acute coronary syndrome in 7 (4.1%; 95% confidence interval [CI]: 1.7 to 8.2), a similar rate of major cardiac events to that in patients without ATD ($n = 80$; 5.5%; 95% CI: 4.4 to 6.8; $p = 0.23$). ATD was not independently associated with 1-year major cardiac events (hazard ratio: 1.32 [95% CI: 0.56 to 3.12]).
Conclusions ATD within the first year and beyond the first month after DES is not exceptional, is usually temporary, and does not appear to have a large impact on risk (53).

A New Strategy for Discontinuation of Dual Antiplatelet Therapy: The RESET Trial (REal Safety and Efficacy of 3-month dual antiplatelet Therapy following Endeavor zotarolimus-eluting stent implantation)

Objectives The goal of this study was to evaluate shorter duration (3 months) dual antiplatelet therapy (DAPT) after drug-eluting stent (DES) implantation.
Background There have been few published reports of prospective randomized clinical studies comparing the safety and efficacy of shorter duration DAPT after DES implantation.

Methods We randomly assigned 2,117 patients with coronary artery stenosis into 2 groups according to DAPT duration and stent type: 3-month DAPT following Endeavor zotarolimus-eluting stent (E-ZES) implantation (E-ZES+3-month DAPT, n = 1,059) versus 12-month DAPT following the other DES implantation (standard therapy, n = 1,058). We hypothesized that the E-ZES+3-month DAPT would be noninferior to the standard therapy for the primary composite endpoint (cardiovascular death, myocardial infarction, stent thrombosis, target\vessel revascularization, or bleeding) at 1 year.

Results The primary endpoint occurred in 40 (4.7%) patients assigned to E-ZES+3-month DAPT compared with 41 (4.7%) patients assigned to the standard therapy (difference: 0.0%; 95% confidence interval [CI]: −2.5 to 2.5; $p = 0.84$; $p < 0.001$ for noninferiority). The composite rates of any death, myocardial infarction, or stent thrombosis were 0.8% and 1.3%, respectively (difference: −0.5%; 95% CI: −1.5 to 0.5; $p = 0.48$). The rates of stent thrombosis were 0.2% and 0.3%, respectively (difference: −0.1%; 95% CI: −0.5 to 0.3; $p = 0.65$) without its further occurrence after cessation of clopidogrel in the E-ZES+3-month DAPT group. The rates of target vessel revascularization were 3.9% and 3.7%, respectively (difference: 0.2%; 95% CI: −2.3 to 2.6; $p = 0.70$).

Conclusions E-ZES+3-month DAPT was noninferior to the standard therapy with respect to the occurrence of the primary endpoint. (REal Safety and Efficacy of a 3-month dual antiplatelet Therapy following E-ZES implantation [RESET]; NCT01145079) (54).

Updated Standardized Endpoint Definitions for Transcatheter Aortic Valve Implantation: The Valve Academic Research Consortium-2 Consensus Document

Objectives The aim of the current Valve Academic Research Consortium (VARC)-2 initiative was to revisit the selection and definitions of transcatheter aortic valve implantation (TAVI) clinical endpoints to make them more suitable to the present and future needs of clinical trials. In addition, this document is intended to expand the understanding of patient risk stratification and case selection.

Background A recent study confirmed that VARC definitions have already been incorporated into clinical and research practice and represent a new standard for consistency in reporting clinical outcomes of patients with symptomatic severe aortic stenosis (AS) undergoing TAVI. However, as the clinical experience with this technology has matured and expanded, certain definitions have become unsuitable or ambiguous.

Methods and Results Two in-person meetings (held in September 2011 in Washington, DC, USA, and in February 2012 in Rotterdam, the Netherlands) involving VARC study group members, independent experts (including surgeons, interventional and non-interventional cardiologists, imaging specialists, neurologists, geriatric specialists, and clinical trialists), the US Food and Drug Administration (FDA), and industry representatives, provided much of the substantive discussion from which this VARC-2 consensus manuscript was derived. This document provides an overview of risk assessment and patient stratification that need to be considered for accurate patient inclusion in studies. Working groups were assigned to define the following clinical endpoints: mortality, stroke, myocardial infarction, bleeding complications, acute kidney injury, vascular complications, conduction disturbances and arrhythmias, and a miscellaneous category including relevant complications not previously categorized. Furthermore, comprehensive echocardiography recommendations are provided for the evaluation of prosthetic valve (dys)function. Definitions for the quality of life assessments are also reported. These endpoints formed the basis for several recommended composite endpoints.

Conclusions This VARC-2 document has provided further standardization of endpoint definitions for studies evaluating the use of TAVI, which will lead to improved comparability and interpretability of the study results, supplying an increasingly growing body of evidence with respect to TAVI and/or surgical aortic valve replacement. This initiative and document can furthermore be used as a model during current endeavors of applying definitions to other transcatheter valve therapies (for example, mitral valve repair) (55).

Cost-Effectiveness and Clinical Effectiveness of Catheter-Based Renal Denervation for Resistant Hypertension

Objectives The purpose of this study was to assess cost-effectiveness and long-term clinical benefits of renal denervation in resistant hypertensive patients.

Background Resistant hypertension affects 12% of hypertensive persons. In the Symplicity HTN-2 randomized controlled trial, catheter-based renal denervation (RDN) lowered systolic blood pressure by 32 ± 23 mm Hg from 178 ± 18 mm Hg at baseline.

Methods A state-transition model was used to predict the effect of RDN and standard of care on 10-year and lifetime probabilities of stroke, myocardial infarction, all coronary heart disease, heart failure, end-stage renal disease, and median survival. We adopted a societal perspective and estimated an incremental cost-effectiveness ratio in U.S. dollars per quality-adjusted life-year, both discounted at 3% per year. Robustness and uncertainty were evaluated using deterministic and probabilistic sensitivity analyses.

Results Renal denervation substantially reduced event probabilities (10-year/lifetime relative risks: stroke 0.70/0.83; myocardial infarction 0.68/0.85; all coronary heart disease 0.78/0.90; heart failure 0.79/0.92; end-stage renal disease 0.72/0.81). Median survival was 18.4 years for RDN versus 17.1 years for standard of care. The discounted

lifetime incremental cost-effectiveness ratio was $3,071 per quality-adjusted life-year. Findings were relatively insensitive to variations in input parameters except for systolic blood pressure reduction, baseline systolic blood pressure, and effect duration. The 95% credible interval for incremental cost-effectiveness ratio was cost-saving to $31,460 per quality-adjusted life-year.

Conclusions The model suggests that catheter-based renal denervation, over a wide range of assumptions, is a cost-effective strategy for resistant hypertension that might result in lower cardiovascular morbidity and mortality (56).

Clinical and Angiographic Outcomes of Patients Treated With Everolimus-Eluting Stents or First-Generation Paclitaxel-Eluting Stents for Unprotected Left Main Disease

Objectives The goal of this study was to compare the outcomes of patients treated with everolimus-eluting stents (EES) with outcomes of patients treated with first-generation paclitaxel-eluting stents (PES) for unprotected left main disease (ULMD).

Background No data exist about the comparison of these 2 types of stents in ULMD.

Methods The primary endpoint of the study was a 1-year composite of cardiac death, nonfatal myocardial infarction, target vessel revascularization, and stroke (MACE). Secondary endpoints were 1-year target vessel failure (TVF) and 9-month angiographic in-segment restenosis >50%.

Results From 2004 to 2010, a total of 390 patients underwent ULMD percutaneous coronary intervention (224 received PES and 166 EES). The 1-year MACE rate was 21.9% in the PES group and 10.2% in the EES group ($p = 0.002$). TVF rate was 20.5% in the PES group and 7.8% in the EES group ($p < 0.001$). The in-segment restenosis rate was 5.2% in the EES group and 15.6% in the PES group ($p = 0.002$). EES and EuroSCORE were the only variables related to the risk of MACE. EES (odds ratio: 0.32; $p = 0.007$) was also independently related to the risk of restenosis.

Conclusions EES implantation for ULMD is associated with a reduced incidence of 1-year MACE, TVF, and restenosis as compared with PES implantation (57).

Reduction in Mortality as a Result of Direct Transport From the Field to a Receiving Center for Primary Percutaneous Coronary Intervention

Objectives This study sought to determine whether mortality complicating ST-segment elevation myocardial infarction (STEMI) was impacted by the design of transport systems.

Background It is recommended that regions develop systems to facilitate rapid transfer of STEMI patients to centers equipped to perform primary percutaneous coronary intervention (PCI), yet the impact on mortality from the design of such systems remains unknown.

Methods Within the framework of a citywide system where all STEMI patients are referred for primary PCI, we compared patients referred directly from the field to a PCI center to patients transported beforehand from the field to a non–PCI-capable hospital. The primary outcome was all-cause mortality at 180 days.

Results A total of 1,389 consecutive patients with STEMI were assessed by the emergency medical services (EMS) and referred for primary PCI: 822 (59.2%) were referred directly from the field to a PCI center, and 567 (40.8%) were transported to a non–PCI-capable hospital first. Death at 180 days occurred in 5.0% of patients transferred directly from the field, and in 11.5% of patients transported from the field to a non–PCI-capable hospital ($p < 0.0001$. After adjusting for baseline characteristics in a multivariable logistic regression model, mortality remained lower among patients referred directly from the field to the PCI center (odds ratio: 0.52, 95% confidence interval: 0.31 to 0.88, $p = 0.01$). Similar results were obtained by using propensity score methods for adjustment.

Conclusions A STEMI system allowing EMS to transport patients directly to a primary PCI center was associated with a significant reduction in mortality. Our results support the concept of STEMI systems that include pre-hospital referral by EMS (58).

Electrocardiographic Q-Wave "Remodeling" in Reperfused ST-Segment Elevation Myocardial Infarction: Validation Study With CMR

Objectives The aim of this study was to evaluate the evolution in Q-wave expression during the first 5 years after a primary, successfully reperfused ST-segment elevation myocardial infarction (MI), using cardiac magnetic resonance (CMR) for infarct location, and to depict changes in infarct size and left ventricular remodeling over time.

Background In the absence of QRS confounders, abnormal Q waves are usually diagnostic of myocardial necrosis. It is hypothesized that Q-wave regression after MI could be related to smaller infarct sizes. Late gadolinium enhancement accurately depicts MI of any age.

Methods Forty-six MI patients underwent electrocardiography and CMR at 1 week (baseline), 4 months, 1 year, and 5 years post-infarction. Conventional CMR parameters were analyzed, and infarct presence, location, and size were assessed using late gadolinium enhancement CMR. Infarct locations were anterior or nonanterior (inferior and/or lateral), using late gadolinium enhancement CMR as a reference. For each time point, patients were classified as having a diagnostic/nondiagnostic electrocardiogram (ECG) using the European Society of Cardiology/American College of Cardiology Foundation/American Heart Association/World Heart Federation consensus criteria for previous Q-wave infarct.

Results At baseline, 11 patients (23%) did not meet the criteria for Q-wave MI. Non–Q-wave infarcts were

significantly smaller than Q-wave infarcts ($p < 0.0001$). All anterior Q-wave infarcts ($n = 17$) were correctly localized, whereas in 7 of 19 nonanterior Q-wave infarcts, the location or extent of the infarct was misjudged by electrocardiography. At 4-month/1-year follow-up, in 10 patients (3 anterior/7 nonanterior), the ECG became nondiagnostic. The ECG remained nondiagnostic at 5-year follow-up. A cutoff infarct size of 6.2% at 1 year yielded a sensitivity of 89% and a specificity of 74% to predict the presence or absence of Q waves.

Conclusions The incidence of nondiagnostic ECGs for previous MI using the current European Society of Cardiology/American College of Cardiology Foundation/American Heart Association/World Heart Federation criteria is substantial and increases with time post-infarction from 23% immediately post-infarction to 44% at 5-year follow-up (59).

Patterns and Predictors of Stress Testing Modality After Percutaneous Coronary Stenting: Data From the NCDR®

Objectives We evaluated temporal trends and geographic variation in choice of stress testing modality after percutaneous coronary intervention (PCI), as well as associations between modality and procedure use after testing.

Background Stress testing is frequently performed post-PCI, but the choices among available modalities (electrocardiography only, nuclear, or echocardiography; pharmacological or exercise stress) and consequences of such choices are not well characterized.

Methods CathPCI Registry® data were linked with identifiable Medicare claims to capture stress testing use between 60 and 365 days post-PCI and procedures within 90 days after testing. Testing rates and modality used were modeled on the basis of patient, procedure, and PCI facility factors, calendar quarter, and Census Divisions using Poisson and logistic regression. Post-test procedure use was assessed using Gray's test.

Results Among 284,971 patients, the overall stress testing rate after PCI was 53.1 per 100 person-years. Testing rates declined from 59.3 in quarter 1 (2006) to 47.1 in quarter 4 (2008), but the relative use of modalities changed little. Among exercise testing recipients, adjusted proportions receiving electrocardiography-only testing varied from 6.8% to 22.8% across Census Divisions; and among exercise testing recipients having an imaging test, the proportion receiving echocardiography (versus nuclear) varied from 9.4% to 34.1%. Post-test procedure use varied among modalities; exercise electrocardiography-only testing was associated with more subsequent stress testing (13.7% vs. 2.9%; $p < 0.001$), but less catheterization (7.4% vs. 14.1%; $p < 0.001$) than imaging-based tests.

Conclusions Modest reductions in stress testing after PCI occurring between 2006 and 2008 cannot be ascribed to trends in use of any single modality. Additional research should assess whether this trend represents better patient selection for testing or administrative policies (e.g., restricted access for patients with legitimate testing needs). Geographic variation in utilization of stress modalities and differences in downstream procedure use among modalities suggest a need to identify optimal use of the different test modalities in individual patients (60).

Comparative Effectiveness of Drug-Eluting Versus Bare-Metal Stents in Elderly Patients Undergoing Revascularization of Chronic Total Coronary Occlusions: Results From the National Cardiovascular Data Registry, 2005–2008

Objectives This study sought to investigate the long-term effectiveness of drug-eluting stents (DES) versus bare-metal stents (BMS).

Background Improved recanalization techniques have increased interest in percutaneous coronary intervention (PCI) for chronic total coronary occlusion (CTO). The long-term effectiveness of DES and BMS is not known.

Methods We used data from 10,261 stable patients age ≥65 years at 889 U.S. hospitals who underwent CTO PCI from January 1, 2005, to December 31, 2008, in the NCDR (National Cardiovascular Data Registry) CathPCI Registry with linked Medicare inpatient claims for follow-up. Patient and procedural characteristics, and 30-month death, myocardial infarction, revascularization, and hospitalization for bleeding were evaluated by stent type. Outcomes following stenting were adjusted and compared using propensity score matching.

Results DES were used for CTO PCI in 8,218 (80%) and BMS in 2,043 (20%). DES patients were younger (74.0 vs. 75.5 years, $p < 0.001$), had longer lesions (18.8 vs. 16.5 mm, $p < 0.001$), received more stents (≥2 stents in 45.7% vs. 37.9%, $p < 0.001$), and underwent multivessel PCI (18.9% vs. 15.1%, $p < 0.001$). DES implantation was associated with a lower hazard of mortality (hazard ratio [HR]: = 0.72, 95% confidence interval [CI]: 0.60 to 0.86, $p < 0.001$), a similar hazard for myocardial infarction (HR: 0.85, 95% CI: 0.61 to 1.19, $p = 0.35$), and subsequent revascularization (HR: 0.94, 95% CI: 0.79 to 1.12, $p = 0.48$), including PCI (HR: 0.98, 95% CI: 0.83 to 1.19, $p = 0.87$) and coronary artery bypass grafting (HR: 0.71, 95% CI: 0.46 to 1.10, $p = 0.12$). Hospitalization for bleeding was also similar for DES versus BMS (HR: 0.92; 95% CI: 0.61 to 1.39, $p = 0.70$).

Conclusions Compared with BMS, DES use in stable patients undergoing CTO PCI was associated with lower mortality, as well as similar myocardial infarction and repeat revascularization rates without an increase in subsequent bleeding requiring hospitalization (61).

Evaluation of Efficacy and Dose Response of Different Paclitaxel-Coated Balloon Formulations in a Novel Swine Model of Iliofemoral In-Stent Restenosis

Objectives The authors aimed to validate a novel iliofemoral in-stent restenosis (ISR) model for the efficacy

evaluation of paclitaxel-coated balloons (PCB) using the familial hypercholesterolemic swine (FHS).

Background Most of the validation work regarding PCB technologies has been performed in the coronary territory of juvenile domestic swine. Although invaluable for safety evaluation, this model is not suited for the evaluation of the efficacy of peripheral PCB technologies.

Methods Twenty-four iliofemoral segments in 12 FHS underwent balloon injury and self-expanding stent placement. After 21 days, the resulting ISR lesions were treated with either 1 $\mu g/mm^2$ dose (n = 8), or 3 $\mu g/mm^2$ dose (n = 8) PCB (Cotavance, Bayer Pharma AG/MEDRAD, Indianola, Pennsylvania), or with an identical uncoated control balloon (n = 8).

Results At termination (28 days after treatment), the percent diameter stenosis by quantitative vascular analysis in the control group was higher (31.2 ± 13.7%) compared with the 1 $\mu g/mm^2$ (19.3 ± 14.0%, 38% reduction) and 3 $\mu g/mm^2$ (8.6 ± 10.7%, 72% reduction) PCB groups. Intravascular ultrasound analysis showed 36% (1 $\mu g/mm^2$ dose, $p = 0.04$) and 55% (3 $\mu g/mm^2$ dose, $p < 0.01$) reductions in neointimal volume stenosis. In the histological analysis, the control group showed the highest degree of percent area stenosis (65 ± 14.3%). The reductions in percent area stenosis was 13.2% ($p = 0.5$) and 26% ($p = 0.04$) in the 1 $\mu g/mm^2$ and 3 $\mu g/mm^2$ dose groups, respectively.

Conclusions The FHS model of iliofemoral ISR demonstrated a dose-dependent effect on the inhibition of neointimal proliferation of a clinically validated PCB technology. This model represents a positive step toward the efficacy evaluation of PCB in the peripheral vascular territory (62).

Predictors of Early, Late, and Very Late Stent Thrombosis After Primary Percutaneous Coronary Intervention With Bare-Metal and Drug-Eluting Stents for ST-Segment Elevation Myocardial Infarction

Objectives The purpose of this study was to evaluate the frequency and predictors of stent thrombosis (ST) after stenting for ST-segment elevation myocardial infarction (STEMI).

Background Stent thrombosis remains a major concern with STEMI patients treated with primary percutaneous coronary intervention.

Methods Consecutive patients (N = 1,640) undergoing stenting for STEMI were prospectively enrolled in our database and followed for 1 to 15 years. Bare-metal stents were implanted from 1995 to 2002, and drug-eluting and bare-metal stents were implanted from 2003 to 2009. Stent thrombosis was defined as definite or probable.

Results Our population had a high risk profile, including a high incidence of Killip class III to IV (11.5%) and STEMI due to ST (10.2%). Stent thrombosis occurred in 124 patients, including 42 with early ST (0 to 30 days), 35 with late ST (31 days to 1 year), and 47 with very late ST (>1 year). The frequency of ST was 2.7% at 30 days, 5.2% at 1 year, and 8.3% at 5 years. Independent predictors of early or late ST were STEMI due to ST (hazard ratio [HR]: 4.38, 95% confidence interval [CI]: 2.27 to 8.45), small stent size (HR: 2.44, 95% CI: 1.49 to 4.00), Killip class III to IV (HR: 2.39, 95% CI: 1.30 to 4.40), and reperfusion time ≤2 h (HR: 2.09, 95% CI: 1.03 to 4.24). Drug-eluting stent was the only independent predictor of very late ST (HR: 3.73, 95% CI: 1.81 to 7.88).

Conclusions Stent thrombosis after primary percutaneous coronary intervention is relatively frequent and continues to increase out to 5 years. New strategies are needed to prevent ST in STEMI patients, and targeted therapies are needed in patients identified at highest risk (63).

Open Versus Endovascular Stent Graft Repair of Abdominal Aortic Aneurysms A Meta-Analysis of Randomized Trials

Objectives This study sought to evaluate the short-, intermediate-, and longer-term outcomes after endovascular versus open repair of abdominal aortic aneurysms (AAA), including both AAA-related and all-cause mortality.

Background Endovascular stent graft placement for AAA has gained broad acceptance as an alternative to open surgical repair due to a lower perioperative morbidity and mortality. The intermediate- and long-term all-cause and aneurysm-related mortality vary among studies. Thus, we sought to perform a meta-analysis of open versus endovascular repair for treating AAA.

Methods Electronic databases were queried for identification of prospective, randomized trials of open surgery versus endovascular stent graft repair of AAA. A total of 10 published papers reporting on 6 studies at different follow-up intervals were identified; they involved 2,899 patients with AAA repair procedures, of whom, 1,470 underwent endovascular stent graft AAA exclusion and 1,429 were treated by open AAA repair.

Results At 30 days, the pooled relative risk of all-cause mortality was lower in the endovascular group (relative risk [RR]: 0.35, 95% confidence interval [CI]: 0.19 to 0.64) than in the open surgery group. At intermediate follow-up, the all-cause mortality had a nonsignificant difference (RR: 0.78, 95% CI: 0.57 to 1.08), the AAA-related mortality was significantly lower (RR: 0.46, 95% CI: 0.28 to 0.74) and reintervention rates were higher (RR: 1.48, 95% CI: 1.06 to 2.08) in the endovascular group than in the open surgery group. At long-term follow-up, there was no significant difference in all-cause mortality (RR: 0.99, 95% CI: 0.85 to 1.15) or AAA-related mortality (RR: 1.58, 95% CI: 0.20 to 12.74), whereas the significant difference in the rate of reinterventions persisted (RR: 2.54, 95% CI: 1.58 to 4.08).

Conclusions In patients randomized to open or endovascular AAA repair, all-cause perioperative mortality, as well as AAA-related mortality at short- and intermediate-term

follow-up are lower in patients undergoing endovascular stent graft placement. This was associated with greater reintervention in the endovascular group noted at intermediate follow-up. Long-term survival appears to converge between the 2 groups (64).

Spontaneous Coronary Artery Dissection: Long-Term Follow-Up of a Large Series of Patients Prospectively Managed With a "Conservative" Therapeutic Strategy

Objectives This study sought to assess the long-term clinical outcome of patients with spontaneous coronary artery dissection (SCD) managed with a conservative strategy.
Background SCD is a rare, but challenging, clinical entity.
Methods A prospective protocol, including a conservative management strategy, was followed. Revascularization was only considered in cases with ongoing/recurrent ischemia. Inflammatory/immunologic markers were systematically obtained.
Results Forty-five consecutive patients (incidence 0.27%) were studied during a 6-year period. Of these, 27 patients (60%) had "isolated" SCD (I-SCD), and 18 had SCD associated with coronary artery disease (A-SCD). Age was 53 ± 11 years, and 26 patients were female. Most patients presented with an acute myocardial infarction. SCD had a diffuse angiographic pattern (length: 31 ± 23 mm). In 11 patients, the diagnosis was confirmed by intracoronary imaging techniques. Sixteen patients (35%) required revascularization during initial admission. One patient died after surgery, but no additional patient experienced recurrent myocardial infarction. No significant inflammatory/immunologic abnormalities were detected. At follow-up (median 730 days), only 3 patients presented with adverse events (1 died of congestive heart failure, and 2 required revascularization). No patient experienced a myocardial infarction or died suddenly. Event-free survival was similar (94% and 88%, respectively) in patients with I-SCD and A-SCD. Notably, at angiographic follow-up, spontaneous "disappearance" of the SCD image was found in 7 of 13 (54%) patients.
Conclusions In this large prospective series of consecutive patients with SCD, a "conservative" therapeutic strategy provided excellent long-term prognosis. Clinical outcome was similar in patients with I-SCD and A-SCD. The natural history of SCD includes spontaneous healing with complete resolution (65).

2-Year Patient-Related Versus Stent-Related Outcomes: The SORT OUT IV (Scandinavian Organization for Randomized Trials With Clinical Outcome IV) Trial

Objectives There are limited head-to-head randomized data on patient-related versus stent-related outcomes for everolimus-eluting stents (EES) and sirolimus-eluting stents (SES).
Background In the SORT OUT IV (Scandinavian Organization for Randomized Trials With Clinical Outcome IV) trial, comparing the EES with the SES in patients with coronary artery disease, the EES was noninferior to the SES at 9 months.
Methods The primary endpoint was a composite: cardiac death, myocardial infarction (MI), definite stent thrombosis, or target vessel revascularization. Safety and efficacy outcomes at 2 years were further assessed with specific focus on patient-related composite (all death, all MI, or any revascularization) and stent-related composite outcomes (cardiac death, target vessel MI, or symptom-driven target lesion revascularization). A total of 1,390 patients were assigned to receive the EES, and 1,384 patients were assigned to receive the SES.
Results At 2 years, the composite primary endpoint occurred in 8.3% in the EES group and in 8.7% in the SES group (hazard ratio [HR]: 0.94, 95% confidence interval [CI]: 0.73 to 1.22). The patient-related outcome: 15.0% in the EES group versus 15.6% in the SES group, (HR: 0.95, 95% CI: 0.78 to 1.15), and the stent-related outcome: 5.2% in the EES group versus 5.3% in the SES group (HR: 0.97, 95% CI: 0.70 to 1.35) did not differ between groups. Rate of definite stent thrombosis was lower in the EES group (0.2% vs. 0.9%, (HR: 0.23, 95% CI: 0.07 to 0.80).
Conclusions At 2-year follow-up, the EES was found to be noninferior to the SES with regard to both patient-related and stent-related clinical outcomes. (The SORT OUT IV TRIAL [SORT OUT IV]; NCT00552877) (66).

A Randomized Comparison of Pulmonary Vein Isolation With Versus Without Concomitant Renal Artery Denervation in Patients With Refractory Symptomatic Atrial Fibrillation and Resistant Hypertension

Objectives The aim of this prospective randomized study was to assess the impact of renal artery denervation in patients with a history of refractory atrial fibrillation (AF) and drug-resistant hypertension who were referred for pulmonary vein isolation (PVI).
Background Hypertension is the most common cardiovascular condition responsible for the development and maintenance of AF. Treating drug-resistant hypertension with renal denervation has been reported to control blood pressure, but any effect on AF is unknown.
Methods Patients with a history of symptomatic paroxysmal or persistent AF refractory to ≥2 antiarrhythmic drugs and drug-resistant hypertension (systolic blood pressure >160 mm Hg despite triple drug therapy) were eligible for enrolment. Consenting patients were randomized to PVI only or PVI with renal artery denervation. All patients were followed ≥1 year to assess maintenance of sinus rhythm and to monitor changes in blood pressure.
Results Twenty-seven patients were enrolled, and 14 were randomized to PVI only, and 13 were randomized to PVI

with renal artery denervation. At the end of the follow-up, significant reductions in systolic (from 181 ± 7 to 156 ± 5, $p < 0.001$) and diastolic blood pressure (from 97 ± 6 to 87 ± 4, $p < 0.001$) were observed in patients treated with PVI with renal denervation without significant change in the PVI only group. Nine of the 13 patients (69%) treated with PVI with renal denervation were AF-free at the 12-month post-ablation follow-up examination versus 4 (29%) of the 14 patients in the PVI-only group ($p = 0.033$).

Conclusions Renal artery denervation reduces systolic and diastolic blood pressure in patients with drug-resistant hypertension and reduces AF recurrences when combined with PVI. (Combined Treatment of Resistant Hypertension and Atrial Fibrillation; NCT01117025) (67).

Vascular Complications After Transcatheter Aortic Valve Replacement: Insights From the PARTNER (Placement of AoRTic TraNscathetER Valve) Trial

Objectives This study sought to identify incidence, predictors, and impact of vascular complications (VC) after transfemoral (TF) transcatheter aortic valve replacement (TAVR).

Background VC after TF-TAVR are frequent and may be associated with unfavorable prognosis.

Methods From the randomized controlled PARTNER (Placement of AoRTic TraNscathetER Valve) trial, a total of 419 patients (177 from cohort B [inoperable] and 242 from cohort A [operable high-risk]) were randomly assigned to TF-TAVR and actually received the designated treatment. First-generation Edwards-Sapien valves and delivery systems were used, via a 22- or 24-F sheath. The 30-day rates of major and minor VC (modified Valve Academic Research Consortium definitions), predictors, and effect on 1-year mortality were assessed.

Results Sixty-four patients (15.3%) had major VC and 50 patients (11.9%) had minor VC within 30 days of the procedure. Among patients with major VC, vascular dissection (62.8%), perforation (31.3%), and access-site hematoma (22.9%) were the most frequent modes of presentation. Major VC, but not minor VC, were associated with significantly higher 30-day rates of major bleeding, transfusions, and renal failure requiring dialysis, and with a significantly higher rate of 30-day and 1-year mortality. The only identifiable independent predictor of major VC was female gender (hazard ratio [HR]: 2.31 [95% confidence interval (CI): 1.08 to 4.98], $p = 0.03$). Major VC (HR: 2.31 [95% CI: 1.20 to 4.43], $p = 0.012$), and renal disease at baseline (HR: 2.26 [95% CI: 1.34 to 3.81], $p = 0.002$) were identified as independent predictors of 1-year mortality.

Conclusions Major VC were frequent after TF-TAVR in the PARTNER trial using first-generation devices and were associated with high mortality. However, the incidence and impact of major VC on 1-year mortality decreased with lower-risk populations (68).

Early Anticoagulation of Bioprosthetic Aortic Valves in Older Patients: Results From the Society of Thoracic Surgeons Adult Cardiac Surgery National Database

Objectives The aim of this study was to evaluate the risks and benefits of short-term anticoagulation in patients receiving aortic valve bioprostheses.

Background Patients receiving aortic valve bioprostheses have an elevated early risk of thromboembolic events; however, the risks and benefits of short-term anticoagulation have been debated with limited evidence.

Methods Our cohort consisted of 25,656 patients ≥65 years of age receiving aortic valve bioprostheses at 797 hospitals within the Society of Thoracic Surgeons Adult Cardiac Surgery Database (2004 to 2006). The associated 3-month incidences of death or readmission for embolic (cerebrovascular accident, transient ischemic attack, and noncerebral arterial thromboembolism) or bleeding events were compared across discharge anticoagulation strategies with propensity methods.

Results In this cohort (median age, 77 years), the 3 most common discharge anticoagulation strategies included: aspirin-only (49%), warfarin-only (12%), and warfarin plus aspirin (23%). Among those receiving aspirin-only, 3-month adverse events were low (death, 3.0%; embolic events, 1.0%; bleeding events, 1.0%). Relative to aspirin-only, those treated with warfarin plus aspirin had a lower adjusted risk of death (relative risk [RR]: 0.80, 95% confidence interval [CI]: 0.66 to 0.96) and embolic event (RR: 0.52, 95% CI: 0.35 to 0.76) but a higher risk of bleeding (RR: 2.80, 95% CI: 2.18 to 3.60). Relative to aspirin-only, warfarin-only patients had a similar risk of death (RR: 1.01, 95% CI: 0.80 to 1.27), embolic events (RR: 0.95, 95% CI: 0.61 to 1.47), and bleeding (RR: 1.23, 95% CI: 0.85 to 1.79). These results were generally consistent across patient subgroups.

Conclusions Death and embolic events were relatively rare in the first 3 months after bioprosthetic aortic valve replacement. Compared with aspirin-only, aspirin plus warfarin was associated with a reduced risk of death and embolic events, but at the cost of an increased bleeding risk (69).

Sex Differences in Mortality After Transcatheter Aortic Valve Replacement for Severe Aortic Stenosis

Objectives The aim of this study was to examine sex differences in outcome after transcatheter aortic valve replacement (TAVR) with real-world data from 2 large centers in Canada.

Background Transcatheter aortic valve replacement is an effective alternative to surgical valve replacement in symptomatic patients with severe aortic stenosis, but the impact of sex on outcomes remains unclear. The PARTNER (Placement of Aortic Transcatheter Valves) 1A trial demonstrated greater benefit of TAVR over surgery in women, but

whether this was due to the poorer surgical outcome of women or better TAVR outcome, compared with men, is unknown.

Methods Consecutive patients (n = 641) undergoing TAVR in Vancouver and Quebec City, Canada, were evaluated. Differences in all-cause mortality were examined with Kaplan-Meier estimates, adjusted logistic regression, and proportional hazards models.

Results Women comprised 51.3% of the cohort. Balloon-expandable valves were used in 97% of cases, with transapical approach in 51.7 % women and 38.1% men. Women had more major vascular complications (12.4% vs. 5.4%, p = 0.003) and borderline significantly more major/life-threatening bleeds (21.6% vs. 15.8%, p = 0.08). At baseline, women had higher aortic gradients and worse renal function but better ejection fractions. Men had more comorbidities: prior myocardial infarction, prior revascularization, and chronic obstructive pulmonary disease. The adjusted odds ratio for 30-day all-cause mortality favored women, 0.39 (95% confidence interval: 0.19 to 0.80; p = 0.01), and this benefit persisted for 2 years, hazard ratio 0.60 (95% confidence interval: 0.41 to 0.88; p = 0.008).

Conclusions Female sex is associated with better short- and long-term survival after TAVR. Added to the PARTNER 1A findings, these results suggest TAVR might be the preferred treatment option for elderly women with symptomatic severe aortic stenosis (70).

The Impact of Frailty Status on Survival After Transcatheter Aortic Valve Replacement in Older Adults With Severe Aortic Stenosis: A Single-Center Experience

Objectives This study sought to evaluate the impact of frailty in older adults undergoing transcatheter aortic valve replacement (TAVR) for symptomatic aortic stenosis.

Background Frailty status impacts prognosis in older adults with heart disease; however, the impact of frailty on prognosis after TAVR is unknown.

Methods Gait speed, grip strength, serum albumin, and activities of daily living status were collected at baseline and used to derive a frailty score among patients who underwent TAVR procedures at a single large-volume institution. The cohort was dichotomized on the basis of median frailty score into frail and not frail groups. The impact of frailty on procedural outcomes (stroke, bleeding, vascular complications, acute kidney injury, and mortality at 30 days) and 1-year mortality was evaluated.

Results Frailty status was assessed in 159 subjects who underwent TAVR (age 86 ± 8 years, Society of Thoracic Surgery Risk Score 12 ± 4). Baseline frailty score was not associated with conventionally ascertained clinical variables or Society of Thoracic Surgery score. Although high frailty score was associated with a longer post-TAVR hospital stay when compared with lower frailty score (9 ± 6 days vs. 6 ± 5 days, respectively, p = 0.004), there were no significant crude associations between frailty status and procedural outcomes, suggesting adequacy of the standard selection process for identifying patients at risk for periprocedural complications after TAVR. Frailty status was independently associated with increased 1-year mortality (hazard ratio: 3.5, 95% confidence interval: 1.4 to 8.5, p = 0.007) after TAVR.

Conclusions Frailty was not associated with increased periprocedural complications in patients selected as candidates to undergo TAVR but was associated with increased 1-year mortality after TAVR. Further studies will evaluate the independent value of this frailty composite in older adults with aortic stenosis (71).

Coronary Endothelial Dysfunction Distal to Stent of First-Generation Drug-Eluting Stents

Objectives This study sought to evaluate the relationship between coronary endothelial function and neointimal coverage after drug-eluting stent (DES) implantation.

Background The mechanisms of endothelial dysfunction after DES implantation remain to be fully elucidated. We hypothesized that poor neointimal coverage after DES implantation may be associated with endothelial dysfunction distal to the stent site.

Methods Sixty-six stable angina patients treated with a first-generation DES were enrolled. At 9-month follow-up, coronary endothelial function was evaluated with intracoronary infusion of incremental doses of acetylcholine (10−8, 10−7, and 10−6 mol/l) and nitroglycerin (200 μg). Vascular responses at the segments proximal and distal to the stent site were angiographically and quantitatively measured. At the same time, the degree of neointimal coverage was evaluated using coronary angioscopy and classified into 4 grades: 0 (no coverage) to 3 (full coverage).

Results We divided the subjects into poor-coverage (grades 0 to 1, n = 33) and good-coverage (grades 2 to 3, n = 33) groups. Acetylcholine induced dose-dependent coronary vasoconstrictions in both groups. At the segment distal to the stent, the magnitude of vasoconstriction to acetylcholine in the poor-coverage group was significantly greater than in the good-coverage group (p < 0.001), whereas vasomotor responses proximal to the stent and vasodilation by nitroglycerine were similar between the 2 groups.

Conclusions Coronary endothelial dysfunction distal to the stent was associated with poor neointimal coverage after DES implantation (72).

Conformational Pulsatile Changes of the Aortic Annulus: Impact on Prosthesis Sizing by Computed Tomography for Transcatheter Aortic Valve Replacement

Objectives This study sought to investigate pulsatile changes of the aortic annulus and their impact on prosthesis selection by computed tomography (CT).

Background Precise noninvasive prosthesis sizing is a prerequisite for transcatheter aortic valve replacement.
Methods A total of 110 patients with severe aortic stenosis (mean age: 82.9 ± 8 years, mean aortic valve area: 0.69 ± 0.18 cm^2) underwent electrocardiogram-gated CT. Aortic annulus dimensions were planimetrically quantified as area-derived diameter (DA = 2 ×√(CSA/π), where CSA is the cross-sectional area) and perimeter-derived diameter (DP = P/π, where P is the length of the perimeter) in 5% increments of the RR interval. Hypothetical prosthesis sizing was based on DA and DP (23-mm prosthesis for <22 mm; 26 mm: 22 to 25 mm; 29 mm: >25 mm) and compared between maximum and traditional cardiac CT reconstruction phases at 35% and 75% of RR. Agreement for prosthesis selection was calculated by κ statistics.
Results DA and DP were increased and eccentricity was reduced during systole, with DA-MAX and DP-MAX most often observed at 20% of RR. DP was consistently larger than DA. Average net differences were 2.0 ± 0.6 mm and 1.7 ± 0.5 mm by DA-MIN versus DA-MAX and DP-MIN versus DP-MAX. Agreement for prosthesis sizing was found in 93 of 110 patients (κ = 0.75) by DA-75% and in 80 of 110 patients (κ = 0.53) by DA-MAX compared with DA-35%; and in 94 of 110 patients (κ = 0.73) by DP-75% and in 93 of 110 patients (κ = 0.73) by DP-MAX compared with DP-35%. With sizing by DA-75% or DP-75%, nominal prosthesis diameter was smaller than DA-MAX or DP-MAX in 15 and 6 patients respectively.
Conclusions Aortic annulus morphology exhibits conformational pulsatile changes throughout the cardiac cycle due to deformation and stretch. These changes affect prosthesis selection. Prosthesis selection by diastolic perimeter- or area-derived dimensions harbors the risk of undersizing (73).

Long-Term Vascular Healing in Response to Sirolimus- and Paclitaxel-Eluting Stents: An Optical Coherence Tomography Study

Objectives This study sought to assess stent strut coverage, malapposition, protrusion, and coronary evaginations as markers of healing 5 years after implantation of sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES), by optical coherence tomography (OCT).
Background Early-generation drug-eluting stents have been shown to delay vascular healing.
Methods A total of 88 event-free patients with 1 randomly selected lesion were suitable for final OCT analysis 5 years after drug-eluting stent implantation. The analytical approach was based on a hierarchical Bayesian random-effects model.
Results OCT analysis was performed at 5 years in 41 SES lesions with 6,380 struts, and in 47 PES lesions with 6,782 struts. A total of 196 struts were uncovered in SES (1.5%) compared with 185 struts in PES lesions (1.0%, 95% credibility interval [CrI]: 0.5 to 1.6; p = 0.32). Malapposed struts were present in 1.2% of SES compared with 0.7% of PES struts (0.7%, 95% CrI: 0.03 to 1.6; p = 0.23). Protruding struts were more frequent among SES (n = 114; 0.8%) than PES lesions (n = 24; 0.1%, 95% CrI: 0.3 to 1.3; p < 0.01). Coronary evaginations were more common among SES- than PES-treated lesions (17 vs. 7 per 100 cross sections, p = 0.003). During extended clinical follow-up, 2 patients suffered from very late stent thrombosis showing a high degree of malapposition, protrusion, and coronary evaginations at the time of OCT investigation.
Conclusions Early-generation drug-eluting stents show a similar degree of strut coverage and malapposition at 5 years of follow-up. Despite an overall low degree of uncovered and malapposed struts in event-free patients, some lesions show a clustering of these characteristics, indicating a heterogeneous healing response, which may be the source for very late adverse events (74).

Association Between Periprocedural Bleeding and Long-Term Outcomes Following Percutaneous Coronary Intervention in Older Patients

Objectives The authors sought to describe the association between post-procedural bleeding and long-term recurrent bleeding, major adverse cardiac events (MACE), and mortality among older patients undergoing percutaneous coronary intervention (PCI).
Background Bleeding complications after PCI are associated with an increased risk for acute morbidity and long-term mortality, but the association of these bleeding complications with other events is unknown.
Methods Patients entered into the National Cardiovascular Data Registry (NCDR) CathPCI Registry (n = 461,311; 946 sites) from January 2004 to December 2008 were linked with claims from the Centers for Medicare & Medicaid Services and grouped according to in-hospital post-PCI bleeding. The association between post-PCI bleeding and 1-, 12-, and 30-month readmission for bleeding, MACE, and all-cause mortality was examined with Cox regression that included patient and procedural characteristics using no bleeding as the reference.
Results Overall, 3.1% (n = 14,107) of patients experienced post-PCI bleeding. Patients who bled were older, more often female, had more medical comorbidities, less often received bivalirudin, and more often underwent PCI via the femoral approach. After adjustment, bleeding after the index procedure was significantly associated with readmission for bleeding (adjusted hazard ratios [95% confidence interval]: 1 month, 1.54 [1.42 to 1.67]; 12 months, 1.52 [1.40 to 1.66]; 30 months, 1.29 [1.11 to 1.50]), MACE (1 month, 1.11 [1.07 to 1.15]; 12 months, 1.17 [1.13 to 1.21]; 30 months, 1.12 [1.06 to 1.19]) and all-cause mortality (1 month, 1.32

[1.26 to 1.38]; 12 months, 1.33 [1.27 to 1.40]); 30 months, 1.22 [1.15 to 1.30]).

Conclusions Post-PCI bleeding complications are associated with an increased risk for short- and long-term recurrent bleeding, MACE, and all-cause mortality. These data underscore the prognostic importance of periprocedural bleeding and the need for identifying strategies to reduce long-term bleeding risk among patients undergoing PCI (75).

Association Between Angiographic Complications and Clinical Outcomes Among Patients With Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention: An EARLY ACS (Early Glycoprotein IIb/IIIa Inhibition in Non–ST-Segment Elevation Acute Coronary Syndrome) Angiographic Substudy

Objectives The goal of this analysis was to determine the association between intraprocedural complications and clinical outcomes among patients with high-risk non–ST-segment elevation acute coronary syndrome (NSTEACS) undergoing percutaneous coronary intervention (PCI).

Background Among patients undergoing PCI for NSTEACS, the relationship between intraprocedural complications and clinical outcomes, independent of epicardial and myocardial perfusion, has not been well characterized.

Methods The EARLY ACS (Early Glycoprotein IIb/IIIa Inhibition in Non–ST-Segment Elevation Acute Coronary Syndrome) trial enrolled 9,406 patients with high-risk NSTEACS undergoing an early invasive strategy. Of these, 1,452 underwent angiographic assessment in an independent core laboratory and did not have a myocardial infarction (MI) between enrollment and angiography. We assessed the relationship between abrupt closure, loss of side branch(es), distal embolization, and no-reflow phenomenon and 30-day clinical outcomes in these patients.

Results Of the patients, 166 (11.4%) experienced an intraprocedural complication. Baseline clinical characteristics were similar between patients who did and did not have complications. The 30-day composite of death or MI was significantly higher among patients with an intraprocedural complication (28.3% vs. 7.8%, odds ratio [OR]: 4.68, 95% confidence interval [CI]: 3.2 to 7.0, $p < 0.001$). Individually, both mortality (3.0% vs. 0.9%, OR: 3.60, 95% CI: 1.2 to 10.5, $p = 0.019$) and MI (27.1% vs. 7.4%, OR: 4.66, 95% CI: 3.1 to 7.0, $p < 0.001$) were significantly increased. After adjusting for differences in post-PCI epicardial and myocardial perfusion, the association with 30-day death or MI remained significant.

Conclusions Among high-risk NSTEACS patients undergoing an invasive strategy, the incidence of intraprocedural complications is high, and the occurrence of these complications is associated with worse clinical outcomes independent of epicardial and myocardial perfusion. (Early Glycoprotein IIb/IIIa Inhibition in Patients With Non–ST-segment Elevation Acute Coronary Syndrome [EARLY ACS]; NCT00089895) (76).

IVUS Detection of Vasa Vasorum Blood Flow Distribution in Coronary Artery Vessel Wall

There is an increased body of evidence to suggest that the vasa vasorum play a major role in the progression and complications of vulnerable plaque leading to acute coronary syndrome. We propose that detecting changes in the flow in the vascular wall by intravascular ultrasound signals can quantify the presence of vasa vasorum. The results obtained in a porcine model of atherosclerosis suggest that intravascular ultrasound-based estimates of blood flow in the arterial wall can be used in vivo in a clinical research setting to establish the density of vasa vasorum as an indicator of plaque vulnerability (77).

Risk of Stroke With Coronary Artery Bypass Graft Surgery Compared With Percutaneous Coronary Intervention

Objectives This study sought to determine whether coronary artery bypass graft (CABG) surgery is associated with an increased risk of stroke compared with percutaneous coronary intervention (PCI).

Background Some, but not all, randomized trials have reported increased rates of stroke with CABG compared with PCI. However, all these studies were powered insufficiently to examine differences in the risk of stroke reliably.

Methods We performed a meta-analysis of 19 trials in which 10,944 patients were randomized to CABG versus PCI. The primary end point was the 30-day rate of stroke. We also determined the rate of stroke at the midterm follow-up and investigated whether there was an interaction between revascularization type and the extent of coronary artery disease on the relative risk of stroke.

Results The 30-day rate of stroke was 1.20% after CABG compared with 0.34% after PCI (odds ratio: 2.94, 95% confidence interval: 1.69 to 5.09, $p < 0.0001$). Similar results were observed after a median follow-up of 12.1 months (1.83% vs. 0.99%, odds ratio: 1.67, 95% confidence interval: 1.09 to 2.56, $p = 0.02$). The extent of coronary artery disease (single vessel vs. multivessel vs. left main) did not affect the relative increase in the risk of stroke observed with CABG compared with PCI at either 30 days ($p = 0.57$ for interaction) or midterm follow-up ($p = 0.08$ for interaction). Similar results were observed when the outcomes in 33,980 patients from 27 observational studies were analyzed.

Conclusions Coronary revascularization by CABG compared with PCI is associated with an increased risk of stroke at 30 days and at the mid-term follow-up (78).

Performance of the HEMORR2HAGES, ATRIA, and HAS-BLED Bleeding Risk–Prediction Scores in Patients With Atrial Fibrillation Undergoing Anticoagulation: The AMADEUS (Evaluating the Use of SR34006 Compared to Warfarin or Acenocoumarol in Patients With Atrial Fibrillation) Study

Objectives The objective of this study was to compare the predictive performance of bleeding risk–estimation tools in a cohort of patients with atrial fibrillation (AF) undergoing anticoagulation.

Background Three bleeding risk–prediction schemes have been derived for and validated in patients with AF: HEMORR2HAGES (Hepatic or Renal Disease, Ethanol Abuse, Malignancy, Older Age, Reduced Platelet Count or Function, Re-Bleeding, Hypertension, Anemia, Genetic Factors, Excessive Fall Risk and Stroke), ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation), and HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile International Normalized Ratio, Elderly, Drugs/Alcohol). The relative predictive values of these bleeding scores have not previously been compared.

Methods We analyzed the dataset from the AMADEUS (Evaluating the Use of SR34006 Compared to Warfarin or Acenocoumarol in Patients With Atrial Fibrillation) trial, a multicenter, randomized, open-label noninferiority study that compared fixed-dose idraparinux with adjustable-dose oral vitamin K antagonist therapy in patients with AF. The principal safety outcome was any clinically relevant bleeding event, which was a composite of major bleeding plus clinically relevant nonmajor bleeding.

Results The HAS-BLED score performed best in predicting any clinically relevant bleeding, reflected both in net reclassification improvement (10.3% and 13% improvement compared with HEMORR2HAGES and ATRIA, respectively) and receiver-operating characteristic (ROC) analyses (c-indexes: 0.60 vs. 0.55 and 0.50 for HAS-BLED vs. HEMORR2AGES and ATRIA, respectively). Using decision-curve analysis, the HAS-BLED score demonstrated superior performance compared with ATRIA and HEMORR2HAGES at any threshold probability for clinically relevant bleeding. HAS-BLED was the only score that demonstrated a significant predictive performance for intracranial hemorrhage (c-index: 0.75; $p = 0.03$). An ATRIA score >3 was not significantly associated with the risk for any clinically relevant bleeding on Cox regression or on ROC analysis (c-index: 0.50; $p = 0.87$).

Conclusions All 3 tested bleeding risk–prediction scores demonstrated only modest performance in predicting any clinically relevant bleeding, although the HAS-BLED score performed better than the HEMORR2HAGES and ATRIA scores, as reflected by ROC analysis, reclassification analysis, and decision-curve analysis. Only HAS-BLED demonstrated a significant predictive performance for intracranial hemorrhage. Given its simplicity, the HAS-BLED score may be an attractive method for the estimation of oral anticoagulant–related bleeding risk for use in clinical practice, supporting recommendations in international guidelines (79).

Pre-Hospital Electrocardiography by Emergency Medical Personnel: Effects on Scene and Transport Times for Chest Pain and ST-Segment Elevation Myocardial Infarction Patients

Objectives This study sought to measure the impact of pre-hospital (PH) electrocardiography (ECG) on scene-to-hospital time for patients with chest pain of cardiac origin and those with ST-segment elevation myocardial infarction (STEMI).

Background Pre-hospital ECG decreases door-to balloon (D2B) time for STEMI patients. However, obtaining a PH ECG might prolong scene time. We investigated the impact of obtaining a PH ECG on both scene and transport times for patients with chest pain suspected of cardiac origin.

Methods City of San Diego Emergency Medical System runsheets of patients with chest pain from January 2003 to April 2008 were analyzed. The scene times and transport times were compared before (from January 2003 to December 2005) and after (from January 2006 to April 2008) implementation of the PH ECG. Among patients with a PH ECG, median scene times and transport times were compared in patients with and without STEMI.

Results There were 21,742 patients evaluated for chest pain during the study period. Implementation of PH ECG resulted in minimal increases in median scene time (19 min, 10 s vs. 19 min, 28 s, $p = 0.002$) and transport time (13 min, 16 s vs. 13 min, 28 s, $p = 0.007$). However, compared with chest pain patients, in STEMI patients ($n = 303$), shorter median scene time (17 min, 51 s vs. 19 min, 31 s, $p < 0.001$), transport time (12 min, 34 s vs. 13 min, 31 s, $p = 0.006$), and scene-to-hospital time was observed (30 min, 45 s vs. 33 min, 29 s, $p < 0.001$).

Conclusions Obtaining a PH ECG for patients with chest pain minimally prolongs scene and transport times. Further, for STEMI patients, both scene times and transport times are actually reduced leading to a potential reduction in total ischemic time (80).

Indirect Comparisons of New Oral Anticoagulant Drugs for Efficacy and Safety When Used for Stroke Prevention in Atrial Fibrillation

Objectives This study sought to perform an indirect comparison analysis of dabigatran etexilate (2 doses), rivaroxaban, and apixaban for their relative efficacy and safety against each other.

Background Data for warfarin compared against the new oral anticoagulants (OACs) in large phase III clinical trials of stroke prevention in atrial fibrillation (AF) are now available for the oral direct thrombin inhibitor, dabigatran

etexilate, in 2 doses (150 mg twice daily [BID], 110 mg BID), and the oral Factor Xa inhibitors, rivaroxaban and apixaban. A "head-to-head" direct comparison of drugs is the standard method for comparing different treatments, but in the absence of such head-to-head direct comparisons, another alternative to assess the relative effect of different treatment interventions would be to perform indirect comparisons, using a common comparator. Nonetheless, any inter-trial comparison is always fraught with major difficulties, and an indirect comparison analysis has many limitations, especially with the inter-trial population differences and thus, should not be overinterpreted.

Methods Indirect comparison analysis was performed using data from the published trials.

Results There was a significantly lower risk of stroke and systemic embolism (by 26%) for dabigatran (150 mg BID) compared with rivaroxaban, as well as hemorrhagic stroke and nondisabling stroke. There were no significant differences for apixaban versus dabigatran (both doses) or rivaroxaban; or rivaroxaban versus dabigatran 110 mg BID in preventing stroke and systemic embolism. For ischemic stroke, there were no significant differences between the new OACs. Major bleeding was significantly lower with apixaban compared with dabigatran 150 mg BID (by 26%) and rivaroxaban (by 34%), but not significantly different from dabigatran 110 mg BID. There were no significant differences between apixaban and dabigatran 110 mg BID in safety endpoints. Apixaban also had lower major or clinically relevant bleeding (by 34%) compared with rivaroxaban. When compared with rivaroxaban, dabigatran 110 mg BID was associated with less major bleeding (by 23%) and intracranial bleeding (by 54%). There were no significant differences in myocardial infarction events between the dabigatran (both doses) and apixaban.

Conclusions Notwithstanding the limitations of an indirect comparison study, we found no profound significant differences in efficacy between apixaban and dabigatran etexilate (both doses) or rivaroxaban. Dabigatran 150 mg BID was superior to rivaroxaban for some efficacy endpoints, whereas major bleeding was significantly lower with dabigatran 110 mg BID or apixaban. Only a head-to-head direct comparison of the different new OACs would fully answer the question of efficacy/safety differences between the new drugs for stroke prevention in AF (81).

Sirolimus-Eluting Stents for Treatment of Infrapopliteal Arteries Reduce Clinical Event Rate Compared to Bare-Metal Stents

Objectives The study investigated the long-term clinical impact of sirolimus-eluting stents (SES) in comparison with bare-metal stents (BMS) in treatment of focal infrapopliteal lesions.

Background There is evidence that SES reduce the risk of restenosis after percutaneous infrapopliteal artery revascularization. No data from randomized trials are available concerning the clinical impact of this finding during long-term follow-up.

Methods The study extended the follow-up period of a prospective, randomized, multicenter, double-blind trial comparing polymer-free SES with placebo-coated BMS in the treatment of focal infrapopliteal de novo lesions. The main study endpoint was the event-free survival rate defined as freedom from target limb amputation, target vessel revascularization, myocardial infarction, and death. Secondary endpoints include amputation rates, target vessel revascularization, and changes in Rutherford-Becker class.

Results The trial included 161 patients. The mean target lesion length was 31 ± 9 mm. Thirty-five (23.3%) patients died during a mean follow-up period of 1,016 ± 132 days. The event-free survival rate was 65.8% in the SES group and 44.6% in the BMS group (log-rank $p = 0.02$). Amputation rates were 2.6% and 12.2% ($p = 0.03$), and target vessel revascularization rates were 9.2% and 20% ($p = 0.06$), respectively. The median (interquartile range) improvement in Rutherford-Becker class was −2 (−3 to −1) in the SES group and −1 (−2 to 0) in the BMS group, respectively ($p = 0.006$).

Conclusions Long-term event-free survival, amputation rates, and changes in Rutherford-Becker class after treatment of focal infrapopliteal lesions are significantly improved with SES in comparison with BMS. (YUKON-Drug-Eluting Stent Below the Knee - Randomised Double-Blind Study [YUKON-BTX]; NCT00664963) (82).

Treatment of Atrial Fibrillation by the Ablation of Localized Sources: CONFIRM (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation) Trial

Objectives We hypothesized that human atrial fibrillation (AF) may be sustained by localized sources (electrical rotors and focal impulses), whose elimination (focal impulse and rotor modulation [FIRM]) may improve outcome from AF ablation.

Background Catheter ablation for AF is a promising therapy, whose success is limited in part by uncertainty in the mechanisms that sustain AF. We developed a computational approach to map whether AF is sustained by several meandering waves (the prevailing hypothesis) or localized sources, then prospectively tested whether targeting patient-specific mechanisms revealed by mapping would improve AF ablation outcome.

Methods We recruited 92 subjects during 107 consecutive ablation procedures for paroxysmal or persistent (72%) AF. Cases were prospectively treated, in a 2-arm 1:2 design, by ablation at sources (FIRM-guided) followed by conventional ablation ($n = 36$), or conventional ablation alone ($n = 71$; FIRM-blinded).

Results Localized rotors or focal impulses were detected in 98 (97%) of 101 cases with sustained AF, each exhibiting 2.1 ± 1.0 sources. The acute endpoint (AF termination or

consistent slowing) was achieved in 86% of FIRM-guided cases versus 20% of FIRM-blinded cases ($p < 0.001$). FIRM ablation alone at the primary source terminated AF in a median 2.5 min (interquartile range: 1.0 to 3.1 min). Total ablation time did not differ between groups (57.8 ± 22.8 min vs. 52.1 ± 17.8 min, $p = 0.16$). During a median 273 days (interquartile range: 132 to 681 days) after a single procedure, FIRM-guided cases had higher freedom from AF (82.4% vs. 44.9%; $p < 0.001$) after a single procedure than FIRM-blinded cases with rigorous, often implanted, electrocardiography monitoring. Adverse events did not differ between groups.

Conclusions Localized electrical rotors and focal impulse sources are prevalent sustaining mechanisms for human AF. FIRM ablation at patient-specific sources acutely terminated or slowed AF, and improved outcome. These results offer a novel mechanistic framework and treatment paradigm for AF. (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation [CONFIRM]; NCT01008722) (83).

Transcatheter Aortic Valve Replacement With the St. Jude Medical Portico Valve: First-in-Human Experience

Objectives The purpose of this study was to demonstrate the feasibility and procedural outcomes with a new self-expanding and repositionable transcatheter heart valve.

Background Transcatheter aortic valve replacement is a viable option for selected patients with severe symptomatic aortic stenosis. However, suboptimal prosthesis positioning may contribute to paravalvular regurgitation, atrioventricular conduction block, and mitral or coronary compromise.

Methods The repositionable Portico valve (St. Jude Medical, Minneapolis, Minnesota) was implanted in 10 patients with severe aortic stenosis utilizing percutaneous femoral arterial access. Patients underwent transthoracic and transesophageal echocardiography and multidetector computed tomography before and after valve implantation. Clinical and echocardiographic follow-up was obtained at 30 days.

Results Device implantation was successful in all patients. Prosthesis recapture and repositioning was performed in 4 patients. Intermittent prosthetic leaflet dysfunction in 1 patient required implantation of a second transcatheter valve. There was 1 minor stroke. At 30-day follow-up, echocardiographic mean transaortic gradient was reduced from 44.9 ± 16.7 mm Hg to 10.9 ± 3.8 mm Hg ($p < 0.001$), and valve area increased from 0.6 ± 0.1 cm^2 to 1.3 ± 0.2 cm^2 ($p < 0.001$). Paravalvular regurgitation was mild or less in 9 patients (90%) and moderate in 1 patient (10%). There were no major strokes, major vascular complications, major bleeds, or deaths. No patient required pacemaker implantation. All patients were in New York Heart Association functional class II or less.

Conclusions Transcatheter aortic valve replacement with the repositionable Portico transcatheter heart valve is feasible, with good short-term clinical and hemodynamic outcomes (84).

Kissing Balloon Inflation in Percutaneous Coronary Interventions

Bifurcation lesions are the most frequently approached complex coronary lesions in everyday interventional practice. Bifurcations complexity relies essentially on their very specific anatomy that is imperfectly handled by current coronary devices and, despite dedicated techniques and drug-eluting stents, percutaneous coronary interventions directed toward the treatment of bifurcations are technically demanding and require proper execution. Kissing balloon (KB) inflation was the first specific bifurcation technique to have been developed for percutaneous bifurcation interventions and continues to currently play an important role. Indeed, KB has been proposed to optimize stent apposition, improve side branch access while correcting stent deformation or distortion. Over the years, the KB technique has been deeply investigated by many different methods, from bench testing and computer simulations to in vivo intravascular imaging and clinical studies, producing a large amount of data pointing out the benefits and limitations of the technique. We sought to provide here a comprehensive overview of all those aspects (85).

Vascular Closure Device Failure in Contemporary Practice

Objectives The goal of this study was to assess the frequency and predictors of vascular closure device (VCD) deployment failure, and its association with vascular complications of 3 commonly used VCDs.

Background VCDs are commonly used following percutaneous coronary intervention on the basis of studies demonstrating reduced time to ambulation, increased patient comfort, and possible reduction in vascular complications as compared with manual compression. However, limited data are available on the frequency and predictors of VCD failure, and the association of deployment failure with vascular complications.

Methods From a de-identified dataset provided by Massachusetts Department of Health, 23,813 consecutive interventional coronary procedures that used either a collagen plug–based ($n = 18,533$), a nitinol clip–based ($n = 2,284$), or a suture-based ($n = 2,996$) VCD between June 2005 and December 2007 were identified. The authors defined VCD failure as unsuccessful deployment or failure to achieve immediate access site hemostasis.

Results Among 23,813 procedures, the VCD failed in 781 (3.3%) procedures (2.1% of collagen plug–based, 6.1% of suture-based, 9.5% of nitinol clip–based VCDs). Patients with VCD failure had an excess risk of "any" (7.7% vs. 2.8%;

$p < 0.001$), major (3.3% vs. 0.8%; $p < 0.001$), or minor (5.8% vs. 2.1%; $p < 0.001$) vascular complications compared with successful VCD deployment. In a propensity score–adjusted analysis, when compared with collagen plug–based VCD (reference odds ratio [OR] = 1.0), nitinol clip–based VCD had 2-fold increased risk (OR: 2.0, 95% confidence interval [CI]: 1.8 to 2.3, $p < 0.001$) and suture-based VCD had 1.25-fold increased risk (OR: 1.25, 95% CI: 1.2 to 1.3, $p < 0.001$) for VCD failure. VCD failure was a significant predictor of subsequent vascular complications for both collagen plug–based VCD and nitinol clip–based VCD, but not for suture-based VCD.

Conclusions VCD failure rates vary depending upon the type of VCD used and are associated with significantly higher vascular complications as compared with deployment successes (86).

The Recanalization of Chronic Total Occlusion Leads to Lumen Area Increase in Distal Reference Segments in Selected Patients: An Intravascular Ultrasound Study

Objectives This study sought to investigate the extent of and factors related to lumen and vessel area change in coronary arteries after total occlusion (TO) recanalization.

Background TO of a coronary artery promotes negative remodeling in distal reference segments. Recanalization can restore blood flow, potentially leading to positive vascular remodeling.

Methods From March 2005 to June 2008, 58 consecutive patients with de novo TO lesions of at least 1-month duration were enrolled. We performed intravascular ultrasound after successful percutaneous coronary intervention and at the 6-month follow-up, and we quantified changes in the distal reference segments.

Results At the 6-month follow-up, there was a significant increase in the mean lumen diameter (+0.21 mm, $p = 0.001$), the mean external elastic membrane diameter (+0.13 mm, $p = 0.010$), the lumen area (+0.87 mm^2, $p < 0.001$), and the external elastic membrane area (+0.85 mm^2, $p = 0.001$) in the distal reference segments and an increase in the left ventricular ejection fraction (+2.77%, $p = 0.010$). Overall, 40 of 58 patients (69%) showed lumen area increase; these patients had increase in lumen diameter by 0.40 ± 0.34 mm ($p < 0.001$) and increase in incomplete stent apposition rate ($p = 0.006$). A TO duration of longer than 3 months (odds ratio [OR]: 14.8; 95% confidence interval [CI]: 1.28 to 172.8, $p = 0.032$), a poor collateral flow (OR: 12.0; 95% CI: 1.92 to 74.2, $p = 0.008$), and statin use (OR: 7.4; 95% CI: 1.03 to 53.6, $p = 0.047$) were independent predictors of lumen area increase.

Conclusions Recanalization of TO led to lumen area increase in two-thirds of the patients. Independent predictors of lumen area increase were occlusion duration, a poor collateral flow, and statin use. These factors could be used as guides in choosing the optimal stent size during percutaneous coronary intervention to TO lesions and optimal medical therapy during follow-up (87).

Radiation Dose Reduction in the Invasive Cardiovascular Laboratory: Implementing a Culture and Philosophy of Radiation Safety

Objectives This paper investigates the effects of sustained practice and x-ray system technical changes on the radiation dose administered to adult patients during invasive cardiovascular procedures.

Background It is desirable to reduce radiation dose associated with medical imaging to minimize the risk of adverse radiation effects to both patients and staff. Several clinical practice and technical changes to elevate radiation awareness and reduce patient radiation dose were implemented under the guidance of a cardiovascular invasive labs radiation safety committee. Practice changes included: intraprocedure radiation dose announcements; reporting of procedures for which the air-kerma exceeded 6,000 mGy, including procedure air-kerma in the clinical report; and establishing compulsory radiation safety training for fellows. Technical changes included establishing standard x-ray imaging protocols, increased use of x-ray beam spectral filters, reducing the detector target dose for fluoroscopy and acquisition imaging, and reducing the fluoroscopy frame rate to 7.5 s^{-1}.

Methods Patient- and procedure-specific cumulative skin dose was calculated from air-kerma values and evaluated retrospectively over a period of 3 years. Data were categorized to include all procedures, percutaneous coronary interventions, coronary angiography, noncardiac vascular angiography and interventions, and interventions to treat structural heart disease. Statistical analysis was based on a comparison of the cumulative skin dose for procedures performed during the first and last quarters of the 3-year study period.

Results A total of 18,115 procedures were performed by 27 staff cardiologists and 65 fellows-in-training. Considering all procedures, the mean cumulative skin dose decreased from 969 to 568 mGy (40% reduction) over 3 years.

Conclusions This work demonstrates that a philosophy of radiation safety, implemented through a collection of sustained practice and x-ray system changes, can result in a significant decrease in the radiation dose administered to patients during invasive cardiovascular procedures (88).

Reduction in Treatment Times Through Formalized Data Feedback: Results From a Prospective Multicenter Study of ST-Segment Elevation Myocardial Infarction

Objectives This study sought to evaluate the effect of systematic data analysis and standardized feedback on treatment times and outcome in a prospective multicenter trial.

Background Formalized data feedback may reduce treatment times in ST-segment elevation myocardial infarction (STEMI).
Methods Over a 15-month period, 1,183 patients presenting with STEMI were enrolled. Six primary percutaneous coronary intervention hospitals in Germany and 29 associated nonpercutaneous coronary intervention hospitals participated. Data from patient contact to balloon inflation were collected and analyzed. Pre-defined quality indicators, including the percentage of patients with pre-announced STEMI, direct handoff in the catheterization laboratory, contact-to-balloon time <90 min, door-to-balloon time <60 min, and door-to-balloon time <30 min were discussed with staff on a quarterly basis.
Results Median door-to-balloon time decreased from 71 to 58 min and contact-to-balloon time from 129 to 103 min between the first and the fifth quarter ($p < 0.05$ for both). Contributing were shorter stays in the emergency department, more direct handoffs from ambulances to the catheterization laboratory (from 22% to 38%, $p < 0.05$), and a slight increase in the number of patients transported directly to the percutaneous coronary intervention facility (primary transport). One-year mortality was reduced in the total group of patients and in the subgroup of patients with primary transport ($p < 0.05$). The sharpest fall in mortality was observed in patients with primary transport and TIMI (Thrombolysis In Myocardial Infarction) risk score ≥3 ($n = 521$) with a decrease in 30-day mortality from 23.1% to 13.3% ($p < 0.05$) and in 1-year mortality from 25.6% to 16.7% ($p < 0.05$).
Conclusions Formalized data feedback is associated with a reduction in treatment times for STEMI and with an improved prognosis, which is most pronounced in high-risk patients. (Feedback Intervention and Treatment Times in ST-Elevation Myocardial Infarction [FITT-STEMI]; NCT00794001) (89).

Impact of Paravalvular Leakage on Outcome in Patients After Transcatheter Aortic Valve Implantation

Objectives The aim of this study was to evaluate the performance of the aortic regurgitation (AR) index as a new hemodynamic parameter in an independent transcatheter aortic valve implantation (TAVI) cohort and validate its application.
Background Increasing evidence associates more-than-mild periprosthetic aortic regurgitation (periAR) with increased mortality and morbidity; therefore precise evaluation of periAR after TAVI is essential. The AR index has been proposed recently as a simple and reproducible indicator for the severity of periAR and predictor of associated mortality.
Methods The severity of periAR was evaluated by echocardiography, angiography, and periprocedural measurement of the dimensionless AR index = ([diastolic blood pressure − left ventricular end-diastolic pressure]/systolic blood pressure) × 100. A cutoff value of 25 was used to identify patients at risk.
Results One hundred twenty-two patients underwent TAVI by use of either the Medtronic CoreValve (Medtronic, Minneapolis, Minnesota) (79.5%) or the Edwards-SAPIEN bioprosthesis (Edwards Lifesciences, Irvine, California) (20.5%). The AR index decreased stepwise from 29.4 ± 6.3 in patients without periAR ($n = 26$) to 28.0 ± 8.5 with mild periAR ($n = 76$), 19.6 ± 7.6 with moderate periAR ($n = 18$), and 7.6 ± 2.6 with severe periAR ($n = 2$) ($p < 0.001$). Patients with AR index <25 had a significantly increased 1-year mortality rate compared with patients with AR index ≥25 (42.3% vs. 14.3%; $p < 0.001$). Even in patients with none/mild periAR, the 1-year mortality risk could be further stratified by an AR index <25 (31.3% vs. 14.3%; $p = 0.04$).
Conclusions The validity of the AR index could be confirmed in this independent TAVI cohort and provided prognostic information that was complementary to the severity of AR (90).

Stem Cell–Based Transcatheter Aortic Valve Implantation: First Experiences in a Pre-Clinical Model

Objectives This study sought to investigate the combination of transcatheter aortic valve implantation and a novel concept of stem cell-based, tissue-engineered heart valves (TEHV) comprising minimally invasive techniques for both cell harvest and valve delivery.
Background TAVI represents an emerging technology for the treatment of aortic valve disease. The used bioprostheses are inherently prone to calcific degeneration and recent evidence suggests even accelerated degeneration resulting from structural damage due to the crimping procedures. An autologous, living heart valve prosthesis with regeneration and repair capacities would overcome such limitations.
Methods Within a 1-step intervention, trileaflet TEHV, generated from biodegradable synthetic scaffolds, were integrated into self-expanding nitinol stents, seeded with autologous bone marrow mononuclear cells, crimped and transapically delivered into adult sheep ($n = 12$). Planned follow-up was 4 h (Group A, $n = 4$), 48 h (Group B, $n = 5$) or 1 and 2 weeks (Group C, $n = 3$). TEHV functionality was assessed by fluoroscopy, echocardiography, and computed tomography. Post-mortem analysis was performed using histology, extracellular matrix analysis, and electron microscopy.
Results Transapical implantation of TEHV was successful in all animals ($n = 12$). Follow-up was complete in all animals of Group A, three-fifths of Group B, and two-thirds of Group C (1 week, $n = 1$; 2 weeks, $n = 1$). Fluoroscopy and echocardiography displayed TEHV functionality demonstrating adequate leaflet mobility and coaptation. TEHV showed intact leaflet structures with

well-defined cusps without signs of thrombus formation or structural damage. Histology and extracellular matrix displayed a high cellularity indicative for an early cellular remodeling and in-growth after 2 weeks.
Conclusions We demonstrate the principal feasibility of a transcatheter, stem cell–based TEHV implantation into the aortic valve position within a 1-step intervention. Its long-term functionality proven, a stem cell–based TEHV approach may represent a next-generation heart valve concept (91).

Transradial Versus Transfemoral Artery Approach for Coronary Angiography and Percutaneous Coronary Intervention in the Extremely Obese

Objectives This study sought to evaluate the safety and efficacy of transradial versus transfemoral access for coronary angiography and percutaneous coronary intervention in patients with a body mass index ≥40 kg/m^2.
Background Coronary angiography is most commonly performed via femoral artery access; however, the optimal approach in extremely obese (EO) patients remains unclear.
Methods Between January 2007 and August 2010, a cohort of consecutive EO patients who underwent coronary angiography was identified in our center's registry of angiography and percutaneous coronary intervention procedures. Of 21,103 procedures, 564 (2.7%) were performed in unique EO patients: 203 (36%) via the transradial approach; and 361 (64%) via the transfemoral approach.
Results The primary outcome, a combined endpoint of major bleeding, access site complications, and nonaccess site complications, occurred in 7.5% of the transfemoral group and 2.0% of the transradial group (odds ratio [OR]: 0.30, 95% confidence interval [CI]: 0.10 to 0.88, p = 0.029), an endpoint driven by reductions in major bleeding (3.3% vs. 0.0%, OR: 0.12, 95% CI: 0 to 0.71, p = 0.015), as well as access site injuries (4.7% vs. 0.0%, OR: 0.08, 95% CI: 0 to 0.48, p = 0.002). There were no differences in nonaccess site complications (1.7% vs. 2.0%, OR: 1.50, 95% CI: 0.41 to 5.55), but transradial access procedures were associated with an increase in procedure time and patient radiation dose (p < 0.05).
Conclusions Transfemoral access for coronary angiography and percutaneous coronary intervention was associated with more bleeding and access site complications when compared with a transradial approach. Important reductions in procedural associated morbidity may be possible with a transradial approach in EO patients (92).

3-Year Clinical Outcomes in the Randomized SORT OUT III Superiority Trial Comparing Zotarolimus- and Sirolimus-Eluting Coronary Stents

Objectives This study sought to examine the 3-year clinical outcomes in patients treated with the Endeavor (Medtronic, Santa Rosa, California) zotarolimus-eluting stent (ZES) or the Cypher (Cordis, Johnson & Johnson, Warren, New Jersey) sirolimus-eluting stent (SES) in routine clinical practice.
Background The long-term clinical outcome in patients treated with ZES in comparison with SES is unclear.
Methods The authors randomized 2,332 patients to ZES (n = 1,162) or SES (n = 1,170) implantation. Endpoints included major adverse cardiac events (MACE), a composite of cardiac death, myocardial infarction, or target vessel revascularization; the individual endpoints of MACE; and definite stent thrombosis.
Results At 3-year follow-up, the MACE rate was higher in patients treated with ZES than in patients treated with SES (148 [12.9%] vs. 116 [10.1%]; hazard ratio [HR]: 1.33, 95% confidence interval [CI]: 1.04 to 1.69; p = 0.022). Target vessel revascularization was more frequent in the ZES group compared with the SES group (103 [9.1%] vs. 76 [6.7%]; HR: 1.40, 95% CI: 1.04 to 1.89; p = 0.025), whereas the occurrence of myocardial infarction (3.8% vs. 3.3%) and cardiac death (2.8% vs. 2.8%) did not differ significantly. Although the rate of definite stent thrombosis was similar at 3-year follow-up (1.1% vs. 1.4%), very late (12 to 36 months) definite stent thrombosis occurred in 0 (0%) patients in the ZES group versus 12 (1.1%) patients in the SES group (p = 0.0005).
Conclusions Although the 3-year MACE rate is higher in patients treated with ZES versus SES, our data highlight a late safety problem concerning definite stent thrombosis with the use of SES. This finding underscores the importance of long-term follow-up in head-to-head comparisons of drug-eluting stents. (Randomized Clinical Comparison of the Endeavor and the Cypher Coronary Stents in Non-selected Angina Pectoris Patients [SORT OUT III]; NCT00660478) (93).

Coronary Vasomotor Control in Obesity and Morbid Obesity: Contrasting Flow Responses With Endocannabinoids, Leptin, and Inflammation

Objectives This study sought to investigate abnormalities in coronary circulatory function in 2 different disease entities of obese (OB) and morbidly obese (MOB) individuals and to evaluate whether these would differ in severity with different profiles of endocannabinoids, leptin, and C-reactive protein (CRP) plasma levels.
Background There is increasing evidence that altered plasma levels of endocannabinoids, leptin, and CRP may affect coronary circulatory function in OB and MOB.
Methods Myocardial blood flow (MBF) responses to cold pressor test from rest and during pharmacologically induced hyperemia were measured with N-13 ammonia positron emission tomography/computed tomography. Study participants (n = 111) were divided into 4 groups based on their body mass index (BMI) (kg/m^2): 1) control group (BMI: 20 to 24.9, n = 30); 2) overweight group (BMI: 25 to 29.9, n = 31), 3) OB group (BMI: 30 to 39.9, n = 25); and 4) MOB group (BMI ≥40, n = 25).

Results The cold pressor test–induced change in endothelium-related MBF response (ΔMBF) progressively declined in overweight and OB groups when compared with the control group [median: 0.19 (interquartile range [IQR] 0.08, 0.27) and 0.11 (0.03, 0.17) vs. 0.27 (0.23, 0.38) ml/g/min; $p \leq 0.01$, respectively], whereas it did not differ significantly between OB and MOB groups [median: 0.11 (IQR: 0.03, 0.17) and 0.09 (−0.01, 0.19) ml/g/min; $p = 0.93$]. Compared with control subjects, hyperemic MBF subjects comparably declined in the overweight, OB, and MOB groups [median: 2.40 (IQR 1.92, 2.63) vs. 1.94 (1.65, 2.30), 2.05 (1.67, 2.38), and 2.14 (1.78, 2.76) ml/g/min; $p \leq 0.05$, respectively]. In OB individuals, ΔMBF was inversely correlated with increase in endocannabinoid anandamide ($r = -0.45$, $p = 0.044$), but not with leptin ($r = -0.02$, $p = 0.946$) or with CRP ($r = -0.33$, $p = 0.168$). Conversely, there was a significant and positive correlation among ΔMBF and elevated leptin ($r = 0.43$, $p = 0.031$) and CRP ($r = 0.55$, $p = 0.006$), respectively, in MOB individuals that was not observed for endocannabinoid anandamide ($r = 0.07$, $p = 0.740$).

Conclusions Contrasting associations of altered coronary endothelial function with increases in endocannabinoid anandamide, leptin, and CRP plasma levels identify and characterize OB and MOB as different disease entities affecting coronary circulatory function (94).

Assessment of Myocardial Scarring Improves Risk Stratification in Patients Evaluated for Cardiac Defibrillator Implantation

Objectives We tested whether an assessment of myocardial scarring by cardiac magnetic resonance imaging (MRI) would improve risk stratification in patients evaluated for implantable cardioverter-defibrillator (ICD) implantation.

Background Current sudden cardiac death risk stratification emphasizes left ventricular ejection fraction (LVEF); however, most patients suffering sudden cardiac death have a preserved LVEF, and many with poor LVEF do not benefit from ICD prophylaxis.

Methods One hundred thirty-seven patients undergoing evaluation for possible ICD placement were prospectively enrolled and underwent cardiac MRI assessment of LVEF and scar. The pre-specified primary endpoint was death or appropriate ICD discharge for sustained ventricular tachyarrhythmia.

Results During a median follow-up of 24 months the primary endpoint occurred in 39 patients. Whereas the rate of adverse events steadily increased with decreasing LVEF, a sharp step-up was observed for scar size >5% of left ventricular mass (hazard ratio [HR]: 5.2; 95% confidence interval [CI]: 2.0 to 13.3). On multivariable Cox proportional hazards analysis, including LVEF and electrophysiological-study results, scar size (as a continuous variable or dichotomized at 5%) was an independent predictor of adverse outcome. Among patients with LVEF >30%, those with significant scarring (>5%) had higher risk than those with minimal or no (≤5%) scarring (HR: 6.3; 95% CI: 1.4 to 28.0). Those with LVEF >30% and significant scarring had risk similar to patients with LVEF ≤30% ($p = 0.56$). Among patients with LVEF ≤30%, those with significant scarring again had higher risk than those with minimal or no scarring (HR: 3.9; 95% CI: 1.2 to 13.1). Those with LVEF ≤30% and minimal scarring had risk similar to patients with LVEF >30% ($p = 0.71$).

Conclusions Myocardial scarring detected by cardiac MRI is an independent predictor of adverse outcome in patients being considered for ICD placement. In patients with LVEF >30%, significant scarring (>5% LV) identifies a high-risk cohort similar in risk to those with LVEF ≤30%. Conversely, in patients with LVEF ≤30%, minimal or no scarring identifies a low-risk cohort similar to those with LVEF >30% (95).

Second-Generation Everolimus-Eluting Stents Versus First-Generation Sirolimus-Eluting Stents in Acute Myocardial Infarction1-Year Results of the Randomized XAMI (XienceV Stent vs. Cypher Stent in Primary PCI for Acute Myocardial Infarction) Trial

Objectives The goal of this study was to compare the efficacy and safety of second-generation everolimus-eluting stents (EES) with first-generation sirolimus-eluting stents (SES) in primary percutaneous coronary intervention (PCI) for acute myocardial infarction (AMI).

Background Drug-eluting stents (DES) in AMI are still feared for possible late and very late stent thrombosis (ST). Newer-generation DES, with more hemocompatible polymers and improved healing, may show promise regarding increased efficacy of DES with improved safety. However, no randomized trials in AMI are available.

Methods A total of 625 patients with AMI were randomized (2:1) to receive EES or SES in the XAMI (XienceV Stent vs Cypher Stent in Primary PCI for Acute Myocardial Infarction) trial. Primary endpoint was major adverse cardiac events (MACE) at 1 year consisting of cardiac death, nonfatal AMI, or any target vessel revascularization. The study was powered for noninferiority of EES. Secondary endpoints comprised ST rates and MACE rate up to 3 years.

Results The MACE rate was 4.0% for EES and 7.7% for SES; the absolute difference was −3.7% (95% confidence interval: −8.28 to −0.03; $p = 0.048$) and relative risk was 0.52 (95% confidence interval: 0.27 to 1.00). One-year cardiac mortality was low at 1.5% for EES versus 2.7% for SES ($p = 0.36$), and 1-year incidence of definite and/or probable ST was 1.2% for EES versus 2.7% for SES ($p = 0.21$).

Conclusions In this all-comer, randomized, multicenter AMI trial, second-generation EES was noninferior to SES, and superiority for MACE was suggested. ST rate in EES at 1-year was low, but long-term follow-up and larger studies

will have to show whether very late ST rates will also be improved in newer DES. (XienceV Stent vs Cypher Stent in Primary PCI for Acute Myocardial Infarction [XAMI]; NTR1123) (96).

Mortality Benefit With Prasugrel in the TRITON–TIMI 38 Coronary Artery Bypass Grafting Cohort: Risk-Adjusted Retrospective Data Analysis

Objectives The objective of this study was to characterize the bleeding, transfusion, and other outcomes of patients related to the timing of prasugrel or clopidogrel withdrawal before coronary artery bypass grafting (CABG).

Background There is little evidence to guide clinical decision making regarding the use of prasugrel in patients who may need urgent or emergency CABG. Experience with performing CABG in the presence of clopidogrel has raised concern about perioperative bleeding complications that are unresolved.

Methods A subset of the TRITON–TIMI 38 study (Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel–Thrombolysis In Myocardial Infarction 38), in which patients with acute coronary syndrome were randomized to treatment with aspirin and either clopidogrel or prasugrel, underwent isolated CABG (N = 346). A supplemental case report form was designed and administered, and the data combined with the existing TRITON–TIMI 38 database. Baseline imbalances were corrected for using elements of the European System for Cardiac Operative Risk Evaluation and The Society of Thoracic Surgeons predictive algorithm.

Results A significantly higher mean 12-h chest tube blood loss (655 ± 580 ml vs. 503 ± 378 ml; p = 0.050) was observed with prasugrel compared with clopidogrel, without significant differences in red blood cell transfusion (2.1 U vs. 1.7 U; p = 0.442) or the total donor exposure (4.4 U vs. 3.0 U; p = 0.463). All-cause mortality was significantly reduced with prasugrel (2.31%) compared with 8.67% with clopidogrel (adjusted odds ratio: 0.26; p = 0.025).

Conclusions Despite an increase in observed bleeding, platelet transfusion, and surgical re-exploration for bleeding, prasugrel was associated with a lower rate of death after CABG compared with clopidogrel. (A Comparison of Prasugrel [CS-747] and Clopidogrel in Acute Coronary Syndrome Subjects Who Are to Undergo Percutaneous Coronary Intervention; NCT00097591) (97).

Prognostic Value of a High On-Clopidogrel Treatment Platelet Reactivity in Bivalirudin Versus Abciximab Treated Non–ST-Segment Elevation Myocardial Infarction PatientsISAR-REACT 4 (Intracoronary Stenting and Antithrombotic Regimen: Rapid Early Action for Coronary Treatment-4) Platelet Substudy

Objectives The ISAR-REACT 4 (Intracoronary Stenting and Antithrombotic Regimen: Rapid Early Action for Coronary Treatment-4) platelet substudy aimed to determine the relevance of high on-clopidogrel treatment platelet reactivity (HPR) in non–ST-segment elevation myocardial infarction patients that received abciximab with unfractionated heparin (UFH) or bivalirudin during percutaneous coronary intervention (PCI).

Background In patients undergoing PCI, HPR has been linked to a higher risk for ischemic events. The influence of HPR on clinical outcomes may differ with regard to the adjunctive antithrombotic treatment administered. In ISAR-REACT 4, bivalirudin treatment showed similar efficacy profiles as compared to abciximab with UFH. The impact of HPR on clinical outcomes in abciximab with UFH versus bivalirudin treated non–ST-segment elevation myocardial infarction patients has never been investigated specifically.

Methods A total of 564 patients (274 in abciximab/UFH group vs. 290 in bivalirudin group) were enrolled in this study. Presence or absence of HPR following clopidogrel loading was determined by platelet function testing on a Multiplate analyzer (Verum Diagnostica, Munich, Germany). Per study group and stratified in HPR and no-HPR patients, the 30-day incidence of a combined efficacy endpoint (death, myocardial infarction, urgent target vessel revascularization) was determined.

Results For abciximab with UFH, the incidence of the efficacy endpoint was similar in HPR versus no-HPR patients (9.4% vs. 6.7%; odds ratio: 1.4; 95% confidence interval: 0.6 to 3.5; p = 0.43). For bivalirudin, the incidence of the efficacy endpoint was significantly higher in HPR versus no-HPR patients (22.0% vs. 5.0%; odds ratio: 5.4; 95% confidence interval: 2.4 to 12.1; p < 0.0001).

Conclusions For patients with a risk profile similar to the subjects enrolled in this platelet substudy, the impact of HPR on clinical outcomes may depend on the type of adjunctive antithrombotic therapy used during PCI. Further investigations are warranted to clarify whether assessment of platelet function may help tailoring antithrombotic therapy during PCI. (Randomized Comparison of Abciximab Plus Heparin With Bivalirudin in Acute Coronary Syndrome [ISAR-REACT 4]; NCT00373451) (98).

Prognostic Utility of Neutrophil Gelatinase-Associated Lipocalin in Predicting Mortality and Cardiovascular Events in Patients With ST-Segment Elevation Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention

Objectives The aim of this study was to investigate the prognostic role of neutrophil gelatinase–associated lipocalin (NGAL) in a large population of patients with ST-segment elevation myocardial infarction.lipocalin (NGAL) in a large population of patients with ST-segment elevation myocardial infarction.

Background NGAL is a glycoprotein released by damaged renal tubular cells and is a sensitive maker of both clinical

and subclinical acute kidney injury. New data have demonstrated that NGAL is also stored in granules of mature neutrophils, and recent data suggest that NGAL may also be involved in the development of atherosclerosis. NGAL is significantly increased in patients with myocardial infarction compared with patients with stable coronary artery disease and healthy subjects. However, the prognostic value of NGAL has never been studied in patients with myocardial infarction.

Methods We included 584 consecutive ST-segment elevation myocardial infarction patients admitted to the heart center of Gentofte University Hospital, Denmark, and treated with primary percutaneous coronary intervention, from September 2006 to December 2008. Blood samples were drawn immediately before primary percutaneous coronary intervention. Plasma NGAL levels were measured using a time-resolved immunofluorometric assay. The endpoints were all-cause mortality (n = 69) and the combined endpoints (n = 116) of major adverse cardiac events (MACE) defined as cardiovascular mortality and admission due to recurrent myocardial infarction or heart failure. The median follow-up time was 23 months (interquartile range, 20 to 24 months).

Results Patients with high NGAL (>75th percentile) had increased risk of all-cause mortality and MACE compared with patients with low NGAL (log-rank test, $p < 0.001$). After adjustment for confounding risk factors chosen by backward elimination by Cox regression analysis, high NGAL remained an independent predictor of all-cause mortality and MACE (hazard ratio: 2.00; 95% confidence interval: 1.16 to 3.44; $p = 0.01$ and hazard ratio: 1.51; 95% confidence interval: 1.00 to 2.30; $p = 0.05$, respectively).

Conclusions High plasma NGAL independently predicts all-cause mortality and MACE in ST-segment elevation myocardial infarction patients treated with primary percutaneous coronary intervention (99).

Ticagrelor Versus Prasugrel in Acute Coronary Syndrome Patients With High On-Clopidogrel Platelet Reactivity Following Percutaneous Coronary Intervention: A Pharmacodynamic Study

Objectives The study aimed to compare the antiplatelet action of ticagrelor with prasugrel in acute coronary syndrome (ACS) patients with high on-treatment platelet reactivity (HTPR) while on clopidogrel after percutaneous coronary intervention (PCI).

Background Newer P2Y12 inhibitors like prasugrel and ticagrelor provide stronger platelet inhibition compared with clopidogrel. Both agents are efficacious in patients with HTPR while on clopidogrel, but direct comparison between them has not yet been reported.

Methods In a prospective, single-center, single-blind study, 44 (of 139 screened, 31.7%) ACS patients with HTPR while on clopidogrel 24 h post-PCI were randomized to either ticagrelor 90 mg twice daily or prasugrel 10 mg once daily for 15 days with a crossover directly to the alternate treatment for another 15 days. HTPR was defined as platelet reactivity units (PRU) ≥235 as assessed by the VerifyNow P2Y12 function assay.

Results The primary endpoint of platelet reactivity at the end of the 2 treatment periods was lower for ticagrelor (32.9 PRU, 95% confidence interval [CI]: 18.7 to 47.2) compared with prasugrel (101.3 PRU, 95% CI: 86.8 to 115.7) with a least squares mean difference of −68.3 PRU (95% CI: −88.6 to −48.1; $p < 0.001$). The secondary endpoint of HTPR rate was 0% for ticagrelor and 2.4% for prasugrel (1 of 42, $p = 0.5$). No patient exhibited a major bleeding event at either treatment group.

Conclusions In patients with ACS exhibiting HTPR while on clopidogrel 24 h post-PCI, ticagrelor produces a significantly higher platelet inhibition compared with prasugrel. (Ticagrelor Versus Prasugrel in Acute Coronary Syndromes After Percutaneous Coronary Intervention; NCT01360437) (100).

Impact of Ischemia-Guided Revascularization With Myocardial Perfusion Imaging for Patients With Multivessel Coronary Disease

Objectives The aim of this study was to evaluate the impact of ischemia-guided (IG) revascularization.

Background The importance of IG revascularization has not been well-determined.

Methods The outcomes of IG revascularization, in which revascularization was performed in the matched coronary artery with the perfusion abnormality on myocardial perfusion image (MPI), were retrospectively compared with those of non-IG revascularization in a registry of 5,340 patients with multivessel coronary disease comprising 2,587 percutaneous coronary interventions (PCIs) with drug-eluting stents and 2,753 coronary artery bypass graft (CABG) surgeries after adjustment with inverse-probability-of-treatment weighting.

Results The MPI was performed in 42.3% of patients, and IG revascularization was performed in 17.3%, including 12.4% in PCI and 21.8% in CABG patients ($p < 0.001$). The incidence of major adverse cardiac and cerebrovascular events (MACCE) including death, myocardial infarction, stroke, or repeat revascularization was significantly lower in the IG than in the non-IG group (16.2% vs. 20.7%; adjusted hazard ratio [aHR]: 0.73; 95% confidence interval [CI]: 0.60 to 0.88; $p = 0.001$), primarily driven by the lower repeat revascularization rate (9.9% vs. 22.8%; aHR: 0.66; 95% CI: 0.49 to 0.90; $p = 0.009$). Subgroup analysis showed that IG reduced the risk of MACCE in PCI (17.4% vs. 22.8%; aHR: 0.59; 95% CI: 0.43 to 0.81; $p = 0.001$) but not in CABG (16.0% vs. 18.5%; aHR: 0.87; 95% CI: 0.67 to 1.14; $p = 0.31$) patients.

Conclusions Ischemia-guided revascularization with MPI, particularly in PCI-treated patients, seems to decrease the

risk of repeat revascularization and MACCE for patients with multivessel disease (101).

Hybrid Thoracoscopic Surgical and Transvenous Catheter Ablation of Atrial Fibrillation

Objectives The purpose of this study was to evaluate the feasibility, safety, and clinical outcomes up to 1 year in patients undergoing combined simultaneous thoracoscopic surgical and transvenous catheter atrial fibrillation (AF) ablation.
Background The combination of the transvenous endocardial approach with the thoracoscopic epicardial approach in a single AF ablation procedure overcomes the limitations of both techniques and should result in better outcomes.
Methods A cohort of 26 consecutive patients with AF who underwent hybrid thoracoscopic surgical and transvenous catheter ablation were followed, with follow-up of up to 1 year.
Results Twenty-six patients (42% with persistent AF) underwent successful hybrid procedures. There were no complications. The mean follow-up period was 470 ± 154 days. In 23% of the patients, the epicardial lesions were not transmural, and endocardial touch-up was necessary. One-year success, defined according to the Heart Rhythm Society, European Heart Rhythm Association, and European Cardiac Arrhythmia Society consensus statement for the catheter and surgical ablation of AF, was 93% for patients with paroxysmal AF and 90% for patients with persistent AF. Two patients underwent catheter ablation for recurrent AF or left atrial flutter after the hybrid procedure.
Conclusions A combined transvenous endocardial and thoracoscopic epicardial ablation procedure for AF is feasible and safe, with a single-procedure success rate of 83% at 1 year (102).

Radial Artery and Saphenous Vein Patency More Than 5 Years After Coronary Artery Bypass Surgery: Results From RAPS (Radial Artery Patency Study)

Objectives The purpose of this study was to present radial and saphenous vein graft (SVG) occlusion results more than 5 years following coronary artery bypass surgery.
Background In the RAPS (Radial Artery Patency Study) study, complete graft occlusion was less frequent in radial artery compared with SVG 1 year post-operatively while functional occlusion (Thrombolysis In Myocardial Infarction flow grade 0, 1, 2) was similar.
Methods A total of 510 patients <80 years of age undergoing primary isolated nonemergent coronary artery bypass grafting with 3-vessel disease were initially enrolled in 9 Canadian centers. Target vessels for the radial artery and study SVG were the right and circumflex coronary arteries, which had >70% proximal stenosis. Within-patient randomization was performed; the radial artery was randomized to either the right or circumflex territory and the study SVG was used for the other territory. The primary endpoint was functional graft occlusion by invasive angiography at least 5 years following surgery. Complete graft occlusion by invasive angiography or computed tomography angiography was a secondary endpoint.
Results A total of 269 patients underwent late angiography (234 invasive angiography, 35 computed tomography angiography) at a mean of 7.7 ± 1.5 years after surgery. The frequency of functional graft occlusion was lower in radial arteries compared with SVGs (28 of 234 [12.0%] vs. 46 of 234 [19.7%]; $p = 0.03$ by McNemar's test). The frequency of complete graft occlusion was also significantly lower in radial compared with SVGs (24 of 269 [8.9%] vs. 50 of 269 [18.6%]; $p = 0.002$).
Conclusions Radial arteries are associated with reduced rates of functional and complete graft occlusion compared with SVGs more than 5 years following surgery. (Multicentre Radial Artery Patency Study: 5 Year Results; NCT00187356) (103).

Long-Term Prognosis Following Resuscitation From Out of Hospital Cardiac Arrest: Role of Percutaneous Coronary Intervention and Therapeutic Hypothermia

Objectives The aim of the study was to assess the influence of percutaneous coronary intervention (PCI) and therapeutic hypothermia (TH) on long-term prognosis.
Background Although hospital care consisting of TH and/or PCI in particular patients resuscitated following out-of-hospital cardiac arrest (OHCA) can improve survival to hospital discharge, there is little evidence regarding how these therapies may impact long-term prognosis.
Methods We performed a cohort investigation of all persons >18 years of age who suffered nontraumatic OHCA and were resuscitated and discharged alive from the hospital between January 1, 2001, and December 31, 2009, in a metropolitan emergency medical service (EMS) system. We reviewed EMS and hospital records, state death certificates, and the national death index to determine clinical characteristics and vital status. Survival analyses were conducted using Kaplan-Meier estimates and multivariable Cox regression. Analyses of TH were restricted to those patients who were comatose at hospital admission.
Results Of the 5,958 persons who received EMS-attempted resuscitation, 1,001 (16.8%) were discharged alive from the hospital. PCI was performed in 384 of 1,001 (38.4%), whereas TH was performed in 241 of 941 (25.6%) persons comatose at hospital admission. Five-year survival was 78.7% among those treated with PCI compared with 54.4% among those not receiving PCI and 77.5% among those treated with TH compared with 60.4% among those not receiving TH (both $p < 0.001$). After adjustment for confounders, PCI was associated with a lower risk of death (hazard ratio [HR]: 0.46 [95% confidence interval [CI]: 0.34 to 0.61]; $p < 0.001$). Likewise, TH was associated with

a lower risk of death (HR: 0.70 [95% CI: 0.50 to 0.97]; p = 0.04).

Conclusions The findings suggested that effects of acute hospital interventions for post-resuscitation treatment extend beyond hospital survival and can positively influence prognosis following the arrest hospitalization (104).

Clinical Application of Cardiovascular Pharmacogenetics

Pharmacogenetics primarily uses genetic variation to identify subgroups of patients who may respond differently to a certain medication. Since its first description, the field of pharmacogenetics has expanded to study a broad range of cardiovascular drugs and has become a mainstream research discipline. Three principle classes of pharmacogenetic markers have emerged: 1) pharmacokinetic; 2) pharmacodynamic; and 3) underlying disease mechanism. In the realm of cardiovascular pharmacogenetics, significant advances have identified markers in each class for a variety of therapeutics, some with a potential for improving patient outcomes. While ongoing clinical trials will determine if routine use of pharmacogenetic testing may be beneficial, the data today support pharmacogenetic testing for certain variants on an individualized, case-by-case basis. Our primary goal is to review the association data for the major pharmacogenetic variants associated with commonly used cardiovascular medications: antiplatelet agents, warfarin, statins, beta-blockers, diuretics, and antiarrhythmic drugs. In addition, we highlight which variants and in which contexts pharmacogenetic testing can be implemented by practicing clinicians. The pace of genetic discovery has outstripped the generation of the evidence justifying its clinical adoption. Until the evidentiary gaps are filled, however, clinicians may choose to target therapeutics to individual patients whose genetic Background indicates that they stand to benefit the most from pharmacogenetic testing (105).

Everolimus-Eluting Stent Implantation for Unprotected Left Main Coronary Artery StenosisThe PRECOMBAT-2 (Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease) Study

Objectives This study sought to evaluate the safety and efficacy of second-generation drug-eluting stents (DES) for patients with unprotected left main coronary artery (ULMCA) stenosis.

Background The clinical benefit of second-generation DES for ULMCA stenosis has not been determined.

Methods The authors assessed 334 consecutive patients who received everolimus-eluting stents (EES) for ULMCA stenosis between 2009 and 2010. The 18-month incidence rates of major adverse cardiac or cerebrovascular events (MACCE), including death, myocardial infarction (MI), stroke, or ischemia-driven target vessel revascularization (TVR), were compared with those of a randomized study comparing patients who received sirolimus-eluting stents (SES) (n = 327) or coronary artery bypass grafts (CABG) (n = 272).

Results EES (8.9%) showed a comparable incidence of MACCE as SES (10.8%; adjusted hazard ratio [aHR] of EES: 0.84; 95% confidence interval [CI]: 0.51 to 1.40; p = 0.51) and CABG (6.7%, aHR of EES: 1.40; 95% CI: 0.78 to 2.54; p = 0.26). The composite incidence of death, MI, or stroke also did not differ among patients receiving EES (3.3%), SES (3.7%; aHR of EES: 0.63; 95% CI: 0.27 to 1.47; p = 0.29), and CABG (4.8%; aHR of EES: 0.67; 95% CI: 0.29 to 1.54; p = 0.34). However, the incidence of ischemia-driven TVR in the EES group (6.5%) was higher than in the CABG group (2.6%, aHR of EES: 2.77; 95% CI: 1.17 to 6.58; p = 0.02), but comparable to SES (8.2%, aHR of EES: 1.14; 95% CI: 0.64 to 2.06; p = 0.65). Angiographic restenosis rates were similar in the SES and EES groups (13.8% vs. 9.2%, p = 0.16).

Conclusions Second-generation EES had a similar 18-month risk of MACCE for ULMCA stenosis as first-generation SES or CABG. (Evaluation of Outcomes of EES Implantation for Unprotected Left Main Coronary Artery Stenosis [PRECOMBAT-2]; NCT01348022) (106).

Drug-Eluting Stent for Left Main Coronary Artery DiseaseThe DELTA Registry: A Multicenter Registry Evaluating Percutaneous Coronary Intervention Versus Coronary Artery Bypass Grafting for Left Main Treatment

Objectives The aim of this study was to compare, in a large all-comers registry, major adverse cardiac and cerebrovascular events (MACCE) after percutaneous coronary intervention (PCI) with first-generation drug-eluting stents (DES) versus coronary artery bypass grafting (CABG) in unprotected left main coronary artery (ULMCA) stenosis.

Background Percutaneous coronary intervention with DES implantation in ULMCA has been shown to be a feasible and safe approach at midterm clinical follow-up.

Methods All consecutive patients with ULMCA stenosis treated by PCI with DES versus CABG were analyzed in this multinational registry. A propensity score analysis was performed to adjust for baseline differences in the overall cohort.

Results In total 2,775 patients were included: 1,874 were treated with PCI versus 901 with CABG. At 1,295 (interquartile range: 928 to 1,713) days, there were no differences, at the adjusted analysis, in the primary composite endpoint of death, cerebrovascular accidents, and myocardial infarction (MI) (adjusted hazard ratio [HR]: 1.11; 95% confidence interval [CI]: 0.85 to 1.42; p = 0.47), mortality

(adjusted HR: 1.16; 95% CI: 0.87 to 1.55; p = 0.32), or composite endpoint of death and MI (adjusted HR: 1.25; 95% CI: 0.95 to 1.64; p = 0.11). An advantage of CABG over PCI was observed in the composite secondary endpoint of MACCE (adjusted HR: 1.64; 95% CI: 1.33 to 2.03; p < 0.0001), driven exclusively by the higher incidence of target vessel revascularization with PCI.

Conclusions In our multinational all-comers registry, no difference was observed in the occurrence of death, cerebrovascular accidents, and MI between PCI and CABG. An advantage of CABG over PCI was observed in the incidence of MACCE, driven by the higher incidence of target vessel revascularization with PCI (107).

Time Course of Endothelium-Dependent and -Independent Coronary Vasomotor Response to Coronary Balloons and Stents: Comparison of Plain and Drug-Eluting Balloons and Stents

Objectives This study sought to determine the time dependency of the endothelium-dependent and -independent vascular responses after percutaneous coronary intervention (PCI) with drug-eluting (DEB) or plain balloons, bare-metal (BMS), and drug-eluting (DES) stents, or controls.

Background Long-term endothelial dysfunction after DES implantation is associated with delayed healing and late thrombosis.

Methods Domestic pigs underwent PCI using DEB or plain balloon, BMS, or DES. The dilated and stented segments, and the proximal reference segments of stents and control arteries were explanted at 5-h, 24-h, 1-week, and 1-month follow-up (FUP). Endothelin-induced vasoconstriction and endothelium-dependent and -independent vasodilation of the arterial segments were determined in vitro and were related to histological results.

Results DES- and BMS-treated arteries showed proneness to vasoconstriction 5 h post-PCI. The endothelium-dependent vasodilation was profoundly (p < 0.05) impaired early after PCI (9.8 ± 3.7%, 13.4 ± 9.2%, 5.7 ± 5.3%, and 7.6 ± 4.7% using plain balloon, DEB, BMS, and DES, respectively), as compared with controls (49.6 ± 9.5%), with slow recovery. In contrast to DES, the endothelium-related vasodilation of vessels treated with plain balloon, DEB, and BMS was increased at 1 month, suggesting enhanced endogenous nitric oxide production of the neointima. The endothelium-independent (vascular smooth muscle–related) vasodilation decreased significantly at 1 day, with slow normalization during FUP. All PCI-treated vessels exhibited imbalance between vasoconstriction–vasodilation, which was more pronounced in DES- and BMS-treated vessels. No correlation between histological parameters and vasomotor function was found, indicating complex interactions between the healing neoendothelium and smooth muscle post-PCI.

Conclusions Coronary arteries treated with plain balloon, DEB, BMS, and DES showed time-dependent loss of endothelial-dependent and -independent vasomotor function, with imbalanced contraction/dilation capacity (108).

Radiation Exposure During Percutaneous Coronary Interventions and Coronary Angiograms Performed by the Radial Compared With the Femoral Route

Objectives This study aimed to compare radiation exposure of patients undergoing percutaneous coronary interventions (PCI) and coronary angiograms (CAG) accessed by the femoral route with the radial route (operator's choice).

Background There are limited and contradictory data on the radiation exposure of patients during PCI and CAG performed by the radial route compared with the femoral route.

Methods Data on the radiation exposure of patients from 3,973 PCI and CAG procedures between June 22, 2004, and December 31, 2008, were prospectively collected and analyzed. A prediction model was made for radiation exposure (dose-area product in Gy·cm^2) based upon the femoral access group, and the group of radial performed procedures was compared to assess differences between observed and expected radiation exposure.

Results Median exposures of patients undergoing a PCI via the femoral route (n = 2,309) was 75 (interquartile range [IQR]: 44 to 135) Gy·cm^2 compared with 72 (IQR: 42 to 134) Gy·cm^2 for radial performed procedures (n = 1,212) (p = 0.30). Median exposure for CAGs was 44 (IQR: 31 to 69) Gy·cm^2 and 40 (IQR: 25 to 65) Gy·cm^2 for, respectively, femoral (n = 314) and radial performed procedures (n = 138), (p = 0.31). Also, the observed radiation exposure in patients undergoing radial PCI or CAGs was not higher than the expected exposure of patients as predicted by the femoral access-based prediction model (71.5 ± 2.3 Gy·cm^2 vs. 79.9 ± 1.8 Gy·cm^2).

Conclusions The study shows that even after correction for the complexity of the procedures, selected procedures performed by the radial route are not associated with higher radiation exposure of patients than selected procedures performed by the femoral route (109).

Serious Infection After Acute Myocardial Infarction: Incidence, Clinical Features, and Outcomes

Objectives The aim of this study was to address the knowledge gap using the APEX-AMI (Assessment of Pexelizumab in Acute Myocardial Infarction) trial database. We also assessed the association between serious infections and 90-day death or death/myocardial infarction (MI).

Background Little is known about the incidence, location, etiological organisms, and outcomes of infection in patients with ST-segment elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention.

Methods We analyzed data from 5,745 STEMI patients enrolled in the APEX-AMI trial. Detailed information on infection was collected for all patients. We described

characteristics of patients according to infection and details of infection. Cox proportional hazards models were used to assess 90-day outcomes among patients with and without infections after adjusting for associated clinical variables and with infection as a time-dependent covariate.

Results Overall, 138 patients developed a serious infection (2.4%), most of whom presented with a single-site infection. The median (25th, 75th percentile) time until diagnosis of infection was 3 (1, 6) days. The most commonly identified organism was *Staphylococcus aureus*, and the main location of infection was the bloodstream. These patients had more comorbidities and lower procedural success at index percutaneous coronary intervention than those without infections. Serious infection was associated with significantly higher rates of 90-day death (adjusted hazard ratio: 5.6; 95% confidence interval: 3.8 to 8.4) and death or MI (adjusted hazard ratio: 4.9; 95% confidence interval: 3.4 to 7.1).

Conclusions Infections complicating the course of patients with STEMI were uncommon but associated with markedly worse 90-day clinical outcomes. Mechanisms for early identification of these high-risk patients as well as design of strategies to reduce their risk of infection are warranted. (Pexelizumab in Conjunction With Angioplasty in Acute Myocardial Infarction [APEX-AMI]; NCT00091637) (110).

Implantation of a Drug-Eluting Stent With a Different Drug (Switch Strategy) in Patients With Drug-Eluting Stent Restenosis: Results From a Prospective Multicenter Study (RIBS III [Restenosis Intra-Stent: Balloon Angioplasty Versus Drug-Eluting Stent])

Objectives This study sought to assess the effectiveness of a strategy of using drug-eluting stents (DES) with a different drug (switch) in patients with DES in-stent restenosis (ISR).

Background Treatment of patients with DES ISR remains a challenge.

Methods The RIBS-III (Restenosis Intra-Stent: Balloon Angioplasty Versus Drug-Eluting Stent) study was a prospective, multicenter study that aimed to assess results of coronary interventions in patients with DES ISR. The use of a different DES was the recommended strategy. The main angiographic endpoint was minimal lumen diameter at 9-month follow-up. The main clinical outcome measure was a composite of cardiac death, myocardial infarction, and target lesion revascularization.

Results This study included 363 consecutive patients with DES ISR from 12 Spanish sites. The different-DES strategy was used in 274 patients (75%) and alternative therapeutic modalities (no switch) in 89 patients (25%). Baseline characteristics were similar in the 2 groups, although lesion length was longer in the switch group. At late angiographic follow-up (77% of eligible patients, median: 278 days) minimal lumen diameter was larger (1.86 $\pm$ 0.7 mm vs. 1.40 $\pm$ 0.8 mm, $p = 0.003$) and recurrent restenosis rate lower (22% vs. 40%, $p = 0.008$) in the different-DES group. At the last clinical follow-up (99% of patients, median: 771 days), the combined clinical endpoint occurred less frequently (23% vs. 35%, $p = 0.039$) in the different-DES group. After adjustment using propensity score analyses, restenosis rate (relative risk: 0.41, 95% confidence interval [CI]: 0.21 to 0.80, $p = 0.01$), minimal lumen diameter (difference: 0.41 mm, 95% CI: 0.19 to 0.62, $p = 0.001$), and the event-free survival (hazard ratio: 0.56, 95% CI: 0.33 to 0.96, $p = 0.038$) remained significantly improved in the switch group.

Conclusions In patients with DES ISR, the implantation of a different DES provides superior late clinical and angiographic results than do alternative interventional modalities (111).

Renal Sympathetic Denervation Using an Irrigated Radiofrequency Ablation Catheter for the Management of Drug-Resistant Hypertension

Objectives This study sought to assess whether renal sympathetic denervation (RSDN) can be achieved using an off-the-shelf saline-irrigated radiofrequency ablation (RFA) catheter typically employed for cardiac tissue ablation.

Background RSDN using a specialized solid-tip RFA catheter has recently been demonstrated to safely reduce systemic blood pressure in patients with refractory hypertension. For cardiac tissue ablation, RFA technology has evolved from nonirrigated to saline-irrigated ablation electrodes to improve both safety and effectiveness.

Methods Ten patients with resistant hypertension underwent renal angiography, followed by bilateral RSDN with a saline-irrigated RFA catheter. Ambulatory blood pressure recordings (24 h) were obtained at baseline, 1, 3, and 6 months after the procedure. Repeat renal angiography was performed during follow-up to assess for arterial stenosis or aneurysm. In 5 patients, pre- and post-procedural serum measures of renal function and sympathetic activity were obtained: aldosterone; metanephrine; normetanephrine; plasma renin activity; and creatinine.

Results Over a 6-month period: 1) the systolic/diastolic blood pressure decreased by $-21/-11$ mm Hg; 2) all patients experienced a decrease in systolic blood pressure of at least 10 mm Hg (range 10 to 40 mm Hg); 3) there was no evidence of renal artery stenosis or aneurysm at repeat angiography; and 4) there was a significant decrease in metanephrine (-12 ± 4, $p = 0.003$), normetanephrine (-18 ± 4, $p = 0.0008$), and aldosterone levels (-60 ± 33 ng/l, $p = 0.02$) at 3 months. There was no significant change in plasma renin activity (-0.2 mg/l/hod, $p = 0.4$). There was no significant change in serum creatinine (-1 mmol/l, $p = 0.4$).

Conclusions These data provide the proof-of-principle that RSDN can be performed using an off-the-shelf saline-irrigated RFA catheter (112).

Optimizing Outcomes During Left Main Percutaneous Coronary Intervention With Intravascular Ultrasound and Fractional Flow Reserve: The Current State of Evidence

Percutaneous coronary intervention (PCI) is an evolving indication for the treatment of unprotected left main coronary arterial (UMLCA) stenoses in selected individuals. Intravascular ultrasound (IVUS)-guided PCI within the epicardial coronary tree has been shown to improve acute procedural results and subsequent clinical outcomes. Similarly, fractional flow reserve (FFR) is rapidly gaining popularity as a means to guide the coronary interventionalist to embark upon a "physiological-based" revascularization strategy. In light of the emergence of PCI for ULMCA stenoses, the lack of randomized trials has meant that there are no systematic guidelines that advocate the routine use of these adjunctive imaging techniques to optimize procedural and clinical outcomes. Given the potential dire clinical consequences of procedural failure during ULMCA PCI, in this review we systematically address the current level of evidence for the use of FFR and IVUS during the assessment for and undertaking of PCI for ULMCA stenoses. In lieu of the current available level of evidence, we recommend the use of FFR for the assessment of (angiographic indeterminate) isolated ostial or midshaft left main coronary arterial (LMCA) stenoses in patients who are considered more appropriate candidates for coronary arterial bypass grafting. In those patients with distal/bifurcation LMCA lesions and in those with diffuse/distal coronary arterial disease, we strongly recommend the liberal use of IVUS. Furthermore, in those patients considered likely candidates for ULMCA PCI, IVUS remains crucial for assessing the degree of lumen compromise and the extent, distribution, and morphology of plaque as well as for the immediate postprocedural quantification of stent deployment (113).

Meta-Analysis of Transcatheter Closure Versus Medical Therapy for Patent Foramen Ovale in Prevention of Recurrent Neurological Events After Presumed Paradoxical Embolism

Objectives In this study, a meta-analysis of observational studies was performed to compare the rate of recurrent neurological events (RNE) between transcatheter closure and medical management of patients with cryptogenic stroke/transient ischemic attack (TIA) and concomitant patent foramen ovale (PFO).

Background A significant controversy surrounds the optimal strategy for treatment of cryptogenic stroke/TIA and coexistent PFO.

Methods We conducted a MEDLINE search with standard search terms to determine eligible studies.

Results Adjusted incidence rates of RNE were 0.8 (95% confidence interval [CI]: 0.5 to 1.1) events and 5.0 (95% CI: 3.6 to 6.9) events/100 person-years (PY) in the transcatheter closure and medical management arms, respectively. Meta-analysis of the limited number of comparative studies and meta-regression analysis suggested that the transcatheter closure might be superior to the medical therapy in prevention of RNE after cryptogenic stroke. Comparison of the anticoagulation and antiplatelet therapy subgroups of the medical arm yielded a significantly lower risk of RNE within patients treated with anticoagulants. Device-related complications were encountered at the rate of 4.1 (95% CI: 3.2 to 5.0) events/100 PY, with atrial arrhythmias being the most frequent complication. After transcatheter closure, RNE did not seem to be related to the pre-treatment shunt size or the presence of residual shunting in the follow-up period. Significant benefit of transcatheter PFO closure was apparent in elderly patients, patients with concomitant atrial septal aneurysm, and patients with thrombophilia.

Conclusions Rates of RNE with transcatheter closure and medical therapy in patients presenting with cryptogenic stroke or TIA were estimated at 0.8 and 5.0 events/100 PY. Further randomized controlled trials are needed to conclusively compare these 2 management strategies (114).

Ischemia Change in Stable Coronary Artery Disease Is an Independent Predictor of Death and Myocardial Infarction

Objectives The aim of this study was to evaluate the independent prognostic significance of ischemia change in stable coronary artery disease (CAD).

Background Recent randomized trials in stable CAD have suggested that revascularization does not improve outcomes compared with optimal medical therapy (MT). In contrast, the nuclear substudy of the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial found that revascularization led to greater ischemia reduction and suggested that this may be associated with improved unadjusted outcomes. Thus, the effects of MT versus revascularization on ischemia change and its independent prognostic significance requires further investigation.

Methods From the Duke Cardiovascular Disease and Nuclear Cardiology Databanks, 1,425 consecutive patients with angiographically documented CAD who underwent 2 serial myocardial perfusion single-photon emission computed tomography scans were identified. Ischemia change was calculated for patients undergoing MT alone, percutaneous coronary intervention, or coronary artery bypass grafting. Patients were followed for a median of 5.8 years after the second myocardial perfusion scan. Cox proportional hazards regression modeling was used to identify factors independently associated with the primary outcome of death or myocardial infarction (MI). Formal risk reclassification analyses were conducted to assess whether the addition of ischemia change to traditional predictors resulted in improved risk classification for death or MI.

Results More MT patients (15.6%) developed $\geq$5% ischemia worsening compared with those undergoing

percutaneous coronary intervention (6.2%) or coronary artery bypass grafting (6.7%) ($p < 0.001$). After adjustment for established predictors, ≥5% ischemia worsening remained a significant independent predictor of death or MI (hazard ratio: 1.634; $p = 0.0019$) irrespective of treatment arm. Inclusion of ≥5% ischemia worsening in this model resulted in significant improvement in risk classification (net reclassification improvement: 4.6%, $p = 0.0056$) and model discrimination (integrated discrimination improvement: 0.0062, $p = 0.0057$).

Conclusions In stable CAD, ischemia worsening is an independent predictor of death or MI, resulting in significantly improved risk reclassification when added to previously known predictors (115).

Role of Echocardiography in Percutaneous Mitral Valve Interventions

Intraprocedural imaging continues to evolve in parallel with advances in percutaneous mitral valve interventions. This didactic review uses several illustrations and rich intraprocedural videos to further describe and demonstrate the role of the most up-to-date echocardiographic and advanced imaging technologies in the patient selection and intraprocedural guidance of percutaneous mitral valve interventions. We will focus on 3 interventions: 1) percutaneous balloon mitral valvuloplasty for mitral stenosis; 2) transcatheter edge-to-edge repair of mitral valve regurgitation; and 3) transcatheter closure of periprosthetic mitral regurgitation. In addition, we discuss potential pitfalls of 3-dimensional transesophageal echocardiography and show examples of this technique (116).

OCT Findings in Patients With Recanalization of Organized Thrombi in Coronary Arteries

Objectives The purpose of this study was to determine the angiographic and optical coherence tomographic (OCT) characteristics of coronary lesions with recanalized thrombi.

Background Although spontaneous recanalization of thrombi has been reported pathologically, it is rarely recognized in clinical practice.

Methods Based on histopathologic features, recanalization of thrombi was defined by characteristics on OCT.

Results Recanalization of thrombi was identified in 6 patients (3 male, 3 female; median age 63 years; age range 54 to 72 years). Based on symptoms, 3 patients were diagnosed with unstable angina; 2 were diagnosed with stable angina; and 1, who had mitral stenosis and huge left atrial thrombi, was diagnosed with post-infarct angina. All had normal serum concentrations of cardiac markers at admission. Angiography showed irregular linear filling defects and haziness. Two patients with near total occlusion had Thrombolysis In Myocardial Infarction (TIMI) flow grade 1 and collaterals, whereas 4 patients had TIMI flow grade 3 and no collaterals. All patients showed OCT findings consistent with recanalized thrombi, which consisted of signal-rich, high backscattered septa that divided the lumen into multiple small cavities communicating with each other. These structures, which had smooth inner borders, created a "Swiss cheese" appearance. Percutaneous coronary intervention was performed in 5 patients with angiographic slow flow or inducible-ischemia as documented by invasive or noninvasive stress tests. The remaining 1 patient with restored coronary flow underwent mitral valve surgery and left atrial thrombectomy.

Conclusions OCT provided details on the characteristics of the organization of thrombi in both chronic total occlusion and subtotal narrowing. Coronary lesions containing recanalized thrombi were characterized by multiple small channels, with most showing functional significance (117).

Clinical Outcomes After Transcatheter Aortic Valve Replacement Using Valve Academic Research Consortium Definitions: A Weighted Meta-Analysis of 3,519 Patients From 16 Studies

Objectives This study sought to perform a weighted meta-analysis to determine the rates of major outcomes after transcatheter aortic valve replacement (TAVR) using Valve Academic Research Consortium (VARC) definitions and to evaluate their current use in the literature.

Background Recently, the published VARC definitions have helped to add uniformity to reporting outcomes after TAVR.

Methods A comprehensive search of multiple electronic databases from January 1, 2011, through October 12, 2011, was conducted using predefined criteria. We included studies reporting at least 1 outcome using VARC definitions.

Results A total of 16 studies including 3,519 patients met inclusion criteria and were included in the analysis. The pooled estimate rates of outcomes were determined according to VARC's definitions: device success, 92.1% (95% confidence interval [CI]: 88.7% to 95.5%); all-cause 30-day mortality, 7.8% (95% CI: 5.5% to 11.1%); myocardial infarction, 1.1% (95% CI: 0.2% to 2.0%); acute kidney injury stage II/III, 7.5% (95% CI: 5.1% to 11.4%); life-threatening bleeding, 15.6% (95% CI: 11.7% to 20.7%); major vascular complications, 11.9% (95% CI: 8.6% to 16.4%); major stroke, 3.2% (95% CI: 2.1% to 4.8%); and new permanent pacemaker implantation, 13.9% (95% CI: 10.6% to 18.9%). Medtronic CoreValve prosthesis use was associated with a significant higher rate of new permanent pacemaker implantation compared with the Edwards prosthesis (28.9% [95% CI: 23.0% to 36.0%] vs. 4.9% [95% CI: 3.9% to 6.2%], $p < 0.0001$). The 30-day safety composite endpoint rate was 32.7% (95% CI: 27.5% to 38.8%) and the 1-year total mortality rate was 22.1% (95% CI: 17.9% to 26.9%).

Conclusions VARC definitions have already been used by the TAVR clinical research community, establishing a new

standard for reporting clinical outcomes. Future revisions of the VARC definitions are needed based on evolving TAVR clinical experiences (118).

First Results of the DEB-AMI (Drug Eluting Balloon in Acute ST-Segment Elevation Myocardial Infarction) TrialA Multicenter Randomized Comparison of Drug-Eluting Balloon Plus Bare-Metal Stent Versus Bare-Metal Stent Versus Drug-Eluting Stent in Primary Percutaneous Coronary Intervention With 6-Month Angiographic, Intravascular, Functional, and Clinical Outcomes

Objectives The goal of this study was to compare angiographic, intravascular imaging, and functional parameters, as well as the clinical outcomes of patients treated with drug-eluting balloon (DEB) plus bare-metal stent (BMS) versus BMS versus drug-eluting stent (DES) for ST-segment elevated acute myocardial infarction (STEMI).

Background Concerns remain regarding the long-term safety of DES in STEMI. DEB could provide an attractive alternative in order to achieve potentially similar effectiveness but limiting the long-term hazards related to late-acquired stent malapposition and thus stent thrombosis.

Methods In this randomized, international, 2-center, single-blinded, 3-arm study, STEMI patients were randomly assigned to group A: BMS; group B: DEB plus BMS; or group C: DES after successful thrombus aspiration. The primary endpoint was 6-month angiographic in-stent late-luminal loss. Secondary endpoints were in-stent binary restenosis, major adverse cardiac events (MACE: cardiac death, myocardial infarction, target vessel revascularization). In a subgroup of patients, stent (mal) apposition (by optical coherence tomography) and endothelial function (by acetylcholine infusion) was assessed.

Results Overall, 150 patients were randomized. Procedural success was achieved in 96.7%. In groups A, B, and C, respectively, late-luminal loss was 0.74 ± 0.57 mm, 0.64 ± 0.56 mm, and 0.21 ± 0.32 mm ($p < 0.01$); binary restenosis was 26.2%, 28.6%, and 4.7% ($p = 0.01$); and MACE rates were 23.5%, 20.0%, and 4.1% ($p = 0.02$), respectively. The median percentage [25th to 75th interquartile range] of uncovered and malapposed stent struts per lesion was 0 [0 to 0.35], 2.84 [0 to 6.63], and 5.21 [3.25 to 14.5] ($p < 0.01$). Significant paradoxical vasoconstriction was seen in groups B and C.

Conclusions In STEMI patients, DEB followed by BMS implantation failed to show angiographic superiority to BMS only. Angiographic results of DES were superior to both BMS and DEB. Moreover, DEB before implantation induced more uncovered and malapposed stent struts than BMS, but less than after DES. (Drug-Eluting Balloon in Acute Myocardial Infarction [DEB-AMI]; NCT00856765) (119).

Recovery of Platelet Function After Discontinuation of Prasugrel or Clopidogrel Maintenance Dosing in Aspirin-Treated Patients With Stable Coronary Disease: The Recovery Trial

Objectives The goal of this study was to assess the offset of the antiplatelet effects of prasugrel and clopidogrel.

Background Guidelines recommend discontinuing clopidogrel at least 5 days and prasugrel at least 7 days before surgery. The pharmacodynamic basis for these recommendations is limited.

Methods Aspirin-treated patients with coronary artery disease were randomly assigned to either prasugrel 10 mg or clopidogrel 75 mg daily for 7 days. Platelet reactivity was measured before study drug administration and for up to 12 days during washout. The primary endpoint was the cumulative proportion of patients returning to baseline reactivity after study drug discontinuation.

Results A total of 56 patients were randomized; 54 were eligible for analysis. Platelet reactivity was lower 24 h after the last dose of prasugrel compared with clopidogrel. After prasugrel, ≥75% of patients returned to baseline reactivity by washout day 7 compared with day 5 after clopidogrel. Recovery time was dependent on the level of platelet reactivity before study drug exposure and the initial degree of platelet inhibition after study drug discontinuation but not on treatment assignment.

Conclusions Recovery time after thienopyridine discontinuation depends on the magnitude of on-treatment platelet inhibition, resulting, on average, in a more delayed recovery with prasugrel compared with clopidogrel. The offset of prasugrel was consistent with current guidelines regarding the recommended waiting period for surgery after discontinuation. (Prasugrel/Clopidogrel Maintenance Dose Washout Study; NCT01014624) (120).

The New York State Cardiac Registries: History, Contributions, Limitations, and Lessons for Future Efforts to Assess and Publicly Report Healthcare Outcomes

In 1988, the New York State Health Commissioner was confronted with hospital-level data demonstrating very large, multiple-year, interhospital variations in short-term mortality and complications for cardiac surgery. The concern with the extent to which these differences were due to variations in patients' pre-surgical severity of illness versus hospitals' quality of care led to the development of clinical registries for cardiac surgery in 1989 and for percutaneous coronary interventions in 1992 in New York. In 1990, the Department of Health released hospitals' risk-adjusted cardiac surgery mortality rates for the first time, and shortly thereafter, similar data were released for hospitals and physicians for percutaneous coronary interventions, cardiac valve surgery, and pediatric cardiac surgery (only hospital data). This practice is still ongoing. The purpose of

this communication is to relate the history of this initiative, including changes or purported changes that have occurred since the public release of cardiac data. These changes include decreases in risk-adjusted mortality, cessation of cardiac surgery in New York by low-volume and high-mortality surgeons, out-of-state referral or avoidance of cardiac surgery/angioplasty for high-risk patients, alteration of contracting choices by insurance companies, and modifications in market share of cardiac hospitals. Evidence related to these impacts is reviewed and critiqued. This communication also includes a summary of numerous studies that used New York's cardiac registries to examine a variety of policy issues regarding the choice and use of cardiac procedures, the comparative effectiveness of competing treatment options, and the examination of the relationship among processes, structures, and outcomes of cardiac care (121).

A Randomized Trial of Prasugrel Versus Clopidogrel in Patients With High Platelet Reactivity on Clopidogrel After Elective Percutaneous Coronary Intervention With Implantation of Drug-Eluting Stents: Results of the TRIGGER-PCI (Testing Platelet Reactivity In Patients Undergoing Elective Stent Placement on Clopidogrel to Guide Alternative Therapy With Prasugrel) Study

Objectives This study sought to investigate the efficacy, safety, and antiplatelet effect of prasugrel as compared with clopidogrel in patients with high on-treatment platelet reactivity (HTPR) after elective percutaneous coronary intervention (PCI).

Background The extent to which prasugrel can correct HTPR and improve clinical outcomes in patients undergoing elective PCI is unknown.

Methods Stable coronary artery disease (CAD) patients with HTPR (>208 $P2Y_{12}$ reaction units [PRU] by the VerifyNow test) after elective PCI with at least 1 drug-eluting stent (DES) were randomly assigned to either prasugrel 10 mg daily or clopidogrel 75 mg daily. Platelet reactivity of the patients on the study drug was reassessed at 3 and 6 months. The study was stopped prematurely for futility because of a lower than expected incidence of the primary endpoint.

Results In 212 patients assigned to prasugrel, PRU decreased from 245 (225 to 273) (median [interquartile range]) at baseline to 80 (42 to 124) at 3 months, whereas in 211 patients assigned to clopidogrel, PRU decreased from 249 (225 to 277) to 241 (194 to 275) ($p < 0.001$ vs. prasugrel). The primary efficacy endpoint of cardiac death or myocardial infarction at 6 months occurred in no patient on prasugrel versus 1 on clopidogrel. The primary safety endpoint of non–coronary artery bypass graft Thrombolysis In Myocardial Infarction major bleeding at 6 months occurred in 3 patients (1.4%) on prasugrel versus 1 (0.5%) on clopidogrel.

Conclusions Switching from clopidogrel to prasugrel in patients with HTPR afforded effective platelet inhibition. However, given the low rate of adverse ischemic events after PCI with contemporary DES in stable CAD, the clinical utility of this strategy could not be demonstrated. (Testing platelet Reactivity In patients underGoing elective stent placement on clopidogrel to Guide alternative thErapy with pRasugrel [TRIGGER-PCI]; NCT00910299) (122).

Quantification and Impact of Untreated Coronary Artery Disease After Percutaneous Coronary Intervention: The Residual SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery) Score

Objectives The purpose of this study was to quantify the extent and complexity of residual coronary stenoses following percutaneous coronary intervention (PCI) and to evaluate its impact on adverse ischemic outcomes.

Background Incomplete revascularization (IR) after PCI is common, and most studies have suggested that IR is associated with a worse prognosis compared with complete revascularization (CR). However, formal quantification of the extent and complexity of residual atherosclerosis after PCI has not been performed.

Methods The baseline Synergy Between PCI With Taxus and Cardiac Surgery (SYNTAX) score (bSS) from 2,686 angiograms from patients with moderate- and high-risk acute coronary syndrome (ACS) undergoing PCI enrolled in the prospective ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial was determined. The SS after PCI was also assessed, generating the "residual" SS (rSS). Patients with rSS >0 were defined as having IR and were stratified by rSS tertiles, and their outcomes were compared to the CR group.

Results The bSS was 12.8 ± 6.7, and after PCI the rSS was 5.6 ± 2.2. Following PCI, 1,084 patients (40.4%) had rSS = 0 (CR), 523 (19.5%) had rSS >0 but ≤2, 578 (21.5%) had rSS >2 but ≤8, and 501 patients (18.7%) had rSS >8. Age, insulin-treated diabetes, hypertension, smoking, elevated biomarkers or ST-segment deviation, and lower ejection fraction were more frequent in patients with IR compared with CR. The 30-day and 1-year rates of ischemic events were significantly higher in the IR group compared with the CR group, especially those with high rSS. By multivariable analysis, rSS was a strong independent predictor of all ischemic outcomes at 1 year, including all-cause mortality (hazard ratio: 1.05, 95% confidence interval: 1.02 to 1.09, $p = 0.006$).

Conclusions The rSS is useful to quantify and risk-stratify the degree and complexity of residual stenosis after PCI. Specifically, rSS >8.0 after PCI in patients with moderate- and high-risk ACS is associated with a poor 30-day and 1-year prognosis. (Comparison of Angiomax Versus Heparin in Acute Coronary Syndromes; NCT00093158) (123).

Post-Conditioning Reduces Infarct Size and Edema in Patients With ST-Segment Elevation Myocardial Infarction

Objectives This study aimed to determine whether post-conditioning at the time of percutaneous coronary intervention could reduce reperfusion-induced myocardial edema in patients with acute ST-segment elevation myocardial infarction (STEMI).

Background Myocardial edema is a reperfusion injury with potentially severe consequences. Post-conditioning is a cardioprotective therapy that reduces infarct size after reperfusion, but no previous studies have analyzed the impact of this strategy on reperfusion-induced myocardial edema in humans.

Methods Fifty patients with STEMI were randomly assigned to either a control or post-conditioned group. Cardiac magnetic resonance imaging was performed within 48 to 72 h after admission. Myocardial edema was measured by T2-weighted sequences, and infarct size was determined by late gadolinium enhancement sequences and creatine kinase release.

Results The post-conditioned and control groups were similar with respect to ischemia time, the size of the area at risk, and the ejection fraction before percutaneous coronary intervention. As expected, post-conditioning was associated with smaller infarct size (13 ± 7 g/m^2 vs. 21 ± 14 g/m^2; $p = 0.01$) and creatine kinase peak serum level (median [interquartile range]: 1,695 [1,118 to 3,692] IU/l vs. 3,505 [2,307 to 4,929] IU/l; $p = 0.003$). At reperfusion, the extent of myocardial edema was significantly reduced in the post-conditioned group as compared with the control group (23 ± 16 g/m^2 vs. 34 ± 18 g/m^2; $p = 0.03$); the relative increase in T2W signal intensity was also significantly lower ($p = 0.02$). This protective effect was confirmed after adjustment for the size of the area at risk.

Conclusions This randomized study demonstrated that post-conditioning reduced infarct size and edema in patients with reperfused STEMI. (Post Cond No Reflow; NCT01208727) (124).

In-Stent Neoathero: sclerosis: A Final Common Pathway of Late Stent Failure

Percutaneous coronary intervention with stenting is the most widely performed procedure for the treatment of symptomatic coronary disease, and drug-eluting stents (DES) have minimized the limitations of bare-metal stents (BMS). Nevertheless, there remain serious concerns about late complications such as in-stent restenosis and late stent thrombosis. Although in-stent restenosis of BMS was considered as a stable condition with an early peak of intimal hyperplasia, followed by a regression period beyond 1 year, recent studies have reported that one-third of patients with in-stent restenosis of BMS presented with acute coronary syndrome that is not regarded as clinically benign. Furthermore, both clinical and histologic studies of DES have demonstrated evidence of continuous neointimal growth during long-term follow-up, which is designated as "late catch-up" phenomenon. Here, we present emerging evidence of de novo neoatherosclerosis based on histology, angioscopy, and intravascular images that provide a new insight for the mechanism of late stent failure. In-stent neoatherosclerosis is an important substrate for late stent failure for both BMS and DES, especially in the extended phase. In light of the rapid progression in DES, early detection of neoatherosclerosis may be beneficial to improving long-term outcome of patients with DES implants (125).

Optimal Treatment of Patients Surviving Out-of-Hospital Cardiac Arrest

Interest in post-resuscitation care has risen with the development of treatment modalities that can affect long-term survival rates even when begun after the systematic ischemia/reperfusion insult associated with cardiac arrest. Mild therapeutic hypothermia has become the foundation for improvement of neurologically favorable survival after cardiac arrest. Reperfusion therapy, specifically early percutaneous coronary intervention, is becoming an important adjunct to therapeutic hypothermia. Identifying which post–cardiac arrest patient had an occluded or unstable coronary vessel is difficult because such events are not reliably predicted by precedent symptoms or standard electrocardiographic analysis. Increasing clinical experience suggests that resuscitated cardiac arrest victims without an obvious noncardiac etiology should undergo emergency coronary angiography and, where indicated, percutaneous coronary intervention. If comatose, they should receive concurrent therapeutic hypothermia. Such an approach can double long-term survival rates among those successfully resuscitated after out-of-hospital cardiac arrest (126).

Safety of Coronary Reactivity Testing in Women With No Obstructive Coronary Artery Disease: Results From the NHLBI-Sponsored WISE (Women's Ischemia Syndrome Evaluation) Study

Objectives This study evaluated the safety of coronary reactivity testing (CRT) in symptomatic women with evidence of myocardial ischemia and no obstructive coronary artery disease (CAD).

Background Microvascular coronary dysfunction (MCD) in women with no obstructive CAD portends an adverse prognosis of a 2.5% annual major adverse cardiovascular event (MACE) rate. The diagnosis of MCD is established by invasive CRT, yet the risk of CRT is unknown.

Methods The authors evaluated 293 symptomatic women with ischemia and no obstructive CAD, who underwent CRT at 3 experienced centers. Microvascular function was assessed using a Doppler wire and injections of adenosine,

acetylcholine, and nitroglycerin into the left coronary artery. CRT-related serious adverse events (SAEs), adverse events (AEs), and follow-up MACE (death, nonfatal myocardial infarction [MI], nonfatal stroke, or hospitalization for heart failure) were recorded.

Results CRT-SAEs occurred in 2 women (0.7%) during the procedure: 1 had coronary artery dissection, and 1 developed MI associated with coronary spasm. CRT-AEs occurred in 2 women (0.7%) and included 1 transient air microembolism and 1 deep venous thrombosis. There was no CRT-related mortality. In the mean follow-up period of 5.4 years, the MACE rate was 8.2%, including 5 deaths (1.7%), 8 nonfatal MIs (2.7%), 8 nonfatal strokes (2.7%), and 11 hospitalizations for heart failure (3.8%).

Conclusions In women undergoing CRT for suspected MCD, contemporary testing carries a relatively low risk compared with the MACE rate in these women. These results support the use of CRT by experienced operators for establishing definitive diagnosis and assessing prognosis in this at-risk population. (Women's Ischemia Syndrome Evaluation [WISE]; NCT00832702) (127).

Risk Profile and 3-Year Outcomes From the SYNTAX Percutaneous Coronary Intervention and Coronary Artery Bypass Grafting Nested Registries

Objectives The aim of this study was to evaluate the use of percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) in "real-world" patients unsuitable for the alternative treatment.

Background No data are available on the risk profile and outcomes of patients that can only undergo PCI or CABG.

Methods In the SYNTAX (Synergy between PCI with TAXUS and Cardiac Surgery) trial, a multidisciplinary Heart Team reached a consensus on whether PCI and CABG could result in clinical equipoise; if so, the patient was randomized. If not, the patient was enrolled in a CABG-ineligible PCI registry or PCI-ineligible CABG registry. A proportion (60%) of patients in the CABG registry was randomly assigned to be followed up for 5 years. No statistical comparisons were performed between randomized and registry patients. Major adverse cardiac or cerebrovascular event (MACCE) rates are presented as observational only.

Results A total of 3,075 patients were treated in the SYNTAX trial; 198 (6.4%) and 1,077 (35.0%) patients were included in PCI and CABG registries, respectively. The main reason for inclusion in the CABG registry was too complex coronary anatomy (70.9%), and the main reason for inclusion in the PCI registry was too high-risk for surgery (70.7%). Three-year MACCE was 38.0% after PCI and 16.4% after CABG. Stratification by SYNTAX score terciles demonstrated a step-wise increase of MACCE rates in both PCI and CABG registries.

Conclusions The SYNTAX Heart Team concluded that PCI and CABG remained the only treatment options for 6.4% and 35.0% of patients, respectively. Inoperable patients with major comorbidities that underwent PCI had high MACCE rates. In patients not suitable for PCI, surgical results were excellent. (SYNTAX Study: TAXUS Drug-Eluting Stent Versus Coronary Artery Bypass Surgery for the Treatment of Narrowed Arteries, NCT00114972) (128).

Contemporary Incidence and Predictors of Stent Thrombosis and Other Major Adverse Cardiac Events in the Year After XIENCE V Implantation: Results From the 8,061-Patient XIENCE V United States Study

Objectives The aim of this study was to identify predictors of clinical events after XIENCE V (Abbott Vascular, Santa Clara, California) stenting.

Background The XIENCE V USA (XIENCE V Everolimus Eluting Coronary Stent System [EECSS] USA Post-Approval) study is a prospective, multicenter, Food and Drug Administration-required post-approval study to examine safety and effectiveness in real-world settings. After an initial 5,062 patients, 2,999 more were included as part of the DAPT (Dual Antiplatelet Therapy) trial (total n = 8,061).

Methods One-year clinical events, including stent thrombosis (ST), cardiac death/myocardial infarction (MI), target lesion failure, and target lesion revascularization, were adjudicated according to Academic Research Consortium criteria, with ST and cardiac death/MI as primary and co-primary endpoints. Demographic, clinical, and procedural variables were assessed by multivariable analysis. A time-dependent covariate assessed the association between DAPT usage and ST.

Results Roughly 61% were off-label; 85.6% remained on DAPT without interruption through 1 year. Incidences of definite/probable ST, cardiac death/MI, target lesion failure, and target lesion revascularization were 0.80% (95% confidence interval [CI]: 0.61% to 1.03%), 7.1% (95% CI: 6.51% to 7.68%), 8.9% (95% CI: 8.30% to 9.60%), and 4.3% (95% CI: 3.82% to 4.75%), respectively. Several independent clinical and angiographic predictors were identified for each outcome. Predictors of ST included DAPT interruption $\leq$30 days (hazard ratio [HR]: 8.63, 95% CI: 2.69 to 27.73, p = 0.0003), renal insufficiency (HR: 3.72, 95% CI: 1.71 to 8.09, p = 0.0009), and total stent length (HR: 1.30, 95% CI: 1.16 to 1.47, p < 0.0001). A DAPT interruption >30 days was not predictive of ST.

Conclusions In this large, real-world population, XIENCE V demonstrated low event rates at 1 year, with several independent predictors. Early DAPT interruption ($\leq$30 days) was the most potent predictor of ST, whereas delayed interruption (>30 days) was not predictive. (XIENCE V Everolimus Eluting Coronary Stent System [EECSS] USA Post-Approval Study; NCT00676520) (129).

Computed Tomographic Angiography–Verified Plaque Characteristics and Slow-Flow Phenomenon During Percutaneous Coronary Intervention

Objectives This study sought to identify whether computed tomographic angiographic (CTA) plaque characteristics are associated with slow-flow phenomenon (SF) during percutaneous coronary intervention (PCI).

Background SF during PCI is associated with myocardial damage and prolonged hospitalization. Intracoronary ultrasound–verified large echolucent lesions have been reported to predict SF.

Methods The authors evaluated pre-PCI CTA plaque characteristics in 40 consecutive patients (male/female, 31/9; age, 69 ± 10 years) with stable angina pectoris who developed SF during PCI; patients with ≥600 Agatston coronary artery calcium score were not included. They were compared with 40 age-, sex-, and culprit coronary artery–matched patients (male/female, 31/9; age, 69 ± 9 years) who underwent PCI during the same period and did not develop SF. Plaque characteristics, including vascular remodeling, plaque consistency, including low-attenuation plaques representing lipid-rich lesions and high-attenuation plaque patterns of calcium deposition, were analyzed.

Results Calcium deposition in the perimeter of a plaque, or circumferential plaque calcification (CPC), was significantly more frequent in the SF group (25 of 40, 63%) than the no-SF group (2 of 40, 5.0%) ($p < 0.001$). Presence of CPC on CTA was confirmed at the same location in the non-enhanced CT during Agatston coronary artery calcium score calculation. The positive remodeling index was significantly higher (1.5 [1.3 to 1.8] vs. 1.2 [1.0 to 1.5]; $p < 0.001$) and plaque density significantly lower (23.5 [9.5 to 40] HU vs. 45 [29 to 86] HU; $p = 0.001$) in the SF group. The conditional logistic regression analysis revealed that CPC, plaque density, and dyslipidemia were the predictors of SF, with CPC being the strongest (odds ratio: 79; 95% confidence interval: 8 to 783, $p < 0.0001$).

Conclusions CTA-verified CPC with low-attenuation plaque and positive remodeling were determinants of SF during PCI. If CTA findings are available in patients undergoing PCI, the interventionists should be aware of the likelihood of SF (130).

Vascular Response of the Segments Adjacent to the Proximal and Distal Edges of the ABSORB Everolimus-Eluting Bioresorbable Vascular Scaffold: 6-Month and 1-Year Follow-Up Assessment: A Virtual Histology Intravascular Ultrasound Study From the First-in-Man ABSORB Cohort B Trial

Objectives This study sought to investigate in vivo the vascular response at the proximal and distal edges of the second-generation ABSORB everolimus-eluting bioresorbable vascular scaffold (BVS).

Background The edge vascular response after implantation of the BVS has not been previously investigated.

Methods The ABSORB Cohort B trial enrolled 101 patients and was divided into B_1 ($n = 45$) and B_2 ($n = 56$) subgroups. The adjacent (5-mm) proximal and distal vessel segments to the implanted ABSORB BVS were investigated at either 6 months (B_1) or 1 year (B_2) with virtual histology intravascular ultrasound (VH-IVUS) imaging.

Results At the 5-mm proximal edge, the only significant change was modest constrictive remodeling at 6 months (Δ vessel cross-sectional area: −1.80% [−3.18; 1.30], $p < 0.05$), with a tendency to regress at 1 year (Δ vessel cross-sectional area: −1.53% [−7.74; 2.48], $p = 0.06$). The relative change of the fibrotic and fibrofatty (FF) tissue areas at this segment were not statistically significant at either time point. At the 5-mm distal edge, a significant increase in the FF tissue of 43.32% [−19.90; 244.28], ($p < 0.05$) 1-year post-implantation was evident. The changes in dense calcium need to be interpreted with caution since the polymeric struts are detected as "pseudo" dense calcium structures with the VH-IVUS imaging modality.

Conclusions The vascular response up to 1 year after implantation of the ABSORB BVS demonstrated some degree of proximal edge constrictive remodeling and distal edge increase in FF tissue resulting in nonsignificant plaque progression with adaptive expansive remodeling. This morphological and tissue composition behavior appears to not significantly differ from the behavior of metallic drug-eluting stents at the same observational time points (131).

The Effect of Patent Foramen Ovale Closure on Visual Aura Without Headache or Typical Aura With Migraine Headache

Objectives The aim of this study was to assess the prevalence of right-to-left (R to L) shunt in patients with visual aura and evaluate the effect of shunt closure on resolution of aura.

Background Right-to-left shunting is associated with migraine headache (MH) with aura. Some patients present with visual aura without headaches. It is unclear whether visual aura without headache is a form of migraine or a transient neurologic dysfunction.

Methods Of patients referred to the University of California, Los Angeles for suspected patent foramen ovale (PFO), 225 had visual aura with or without MH. Patients were assessed for a shunt and evaluated for MH and/or visual aura. They were divided into 3 groups: 1) visual aura associated with MH; 2) visual aura unrelated in time to MH; and 3) visual aura without MH. The frequency of R to L shunt was compared with a control group of 200 patients. Eighty patients underwent PFO closure. Residual shunts, MH, and visual aura were reassessed after 3 and 12 months.

Results The prevalence of R to L shunt in Groups A, B, and C was 96%, 72%, and 67%, respectively, versus 18% in the control group ($p < 0.0001$). The frequency of shunting

was similar in Group B versus Group C, but much higher in all 3 groups compared with control subjects. Twelve months after PFO closure, symptoms of aura were resolved in 52%, 75%, and 80% of patients in Groups A, B, and C, respectively (p = NS).

Conclusions The similar distribution of R to L shunting in all 3 patient groups and the correlation between PFO closure and improvement of aura suggests a similar pathophysiology between the presence of PFO and the visual aura phenomenon, whether or not headache is present in the symptom complex (132).

A Global Risk Approach to Identify Patients With Left Main or 3-Vessel Disease Who Could Safely and Efficaciously Be Treated With Percutaneous Coronary Intervention: The SYNTAX Trial at 3 Years

Objectives The aim of this study was to assess the additional value of the Global Risk—a combination of the SYNTAX Score (SXscore) and additive EuroSCORE—in the identification of a low-risk population, who could safely and efficaciously be treated with coronary artery bypass graft surgery (CABG) or percutaneous coronary intervention (PCI).

Background PCI is increasingly acceptable in appropriately selected patients with left main stem or 3-vessel coronary artery disease.

Methods Within the SYNTAX Trial (Synergy between PCI with TAXUS and Cardiac Surgery Trial), all-cause death and major adverse cardiac and cerebrovascular events (MACCE) were analyzed at 36 months in low (GRC_{LOW}) to high Global Risk groups, with Kaplan-Meier, log-rank, and Cox regression analyses.

Results Within the randomized left main stem population (n = 701), comparisons between GRC_{LOW} groups demonstrated a significantly lower mortality with PCI compared with CABG (CABG: 7.5%, PCI: 1.2%, hazard ratio [HR]: 0.16, 95% confidence interval [CI]: 0.03 to 0.70, p = 0.0054) and a trend toward reduced MACCE (CABG: 23.1%, PCI: 15.8%, HR: 0.64, 95% CI: 0.39 to 1.07, p = 0.088). Similar analyses within the randomized 3-vessel disease population (n = 1,088) demonstrated no statistically significant differences in mortality (CABG: 5.2%, PCI: 5.8%, HR: 1.14, 95% CI: 0.57 to 2.30, p = 0.71) or MACCE (CABG: 19.0%, PCI: 24.7%, HR: 1.35, 95% CI: 0.95 to 1.92, p = 0.10). Risk-model performance and reclassification analyses demonstrated that the EuroSCORE—with the added incremental benefit of the SXscore to form the Global Risk—enhanced the risk stratification of all PCI patients.

Conclusions In comparison with the SXscore, the Global Risk, with a simple treatment algorithm, substantially enhances the identification of low-risk patients who could safely and efficaciously be treated with CABG or PCI (133).

Pathology of Drug-Eluting Versus Bare-Metal Stents in Saphenous Vein Bypass Graft Lesions

Objectives The purpose of this study was to assess the pathological responses of atherosclerotic saphenous vein bypass grafts (SVBGs) to drug-eluting stents (DES) versus bare-metal stents (BMS).

Background Repeat bypass surgery is typically associated with a high rate of morbidity and mortality. Percutaneous coronary interventions have emerged as the preferred treatment; however, only limited data are available on SVBGs pathological responses to DES and BMS.

Methods Formalin-fixed SVBG of >2 years duration (n = 31) were collected to histologically characterize advanced atherosclerotic lesions in native SVBG. In a separate group, SVBGs treated with DES (n = 9) and BMS (n = 9) for >30 days duration were assessed for morphological and morphometric changes.

Results Necrotic core lesions were identified in 25% of SVBG sections, and plaque rupture with luminal thrombosis was observed in 6.3% of histological sections (32% [10 of 31] vein grafts examined). Morphometry of DES demonstrated reduction in neointimal thickening versus BMS (0.13 mm [interquartile range: 0.06 to 0.16 mm] vs. 0.30 mm [interquartile range: 0.20 to 0.48 mm], p = 0.004). DES lesions also showed greater delayed healing characterized by increased peristrut fibrin deposition, higher percentage of uncovered struts, and less endothelialization compared with BMS. Stent fractures (DES 56% vs. BMS 11%, p = 0.045) and late stent thrombosis (DES 44% vs. BMS 0%, p = 0.023) were more common in DES versus BMS.

Conclusions Advanced SVBG atherosclerotic lesions are characterized by large hemorrhagic necrotic cores. Stenting of such lesions is associated with delayed vascular healing and late thrombosis particularly following DES implantation, which may help explain the higher rates of cardiovascular events observed in SVBG stenting as compared with native coronary arteries (134).

Influence of Genetic Polymorphisms on the Effect of High- and Standard-Dose Clopidogrel After Percutaneous Coronary Intervention: The GIFT (Genotype Information and Functional Testing) Study

Objectives This study sought to evaluate the influence of single nucleotide polymorphisms (SNPs) on the pharmacodynamic effect of high- or standard-dose clopidogrel after percutaneous coronary intervention (PCI).

Background There is a lack of prospective, multicenter data regarding the effect of different genetic variants on clopidogrel pharmacodynamics over time in patients undergoing PCI.

Methods The GRAVITAS (Gauging Responsiveness with A VerifyNow assay–Impact on Thrombosis And Safety) trial screened patients with platelet function testing after

PCI and randomly assigned those with high on-treatment reactivity (OTR) to either high- or standard-dose clopidogrel; a cohort of patients without high OTR were also followed. DNA samples obtained from 1,028 patients were genotyped for 41 SNPs in 17 genes related to platelet reactivity. After adjusting for clinical characteristics, the associations between the SNPs and OTR using linear regression were evaluated.

Results *CYP2C19*2* was significantly associated with OTR at 12 to 24 h ($R^2 = 0.07$, $p = 2.2 \times 10^{-15}$), 30 days ($R^2 = 0.10$, $p = 1.3 \times 10^{-7}$), and 6 months after PCI ($R^2 = 0.07$, $p = 1.9 \times 10^{-11}$), whereas *PON1*, *ABCB1 3435 C→T*, and other candidate SNPs were not. Carriers of 1 and 2 reduced-function *CYP2C19* alleles were significantly more likely to display persistently high OTR at 30 days and 6 months, irrespective of treatment assignment. The portion of the risk of persistently high OTR at 30 days attributable to reduced-function *CYP2C19* allele carriage was 5.2% in the patients randomly assigned to high-dose clopidogrel.

Conclusions *CYP2C19*, but not *PON1* or *ABCB1,* is a significant determinant of the pharmacodynamic effects of clopidogrel, both early and late after PCI. In patients with high OTR identified by platelet function testing, the *CYP2C19* genotype provides limited incremental information regarding the risk of persistently high reactivity with clopidogrel 150-mg maintenance dosing. (Genotype Information and Functional Testing Study [GIFT]; NCT00992420) (135).

Appropriateness of Coronary Revascularization for Patients Without Acute Coronary Syndromes

Objectives The purpose of this study was to determine appropriateness of percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) surgery performed in New York for patients without acute coronary syndrome (ACS) or previous CABG surgery.

Background The American College of Cardiology Foundation (ACCF) and 6 other societies recently published joint appropriateness criteria for coronary revascularization.

Methods Data from patients who underwent CABG surgery and PCI without acute coronary syndrome or previous CABG surgery in New York in 2009 and 2010 were used to assess appropriateness and to examine the variation across hospitals in inappropriateness ratings.

Results Of the 8,168 patients undergoing CABG surgery in New York without ACS/prior CABG who could be rated, 90.0% were appropriate for revascularization, 1.1% were inappropriate, and 8.6% were uncertain. Of the 33,970 PCI patients eligible for rating, 28% lacked sufficient information to be rated. Of the patients who could be rated, 36.1% were appropriate, 14.3% were inappropriate, and 49.6% were uncertain. A total of 91% of the patients undergoing PCI who were classified as inappropriate had 1- or 2-vessel disease without proximal left anterior descending artery disease and had no or minimal anti-ischemic medical therapy.

Conclusions For patients without ACS/prior CABG, only 1% of patients undergoing CABG surgery who could be rated were found to be inappropriate for the procedure according to the ACCF appropriateness criteria, but 14% of the PCI patients who could be rated were found to be inappropriate, and 28% lacked enough noninvasive test information to be rated (136).

Impact of Coronary Plaque Composition on Cardiac Troponin Elevation After Percutaneous Coronary Intervention in Stable Angina Pectoris: A Computed Tomography Analysis

Objectives The authors used multidetector computed tomography (MDCT) to study the relation between culprit plaque characteristics and cardiac troponin T (cTnT) elevation after percutaneous coronary intervention (PCI).

Background Percutaneous coronary intervention is often complicated by post-procedural myocardial necrosis manifested by elevated cardiac biomarkers.

Methods Stable angina patients (n = 107) with normal pre-PCI cTnT levels underwent 64-slice MDCT before PCI to evaluate plaque characteristics of culprit lesions. Patients were divided into 2 groups according to presence (group I, n = 36) or absence (group II, n = 71) of post-PCI cTnT elevation ≥3 times the upper limit of normal (0.010 ng/ml) at 24 h after PCI.

Results Computed tomography attenuation values were significantly lower in group I than in group II (43.0 [26.5 to 75.7] HU vs. 94.0 [65.0 to 109.0] HU, $p < 0.001$). Remodeling index was significantly greater in group I than in group II (1.20 ± 0.18 vs. 1.04 ± 0.15, $p < 0.001$). Spotty calcification was observed significantly more frequently in group I than in group II (50% vs. 11%, $p < 0.001$). Multivariate analysis showed presence of positive remodeling (remodeling index >1.05; odds ratio: 4.54; 95% confidence interval: 1.36 to 15.9; $p = 0.014$) and spotty calcification (odds ratio: 4.27; 95% confidence interval: 1.30 to 14.8; $p = 0.016$) were statistically significant independent predictors for cTnT elevation. For prediction of cTnT elevation, the presence of all 3 variables (CT attenuation value <55 HU; remodeling index >1.05, and spotty calcification) showed a high positive predictive value of 94%, and their absence showed a high negative predictive value of 90%.

Conclusions MDCT may be useful in detecting which lesions are at high risk for myocardial necrosis after PCI (137).

Temporal Trends in and Factors Associated With Bleeding Complications Among Patients Undergoing Percutaneous Coronary Intervention: A Report From the National Cardiovascular Data CathPCI Registry

Objectives The purpose of this study was to examine temporal trends in post-percutaneous coronary intervention

(PCI) bleeding among patients with elective PCI, unstable angina (UA)/non–ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI).

Background The impact of bleeding avoidance strategies on post-PCI bleeding rates over time is unknown.

Methods Using the CathPCI Registry, we examined temporal trends in post-PCI bleeding from 2005 to 2009 among patients with elective PCI (n = 599,524), UA/NSTEMI (n = 836,103), and STEMI (n = 267,632). We quantified the linear time trend in bleeding using 3 sequential logistic regression models: 1) clinical factors; 2) clinical + vascular access strategies (femoral vs. radial, use of closure devices); and 3) clinical, vascular strategies + antithrombotic treatments (anticoagulant ± glycoprotein IIb/IIIa inhibitor [GPI]). Changes in the odds ratio for time trend in bleeding were compared using bootstrapping and converted to risk ratio.

Results An approximate 20% reduction in post-PCI bleeding was seen (elective PCI: 1.4% to 1.1%; UA/NSTEMI: 2.3% to 1.8; STEMI: 4.9% to 4.5%). Radial approach remained low (<3%), and closure device use increased marginally from 44% to 49%. Bivalirudin use increased (17% to 30%), whereas any heparin + GPI decreased (41% to 28%). There was a significant 6% to 8% per year reduction in annual bleeding risk in UA/NSTEMI and elective PCI, but not in STEMI. Antithrombotic strategies were associated with roughly half of the reduction in annual bleeding risk: change in risk ratio from 7.5% to 4% for elective PCI, and 5.7% to 2.8% for UA/NSTEMI (both p <0.001).

Conclusions The nearly 20% reduction in post-PCI bleeding over time was largely due to temporal changes in antithrombotic strategies. Further reductions in bleeding complications may be possible as bleeding avoidance strategies evolve, especially in STEMI (138).

Intraprocedural Thrombotic Events During Percutaneous Coronary Intervention in Patients With Non–ST-Segment Elevation Acute Coronary Syndromes Are Associated With Adverse Outcomes: Analysis From the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) Trial

Objectives The purpose of this study was to assess the prognostic impact of intraprocedural thrombotic events (IPTE) during percutaneous coronary intervention (PCI).

Background Ischemic complications of PCI are infrequent but prognostically important. How often these events are a consequence of intraprocedural complications is unknown, with only limited data assessing the occurrence and importance of IPTE.

Methods A total of 3,428 patients who underwent PCI for non–ST-segment elevation acute coronary syndrome in the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial underwent detailed frame-by-frame core laboratory angiographic analysis. An IPTE, defined as the development of new or increasing thrombus, abrupt vessel closure, no reflow, slow reflow, or distal embolization at any time during the procedure, occurred in 121 patients (3.5%).

Results Patients with IPTE had higher in-hospital, 30-day, and 1-year major adverse cardiac event rates than patients without IPTE (25.6% vs. 6.3% in-hospital, 30.6% vs. 9.3% at 30 days, and 37.0% vs. 20.5% at 1 year; p < 0.0001 for each). An IPTE was strongly associated with Q-wave myocardial infarction and out-of-laboratory definite/probable stent thrombosis (in-hospital 3.3% vs. 0.5%, p = 0.006; 30 days 5.8% vs. 1.3%, p < 0.0001; and 1 year 6.7% vs. 2.0%, p = 0.0002). Unplanned revascularization, target vessel revascularization, and major bleeding not associated with coronary artery bypass graft surgery were also increased among patients with IPTE, as was overall 30-day mortality (3.3% vs. 0.7%, p = 0.002). Moreover, IPTE was an independent predictor of 30-day and 1-year composite death/myocardial infarction, stent thrombosis, and major adverse cardiac events.

Conclusions Although infrequent among patients undergoing early PCI for moderate and high-risk non–ST-segment elevation acute coronary syndrome, IPTE was strongly associated with subsequent adverse outcomes including death, myocardial infarction, and stent thrombosis (139).

Spotty Calcification as a Marker of Accelerated Progression of Coronary Atherosclerosis: Insights From Serial Intravascular Ultrasound

Objectives The purpose of this study was to determine atheroma progression in patients with spotty calcification.

Background Although extensively calcified atherosclerotic lesions have been proposed to be clinically quiescent, the presence of spotty calcification within plaque has been reported to be associated with an increased incidence of ischemic cardiovascular events. The relationship between spotty calcification and disease progression has not been investigated.

Methods A total of 1,347 stable patients with angiographic coronary artery disease underwent serial evaluation of atheroma burden with intravascular ultrasound imaging. Patients with spotty calcification were identified based on the presence of lesions (1 to 4 mm in length) containing an arc of calcification of <90°. Clinical characteristics and disease progression were compared between patients with spotty calcification (n = 922) and those with no calcification (n = 425).

Results Patients with spotty calcification were older (age 56 years vs. 54 years; p = 0.001), more likely to be male (68% vs. 54%; p = 0.01), and have a history of diabetes mellitus (30% vs. 24%; p = 0.01) and myocardial infarction (28% vs. 20%; p = 0.004), and have lower on-treatment

high-density lipoprotein cholesterol levels (48 ± 16 mg/dl vs. 51 ± 17 mg/dl; p = 0.001). Patients with spotty calcification demonstrated a greater percent atheroma volume (PAV) (36.0 ± 7.6% vs. 29.0 ± 8.5%; p < 0.001) and total atheroma volume (174.6 ± 71.9 mm^3 vs. 133.9 ± 64.9 mm^3; p < 0.001). On serial evaluation, spotty calcification was associated with greater progression of PAV (+0.43 ± 0.07% vs. +0.02 ± 0.11%; p = 0.002). Although intensive low-density lipoprotein cholesterol and blood pressure lowering therapy slowed disease progression, these efficacies were attenuated in patients with spotty calcification.

Conclusions The presence of spotty calcification is associated with more extensive and diffuse coronary atherosclerosis and accelerated disease progression despite use of medical therapies (140).

Metabolomic Profile of Human Myocardial Ischemia by Nuclear Magnetic Resonance Spectroscopy of Peripheral Blood Serum: A Translational Study Based on Transient Coronary Occlusion Models

Objectives The aim of this study was to investigate the metabolomic profile of acute myocardial ischemia (MIS) using nuclear magnetic resonance spectroscopy of peripheral blood serum of swine and patients undergoing angioplasty balloon–induced transient coronary occlusion.

Background Biochemical detection of MIS is a major challenge. The validation of novel biosignatures is of utmost importance.

Methods High-resolution nuclear magnetic resonance spectroscopy was used to profile 32 blood serum metabolites obtained (before and after controlled ischemia) from swine (n = 9) and patients (n = 20) undergoing transitory MIS in the setting of planned coronary angioplasty. Additionally, blood serum of control patients (n = 10) was sequentially profiled. Preliminary clinical validation of the developed metabolomic biosignature was undertaken in patients with spontaneous acute chest pain (n = 30).

Results Striking differences were detected in the blood profiles of swine and patients immediately after MIS. MIS induced early increases (10 min) of circulating glucose, lactate, glutamine, glycine, glycerol, phenylalanine, tyrosine, and phosphoethanolamine; decreases in choline-containing compounds and triacylglycerols; and a change in the pattern of total, esterified, and nonesterified fatty acids. Creatine increased 2 h after ischemia. Using multivariate analyses, a biosignature was developed that accurately detected patients with MIS both in the setting of angioplasty-related MIS (area under the curve 0.94) and in patients with acute chest pain (negative predictive value 95%).

Conclusions This study reports, to the authors' knowledge, the first metabolic biosignature of acute MIS developed under highly controlled coronary flow restriction. Metabolic profiling of blood plasma appears to be a promising approach for the early detection of MIS in patients (141).

Transfemoral Aortic Valve Replacement With the Edwards SAPIEN and Edwards SAPIEN XT Prosthesis Using Exclusively Local Anesthesia and Fluoroscopic Guidance: Feasibility and 30-Day Outcomes

Objectives The authors report the feasibility and 30-day outcomes of transfemoral aortic valve replacement (TAVR), using the Edwards SAPIEN (Edwards Lifesciences, Irvine, California) and Edwards SAPIEN XT (Edwards Lifesciences) prosthesis, implanted using exclusively local anesthesia and fluoroscopic guidance.

Background Transfemoral TAVR is often managed with general anesthesia. However, a simplified percutaneous approach using local anesthesia has become more popular because it offers multiple advantages in an elderly and fragile population.

Methods Between May 2006 and January 2011, the authors prospectively evaluated 151 consecutive patients (logistic EuroSCORE: 22.8 ± 11.8%) who underwent TAVR (SAPIEN: n = 78, SAPIEN XT: n = 73) using only local anesthesia and fluoroscopic guidance. The primary endpoint was a combination of all-cause mortality, major stroke, life-threatening bleeding, stage 3 acute kidney injury (AKI), periprocedural myocardial infarction (MI), major vascular complication, and repeat procedure for valve-related dysfunction at 30 days.

Results Transarterial femoral approach was surgical in all SAPIEN procedures and percutaneous in 97.3% of SAPIEN XT, using the ProStar vascular closure device, and was well tolerated in all cases. Conversion to general anesthesia was required in 3.3% (SAPIEN cases) and was related to complications. Vasopressors were required in 5.5%. Procedural success was 95.4%. The combined-safety endpoint was reached in 15.9%, including overall mortality (6.6%), major stroke (2.0%), life-threatening bleeding (7.9%), stage 3 AKI (0.7%), periprocedural MI (1.3%), major vascular complication (7.9%), and repeat procedure for valve-related dysfunction (2.0%) at 30 days. A permanent pacemaker was required in 5.3%.

Conclusions This single-center, prospective registry demonstrated the feasibility and safety of a simplified transfemoral TAVR performed using only local anesthesia and fluoroscopic guidance in high surgical risk patients with severe aortic stenosis (142).

Percutaneous Management of Vascular Complications in Patients Undergoing Transcatheter Aortic Valve Implantation

Objectives This study sought to investigate the feasibility and safety of percutaneous management of vascular complications after transcatheter aortic valve implantation (TAVI).

Background Vascular complications after TAVI are frequent and outcomes after percutaneous management of these adverse events not well established.
Methods Between August 2007 and July 2010, 149 patients underwent transfemoral TAVI using a percutaneous approach. We compared outcomes of patients undergoing percutaneous management of vascular complications with patients free from vascular complications and performed duplex ultrasonography, fluoroscopy, and multislice computed tomography during follow-up.
Results A total of 27 patients (18%) experienced vascular complications consisting of incomplete arteriotomy closure (n = 19, 70%), dissection (n = 3, 11%), arterial perforation (n = 3, 11%), arterial occlusion (n = 1, 4%), and pseudoaneurysm (n = 1, 4%). Percutaneous stent graft implantation was successful in 21 of 23 (91%) patients, whereas 2 patients were treated by manual compression, 2 patients underwent urgent surgery, and 2 patients required delayed surgery. Rates of major adverse cardiac events at 30 days were similar among patients undergoing percutaneous management of vascular complications and those without vascular complications (9% vs. 8%, p = 1.00). After a median follow-up of 10.9 months, imaging showed no evidence of hemodynamically significant stenosis (mean peak velocity ratio: 1.2 ± 0.4). Stent fractures were observed in 4 stents (22%, type I [6%], type II [16%]) and were clinically silent in all cases.
Conclusions Vascular complications after TAVI can be treated percutaneously as a bailout procedure with a high rate of technical success, and clinical outcomes are comparable to patients without vascular complications. Stent patency is high during follow-up, although stent fractures require careful scrutiny (143).

Predictive Factors, Efficacy, and Safety of Balloon Post-Dilation After Transcatheter Aortic Valve Implantation With a Balloon-Expandable Valve

Objectives This study sought to evaluate the predictive factors, effects, and safety of balloon post-dilation (BPD) for the treatment of significant paravalvular aortic regurgitation (AR) after transcatheter aortic valve implantation (TAVI).
Background Very few data exist on BPD after TAVI with a balloon-expandable valve.
Methods A total of 211 patients who underwent TAVI with a balloon-expandable valve were included. BPD was performed after TAVI if paravalvular AR ≥2 was identified by transesophageal echocardiography. Clinical events and echocardiographic data were prospectively recorded, and median follow-up was 12 (6 to 24) months.
Results BPD was performed in 59 patients (28%), leading to a reduction in at least 1 degree of AR in 71% of patients, with residual AR <2 in 54% of the patients. The predictors of the need for BPD were the degree of valve calcification and transfemoral approach, with valve calcification volume >2,200 and >3,800 mm^3 best determining the need for and a poor response to BPD, respectively. Patients who underwent BPD had a higher incidence of cerebrovascular events at 30 days (11.9% vs. 2.0%, p = 0.006), with most (83%) events within the 24 h after the procedure occurring in patients who had BPD. No significant changes in valve area or AR degree were observed at follow-up in BPD and no-BPD groups.
Conclusions BPD was needed in about one-fourth of the patients undergoing TAVI with a balloon-expandable valve and was successful in about one-half of them. A higher degree of valve calcification and transfemoral approach predicted the need for BPD. BPD was not associated with any deleterious effect on valve function at mid-term follow-up, but a higher rate of cerebrovascular events was observed in patients who had BPD (144).

Evaluation of Multidimensional Geriatric Assessment as a Predictor of Mortality and Cardiovascular Events After Transcatheter Aortic Valve Implantation

Objectives This study evaluated Multidimensional Geriatric Assessment (MGA) as predictor of mortality and major adverse cardiovascular and cerebral events (MACCE) after transcatheter aortic valve implantation (TAVI).
Background Currently used global risk scores do not reliably estimate mortality and MACCE in these patients.
Methods This prospective cohort comprised 100 consecutive patients ≥70 years undergoing TAVI. Global risk scores (Society of Thoracic Surgeons [STS] score, EuroSCORE) and MGA-based scores (cognition, nutrition, mobility, activities of daily living [ADL], and frailty index) were evaluated as predictors of all-cause mortality and MACCE 30 days and 1 year after TAVI in regression models.
Results In univariable analyses, all predictors were significantly associated with mortality and MACCE at 30 days and 1 year, except for the EuroSCORE at 30 days and instrumental ADL at 30 days and 1 year. Associations of cognitive impairment (odds ratio [OR]: 2.98, 95% confidence interval [CI]: 1.07 to 8.31), malnutrition (OR: 6.72, 95% CI: 2.04 to 22.17), mobility impairment (OR: 6.65, 95% CI: 2.15 to 20.52), limitations in basic ADL (OR: 3.63, 95% CI: 1.29 to 10.23), and frailty index (OR: 3.68, 95% CI: 1.21 to 11.19) with 1-year mortality were similar compared with STS score (OR: 5.47, 95% CI: 1.48 to 20.22) and EuroSCORE (OR: 4.02, 95% CI: 0.86 to 18.70). Similar results were found for 30-day mortality and MACCE. Bivariable analyses, including STS score or EuroSCORE suggested independent associations of MGA-based scores (e.g., OR of frailty index: 3.29, 95% CI: 1.06 to 10.15, for 1-year mortality in a model including EuroSCORE).
Conclusions This study provides evidence that risk prediction can be improved by adding MGA-based information to global risk scores. Larger studies are needed for

the development and validation of improved risk prediction models (145).

Need for Permanent Pacemaker as a Complication of Transcatheter Aortic Valve Implantation and Surgical Aortic Valve Replacement in Elderly Patients With Severe Aortic Stenosis and Similar Baseline Electrocardiographic Findings

Objectives The aim of this study was to compare the incidence and predictive factors of complete atrioventricular block (AVB) and permanent pacemaker implantation (PPI) after transcatheter aortic valve implantation (TAVI) versus surgical aortic valve replacement (SAVR).
Background No data exist on the need for PPI after TAVI versus SAVR in patients with similar baseline electrocardiographic (ECG) findings.
Methods A total of 411 patients with severe aortic stenosis (AS) and no prior pacemaker who underwent TAVI with the balloon-expandable Edwards valve (Edwards Lifesciences, Irvine, California) were matched (1:1) with 411 elderly patients with severe AS who underwent isolated SAVR on the basis of baseline ECG findings. The incidence, reasons, and predictive factors for PPI within 30 days after the procedure were compared between groups.
Results Mean age was similar in both groups ($p = 0.11$), and the TAVI group had a higher Society of Thoracic Surgeons score ($p < 0.001$). The rate of new PPI was higher after TAVI (7.3%) compared with SAVR (3.4%), $p = 0.014$. Complete AVB and severe symptomatic bradycardia, respectively, were the reasons for PPI in the TAVI (5.6% and 1.7%, respectively) and SAVR (2.7% and 0.7%, respectively) groups ($p = 0.039$ for complete AVB, p = NS for symptomatic bradycardia). The presence of baseline right bundle branch block was the only variable associated with PPI in the TAVI group (odds ratio: 8.61, 95% confidence interval: 3.14 to 23.67, $p < 0.0001$), whereas no variable was found in the SAVR group.
Conclusions Transcatheter aortic valve implantation was associated with a higher rate of complete AVB and PPI compared with SAVR in elderly patients with severe AS and similar baseline ECG findings. The presence of baseline right bundle branch block correlated with the need for PPI in the TAVI group (146).

Multicenter Evaluation of Edwards SAPIEN Positioning During Transcatheter Aortic Valve Implantation With Correlates for Device Movement During Final Deployment

Objectives This study sought to evaluate the exact location of Edwards SAPIEN (Edwards Lifesciences, Irvine, California) devices in different stages of implantation and to quantify possible operator-independent device movement during final deployment.
Background Accurate device positioning during transcatheter aortic valve implantation is crucial in order to achieve optimal results.
Methods This multicenter study consisted of 68 procedures with reliable pacemaker capture. Device positions were assessed using fluoroscopic images and the C-THV system (Paieon Medical, Rosh Ha'Ayin, Israel).
Results The location after implantation was significantly higher than in the final stage of rapid pacing: $16.7 \pm 16.3\%$ of device height below the plane of the lower sinus border versus $32.6 \pm 13.8\%$, $p < 0.0001$. Operator-independent device-center upper movement during final deployment was 2 ± 1.43 mm, range: -1.3 to 4.6 mm. Device movement was asymmetrical, occurring more in the lower part of the device than in its upper part (3.2 ± 1.4 mm vs. 0.75 ± 1.5 mm, $p < 0.001$), resulting in device shortening. Multivariate analysis revealed that moderate and severe aortic valve calcification had 49% higher upward movement than mild calcification ($p = 0.03$), and aortic sinus volume was negatively correlated with movement size ($r = -0.35$, $p = 0.005$). This movement was independent of device version (SAPIEN vs. SAPIEN XT), procedural access (transfemoral vs. transapical), and interventricular septum width.
Conclusions The final Edwards SAPIEN position is mostly aortic in relation to the lower sinus border. There is an operator-independent upward movement of the device center during the final stage of implantation. Anticipated upward movement of the device should influence its positioning before final deployment (147).

Distribution of Calcium in the Ascending Aorta in Patients Undergoing Transcatheter Aortic Valve Implantation and Its Relevance to the Transaortic Approach

Objectives This study sought to identify how many patients suitable for transcatheter aortic valve implantation (TAVI) would have a contraindication for the transaortic (TAo) approach due to ascending aortic calcification.
Background TAo is an emerging approach for implantation of the Sapien valve through the ascending aorta. A "porcelain aorta" is often considered a contraindication for the TAo approach. This may not always be true, as the TAo procedure requires a small calcium-free area for the purse-string suture, usually in the upper outer quadrant of the distal ascending aorta, identified as the "TAo zone."
Methods A total of 237 patients underwent TAVI between February 2008 and June 2011. Multislice computed tomography scans (MSCT) were analyzed for distribution of calcium with special attention to the TAo zone. Each MSCT was interrogated in cross section and three dimensional (3D) reconstructions. Correlation between the calcium distribution on MSCT and the 3D reconstruction with the clinical findings was sought in patients undergoing the TAo procedure.

Results The vast majority of patients had calcification in the aortic arch (n = 154, 64.9%) and aortic root (n = 220, 92.8%). Of the 237 patients, only 1 patient had diffuse calcification in the ascending aorta, including the TAo zone, thus precluding a TAo procedure. MSCT and 3D reconstruction data in the 33 patients who underwent a TAo procedure, including 6 who were identified as having porcelain aorta preoperatively, correlated very well with the absence of calcium in the TAo zone during surgery. There were no post-procedure neurological events in this group.
Conclusions Conventionally defined porcelain aorta should not be considered a contraindication for performing TAVI by the TAo approach (148).

Structural Integrity of Balloon-Expandable Stents After Transcatheter Aortic Valve Replacement: Assessment by Multidetector Computed Tomography

Objectives This study sought to evaluate the structural integrity of balloon-expandable stents used in transcatheter aortic valve replacement.
Background Underexpansion, deformation, or fracture of stent frames may affect transcatheter heart valve (THV) function and durability.
Methods Patients >1 year after transcatheter aortic valve replacement underwent multidetector computed tomography. Geometry of the stent frame was assessed for circularity; eccentricity; minimum and maximum external diameter; and expansion at the inflow, mid-stent, and outflow levels, as well as for stent fracture. THV noncircularity was defined as stent eccentricity >10% (1 − minimum diameter/maximum diameter) and THV underexpansion when expansion <90% (multidetector computed tomography derived external valve area/nominal external valve area). Echocardiography was performed after implantation and annually.
Results Fifty patients underwent multidetector computed tomography at an average of 2.5 ± 0.9 years after transcatheter aortic valve replacement (35 Sapien, 8 Sapien XT, and 7 Cribier-Edwards valves [all Edwards Lifesciences, Irvine, California). The mean external diameter for the 23- and 26-mm valves was 23.3 ± 0.9 mm and 25.9 ± 0.9 mm, respectively. Circularity was present in 96% (48 of 50) and median eccentricity was 2.0% (interquartile range: 1.2% to 3.0%). Mean THV expansion was 104.1 ± 7.4%, which increased from stent inflow to outflow (100.8 ± 7.6% vs. 108.1 ± 6.9%, $p < 0.001$). Stent fracture was not observed. Underexpanded valves (8% [4 of 50]) and noncircular valves (4% [2 of 50]) demonstrated stable hemodynamic function on annual echocardiography.
Conclusions Balloon-expandable aortic valves have excellent rates of circularity with low eccentricity and maintain full expansion without stent fracture at an average 2.5 years after implantation (149).

Transcatheter Valve-In-Valve Implantation for Failed Balloon-Expandable Transcatheter Aortic Valves

Objectives This study sought to evaluate outcomes after implantation of a second transcatheter heart valve (THV-in-THV) for acute THV failure.
Background Aortic regurgitation after transcatheter aortic valve replacement (TAVR) may be valvular due to prosthetic leaflet dysfunction or paravalvular due to poor annular sealing.
Methods Patients undergoing aortic balloon-expandable TAVR at 3 centers were prospectively evaluated at baseline, intraprocedurally, at hospital discharge, and annually.
Results Of 760 patients undergoing TAVR, 21 (2.8%) received a THV-in-THV implant due to acute, severe regurgitation. Aortic regurgitation was paravalvular in 18 patients and transvalvular in the remaining 3 patients. THV-in-THV implantation was technically successful in 19 patients (90%) and unsuccessful in 2 patients (10%), who subsequently underwent open heart surgery. Mortality at 30 days and 1 year was 14.3% and 24%, respectively. After successful THV-in-THV, mean aortic valve gradient fell from 37 ± 12 mm Hg to 13 ± 5 mm Hg ($p < 0.01$); aortic valve area increased from 0.64 ± 0.14 cm^2 to 1.55 ± 0.27 cm^2 ($p < 0.01$); and paravalvular aortic regurgitation was none in 4 patients, mild in 13 patients, and moderate in 2 patients. At 1-year follow-up, 1 patient had moderate and the others had mild or no paravalvular leaks. The mean transvalvular gradient was 15 ± 4 mm Hg, which was higher than in patients undergoing conventional TAVR (11 ± 4 mm Hg, $p = 0.02$).
Conclusions THV-in-THV implantation is feasible and results in satisfactory short- and mid-term outcomes (150).

Factors Predicting and Having an Impact on the Need for a Permanent Pacemaker After CoreValve Prosthesis Implantation Using the New Accutrak Delivery Catheter System

Objectives The purpose of this study was to evaluate the need for a permanent pacemaker after transcatheter aortic valve implantation with the CoreValve prosthesis (Medtronic, Inc., Minneapolis, Minnesota) using the new Accutrak delivery system (Medtronic, Inc.).
Background The need for a permanent pacemaker is a recognized complication after transcatheter aortic valve implantation with the CoreValve prosthesis.
Methods Between April 23, 2008 and May 31, 2011, 195 consecutive patients with symptomatic aortic valve stenosis underwent transcatheter aortic valve implantation using the self-expanding CoreValve prosthesis. In 124 patients, the traditional delivery system was used, and in 71 patients, the Accutrak delivery system was used.
Results There were no significant differences in baseline electrocardiographic characteristics between the traditional system and the Accutrak patients: PR interval: 153 ± 46 mm

versus 165 ± 30 mm, p = 0.12; left bundle branch block: 22 (20.2%) versus 8 (12.7%), p = 0.21; right bundle branch block: 21 (19.3%) versus 8 (12.7%), p = 0.26. The depth of the prosthesis in the left ventricular outflow tract was greater with the traditional system than with the Accutrak system (9.6 ± 3.2 mm vs. 6.4 ± 3 mm, p < 0.001) and the need for a permanent pacemaker was higher with traditional system than with Accutrak (35.1% vs. 14.3%, p = 0.003). The predictors of the need for a pacemaker were the depth of the prosthesis in the left ventricular outflow tract (hazard ratio [HR]: 1.2, 95% confidence interval [CI]: 1.08 to 1.34, p < 0.001), pre-existing right bundle branch block (HR: 3.5, 95% CI: 1.68 to 7.29, p = 0.001), and use of the traditional system (HR: 27, 95% CI: 2.81 to 257, p = 0.004).

Conclusions The new Accutrak delivery system was associated with less deep prosthesis implantation in the left ventricular outflow tract, which could be related to the lower rate of permanent pacemaker requirement (151).

Pathology of Transcatheter Valve Therapy

Objectives This study sought to report on the pathology of transcatheter aortic valves explanted at early and late time points after transcatheter aortic valve implantation.

Background Information on pathological findings following transcatheter aortic valve implantation is scarce, particularly late after transcatheter aortic valve implantation.

Methods This study included 20 patients (13 men, median age 80 years [interquartile range: 72 to 84] years) with previous transcatheter aortic valve implantation with a valve explanted at autopsy (n = 17) or surgery (n = 3) up to 30 months after implantation (10 transapical and 10 transfemoral procedures).

Results Structural valve degeneration was not seen, although fibrous tissue ingrowth was observed at later time points with minimal effects on cusp mobility in 1 case. Minor alterations in valve configuration or placement were observed in up to 50% of cases, but they were not accompanied by substantial changes in valve function or reliably associated with chest compressions. Vascular or myocardial injury was common, especially within 30 days of transcatheter aortic valve implantation (about 69%), with the latter associated with left coronary ostial occlusion by calcified native aortic valve tissue in 2 cases. Mild to severe myocardial amyloidosis was present in nearly 33% of cases and likely played a role in the poor outcome of 3 patients. Endocarditis, migration of the valve, and embolization during the procedure led to surgical valve removal.

Conclusions Structural degeneration was not seen and minor alterations of valve configuration or placement did not affect valve function and were not reliably caused by chest compressions. Vascular or myocardial injury is very common early after transcatheter aortic valve implantation and myocardial amyloidosis represents a relatively frequent potentially significant comorbid condition (152).

Transcatheter Aortic Valve Implantation in Patients With Low-Flow, Low-Gradient Aortic Stenosis

Objectives The purpose of this study was to evaluate the efficacy and outcome of transcatheter aortic valve implantation (TAVI) in patients with low-flow, low-gradient aortic stenosis (LG-AS).

Background Patients with LG-AS have a poor prognosis with medical treatment and a high risk for surgical aortic valve replacement.

Methods Between January 2009 and June 2010, a total of 1,302 patients underwent TAVI for severe AS and were prospectively included in the multicenter German TAVI registry.

Results LG-AS was present in 149 patients (11.4%; mean age: 80.2 ± 6.3 years). In this subgroup, the EuroSCORE was significantly higher (26.8 ± 16.6 vs. 20.0 ± 13.3; p < 0.0001) compared with patients with high-gradient AS (HG-AS). The procedural success rate (LG-AS: 95.3% vs. HG-AS: 97.5%; p = 0.13) and the rate of TAVI-associated complications were comparable in both groups (new pacemaker: 27.0% vs. 28.1%; p = 0.76; cerebrovascular events: 3.4% vs. 3.1%, p = 0.83). However, post-operative low-output syndrome occurred more frequently in the LG-AS-group (LG-AS: 14.9% vs. HG-AS: 5.7%, p < 0.0001), and mortality at 30 days and 1 year was significantly higher in this subgroup (LG-AS: 12.8% and 36.9% vs. HG-AS: 7.4% and 18.1%; p < 0.001 and p < 0.0001, respectively). Post-operative New York Heart Association functional class improved, and self-assessed quality of life increased significantly, demonstrating a substantial benefit in the LG-AS group at 30 days and 1 year after TAVI.

Conclusions In high-risk patients with LG-AS, TAVI is associated with a significantly higher mortality at 30 days and at 1 year. However, long-term survivors benefit from TAVI with functional improvement and a significantly increased quality of life. Therefore, in view of the poor prognosis with medical treatment, TAVI should be considered an option in high-risk patients with LG-AS (153).

Direct Percutaneous Access Technique for Transaxillary Transcatheter Aortic Valve Implantation: "The Hamburg Sankt Georg Approach"

Objectives This study questioned whether transaxillary transcatheter aortic valve implantation (TAVI) is feasible as a true percutaneous approach using percutaneous closure devices.

Background Transaxillary TAVI is gaining increasing acceptance as an alternative to the transfemoral route; however, the access has always been done via surgical cut-down so far.

Methods Between August 2010 and September 2011, a total of 24 high-risk patients with severe aortic valvular

stenosis underwent a percutaneous TAVI procedure by direct puncture of the axillary artery without surgical cut-down. For safety reasons and as a target for the puncture, a wire was advanced via the ipsilateral brachial artery. Moreover, a balloon was placed into the subclavian artery via the femoral artery for temporary vessel blockade before percutaneous vessel closure. Vascular closure was performed using either the ProStar XL system (Abbott Vascular Devices, Redwood City, California) or 2 ProGlide systems (Abbott Vascular Devices).

Results The true percutaneous approach was successfully completed in all patients (14 left and 8 right axillary artery cases). Overall mortality at 30 days was 8.3%. Acute vascular closure device success was achieved in 17 patients (71%). Vascular closure device success rate was 100% for the ProGlide device and 37% for the ProStar device, respectively. Seven patients (29%) with failing closure devices were treated by endovascular stent graft implantation without the need for surgical repair. For the last 12 treated patients, direct closure was achieved in 11 patients.

Conclusions Direct puncture of the axillary artery for TAVI is feasible and safe if a wire is placed into the subclavian artery via the ipsilateral brachial artery (154).

Impact of Aortic Regurgitation After Transcatheter Aortic Valve Implantation: Results From the REVIVAL Trial

Objectives Understanding the severity of aortic regurgitation (AR) after transcatheter aortic valve implantation, its impact on left ventricular (LV) structure and function, and the structural factors associated with worsening AR could lead to improvements in patient selection, implantation technique, and valve design.

Background Initial studies in patients at high risk of surgical aortic valve replacement have reported both central valvular and paravalvular AR after transcatheter aortic valve implantation.

Methods Transthoracic echocardiograms were quantified from 95 patients in the REVIVAL (TRanscatheter EndoVascular Implantation of VALves) trial. Transthoracic echocardiograms were obtained before implantation of the Edwards-Sapien valve (Edwards Lifesciences, Irvine, California) and thereafter at selected intervals. Measurements included LV internal diameters and volumes, ejection fraction, aortic valve area, and the degree of aortic regurgitation. Measures of degree of native leaflet mobility, thickness, and calcification, as well as left ventricular outflow tract, aortic annulus, and aortic root diameters were also made.

Results Eighty-four patients remained after 11 were excluded; 26 (29.8%) died over a period of 3 years. At 24 h post-implantation, 75% had some degree of AR, mostly paravalvular. By 1 year, the mean AR grade increased slightly, but not significantly (1.1 ± 0.8 to 1.3 ± 0.9), and all measures of LV structure and function improved (LV ejection fraction, 50.7 ± 16.1% to 59.4 ± 14.0%). Native aortic leaflet calcification and annulus diameter correlated significantly with the severity of AR at 1 year ($p < 0.05$).

Conclusions AR after transcatheter aortic valve implantation is frequent but is rarely more than mild. Although AR progresses, it is not associated with a harmful impact on LV structure and function over the first year. Native valve calcification and aortic annulus diameter influence the degree of AR at 6 months (155).

High Platelet Reactivity on Clopidogrel Therapy Correlates With Increased Coronary Atherosclerosis and Calcification: A Volumetric Intravascular Ultrasound Study

Objectives This study sought to evaluate the relationship between platelet reactivity and atherosclerotic burden in patients undergoing percutaneous coronary intervention (PCI) with pre-intervention volumetric intravascular ultrasound (IVUS) imaging.

Background Atherosclerosis progresses by the pathologic sequence of subclinical plaque rupture, thrombosis, and healing. In this setting, increased platelet reactivity may lead to more extensive arterial thrombosis at the time of plaque rupture, leading to a more rapid progression of the disease. Alternatively, abnormal vessel wall biology with advanced atherosclerosis is known to enhance platelet reactivity. Therefore, it is possible that by either mechanism, increased platelet reactivity may be associated with greater atherosclerotic burden.

Methods This study included patients who underwent PCI with pre-intervention IVUS imaging and platelet reactivity functional assay ($P2Y_{12}$ reaction units) performed >16 h after PCI, after the stabilization of clopidogrel therapy (administered before PCI). Platelet reactivity >230 $P2Y_{12}$ reaction units defined high on-treatment platelet reactivity (HPR).

Results Among 335 patients (mean age 65.0 years, 71% men), there were 109 patients with HPR (32.5%) and 226 without HPR (67.5%), with HPR being associated with diabetes and chronic renal insufficiency. By IVUS analysis, patients with HPR had significantly greater target lesion calcium lengths, calcium arcs, and calcium indexes. Furthermore, patients with HPR tended to have longer lesions and greater volumetric dimensions, indicating higher plaque volume, larger total vessel volume, and also greater luminal volume, despite similar plaque burden. By multivariate analysis controlling for baseline clinical variables, HPR was the single consistent predictor of all IVUS parameters examined, including plaque volume, calcium length, and calcium arc.

Conclusions Increased platelet reactivity on clopidogrel treatment, defined as >230 $P2Y_{12}$ reaction units, is associated with greater coronary artery atherosclerotic disease burden and plaque calcification (156).

Noninvasive Programmed Ventricular Stimulation Early After Ventricular Tachycardia Ablation to Predict Risk of Late Recurrence

Objectives The goal of this study was to evaluate the ability of noninvasive programmed stimulation (NIPS) after ventricular tachycardia (VT) ablation to identify patients at high risk of recurrence.

Background Optimal endpoints for VT ablation are not well defined.

Methods Of 200 consecutive patients with VT and structural heart disease undergoing ablation, 11 had clinical VT inducible at the end of ablation and 11 recurred spontaneously. Of the remaining 178 patients, 132 underwent NIPS through their implantable cardioverter-defibrillator 3.1 ± 2.1 days after ablation. At 2 drive cycle lengths, single, double, and triple right ventricular extrastimuli were delivered to refractoriness. Clinical VT was defined by comparison with 12-lead electrocardiograms and stored implantable cardioverter-defibrillator electrograms from spontaneous VT episodes. Patients were followed for 1 year.

Results Fifty-nine patients (44.7%) had no VT inducible at NIPS; 49 (37.1%) had inducible nonclinical VT only; and 24 (18.2%) had inducible clinical VT. Patients with inducible clinical VT at NIPS had markedly decreased 1-year VT-free survival compared to those in whom no VT was inducible (<30% vs. >80%; p = 0.001), including 33% recurring with VT storm. Patients with inducible nonclinical VT only, had intermediate 1-year VT-free survival (65%).

Conclusions When patients with VT and structural heart disease have no VT or nonclinical VT only inducible at the end of ablation or their condition is too unstable to undergo final programmed stimulation, NIPS should be considered in the following days to further define risk of recurrence. If clinical VT is inducible at NIPS, repeat ablation may be considered because recurrence over the following year is high (157).

Heparanase Regulates Thrombosis in Vascular Injury and Stent-Induced Flow Disturbance

Objectives The purpose of this study was to examine the role of heparanase in controlling thrombosis following vascular injury or endovascular stenting.

Background The use of endovascular stents are a common clinical intervention for the treatment of arteries occluded due to vascular disease. Both heparin and heparan sulfate are known to be potent inhibitors of thrombosis. Heparanase is the major enzyme that degrades heparan sulfate in mammalian cells. This study examined the role of heparanase in controlling thrombosis following vascular injury and stent-induced flow disturbance.

Methods This study used mice overexpressing human heparanase and examined the time to thrombosis using a laser-induced arterial thrombosis model in combination with vascular injury. An ex vivo system was used to examine the formation of thrombus to stent-induced flow disturbance.

Results In the absence of vascular injury, wild type and heparanase overexpressing (HPA Tg) mice had similar times to thrombosis in a laser-induced arterial thrombosis model. However, in the presence of vascular injury, the time to thrombosis was dramatically reduced in HPA Tg mice. An ex vivo system was used to flow blood from wild type and HPA Tg mice over stents and stented arterial segments from both animal types. These studies demonstrate markedly increased thromboses on stents with blood isolated from HPA Tg mice in comparison to blood from wild type animals. We found that blood from HPA Tg animals had markedly increased thrombosis when applied to stented arterial segments from either wild type or HPA Tg mice.

Conclusions Taken together, this study's results indicate that heparanase is a powerful mediator of thrombosis in the context of vascular injury and stent-induced flow disturbance (158).

Coronary Arterial 18F-Sodium Fluoride Uptake: A Novel Marker of Plaque Biology

Objectives With combined positron emission tomography and computed tomography (CT), we investigated coronary arterial uptake of 18F-sodium fluoride (18F-NaF) and 18F-fluorodeoxyglucose (18F-FDG) as markers of active plaque calcification and inflammation, respectively.

Background The noninvasive assessment of coronary artery plaque biology would be a major advance particularly in the identification of vulnerable plaques, which are associated with specific pathological characteristics, including microcalcification and inflammation.

Methods We prospectively recruited 119 volunteers (72 ± 8 years of age, 68% men) with and without aortic valve disease and measured their coronary calcium score and 18F-NaF and 18F-FDG uptake. Patients with a calcium score of 0 were used as control subjects and compared with those with calcific atherosclerosis (calcium score >0).

Results Inter-observer repeatability of coronary 18F-NaF uptake measurements (maximum tissue/background ratio) was excellent (intra-class coefficient 0.99). Activity was higher in patients with coronary atherosclerosis (n = 106) versus control subjects (1.64 ± 0.49 vs. 1.23 ± 0.24; p = 0.003) and correlated with the calcium score (r = 0.652, p < 0.001), although 40% of those with scores >1,000 displayed normal uptake. Patients with increased coronary 18F-NaF activity (n = 40) had higher rates of prior cardiovascular events (p = 0.016) and angina (p = 0.023) and higher Framingham risk scores (p = 0.011). Quantification of coronary 18F-FDG uptake was hampered by myocardial activity and was not increased in patients with atherosclerosis versus control subjects (p = 0.498).

Conclusions 18F-NaF is a promising new approach for the assessment of coronary artery plaque biology. Prospective studies with clinical outcomes are now needed to assess

whether coronary 18F-NaF uptake represents a novel marker of plaque vulnerability, recent plaque rupture, and future cardiovascular risk. (An Observational PET/CT Study Examining the Role of Active Valvular Calcification and Inflammation in Patients With Aortic Stenosis; NCT01358513) (159).

Prolongation of QTc and Risk of Stroke: The REGARDS (REasons for Geographic and Racial Differences in Stroke) Study

Objectives The purpose of this study was to examine the association between prolongation of QT interval corrected for heart rate (QTc) with incident stroke.

Background Unlike cardiovascular morbidity and mortality, little is known about the relationship between QTc and risk of stroke.

Methods A total of 27,411 participants age 45 years and older without previous stroke from the REGARDS (REasons for Geographic and Racial Differences in Stroke) study were included in this analysis. QTc was calculated using Framingham formula (QTc_{Fram}). Stroke cases were identified and adjudicated during up to 8.2 years of follow-up (median, 5.1 years).

Results The risk of incident stroke in study participants with prolonged QTc_{Fram} was almost 3 times the risk in those with normal QTc_{Fram} (hazard ratio [HR] [95% confidence interval (CI)]: 2.88 [2.12 to 3.92], $p < 0.0001$). After adjustment for demographics (age, race, and sex), traditional stroke risk factors (antihypertensive medication use, systolic blood pressure, current smoking, diabetes, left ventricular hypertrophy, atrial fibrillation, and previous cardiovascular disease), warfarin use, aspirin use, QRS duration and use of QTc-prolonging drugs, the risk of stroke remained significantly high (HR [95% CI]: 1.67 [1.16 to 2.41], $p = 0.0061$) and was consistent across several subgroups of REGARDS study participants. Similar results were obtained when the risk of stroke was estimated per 1-SD increase in QTc_{Fram}, (HR [95% CI]: 1.12 [1.03 to 1.21], $p = 0.0053$ in multivariable-adjusted model) and when other QTc correction formulas including those of Hodge, Bazett, and Fridericia were used.

Conclusions QTc prolongation is associated with a significantly increased risk of incident stroke independent of traditional stroke risk factors. Examining the risk of stroke associated with QTc-prolonging drugs may be warranted (160).

New Oral Anticoagulants in Atrial Fibrillation and Acute Coronary Syndromes: ESC Working Group on Thrombosis—Task Force on Anticoagulants in Heart Disease Position Paper

Until recently, vitamin K antagonists were the only available oral anticoagulants, but with numerous limitations that prompted the introduction of new oral anticoagulants targeting the single coagulation enzymes thrombin (dabigatran) or factor Xa (apixaban, rivaroxaban, and edoxaban) and given in fixed doses without coagulation monitoring. Here we review the pharmacology and the results of clinical trials with these new agents in stroke prevention in atrial fibrillation and secondary prevention after acute coronary syndromes, providing perspectives on their future incorporation into clinical practice. In phase III trials in atrial fibrillation, compared with warfarin, dabigatran etexilate 150 mg B.I.D. reduced the rates of stroke/systemic embolism without any difference in major bleeding; dabigatran etexilate 110 mg B.I.D. had similar efficacy with decreased bleeding; apixaban 5 mg B.I.D. reduced stroke, systemic embolism, and mortality as well as major bleeding; and rivaroxaban 20 mg Q.D. was noninferior to warfarin for stroke and systemic embolism without a difference in major bleeding. All these agents reduced intracranial hemorrhage. Edoxaban is currently being evaluated in a further large phase III trial. Apixaban and rivaroxaban were evaluated in phase III trials for prevention of recurrent ischemia in patients with acute coronary syndromes who were mostly receiving dual antiplatelet therapy, with conflicting results on efficacy but consistent results for increased major bleeding. Overall, the new oral anticoagulants are poised to replace vitamin K antagonists for many patients with atrial fibrillation and may have a role after acute coronary syndromes. Although convenient to administer and manage, they present challenges that need to be addressed (161).

A Randomized Controlled Trial in Second-Generation Zotarolimus-Eluting Resolute Stents Versus Everolimus-Eluting Xience V Stents in Real-World Patients: The TWENTE Trial

Objectives The aim of this study was to compare the safety and efficacy of Resolute zotarolimus-eluting stents (ZES) (Medtronic Cardiovascular, Santa Rosa, California) with Xience V everolimus-eluting stents (EES) (Abbott Vascular Devices, Santa Clara, California) at 1-year follow-up.

Background Only 1 randomized trial previously compared these stents.

Methods This investigator-initiated, patient-blinded, randomized noninferiority study had limited exclusion criteria (acute ST-segment elevation myocardial infarctions not eligible). Patients ($n = 1,391$; 81.4% of eligible population) were randomly assigned to ZES ($n = 697$) or EES ($n = 694$). Liberal use of stent post-dilation was encouraged. Cardiac biomarkers were systematically assessed. The primary endpoint was target vessel failure (TVF), a composite of cardiac death, myocardial infarction not clearly attributable to non-target vessels, and clinically indicated target-vessel revascularization. An external independent research organization performed clinical event adjudication (100% follow-up data available). Analysis was by intention-to-treat.

Results Acute coronary syndromes were present in 52% and "off-label" feature in 77% of patients. Of the lesions, 70% were type B2/C; the post-dilation rate was very high (82%). In ZES and EES, TVF occurred in 8.2% and 8.1%, respectively (absolute risk-difference 0.1%; 95% confidence interval: −2.8% to 3.0%, $p_{noninferiority} = 0.001$). There was no significant between-group difference in TVF components. The definite-or-probable stent thrombosis rates were relatively low and similar for ZES and EES (0.9% and 1.2%, respectively, $p = 0.59$). Definite stent thrombosis rates were also low (0.58% and 0%, respectively, $p = 0.12$). In EES, probable stent thrombosis beyond day 8 was observed only in patients not adhering to dual antiplatelet therapy.
Conclusions Resolute ZES were noninferior to Xience V EES in treating "real-world" patients with a vast majority of complex lesions and "off-label" indications for drug-eluting stents, which were implanted with liberal use of post-dilation. (The Real-World Endeavor Resolute Versus XIENCE V Drug-Eluting SteNt Study: Head-to-head Comparison of Clinical Outcome After Implantation of Second Generation Drug-eluting Stents in a Real World Scenario; NCT01066650) (162).

A Randomized, Multicenter, Single-Blinded Trial Comparing Paclitaxel-Coated Balloon Angioplasty With Plain Balloon Angioplasty in Drug-Eluting Stent Restenosis: The PEPCAD-DES Study

Objectives This study sought to define the impact of paclitaxel-coated balloon angioplasty for treatment of drug-eluting stent restenosis compared with uncoated balloon angioplasty alone.
Background Drug-coated balloon angioplasty is associated with favorable results for treatment of bare-metal stent restenosis.
Methods In this prospective, single-blind, multicenter, randomized trial, the authors randomly assigned 110 patients with drug-eluting stent restenoses located in a native coronary artery to paclitaxel-coated balloon angioplasty or uncoated balloon angioplasty. Dual antiplatelet therapy was prescribed for 6 months. Angiographic follow-up was scheduled at 6 months. The primary endpoint was late lumen loss. The secondary clinical endpoint was a composite of cardiac death, myocardial infarction attributed to the target vessel, or target lesion revascularization.
Results There was no difference in patient baseline characteristics or procedural results. Angiographic follow-up rate was 91%. Treatment with paclitaxel-coated balloon was superior to balloon angioplasty alone with a late loss of 0.43 ± 0.61 mm versus 1.03 ± 0.77 mm ($p < 0.001$), respectively. Restenosis rate was significantly reduced from 58.1% to 17.2% ($p < 0.001$), and the composite clinical endpoint was significantly reduced from 50.0% to 16.7% ($p < 0.001$), respectively.
Conclusions Paclitaxel-coated balloon angioplasty is superior to balloon angioplasty alone for treatment of drug-eluting stent restenosis. (PEPCAD DES–Treatment of DES-In-Stent Restenosis With SeQuent® Please Paclitaxel Eluting PTCA Catheter [PEPCAD-DES]; NCT00998439) (163).

The PROFI Study (Prevention of Cerebral Embolization by Proximal Balloon Occlusion Compared to Filter Protection During Carotid Artery Stenting): A Prospective Randomized Trial

Objectives The objective of this study was to compare the cerebral embolic load of filter-protected versus proximal balloon–protected carotid artery stenting (CAS).
Background Randomized trials comparing filter-protected CAS with carotid endarterectomy revealed a higher periprocedural stroke rate after CAS. Proximal balloon occlusion may be more effective in preventing cerebral embolization during CAS than filters.
Methods Patients undergoing CAS with cerebral embolic protection for internal carotid artery stenosis were randomly assigned to proximal balloon occlusion or filter protection. The primary endpoint was the incidence of new cerebral ischemic lesions assessed by diffusion-weighted magnetic resonance imaging. Secondary endpoints were the number and volume of new ischemic lesions and major adverse cardiovascular and cerebral events (MACCE).
Results Sixty-two consecutive patients (mean age: 71.7 years, 76.4% male) were randomized. Compared with filter protection (n = 31), proximal balloon occlusion (n = 31) resulted in a significant reduction in the incidence of new cerebral ischemic lesions (45.2% vs. 87.1%, $p = 0.001$). The number (median [range]: 2 [0 to 13] vs. 0 [0 to 4], $p = 0.0001$) and the volume (0.47 [0 to 2.4] cm^3 vs. 0 [0 to 0.84] cm^3, $p = 0.0001$) of new cerebral ischemic lesions were significantly reduced by proximal balloon occlusion. Lesions in the contralateral hemisphere were found in 29.0% and 6.5% of patients (filter vs. balloon occlusion, respectively, $p = 0.047$). The 30-day MACCE rate was 3.2% and 0% for filter versus balloon occlusion, respectively (p = NS).
Conclusions In this randomized trial of patients undergoing CAS, proximal balloon occlusion as compared with filter protection significantly reduced the embolic load to the brain (164).

A Multicenter Randomized Trial Comparing Amphilimus- With Paclitaxel-Eluting Stents in De Novo Native Coronary Artery Lesions

Objectives This study sought to demonstrate the noninferiority of polymer-free amphilimus-eluting stents (Cre8, CID, Saluggia, Italy) versus permanent-polymer paclitaxel-eluting stents (Taxus Liberté, Boston Scientific, Natick, Massachusetts) in de novo percutaneous coronary intervention.
Background Although the efficacy of the drug-eluting stent has been well established, the risk-benefit balance is

still suboptimal, and the safety of polymers remains uncertain.

Methods Patients undergoing percutaneous coronary intervention for de novo lesions were randomly assigned 1:1 to Cre8 or Taxus Liberté stents. Primary endpoint was 6-month angiographic in-stent late lumen loss (LLL) within a noninferiority scope. Six-month intravascular ultrasound was performed in 20% of the patients. All patients will be clinically followed up to 5 years.

Results Out of 323 patients enrolled, 162 received Cre8 and 161 Taxus Liberté stents. In-stent LLL was significantly lower in Cre8 group (0.14 ± 0.36 mm vs. 0.34 ± 0.40 mm, p noninferiority <0.0001, p superiority <0.0001). Clinical endpoints (cardiac death, myocardial infarction, target lesion revascularization, and stent thrombosis) up to 12 months did not differ significantly between the groups.

Conclusions The Cre8 stent in de novo lesions showed significantly lower in-stent LLL at 6 months than the Taxus Liberté stent did, with a trend toward better 12-month clinical safety and efficacy results. (International Randomized Comparison Between DES Limus Carbostent and Taxus Drug-Eluting Stents in the Treatment of De Novo Coronary Lesions [NEXT]; NCT01373502) (165).

Cross-Sectional Computed Tomographic Assessment Improves Accuracy of Aortic Annular Sizing for Transcatheter Aortic Valve Replacement and Reduces the Incidence of Paravalvular Aortic Regurgitation

Objectives In an effort to define the gold standard for annular sizing for transcatheter aortic valve replacement (TAVR), we sought to critically analyze and compare the predictive value of multiple measures of the aortic annulus for post-TAVR paravalvular (PV) regurgitation and then assess the impact of a novel cross-sectional computed tomographic (CT) approach to annular sizing.

Background Recent studies have shown clear discrepancies between conventional 2-dimensional (2D) echocardiographic and CT measurements. In terms of aortic annular measurement for TAVR, such findings have lacked the outcome analysis required to inform clinical practice.

Methods The discriminatory value of multiple CT annular measures for post-TAVR PV aortic regurgitation was compared with 2D echocardiographic measures. TAVR outcomes with device selection according to aortic annular sizing using a traditional 2D transesophageal echocardiography–guided or a novel CT-guided approach were also studied.

Results In receiver-operating characteristic models, cross-sectional CT parameters had the highest discriminatory value for post-TAVR PV regurgitation: This was with the area under the curve for [maximal cross-sectional diameter minus prosthesis size] of 0.82 (95% confidence interval: 0.69 to 0.94; p < 0.001) and that for [circumference-derived cross-sectional diameter minus prosthesis size] of 0.81 (95% confidence interval: 0.7 to 0.94; p < 0.001). In contrast, traditional echocardiographic measures were nondiscriminatory in relation to post-TAVR PV aortic regurgitation. The prospective application of a CT-guided annular sizing approach resulted in less PV aortic regurgitation of grade worse than mild after TAVR (7.5% vs. 21.9%; p = 0.045).

Conclusions Our data lend strong support to 3-dimensional cross-sectional measures, using CT as the new gold standard for aortic annular evaluation for TAVR with the Edwards SAPIEN device (166).

Impact of Metabolic Syndrome on Procedural Outcomes in Patients With Atrial Fibrillation Undergoing Catheter Ablation

Objectives The aim of this study was to investigate impact of metabolic syndrome (MS) on outcomes of catheter ablation in patients with atrial fibrillation (AF) in terms of recurrence and quality of life (QoL).

Background MS, a proinflammatory state with hypertension, diabetes, dyslipidemia, and obesity, is presumed to be a close associate of AF.

Methods In this prospective study, 1,496 consecutive patients with AF undergoing first ablation (29% with paroxysmal AF, 26% with persistent AF, and 45% with long-standing persistent AF) were classified into those with MS (group 1; n = 485) and those without MS (group 2; n = 1,011). Patients were followed for recurrence and QoL. The Medical Outcomes Study SF-36 Health Survey was used to assess QoL at baseline and 12 month after ablation.

Results After 21 ± 7 months of follow-up, 189 patients in group 1 (39%) and 319 in group 2 (32%) had arrhythmia recurrence (p = 0.005). When stratified by AF type, patients with nonparoxysmal AF in group 1 failed more frequently compared with those in group 2 (150 [46%] vs. 257 [35%], p = 0.002); no difference existed in the subgroup with paroxysmal AF (39 [25%] vs. 62 [22%], p = 0.295). Group 1 patients had significantly lower baseline scores on all SF-36 Health Survey subscales. At follow-up, both mental component summary (Δ5.7 ± 2.5, p < 0.001) and physical component summary (Δ9.1 ± 3.7, p < 0.001) scores improved in group 1, whereas only mental component summary scores (Δ4.6 ± 2.8, p = 0.036) were improved in group 2. In the subgroup with nonparoxysmal AF, MS, sex, C-reactive protein ≥0.9 mg/dl, and white blood cell count were independent predictors of recurrence.

Conclusions Baseline inflammatory markers and the presence of MS predicted higher recurrence after single-catheter ablation only in patients with nonparoxysmal AF. Additionally, significant improvements in QoL were observed in the post-ablation MS population (167).

3-Dimensional Aortic Annular Assessment by Multidetector Computed Tomography Predicts Moderate or Severe Paravalvular Regurgitation After Transcatheter Aortic Valve Replacement: A Multicenter Retrospective Analysis

Objectives This study sought to analyze multidetector computed tomography (MDCT) 3-dimensional aortic annular dimensions for the prediction of paravalvular aortic regurgitation (PAR) following transcatheter aortic valve replacement (TAVR).

Background Moderate or severe PAR after TAVR is associated with increased morbidity and mortality.

Methods A total of 109 consecutive patients underwent MDCT pre-TAVR with a balloon expandable aortic valve. Differences between transcatheter heart valve (THV) size and MDCT measures of annular size (mean diameter, area, and circumference) were analyzed concerning prediction of PAR. Patients with THV malposition (n = 7) were excluded. In 50 patients, MDCT was repeated after TAVR to assess THV eccentricity (1 − short diameter/long diameter) and expansion (MDCT measured THV area/nominal THV area).

Results Moderate or severe PAR (13 of 102) was associated with THV undersizing (THV diameter − mean diameter = −0.7 ± 1.4 mm vs. 0.9 ± 1.8 mm for trivial to mild PAR, $p < 0.01$). The difference between THV size and MDCT annular size was predictive of PAR (mean diameter: area under the curve [AUC]: 0.81, 95% confidence interval [CI]: 0.68 to 0.88; area: AUC: 0.80, 95% CI: 0.65 to 0.90; circumference: AUC: 0.76, 95% CI: 0.59 to 0.91). Annular eccentricity was not associated with PAR (AUC: 0.58, 95% CI: 0.46 to 0.75). We found that 35.3% (36 of 102) and 45.1% (46 of 102) of THVs were undersized relative to the MDCT mean diameter and area, respectively. THV oversizing relative to the annular area was not associated with THV eccentricity or underexpansion (oversized vs. undersized THVs; expansion: 102.7 ± 5.3% vs. 106.1 ± 5.6%, $p = 0.03$; eccentricity: median: 1.7% [interquartile range: 1.4% to 3.0%] vs. 1.7% [interquartile range: 1.1% to 2.7%], $p = 0.28$).

Conclusions MDCT-derived 3-dimensional aortic annular measurements are predictive of moderate or severe PAR following TAVR. Oversizing of THVs may reduce the risk of moderate or severe PAR (168).

A Randomized, 2-Period, Crossover Design Study to Assess the Effects of Dexlansoprazole, Lansoprazole, Esomeprazole, and Omeprazole on the Steady-State Pharmacokinetics and Pharmacodynamics of Clopidogrel in Healthy Volunteers

Objectives The aim of this study was to assess the effects of different proton pump inhibitors (PPIs) on the steady-state pharmacokinetics and pharmacodynamics of clopidogrel.

Background Metabolism of clopidogrel requires cytochrome P450s (CYPs), including CYP2C19. However, PPIs may inhibit CYP2C19, potentially reducing the effectiveness of clopidogrel.

Methods A randomized, open-label, 2-period, crossover study of healthy subjects (n = 160, age 18 to 55 years, homozygous for CYP2C19 extensive metabolizer genotype, confined, standardized diet) was conducted. Clopidogrel 75 mg with or without a PPI (dexlansoprazole 60 mg, lansoprazole 30 mg, esomeprazole 40 mg, or, as a positive control to maximize potential interaction and demonstrate assay sensitivity, omeprazole 80 mg) was given daily for 9 days. Pharmacokinetics and pharmacodynamics were assessed on days 9 and 10. Pharmacodynamic end-points were vasodilator-stimulated phosphoprotein $P2Y_{12}$ platelet reactivity index, maximal platelet aggregation to 5 and 20 μmol/l adenosine diphosphate, and VerifyNow P2Y12 platelet response units.

Results Pharmacokinetic and pharmacodynamic responses with omeprazole demonstrated assay sensitivity. The area under the curve for clopidogrel active metabolite decreased significantly with esomeprazole but not with dexlansoprazole or lansoprazole. Similarly, esomeprazole but not dexlansoprazole or lansoprazole significantly reduced the effect of clopidogrel on vasodilator-stimulated phosphoprotein platelet reactivity index. All PPIs decreased the peak plasma concentration of clopidogrel active metabolite (omeprazole > esomeprazole > lansoprazole > dexlansoprazole) and showed a corresponding order of potency for effects on maximal platelet aggregation and platelet response units.

Conclusions Generation of clopidogrel active metabolite and inhibition of platelet function were reduced less by the coadministration of dexlansoprazole or lansoprazole with clopidogrel than by the coadministration of esomeprazole or omeprazole. These results suggest that the potential of PPIs to attenuate the efficacy of clopidogrel could be minimized by the use of dexlansoprazole or lansoprazole rather than esomeprazole or omeprazole. (A Study of the Effects of Multiple Doses of Dexlansoprazole, Lansoprazole, Omeprazole or Esomeprazole on the Pharmacokinetics and Pharmacodynamics of Clopidogrel in Healthy Participants; NCT00942175) (169).

Provoked Exercise Desaturation in Patent Foramen Ovale and Impact of Percutaneous Closure

Objectives This study was designed to assess the prevalence of provoked exercise desaturation (PED) in patients with patent foramen ovale (PFO) referred for cardiovascular evaluation and to evaluate the impact of PFO closure.

Background Platypnea orthodeoxia syndrome is a rare, mechanistically obscure consequence of PFO that results in oxygen desaturation during postural changes. In our clinical experience, however, it is far less common than desaturation during exercise.

Methods This was a single-center prospective study of 50 patients with newly diagnosed PFO. Each patient

underwent standardized assessment for arterial oxygen saturation with pulse oximetry during postural changes and stair climbing exercise. Provoked exercise desaturation was defined as a desaturation of at least 8% from baseline to <90%. All patients who underwent closure were reevaluated 3 months after the procedure. Those with baseline PED were similarly reassessed for desaturation at follow-up.
Results Mean age of the cohort was 46 ± 17 years, 74% were female, 30% had migraines, and 48% had experienced a cerebrovascular event. Seventeen patients (34%) demonstrated PED. Provoked exercise desaturation patients seemed demographically similar to non-PED patients. Ten PED patients underwent PFO closure (2 surgical, and 8 percutaneous). Drop in oxygen saturation was improved by an average of 10.1 ± 4.2% after closure ($p < 0.001$), and New York Heart Association functional class improved by a median of 1.5 classes (interquartile range: 0.75 to 2.00, $p = 0.008$).
Conclusions One-third of patients referred for assessment of PFO experience oxygen desaturation during stair exercise. Closure of PFO seems to ameliorate this phenomenon and improve functional status (170).

Successful Recanalization of Chronic Total Occlusions Is Associated With Improved Long-Term Survival

Objectives This study investigated the impact of procedural success on mortality following chronic total occlusion (CTO) percutaneous coronary intervention (PCI) in a large cohort of patients in the drug-eluting stent era.
Background Despite advances in expertise and technologies, many patients with CTO are not offered PCI.
Methods A total of 6,996 patients underwent elective PCI for stable angina at a single center (2003 to 2010), 836 (11.9%) for CTO. All-cause mortality was obtained to 5 years (median: 3.8 years; interquartile range: 2.0 to 5.4 years) and stratified according to successful chronic total occlusion (sCTO) or unsuccessful chronic total occlusion (uCTO) recanalization. Major adverse cardiac events (MACE) included myocardial infarction (MI), urgent revascularization, stroke, or death.
Results A total of 582 (69.6%) procedures were successful. Stents were implanted in 97.0% of successful procedures (mean: 2.3 ± 0.1 stents per patient, 73% drug-eluting). Prior revascularization was more frequent among uCTO patients: coronary artery bypass grafting (CABG) (16.5% vs. 7.4%; $p < 0.0001$), PCI (36.0% vs. 21.2%; $p < 0.0001$). Baseline characteristics were otherwise similar. Intraprocedural complications, including coronary dissection, were more frequent in unsuccessful cases (20.5% vs. 4.9%; $p < 0.0001$), but did not affect in-hospital MACE (3% vs. 2.1%; p = NS). All-cause mortality was 17.2% for uCTO and 4.5% for sCTO at 5 years ($p < 0.0001$). The need for CABG was reduced following sCTO (3.1% vs. 22.1%; $p < 0.0001$). Multivariate analysis demonstrated that procedural success was independently predictive of mortality (hazard ratio [HR]: 0.32 [95% confidence interval (CI): 0.18 to 0.58]), which persisted when incorporating a propensity score (HR: 0.28 [95% CI: 0.15 to 0.52]).
Conclusions Successful CTO PCI is associated with improved survival out to 5 years. Adoption of techniques and technologies to improve procedural success may have an impact on prognosis (171).

Relationship Between Fractional Flow Reserve and Angiographic and Intravascular Ultrasound Parameters in Ostial Lesions: Major Epicardial Vessel Versus Side Branch Ostial Lesions

Objectives This study sought to assess the relationship of coronary angiography, intravascular ultrasound (IVUS) and fractional flow reserve (FFR) between major epicardial vessel (MV) and side branch (SB) ostial lesions.
Background Evaluation of ostial lesions is clinically very important. However, anatomical parameters have limitations in the prediction of the functional significance of coronary stenoses.
Methods IVUS and FFR measurement were performed in 93 lesions (MV: 38, SB: 55). Optimal angiographic and IVUS criteria and their diagnostic accuracy for functionally significant stenoses (FFR ≤0.8) were assessed.
Results In MV ostial lesions, FFR had correlation with angiographic percent diameter stenosis ($r = -0.68$, $p < 0.001$), minimum lumen area (MLA) by IVUS ($r = 0.55$, $p < 0.001$), percent plaque burden ($r = -0.42$, $p = 0.011$), and percent area stenosis ($r = -0.49$, $p = 0.003$). Meanwhile, FFR had no correlation with angiographic percent diameter stenosis ($r = -0.067$, $p = 0.635$) and weak correlation with MLA ($r = 0.30$, $p = 0.026$) in SB ostial lesions. In MV ostial lesions, best cutoff value of angiographic percent diameter stenosis, MLA, percent plaque burden, and percent area stenosis to determine the functional significance was 53%, 3.5 mm^2, 70%, and 50%. However, a statistically significant cutoff value of percent diameter stenosis and MLA could not be found in SB ostial lesions.
Conclusions The relations between angiographic/IVUS parameters and FFR were different between MV and SB ostial lesions. Angiographic and IVUS parameters had poor diagnostic accuracy in predicting the functional significance of SB ostial lesions. (Main Branch Versus Side Branch Ostial Lesion; NCT01335659) (172).

Use of a Novel Crossing and Re-Entry System in Coronary Chronic Total Occlusions That Have Failed Standard Crossing Techniques: Results of the FAST-CTOs (Facilitated Antegrade Steering Technique in Chronic Total Occlusions) Trial

Objectives This study sought to examine the efficacy and safety of 3 novel devices to recanalize coronary chronic total occlusions (CTOs).

Background Successful percutaneous coronary intervention (PCI) of CTOs improves clinical outcome in appropriately selected patients. CTO PCI success, however, remains suboptimal.
Methods A new crossing catheter and re-entry system was evaluated in a prospective, multicenter, single-arm trial of CTO lesions refractory to standard PCI techniques. The primary efficacy endpoint was the frequency of true lumen guidewire placement distal to the CTO (technical success).
Results Enrollment included 147 patients with 150 CTOs. The mean lesion length was 41 ± 17 mm. A crossing catheter crossed 56 lesions into the distal true lumen, and a re-entry catheter facilitated tapered-wire cannulation of the distal lumen in 59 CTOs initially crossed subintimally (77% technical success). Success in the first 75 CTOs was 67%, rising to 87% in the last 75 CTOs. Mean fluoroscopy and procedure times were 45 ± 16 min and 90 ± 12 min, respectively, each significantly shorter than in historical controls ($p < 0.0001$ for both). Coronary perforation occurred in 14 cases (9.3%), requiring treatment in 3 cases (prolonged balloon inflation, with additional coil embolization in 1 case). No tamponade or hemodynamic instability occurred. Six patients had periprocedural non–ST-segment elevation myocardial infarction. No emergency surgery, ST-segment elevation myocardial infarction, or cardiac reintervention occurred. Two deaths occurred within 30 days, neither as a direct result of the procedure. The 30-day major adverse cardiac event rate was 4.8%.
Conclusions In CTOs failing standard techniques, use of a new crossing and re-entry system results in a high success rate without increasing complications (173).

Risk Factors and Outcomes of Post-Procedure Heart Blocks After Transcatheter Device Closure of Perimembranous Ventricular Septal Defect

Objectives The aim of this study was to analyze the risk factors and mid-term outcomes associated with post-procedure heart blocks (PPHBs) after transcatheter closure of perimembranous ventricular septal defect (pmVSD).
Background The development of heart blocks remains a major challenge for transcatheter closure of pmVSD.
Methods Transcatheter closure of pmVSD was carried out in 228 patients. Electrocardiography and 24-h Holter monitoring were performed before the procedure, within 1 week after the procedure, then 1, 3, 6, and 12 months, and every year thereafter.
Results Thirty-three patients (14.5%) who received transcatheter closure of pmVSD developed PPHBs. PPHBs included right bundle branch block (57.6%), left bundle branch block (24.2%), and atrioventricular block (18.2%). High-degree atrioventricular blocks occurred in 4 patients and recovered to normal conduction after intravenous administration of hydrocortisone. PPHBs recovered to normal conduction in 21 patients by the time of hospital discharge. Compared with the patients without PPHBs, the patients suffering PPHBs were characterized by a significantly longer distance between the aortic valve and the defect (DAVD), a shorter distance from the lower rim of the defect to the septal leaflet of the tricuspid valve (DLRD-SLTV), and a larger diameter difference between the occluder and ventricular septal defect (DDOV). The earlier the PPHBs developed after the procedure, the more difficult the recovery to normal conduction.
Conclusions The outcome of PPHBs after transcatheter closure of pmVSD was satisfactory, as most patients recovered to normal conduction. Measurements of DLRD-SLTV, DAVD, and DDOV may be useful in predicting the incidence of PPHBs (174).

A Percutaneous Treatment Algorithm for Crossing Coronary Chronic Total Occlusions

Coronary chronic total occlusions (CTOs) are frequently identified during coronary angiography and remain the most challenging lesion group to treat. Patients with CTOs are frequently left unrevascularized due to perceptions of high failure rates and technical complexity even if they have symptoms of coronary disease or ischemia. In this review, the authors describe a North American contemporary approach for percutaneous coronary interventions for CTO. Two guide catheters are placed to facilitate seamless transition between antegrade wire–based, antegrade dissection re-entry–based, and retrograde (wire or dissection re-entry) techniques, the "hybrid" interventional strategy. After dual coronary injection is performed, 4 angiographic parameters are assessed: 1) clear understanding of location of the proximal cap using angiography or intravascular ultrasonography; 2) lesion length; 3) presence of branches, as well as size and quality of the target vessel at the distal cap; and 4) suitability of collaterals for retrograde techniques. On the basis of these 4 characteristics, an initial strategy and rank order hierarchy for technical approaches is established. Radiation exposure, contrast utilization, and procedure time are monitored throughout the procedure, and thresholds are established for intraprocedural strategy conversion to maximize safety, efficiency, and effectiveness (175).

Nobori Stent Shows Less Vascular Inflammation and Early Recovery of Endothelial Function Compared With Cypher Stent

Objectives The current study sought to examine inflammation at the stented segments of Nobori (Terumo Corporation, Tokyo, Japan) and Cypher (Cordis, Miami, Florida) drug-eluting stents (DES), as well as free radical production and endothelial function of the adjacent non-stented segments in a pig coronary model.
Background Nobori is a novel DES, incorporating a biolimus A9-eluting biodegradable polymer coated only on the abluminal surface of the stent. These unique features may favorably affect inflammation and endothelial function, as

compared to the currently marketed DES. Presently, preclinical data on direct comparison of the various generations of DES are not available.

Methods A total of 18 DES were implanted in pig coronary arteries and subsequently explanted at 1 month. Stented segments were assessed by angiography and histology. Ex vivo vasomotor function and superoxide production in segments proximal and distal to the stent were determined. The vasoconstriction, endothelial-dependent relaxation, and endothelial-independent relaxation of proximal and distal nonstented segments were measured.

Results Histological evaluation revealed lower inflammatory response with Nobori than with Cypher DES. There is trend for lower angiographic percentage diameter stenosis in Nobori versus Cypher groups ($p = 0.054$). There was increased endothelium-dependent relaxation, decreased endothelin-1–mediated contraction, and less superoxide production in the vessel segments proximal and distal to Nobori versus Cypher stents.

Conclusions Our data show significantly lower inflammatory response in the stented segments, and rapid recovery of endothelial function of peristent segments in the Nobori group compared with Cypher DES group at 1 month in porcine coronary artery model (176).

Maximal Hyperemia in the Assessment of Fractional Flow ReserveIntracoronary Adenosine Versus Intracoronary Sodium Nitroprusside Versus Intravenous Adenosine: The NASCI (Nitroprussiato Versus Adenosina nelle Stenosi Coronariche Intermedie) Study

Objectives This study sought to compare increasing doses of intracoronary (IC) adenosine or IC sodium nitroprusside versus intravenous (IV) adenosine for fractional flow reserve (FFR) assessment.

Background Maximal hyperemia is the critical prerequisite for FFR assessment. Despite IV adenosine currently representing the recommended approach, IC administration of adenosine or other coronary vasodilators constitutes a valuable alternative in everyday practice. However, it is surprisingly unclear which IC strategy allows the achievement of FFR values comparable to IV adenosine.

Methods Fifty intermediate coronary stenoses ($n = 45$) undergoing FFR measurement were prospectively and consecutively enrolled. Hyperemia was sequentially induced by incremental boli of IC adenosine (ADN) (60 μg ADN60, 300 μg ADN300, 600 μg ADN600), by IC sodium nitroprusside (NTP) (0.6 μg/kg bolus) and by IV adenosine infusion (IVADN) (140 μg/kg/min). FFR values, symptoms, and development of atrioventricular block were recorded.

Results Incremental doses of IC adenosine and NTP were well tolerated and associated with fewer symptoms than IVADN. Intracoronary adenosine doses (0.881 ± 0.067, 0.871 ± 0.068, and 0.868 ± 0.070 with ADN60, ADN300, and ADN600, respectively) and NTP (0.892 ± 0.072) induced a significant decrease of FFR compared with baseline levels ($p < 0.001$). Notably, ADN600 only was associated with FFR values similar to IVADN (0.867 ± 0.072, $p = 0.28$). Among the 10 patients with FFR values ≤ 0.80 with IVADN, 5 were correctly identified also by ADN60, 6 by ADN300, 7 by ADN600, and 6 by NTP.

Conclusions Intracoronary adenosine, at doses higher than currently suggested, allows obtaining FFR values similar to IV adenosine. Intravenous adenosine, which remains the gold standard, might thus be reserved for those lesions with equivocal FFR values after high (up to 600 μg) IC adenosine doses (177).

Differences in Neointimal Thickness Between the Adluminal and the Abluminal Sides of Malapposed and Side-Branch Struts in a Polylactide Bioresorbable Scaffold: Evidence In Vivo About the Abluminal Healing Process

Objectives The goal of this study was to describe the neointimal healing on the abluminal side (ABL) of malapposed (ISA) struts and nonapposed side-branch (NASB) struts in terms of coverage by optical coherence tomography (OCT) and in comparison with the adluminal side (ADL).

Background The neointimal healing on the ABL of ISA and NASB struts has never to our knowledge been explored in vivo and could be involved in the correction of acute malapposition. The bioresorbable vascular scaffold (BVS) is made of a translucent polymer that enables imaging of the ABL with OCT.

Methods Patients enrolled in the ABSORB B (ABSORB Clinical Investigation Cohort B) study were treated with implantation of a BVS and imaged with OCT at 6 months. Thickness of coverage on the ADL and ABL of ISA and NASB struts was measured by OCT.

Results Twenty-eight patients were analyzed; 114 (2.4%) struts were malapposed or at side branches. In 76 ISA struts (89.4%) and 29 NASB struts (100%), the thickness of ABL coverage was >30 μm. Coverage was thicker on the ABL than on the ADL side (101 vs. 71 μm; 95% confidence interval [CI] of the difference: 20 to 40 μm). In 70 struts (60.7%, 95% CI: 50.6% to 70.0%), the neointimal coverage was thicker on the ABL, versus only 20 struts (18.5%, 95% CI: 11.6% to 28.1%) with thicker neointimal coverage on the ADL side (odds ratio: 3.35, 95% CI: 2.22 to 5.07).

Conclusions Most of the malapposed and side-branch struts are covered on the ABL side 6 months after BVS implantation, with thicker neointimal coverage than on the ADL side. The physiological correction of acute malapposition involves neointimal growth from the strut to the vessel wall or bidirectional. (ABSORB Clinical Investigation, Cohort B [ABSORB B]; NCT00856856) (178).

A Practical Guide to Multimodality Imaging of Transcatheter Aortic Valve Replacement

The advent of transcatheter aortic valve replacement (TAVR) is one of the most widely anticipated advances in the care of patients with severe aortic stenosis. This procedure is unique in many ways, one of which is the need for a multimodality imaging team-based approach throughout the continuum of the care of TAVR patients. Pre-procedural planning, intra-procedural implantation optimization, and long-term follow-up of patients undergoing TAVR require the expert use of various imaging modalities, each of which has its own strengths and limitations. Divided into 3 sections (pre-procedural, intraprocedural, and long-term follow-up), this review offers a single source for expert opinion and evidence-based guidance on how to incorporate the various modalities at each step in the care of a TAVR patient. Although much has been learned in the short span of time since TAVR was introduced, recommendations are offered for clinically relevant research that will lead to refinement of best practice strategies for incorporating multimodality imaging into TAVR patient care (179).

Feasibility and Safety of Dabigatran Versus Warfarin for Periprocedural Anticoagulation in Patients Undergoing Radiofrequency Ablation for Atrial Fibrillation: Results From a Multicenter Prospective Registry

Objectives The purpose of this study was to evaluate the feasibility and safety of periprocedural dabigatran during atrial fibrillation (AF) ablation.

Background AF ablation requires optimal periprocedural anticoagulation for minimizing bleeding and thromboembolic complications. The safety and efficacy of dabigatran as a periprocedural anticoagulant for AF ablation are unknown.

Methods We performed a multicenter, observational study from a prospective registry including all consecutive patients undergoing AF ablation in 8 high-volume centers in the United States. All patients receiving dabigatran therapy who underwent AF ablation on periprocedural dabigatran, with the dose held on the morning of the procedure, were matched by age, sex, and type of AF with an equal number of patients undergoing AF ablation with uninterrupted warfarin therapy over the same period.

Results A total of 290 patients, including 145 taking periprocedural dabigatran and an equal number of matched patients taking uninterrupted periprocedural warfarin, were included in the study. The mean age was 60 years with 79% being male and 57% having paroxysmal AF. Both groups had a similar $CHADS_2$ score, left atrial size, and left ventricular ejection fraction. Three thromboembolic complications (2.1%) occurred in the dabigatran group compared with none in the warfarin group ($p = 0.25$). The dabigatran group had a significantly higher major bleeding rate (6% vs. 1%; $p = 0.019$), total bleeding rate (14% vs. 6%; $p = 0.031$), and composite of bleeding and thromboembolic complications (16% vs. 6%; $p = 0.009$) compared with the warfarin group. Dabigatran use was confirmed as an independent predictor of bleeding or thromboembolic complications (odds ratio: 2.76, 95% confidence interval: 1.22 to 6.25; $p = 0.01$) on multivariate regression analysis.

Conclusions In patients undergoing AF ablation, periprocedural dabigatran use significantly increases the risk of bleeding or thromboembolic complications compared with uninterrupted warfarin therapy (180).

Functional Measurement of Coronary Stenosis

Fractional flow reserve (FFR) is considered nowadays as the gold standard for invasive assessment of physiologic stenosis significance and an indispensable tool for decision making in coronary revascularization. Use of FFR in the catheterization laboratory accurately identifies which lesions should be stented and improves the outcome in most elective clinical and angiographic conditions. Recently, FFR has been upgraded to a class IA classification in multivessel percutaneous coronary intervention in the guidelines on coronary revascularization of the European Society of Cardiology. In this state-of-the-art paper, the basic concept of FFR and its application, characteristics, and use in several subsets of patients are discussed from a practical point of view (181).

Morphometric Assessment of Coronary Stenosis Relevance With Optical Coherence Tomography: A Comparison With Fractional Flow Reserve and Intravascular Ultrasound

Objectives The study sought to assess the diagnostic efficiency of optical coherence tomography (OCT) in identifying hemodynamically severe coronary stenoses as determined by fractional flow reserve (FFR). Concomitant OCT and intravascular ultrasound (IVUS) area measurements were performed in a subgroup of patients to compare the diagnostic efficiency of both techniques.

Background The value of OCT to determine stenosis severity remains unsettled.

Methods Sixty-one stenoses with intermediate angiographic severity were studied in 56 patients. Stenoses were labeled as severe if FFR $\leq$0.80. OCT interrogation was performed in all cases, with concomitant IVUS imaging in 47 cases.

Results Angiographic stenosis severity was 50.9 $\pm$ 8% diameter stenosis with 1.28 $\pm$ 0.3 mm minimal lumen diameter. FFR was $\leq$0.80 in 28 (45.9%) stenoses. An overall moderate diagnostic efficiency of OCT was found (area under the curve [AUC]: 0.74; 95% confidence interval [CI]: 0.61 to 0.84), with sensitivity/specificity of 82%/63% associated with an optimal cutoff value of 1.95 mm^2. Comparison of the results in patients with simultaneous IVUS and OCT imaging revealed no significant differences in the

diagnostic efficiency of OCT (AUC: 0.70; 95% CI: 0.55 to 0.83) and IVUS (AUC. 0.63; 95% CI: 0.47 to 0.77; $p = 0.19$). Sensitivity/specificity for IVUS was 67%/65% for an optimal cutoff value of 2.36 mm^2. In the subgroup of small vessels (reference diameter <3 mm) OCT showed a significantly better diagnostic efficiency (AUC: 0.77; 95% CI: 0.60 to 0.89) than IVUS (AUC: 0.63; 95% CI: 0.46 to 0.78) to identify functionally significant stenoses ($p = 0.04$).
Conclusions OCT has a moderate diagnostic efficiency in identifying hemodynamically severe coronary stenoses. Although OCT seems slightly superior to IVUS for this purpose (particularly in vessels <3 mm), its low specificity precludes its use as a substitute of FFR for functional stenosis assessment (182).

Consensus Standards for Acquisition, Measurement, and Reporting of Intravascular Optical Coherence Tomography Studies: A Report From the International Working Group for Intravascular Optical Coherence Tomography Standardization and Validation

Objectives The purpose of this document is to make the output of the International Working Group for Intravascular Optical Coherence Tomography (IWG-IVOCT) Standardization and Validation available to medical and scientific communities, through a peer-reviewed publication, in the interest of improving the diagnosis and treatment of patients with atherosclerosis, including coronary artery disease.
Background Intravascular optical coherence tomography (IVOCT) is a catheter-based modality that acquires images at a resolution of ~10 μm, enabling visualization of blood vessel wall microstructure in vivo at an unprecedented level of detail. IVOCT devices are now commercially available worldwide, there is an active user base, and the interest in using this technology is growing. Incorporation of IVOCT in research and daily clinical practice can be facilitated by the development of uniform terminology and consensus-based standards on use of the technology, interpretation of the images, and reporting of IVOCT results.
Methods The IWG-IVOCT, comprising more than 260 academic and industry members from Asia, Europe, and the United States, formed in 2008 and convened on the topic of IVOCT standardization through a series of 9 national and international meetings.
Results Knowledge and recommendations from this group on key areas within the IVOCT field were assembled to generate this consensus document, authored by the Writing Committee, composed of academicians who have participated in meetings and/or writing of the text.
Conclusions This document may be broadly used as a standard reference regarding the current state of the IVOCT imaging modality, intended for researchers and clinicians who use IVOCT and analyze IVOCT data (183).

Mechanical Aortic Valve Replacement in Young Women Planning on Pregnancy: Maternal and Fetal Outcomes Under Low Oral Anticoagulation, a Pilot Observational Study on a Comprehensive Pre-Operative Counseling Protocol

Objectives This pilot prospective observational study aimed to evaluate the maternal and fetal outcomes of pregnancies under low-dose oral anticoagulation therapy after aortic mechanical replacement.
Background Need for valve replacement is still an issue for young women with native valve disease who are planning on future pregnancy. Choice of replacement device is a challenging clinical task.
Methods A comprehensive pre-operative counseling protocol to guide choice of replacement device was developed. The pre-operative anticoagulation trial to determine the warfarin daily dosage needed to reach target international normalized ratio (INR) represented the main stem of such protocol. Pregnancies on low-dose anticoagulation therapy (target INR: 1.5 to 2.5) were allowed in a highly selected subset of mechanical aortic valve recipients.
Results Twenty-two patients of 40 originally referred for native valve disease surgery requiring valve replacement, safely underwent the pre-operative anticoagulation challenge. No maternal or fetal complications were detected in 16 pregnancies under low oral anticoagulation. Patterns of warfarin daily dosage and induced INRs were characterized during pregnancy.
Conclusions In this small sample observational study, a pre-operative anticoagulation therapy trial helped young women scheduled for valve replacement to acquire complete information as to the choice of prosthetic device. In selected third-generation mechanical aortic prosthesis recipients, low-dose anticoagulation therapy seems safe and feasible for both mother and fetus. Further studies are needed to validate this approach (184).

Randomized Trial of Optimal Treatment Strategies for In-Stent Restenosis After Drug-Eluting Stent Implantation

Objectives The purpose of this study is to compare the efficacy of the treatment strategies for in-stent restenosis (ISR) of drug-eluting stents (DES) according to the morphologic pattern of restenosis.
Background Optimal treatment strategies for ISR within DES have not been adequately addressed yet.
Methods Patients with ISR of DES were randomized according to the lesion length to compare outcomes of sirolimus-eluting stent (SES) versus cutting balloon angioplasty for focal type (≤10 mm) and SES versus everolimus-eluting stent (EES) for diffuse type (>10 mm). The primary endpoint was in-segment late loss at 9 months. Overall 162 patients, 96 with focal ISR and 66 with diffuse ISR, were enrolled.

Results In focal lesions, in-segment late loss was significantly higher in the cutting balloon group (n = 48) than in the SES group (n = 48; 0.25 mm, interquartile range [IQR]: −0.01 to 0.68 mm vs. 0.06 mm, IQR: −0.08 to 0.17 mm; p = 0.04). Consequently, in-segment restenosis rate tended to be higher in the cutting balloon group than in the SES group (20.7% vs. 3.1%, p = 0.06) with comparable incidences of the composite of death, myocardial infarction, or target vessel revascularization at 12 months of clinical follow up (6.3% vs. 6.3%, p > 0.99). In 66 cases of diffuse ISR, in-segment late loss (0.11 mm, IQR: −0.02 to 0.30 mm; vs. 0.00 mm, IQR: −0.08 to 0.25 mm; p = 0.64), in-segment restenosis rate (5.0% vs. 14.3%, p = 0.32), and the composite incidence of death, myocardial infarction, or target lesion revascularization (9.6% vs. 8.8%, p > 0.99) did not differ between SES group (n = 32) and EES group (n = 34).

Conclusions For lesions of focal DES restenosis, repeat implantation of SES is more effective in reducing late luminal loss and subsequent restenosis rate than cutting balloon angioplasty. For diffuse DES restenosis, implantation of SES or EES is comparably effective in terms of angiographic and clinical outcomes (185).

Current Perspectives on Coronary Chronic Total Occlusions: The Canadian Multicenter Chronic Total Occlusions Registry

Objectives The purpose of this study was to determine the prevalence, clinical characteristics, and management of coronary chronic total occlusions (CTOs) in current practice.

Background There is little evidence in contemporary literature concerning the prevalence, clinical characteristics, and treatment decisions regarding patients who have coronary CTOs identified during coronary angiography.

Methods Consecutive patients undergoing nonurgent coronary angiography with CTO were prospectively identified at 3 Canadian sites from April 2008 to July 2009. Patients with previous coronary artery bypass graft surgery or presenting with acute ST-segment elevation myocardial infarction were excluded. Detailed baseline clinical, angiographic, electrocardiographic, and revascularization data were collected.

Results Chronic total occlusions were identified in 1,697 (18.4%) patients with significant coronary artery disease (>50% stenosis in ≥1 coronary artery) who were undergoing nonemergent angiography. Previous history of myocardial infarction was documented in 40% of study patients, with electrocardiographic evidence of Q waves corresponding to the CTO artery territory in only 26% of cases. Left ventricular function was normal in >50% of patients with CTO. Half the CTOs were located in the right coronary artery. Almost half the patients with CTO were treated medically, and 25% underwent coronary artery bypass graft surgery (CTO bypassed in 88%). Percutaneous coronary intervention was done in 30% of patients, although CTO lesions were attempted in only 10% (with 70% success rate).

Conclusions Chronic total occlusions are common in contemporary catheterization laboratory practice. Prospective studies are needed to ascertain the benefits of treatment strategies of these complex patients (186).

Platelet Biology and Response to Antiplatelet Therapy in Women: Implications for the Development and Use of Antiplatelet Pharmacotherapies for Cardiovascular Disease

Women are underrepresented in cardiovascular studies, even as their preponderance in the aging population steadily increases. Although concerns have been raised about the differential benefit of antiplatelet medications for women, the propensity for increased bleeding among women has also been recognized. A better understanding of the factors contributing to the observed sex-related differences in platelet biology is warranted. These factors include differences in the frequency and expression of genetic polymorphisms affecting platelet responsiveness to agonists (with and without antiplatelet therapies), which might be obtained through population-based studies and in large controlled clinical trials; inflammatory marker levels and their influence on atherothrombotic risk, and the role of specific hormones in mediating platelet activation and function. Knowledge gained about these mechanistic factors might inform the development of sex-specific antithrombotic treatment regimens that confer optimized safety and efficacy (187).

Histopathologic Characterization of Chronic Radiofrequency Ablation Lesions for Pulmonary Vein Isolation

Objectives This study describes the histopathologic and electrophysiological findings in patients with recurrence of atrial fibrillation (AF) after pulmonary vein (PV) isolation who underwent a subsequent surgical maze procedure.

Background The recovery of PV conduction is commonly responsible for recurrence of AF after catheter-based PV isolation.

Methods Twelve patients with recurrent AF after acutely successful catheter-based antral PV isolation underwent a surgical maze procedure. Full-thickness surgical biopsy specimens were obtained from the PV antrum in areas of visible endocardial scar. Before biopsy, intraoperative epicardial electrophysiological recordings were taken from each PV using a circular mapping catheter.

Results Twenty-two PVs were biopsied from the 12 patients 8 ± 11 months after ablation. Eleven of the 22 specimens (50%) revealed transmural scar, and 11 (50%) showed viable myocardium with or without scar. Each biopsy specimen demonstrated evidence of injury, most commonly endocardial thickening (n = 21 [95%]) and

fibrous scar (n = 18 [82%]). Seven of the 22 specimens (32%) showed conduction block at surgery. Transmural scar was more likely to be seen in the biopsy specimens from the PVs with conduction block than in specimens from the PVs showing reconnection. However, viable myocardium alone or mixed with scar was seen in 2 specimens from PVs with conduction block.

Conclusions PVs showing electrical reconnection after catheter-based antral ablation frequently reveal anatomic gaps or nontransmural lesions at the sites of catheter ablation. Nontransmural lesions are noted in some PVs with persistent conduction block, suggesting that lesion geometry may influence PV conduction. The histological findings show that nontransmural ablation can produce a dynamic cellular substrate with features of reversible injury. Delayed recovery from injury may explain late recurrences of AF after PV isolation (188).

The Clinical Impact of Incomplete Left Atrial Appendage Closure With the Watchman Device in Patients With Atrial Fibrillation: A PROTECT AF (Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients With Atrial Fibrillation) Substudy

Objectives The purpose of this study was to investigate the frequency and clinical impact of incomplete left atrial appendage (LAA) sealing and consequent peri-device residual blood flow in patients undergoing percutaneous LAA closure with the Watchman device (Atritech, Inc., Plymouth, Minnesota).

Background During percutaneous LAA closure for stroke prophylaxis, the geometric variability of the LAA ostium may result in an incomplete seal of the LAA. On the one hand, this could enhance thrombus formation and embolization of thrombi around the device into the circulation; on the other hand, the relatively small size of these leaks may preclude clinically relevant embolizations.

Methods Patients randomly assigned to device implantation in the PROTECT AF (Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients With Atrial Fibrillation) trial were analyzed. Transesophageal echocardiography was performed at 45 days, 6 months, and 12 months. Per the study protocol, patients discontinued warfarin therapy if the 45-day Transesophageal echocardiogram revealed either minimal or no peri-device flow (jet $\leq$5 mm width). The impact of peri-device flow severity, defined as minor, moderate, or major ($<$1 mm, 1 mm to 3 mm, $>$3 mm, respectively) on the composite primary efficacy endpoint (stroke, systemic embolism, and cardiovascular death) is expressed as hazard ratio (HR) with 95% confidence interval (CI).

Results Transesophageal echocardiography follow-up revealed that 32.0% of implanted patients had at least some degree of peri-device flow at 12 months. The HR of the primary efficacy endpoint per 1 mm larger per-device flow was 0.84 (95% CI: 0.62 to 1.14; p = 0.256). Compared to patients with no peri-device flow, the HRs were 0.85 (95% CI: 0.11 to 6.40), 0.83 (95% CI: 0.33 to 2.09), and 0.48 (95% CI: 0.11 to 2.09) for minor, moderate, and major peri-device flow, respectively (p = 0.798). Compared to patients with no peri-device flow who discontinued warfarin, the HR for patients with any peri-device flow and continuing warfarin was 0.63 (95% CI: 0.14 to 2.71; p = 0.530).

Conclusions These data indicate that residual peri-device flow into the LAA after percutaneous closure with the Watchman device was common, and is not associated with an increased risk of thromboembolism. This finding should be interpreted with caution as the low event rate decreases the confidence of this conclusion (189).

Prasugrel Versus Tirofiban Bolus With or Without Short Post-Bolus Infusion With or Without Concomitant Prasugrel Administration in Patients With Myocardial Infarction Undergoing Coronary Stenting: The FABOLUS PRO (Facilitation through Aggrastat By drOpping or shortening Infusion Line in patients with ST-segment elevation myocardial infarction compared to or on top of PRasugrel given at loading dOse) Trial

Objectives The authors sought to compare the effect on inhibition of platelet aggregation (IPA) of prasugrel therapy versus tirofiban bolus with or without a post-bolus short drug infusion in ST-segment elevation myocardial infarction (STEMI) patients.

Background The degree and rapidity of IPA after prasugrel alone with or without concomitant glycoprotein IIb/IIIa inhibition in STEMI patients is unknown.

Methods A total of 100 STEMI patients randomly received prasugrel 60 mg versus 25 μg/kg tirofiban bolus with or without post-bolus 2-h infusion of tirofiban, with or without concomitant prasugrel. IPA at light transmission aggregometry was performed throughout 24 h. The primary endpoint was IPA stimulated with 20 μmol/l adenosine diphosphate (ADP) at 30 min.

Results At 30 min, patients in the prasugrel group showed a significantly lower IPA to 20 μmol/l ADP stimulation as compared with tirofiban-treated patients (36 ± 35 vs. 87 ± 31, p $<$ 0.0001). Similarly, patients taking prasugrel showed a suboptimal degree of platelet inhibition for at least 2 h compared with tirofiban patients. Post-bolus tirofiban infusion was necessary to maintain a high level of IPA beyond 1 h after bolus administration if concomitant clopidogrel was given, whereas the bolus-only tirofiban and concomitant prasugrel led to the higher and more consistent IPA levels after both ADP and thrombin receptor-activating peptide stimuli than either therapy alone.

Conclusions Our study shows that prasugrel administration leads to a suboptimal IPA for at least 2 h in STEMI

patients. Yet, prasugrel, given in association with a bolus only of glycoprotein IIb/IIIa inhibitor, obviates the need of post-bolus infusion and almost completely abolishes residual variability of IPA after treatment. (Facilitation through Aggrastat By drOpping or shortening Infusion Line in patients with ST-segment elevation myocardial infarction compared to or on top of PRasugrel given at loading dOse [The FABOLUS PRO trial]; NCT01336348) (190).

Long-Term Follow-Up After Treatment of Coronary In-Stent Restenosis With a Paclitaxel-Coated Balloon Catheter

Objectives This study presents long-term clinical follow-up, including binary restenosis rate and major adverse cardiovascular events, of the PACCOCATH-ISR (Treatment of In-Stent Restenosis by Paclitaxel Coated PTCA Balloons) I and II trial.

Background The PACCOCATH-ISR trial was a first-in-human study with a drug-coated balloon catheter and the first study for the treatment of coronary ISR with a drug-coated balloon. So, far no long-term follow-up data have been presented.

Methods This study enrolled 108 patients in a randomized, double-blinded multicenter trial on the efficacy and safety of a paclitaxel-coated balloon (3 $\mu g/mm^2$ balloon surface; PACCOCATH [Bayer AG, Germany]) compared with an uncoated balloon. The main inclusion criteria were a diameter stenosis of $\geq$70% and <30-mm length with a vessel diameter of 2.5 to 3.5 mm. The primary endpoint was angiographic late lumen loss in-segment after 6 months. Combined antiplatelet therapy was continued only for 1 month followed by treatment with aspirin alone.

Results During a follow-up of 5.4 $\pm$ 1.2 years, the clinical event rate was significantly reduced in patients treated with the drug-coated balloon (major adverse cardiovascular events: 59.3% vs. 27.8%, $p = 0.009$), which was mainly driven by the reduction of target lesion revascularization from 38.9% to 9.3% ($p = 0.004$).

Conclusions Treatment of coronary ISR with paclitaxel-coated balloon catheters is safe and persistently reduces repeat revascularization during long-term follow-up. The initial results were sustained over the 5-year period. (Treatment of In-Stent Restenosis by Paclitaxel Coated PTCA Balloons [PACCOCATH ISR I]; NCT00106587. Treatment of In-Stent Restenosis by Paclitaxel Coated PTCA Balloons [PACCOCATH ISR II]; NCT00409981) (191).

A Therapeutic Window for Platelet Reactivity for Patients Undergoing Elective Percutaneous Coronary Intervention: Results of the ARMYDA-PROVE (Antiplatelet therapy for Reduction of MYocardial Damage during Angioplasty–Platelet Reactivity for Outcome Validation Effort) Study

Objectives This study sought to validate the ability of the VerifyNow P2Y12 assay (Accumetrics, San Diego, California) in predicting both ischemic and bleeding events after elective percutaneous coronary intervention (PCI).

Background High and low levels of platelet reactivity are associated with ischemic and bleeding events, respectively, after PCI.

Methods A total of 732 patients on dual antiplatelet therapy undergoing elective PCI were recruited. Platelet reactivity was measured before PCI. The primary endpoint was the 30-day incidence of net adverse clinical events (NACE), defined as the occurrence of ischemic or bleeding events, in relation to $P2Y_{12}$ reaction unit (PRU) distribution.

Results At receiver-operating characteristic curve analysis, PRU values could significantly discriminate between patients with and without bleeding events (area under the curve [AUC]: 0.72; 95% confidence interval [CI]: 0.65 to 0.80; $p < 0.0001$) and those with and without ischemic events (AUC: 0.68; 95% CI: 0.61 to 0.76; $p < 0.0001$). The optimal cutoffs for bleeding (PRU $\leq$178) and ischemic events (PRU $\geq$239) were used to define 3 groups: low platelet reactivity (LPR) (LPR = PRU $\leq$178), normal platelet reactivity (NPR) (NPR = PRU 179 to 238), and high platelet reactivity (HPR) (HPR = PRU $\geq$239). The incidence of NACE was 14.1% in the LPR group, 7.8% in the NPR group ($p = 0.025$ vs. LPR group), and 15.4% in the HPR group ($p = 0.005$ vs. NPR group). At multivariate analysis, PRU values in the NPR group were an independent predictor of reduced risk of 30-day NACE (odds ratio: 0.47, 95% CI: 0.27 to 0.81).

Conclusions A therapeutic window for platelet reactivity measured with the VerifyNow P2Y12 assay can be identified using specific thresholds that define a group of patients at lower risk for both ischemic and bleeding events. Adjunctive measures may be beneficial in patients with higher or lower platelet reactivity in order to improve clinical outcomes after PCI (192).

Cigarette Smoking Is Associated With a Dose-Response Effect in Clopidogrel-Treated Patients With Diabetes Mellitus and Coronary Artery Disease: Results of a Pharmacodynamic Study

Objectives This study sought to assess the presence of a dose-response effect of cigarette smoking and its impact on high on-treatment platelet reactivity (HPR) in patients with diabetes mellitus treated with clopidogrel.

Background Cigarette smoking is an inducer of cytochrome P450 1A2, a hepatic enzyme involved in clopidogrel metabolism. If cigarette smoking is associated with a dose-response effect on pharmacodynamic measures in clopidogrel-treated patients is unknown.

Methods A total of 134 type 2 diabetes mellitus patients on maintenance aspirin and clopidogrel therapy were studied. Patients were divided into 3 groups according to cotinine levels: <3 ng/ml (nonsmokers), 3 to 199 ng/ml (light smokers), and $\geq$200 ng/ml (heavy smokers). Platelet

function was assessed by light transmittance aggregometry, VerifyNow P2Y12 assay (Accumetrics, San Diego, California), and vasodilator-stimulated phosphoprotein. Rates of HPR were defined using established cutoff values.

Results A dose-response effect was observed for all pharmacodynamic parameters tested. Serum cotinine levels were inversely associated with platelet reactivity as assessed by light transmittance aggregometry using 5 and 20 μmol/l adenosine diphosphate ($p < 0.0001$ for all). Accordingly, platelet disaggregation increased with levels of serum cotinine ($p < 0.0001$). Similar results were found with $P2Y_{12}$ reaction units ($p < 0.0001$) and inhibition of platelet aggregation ($p = 0.005$) as defined by VerifyNow P2Y12 testing, and platelet reactivity index ($p = 0.002$) as assessed by vasodilator-stimulated phosphoprotein. Higher serum cotinine levels were significantly associated with lower rates of HPR, as defined according to various pharmacodynamic cutoff measures.

Conclusions Cigarette smoking is associated with a dose-response effect on clopidogrel-induced antiplatelet effects and lower rates of HPR in diabetes mellitus patients (193).

Comparison of Drug-Eluting and Bare-Metal Stents for Primary Percutaneous Coronary Intervention With or Without Abciximab in ST-Segment Elevation Myocardial Infarction: DEBATER: The Eindhoven Reperfusion Study

Objectives The goal of this study was to demonstrate superiority of sirolimus-eluting stents (SES) over bare-metal stents (BMS) and of abciximab over no abciximab in primary percutaneous coronary intervention (PCI).

Background Drug-eluting stents (DES) are increasingly used in primary PCI, but the recommendations for use in primary PCI are based on a few randomized controlled trials with selected patients. The usefulness of abciximab in primary PCI is not established.

Methods Nine hundred seven patients referred to the Catharina Hospital were randomized to SES or BMS, and to abciximab or no abciximab in a prospective, randomized, open 2 × 2 factorial trial with blinded evaluation. Primary endpoint was major adverse cardiac and cerebrovascular events (MACCE), defined as the composite of death, myocardial infarction (MI), stroke, repeat revascularization, and bleeding at 1 year (stent arm) and the composite of death, target vessel MI, target vessel revascularization (TVR), and bleeding at 30 days (abciximab arm).

Results At 1 year, the rate of MACCE was lower in the SES arm (16.5% vs. 25.8%, $p = 0.001$), mainly driven by less repeat revascularization (9.8% vs. 16.8%; $p = 0.003$) and without influencing the cumulative incidence of death and MI (5.2% vs. 5.8%; $p = 0.68$). At 30 days, the rate of the composite of death, target vessel MI, TVR, and bleeding was lower in the abciximab arm (8.2% vs. 12.4%, $p = 0.04$), mainly driven by less TVR due to less stent thrombosis (1.2% vs.7.4%, $p < 0.001$). However, bleeding complications occurred more frequently in the abciximab group (5.7% vs. 2.8%, $p = 0.03$).

Conclusions Primary PCI with SES reduces adverse events at 1 year, mainly by reduction of repeat revascularization, whereas abciximab reduces early stent thrombosis, at the expense of more bleeding complications. (Comparison of Drug Eluting and Bare Metal Stents With or Without Abciximab in ST Elevation Myocardial Infarction [DEBATER]; NCT00986050) (194).

Clinical Evaluation of a Paclitaxel-Eluting Balloon for Treatment of Femoropopliteal Arterial Disease: 12-Month Results From a Multicenter Italian Registry

Objectives This study evaluated the use of a paclitaxel-eluting balloon (PEB) for treatment of femoropopliteal arterial disease.

Background Conventional balloon angioplasty and stenting in this setting is associated with high restenosis rates within 12 months. Recent data suggest that PEB use may reduce restenosis. Twelve-month outcomes following PEB use with provisional stenting are described.

Methods This prospective registry enrolled patients (Rutherford class 2 to 4) with reference vessel diameter of 3 to 7 mm and lesion/occlusion length ≤15 cm. Endpoints included primary patency rate, target lesion revascularization, and changes in Rutherford class and ankle-brachial index. Walking capacity, absolute claudication distance, and quality of life were also assessed.

Results The registry enrolled 105 patients. Baseline ankle-brachial index was 0.56 ± 0.15. Baseline Rutherford classification was class 2 or 3 for most patients (91.5%). Most lesions were located in the superficial femoral artery (77.1%). Mean lesion length was 76.3 ± 38.3 mm; 29.8% of lesions were total occlusions. The device was successfully used in all patients and only 12.3% of lesions required stenting. At 12-month follow-up, 92 of 105 patients (87.6%) were evaluable; the primary patency rate was 83.7%; the target lesion revascularization rate was 7.6%; 85.6% of patients were Rutherford class 0 or 1; and mean ankle-brachial index was 0.86 ± 0.15. Quality of life and absolute claudication distance showed significant improvement from baseline to 12-month follow-up.

Conclusions PEB treatment of femoropopliteal arterial disease resulted in consistent clinical improvement across multiple endpoints with a low rate of stenting and target lesion revascularization (195).

Impact of Sex on Clinical and Angiographic Outcomes Among Patients Undergoing Revascularization With Drug-Eluting Stents

Objectives The goal of this study was to investigate sex-based differences in long-term clinical and angiographic outcomes after coronary revascularization with drug-eluting stents (DES).

Background The impact of sex on clinical and angiographic outcomes following revascularization with DES is not well established.
Methods Individual patient data from 3 all-comers randomized DES trials (SIRTAX, LEADERS, RESOLUTE All-Comers) were pooled. Of 5,011 patients, 4,885 (97.5%) completed 2-year follow-up (1,164 women, 3,721 men). Protocol-mandated angiographic follow-up was available for 1,561 lesions (351 among women, 1,210 among men). The primary endpoint was the composite of cardiac death and myocardial infarction (MI) at 2 years.
Results At baseline, women, as compared with men, were older, more frequently had diabetes, obesity, and hypertension, less frequently had smoking habits, previous MI, and previous surgical revascularization, and had a smaller reference diameter of the target vessel as well as a lower SYNTAX score. After adjustment for baseline differences, women and men had a similar risk of cardiac death or MI (odds ratio [OR]: 1.13, 95% confidence interval [CI]: 0.82 to 1.56, p = 0.44), cardiac death (OR: 1.04, 95% CI: 0.61 to 1.80, p = 0.87), and MI (OR: 1.07, 95% CI: 0.75 to 1.53, p = 0.71) at 2 years. Similarly, risks of target lesion revascularization (OR: 1.09, 95% CI: 0.77 to 1.54, p = 0.62), target vessel revascularization (OR: 0.88, 95% CI: 0.63 to 1.22, p = 0.43), and definite or probable stent thrombosis (OR: 0.73, 95% CI: 0.38 to 1.38, p = 0.33) were comparable for women and men. Follow-up angiography showed no differences in terms of in-stent late loss (0.18 ± 0.54 mm vs. 0.20 ± 0.99 mm, p = 0.76) and in-segment binary restenosis (8.5% vs. 8.5%, p = 0.76).
Conclusions The unrestricted use of DES is associated with similar long-term safety and efficacy among women and men with coronary artery disease. (Sirolimus-Eluting Versus Paclitaxel-Eluting Stents for Coronary Revascularization [SIRTAX]; NCT00297661, LEADERS Trial Limus Eluted From A Durable Versus ERodable Stent Coating [LEADERS]; NCT00389220, RESOLUTE-III All-comers Trial: A Randomized Comparison of a Zotarolimus-Eluting Stent With an Everolimus-Eluting Stent for Percutaneous Coronary Intervention [RESOLUTE All-Comers]; NCT00617084) (196).

Transcatheter Mitral Valve-in-Valve Implantation in Patients With Degenerated Bioprostheses

Objectives This study reports the results of a series of transapical mitral valve-in-valve implantations and aims to offer guidance on technical aspects of the procedure.
Background Mitral valve reoperations due to failing bioprostheses are associated with high morbidity and mortality. Transcatheter techniques may evolve as complementary approaches to surgery in these high-risk patients.
Methods Six patients (age 75 ± 15 years) received transapical implantation of a balloon-expandable pericardial heart valve into a degenerated bioprosthesis (range 27 to 31 mm) in mitral position at our institution. All patients were considered high risk for surgical valve replacement (logistic EuroSCORE: 33 ± 15%) after evaluation by an interdisciplinary heart team. Procedural and clinical outcomes were analyzed.
Results Implantation was successful in all patients with reduction of mean transvalvular gradients from 11.3 ± 5.2 mm Hg to 5.5 ± 3.6 mm Hg (p = 0.016) and median regurgitation from grade 3.0 (interquartile range [IQR]: 2.7 to 3.1) to 0 (IQR: 0 to 1.0, p = 0.033) with trace paravalvular regurgitation remaining in 2 patients. Apical bleeding occurred in 2 patients requiring rethoracotomy in 1 and resuscitation in a second patient, the latter of whom died on postoperative day 6. In the remaining patients, median New York Heart Association functional class improved from 3.0 (IQR: 3.0 to 3.5) to 2.0 (IQR: 1.5 to 2.0, p = 0.048) over a median follow-up of 70 (IQR: 25.5 to 358) days.
Conclusions With acceptable results in a high-risk population, transapical mitral valve-in-valve implantation can be considered as a complementary approach to reoperative mitral valve surgery in select patients (197).

Different Prognostic Significance of High On-Treatment Platelet Reactivity as Assessed by the Verify: Now P2Y12 Assay After Coronary Stenting in Patients With and Without Acute Myocardial Infarction

Objectives This study compared the prognostic role of high on-treatment platelet reactivity (HTPR) in predicting thrombotic events in a Korean population undergoing percutaneous coronary intervention (PCI) in the acute myocardial infarction (AMI) and non-AMI setting.
Background The prognostic significance and optimal cutoff of HTPR might differ according to a given clinical condition, such as AMI and ethnicity.
Methods On-treatment platelet reactivity was measured with a VerifyNow P2Y12 assay (Accumetrics, San Diego, California) in 1,226 patients (824 men; age 65 ± 10 years), including 413 AMI cases, 12 to 24 h after PCI between March 2008 and March 2010. The prevalence of cardiovascular (CV) events defined as a composite of death from CV causes, nonfatal myocardial infarction, or stent thrombosis at 1-year follow-up were compared according to HTPR between patients with and without AMI.
Results The optimal cutoff for HTPR was 272 IU of the $P2Y_{12}$ reaction unit (PRU) (area under the curve: 0.708; 95% confidence interval [CI]: 0.607 to 0.809, p = 0.03), which was the upper-tertile threshold. Among AMI patients, 1-year CV events occurred more frequently in patients with versus without HTPR (n = 14 [8.8%] vs. n = 1 [0.4%], p < 0.001), whereas there was no difference in the composite endpoint on the basis of HTPR in patients without AMI (n = 7 [2.8%] vs. n = 8 [1.4%], p = 0.193).
Conclusions Increased residual platelet reactivity is related to post-discharge CV events in subjects with AMI, whereas

the prognostic significance of HTPR seems to be attenuated in patients with stable coronary disease after PCI (198).

Renal Denervation for Hypertension

Systemic hypertension is a major burden to the individual and society. Its association with major adverse cardiac and cerebral events and favorable effects of antihypertensive therapy are undisputed. However, despite multidrug therapy, blood pressures are frequently suboptimally controlled. Moreover, adverse drug effects often interfere with patients' lifestyles and affect compliance. Therefore, alternative treatment strategies have been explored. Most recently, attention has been redirected to the sympathetic nervous system (SNS) in the pathogenesis of hypertension. In addition, interruption of the renal SNS in humans with resistant hypertension has been studied with promising results. The following review provides an overview of the anatomy and physiology of the renal SNS, the rational for manipulating the SNS, and the results of therapeutic renal sympathetic denervation (199).

Incidence of Overall Bleeding in Patients Treated With Intra-Aortic Balloon Pump During Percutaneous Coronary Intervention: 12-Year Milan Experience

Objectives This study aims to report a "real-world" experience of in hospital complications and clinical outcome of a large cohort of consecutive patients who underwent percutaneous coronary intervention (PCI) with intra-aortic balloon pump counterpulsation (IABP) support, from a tertiary care center over a 12-year period.
Background The incidence of vascular complications in patients treated with PCI and IABP is expected to be higher due to simultaneous puncture of femoral arteries, larger IABP sheath size, and longer duration of IABP therapy.
Methods A total of 360 consecutive patients (mean age of 65.9 ± 11.2 years; 80.6% male) who required an IABP support during percutaneous PCI were classified into 3 groups: Urgent: 133 patients (36.9%) admitted with acute coronary syndrome in whom IABP therapy was started before urgent PCI; Emergent: 56 patients (15.6%) in whom emergent IABP insertion was required to manage hypotension during PCI; and Elective: 171 patients (47.5%) with stable angina pectoris in whom IABP was inserted before elective PCI. Overall bleeding was defined according to the newest the Bleeding Academic Research Consortium (BARC) definition criteria.
Results BARC bleeding occurred in 68 patients (19%), with the highest incidence noted in the Urgent group (31.1%), in comparison with the Emergent (26.8%) and Elective (7%) groups, $p < 0.0001$. Bleeding related to the IABP access site was 7.5%, which accounted for 82% of any access site–related bleeding. It was significantly higher in the Urgent group (12.8%) compared with the Elective (4.1%) and Emergent (5.4%) groups. At multivariate analysis, IABP treatment duration and renal impairment were the only independent predictors of BARC bleeding.
Conclusions Bleeding related to the IABP access site was significantly higher in the Urgent group and accounted for more than two-thirds of overall access site–related bleeding. IABP treatment duration and renal impairment were independent predictors of overall bleeding (200).

Residual Plaque Burden in Patients With Acute Coronary Syndromes After Successful Percutaneous Coronary Intervention

Objectives The aim of this study was to characterize and evaluate the clinical impact of untreated atherosclerotic disease after percutaneous coronary intervention (PCI) in patients with acute coronary syndromes (ACS).
Background Residual atherosclerotic disease after successful PCI may predispose future major adverse cardiovascular events (MACE). Compared with intravascular ultrasound (IVUS), angiography underestimates the presence and severity of coronary artery disease.
Methods Following successful PCI of all clinically significant lesions in 697 patients with ACS, 3-vessel grayscale and radiofrequency IVUS was performed. Lesions were prospectively characterized, and patients were followed for a median of 3.4 years. A total of 3,229 untreated lesions (4.89 ± 1.98 lesions/patient) were identified by IVUS, with mean plaque burden (PB) of 49.6 ± 4.2%.
Results By angiography these nonculprit lesions were mild, with mean diameter stenosis of 38.9 ± 15.3%. At least 1 lesion with a PB ≥70% (PB70 lesion) was found in 220 (33%) patients. By multivariable analysis, a history of prior PCI and angiographic 3-vessel disease were independent predictors of PB70 lesions. Patients with PB70 lesions had greater total percent plaque volume, normalized PB, fibroatheromas, thin-cap fibroatheromas, and normalized volumes of necrotic core and dense calcium. Patients with PB70 lesions had greater 3-year rates of MACE due to untreated nonculprit lesions (20.8% vs. 7.7%, $p < 0.0001$). Among imaged nonculprit lesions, the proportion of PB70 lesions causing MACE was significantly greater than non-PB70 lesions (8.7% vs. 1.0%, $p < 0.0001$).
Conclusions After successful PCI of all angiographically significant lesions, overall untreated atherosclerotic burden remains high, and PB70 lesions are frequently present in the proximal and mid-coronary tree. Patients with PB70 lesions have greater atherosclerosis throughout the coronary tree, have more thin-cap fibroatheromas, and are at increased risk for future cardiovascular events. (PROSPECT: An Imaging Study in Patients With Unstable Atherosclerotic Lesions; NCT00180466) (201).

Longitudinal Distribution of Plaque Burden and Necrotic Core–Rich Plaques in Nonculprit Lesions of Patients Presenting With Acute Coronary Syndromes

Objectives In this substudy of the PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) study, we examined the longitudinal distribution of atherosclerotic plaque burden, virtual histology–intravascular ultrasound (VH-IVUS) characterized necrotic core (NC) content and VH–thin-cap fibroatheroma (TCFA) distribution in nonculprit lesions of patients presenting with acute coronary syndromes.

Background Previous analyses suggested that vulnerable plaques and acute myocardial infarction may occur more frequently in the proximal than the distal coronary tree.

Methods A total of 4,234 proximal, mid, and distal 30-mm-long segments of each epicardial coronary artery were compared with each other and to the left main coronary artery (LMCA).

Results Combining IVUS data from all 3 arteries, there was a gradient in plaque burden from the proximal (42.4%) to mid (37.6%) to distal (32.6%) 30-mm-long segments ($p < 0.0001$). Overall, 67.4% of proximal, 41.0% of mid, and 29.7% of distal 30-mm-long segments contained at least 1 lesion (plaque burden >40%). Proportion of NC, however, was similar in the proximal and mid 30-mm-long segments of all arteries (10.3% [interquartile range (IQR): 4.8% to 16.7%] vs. 10.6% [IQR: 5.0% to 18.1%], $p = 0.25$), but less in the distal 30-mm-long segment (9.1% [IQR: 3.7% to 17.8%], $p = 0.03$ compared with the proximal segment and $p = 0.003$ compared with the mid segment). Overall, 17.3% of proximal, 11.5% of mid, and 9.1% of distal 30-mm-long segments had at least 1 lesion that was classified as VH-TCFA ($p < 0.0001$). Comparing the LMCA with the combined cohort of proximal left anterior descending, left circumflex, and right coronary artery 30-mm-long segments: 1) plaque burden was less (35.4% [IQR: 28.8% to 43.5%] vs. 40.9% [IQR: 33.3% to 48.0%], $p < 0.0001$); 2) fewer LMCAs contained at least 1 lesion (17.5%, $p < 0.0001$); 3) there was less NC (6.5% [IQR: 2.9% to 12.2%] vs. 9.3% [IQR: 4.3% to 15.9%], $p < 0.0001$); and 4) LMCAs rarely contained a VH-TCFA (1.8%, $p < 0.0001$).

Conclusions The current analysis appears to confirm that lesions that are responsible for acute coronary events (large, plaque burden–rich in NC) are somewhat more likely to be present in the proximal than the distal coronary tree, except for the LMCA (202).

Plaque Composition and Clinical Outcomes in Acute Coronary Syndrome Patients With Metabolic Syndrome or Diabetes

Objectives The goal of this study was to characterize the extent and composition of coronary atherosclerosis in patients with diabetes mellitus or the metabolic syndrome (Met Syn) presenting with acute coronary syndromes (ACS).

Background Diabetes and Met Syn patients have increased rates of major adverse cardiac events (MACE), yet a systematic description of nonculprit lesions for these high-risk groups is incomplete.

Methods In the PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) study, ACS patients underwent 3-vessel quantitative coronary angiography, grayscale, and radiofrequency intravascular ultrasound after successful percutaneous coronary intervention (PCI). Subsequent MACE (cardiac death or arrest, myocardial infarction, or rehospitalization for unstable or progressive angina) were adjudicated to the originally treated culprit versus untreated nonculprit lesions in 3 patient groups: 1) diabetes; 2) Met Syn; and 3) neither. Median length of follow-up was 3.4 years.

Results Of 673 patients, 119 (17.7%) had diabetes and 239 (35.5%) had Met Syn. The cumulative 3-year MACE rate was 29.4% in patients with diabetes, 21.3% with Met Syn, and 17.4% with neither ($p = 0.03$). MACE adjudicated to untreated nonculprit lesions occurred in 18.7%, 11.7%, and 9.7% of patients, respectively ($p = 0.06$). Nonculprit lesions in diabetes and Met Syn patients were longer and had greater plaque burden, smaller lumen areas, with greater necrotic core and calcium content. Diabetes and Met Syn patients with future MACE had greater necrotic core and calcification compared with the normal cardiometabolic group.

Conclusions In this PCI ACS population, patients with diabetes and Met Syn had higher 3-year MACE rates. Lesion length, plaque burden, necrotic core, and calcium content were significantly greater among nonculprit lesions of patients with diabetes and Met Syn, but only necrotic core and calcium were significantly greater in the nonculprit lesions of patients with a future MACE in this exploratory analysis (203).

Natural History of Coronary Atherosclerosis by Multislice Computed Tomography

Objectives This study sought to analyze the natural history of coronary atherosclerosis by multislice computed tomography (MSCT) and assess the serial changes in coronary plaque burden, lumen dimensions, and arterial remodeling.

Background MSCT can comprehensively assess coronary atherosclerosis by combining lumen and plaque size parameters.

Methods Thirty-two patients with acute coronary syndromes underwent 64-slice computed tomography angiography after percutaneous coronary intervention at baseline and after a median of 39 months. All patients received contemporary medical treatment. All available coronary segments in every subject were analyzed. The progression of atherosclerosis per segment and per patient was assessed by means of change in percent atheroma

volume (PAV), change in normalized total atheroma volume (TAVnorm), and percent change in TAV (% change in TAV). Serial coronary remodeling was also assessed. Measures of lumen stenosis included percent diameter stenosis (%DS), minimum lumen diameter (MLD), percent area stenosis (%AS), and minimum lumen area (MLA). For each patient, the mean of all matched segments was calculated at the 2 time points. Clinical events at follow-up were documented.

Results The PAV did not change significantly (−0.15 ± 3.64%, p = 0.72). The mean change in TAVnorm was 47.36 ± 143.24 mm^3 (p = 0.071), and the % change in TAV was 6.7% (p = 0.029). The MLD and MLA increased by 0.15 mm (−0.09 to 0.24, p = 0.039) and 0.52 mm^2 (−0.38 to 1.04, p = 0.034) respectively, which was accompanied by vessel enlargement, with 53% of the patients showing expansive positive remodeling. Patients with clinical events had a larger TAVnorm at baseline (969.72 mm^3 vs. 810.77 mm^3, p = 0.010).

Conclusions MSCT can assess the progression of coronary atherosclerosis and may be used for noninvasive monitoring of pharmacological interventions in coronary artery disease. (PROSPECT: An Imaging Study in Patients With Unstable Atherosclerotic Lesions; NCT00180466) (204).

Relationship Between Palpography and Virtual Histology in Patients With Acute Coronary Syndromes

Objectives The purpose of this study was to correlate adverse events at long-term follow-up in patients after an acute coronary syndrome with coronary plaque characteristics derived from simultaneous evaluation of their mechanical and compositional properties using virtual histology (intravascular ultrasound virtual histology) and palpography.

Background Fibroatheroma is the plaque morphology with the highest risk of causing adverse cardiac events. Palpography can potentially assess the local mechanical plaque properties with the possibility of identifying fibroatheroma with the highest risk of rupture.

Methods A total of 114 patients with acute coronary syndrome from the PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) trial underwent a single ultrasound imaging investigation of their 3 coronary vessels with the co-registration of intravascular ultrasound virtual histology and palpography. Major adverse cardiac events (MACE) (cardiac death, cardiac arrest, myocardial infarction, or unstable or progressive angina) were collected up to a median follow-up of 3.4 years and adjudicated to originally treated culprit versus untreated nonculprit lesions.

Results In total, 488 necrotic core–rich plaques were identified and subclassified as thin-cap fibroatheroma (n = 111), calcified thick-cap fibroatheroma (n = 213), and noncalcified thick-cap fibroatheroma (n = 164) and matched to their co-registered palpography data. A total of 16 MACE, adjudicated to untreated nonculprit lesions, were recorded at follow-up. In patients in whom MACE developed, fibroatheroma were larger (plaque area 10.0 mm^2 [range: 8.4 to 11.6 mm^2] vs. 8.2 mm^2 [range: 7.7 to 8.8 mm^2] (p = 0.03) compared with patients who were MACE free. By palpography, the maximum and the density strain values did not differ between the varying subtypes of fibroatheroma of patients with or without MACE during follow-up.

Conclusions In acute coronary syndromes, patients treated with stents and contemporary pharmacotherapy, palpography did not provide additional diagnostic information for the identification of fibroatheroma with a high risk of rupture and MACE during long-term follow-up. (Providing Regional Observations to Study Predictors of Events in the Coronary Tree [PROSPECT]: An Imaging Study in Patients With Unstable Atherosclerotic Lesions; NCT00180466) (205).

Adverse Cardiovascular Events Arising From Atherosclerotic Lesions With and Without Angiographic Disease Progression

Objectives The aim of this study was to use angiography and grayscale and intravascular ultrasound–virtual histology to assess coronary lesions that caused events during a median follow-up period of 3.4 years.

Background Vulnerable plaque-related events are assumed to be the result of substantial progression of insignificant lesions.

Methods In the PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) study, 697 patients with acute coronary syndromes underwent treatment of all culprit lesions followed by 3-vessel imaging to assess the natural history of culprit and untreated nonculprit (NC) lesions. Future adverse cardiovascular events adjudicated to NC lesions were divided into those with versus without substantial lesion progression (SLP) (≥20% angiographic diameter stenosis increase).

Results NC lesion events occurred in 72 patients, 44 (61%) with and 28 (39%) without SLP. Myocardial infarctions (n = 6) occurred only in patients with SLP. Conversely, patients without SLP presented only with unstable or increasing angina requiring rehospitalization. Lesions with versus without SLP occurred later (median time to event 401 vs. 223 days, p = 0.07); were less severe at baseline (median diameter stenosis 26.4% vs. 53.8%, p < 0.0001) but more severe at the time of the event (mean diameter stenosis 73.8% vs. 56%, p < 0.0001); and had comparable baseline median plaque burden (68.7% vs. 70.1%, p = 0.17), minimum luminal area (3.7 vs. 4.0 mm^2, p = 0.60), and intravascular ultrasound–virtual histology phenotype (83.3% vs. 90.9%, p = 0.68; classified as fibroatheromas at baseline).

Conclusions NC lesions responsible for future cardiovascular events showed angiographic increase during 3.4 years of follow-up, whereas SLP underlay many but not all of them. NC events due to lesions with SLP were

angiographically less severe and presented with a delayed time course but were otherwise indistinguishable from NC events that were not associated with SLP (206).

Plaque Composition by Intravascular Ultrasound and Distal Embolization After Percutaneous Coronary Intervention

Distal embolization after percutaneous coronary intervention occurs in 15% to 70% of patients, depending on the sensitivity of the diagnostic modality used, and is associated with a poor prognosis after elective and primary percutaneous coronary intervention. It has been hypothesized that imaging of the plaque composition can identify coronary artery lesions that are predisposed to causing distal embolization. This review report aims to summarize all currently available published data on the use of assessment of atherosclerotic plaque composition by virtual histology intravascular ultrasound (VH-IVUS) to predict the occurrence of distal embolization. A systematic review of the literature was performed. We searched Medline, ISI Web of Knowledge, and the Cochrane Library from January 2002 until March 2011. When a study was found to be relevant, the manuscript was obtained and reviewed. A total of 11 studies were identified investigating the relationship between plaque composition assessed by VH-IVUS and distal embolization. Although all studies used the same equipment to perform and analyze VH-IVUS, there was considerable heterogeneity in patient characteristics, outcome definitions, and reporting of VH-IVUS findings. Nevertheless, the necrotic core plaque component—either by itself or as a constituent of a VH thin cap fibroatheroma—was associated with distal embolization in all but 2 of the 11 reviewed studies. Therefore, identification of lesions with large amounts of necrotic core on VH-IVUS could identify lesions that might benefit from the selective use of embolic protection devices (207).

Definitions and Methodology for the Grayscale and Radiofrequency Intravascular Ultrasound and Coronary Angiographic Analyses

Objectives In a prospective study of the natural history of coronary atherosclerosis using angiography and grayscale and radiofrequency intravascular ultrasound (IVUS)–virtual histology (VH), larger plaque burden, smaller luminal area, and plaque composition thin-cap fibroatheroma emerged as independent predictors of future adverse cardiovascular events.

Background The methodology for IVUS-VH classification for an in vivo natural history study and the prospective image mapping by angiography and grayscale and IVUS-VH have not been established.

Methods All culprit and nonculprit lesions (defined as ≥30% angiographic visual diameter stenoses) were analyzed. Three epicardial vessels as well as all ≥1.5-mm-diameter side branches were divided into 29 CASS (Coronary Artery Surgery Study) segments. Each CASS segment was then subdivided into 1.5-mm-long subsegments, and dimensions were analyzed. All grayscale and IVUS-VH slices from the proximal 6 to 8 cm of the 3 coronary arteries were analyzed, with lesions defined as having more than 3 consecutive slices with ≥40% plaque burden categorized as: 1) VH thin-cap fibroatheroma; 2) thick-cap fibroatheroma; 3) pathological intimal thickening; 4) fibrotic plaque; or 5) fibrocalcific plaque. The locations of angiographic and grayscale and IVUS-VH lesions were recorded in relation to the corresponding coronary artery ostium and nearby side branches.

Results The 3-year cumulative rate of major adverse cardiovascular events was 20.4%. Events were adjudicated to culprit lesions in 12.9% of patients and to nonculprit lesions in 11.6%. On multivariate analysis, nonculprit lesions associated with recurrent events were characterized by a plaque burden ≥70% (hazard ratio: 5.03; 95% confidence interval: 2.51 to 10.11; $p < 0.0001$), a minimal luminal area ≤4.0 mm^2 (hazard ratio: 3.21; 95% confidence interval: 1.61 to 6.42; $p = 0.001$), and IVUS-VH phenotype of a thin-cap fibroatheroma (hazard ratio: 3.35; 95% confidence interval: 1.77 to 6.36; $p < 0.001$).

Conclusions Three-vessel multimodality coronary artery imaging was feasible and allowed the identification of lesion-level predictors for future events in this natural history study (208).

Characteristics and Clinical Significance of Angiographically Mild Lesions in Acute Coronary Syndromes

Objectives The aim of this study was to assess whether residual nonculprit (NC) lesions, defined as visual diameter stenosis ≥30% after successful percutaneous coronary intervention, affect the rate of future events in patients with acute coronary syndromes.

Background In patients with acute coronary syndromes, approximately one-half of recurrent events after percutaneous coronary intervention arise from untreated lesions.

Methods Patients enrolled in PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) were divided into 3 groups: those with no NC lesions, 1 NC lesion, or ≥2 NC lesions. Time to events for major adverse cardiac events was estimated up to 3 years.

Results Among 697 patients, 13.3% had no NC lesions, 19.7% had 1 NC lesion, and 67.0% had ≥2 NC lesions. The median diameter stenoses of the NC lesions in the latter 2 groups were 36.7% (interquartile range: 31.0% to 43.4%) and 37.4% (interquartile range: 32.0% to 46.5%), respectively ($p = 0.22$). At least 1 thin-cap fibroatheroma was present in one-half the patients in each group. At 3 years, the incidence of major adverse cardiac events was 8.5%, 15.2%, and 24.3%, respectively ($p = 0.0009$). NC lesion–related events occurred in 0%, 5.0%, and 15.9% of patients, respectively ($p < 0.0001$). Of 105 NC lesion–related clinical

events occurring during follow-up, 73 (69.5%) originated from angiographically evident baseline NC lesions (of which 36 had diameter stenosis >50%), while the other 32 arose from normal or near normal segments.

Conclusions Residual NC lesions are common after percutaneous coronary intervention for acute coronary syndromes and portend a higher rate of recurrent ischemic events within 3 years, especially when angiographically more severe. Conversely, the absence of NC lesions by angiography is highly predictive of freedom from events not related to the originally treated culprit lesion(s) (209).

ACCF/SCAI/STS/AATS/AHA/ASNC/HFSA/SCCT 2012 Appropriate Use Criteria for Coronary Revascularization Focused Update: A Report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, Society for Cardiovascular Angiography and Interventions, Society of Thoracic Surgeons, American Association for Thoracic Surgery, American Heart Association, American Society of Nuclear Cardiology, and the Society of Cardiovascular Computed Tomography

The American College of Cardiology Foundation (ACCF), Society for Cardiovascular Angiography and Interventions, Society of Thoracic Surgeons, and the American Association for Thoracic Surgery, along with key specialty and subspecialty societies, conducted an update of the appropriate use criteria (AUC) for coronary revascularization frequently considered. In the initial document, 180 clinical scenarios were developed to mimic patient presentations encountered in everyday practice and included information on symptom status, extent of medical therapy, risk level as assessed by noninvasive testing, and coronary anatomy. This update provides a reassessment of clinical scenarios the writing group felt to be affected by significant changes in the medical literature or gaps from prior criteria. The methodology used in this update is similar to the initial document, and the definition of appropriateness was unchanged. The technical panel scored the clinical scenarios on a scale of 1 to 9. Scores of 7 to 9 indicate that revascularization is considered appropriate and likely to improve patients' health outcomes or survival. Scores of 1 to 3 indicate revascularization is considered inappropriate and unlikely to improve health outcomes or survival. Scores in the mid-range (4 to 6) indicate a clinical scenario for which the likelihood that coronary revascularization will improve health outcomes or survival is uncertain.

In general, as seen with the prior AUC, the use of coronary revascularization for patients with acute coronary syndromes and combinations of significant symptoms and/or ischemia is appropriate. In contrast, revascularization of asymptomatic patients or patients with low-risk findings on noninvasive testing and minimal medical therapy are viewed less favorably. The technical panel felt that based on recent studies, coronary artery bypass grafting remains an appropriate method of revascularization for patients with high burden of coronary artery disease (CAD). Additionally, percutaneous coronary intervention may have a role in revascularization of patients with high burden of CAD. The primary objective of the appropriate use criteria is to improve physician decision making and patient education regarding expected benefits from revascularization and to guide future research (210).

Prognostic Value of Myocardial Viability by Delayed-Enhanced Magnetic Resonance in Patients With Coronary Artery Disease and Low Ejection Fraction: Impact of Revascularization Therapy

Objectives The purpose of this study was to evaluate the impact of myocardial viability assessment by delayed-enhanced cardiac magnetic resonance (DE-CMR) and of revascularization therapy on survival in patients with coronary artery disease (CAD) and low ejection fraction (EF).

Background Prior studies have shown that DE-CMR predicts recovery of left ventricular (LV) dysfunction after revascularization.

Methods The authors prospectively evaluated survival of 144 consecutive patients (130 males, age 65 ± 11 years) with CAD and LV dysfunction (EF: 24 ± 7%) undergoing DE-CMR. Eighty-six patients underwent complete revascularization of dysfunctional myocardium (79 coronary artery bypass grafting, 7 percutaneous coronary intervention), whereas 58 patients remained under medical treatment.

Results Over the 3-year median follow-up, 49 patients died. Three-year survival was significantly worse in medically treated patients with dysfunctional viable than with nonviable myocardium (48% vs. 77% survival, $p = 0.02$). By contrast, in revascularized patients, survival was similar whether myocardium was viable or not (88% and 71% survival, respectively, $p = NS$). Hazard of death of viable myocardium remaining under medical treatment versus complete revascularization was 4.56 (95% confidence interval [CI]: 1.93 to 10.8). Cox multivariate analysis indicated that interaction of revascularization and viability provided significant additional value (chi-square test = 13.1, $p = 0.004$) to baseline predictors of survival (New York Heart Association functional class, wall motion score, and peripheral artery disease). More importantly, in 43 pairs of propensity score–matched patients, hazard of death (hazard ratio: 2.5 [95% CI: 1.1 to 6.1], $p = 0.02$) remained significantly higher for medically treated patients rather than for those with fully revascularized viable myocardium.

Conclusions Without revascularization, presence of dysfunctional viable myocardium by DE-CMR is an independent predictor of mortality in patients with ischemic LV dysfunction. This observation may be useful for preoperative selection of patients for revascularization (211).

Transient Impairment of Vasomotion Function After Successful Chronic Total Occlusion Recanalization

Objectives The aim of our study was to assess coronary vasomotion after successful revascularization of chronic total occlusion (CTO).

Background It is largely unknown whether the recovery of anterograde flow after CTO recanalization with drug-eluting stent implantation affects vascular function in distal coronary segments.

Methods One hundred consecutive CTOs successfully treated with drug-eluting stents underwent coronary diameter measurement after intracoronary nitroglycerin injection 5, 20, and 35 mm distal to the stented coronary segment using 3-dimensional quantitative coronary angiography. In a subgroup of 14 patients, coronary vasomotion was tested in distal segments: incremental atrial pacing for endothelium-dependent cases; and intracoronary nitroglycerin injection for endothelium-independent cases. In another subgroup of 13 patients, distal vessels were assessed by intracoronary ultrasounds.

Results Vessel diameters significantly increased at follow-up as compared to baseline values (2.0 ± 0.52 mm vs. 2.25 ± 0.50 mm, 1.76 ± 0.49 mm vs. 2.05 ± 0.58 mm, 1.54 ± 0.53 mm vs. 2.04 ± 0.58 mm, at each segment analyzed; $p < 0.001$). At baseline, distal segments failed to respond to both endothelium-dependent and -independent stimuli. At follow-up, atrial pacing induced vasoconstriction, whereas nitroglycerine administration resulted in significant vasodilation ($p < 0.05$). Intracoronary ultrasounds failed to show changes of the cross-sectional area of distal segments at follow-up angiography.

Conclusions Recanalization of CTO is followed by a hibernation of vascular wall at distal coronary segments that fail to respond to endothelium-dependent and -independent stimuli. Distal vessel diameter increases over time in the absence of positive remodeling and in spite of persistent endothelial dysfunction. This severe impairment of vasomotor tone after CTO reopening suggests that intracoronary ultrasound assessment is of paramount importance for the selection of stent size (212).

Role of AV Nodal Ablation in Cardiac Resynchronization in Patients With Coexistent Atrial Fibrillation and Heart FailureA Systematic Review

Objectives The aim of this study was to systematically review the medical literature to evaluate the impact of AV nodal ablation in patients with heart failure and coexistent atrial fibrillation (AF) receiving cardiac resynchronization therapy (CRT).

Background CRT has a substantial evidence base in patients in sinus rhythm with significant systolic dysfunction, symptomatic heart failure, and prolonged QRS duration. The role of CRT is less well established in AF patients with coexistent heart failure. AV nodal ablation has recently been suggested to improve outcomes in this group.

Methods Electronic databases and reference lists through September 15, 2010, were searched. Two reviewers independently evaluated citation titles, abstracts, and articles. Studies reporting the outcomes after AV nodal ablation in patients with AF undergoing CRT for symptomatic heart failure and left ventricular dyssynchrony were selected. Data were extracted from 6 studies, including 768 CRT-AF patients, composed of 339 patients who underwent AV nodal ablation and 429 treated with medical therapy aimed at rate control alone.

Results AV nodal ablation in CRT-AF patients was associated with significant reductions in all-cause mortality (risk ratio: 0.42 [95% confidence interval: 0.26 to 0.68]), cardiovascular mortality (risk ratio: 0.44 [95% confidence interval: 0.24 to 0.81]), and improvement in mean New York Heart Association functional class (risk ratio: −0.52 [95% confidence interval: −0.87 to −0.17]).

Conclusions AV nodal ablation was associated with a substantial reduction in all-cause mortality and cardiovascular mortality and with improvements in New York Heart Association functional class compared with medical therapy in CRT-AF patients. Randomized controlled trials are warranted to confirm the efficacy and safety of AV nodal ablation in this patient population (213).

Prognostic Value of Myocardial Contrast Delayed Enhancement With 64-Slice Multidetector Computed Tomography After Acute Myocardial Infarction

Objectives This study evaluated the clinical value of myocardial contrast delayed enhancement (DE) with multidetector computed tomography (MDCT) for predicting clinical outcome after acute myocardial infarction (AMI).

Background Although some studies have described the use of MDCT for assessment of myocardial viability after AMI, clinical experience remains limited.

Methods In 102 patients with first AMI, 64-slice MDCT without iodine reinjection was performed immediately following successful percutaneous coronary intervention (PCI). We measured the size of myocardial contrast DE on MDCT and compared it with clinical outcome. Primary composite cardiac events were cardiac death or hospitalization for worsening heart failure.

Results Among the 102 patients (24 ± 10 months follow-up), 19 patients experienced primary composite cardiac events (cardiac death, $n = 7$; heart failure, $n = 12$). Kaplan-Meier analysis showed higher risk of cardiac events for patients in the third tertile of myocardial contrast DE size (≥36 g) than for those in the other 2 tertiles ($p < 0.0001$). Multivariable Cox proportional hazards regression analysis indicated that myocardial contrast DE size (adjusted hazard ratio [HR] for tertile 3 vs. 1: 16.1, 95% confidence

interval [CI]: 1.45 to 72.4, p = 0.022; HR for tertile 3 vs. 2: 5.06, 95% CI: 1.25 to 22.7, p = 0.039) was a significant independent predictor for cardiac events after adjustment for Thrombolysis In Myocardial Infarction risk score, left ventricular ejection fraction, total defect score on single-photon emission CT with technetium tetrofosmin, and transmural extent of myocardial contrast DE on MDCT.

Conclusions Myocardial contrast DE size on MDCT immediately after primary PCI may provide promising information for predicting clinical outcome in patients with AMI (214).

Characteristics and Long-Term Outcomes of Percutaneous Revascularization of Unprotected Left Main Coronary Artery Stenosis in the United StatesA Report From the National Cardiovascular Data Registry, 2004 to 2008

Objectives This study sought to assess percutaneous coronary intervention (PCI) for unprotected left main coronary artery (ULMCA) stenosis in routine U.S. clinical practice.

Background Percutaneous coronary intervention for ULMCA stenosis is controversial; however, current use and outcomes of ULMCA PCI in routine U.S. clinical practice have not been described.

Methods We evaluated 5,627 patients undergoing ULMCA PCI at 693 centers within the National Cardiovascular Data Registry Catheterization Percutaneous Coronary Intervention Registry for temporal trends in PCI use (2004 to 2008), patient characteristics, and in-hospital mortality. Thirty-month mortality and composite major adverse events (death, myocardial infarction, and revascularization) with drug-eluting versus bare-metal stents were compared using inverse probability weighted (IPW) hazard ratios (HRs) in a nonrandomized Medicare-linked (age ≥65 years) patient cohort (n = 2,765).

Results ULMCA PCI was performed in 4.3% of patients with ULMCA stenosis. Unadjusted in-hospital mortality rates ranged from 2.9% for elective cases to 45.1% for emergent/salvage cases. By 30 months, 57.9% of the elderly ULMCA PCI population experienced death, myocardial infarction, or revascularization, and 42.7% died. Patients receiving drug-eluting stents (versus bare-metal stents) had a lower 30-month mortality (IPW HR: 0.84, 95% confidence interval [CI]: 0.73 to 0.96), but the composite of major adverse events were similar (IPW HR: 0.95, 95% CI: 0.84 to 1.06).

Conclusions In the United States, ULMCA PCI is performed in <5% of patients with ULMCA disease and is generally reserved for those at high procedural risk. Adverse events are common in elderly patients and are related to patient and procedural characteristics, including stent type (215).

Sex-Related Differences in Clinical Presentation and Outcome of Transcatheter Aortic Valve Implantation for Severe Aortic Stenosis

Objectives The purpose of this study was to clarify the impact of sex-related differences in transcatheter aortic valve implantation (TAVI) for high-risk patients with severe aortic stenosis.

Background Although TAVI is becoming a mature technique, the impact of sex differences remains unclear.

Methods The TAVI patients were included prospectively in a dedicated database from October 2006. The proportion of women (n = 131) was similar to that of men (n = 129). The Edwards valve (85.4%) and CoreValve (14.6%) were used through the transfemoral (65.0%), subclavian (3.1%), or transapical (31.9%) approach. All events were defined according to Valve Academic Research Consortium criteria.

Results Age was similar (83.1 ± 6.3 years), but women had less coronary and peripheral disease, less previous cardiac surgery, higher ejection fraction, and lower EuroSCORE (European System for Cardiac Operative Risk Evaluation [22.3 ± 9.0% vs. 26.2 ± 13.0%, p = 0.005]). Minimal femoral size (7.74 ± 1.03 mm vs. 8.55 ± 1.34 mm, p < 0.001), annulus size (20.9 ± 1.4 vs. 22.9 ± 1.7 mm, p < 0.001), and valve size (23.9 ± 1.6 mm vs. 26.3 ± 1.5 mm, p < 0.001) were smaller in women. Device success was similar (90.8% vs. 88.4%, p = 0.516) despite more frequent iliac complications (9.0% vs. 2.5%, p = 0.030). Residual mean aortic pressure gradient (11.6 ± 4.9 vs. 10.9 ± 4.9, p = 0.279) was also similar. The 1-year survival rate was higher for women, 76% (95% confidence interval: 72% to 80%), than for men, 65% (95% confidence interval: 60% to 69%); and male sex (hazard ratio: 1.62, 95% confidence interval: 1.03 to 2.53, p = 0.037) was identified as a predictor of midterm mortality by Cox regression analysis.

Conclusions Female sex is associated with better baseline clinical characteristics and improved survival, and is identified as a predictor of midterm survival after TAVI (216).

Impact of Statin Therapy on Plaque Characteristics as Assessed by Serial OCT, Grayscale and Integrated Backscatter–IVUS

Objectives The purpose of this study was to evaluate the effect of statin treatment on coronary plaque composition and morphology by optical coherence tomography (OCT), grayscale and integrated backscatter (IB) intravascular ultrasound (IVUS) imaging.

Background Although previous studies have demonstrated that statins substantially improve cardiac mortality, their precise effect on the lipid content and fibrous cap thickness of atherosclerotic coronary lesions is less clear. While IVUS lacks the spatial resolution to accurately assess fibrous cap thickness, OCT lacks the penetration of IVUS. We used

a combination of OCT, grayscale and IB-IVUS to comprehensively assess the impact of pitavastatin on plaque characteristics.

Methods Prospective serial OCT, grayscale and IB-IVUS of nontarget lesions was performed in 42 stable angina patients undergoing elective coronary intervention. Of these, 26 received 4 mg pitavastatin after the baseline study; 16 subjects who refused statin treatment were followed with dietary modification alone. Follow-up imaging was performed after a median interval of 9 months.

Results Grayscale IVUS revealed that in the statin-treated patients, percent plaque volume index was significantly reduced over time (48.5 ± 10.4%, 42.0 ± 11.1%; p = 0.033), whereas no change was observed in the diet-only patients (48.7 ± 10.4%, 50.4 ± 11.8%; p = NS). IB-IVUS identified significant reductions in the percentage lipid volume index over time (34.9 ± 12.2%, 28.2 ± 7.5%; p = 0.020); no change was observed in the diet-treated group (31.0 ± 10.7%, 33.8 ± 12.4%; p = NS). While OCT demonstrated a significant increase in fibrous cap thickness (140 ± 42 μm, 189 ± 46 μm; p = 0.001), such changes were not observed in the diet-only group (140 ± 35 μm, 142 ± 36 μm; p = NS). Differences in the changes in the percentage lipid volume index (−6.8 ± 8.0% vs. 2.8 ± 9.9%, p = 0.031) and fibrous cap thickness (52 ± 32 μm vs. 2 ± 22 μm, p < 0.001) over time between the pitavastatin and diet groups were highly significant.

Conclusions Statin treatment induces favorable plaque morphologic changes with an increase in fibrous cap thickness, and decreases in both percentage plaque and lipid volume indexes (217).

Percutaneous Coronary Intervention Use in the United States: Defining Measures of Appropriateness

Appropriate utilization of percutaneous coronary intervention (PCI) and medical therapy is deservedly a national healthcare policy priority for the United States. Because PCI is both common and costly, appraisal of appropriateness is warranted. The initial appropriate use criteria (AUC) have been developed for coronary revascularization procedures and investigators recently reported the appropriateness for the approximately 500,000 PCI procedures performed at centers participating in the National Cardiovascular Data Registry. The AUC have broad implications for both healthcare providers and our patients and will be used as the basis for indications, referral patterns, treatment options, physician education, shared decision-making, and reimbursement for years to come. While we acknowledge the importance of thoughtfully assessing appropriateness for all medical procedures including PCI, there are a number of concerns with the current AUC and methods used to report appropriateness that warrant expanded commentary (218).

Principles of Percutaneous Paravalvular Leak Closure

Paravalvular regurgitation affects 5% to 17% of all surgically implanted prosthetic heart valves. Patients who have paravalvular regurgitation can be asymptomatic or present with hemolysis or heart failure, or both. Reoperation is associated with increased morbidity and is not always successful because of underlying tissue friability, inflammation, or calcification. Comprehensive echocardiographic imaging with transthoracic and real-time 3-dimensional transesophageal echocardiography is key for characterizing the defect location, size, and shape. For paramitral defects, an antegrade transseptal approach can usually be guided by biplane fluoroscopy, and real-time 3-dimensional transesophageal echocardiography can usually be performed successfully. Alternative approaches to paramitral defects include retrograde transaortic cannulation or transapical access and retrograde cannulation. For oblong or crescentic defects, the simultaneous or sequential deployment of 2 smaller devices, as opposed to 1 large device, results in a higher degree of procedural success and safety because the risk of impingement on the prosthetic leaflets is minimized. Most para-aortic defects can be approached in a retrograde manner and closed with a single device. With careful anatomical assessment, procedural planning, and procedural execution, successful closure rates of 90% or more should be attainable with a low risk of device impingement on the prosthetic valve or embolization (219).

Long-Term Comparison of Everolimus- and Sirolimus-Eluting Stents in Patients With Acute Coronary Syndromes

Objectives The goal of this study was to compare the long-term clinical outcome between everolimus-eluting stent (EES) and sirolimus-eluting stent (SES) in patients with acute coronary syndromes (ACS).

Background EES have not been directly compared with SES in ACS patients to date.

Methods Between 2004 and 2009, 1,746 consecutive ACS patients (ST-segment elevation ACS [STE-ACS]: 33.5%; non–ST-segment elevation ACS [NSTE-ACS]: 66.5%) were treated with EES (n = 903) or SES (n = 843). Using propensity score matching, clinical outcome was compared among 705 matched pairs of ACS patients treated with EES and SES.

Results Through 3 years, the primary endpoint—the composite of death, myocardial infarction (MI), and target vessel revascularization (TVR)—occurred in 13.8% of EES- and 17.7% of SES-treated ACS patients (hazard ratio [HR]: 0.72, 95% confidence interval [CI]: 0.54 to 0.95, p = 0.02). The difference in favor of EES was driven by a lower risk of TVR (5.7% vs. 8.8%, HR: 0.65, 95% CI: 0.43 to 0.98, p = 0.04) and a trend toward a lower risk of MI (2.1% vs. 3.3%, HR: 0.56, 95% CI: 0.29 to 1.12, p = 0.10). The risk of

death (7.2% vs. 8.8%, HR: 0.75, 95% CI: 0.50 to 1.10, p = 0.14) showed no difference between EES and SES. The treatment effect in favor of EES for the primary endpoint was similar for patients with STE-ACS (16.4% vs. 18.5%, HR: 0.80, 95% CI: 0.50 to 1.27) and NSTE-ACS (12.4% vs. 17.3%; HR: 0.67, 95% CI: 0.47 to 0.96; $p_{for\ interaction}$ = 0.56) and across major subgroups. Definite (0.4% vs. 1.8%, p = 0.03), and definite or probable stent thrombosis (3.4% vs. 6.1%, p = 0.02) were less frequent among EES- than SES-treated ACS patients.

Conclusions Among patients with ACS, the unrestricted use of EES is associated with improved clinical outcome compared with SES during long-term follow-up to 3 years. Notably, the risk of stent thrombosis was lower among EES-treated ACS patients (220).

Timing of Angiography With a Routine Invasive Strategy and Long-Term Outcomes in Non–ST-Segment Elevation Acute Coronary Syndrome: A Collaborative Analysis of Individual Patient Data From the FRISC II (Fragmin and Fast Revascularization During Instability in Coronary Artery Disease), ICTUS (Invasive Versus Conservative Treatment in Unstable Coronary Syndromes), and RITA-3 (Intervention Versus Conservative Treatment Strategy in Patients With Unstable Angina or Non-ST Elevation Myocardial Infarction) Trials

Objectives This study sought to investigate long-term outcomes after early or delayed angiography in patients with non–ST-segment elevation acute coronary syndrome (nSTE-ACS) undergoing a routine invasive management.

Background The optimal timing of angiography in patients with nSTE-ACS is currently a topic for debate.

Methods Long-term follow-up after early (within 2 days) angiography versus delayed (within 3 to 5 days) angiography was investigated in the FRISC-II (Fragmin and Fast Revascularization During Instability in Coronary Artery Disease), ICTUS (Invasive Versus Conservative Treatment in Unstable Coronary Syndromes), and RITA-3 (Intervention Versus Conservative Treatment Strategy in Patients With Unstable Angina or Non-ST Elevation Myocardial Infarction) (FIR) nSTE-ACS patient-pooled database. The main outcome was cardiovascular death or myocardial infarction up to 5-year follow-up. Hazard ratios (HR) were calculated with Cox regression models. Adjustments were made for the FIR risk score, study, and the propensity of receiving early angiography using inverse probability weighting.

Results Of 2,721 patients originally randomized to the routine invasive arm, consisting of routine angiography and subsequent revascularization if suitable, 975 underwent early angiography and 1,141 delayed angiography. No difference was observed in 5-year cardiovascular death or myocardial infarction in unadjusted (HR: 1.06, 95% confidence interval [CI]: 0.79 to 1.42, p = 0.61) and adjusted (HR: 0.93, 95% CI: 0.75 to 1.16, p = 0.54) Cox regression models.

Conclusions In the FIR database of patients presenting with nSTE-ACS, the timing of angiography was not related to long-term cardiovascular mortality or myocardial infarction. (Invasive Versus Conservative Treatment in Unstable Coronary Syndromes [ICTUS]; ISRCTN82153174. Intervention Versus Conservative Treatment Strategy in Patients With Unstable Angina or Non-ST Elevation Myocardial Infarction [the Third Randomised Intervention Treatment of Angina Trials (RITA-3)]; ISRCTN07752711) (221).

Functional Assessment of Jailed Side Branches in Coronary Bifurcation Lesions Using Fractional Flow Reserve

Objectives This study was designed to assess the functional significance of side branches after stent implantation in main vessels using fractional flow reserve (FFR).

Background Little is known about the functional significance of side branches after stent implantation in main vessels in coronary bifurcation lesions.

Methods Between May 2007 and January 2011, 230 side branches in 230 patients after stent implantation in main vessels were assessed by FFR and were consecutively enrolled.

Results Median FFR at the side branch was 0.91 (interquartile range: 0.85 to 0.95). There was a negative correlation between the diameter stenosis (DS) by quantitative coronary angiography (QCA) and FFR of side branch (r = −0.21, p = 0.002), but only 41 (17.8%) side branches were functionally significant after stent implantation in the main vessel. Among 67 side branches with >50% DS by QCA, 19 (28.4%) had FFR ≤0.80, and among 163 side branches with ≤50% DS by QCA, 22 (13.5%) had FFR ≤0.80 after stent implantation in main vessels. On the basis of receiver-operating characteristic curves, the optimal cutoff value of DS by QCA of the side branch was 54.9%, and the area under the curve was 0.64 (95% confidence interval [CI]: 0.58 to 0.71, p < 0.001) with a 41.5% sensitivity, an 83.1% specificity, a 34.7% positive predictive value, an 86.3% negative predictive value, and a 75.7% accuracy. Multivariate binary logistic regression analysis identified DS by QCA (odds ratio [OR]: 1.04, 95% CI: 1.02 to 1.06, p = 0.001) and reference vessel diameter (OR: 0.28, 95% CI: 0.10 to 0.77, p = 0.014) before stent implantation as independent predictors of the side branches with FFR ≤0.80 after stent implantation.

Conclusions Most side branch lesions do not have functional significance after stent implantation in the main vessel, and quantitative coronary angiography is unreliable in assessing the functional severity of these lesions (222).

Procedural Factors Associated With Percutaneous Coronary Intervention-Related Ischemic Stroke

Objectives This study sought to determine whether procedural factors during percutaneous coronary intervention (PCI) are associated with the occurrence of ischemic stroke or transient ischemic attack (PCI-stroke).

Background Stroke is a devastating complication of PCI. Demographic predictors are nonmodifiable. Whether PCI-stroke is associated with procedural factors, which may be modifiable, is unknown.

Methods We performed a single-center retrospective study of 21,497 PCI hospitalizations between 1994 and 2008. We compared procedural factors from patients who suffered an ischemic stroke or transient ischemic attack related to PCI ($n = 79$) and a control group ($n = 158$), and matched them 2:1 based on a predicted probability of stroke developed from a logistic regression model.

Results PCI-stroke procedures involved the use of more catheters (median: 3 [quarter (Q) 1, Q3: 3, 4] vs. 3 [Q1, Q3: 2, 3], $p < 0.001$), greater contrast volumes (250 ml vs. 218 ml, $p = 0.006$), and larger guide caliber (median: 7-F [Q1, Q3: 6, 8] vs. 6-F [Q1, Q3: 6, 8], $p < 0.001$). The number of lesions attempted (1.7 ± 0.8 vs. 1.5 ± 0.8, $p = 0.14$) and stents placed (1.4 ± 1.2 vs. 1.2 ± 1.1, $p = 0.35$) were similar between groups, but PCI-stroke patients were more likely to have undergone rotational atherectomy (10% vs. 3%, $p = 0.029$). Overall procedural success was lower in the PCI-stroke group compared with controls (71% vs. 85%, $p = 0.017$). Evaluation of the entire PCI population revealed no difference in the rate of PCI-stroke between radial and femoral approaches (0.4% vs. 0.4%, $p = 0.78$).

Conclusions Ischemic stroke related to PCI is associated with potentially modifiable technical parameters. Careful procedural planning is warranted, particularly in patients at increased risk (223).

Clinical Presentation, Management, and Outcomes of Angiographically Documented Early, Late, and Very Late Stent Thrombosis

Objectives The aim of this study was to describe differences in treatment and in-hospital mortality of early, late, and very late stent thrombosis (ST).

Background Early, late, and very late ST may differ in clinical presentation, management, and in-hospital outcomes.

Methods We analyzed definite (angiographically documented) ST cases identified from February 2009 to June 2010 in the CathPCI Registry. We stratified events by timing of presentation: early ($\leq$1 month), late (1 to 12 months), or very late ($\geq$12 months) following stent implantation. Multivariable logistic regression modeling was performed to compare in-hospital mortality for each type of ST after adjusting for baseline comorbidities.

Results During the study period, 7,315 ST events were identified in 7,079 of 401,662 patients (1.8%) presenting with acute coronary syndromes. This ST cohort consisted of 1,391 patients with early ST (19.6%), 1,370 with late ST (19.4%), and 4,318 with very late ST (61.0%). Subjects with early ST had a higher prevalence of black race and diabetes, whereas subjects with very late ST had a higher prevalence of white race and a lower prevalence of prior myocardial infarction or diabetes. In-hospital mortality was significantly higher in early ST (7.9%) compared with late (3.8%) and very late ST (3.6%, $p < 0.001$). This lower mortality for late and very late ST persisted after multivariable adjustment (odds ratio: 0.53 [95% confidence interval (CI): 0.36 to 0.79] and 0.58 [95% CI: 0.43 to 0.79], respectively).

Conclusions Significant differences exist in the presentation and outcomes of early, late, and very late ST. Among patients with acute coronary syndromes who are undergoing percutaneous coronary intervention for angiographically documented ST, early ST is associated with the highest in-hospital mortality (224).

Endothelial and Smooth Muscle Cells Dysfunction Distal to Recanalized Chronic Total Coronary Occlusions and the Relationship With the Collateral Connection Grade

Objectives This study sought to assess the vascular function in patients with chronic total coronary occlusions (CTO) immediately after successful percutaneous recanalization and its relation with the pre-existing collateral circulation.

Background CTOs represent a long-acting occlusion of a coronary vessel, in which the progressively developed collateral circulation may limit ischemia and symptoms. However, it is unknown if the coronary segment distal to the occlusion has a preserved vascular function.

Methods We prospectively enrolled 19 consecutive patients, after percutaneous coronary intervention of a CTO. Luminal diameter, measured by quantitative coronary angiography, and coronary blood flow at level of epicardial coronary artery distal to the treated CTO was assessed before and after administration of acetylcholine (Ach), adenosine, and nitroglycerin (NTG). Collaterals were assessed angiographically by grading of Rentrop and of collateral connections (CC1: threadlike continuous connection; CC2: side branch–like connection).

Results Overall, Ach and adenosine caused coronary artery vasoconstriction ($p = 0.001$ and $p = 0.004$, respectively), whereas NTG failed to induce vasodilation ($p = 0.084$). Coronary blood flow significantly decreased with Ach ($p = 0.005$), significantly increased with NTG ($p = 0.035$), and did not change with adenosine ($p = 0.470$). Patients with CC2 collaterals ($n = 8$) had less vasoconstriction response and reduction in coronary blood flow after Ach ($p = 0.005$ and $p = 0.008$, respectively), and better vasomotor response to NTG ($p = 0.029$) than patients with CC1 collaterals ($n = 11$).

Conclusions Significant endothelial and smooth muscle dysfunction is present in the distal segments of successfully recanalized CTOs, and that seems to be more pronounced in the presence of a low grading of collateral circulation (225).

Patient Safety and Outcomes From Live Case Demonstrations of Interventional Cardiology Procedures

Objectives The goal of this study was to examine the safety and results of interventional procedures performed during the broadcast of live case demonstrations.
Background Professional meetings using live case demonstrations to present cutting-edge technology are considered a valuable educational resource. There is an ongoing discussion on whether patients who are treated during live case demonstrations are exposed to a higher risk.
Methods Between 1998 and 2010, 101 patients were treated during live transmissions from a single center in 15 invasive-cardiology conferences. Technical success was defined as the ability to effectively perform the planned procedure without any major complication. The primary endpoint of the study was the composite occurrence of death, myocardial infarction, or stroke.
Results The interventional procedures included coronary (n = 66), carotid (n = 15), peripheral (n = 1), valvular (n = 2), congenital heart disease (n = 12), and complex electrophysiological mapping and ablation interventions (n = 7). In 4 cases, the intended procedure was not done. The procedure was technically successful in 95%. In 5 cases, the procedure was unsuccessful because of the inability to cross a chronic total occlusion. There were no deaths during the hospital stay, and the composite primary endpoint occurred in 2 patients: a minor stroke following an atrial fibrillation ablation and a rise in serum troponin levels after percutaneous coronary intervention. These results were no different from those of 66 matched controls who underwent procedures performed by the same operators but not as live case demonstrations (relative risk: 0.32; 95% confidence interval: 0.02 to 3.62, p = 0.62).
Conclusions In this consecutive series of interventional cardiology procedures that were performed by expert operators during live demonstration courses, the procedural and 30-day clinical outcomes were similar to those found in daily practice and to those that have been reported in the contemporary published data. These results suggest that broadcasting live case demonstrations in selected patients from selected centers may be safe (226).

Protective Effect of Telmisartan Against Endothelial Dysfunction After Coronary Drug-Eluting Stent Implantation in Hypertensive Patients

Objectives The aim of this prospective, randomized study was to evaluate the effects of telmisartan, compared with the calcium-channel blocker amlodipine, on endothelial function after coronary drug-eluting stent (DES) implantation in hypertensive patients.
Background DES implantation impairs local endothelial function, which may be associated with future cardiovascular events. Telmisartan, which has unique peroxisome proliferator-activated-receptor-gamma–mediated effects in addition to its renin-angiotensin system–inhibition effects, has favorable effects on endothelial function.
Methods Fifty-one hypertensive patients with coronary artery stenosis but without coronary artery spasm, treated with a sirolimus-eluting stent, were randomly assigned to either the telmisartan (25 cases) or amlodipine (26 cases) treatment groups. At baseline and at 3 months after DES implantation, endothelium-dependent and -independent vasomotion were evaluated by quantitative coronary angiography under the condition of medication withdrawal. The mean luminal diameter of a 20-mm coronary segment, beginning 5 mm distal to the stent, was measured before and after infusion of intracoronary acetylcholine (10^{-7}, 10^{-6} mol/l) and then again after infusion of nitroglycerin.
Results Blood pressure was comparable between groups at baseline and after 3 months. Vasoconstriction after acetylcholine infusion at 3 months (impaired endothelial function) was less pronounced in the telmisartan group than in the amlodipine group ($p < 0.0001$), although there was no significant difference between the 2 groups before DES implantation. The response to nitroglycerin did not differ between groups before or at 3 months after DES implantation.
Conclusions Telmisartan, compared with amlodipine, significantly ameliorated endothelial dysfunction after DES implantation in terms of vasoconstriction induced by acetylcholine (227).

No Evidence of "Obesity Paradox" After Treatment With Drug-Eluting Stents in a Routine Clinical Practice: Results From the Prospective Multicenter German DES.DE (German Drug-Eluting Stent) Registry

Objectives The aim of this study was to compare clinical outcomes among unselected patients stratified in categories of body mass index, who underwent percutaneous coronary intervention (PCI) with either sirolimus-eluting or paclitaxel-eluting stents.
Background Overweight and obesity are often considered risk factors for cardiovascular events. However, recent studies have associated obesity with better outcomes after PCI with bare-metal stents. Data from routine clinical practice using drug-eluting stents (DES) focusing on this "obesity paradox" are not available.
Methods We used data from DES.DE (German Drug-Eluting Stent) registry to compare in-hospital and 1-year outcomes among unselected patients undergoing PCI with DES implantation. Primary endpoints were the rate of

major adverse cardiac and cerebrovascular events (MACCE) (defined as the composite of death, myocardial infarction, and stroke) and target vessel revascularization (TVR).

Results Between October 2005 and 2006, 1,436 normal weight, 2,839 overweight, and 1,531 obese patients treated with DES were enrolled at 98 sites. Baseline clinical parameters were more severe in overweight and obese patients; 1-year follow-up comparison between groups revealed similar rates of all-cause death (3.3% vs. 2.4% vs. 2.4%; p = 0.17), MACCE (7.1% vs. 5.6% vs. 5.5%; p = 0.09), and TVR in survivors (10.9% vs. 11.7% vs. 11.6%; p = 0.56) in normal weight individuals compared with overweight or obese patients. Such results persisted after risk-adjustment for heterogeneous baseline characteristics of groups and were independent of the types of DES.

Conclusions DES.DE revealed no evidence of "obesity paradox" in a routine clinical practice using DES (228).

True Percutaneous Approach for Transfemoral Aortic Valve Implantation Using the Prostar XL Device: Impact of Learning Curve on Vascular Complications

Objectives The purpose of this study was to evaluate the incidence of vascular complications and the predictors of Prostar failure for a "true percutaneous approach" in transfemoral transcatheter aortic valve implantation (TAVI).

Background Safety and efficacy of a true percutaneous approach in transfemoral-TAVI has not been described in a large prospective cohort.

Methods Among 264 patients included in our prospective TAVI database (October 2006 to December 2010), transfemoral-TAVI was performed in 170 patients. True percutaneous approach was performed in 142 consecutive patients since March 2008. Successful closure with Prostar was defined as adequate hemostasis without Prostar-related vascular complications. We compared the incidence of vascular complications in our early and late experience.

Results Patients were 83.0 ± 7.2 years old and with a EuroSCORE of 24.0 ± 11.6%. The Edwards valve (Edwards Lifesciences, Irvine, California) (18- to 24-F) was used in 109 cases and the CoreValve (Medtronic, Minneapolis, Minnesota) (18-F) in 31. The sheath outer diameter to minimal femoral diameter ratio (SFAR) was 0.96 ± 0.14. Successful closure was achieved in 90.7%, and was significantly increased (95.7% vs. 85.7%, p = 0.047) in the late experience group. Cross-over to surgery was required in 3.6%. Vascular complications occurred in 20.0%, and were significantly lower in the late experience group (11.4% vs. 28.6%, p = 0.012). Major vascular complications (2.9% vs. 14.3%, p = 0.018) were decreased in the late experience group. Early experience (hazard ratio [HR]: 3.66, 95% confidence interval [CI]: 1.04 to 13.89, p = 0.047) and SFAR (HR: 110.80, 95% CI: 1.15 to 10,710.73, p = 0.044) predicted Prostar failure by univariate analysis.

Conclusions Experience reduced major vascular complications in a true percutaneous approach for transfemoral-TAVI. Further application of this less invasive strategy is feasible and may be beneficial, in this high-risk patient cohort (229).

Silent Ischemia: Clinical Relevance

Myocardial ischemia can occur without overt symptoms. In fact, asymptomatic (or silent) ST-segment depression during ambulatory electrocardiogram monitoring occurs more often than symptomatic ST-segment depression in patients with coronary artery disease. Initial studies documented that silent ischemia provided independent prediction of adverse outcomes in patients with known and unknown coronary artery disease. The ACIP (Asymptomatic Cardiac Ischemia Pilot Study) enrolled patients in the 1990s and found that revascularization was better than medical therapy in reducing silent ischemic episodes and possibly cardiovascular (CV) events. However, the more recent COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial found similar CV event rates between patients treated with optimal medical therapy alone and those treated with optimal medical therapy plus percutaneous revascularization. Therefore, in the current era, medical therapy appears to be as effective as revascularization in suppressing symptomatic ischemia and preventing CV events. COURAGE was not designed to evaluate changes in the frequency of silent ischemia. Therefore, silent ischemia may persist despite current-era treatment and might still identify patients with increased risk of CV events. Also, silent ischemia is likely to occur frequently in heart transplant patients with denervated hearts and coronary allograft vasculopathy, and future study aimed at improving the management of silent ischemia in this population is warranted. Additionally, future research is warranted to study the effect of newer medical therapies such as ranolazine or selected use of revascularization (for example, guided by fractional flow reserve) in those patients with persistent silent ischemia despite optimal current-era medical therapy (230).

Survival in Patients With Poorly Compressible Leg Arteries

Objectives This study sought to compare survival of patients with poorly compressible arteries (PCA) to those with a normal ankle-brachial index (ABI) and those with peripheral arterial disease (PAD).

Background Limited data are available regarding survival in patients with PCA identified in the clinical setting by noninvasive lower extremity arterial evaluation.

Methods We conducted a historical cohort study of consecutive patients who underwent outpatient, noninvasive lower extremity arterial evaluation at the Mayo Clinic, Rochester, Minnesota, from January 1998 through December 2007, and who were followed for a mean duration

of 5.8 ± 3.1 years. An ABI 1.00 to 1.30 was considered normal, PAD was defined as a resting or post-exercise ABI ≤0.90, and PCA defined as an ABI ≥1.4 and/or an ankle systolic blood pressure >255 mm Hg. Patients were followed for all-cause mortality through September 30, 2009.

Results Of 16,493 individuals (mean age 67.8 ± 13.0 years, 59% male); 29% had normal ABI, 54% had PAD, and 17% had PCA. During follow-up (mean duration 5.8 ± 3.1 years), 4,365 patients (26%) died. The percent alive at the end of the study period was 88%, 70%, and 60% for normal ABI, PAD, and PCA, respectively. After adjustment for age, sex, cardiovascular risk factors, comorbid conditions, and medication use, the hazard ratios (95% confidence intervals) of death associated with PCA were 2.0 (1.8 to 2.2) and 1.3 (1.2 to 1.4) compared with the normal ABI and PAD groups, respectively.

Conclusions Patients identified by noninvasive vascular testing to have poorly compressible leg arteries have poor survival, worse than those with a normal ABI or those with PAD (231).

Improvements in Transcatheter Aortic Valve Implantation Outcomes in Lower Surgical Risk Patients: A Glimpse Into the Future

Objectives The purpose of this study was to investigate the evolution of patient selection criteria for transcatheter aortic valve implantation (TAVI) and its impact on clinical outcomes.

Background Anecdotal evidence suggests that patient selection for TAVI is shifting toward lower surgical risk patients. The extent of this shift and its impact on clinical outcomes, however, are currently unknown.

Methods We conducted a single-center study that sub-categorized TAVI patients into quartiles (Q1 to Q4) defined by enrollment date. These subgroups were subsequently examined for differences in baseline characteristics and 30-day and 6-month mortality rate. The relationship between quartiles and mortality rate was examined using unadjusted and adjusted (for baseline characteristics) Cox proportional hazard models.

Results Each quartile included 105 patients (n = 420). Compared with Q4 patients, Q1 patients had higher logistic EuroSCORES (25.4 ± 16.1% vs. 17.8 ± 12.0%, p < 0.001), higher Society of Thoracic Surgeons scores (7.1 ± 5.5% vs. 4.8 ± 2.6%, p > 0.001), and higher median N-terminal pro–B-type natriuretic peptide levels (3,495 vs. 1,730 ng/dl, p < 0.046). From Q1 to Q4, the crude 30-day and 6-month mortality rate decreased significantly from 11.4% to 3.8% (unadjusted hazard ratio [HR]: 0.33; 95% confidence interval [CI]: 0.11 to 1.01; p = 0.053) and from 23.5% to 12.4% (unadjusted HR: 0.49; 95 CI: 0.25 to 0.95; p = 0.07), respectively. After adjustment for baseline characteristics, there were no significant differences between Q1 and Q4 in 30-day mortality rate (adjusted HR ratio: 0.29; 95% CI: 0.08 to 1.08; p = 0.07) and 6-month mortality rate (HR: 0.67; 95% CI: 0.25 to 1.77; p = 0.42).

Conclusions The results of this study demonstrate an important paradigm shift toward the selection of lower surgical risk patients for TAVI. Significantly better clinical outcomes can be expected in lower than in higher surgical risk patients undergoing TAVI (232).

Hypothermia Therapy: Neurological and Cardiac Benefits

Due to its protective effect on the brain and the myocardium, hypothermia therapy (HT) has been extensively studied in cardiac arrest patients with coma as well as in patients presenting with acute myocardial infarction (MI). In the setting of cardiac arrest, randomized studies have shown that HT decreases mortality and improves neurological outcomes. Subsequent guidelines have therefore recommended cooling (32°C to 34°C) for 12 to 24 h in unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest due to ventricular fibrillation. Observational studies have also confirmed the feasibility of this therapy in clinical practice and support its early application in patients with nonventricular fibrillation cardiac arrest and in post-resuscitation circulatory shock. In patients with acute MI, available clinical evidence does not yet support HT as the standard of care, because no study to date has shown a clear net benefit in such a cohort. After a brief review of the mechanisms of action for HT, we provide a review of the clinical evidence, cooling techniques, and potential adverse effects associated with HT in the setting of post-cardiac arrest patient and acute MI (233).

Percutaneous Coronary Intervention and Drug-Eluting Stent Use Among Patients ≥85 Years of Age in the United States

Objectives This study assessed the comparative effectiveness of drug-eluting stents (DES) versus bare-metal stents (BMS) among patients ≥85 years of age.

Background Despite an aging population, little is known about the comparative effectiveness of DES versus BMS among patients age ≥85 years undergoing percutaneous coronary intervention (PCI).

Methods We examined 471,006 PCI patients age ≥65 years at 947 hospitals in the National Cardiovascular Data Registry between 2004 and 2008 and linked to Medicare claims data. Long-term outcomes (median follow-up 640.8 ± 423.5 days) were compared between users of DES and BMS.

Results Patients age ≥85 years comprise an increasing proportion of PCIs performed among elderly subjects, yet rates of DES use declined the most in this age group. Compared with BMS, use of DES was associated with lower mortality: age ≥85 years, 29% versus 38% (adjusted hazard ratio [HR]: 0.80 [95% confidence interval (CI): 0.77 to

0.83]); age 75 to 84 years, 17% versus 25% (HR: 0.77 [95% CI: 0.75 to 0.79]); and age 65 to 74 years, 10% versus 16% (HR: 0.73 [95% CI: 0.71 to 0.75]). However, the adjusted mortality difference narrowed with increasing age ($p_{interaction}$ <0.001). In contrast, the adjusted HR for myocardial infarction rehospitalization associated with DES use was significantly lower with increasing age: age ≥85 years, 9% versus 12% (HR: 0.77 [95% CI: 0.71 to 0.83]); age 75 to 84 years, 7% versus 9% (HR: 0.81 [95% CI: 0.77 to 0.84]); and age 65 to 74 years, 7% versus 8% (HR: 0.84 [95% CI: 0.80 to 0.88]) ($p_{interaction}$ <0.001).

Conclusions In this national study of older patients undergoing PCI, declines in DES use were most pronounced among those aged ≥85 years, yet lower adverse-event rates associated with DES versus BMS use were observed (234).

Incidence, Predictive Factors, and Prognostic Value of New-Onset Atrial Fibrillation Following Transcatheter Aortic Valve Implantation

Objectives This study sought to evaluate the incidence, predictive factors, and prognostic value of new-onset atrial fibrillation (NOAF) following transcatheter aortic valve implantation (TAVI).

Background Very few data exist on the occurrence of NOAF following TAVI.

Methods A total of 138 consecutive patients with no prior history of atrial fibrillation (AF) underwent TAVI with a balloon-expandable valve. Patients were on continuous electrocardiogram monitoring until hospital discharge, and NOAF was defined as any episode of AF lasting >30 s. All clinical, echocardiographic, procedural, and follow-up data were prospectively collected.

Results NOAF occurred in 44 patients (31.9%) at a median time of 48 h (interquartile range: 0 to 72 h) following TAVI. The predictive factors of NOAF were left atrial (LA) size (odds ratio [OR]: 1.21 for each increase in 1 mm/m^2, 95% confidence interval [CI]: 1.09 to 1.34, $p < 0.0001$) and transapical approach (OR: 4.08, 95% CI: 1.35 to 12.31, $p = 0.019$). At 30-day follow-up, NOAF was associated with a higher rate of stroke/systemic embolism (13.6% vs. 3.2%, $p = 0.021$, $p = 0.047$ after adjustment for baseline differences between groups), with no differences in mortality rate between groups (NOAF: 9.1%, no-NOAF: 6.4%, $p = 0.57$). At a median follow-up of 12 months (interquartile range: 5 to 20 months), a total of 27 patients (19.6%) had died, with no differences between the NOAF (15.9%) and no-NOAF (21.3%) groups, $p = 0.58$. The cumulative rate of stroke and stroke/systemic embolism at follow-up were 13.6% and 15.9%, respectively, in the NOAF group versus 3.2% in the no-NOAF group ($p = 0.039$, adjusted $p = 0.037$ for stroke; $p = 0.020$, adjusted $p = 0.023$ for stroke/systemic embolism).

Conclusions NOAF occurred in about one-third of the patients with no prior history of AF undergoing TAVI and its incidence was increased in patients with larger LA size and those undergoing transapical TAVI. NOAF was associated with a higher rate of stroke/systemic embolism, but not a higher mortality, at 30 days and at 1-year follow-up (235).

Percutaneous Aortic Valve Replacement: Vascular Outcomes With a Fully Percutaneous Procedure

Objectives The aim of this study was to evaluate vascular complications in a consecutive patient population undergoing transfemoral percutaneous aortic valve replacement (PAVR) applying current Valve Academic Research Consortium definitions.

Background Vascular complications have been the major cause of mortality and morbidity associated with PAVR. Both open surgical and fully percutaneous access site strategies have been advocated.

Methods All patients undergoing transfemoral PAVR during fiscal years 2009 and 2010 were prospectively evaluated at baseline, after the procedure, and at 30 days.

Results PAVR was performed in 137 consecutive patients. All but 1 patient underwent planned arteriotomy closure using a percutaneous pre-closure technique. Smaller sheaths, rigorous angiographic and computed tomographic screening and patient selection, and percutaneous vascular repair techniques were increasingly used over this period. From 2009 to 2010, major vascular complications decreased from 8% to 1% ($p = 0.06$), minor vascular complications decreased from 24% to 8% ($p < 0.01$), major bleeds fell from 14% to 1% ($p < 0.01$), and unplanned surgery decreased from 28% to 2% ($p < 0.01$). A minimal artery diameter smaller than the external sheath diameter, moderate or severe calcification, and peripheral vascular disease were associated with higher vascular complication rates.

Conclusions Vascular complications occur more often if the minimal artery diameter is smaller than the external sheath diameter, in the presence of moderate or severe calcification, and in patients with peripheral vascular disease. With careful patient selection, advanced interventional techniques, and a fully percutaneous procedure, marked reductions in vascular and bleeding complications can be achieved (236).

Procedural Complications, Rehospitalizations, and Repeat Procedures After Catheter Ablation for Atrial Fibrillation

Objectives The purpose of this study was to estimate rates and identify predictors of inpatient complications and 30-day readmissions, as well as repeat hospitalization rates for arrhythmia recurrence following atrial fibrillation (AF) ablation.

Background AF is the most common clinically significant arrhythmia and is associated with increased morbidity and mortality. Radiofrequency or cryotherapy ablation of AF is

a relatively new treatment option, and data on post-procedural outcomes in large general populations are limited.
Methods Using data from the California State Inpatient Database, we identified all adult patients who underwent their first AF ablation from 2005 to 2008. We used multivariable logistic regression to identify predictors of complications and/or 30-day readmissions and Kaplan-Meier analyses to estimate rates of all-cause and arrhythmia readmissions.
Results Among 4,156 patients who underwent an initial AF ablation, 5% had periprocedural complications, most commonly vascular, and 9% were readmitted within 30 days. Older age, female, prior AF hospitalizations, and less hospital experience with AF ablation were associated with higher adjusted risk of complications and/or 30-day readmissions. The rate of all-cause hospitalization was 38.5% by 1 year. The rate of readmission for recurrent AF, atrial flutter, and/or repeat ablation was 21.7% by 1 year and 29.6% by 2 years.
Conclusions Periprocedural complications occurred in 1 of 20 patients undergoing AF ablation, and all-cause and arrhythmia-related rehospitalizations were common. Older age, female sex, prior AF hospitalizations, and recent hospital procedure experience were associated with a higher risk of complications and/or 30-day readmission after AF ablation (237).

Classification and Clinical Impact of Restenosis After Femoropopliteal Stenting

Objectives The purpose of this study was to investigate the relationship between angiographic patterns of in-stent restenosis (ISR) after femoropopliteal (FP) stenting and the frequency of refractory ISR.
Background In-stent restenosis after FP stenting is an unsolved problem. The incidence and predictors of refractory restenosis remain unclear.
Methods This study was a multicenter, retrospective observational study. From September 2000 to December 2009, 133 restenotic lesions after FP artery stenting were classified by angiographic pattern: class I included focal lesions (≤50 mm in length), class II included diffuse lesions (>50 mm in length), and class III included totally occluded ISR. All patients were treated by balloon angioplasty for at least 60 s. Recurrent ISR or occlusion was defined as ISR or occlusion after target lesion revascularization. Restenosis was defined as >2.4 of the peak systolic velocity ratio by duplex scan or >50% stenosis by angiography.
Results Sixty-four percent of patients were male, 67% had diabetes mellitus, and 24% underwent hemodialysis. Class I pattern was found in 29% of the limbs, class II in 38%, and class III in 33%. Mean follow-up period was 24 ± 17 months. All-cause death occurred in 14 patients; bypass surgery was performed in 11 limbs, and major amputation was performed in 1 limb during the follow-up. Kaplan-Meier survival curves showed that the rate of recurrent ISR at 2 years was 84.8% in class III patients compared with 49.9% in class I patients ($p < 0.0001$) and 53.3% in class II patients ($p = 0.0003$), and the rate of recurrent occlusion at 2 years was 64.6% in class III patients compared with 15.9% in class I patients ($p < 0.0001$) and 18.9% in class II patients ($p < 0.0001$).
Conclusions Restenotic patterns after FP stenting are important predictors of recurrent ISR and occlusion (238).

Ex Vivo Assessment of Vascular Response to Coronary Stents by Optical Frequency Domain Imaging

Objectives This study sought to examine the capability of optical frequency domain imaging (OFDI) to characterize various morphological and histological responses to stents implanted in human coronary arteries.
Background A precise assessment of vascular responses to stents may help stratify the risk of future adverse events in patients who have been treated with coronary stents.
Methods Fourteen human stented coronary segments with implant duration ≥1 month from 10 hearts acquired at autopsy were interrogated ex vivo by OFDI and intravascular ultrasound (IVUS). Comparison with histology was assessed in 134 pairs of images where the endpoints were to investigate: 1) accuracy of morphological measurements; 2) detection of uncovered struts; and 3) characterization of neointima.
Results Although both OFDI and IVUS provided a good correlation of neointimal area with histology, the correlation of minimum neointimal thickness was inferior in IVUS ($R^2 = 0.39$) as compared with OFDI ($R^2 = 0.67$). Similarly, IVUS showed a weak correlation of the ratio of uncovered to total stent struts per section (RUTSS) ($R^2 = 0.24$), whereas OFDI maintained superiority ($R^2 = 0.66$). In a more detailed analysis by OFDI, identification of individual uncovered struts demonstrated a sensitivity of 77.9% and specificity of 96.4%. Other important morphological features such as fibrin accumulation, excessive inflammation (hypersensitivity), and in-stent atherosclerosis were characterized by OFDI; however, the similarly dark appearance of these tissues did not allow for direct visual discrimination. The quantitative analysis of OFDI signal reflections from various in-stent tissues demonstrated distinct features of organized thrombus and accumulation of foamy macrophages.
Conclusions The results of the present study reinforce the potential of OFDI to detect vascular responses that may be important for the understanding of long-term stent performance, and indicate the capability of this technology to serve as a diagnostic indicator of clinical success (239).

The Retrograde Technique for Recanalization of Chronic Total Occlusions: A Step-by-Step Approach

Chronic total occlusion recanalization still represents the final frontier in percutaneous coronary intervention.

Retrograde chronic total occlusion recanalization has recently become an essential complement to the classical antegrade approach. In experienced hands, the retrograde technique currently has a high success rate with a low complication profile, despite frequent utilization in the most anatomically and clinically complex patients. Since its initial description, important changes have occurred that make the technique faster and more successful. We propose a step-by-step approach of the technique as practiced at experienced centers in North America. Because the technique can vary substantially, we describe the different alternatives to each step and offer what we perceived to be the most efficient techniques (240).

Contemporary Use and Effectiveness of N-Acetylcysteine in Preventing Contrast-Induced Nephropathy Among Patients Undergoing Percutaneous Coronary Intervention

Objectives The aim of this study was to examine the use of and outcomes associated with use of *N*-acetylcysteine (NAC) in real-world practice.

Background The role of NAC in the prevention of contrast-induced nephropathy (CIN) is controversial, leading to widely varying recommendations for its use.

Methods Use of NAC was assessed in consecutive patients undergoing nonemergent percutaneous coronary intervention from 2006 to 2009 in the Blue Cross Blue Shield of Michigan Cardiovascular Consortium, a large multicenter quality improvement collaborative. We examined the overall prevalence of NAC use in these patients and then used propensity matching to link its use with clinical outcomes, including CIN, nephropathy-requiring dialysis, and death.

Results Of the 90,578 percutaneous coronary interventions performed during the study period, NAC was used in 10,574 (11.6%) procedures, with its use steadily increasing over the study period. Patients treated with NAC were slightly older and more likely to have baseline renal insufficiency and other comorbidities. In propensity-matched, risk-adjusted models, we found no differences in outcomes between patients treated with NAC and those not receiving NAC for CIN (5.5% vs. 5.5%, $p = 0.99$), nephropathy-requiring dialysis (0.6% vs. 0.6%, $p = 0.69$), or death (0.6% vs. 0.8%, $p = 0.15$). These findings were consistent across many prespecified subgroups.

Conclusions Use of NAC is common and has steadily increased over the study period but does not seem to be associated with improved clinical outcomes in real-world practice (241).

Examination of the In Vivo Mechanisms of Late Drug-Eluting Stent Thrombosis: Findings From Optical Coherence Tomography and Intravascular Ultrasound Imaging

Objectives This study investigated the role of uncovered stent struts on late stent thrombosis (LST) after drug-eluting stent (DES) implantation with optical coherence tomography (OCT).

Background Autopsy studies have identified delayed healing and lack of endothelialization of DES struts as the hallmarks of LST. DES strut coverage has not previously been examined in vivo in patients with LST.

Methods We studied 54 patients, including 18 with DES LST (median 615 days after implant) undergoing emergent percutaneous coronary interventions and 36 matched DES control subjects undergoing routine repeat OCT and intravascular ultrasound (IVUS) who did not experience LST for ≥3 years. Thrombus aspiration was performed during emergent percutaneous coronary intervention before OCT and IVUS assessment.

Results By OCT, patients with LST—compared with control subjects—had a higher percentage of uncovered (median [interquartile range]) (12.27 [5.50 to 23.33] vs. 4.14 [3.00 to 6.22], $p < 0.001$) and malapposed (4.60 [1.85 to 7.19] vs. 1.81 [0.00 to 2.99], $p < 0.001$) struts. The mean neointimal thickness was similar in the 2 groups (0.23 ± 0.17 mm vs. 0.17 ± 0.09 mm, $p = 0.28$). By IVUS, stent expansion was comparable in the 2 groups, although positive remodeling was increased in patients with LST (mean vessel cross-section area 19.4 ± 5.8 mm^2 vs. 15.1 ± 4.6 mm^2, $p = 0.003$). Thrombus aspiration demonstrated neutrophils and eosinophils in most cases. By multivariable analysis, the length of segment with uncovered stent struts by OCT and the remodeling index by IVUS were independent predictors of LST.

Conclusions In this in vivo case-controlled study, the presence of uncovered stent struts as assessed by OCT and positive vessel remodeling as imaged by IVUS were associated with LST after DES (242).

Quantifying the Learning Curve in the Use of a Novel Vascular Closure Device: An Analysis of the NCDR (National Cardiovascular Data Registry) CathPCI Registry

Objectives This study sought to quantify the learning curve for the safety and effectiveness of a newly introduced vascular closure device through evaluation of the NCDR (National Cardiovascular Data Registry) CathPCI clinical outcomes registry.

Background The impact of learning on the clinical outcomes complicates the assessment of the safety and efficacy during the early experience with newly introduced medical devices.

Methods We performed a retrospective analysis of the relationship between cumulative institutional experience and clinical device success, defined as device deployment success and freedom from any vascular complications, for the StarClose vascular closure device (Abbott Vascular, Redwood City, California). Generalized estimating equation modeling was used to develop risk-adjusted clinical success predictions that were analyzed to quantify learning curve rates.

Results A total of 107,710 procedures used at least 1 StarClose deployment, between January 1, 2006, and December 31, 2007, with overall clinical success increasing from 93% to 97% during the study period. The learning curve was triphasic, with an initial rapid learning phase, followed by a period of declining rates of success, followed finally by a recovery to a steady-state rate of improved device success. The rates of learning were influenced positively by diagnostic (vs. percutaneous coronary intervention) procedure use and teaching status and were affected inversely by annual institutional volume.

Conclusions An institutional-level learning curve for the initial national experience of StarClose was triphasic, likely indicating changes in patient selection and expansion of number of operators during the initial phases of device adoption. The rate of learning was influenced by several institutional factors, including overall procedural volume, utilization for percutaneous coronary intervention procedures, and teaching status (243).

The Sirolimus-Eluting Cypher Select Coronary Stent for the Treatment of Bare-Metal and Drug-Eluting Stent Restenosis: Insights From the e-SELECT (Multicenter Post-Market Surveillance) Registry

Objectives This study sought to compare the 1-year safety and efficacy of Cypher Select or Cypher Select Plus (Cordis Corporation, Bridgewater, New Jersey) sirolimus-eluting stents (SES) with the treatment of bare-metal stents (BMS) and drug-eluting stent (DES) in-stent restenosis (ISR) in nonselected, real-world patients.

Background There is paucity of consistent data on DES for the treatment of ISR, especially, DES ISR.

Methods The e-SELECT (Multicenter Post-Market Surveillance) registry is a Web-based, multicenter and international registry encompassing virtually all subsets of patients and lesions treated with at least 1 SES during the period from 2006 to 2008. We enrolled in this pre-specified subanalysis all patients with at least 1 clinically relevant BMS or DES ISR treated with SES. Primary endpoint was major adverse cardiac events and stent thrombosis rate at 1 year.

Results Of 15,147 patients enrolled, 1,590 (10.5%) presented at least 1 ISR (BMS group, n = 1,235, DES group, n = 355). Patients with DES ISR had higher incidence of diabetes (39.4% vs. 26.9%, $p < 0.001$), renal insufficiency (5.8% vs. 2.3%, $p = 0.003$), and prior coronary artery bypass graft (20.5% vs. 11.8%, $p < 0.001$). At 1 year, death (1.4% for BMS vs. 2.1% for DES, $p = 0.3$) and myocardial infarction (2.4% for BMS and 3.3% for DES, $p = 0.3$) rates were similar, whereas ischemia-driven target lesion revascularization and definite/probable late stent thrombosis were higher in patients with DES ISR (6.9% vs. 3.1%, $p = 0.003$, and 1.8% vs. 0.5%, $p = 0.04$, respectively).

Conclusions Use of SES for either BMS or DES ISR treatment is safe and associated with low target lesion revascularization recurrence and no apparent safety concern (244).

Angiographic Stent Thrombosis at Coronary Bifurcations: Short- and Long-Term Prognosis

Objectives This study sought to describe the presentation, management, and outcomes of patients presenting with angiographic definite stent thrombosis (ST) at coronary bifurcations.

Background The development of drug-eluting stents has made it increasingly feasible to treat bifurcation lesions percutaneously. However, ST at coronary bifurcations may be associated with greater mortality than ST elsewhere.

Methods We analyzed a multicenter California registry comprising all cases of angiographic definite ST at 5 academic hospitals from 2005 to 2010. Stenting was defined as occurring at a bifurcation if the main vessel stent crossed a side branch ≥2.0 mm in diameter (provisional single-stent approach), or if there was a prior 2-stent bifurcation approach.

Results Among 173 cases of angiographic definite ST, we identified 20 cases of ST at coronary bifurcations. Nine of 20 bifurcation ST (45%) occurred with a stent present in both the parent and branch vessel. Eight cases had thrombus present in both the parent and side branch vessels. In-hospital mortality was much higher for subjects with bifurcation ST than ST at a nonbifurcation site (20% vs. 2%, $p < 0.0001$). During a median follow-up of 2.3 years, ST at a coronary bifurcation was associated with increased long-term mortality (hazard ratio [HR]: 3.3, 95% confidence interval [CI]: 1.4 to 7.7, $p = 0.007$) and a significantly higher risk for major adverse cardiovascular events (HR: 2.2, 95% CI: 1.04 to 4.8, $p = 0.04$) relative to ST at a nonbifurcation site.

Conclusions ST at coronary bifurcations is associated with a higher in-hospital and long-term mortality than ST at nonbifurcation lesions. (Stent Thrombus in Acute Coronary Syndromes; NCT00931502) (245).

Transcatheter Aortic Valve Implantation: Assessing the Learning Curve

Objectives The aim of this study was to assess the learning curve for the implantation of the percutaneous aortic valve via the transfemoral route.

Background Transcutaneous aortic valve insertion is a fundamentally new procedure for the treatment of aortic valve stenosis. The number of cases needed to gain proficiency with concomitant ease and familiarity (i.e., the "learning curve") with the procedure is unknown.

Methods We performed a retrospective analysis of the first 44 consecutive patients who underwent transcatheter aortic valve implantation as part of the PARTNER (Placement of Aortic Transcatheter Valves) trial at our institution between November 2008 and May 2011.

Results The median age of the patients was 83 years (interquartile range: 77 to 87 years) and a median Society of Thoracic Surgery risk score of 9.6. Pre-procedural assessment of the aortic valve revealed a mean gradient of 53.5 mm Hg, mean aortic valve area of 0.7 mm^2, and a median ejection fraction of 59.5%. Patients were divided into tertiles based on sequence. Significant decreases in median contrast volume (180 to 160 to 130 ml, $p = 0.003$), valvuloplasty to valve deployment time (12.0 to 11.6 to 7.0 min, $p < 0.001$) and fluoroscopy times, from 26.1 to 17.2 and 14.3 min occurred from tertiles 1 to 3, $p < 0.001$. Significant decreases in radiation doses were also seen across the 3 tertiles, $p < 0.001$. The 30-day mortality for the entire cohort was 11%.

Conclusions Experience accumulated over 44 transfemoral aortic valve implantations led to significant decreases in procedural times, radiation, and contrast volumes. Our data show increasing proficiency with evidence of plateau after the first 30 cases. More studies are needed to confirm these findings (246).

Percutaneous Edge-to-Edge Mitral Valve Repair in High-Surgical-Risk Patients: Do We Hit the Target?

Objectives This study sought to assess the feasibility and safety of percutaneous edge-to-edge mitral valve (MV) repair in patients with an unacceptably high operative risk.

Background MV repair for mitral regurgitation (MR) can be accomplished by use of a clip that approximates the free edges of the mitral leaflets.

Methods All patients were declined for surgery because of a high logistic EuroSCORE (>20%) or the presence of other specific surgical risk factors. Transthoracic echocardiography was performed before and 6 months after the procedure. Differences in New York Heart Association (NYHA) functional class, quality of life (QoL) using the Minnesota questionnaire, and 6-min walk test (6-MWT) distances were reported.

Results Fifty-five procedures were performed in 52 patients (69.2% male, age 73.2 ± 10.1 years, logistic EuroSCORE 27.1 ± 17.0%). In 3 patients, partial clip detachment occurred; a second clip was placed successfully. One patient experienced cardiac tamponade. Two patients developed inguinal bleeding, of whom 1 needed surgery. Six patients (11.5%) died during 6-month follow-up (5 patients as a result of progressive heart failure and 1 noncardiac death). The MR grade before repair was ≥3 in 100%; after 6 months, a reduction in MR grade to ≤2 was present in 79% of the patients. Left ventricular (LV) end-diastolic diameter, LV ejection fraction, and systolic pulmonary artery pressure improved significantly. Accompanied improvements in NYHA functional class, QoL index, 6-MWT distances, and log N-terminal pro–B-type natriuretic peptide were observed.

Conclusions In a high-risk population, MR reduction can be achieved by percutaneous edge-to-edge valve repair, resulting in LV remodeling with improvement of functional capacity after 6 months (247).

Kissing Balloon or Sequential Dilation of the Side Branch and Main Vessel for Provisional Stenting of Bifurcations: Lessons From Micro-Computed Tomography and Computational Simulations

Objectives This study sought to evaluate post-dilation strategies in bifurcation stenting.

Background In bifurcation stenting practice, it is still controversial how post-dilation should be performed and whether the kissing balloon (KB) technique is mandatory when only the main vessel (MV) receives a stent.

Methods A series of drug-eluting stents (DES) ($n = 26$) were deployed in a coronary bifurcation model following a provisional approach. After the deployment of the stent in the MV, post-dilation with the KB technique was compared with a 2-step, sequential post-dilation of the side branch (SB) and MV without kissing.

Results The percentage of the SB lumen area free of stent struts was similar after KB (79.1 ± 8.7%) and after the 2-step sequence (74.4 ± 11.6%, $p = 0.25$), a considerable improvement compared with MV stenting only without dilation of the stent at the SB ostium (30.8 ± 7.8%, $p < 0.0001$). The rate of strut malapposition in the ostium was 21.3 ± 9.2% after KB and 24.9 ± 10.4% after the 2-step sequence, respectively, a significant reduction compared with a simple SB dilation (55.3 ± 16.8%, $p < 0.0001$) or MV stenting only (47.0 ± 8.5%, $p < 0.0005$). KB created a significant elliptical overexpansion of the MV lumen, inducing higher stress concentration proximal to the SB. KB also led to a higher risk of incomplete stent apposition at the proximal stent edge (30.7 ± 26.4% vs. 2.8 ± 9.6% for 2-step, $p = 0.0016$).

Conclusions Sequential 2-step post-dilation of the SB and MV may offer a simpler and more efficient alternative to final KB technique for provisional stenting of bifurcations (248).

Transradial Versus Transfemoral Intervention for Acute Myocardial Infarction: A Propensity Score-Adjusted and -Matched Analysis From the REAL (REgistro regionale AngiopLastiche dell'Emilia-Romagna) Multicenter Registry

Objectives This study sought to assess whether transradial intervention, by minimizing access-site bleeding and vascular events, improves outcomes in patients with ST-segment elevation myocardial infarction compared with the transfemoral approach.

Background Bleeding and consequent blood product transfusions have been causally associated with a higher mortality rate in patients with myocardial infarction undergoing coronary angioplasty.

Methods We identified all adults undergoing percutaneous intervention for acute myocardial infarction in

Emilia-Romagna, a region in the north of Italy of 4 million residents, between January 1, 2003, and July 30, 2009, at 12 referral hospitals using a region-mandated database of percutaneous coronary intervention procedures. Differences in the risk of death at 2 years between patients undergoing transfemoral versus transradial intervention, assessed on an intention-to-treat basis, were determined from vital statistics records and compared based on propensity score adjustment and matching.

Results A total of 11,068 patients were treated for acute myocardial infarction (8,000 via transfemoral and 3,068 via transradial route). According to analysis of matched pairs, the 2-year, risk-adjusted mortality rates were lower for the transradial than for the transfemoral group (8.8% vs. 11.4%; $p = 0.0250$). The rate of vascular complications requiring surgery or need for blood transfusion were also significantly decreased in the transradial group (1.1% vs. 2.5%, $p = 0.0052$).

Conclusions In patients undergoing angioplasty for acute myocardial infarction, transradial treatment is associated with decreased 2-year mortality rates and a reduction in the need for vascular surgery and/or blood transfusion compared with transfemoral intervention (249).

Prevention of Contrast Nephropathy by Furosemide With Matched Hydration: The MYTHOS (Induced Diuresis With Matched Hydration Compared to Standard Hydration for Contrast Induced Nephropathy Prevention) Trial

Objectives This study investigated the effect of furosemide-forced diuresis and intravenous saline infusion matched with urine output, using a novel dedicated device designed for contrast-induced nephropathy (CIN) prevention.

Background CIN is a frequent cause of acute kidney injury associated with increased morbidity and mortality.

Methods A total of 170 consecutive patients with chronic kidney disease (CKD) undergoing coronary procedures were randomized to either furosemide with matched hydration (FMH group, $n = 87$) or to standard intravenous isotonic saline hydration (control group; $n = 83$). The FMH group received an initial 250-ml intravenous bolus of normal saline over 30 min followed by an intravenous bolus (0.5 mg/kg) of furosemide. Hydration infusion rate was automatically adjusted to precisely replace the patient's urine output. When a urine output rate >300 ml/h was obtained, patients underwent the coronary procedure. Matched fluid replacement was maintained during the procedure and for 4 h post-treatment. The definition of CIN was a ≥25% or ≥0.5 mg/dl rise in serum creatinine over baseline.

Results In the FMH group, no device- or therapy-related complications were observed. Four (4.6%) patients in the FMH group developed CIN versus 15 (18%) controls ($p = 0.005$). A lower incidence of cumulative in-hospital clinical complications was also observed in FMH-treated patients than in controls (8% vs. 18%; $p = 0.052$).

Conclusions In patients with CKD undergoing coronary procedures, furosemide-induced high urine output with matched hydration significantly reduces the risk of CIN and may be associated with improved in-hospital outcome. (Induced Diuresis With Matched Hydration Compared to Standard Hydration for Contrast Induced Nephropathy Prevention [MYTHOS]; NCT00702728) (250).

The Leipzig Prospective Vascular Ultrasound Registry in Radial Artery Catheterization: Impact of Sheath Size on Vascular Complications

Objectives This study investigated the impact of sheath size on the rate of radial artery occlusions (RAO) (primary objective) and other access site complications (hemorrhage, pseudoaneurysm, arteriovenous fistula) as secondary Objectives after transradial coronary catheterization.

Background The number of vascular access complications in the published data ranges from 5% to 38% after transradial catheterization.

Methods Between November 2009 and August 2010, 455 patients 65.3 ± 10.9 years of age (62.2% male) with transradial access with 5-F ($n = 153$) or 6-F ($n = 302$) arterial sheaths were prospectively recruited. Duplex sonography was obtained in each patient before discharge. Patients with symptomatic RAO were treated with low-molecular-weight heparin (LMWH), and a follow-up was performed.

Results The incidence of access site complications was 14.4% with 5-F sheaths compared with 33.1% with 6-F sheaths ($p < 0.001$). Radial artery occlusion occurred in 13.7% with 5-F sheaths compared with 30.5% with 6-F sheaths ($p < 0.001$). There was no difference between groups with regard to hemorrhage, pseudoaneurysms, or arteriovenous fistulas. Female sex, larger sheath size, peripheral arterial occlusive disease, and younger age independently predicted RAO in multivariate analysis. In total, 42.5% of patients with RAO were immediately symptomatic; another 7% became symptomatic within a mean of 4 days. Of patients with RAO, 59% were treated with LMWH. The recanalization rates were significantly higher in patients receiving LMWH compared with conventional therapy (55.6% vs. 13.5%, $p < 0.001$) after a mean of 14 days.

Conclusions The incidence of RAO by vascular ultrasound was higher than expected from previous data, especially in patients who underwent the procedure with larger sheaths (251).

A Point-of-Care Platelet Function Assay and C-Reactive Protein for Prediction of Major Cardiovascular Events After Drug-Eluting Stent Implantation

Objectives This study sought to investigate clinical utility of on-site platelet function test and C-reactive protein

(CRP) in patients undergoing percutaneous coronary intervention (PCI).

Background Data on long-term prognostic value of high on-treatment platelet reactivity (HTPR) on clopidogrel after PCI are limited. As a distinct biological pathway, CRP has been suggested to be associated with post-PCI atherothrombotic events.

Methods We evaluated 2,849 patients who received drug-eluting stents (DES) and had post-PCI VerifyNow P2Y12 assays (Accumetrics, San Diego, California) performed. Among them, baseline CRP measurement was available in 2,546 patients. The primary endpoint was a composite of all-cause death, nonfatal myocardial infarction, stent thrombosis, and stroke.

Results During follow-up (median, 2.2 years), the occurrence of the primary endpoint did not significantly differ among patients with and without HTPR (2.8% vs. 2.4% at 2 years; hazard ratio [HR]: 1.33, 95% confidence interval [CI]: 0.88 to 2.01; $p = 0.18$). By contrast, patients with elevated CRP levels were at significantly higher risk for the primary endpoint, as compared with those with nonelevated CRP levels (5.6% vs. 1.7% at 2 years; HR: 2.81, 95% CI:, 1.83 to 4.31; $p < 0.001$). The VerifyNow test had no incremental usefulness to classify long-term risk. However, the incorporation of CRP into a model with conventional clinical and procedural risk factors significantly improved the C-statistic for the prediction of the primary endpoint (0.729 to 0.759; $p = 0.03$).

Conclusions We failed to identify that HTPR measured by VerifyNow P2Y12 assay was significantly associated with long-term atherothrombotic risks in patients receiving DES. However, elevated CRP levels were significantly associated with worse outcomes and had incremental predictive values over conventional risk factors (252).

Impact of Body Weight and Extreme Obesity on the Presentation, Treatment, and In-Hospital Outcomes of 50,149 Patients With ST-Segment Elevation Myocardial Infarction: Results From the NCDR (National Cardiovascular Data Registry)

Objectives The aim of this study was to assess the impact of extreme (class III) obesity (body mass index [BMI] $\geq$40 kg/m^2) on care and outcomes in patients with ST-segment elevation myocardial infarction (STEMI).

Background Although its prevalence is increasing rapidly, little is known about the impact of extreme obesity on STEMI presentation, treatments, complication rates, and outcomes.

Methods The relationship between BMI and baseline characteristics, treatment patterns, and risk-adjusted in-hospital outcomes was quantified for 50,149 patients with STEMI from the National Cardiovascular Data Registry (NCDR) ACTION Registry–GWTG.

Results The proportions of patients with STEMI by BMI category were as follows: underweight (BMI <18.5 kg/m^2) 1.6%, normal weight (18.5 kg/m^2 $\leq$BMI <25 kg/m^2) 23.5%, overweight (25 kg/m^2 $\leq$BMI <30 kg/m^2) 38.7%, class I obese (30 kg/m^2 $\leq$BMI <35 kg/m^2) 22.4%, class II obese (35 kg/m^2 $\leq$BMI <40 kg/m^2) 8.7%, and class III obese 5.1%. Extreme obesity was associated with younger age at STEMI presentation (median age 55 years for class III obese vs. 66 years for normal weight); a higher prevalence of diabetes, hypertension, and dyslipidemia; a lower prevalence of smoking; and less extensive coronary artery disease and higher left ventricular ejection fraction. Process-of-care measures were similar across BMI categories, including the extremely obese. Using class I obesity as the referent, risk-adjusted in-hospital mortality rates were significantly higher only for class III obese patients (adjusted odds ratio: 1.64; 95% confidence interval: 1.32 to 2.03).

Conclusions Patients with extreme obesity present with STEMI at younger ages and have less extensive coronary artery disease, better left ventricular systolic function, and similar processes and quality of care. Despite these advantages, extreme obesity remains independently associated with higher in-hospital mortality (253).

Percutaneous Radiofrequency Septal Reduction for Hypertrophic Obstructive Cardiomyopathy in Children

Objectives The aim of this study was to assess the efficacy of radiofrequency catheter ablation (RFCA) in the treatment of hypertrophic obstructive cardiomyopathy in children.

Background Hypertrophic obstructive cardiomyopathy is an uncommon cause of left ventricular outflow tract obstruction in children. In symptomatic patients, open heart surgical myectomy has hitherto been the only therapeutic option.

Methods In 32 children, at a median age of 11.1 (range 2.9 to 17.5) years and weight of 31 (15 to 68) kg, ablation of the hypertrophied septum was performed using a cool-tip ablation catheter via a femoral arterial approach. The median number of lesions was 27 (10 to 63) and fluoroscopic time was 24 (12 to 60) min.

Results The majority of patients demonstrated an immediate decrease in the catheter pullback gradient (mean 78.5 $\pm$ 26.2 mm Hg pre-RFCA versus mean 36.1 $\pm$ 16.5 mm Hg post-RFCA, $p < 0.01$) and a further reduction in the Doppler echocardiographic gradient (mean 96.9 $\pm$ 27.0 mm Hg pre-RFCA versus 32.7 $\pm$ 27.1 mm Hg post-RFCA, $p < 0.01$) at follow-up. One patient died due to a paradoxical increase in left ventricular outflow tract obstruction, and another had persistent atrioventricular block that required permanent pacing. Six patients required further procedures (surgery, pacing, or further RFCA) during a median follow-up of 48 (3 to 144) months.

Conclusions The preliminary results of RFCA for septal reduction in children with hypertrophic cardiomyopathy are promising and merit further evaluation (254).

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Stent Longitudinal Integrity: Bench Insights Into a Clinical Problem

Objectives Standardized bench-top compression and elongation testing was undertaken to assess the longitudinal strength of contemporary stents. Insights gained may improve clinical stent choice and deployment techniques, and facilitate future stent design improvements.

Background The hoops of coronary stents provide radial support, and connectors hold hoops together. Strut material, shape, and thickness, along with connector number and configuration, provide the balance between stent flexibility and longitudinal integrity. Longitudinal distortion manifests as length change, strut overlap, strut separation, malapposition, and luminal obstruction. These may predispose to restenosis and stent thrombosis, obstruct passage of devices, be misinterpreted as strut fracture, and require additional stenting.

Methods The force required to compress and to elongate 7 contemporary stents was measured with an Instron universal testing machine (Norwood, Massachusetts). Stents deployed in a silicone phantom damaged by a balloon or guide catheter were imaged by microcomputed tomography to understand better the appearances and effects of longitudinal distortion.

Results Stents with 2 connectors (Boston Scientific [Natick, Massachusetts] Omega and Medtronic [Santa Rosa, California] Driver) required significantly less force to be compressed up to 5 mm and elongated by 1 mm than designs with more connectors. The 6-connector Cypher Select required significantly more force to be elongated 5 mm than other designs.

Conclusions Stents with 2 connectors between hoops have less longitudinal strength when exposed to compressing or elongating forces than those with more connectors. This independent, standardized study may assist stent selection in clinical situations where longitudinal integrity is important, and may aid future design improvements.Stent longitudinal strength, the resistance to shortening or elongation, appears related to the number of connectors between hoops. Using a standardized testing protocol, designs with 2 connectors were more likely to shorten or elongate than those with more connectors. Distortion may be recognized clinically as bunching or separation of struts, and may be confused with strut fracture. Without post-dilation or further stent deployment, the patient may be at increased risk for adverse clinical events. A stent design change ensuring 3 connectors, especially at the proximal end of a stent, should increase longitudinal integrity, but perhaps at the expense of stent flexibility (255).

A New Era of Prospective Real-World Safety Evaluation: Primary Report of XIENCE V USA (XIENCE V Everolimus Eluting Coronary Stent System Condition-of-Approval Post-Market Study)

The XIENCE V USA (XIENCE V Everolimus Eluting Coronary Stent System Condition-of-Approval Post-Market Study) sought to evaluate the safety of everolimus-eluting coronary stent systems in a real-world population with a total of 5,054 participants (1,875 standard-risk; 3,179 extended-risk). At 1 year, the rate of Academic Research Consortium-defined definite and probable stent thrombosis was 0.84%, and the composite rate of cardiac death and Academic Research Consortium-defined myocardial infarction was 6.5%. Consistent safety outcomes between the matched standard-risk cohorts from the XIENCE V USA study and the SPIRIT IV randomized trial (Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System in the Treatment of Subjects With de Novo Native Coronary Artery Lesions) suggest that this study affords a reliable benchmark for understanding the safety of everolimus-eluting coronary stent systems in real-world clinical practice.

Objectives The XIENCE V USA (XIENCE V Everolimus Eluting Coronary Stent System Condition-of-Approval Post-Market study) sought to: 1) evaluate the safety of everolimus-eluting coronary stent systems (EECSS) in a contemporary cohort of real-world subjects; and 2) prospectively test the quality of event reporting with analysis of matched patients from the randomized SPIRIT IV (Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System in the Treatment of Subjects With de Novo Native Coronary Artery Lesions) trial.

Background Randomized trials have demonstrated the safety and efficacy of EECSS in selected "standard-risk" patients.

Methods The XIENCE V USA trial was a prospective, multicenter, single-arm study in unselected patients. The primary endpoint was Academic Research Consortium (ARC)-defined definite and probable stent thrombosis (ST); the co-primary endpoint was the composite of cardiac death and myocardial infarction at 1 year. Secondary analyses included: 1) stratification by standard-risk and extended-risk cohorts; and 2) late ST after dual antiplatelet therapy interruption.

Results Of 5,054 participants (1,875 standard-risk; 3,179 extended-risk), 4,958 (98.1%) reached 1-year follow-up. The rate of ARC-defined definite and probable ST was 0.84% (95% confidence interval [CI]: 0.60% to 1.14%) in the overall population and 0.33% (95% CI: 0.12% to 10.72%) and 1.14% (95% CI: 0.80% to 11.58%) in the standard-risk and extended-risk cohorts, respectively. No late ST was observed after dual antiplatelet therapy interruption in either cohort after 6 months. The composite rate of cardiac death and ARC-defined myocardial infarction was 6.5% (95% CI: 5.79% to 17.17%) in the overall population, 3.8% (95% CI: 2.98% to 14.78%) in the standard-risk cohort, and 8.0% (95% CI: 7.09% to 19.02%) in the extended-risk cohort.

Conclusions This study comprehensively reports ST rates for EECSS in a contemporary real-world population. The absence of ST after dual antiplatelet therapy interruption beyond 6 months in standard-risk and high-risk patients is

notable. Consistent safety outcomes between matched standard-risk cohorts from the XIENCE V USA study and the SPIRIT IV randomized trial suggest that this study affords a reliable benchmark for understanding the safety of EECSS in the context of real-world clinical practice. (XIENCE V Everolimus Eluting Coronary Stent System [EECSS] USA Post-Approval Study; NCT00676520) (256).

A High-Risk Period for Cerebrovascular Events Exists After Transcatheter Aortic Valve Implantation

Objectives This study assesses if there exists a high-risk period for cerebrovascular events (CeV)after transcatheter aortic valve implantation (TAVI).

Background Even though acute strokes after TAVI have been described, it is uncertain if stroke rates continue to remain high in the early months after TAVI. Furthermore, the optimal dose and duration of thromboprophylaxis is unclear.

Methods Patients who underwent TAVI were evaluated at baseline, at discharge, at 1 and 6 months, and yearly. Risk factors for CeV events, procedural details, and antithrombotic therapy were recorded. Outcomes assessed were CeV events and death. The timing of such events, predictors, and impact on survival were analyzed.

Results A total of 253 patients were assessed. Median age was 85 years. The median Society of Thoracic Surgeons score was 8.1% (interquartile range [IQR]: 5.5% to 12.0%). Risk factors included smoking (47%), hypertension (70%), dyslipidemia (66%), and diabetes mellitus (25%). Twenty-three percent had known cerebrovascular disease and 39% had atrial fibrillation. Median follow-up was 455 days (IQR: 160 to 912 days) at which time 23 patients experienced a CeV event. The incidence was highest in the first 24 h but remained high for 2 months. In-hospital mortality rate after a CeV event was 21%. A prior history of CeV disease was an independent predictor of an event (hazard ratio: 4.23, 95% CI: 1.60 to 11.11, $p = 0.004$).

Conclusions The incidence of CeV events is highest within 24 h of TAVI, but this risk may remain elevated for up to 2 months. A prior history of cerebrovascular disease is an independent predictor. This may have implications for patient selection and antithrombotic strategies (257).

30-Day Readmission for Patients Undergoing Percutaneous Coronary Interventions in New York State

Objectives This study sought to report percutaneous coronary intervention (PCI) 30-day readmission rates, identify the impact of staged (planned) readmissions on overall readmission rates, determine the significant predictors of unstaged readmissions after PCI, and specify the reasons for readmissions.

Background Hospital readmissions occur frequently and incur substantial costs. PCI are among the most common and costly procedures, and little is known about the nature and extent of readmissions for PCI.

Methods We retrospectively analyzed 30-day readmissions after PCI using the nation's largest statewide PCI registry to identify 40,093 New York State patients who underwent PCI between January 1, 2007, and November 30, 2007. Demographic variables, pre-procedural risk factors, complications of PCI, and length of stay were considered as potential predictors of readmission, and reasons for readmission were identified from New York's administrative database using principal diagnoses.

Results A total of 15.6% of all PCI patients were readmitted within 30 days, and 20.6% of these readmissions were staged. Among unstaged readmissions, the most common reasons for readmission were chronic ischemic heart disease (22.5%), chest pain (10.8%), and heart failure (8.2%). A total of 2,015 patients (32.2% of readmissions) underwent a repeat PCI. Thirteen demographic and diagnostic risk factors, as well as longer lengths of stay, were all associated with higher readmission rates.

Conclusions Future efforts to reduce readmissions should be directed toward the recognition of patients most at risk, and the reasons they are readmitted. Staging also should be examined from a cost-effectiveness standpoint as a function of patients' unique risk factors (258).

Serial In Vivo Intravascular Ultrasound-Based Echogenicity Changes of Everolimus-Eluting Bioresorbable Vascular Scaffold During the First 12 Months After Implantation: Insights From the ABSORB B Trial

Because the bioresorption of the ABSORB bioresorbable vascular scaffold (Abbott Vascular, Santa Clara, California) is characterized by a diminishing gray-level intensity of the struts over time, the evaluation of quantitative changes in hyperechogenicity can be useful to follow the in vivo degradation of the scaffold. Whereas the first ABSORB generation showed at 6 months a 50% reduction in hyperechogenicity, the second ABSORB generation (1.1), designed to prolong the duration of luminal scaffolding, showed a 15% and 20% reduction in hyperechogenicity at 6 and 12 months, respectively, compared with post-implantation. These findings confirm the value of the manufacturing changes and suggest a slower degradation rate of the scaffold.

Objectives This study sought to investigate quantitative and homogeneity differential echogenicity changes of the ABSORB scaffold (1.1) during the first year after implantation.

Background The imaging of the ABSORB bioresorbable vascular scaffold degradation by intravascular ultrasound (IVUS) has previously demonstrated diminishing gray-level intensity of the struts over time that can be evaluated by IVUS-based differential echogenicity. The first generation

of ABSORB (1.0) showed a 50% reduction in hyperechogenicity at 6 months and restoration of the pre-ABSORB implantation values at 2 years. The second generation of ABSORB (1.1), investigated in the ABSORB B trial, was modified to prolong the duration of luminal scaffolding.

Methods A total of 63 patients were examined by IVUS immediately post-implantation and at 6-month (Cohort B1, n = 28) or 12-month (Cohort B2, n = 35) follow-up. IVUS-based tissue composition analysis software was used to quantify changes in hyperechogenicity over time in the scaffolded regions. Relative changes in hyperechogenicity were calculated as: 100 × (% hyperechogenicity at follow-up − % hyperechogenicity at baseline)/% hyperechogenicity at baseline.

Results At 6- and 12-month follow-up, there was a 15% (from 22.58 ± 9.77% to 17.42 ± 6.69%, p = 0.001) and 20% (from 23.51 ± 8.57% to 18.25 ± 7.19%, p < 0.001) reduction in hyperechogenicity, respectively, compared with post-implantation values. No difference in hyperechogenicity changes were observed between the proximal, medial, or distal part of the scaffolded segment.

Conclusions Quantitative differential echogenicity changes of the ABSORB scaffold (1.1) during the first 12 months after implantation are lower compared with those previously observed with its first generation (1.0), confirming the value of the manufacturing changes and suggesting a slower degradation rate of the scaffold (259).

Intracoronary Optical Diagnostics: Current Status, Limitations, and Potential

Optical coherence tomography (OCT), is a novel intravascular imaging modality analogous to intravascular ultrasound but uses light instead of sound. This review details the background, development, and status of current investigation using OCT, and discusses advantages, limitations, and likely future developments. It provides indications for possible future clinical use, and places OCT in the context of current intravascular imaging in what is a rapidly changing field of investigation (260).

Carotid Artery Stenting in Acute Stroke

Objectives The purpose of this study is to demonstrate the technical success of carotid artery stenting in acute extracranial internal carotid artery (ICA) occlusion as well as the benefit in clinical outcome.

Background Stroke caused by acute occlusion of the ICA is associated with a significant level of morbidity and mortality. For this type of lesion, treatment with standard intravenous thrombolysis alone leads to a good clinical outcome in only 17% of the cases, with a death rate as high as 55%. Recanalization of the occluded ICA can lead to an improvement in acute symptoms of stroke, prevent possible deterioration, and reduce long-term stroke risk. At present, there is no consensus treatment for patients with acute ischemic stroke presenting with severe clinical symptoms due to atherosclerotic occlusion of the extracranial ICA.

Methods Carotid artery stenting was performed in 22 patients with acute atherosclerotic extracranial ICA occlusion within 6 h of stroke symptom onset. In 18 patients, there was an additional intracranial occlusion at the level of the terminal segment of the ICA (n = 4) and at the level of the middle cerebral artery (n = 14). Intracranial occlusions were either treated with the Penumbra system or the Solitaire stent–based recanalization system, or a combination of mechanical recanalization and intra-arterial thrombolysis. Recanalization results were assessed by angiography immediately after the procedure. The neurologic status was evaluated before and after the treatment with a follow-up as long as 90 days using the National Institutes of Health Stroke Scale and the modified Rankin Scale.

Results Successful revascularization of extracranial ICA with acute stent implantation was achieved in 21 patients (95%). There was no acute stent thrombosis. After successful recanalization of the origin of the ICA, the intracranial recanalization with Thrombolysis In Myocardial Infarction flow grade 2/3 was achieved in 11 of the 18 patients (61%). The overall recanalization rate (extracranial and intracranial) was 14 of 22 patients (63%). Nine patients (41%) had a modified Rankin Scale score of ≤2 at 90 days. The mortality rate was 13.6% at 90 days.

Conclusions Carotid artery stenting in acute atherosclerotic extracranial ICA occlusion with severe stroke symptoms is feasible, safe, and useful within the first 6 h after symptom onset (261).

CHADS2 and CHA2DS2-VASc Scores in the Prediction of Clinical Outcomes in Patients With Atrial Fibrillation After Catheter Ablation

Objectives This study aimed to evaluate whether $CHADS_2$ and CHA_2DS_2-VASc scores are useful for risk stratification in patients after catheter ablation of atrial fibrillation (AF).

Background AF is associated with increased risk of cardiovascular events. However, limited data are available on the predictors of adverse events in patients with AF after catheter ablation.

Methods A total of 565 patients with AF who underwent catheter ablation were enrolled in the study. The clinical endpoint was occurrence of thromboembolic events (ischemic stroke, transient ischemic attack, peripheral embolism, or pulmonary embolisms) or death during follow-up after catheter ablation.

Results During a follow-up of 39.2 ± 22.6 months, 27 patients (4.8%) experienced adverse events. Both the $CHADS_2$ and CHA_2DS_2-VASc scores were useful predictors of events in separate multivariate models. The areas under the receiver-operator characteristic curves based on the $CHADS_2$ and CHA_2DS_2-VASc scores in predicting

events were 0.785 and 0.830, respectively. Although the difference did not reach statistical significance ($p = 0.116$), the CHA_2DS_2-VASc score could be used to further stratify the patients with $CHADS_2$ scores of 0 or 1 into 2 groups with different event rates (7.1% vs. 1.1%, $p = 0.003$) at a cutoff value of 2.

Conclusions The $CHADS_2$ and CHA_2DS_2-VASc scores are useful predictors of adverse events after catheter ablation of AF (262).

Alcohol Septal Ablation for the Treatment of Hypertrophic Obstructive Cardiomyopathy: A Multicenter North American Registry

Objectives The purpose of the study is to identify the predictors of clinical outcome (mortality and survival without repeat septal reduction procedures) of alcohol septal ablation for the treatment of patients with hypertrophic obstructive cardiomyopathy.

Background Alcohol septal ablation is used for treatment of medically refractory hypertrophic obstructive cardiomyopathy patients with severe outflow tract obstruction. The existing literature is limited to single-center results, and predictors of clinical outcome after ablation have not been determined. Registry results can add important data.

Methods Hypertrophic obstructive cardiomyopathy patients ($N = 874$) who underwent alcohol septal ablation were enrolled. The majority (64%) had severe obstruction at rest, and the remaining had provocable obstruction. Before ablation, patients had severe dyspnea (New York Heart Association [NYHA] functional class III or IV: 78%) and/or severe angina (Canadian Cardiovascular Society angina class III or IV: 43%).

Results Significant improvement ($p < 0.01$) occurred after ablation (~5% in NYHA functional classes III and IV, and 8 patients in Canadian Cardiovascular Society angina class III). There were 81 deaths, and survival estimates at 1, 5, and 9 years were 97%, 86%, and 74%, respectively. Left anterior descending artery dissections occurred in 8 patients and arrhythmias in 133 patients. A lower ejection fraction at baseline, a smaller number of septal arteries injected with ethanol, a larger number of ablation procedures per patient, a higher septal thickness post-ablation, and the use beta-blockers post-ablation predicted mortality.

Conclusions Variables that predict mortality after ablation, include baseline ejection fraction and NYHA functional class, the number of septal arteries injected with ethanol, post-ablation septal thickness, beta-blocker use, and the number of ablation procedures (263).

Safety and Efficacy of Antiplatelet and Antithrombotic Therapy in Acute Coronary Syndrome Patients With Chronic Kidney Disease

Chronic kidney disease (CKD) is prevalent and affects an ever-increasing proportion of patients presenting with acute coronary syndrome (ACS). Patients with CKD have a higher risk of ACS and significantly higher mortality, and are also predisposed to increased bleeding complications. Antiplatelet and antithrombotic drugs form the bedrock of management of patients with ACS. Most randomized trials of these drugs exclude patients with CKD, and current guidelines for management of these patients are largely based on these trials. We aim to review the safety and efficacy of these drugs in patients with CKD presenting with ACS (264).

Stroke Associated With Surgical and Transcatheter Treatment of Aortic Stenosis: A Comprehensive Review

Stroke is a potential complication of treating patients with aortic stenosis via surgical aortic valve replacement (AVR), transcatheter aortic valve replacement (TAVR), and balloon aortic valvuloplasty. Because there are limited and heterogeneous data on the incidence, risk factors, and outcomes of stroke among patients being treated for aortic stenosis, we performed a comprehensive review of the literature. The risk of stroke after AVR in the general population is approximately 1.5%, and the risk is increased (to approximately 2% to 4%) in older and higher-risk patients. Strokes were reported in 1.5% to 6% of patients treated with TAVR, and in the only randomized trial of AVR versus TAVR, there was an increased risk of 30-day strokes (minor and major strokes and transient ischemic attacks) with TAVR (5.5% vs. 2.4%, $p = 0.04$) (265).

Multimodality Imaging in Transcatheter Aortic Valve Implantation and Post-Procedural Aortic Regurgitation: Comparison Among Cardiovascular Magnetic Resonance, Cardiac Computed Tomography, and Echocardiography

Objectives The purpose of this study was to determine imaging predictors of aortic regurgitation (AR) after transcatheter aortic valve implantation (TAVI) and the agreement and reproducibility of cardiovascular magnetic resonance (CMR), cardiac computed tomography (CCT), and transthoracic echocardiography (TTE) in aortic root assessment.

Background The optimal imaging strategy for planning TAVI is unclear with a paucity of comparative multimodality imaging data. The association between aortic root morphology and outcomes after TAVI also remains incompletely understood.

Methods A total of 202 consecutive patients assessed by CMR, CCT, and TTE for TAVI were studied. Agreement and variability among and within imaging modalities was assessed by Bland-Altman analysis. Postoperative AR was assessed by TTE.

Results Of the 202 patients undergoing TAVI assessment with both CMR and TTE, 133 also underwent CCT. Close

agreement was observed between CMR and CCT in dimensions of the aortic annulus (bias, −0.4 mm; 95% limits of agreement: −5.7 to 5.0 mm), and similarly for sinus of Valsalva, sinotubular junction, and ascending aortic measures. Agreement between TTE-derived measures and either CMR or CCT was less precise. Intraobserver and interobserver variability were lowest with CMR. The presence and severity of AR after TAVI were associated with larger aortic valve annulus measurements by both CMR ($p = 0.03$) and CCT ($p = 0.04$) but not TTE-derived measures ($p = 0.10$). Neither CCT nor CMR measures of annulus eccentricity, however, predicted AR after TAVI ($p = 0.33$ and $p = 0.78$, respectively).

Conclusions In patients undergoing imaging assessment for TAVI, the presence and severity of AR after TAVI were associated with larger aortic annulus measurements by both CMR and CCT, but not TTE. Both CMR and CCT provide highly reproducible information in the assessment of patients undergoing TAVI (266).

Long-Term Outcomes After Transcatheter Aortic Valve Implantation in High-Risk Patients With Severe Aortic Stenosis: The U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry

Objectives The objective was to define the characteristics of a real-world patient population treated with transcatheter aortic valve implantation (TAVI), regardless of technology or access route, and to evaluate their clinical outcome over the mid to long term.

Background Although a substantial body of data exists in relation to early clinical outcomes after TAVI, there are few data on outcomes beyond 1 year in any notable number of patients.

Methods The U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry was established to report outcomes of all TAVI procedures performed within the United Kingdom. Data were collected prospectively on 870 patients undergoing 877 TAVI procedures up until December 31, 2009. Mortality tracking was achieved in 100% of patients with mortality status reported as of December 2010.

Results Survival at 30 days was 92.9%, and it was 78.6% and 73.7% at 1 year and 2 years, respectively. There was a marked attrition in survival between 30 days and 1 year. In a univariate model, survival was significantly adversely affected by renal dysfunction, the presence of coronary artery disease, and a nontransfemoral approach; whereas left ventricular function (ejection fraction <30%), the presence of moderate/severe aortic regurgitation, and chronic obstructive pulmonary disease remained the only independent predictors of mortality in the multivariate model.

Conclusions Midterm to long-term survival after TAVI was encouraging in this high-risk patient population, although a substantial proportion of patients died within the first year (267).

Impact of Platelet Reactivity on Clinical Outcomes After Percutaneous Coronary Intervention: A Collaborative Meta-Analysis of Individual Participant Data

Objectives The purpose of the study was to systematically evaluate the significance of platelet reactivity on clopidogrel treatment on adverse cardiovascular events using a collaborative meta-analysis using patient-level data for the VerifyNow P2Y12 assay (Accumetrics, San Diego, California).

Background Clinical evidence has been controversial regarding the influence of clopidogrel on treatment platelet reactivity and ischemic outcomes.

Methods MEDLINE, Scopus, and the Cochrane library databases were searched through January 2010. A database containing individual patient-level time-to-event data was generated from identified studies. The primary outcome of interest was a composite of death, myocardial infarction (MI), or stent thrombosis. Secondary outcomes included the incidence of: 1) death; 2) MI; and 3) stent thrombosis.

Results A total of 6 studies with 3,059 patients was included. In each study, clopidogrel responsiveness was assessed using the same point-of-care assay after percutaneous coronary intervention. The primary endpoint occurred more frequently in higher quartiles of $P2Y_{12}$ reaction unit (PRU) values: quartile I, 5.8%; quartile II, 6.9%; quartile III, 10.9%; quartile IV, 15.8% ($p < 0.001$). Taking quartile I as referent, the hazard ratios (HRs) for the primary endpoint were as follows: quartile II, HR: 1.13 (95% confidence interval [CI]: 0.72 to 1.78; $p = 0.60$); quartile III, HR: 1.82 (95% CI: 1.20 to 2.75; $p = 0.005$); quartile IV, HR: 2.62 (95% CI: 1.78 to 3.87; $p < 0.001$). On a continuous scale, every 10-U increase in PRU was associated with a significantly higher rate of the primary endpoint (HR: 1.04; 95% CI: 1.03 to 1.06; $p < 0.0001$). According to receiver-operating characteristic curve analysis, a PRU value of 230 appeared to best predict death, MI, or stent thrombosis ($p < 0.001$). A PRU value ≥230 was associated with a higher rate of the composite primary endpoint (HR: 2.10; 95% CI: 1.62 to 2.73; $p < 0.0001$), as well as the individual endpoints of death (HR: 1.66; 95% CI: 1.04 to 2.68; $p = 0.04$), MI (HR: 2.04; 95% CI: 1.51 to 2.76; $p < 0.001$), and stent thrombosis (HR: 3.11; 95% CI: 1.50 to 6.46; $p = 0.002$).

Conclusions In this collaborative meta-analysis, the level of on-treatment platelet reactivity according to the $P2Y_{12}$ assay is associated with long-term cardiovascular events after percutaneous coronary intervention, including death, MI, and stent thrombosis (268).

Carotid Revascularization Immediately Before Urgent Cardiac Surgery: Practice Patterns Associated With the Choice of Carotid Artery Stenting or Endarterectomy: A Report From the CARE (Carotid Artery Revascularization and Endarterectomy) Registry

Objectives We describe characteristics associated with use of endarterectomy (CEA) versus stenting (CAS) in patients before urgent cardiac surgery.

Background The optimal modality of carotid revascularization preceding cardiac surgery is unknown.

Methods Retrospective evaluation of the CARE (Carotid Artery Revascularization and Endarterectomy) registry from January 2005 to April 2010 was performed on patients undergoing CEA or CAS preceding urgent cardiac surgery within 30 days. Baseline characteristics were compared, and multivariate adjustment was performed.

Results Of 451 patients who met study criteria, 255 underwent CAS and 196 underwent CEA. Both procedures increased over time to a similar degree ($p = 0.18$). Patients undergoing CAS had more frequent history of peripheral artery disease (38.2% vs. 26.5%, $p < 0.01$), neck surgery (5.5% vs. 1.0%, $p = 0.01$), neck radiation (4.3% vs. 1.0%, $p = 0.04$), left-main coronary disease (34.8% vs. 23.5%, $p < 0.01$), neurological events (45.8% vs. 31.3%, $p < 0.01$), carotid intervention (20.8% vs. 7.6%, $p < 0.01$), and higher baseline creatinine (1.3 vs. 1.1 mg/dl, $p = 0.02$). The target carotid arteries of CAS patients were more likely to be symptomatic in the 6 months before revascularization and have restenosis from prior CEA. Patients undergoing CAS had a lower American Society of Anesthesiology grade. Midwest hospitals were less likely to perform CAS than CEA, whereas in the other regions CAS was more common ($p < 0.01$). Non-Caucasian race, a history of heart failure, previous carotid procedures, prior stroke, left main coronary artery stenosis, lower American Society of Anesthesiology grade, and teaching hospital were independent predictors of patients who would receive CAS.

Conclusions Carotid artery stenting and CEA have increased among patients undergoing urgent cardiac surgery. Patients who underwent CAS had more vascular disease but lower acute pre-surgical risk. Significant regional variation in procedure selection exists (269).

Carotid Artery Stenting and Cardiac Surgery in Symptomatic Patients

Objectives The purpose of this study was to evaluate the feasibility and safety of the combined outcome of carotid artery stenting (CAS) and coronary artery bypass graft (CABG) surgery in neurologically symptomatic patients.

Background The risk of perioperative stroke in patients undergoing CABG who report a prior history of transient ischemic attack or stroke has been associated with a 4-fold increased risk as compared to the risk for neurologically asymptomatic patients. It seems appropriate to offer prophylactic carotid endarterectomy to neurologically symptomatic patients who have significant carotid artery disease and are scheduled for CABG. The CAS-CABG outcome for symptomatic patients remains underreported, notwithstanding randomized data supporting CAS for high-risk patients.

Methods In a prospective, single-center study, the periprocedural and long-term outcomes of 57 consecutive patients who underwent CAS before cardiac surgery were analyzed.

Results The procedural success rate of CAS was 98%. The combined death, stroke, and myocardial infarction rate was 12.3%. The death and major stroke rate from time of CAS to 30 days after cardiac surgery was 3.5%. The myocardial infarction rate from time of CAS to 30 days after cardiac surgery was 1.5%.

Conclusions This is the first single-center study reporting the combined outcome of CAS-CABG in symptomatic patients. The periprocedural complication rate and long-term results of the CAS-CABG strategy in this high-risk population support the reliability of this approach. In such a high-risk population, this strategy might offer a valuable alternative to the combined surgical approach; however, a large randomized trial is clearly warranted (270).

Contemporary Clinical Applications of Coronary Intravascular Ultrasound

Intravascular ultrasound (IVUS) provides valuable information on the coronary vascular lumen and wall and has been an important tool in the cardiac catheterization laboratory for over 2 decades. The major utility of IVUS relates to optimizing stent deployment, particularly in complex lesions. In percutaneous coronary intervention with bare-metal stents, IVUS guidance reduces restenosis. In percutaneous coronary intervention with drug-eluting stents, IVUS guidance may reduce rates of stent thrombosis with little affect on restenosis. The benefit of IVUS guidance is most important in complex lesion subsets, such as left main and bifurcation lesions, where studies suggest that IVUS guidance may reduce mortality. Whereas IVUS luminal area measurements have been used to assess intermediate lesion severity, recent studies have demonstrated that IVUS accurately identifies nonischemic lesions for which percutaneous coronary intervention can be safely deferred, but cannot accurately predict hemodynamically significant lesions and should not solely be used to justify revascularization. In the current review, we focus on clinical applications of IVUS in interventional cardiology (271).

Aortic Annulus Diameter Determination by Multidetector Computed Tomography: Reproducibility, Applicability, and Implications for Transcatheter Aortic Valve Implantation

Objectives This study sought to determine the most reproducible multidetector computed tomography (MDCT)

measurements of the aortic annulus and to determine methods to improve the applicability of these measurements for transcatheter aortic valve implantation.

Background The reproducibility and applicability of MDCT annular measurements to guide transcatheter aortic valve implantation remain unclear.

Methods Annular measurements were performed in 50 patients planed for transcatheter aortic valve implantation in multiple planes: basal ring (short- and long-axis, mean diameter, area-derived diameter), coronal, sagittal, and 3-chamber projections. A theoretical model was developed taking into account the differences between the most reproducible MDCT measurements and transesophageal echocardiography to guide valve size choice.

Results The most reproducible measurements were the area-derived diameter and basal ring average diameter (inter-reader intraclass correlation coefficient: 0.87 [95% confidence interval: 0.81 to 0.92] and 0.80 [95% confidence interval: 0.70 to 0.87]; respectively; intrareader >0.90 for all readers). These were generally larger than transesophageal echocardiography diameters (mean difference of 1.5 ± 1.6 mm and 1.1 ± 1.7 mm, respectively). When a strategy of valve-sizing is undertaken using these CT measurements using an echocardiographic sizing scale, a different THV size would be selected in 44% and 40% of cases, respectively. When adjusting the sizing cutoffs to account for the differences in observed diameters, this was reduced to 10% to 12% ($p < 0.01$ for both, respectively).

Conclusions The most reproducible MDCT measurements of the annulus are the area-derived diameter and basal ring average diameter, with derived values generally larger than those obtained with echocardiography. If MDCT is used for valve sizing, a strategy incorporating these differences may be important. MDCT using these easily derived measurements may be ideally suited to sizing transcatheter aortic valves as they account for the eccentricity of the aortic annulus, are reproducible, and are noninvasive (272).

Valve-in-Valve Transcatheter Aortic Valve Implantation for Degenerated Bioprosthetic Heart Valves

Objectives We sought to analyze outcomes of patients with degenerated surgically implanted bioprosthetic heart valves undergoing valve-in-valve (viv) transcatheter aortic valve implantation (TAVI).

Background Redo cardiac surgery for degenerated bioprosthetic heart valves is associated with increased risks, particular in elderly patients with comorbidities. For these patients, TAVI may be an attractive, less invasive treatment option.

Methods Data from 47 patients age 64 to 97 years (logistic euroSCORE: 35.0 ± 18.5%) undergoing transfemoral (n = 25) or transapical (n = 22) viv-TAVI for failed bioprosthetic aortic valves 113 ± 65 months after initial surgery at 9 clinical sites in Germany and Switzerland were analyzed.

Results Valve-in-valve TAVI was technically successful in all patients, with 2 patients requiring bailout implantation of a second TAVI prosthesis for severe regurgitation during the procedure. There was 1 procedural death as the result of low-output failure. Valvular function after viv-TAVI was excellent with respect to valve competence, but increased transvalvular gradients ≥20 mm Hg were noted in 44% of patients. Vascular access complications occurred in 6 (13%) patients, and 5 (11%) patients required new pacemaker implantation after viv-TAVI. Renal failure requiring dialysis occurred in 4 (9%) patients. Mortality at 30 days was 17% (1 procedural and 7 post-procedural deaths), with 3 of 8 fatalities the result of non–valve-related septic complications.

Conclusions Valve-in-valve TAVI can be performed with high technical success rates, acceptable post-procedural valvular function, and excellent functional improvement. However, in these predominantly elderly high-risk patients with multiple comorbidities, viv-TAVI was associated with 17% mortality, often because of septic complications arising in the post-operative phase (273).

Impact of Lesion Length and Vessel Size on Clinical Outcomes After Percutaneous Coronary Intervention With Everolimus- Versus Paclitaxel-Eluting Stents: Pooled Analysis From the SPIRIT (Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System) and COMPARE (Second-generation everolimus-eluting and paclitaxel-eluting stents in real-life practice) Randomized Trials

Objectives The aim of this study was to investigate the impact of reference vessel diameter (RVD) and lesion length (LL) on the relative safety and efficacy of everolimus-eluting stents (EES) and paclitaxel-eluting stents (PES).

Background Lesion length and RVD are well-known predictors of adverse events after percutaneous coronary intervention.

Methods Patient-level data were pooled from the randomized SPIRIT (Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System) II, III, IV and COMPARE (Second-generation everolimus-eluting and paclitaxel-eluting stents in real-life practice) trials. Quantitative angiographic core laboratory data were available for 6,183 patients randomized to EES (n = 3,944) or PES (n = 2,239). Long lesions and small vessels were defined as LL >median (13.4 mm) and RVD ≤median (2.65 mm), respectively. Major adverse cardiac events (MACE) (consisting of cardiac death, myocardial infarction, or ischemia-driven target lesion revascularization) were assessed at 2 years, according to stent type in 3 groups: short lesions in large vessels (group A, n = 1,297); long lesions or small vessels but not both (group B, n = 2,981); and long lesions in small vessels (group C, n = 1,905).

Results The pooled 2-year MACE rates were 5.6%, 8.2%, and 10.4% in Groups A, B, and C, respectively

($p < 0.0001$). There was no significant interaction between lesion group and stent type ($p = 0.64$), indicating lower MACE with EES compared with PES regardless of LL and RVD. However, the absolute difference was largest in Groups B and C. In Group A, 2-year MACE rates were not significantly different between EES and PES (4.8% vs. 7.0%, respectively, $p = 0.11$). In contrast, EES was associated with lower 2-year rates of MACE in Group B (6.6% vs. 11.2%, $p < 0.01$) and in Group C (9.1% vs. 12.7%, $p = 0.008$) as well as lower rates of myocardial infarction, target lesion revascularization, and stent thrombosis. Multivariable analysis confirmed EES versus PES as an independent predictor of freedom from MACE in Groups B and C.

Conclusions Patients with short lesions in large vessels have low rates of MACE at 2 years after treatment with either EES or PES. In higher-risk patients with long lesions and/or small vessels, EES results in significant improvements in both clinical safety and efficacy outcomes. (A Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System in the Treatment of Patients With de Novo Native Coronary Artery Lesions; NCT00180310; SPIRIT III: A Clinical Evaluation of the Investigational Device XIENCE V Everolimus Eluting Coronary Stent System [EECSS] in the Treatment of Subjects With de Novo Native Coronary Artery Lesions; NCT00180479; SPIRIT IV Clinical Trial: Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System in the Treatment of Subjects With de Novo Native Coronary Artery Lesions; NCT00307047; A Randomized Controlled Trial of Everolimus-eluting Stents and Paclitaxel-eluting Stents for Coronary Revascularization in Daily Practice: The COMPARE Trial; NCT01016041) (274).

Fractional Flow Reserve in Unstable Angina and Non–ST-Segment Elevation Myocardial Infarction: Experience From the FAME (Fractional flow reserve versus Angiography for Multivessel Evaluation) Study

Objectives The aim of this study was to study whether there is a difference in benefit of fractional flow reserve (FFR) guidance for percutaneous coronary intervention (PCI) in multivessel coronary disease in patients with unstable angina (UA) or non–ST-segment elevation myocardial infarction (NSTEMI), compared with stable angina (SA).

Background The use of FFR to guide PCI has been well established for patients with SA. Its use in patients with UA or NSTEMI has not been investigated prospectively.

Methods In the FAME (Fractional flow reserve versus Angiography for Multivessel Evaluation) study 1,005 patients with multivessel disease amenable to PCI were included and randomized to either angiography-guided PCI of all lesions ≥50% or FFR-guided PCI of lesions with an FFR ≤0.80. Patients admitted for UA or NSTEMI with positive troponin but total creatine kinase <1,000 U/l were eligible for inclusion. We determined 2-year major adverse cardiac event rates of these patients and compared it with stable patients.

Results Of 1,005 patients, 328 had UA or NSTEMI. There was no evidence for heterogeneity among the subgroups for any of the outcome variables (all p values >0.05). Using FFR to guide PCI resulted in similar risk reductions of major adverse cardiac events and its components in patients with UA or NSTEMI, compared with patients with SA (absolute risk reduction of 5.1% vs. 3.7%, respectively, $p = 0.92$). In patients with UA or NSTEMI, the number of stents was reduced without increase in hospital stay or procedure time and with less contrast use, in similarity to stable patients.

Conclusions The benefit of using FFR to guide PCI in multivessel disease does not differ between patients with UA or NSTEMI, compared with patients with SA (275).

Intravascular Ultrasound-Derived Predictors for Fractional Flow Reserve in Intermediate Left Main Disease

Objectives The aim of this study was to determine the best intravascular ultrasound (IVUS) criteria for predicting physiological significance of left main (LM) stenosis with fractional flow reserve (FFR) as the standard.

Background For identifying significant LM disease, optimal cutoff of minimal lumen area (MLA) and its accuracy remain debatable.

Methods We identified 55 patients (31 stable and 24 unstable angina) with an isolated LM lesion of 30% to 80% angiographic diameter stenosis who underwent IVUS and invasive physiological assessment before intervention.

Results The FFR at maximum hyperemia significantly correlated with IVUS-measured MLA within the LM ($r = 0.623$, $p < 0.001$), plaque burden ($r = -0.548$, $p < 0.001$), angiographic diameter stenosis ($r = -0.449$, $p = 0.002$), and angiographic length of the lesion ($r = -0.292$, $p = 0.046$). The FFR was significantly lower in 18 lesions with plaque rupture than 37 lesions without plaque rupture (0.76 ± 0.09 vs. 0.82 ± 0.09, $p = 0.018$). The independent determinants of FFR as a continuous variable were MLA (beta = 0.598, $p < 0.001$) and plaque rupture (beta = −0.255, $p = 0.038$). Furthermore, the MLA within the LM was the only independent determinant for FFR <0.80 (adjusted odds ratio: 0.312, $p < 0.001$) and for FFR <0.75 (adjusted odds ratio: 0.196, $p = 0.001$). The IVUS MLA value within the LM that best predicted FFR <0.80 was <4.8 mm^2 (89% sensitivity, 83% specificity). In addition, the cutoff value of plaque burden to predict FFR <0.80 was ≥72% (73% sensitivity, 79% specificity). The best cutoff values of the MLA and plaque burden for predicting FFR <0.75 were <4.1 mm^2 (95% sensitivity, 83% specificity) and ≥76% (79% sensitivity, 80% specificity), respectively.

Conclusions In isolated LM disease, an IVUS-derived MLA <4.8 mm^2 is a useful criterion for predicting FFR <0.80 (276).

Long-Term Follow-Up After Fractional Flow Reserve–Guided Treatment Strategy in Patients With an Isolated Proximal Left Anterior Descending Coronary Artery Stenosis

Objectives This study sought to evaluate the long-term clinical outcome of patients with an angiographically intermediate left anterior descending coronary artery (LAD) stenosis in whom the revascularization strategy was based on fractional flow reserve (FFR).

Background When revascularization is based mainly on angiographic guidance, a number of hemodynamically nonsignificant stenoses will be revascularized.

Methods In 730 patients with a 30% to 70% isolated stenosis in the proximal LAD and no significant valvular disease, FFR measurements were obtained to guide treatment strategy. When FFR was ≥0.80, the patients (n = 564) were treated medically (medical group); when FFR was <0.80, the patients (n = 166) underwent a revascularization procedure (revascularization group; 13% coronary artery bypass graft surgery and 87% percutaneous coronary intervention). A 100% long-term clinical follow-up (median follow-up: 40 months) was obtained. The 5-year survival of the medical group was compared with that of a reference population. For each patient, 4 controls were selected from an age- and sex-matched control population.

Results The 5-year survival estimate was 92.9% in the medical group versus 89.6% in the controls (p = 0.74). The mean diameter stenosis was significantly smaller in the medical than in the revascularization group (39 ± 14% vs. 54 ± 13%, p < 0.0001), but there was a large overlap between both groups. The 5-year event-free survival estimates (death, myocardial infarction, and target vessel revascularization) were 89.7% and 68.5%, respectively (p < 0.0001).

Conclusions Medical treatment of patients with a hemodynamically nonsignificant stenosis (FFR ≥0.80) in the proximal LAD is associated with an excellent long-term clinical outcome with survival at 5 years similar to an age- and sex-matched control population (277).

Transcatheter Valve-in-Valve Implantation Using CoreValve Revalving System for Failed Surgical Aortic Bioprostheses

Objectives The purpose of this study was to evaluate the performance of CoreValve Revalving System (CRS) (Medtronic, Minneapolis, Minnesota) implantation in patients with failed aortic bioprostheses.

Background Transcatheter aortic valve implantation with the CRS is an effective option in high-risk patients with severe aortic stenosis. It may be an option for patients with a failed aortic bioprosthesis, especially when the risk of a surgical redo is deemed prohibitive.

Methods CRS "valve-in-valve" implantation was performed in 25 high-risk patients with a failed bioprosthesis. Their mean age was 82.4 ± 3.2 years. New York Heart Association functional classes III and IV were present in 21 and 4 patients, respectively. The logistic EuroSCORE was 31.5 ± 14.8%, whereas the Society of Thoracic Surgeons score was 8.2 ± 4.2. Patients/prostheses were divided in type A (mainly stenotic, n = 9) and type B (mainly regurgitant, n = 16).

Results The implantation success rate was 100%. In group A, the peak aortic gradient significantly decreased from 77.6 ± 21.6 mm Hg to 34.6 ± 19.4 mm Hg (p = 0.001). In all but 2 patients in group B, no significant regurgitation was observed post-implantation. No patients died during the procedure. At 30 days, there were 3 deaths (12%), 2 myocardial infarctions (8%), and 3 atrioventricular blocks requiring pacemaker implantation (12%). At a mean follow-up of 6 months, there were another death (survival rate of 84%) and a pacemaker implantation (cumulative incidence of 16%). New York Heart Association functional class improved in all patients to I and II.

Conclusions CRS implantation was feasible and effective regardless of the prevalent mode of failure. This finding may significantly affect the treatment of patients with a failed bioprosthesis deemed at a prohibitive risk for surgical redo (278).

Safety and Efficacy of Drug-Eluting Stents in Older Patients With Chronic Kidney Disease: A Report From the Linked CathPCI Registry–CMS Claims Database

Objectives The purpose of this study was to determine the safety and efficacy of drug-eluting stents (DES) compared with bare-metal stents (BMS) in older patients with chronic kidney disease (CKD).

Background DES may be associated with late death and myocardial infarction (MI) secondary to stent thrombosis. However, data on outcomes in older patients with CKD are limited.

Methods We estimated the glomerular filtration rate (GFR) of 283,593 patients 65 years of age and older who underwent stent implantation between 2004 and 2007. In propensity-matched cohorts grouped by GFR, the association between DES and BMS and the risk of death, MI, revascularization, and major bleeding was examined.

Results A total of 121,446 patients (42.8%) had CKD (GFR <60 ml/min/1.73 m^2). The 30-month mortality rate for patients on long-term dialysis was 52.0%. In propensity-matched pairs, placement of a DES compared with a BMS in patients with normal renal function was associated with significant reductions in 30-month revascularization (hazard ratio [HR]: 0.91; 95% confidence interval [CI]: 0.86 to 0.95), MI (HR: 0.77; 95% CI: 0.71 to 0.83), and death (HR: 0.73; 95% CI: 0.69 to 0.77), but no difference in

bleeding (HR: 0.89; 95% CI: 0.79 to 1.00). Lower MI and mortality rates were also observed after DES compared with BMS implantation in all CKD subgroups with the exception of MI in the long-term dialysis group. Decreased rates of revascularization did not extend to any subgroup of patients with CKD.

Conclusions The safety of DES compared with BMS is observed in all patients regardless of renal function and is associated with reduced rates of MI and death in some subsets of patients with CKD (279).

Everolimus-Eluting Versus Sirolimus-Eluting Stents in Patients Undergoing Percutaneous Coronary Intervention: The EXCELLENT (Efficacy of Xience/Promus Versus Cypher to Reduce Late Loss After Stenting) Randomized Trial

Objectives The goal of this study was to compare the angiographic outcomes of everolimus-eluting stents (EES) and sirolimus-eluting stents (SES) in a head-to-head manner.

Background EES have been shown to be superior to paclitaxel-eluting stents in inhibiting late loss (LL) and clinical outcome. Whether EES may provide similar angiographic and clinical outcomes compared with SES is undetermined.

Methods This was a prospective, randomized, open-label, multicenter trial to demonstrate the noninferiority of EES compared with SES in preventing LL at 9 months. A total of 1,443 patients undergoing percutaneous coronary intervention were randomized 3:1 to receive EES or SES. Routine follow-up angiography was recommended at 9 months. The primary endpoint was in-segment LL at 9 months, and major secondary endpoints included in-stent LL at 9 months, target lesion failure, cardiac death, nonfatal myocardial infarction, target lesion revascularization, and stent thrombosis at 12 months. Data were managed by an independent management center, and clinical events were adjudicated by an independent adjudication committee.

Results Clinical follow-up was available in 1,428 patients and angiographic follow-up in 924 patients (1,215 lesions). The primary endpoint of the study (in-segment LL at 9 months) was 0.11 ± 0.38 mm and 0.06 ± 0.36 mm for EES and SES, respectively (p for noninferiority = 0.0382). The in-stent LL was also noninferior (EES 0.19 ± 0.35 mm; SES 0.15 ± 0.34 mm; p for noninferiority = 0.0121). The incidence of clinical endpoints was not statistically different between the 2 groups, including target lesion failure (3.75% vs. 3.05%; p = 0.53) and stent thrombosis (0.37% vs. 0.83%; p = 0.38).

Conclusions EES were noninferior to SES in inhibition of LL after stenting, which was corroborated by similar rates of clinical outcomes. (Efficacy of Xience/Promus Versus Cypher in Reducing Late Loss After Stenting [EXCELLENT]; NCT00698607) (280).

Hemodynamic and Clinical Impact of Prosthesis–Patient Mismatch After Transcatheter Aortic Valve Implantation

Objectives This study examined the mid-term hemodynamic and clinical impact of prosthesis–patient mismatch (PPM) in patients undergoing transcatheter aortic valve implantation (TAVI) with balloon-expandable valves.

Background PPM can be observed after aortic valve surgery. However, little is known about the incidence of PPM in patients undergoing TAVI.

Methods Echocardiography and clinical assessment were performed in 165 patients at baseline, before hospital discharge, and at 6 months after TAVI. PPM was defined as an indexed effective orifice area ≤ 0.85 cm^2/m^2.

Results Thirty patients (18.2%) showed PPM before hospital discharge. At baseline, patients with PPM had a larger body surface area (1.84 ± 0.18 m^2 vs. 1.73 ± 0.18 m^2, p = 0.003) and a greater severity of aortic stenosis (indexed valve area 0.35 ± 0.09 cm^2/m^2 vs. 0.40 ± 0.10 cm^2/m^2, p = 0.005) than patients without PPM. Patients with PPM demonstrated a slower and smaller reduction in mean transaortic gradient, limited left ventricular (LV) mass regression, and left atrial volume reduction over 6 months compared with patients without PPM. LV filling pressure, measured by E/e′, tended to remain elevated in patients with PPM. Importantly, a higher proportion of patients with PPM did not improve in New York Heart Association functional class compared with patients without PPM (36.7% vs. 1.5%, p < 0.001), although major adverse valve-related and cardiovascular events did not differ between the 2 groups.

Conclusions PPM may be observed after TAVI and when present may be accompanied by less favorable changes in transvalvular hemodynamics, limited LV mass regression, persistent elevated LV filling pressure, and less improvement in clinical functional status (281).

Impact of In-Hospital Major Bleeding on Late Clinical Outcomes After Primary Percutaneous Coronary Intervention in Acute Myocardial Infarction: The HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) Trial

Objectives We aimed to investigate the long-term prognosis of patients with in-hospital major bleeding (IHMB).

Background The effect of IHMB on the long-term prognosis of patients undergoing primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction is unknown.

Methods Primary PCI was performed in 3,345 (92.9%) of 3,602 patients in the HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trial; in-hospital protocol-defined non–coronary artery bypass graft–related major bleeding developed in 231 (6.9%). We examined medication use at

discharge, mortality, and major adverse cardiovascular events (composite of death, reinfarction, stroke, or ischemic target vessel revascularization) at 3-year follow-up in patients with and without IHMB.

Results At 3-year follow-up, patients with IHMB had higher mortality (24.6% vs. 5.4%, $p < 0.0001$) and major adverse cardiovascular events (40.3% vs. 20.5%, $p < 0.0001$). The deleterious effect of major bleeding was observed within 1 month, between 1 month and 1 year, and between 1 and 3 years. IHMB was an independent predictor of mortality (hazard ratio: 2.80; 95% confidence interval: 1.89 to 4.16, $p < 0.0001$) at 3-year follow up.

Conclusions Patients with IHMB after primary PCI have significantly increased 3-year rates of morbidity and mortality. Further investigation is warranted to understand the mechanisms underlying this relationship and to further improve outcomes in patients with ST-segment myocardial infarction. (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction [HORIZONS-AMI]; NCT00433966) (282).

Comparative Effectiveness and Cost-Effectiveness of Computed Tomography Screening for Coronary Artery Calcium in Asymptomatic Individuals

Objectives The aim of this study was to assess the (cost-) effectiveness of screening asymptomatic individuals at intermediate risk of coronary heart disease (CHD) for coronary artery calcium with computed tomography (CT).

Background Coronary artery calcium on CT improves prediction of CHD.

Methods A Markov model was developed on the basis of the Rotterdam Study. Four strategies were evaluated: 1) current practice; 2) current prevention guidelines for cardiovascular disease; 3) CT screening for coronary calcium; and 4) statin therapy for all individuals. Asymptomatic individuals at intermediate risk of CHD were simulated over their remaining lifetime. Quality-adjusted life years (QALYs), costs, and incremental cost-effectiveness ratios were calculated.

Results In men, CT screening was more effective and more costly than the other 3 strategies (CT vs. current practice: +0.13 QALY [95% confidence interval (CI): 0.01 to 0.26], +$4,676 [95% CI: $3,126 to $6,339]; CT vs. statin therapy: +0.04 QALY [95% CI: −0.02 to 0.13], +$1,951 [95% CI: $1,170 to $2,754]; and CT vs. current guidelines: +0.02 QALY [95% CI: −0.04 to 0.09], +$44 [95% CI: −$441 to $486]). The incremental cost-effectiveness ratio of CT calcium screening was $48,800/QALY gained. In women, CT screening was more effective and more costly than current practice (+0.13 QALY [95% CI: 0.02 to 0.28], +$4,663 [95% CI: $3,120 to $6,277]) and statin therapy (+0.03 QALY [95% CI: −0.03 to 0.12], +$2,273 [95% CI: $1,475 to $3,109]). However, implementing current guidelines was more effective compared with CT screening (+0.02 QALY [95% CI: −0.03 to 0.07]), only a little more expensive (+$297 [95% CI: −$8 to $633]), and had a lower cost per additional QALY ($33,072/QALY vs. $35,869/QALY). Sensitivity analysis demonstrated robustness of results in women but considerable uncertainty in men.

Conclusions Screening for coronary artery calcium with CT in individuals at intermediate risk of CHD is probably cost-effective in men but is unlikely to be cost-effective in women (283).

Benefit of Early Statin Therapy in Patients With Acute Myocardial Infarction Who Have Extremely Low Low-Density Lipoprotein Cholesterol

Objectives We investigated whether statin therapy could be beneficial in patients with acute myocardial infarction (AMI) who have baseline low-density lipoprotein cholesterol (LDL-C) levels below 70 mg/dl.

Background Intensive lipid-lowering therapy with a target LDL-C value <70 mg/dl is recommended in patients with very high cardiovascular risk. However, whether to use statin therapy in patients with baseline LDL-C levels below 70 mg/dl is controversial.

Methods We analyzed 1,054 patients with AMI who had baseline LDL-C levels below 70 mg/dl and survived at discharge from the Korean Acute MI Registry between November 2005 and December 2007. They were divided into 2 groups according to the prescribing of statins at discharge (statin group n = 607; nonstatin group n = 447). The primary endpoint was the composite of 1-year major adverse cardiac events, including death, recurrent MI, target vessel revascularization, and coronary artery bypass grafting.

Results Statin therapy significantly reduced the risk of the composite primary endpoint (adjusted hazard ratio [HR]: 0.56; 95% confidence interval [CI]: 0.34 to 0.89; p = 0.015). Statin therapy reduced the risk of cardiac death (HR: 0.47; 95% CI: 0.23 to 0.93; p = 0.031) and coronary revascularization (HR: 0.45, 95% CI: 0.24 to 0.85; p = 0.013). However, there were no differences in the risk of the composite of all-cause death, recurrent MI, and repeated percutaneous coronary intervention rate.

Conclusions Statin therapy in patients with AMI with LDL-C levels below 70 mg/dl was associated with improved clinical outcome (284).

Microembolization During Carotid Artery Stenting in Patients With High-Risk, Lipid-Rich Plaque: A Randomized Trial of Proximal Versus Distal Cerebral Protection

Objectives The goal of this study was to compare the rate of cerebral microembolization during carotid artery stenting (CAS) with proximal versus distal cerebral protection in patients with high-risk, lipid-rich plaque.

Background Cerebral protection with filters partially reduces the cerebral embolization rate during CAS.

Proximal protection has been introduced to further decrease embolization risk.

Methods Fifty-three consecutive patients with carotid artery stenosis and lipid-rich plaque were randomized to undergo CAS with proximal protection (MO.MA system, n = 26) or distal protection with a filter (FilterWire EZ, n = 27). Microembolic signals (MES) were assessed by using transcranial Doppler during: 1) lesion wiring; 2) predilation; 3) stent crossing; 4) stent deployment; 5) stent dilation; and 6) device retrieval/deflation. Diffusion-weighted magnetic resonance imaging was conducted before CAS, after 48 h, and after 30 days.

Results Patients in the MO.MA group had higher percentage diameter stenosis (89 ± 6% vs. 86 ± 5%, p = 0.027) and rate of ulcerated plaque (35% vs. 7.4%; p = 0.019). Compared with use of the FilterWire EZ, MO.MA significantly reduced mean MES counts (p < 0.0001) during lesion crossing (mean 18 [interquartile range (IQR): 11 to 30] vs. 2 [IQR: 0 to 4]), stent crossing (23 [IQR: 11 to 34] vs. 0 [IQR: 0 to 1]), stent deployment (30 [IQR: 9 to 35] vs. 0 [IQR: 0 to 1]), stent dilation (16 [IQR: 8 to 30] vs. 0 [IQR: 0 to 1]), and total MES (93 [IQR: 59 to 136] vs. 16 [IQR: 7 to 36]). The number of patients with MES was higher with the FilterWire EZ versus MO.MA in phases 3 to 5 (100% vs. 27%; p < 0.0001). By multivariate analysis, the type of brain protection was the only independent predictor of total MES number. No significant difference was found in the number of patients with new post-CAS embolic lesion in the MO.MA group (2 of 14, 14%) as compared with the FilterWire EZ group (9 of 21, 42.8%).

Conclusions In patients with high-risk, lipid-rich plaque undergoing CAS, MO.MA led to significantly lower microembolization as assessed by using MES counts. (Carotid Stenting in Patients With High Risk Carotid Stenosis ["Soft Plaque"] [MOMA]; NCT01274676) (285).

Evaluation of the Second Generation of a Bioresorbable Everolimus-Eluting Vascular Scaffold for the Treatment of De Novo Coronary Artery Stenosis: 12-Month Clinical and Imaging Outcomes

Objectives The aim of this study was to demonstrate that the prevention of early scaffold area shrinkage of the ABSORB BVS (Rev.1.1, Abbott Vascular, Santa Clara, California) was sustained and not simply delayed by a few months.

Background With improved scaffold design and modified manufacturing process of its polymer, the second iteration of ABSORB (BVS 1.1) has improved performance to prevent a scaffold area reduction at 6 months.

Methods Fifty-six patients were enrolled and received 57 ABSORB scaffolds. Quantitative coronary angiography, intravascular ultrasound (IVUS), analysis of radiofrequency backscattering, echogenicity and optical coherence tomography (OCT) were performed at baseline and at 12-month follow-up.

Results Overall the scaffold area remained unchanged with IVUS as well as with OCT, whereas the radiofrequency backscattering and the echogenicity of the struts decreased by 16.8% (p < 0.001) and 20% (p < 0.001), respectively; more specifically, the strut core area on OCT decreased by 11.4% (p = 0.003). Despite the absence of scaffold area loss, pharmacological vasomotion was restored. On an intention-to-treat basis, the angiographic late lumen loss amounted to 0.27 ± 0.32 mm with an IVUS relative decrease in minimal lumen area of 1.94% (p = 0.12), without significant changes in mean lumen area. The OCT at follow-up showed that 96.69% of the struts were covered and that malapposition, initially observed in 18 scaffolds was only detected at follow-up in 4 scaffolds. Two patients experienced peri-procedural and iatrogenic myocardial infarction, respectively, whereas 2 underwent repeat intervention, resulting in the major adverse cardiac event rate of 7.1% (4 of 56).

Conclusions The 12-month performance of the second-generation ABSORB bioresorbable everolimus-eluting scaffold justifies the conduct of a randomized trial against current best standards. (A Clinical Evaluation of the Bioabsorbable Everolimus Eluting Coronary Stent System [BVS EECSS] in the Treatment of Patients With de Novo Native Coronary Artery Lesions; NCT00856856) (286).

Health-Related Quality of Life After Carotid Stenting Versus Carotid Endarterectomy: Results From CREST (Carotid Revascularization Endarterectomy Versus Stenting Trial)

Objectives The purpose of this study was to compare health-related quality of life (HRQOL) outcomes in patients treated with carotid artery stenting (CAS) versus carotid endarterectomy (CEA).

Background In CREST (Carotid Revascularization Endarterectomy versus Stenting Trial), the largest randomized trial of carotid revascularization to date, there was no significant difference in the primary composite endpoint, but rates of stroke and myocardial infarction (MI) differed between CAS and CEA. To help guide individualized clinical decision making, we compared HRQOL among patients enrolled in the CREST study. We also performed exploratory analyses to evaluate the association between periprocedural complications and HRQOL.

Methods We measured HRQOL at baseline, and after 2 weeks, 1 month, and 1 year among 2,502 patients randomly assigned to either CAS or CEA in the CREST study. The HRQOL was assessed using the Medical Outcomes Study Short-Form 36 (SF-36) and 6 disease-specific scales designed to study HRQOL in patients undergoing carotid revascularization.

Results At both 2 weeks and 1 month, CAS patients had better outcomes for multiple components of the SF-36, with large differences for role physical function, pain, and the

physical component summary scale (all $p < 0.01$). On the disease-specific scales, CAS patients reported less difficulty with driving, eating/swallowing, neck pain, and headaches but more difficulty with walking and leg pain (all $p < 0.05$). However, by 1 year, there were no differences in any HRQOL measure between CAS and CEA. In the exploratory analyses, periprocedural stroke was associated with poorer 1-year HRQOL across all SF-36 domains, but periprocedural MI or cranial nerve palsy were not.

Conclusions Among patients undergoing carotid revascularization, CAS is associated with better HRQOL during the early recovery period as compared with CEA—particularly with regard to physical limitations and pain—but these differences diminish over time and are not evident after 1 year. Although CAS and CEA are associated with similar overall HRQOL at 1 year, event-specific analyses confirm that stroke has a greater and more sustained impact on HRQOL than MI. (Carotid Revascularization Endarterectomy versus Stenting Trial [CREST]; NCT00004732) (287).

Outcome Comparison of 600- and 300-mg Loading Doses of Clopidogrel in Patients Undergoing Primary Percutaneous Coronary Intervention for ST-Segment Elevation Myocardial Infarction: Results From the ARMYDA-6 MI (Antiplatelet therapy for Reduction of MYocardial Damage during Angioplasty-Myocardial Infarction) Randomized Study

Objectives The purpose of this study was to compare 600- and 300-mg clopidogrel loading doses in patients with ST-segment elevation myocardial infarction (STEMI).

Background Given the high thrombotic risk of patients with STEMI, greater platelet inhibition may improve outcome in those patients receiving percutaneous coronary intervention (PCI). Although observational data suggest that pretreatment with a 600-mg clopidogrel loading dose may be more effective than the 300-mg regimen in primary PCI, this hypothesis has never been tested in a randomized study.

Methods A total of 201 patients undergoing primary PCI for STEMI randomly received a 600-mg ($n = 103$) or 300-mg ($n = 98$) clopidogrel loading dose before the procedure. The primary endpoint was the evaluation of the infarct size, defined as the area under the curve of cardiac markers.

Results Infarct size was significantly lower in the high-dose regimen: median creatine kinase-myocardial band 2,070 ng/ml (interquartile range [IQR]: 815 to 2,847 ng/ml) versus 3,049 ng/ml (IQR: 1,050 to 7,031 ng/ml) in the 300-mg group, $p = 0.0001$; troponin-I 255 ng/ml (IQR: 130 to 461 ng/ml) versus 380 ng/ml (IQR: 134 to 1,406 ng/ml), $p < 0.0001$. In the 600-mg arm, Thrombolysis In Myocardial Infarction flow grade <3 after PCI was less frequent (5.8% vs. 16.3%, $p = 0.031$), left ventricular ejection fraction at discharge was improved (52.1 ± 9.5% vs. 48.8 ± 11.3%, $p = 0.026$), 30-day major adverse cardiovascular events were fewer (5.8% vs. 15%, $p = 0.049$), and bleeding/entry site complications were not increased (secondary endpoints).

Conclusions In STEMI patients, pre-treatment with a 600-mg clopidogrel loading dose before primary PCI was associated with a reduction of the infarct size compared with a 300-mg loading dose, as well as with improvement of angiographic results, residual cardiac function, and 30-day major adverse cardiovascular events; further studies are warranted to evaluate impact of such strategy on survival (288).

Dual Antiplatelet Therapy Duration and Clinical Outcomes Following Treatment With Zotarolimus-Eluting Stents

Objectives We sought to evaluate differences in late safety outcomes relative to dual antiplatelet therapy (DAPT) duration in patients treated with zotarolimus-eluting stents (ZES).

Background Despite treatment recommendations for at least 12 months of DAPT following drug-eluting stent revascularization, device-specific outcomes relative to DAPT duration are absent.

Methods Among 2,032 patients undergoing percutaneous coronary revascularization with ZES in 5 trials, late safety events were compared relative to DAPT duration for patients with ≥6 months DAPT adherence and survival free of major ischemic and bleeding events.

Results A total of 1,414 event-free patients on DAPT at 6 months were identified. Patient group comparisons relative to DAPT included: 6 months versus ≥12 months, and 6 months versus ≥24 months. Through 3 years, risk-adjusted ischemic event rates did not significantly differ between groups: 6 versus ≥12 months: death (2.7% vs. 2.2%), myocardial infarction (MI, 0.3% vs. 1.1%), and definite/probable stent thrombosis (ST, 0.3% vs. 0%); 6 versus ≥24 months: death (1.6% vs. 1.6%), MI (0.4% vs. 1.2%), and definite/probable ST (0.1% vs. 0.2%). Composite events also did not statistically vary between DAPT durations. In multivariable analysis, 6-month versus longer DAPT duration was not associated with increased likelihood of thrombotic events at 3-year follow-up. Major bleeding was negligible across groups.

Conclusions Among patients treated with ZES, late-term events of death, MI, stroke, and ST do not significantly differ between patients taking 6 months DAPT compared with continuation beyond 1 year. These findings merit further study to identify the appropriate duration of DAPT according to specific drug-eluting stents (289).

Assessing the Temporal Course of Neointimal Hyperplasia Formation After Different Generations of Drug-Eluting Stents

Objectives This study sought to assess the temporal course of neointimal hyperplasia (NIH) formation following

implantation of 2 different generations of drug-eluting stents (DES).

Background The amount of NIH following DES implantation correlates with the potency of the antiproliferative drug, its kinetic release, as well as some individual characteristics, as the presence of diabetes mellitus (DM). Recently, some publications have suggested a continuous growth of NIH following DES, which in some cases, might result in late "catch-up."

Methods Twenty-five patients with single, de novo lesions were treated with sirolimus-eluting stents (SES) (n = 12) and biolimus-eluting stents (BES) (n = 13) and underwent intravascular ultrasound evaluation immediately after the procedure and at 9-month and 5-year follow-ups. The primary endpoint was the comparison of the percentage of NIH obstruction between mid- and long-term follow-up.

Results Mean age was 59 years and 28% of patients had DM. Overall, the percentage of NIH obstruction significantly increased from 9 months to 5 years (1.3% at first follow-up vs. 4.8% at second follow-up, p = 0.002). There was no significant difference in the variation of vessel volume ($\Delta = -0.70$ mm^3/mm BES vs. $\Delta = 0.18$ mm^3/mm SES, p = 0.56), lumen volume ($\Delta = 0.40$ mm^3/mm BES vs. $\Delta = -0.05$ mm^3/mm SES, p = 0.71), and percentage of NIH obstruction ($\Delta = 3.0\%$ BES vs. $\Delta = 3.8\%$ SES, p = 0.55) among DES. However, diabetic patients had a marked NIH increase along the years (NIH volume at second follow-up: 10.15 mm^3 DM vs. 5.11 mm^3 non-DM, p = 0.028).

Conclusions The present serial intravascular ultrasound assessment supports the occurrence of continuous NIH growth following different generations of DES. These findings seem to be particularly more pronounced among patients with DM (290).

Clinical Utility of Regadenoson for Assessing Fractional Flow Reserve

Objectives The aim of this study was to evaluate the efficacy of regadenoson, in comparison with adenosine, for assessing fractional flow reserve (FFR) of intermediate coronary artery stenoses (CAS).

Background Fractional flow reserve is an established invasive method for assessing the physiological significance of CAS. Regadenoson, a selective A_{2A} receptor agonist, is an approved hyperemic agent for pharmacological stress imaging, but its role for measuring FFR is unknown.

Methods This prospective, single-center study enrolled 25 consecutive patients with intermediate CAS discovered during elective angiography (25 lesions). In each patient, FFR of the CAS was measured first by IV adenosine (140 μg/kg/min), followed by IV regadenoson (400 μg bolus). The intrapatient FFR correlation between adenosine and regadenoson was evaluated.

Results The mean age was 63 ± 11 years, and mean left ventricular ejection fraction was 58 ± 11%. Most patients were male (52%) and had hypertension (84%) and dyslipidemia (84%), with 24% having diabetes mellitus and 20% chronic obstructive pulmonary disease. The CAS was visually estimated during angiography (mean 58 ± 9%) and most often found in the left anterior descending coronary artery (48%). A strong, linear correlation of FFR was noted with adenosine and regadenoson ($r = 0.985$, $p < 0.001$). A hemodynamically significant lesion (FFR ≤0.80) was present in 52% with no reclassification of significance between adenosine and regadenoson. No serious events occurred with administration of either drug.

Conclusions Our results suggest that a single IV bolus of regadenoson is as effective as an intravenous infusion of adenosine for measuring FFR and, given its ease of use, should be considered for FFR measurement in the catheterization laboratory (291).

Effects of Increasing Doses of Intracoronary Adenosine on the Assessment of Fractional Flow Reserve

Objectives The purpose of this study was to investigate the effects of increasing dose of intracoronary adenosine on fractional flow reserve (FFR) measurement.

Backgrounds FFR is a validated method for the assessment of the severity of coronary artery stenosis. It is based on the change in the pressure gradient across the stenosis after the achievement of maximal hyperemia of the coronary microcirculation that may be obtained by either intracoronary bolus or intravenous infusion of adenosine. No study has explored so far the effects of very high doses of intracoronary adenosine on FFR.

Methods FFR was assessed in 46 patients with 50 intermediate lesions during cardiac catheterization by pressure-recording guidewire (PrimeWire, Volcano, San Diego, California). FFR was calculated as the ratio of the distal coronary pressure to the aortic pressure at hyperemia. Increasing doses of adenosine were administrated (60, 120, 180, 360, and 720 μg) as intracoronary boluses. Exclusion criteria were: 1) allergy to adenosine; 2) baseline bradycardia (heart rate <50 beats/min); 3) hypotension (blood pressure <90 mm Hg); and 4) refusal to provide signed informed consent.

Results High doses of intracoronary adenosine were well tolerated, with no major side effects. Increasing doses up to 720 μg progressively decreased FFR values and increased the percentage of patients showing an FFR <0.75. Among angiographic parameters, both percent stenosis and lesion length were independently associated with lower FFR values.

Conclusions This study shows that high doses of intracoronary adenosine (up to 720 μg) increased the sensitivity of FFR in the detection of hemodynamically relevant coronary stenoses. Furthermore, lesion length and stenosis severity were independent angiographic determinants of FFR (292).

Comparison of Everolimus- and Sirolimus-Eluting Stents in Patients With Long Coronary Artery Lesions: A Randomized LONG-DES-III (Percutaneous Treatment of LONG Native Coronary Lesions With Drug-Eluting Stent-III) Trial

Objectives This study compared everolimus-eluting stents (EES) and sirolimus-eluting stents (SES) for long coronary lesions.

Background Outcomes remain relatively unfavorable for stent-based coronary intervention of lesions with long diseased segments.

Methods This randomized, multicenter, prospective trial compared the use of long EES with SES in 450 patients with long (≥25 mm) native coronary lesions. The primary endpoint of the trial was in-segment late luminal loss at 9-month angiographic follow-up.

Results The EES and SES groups had similar baseline characteristics. Lesion length was 34.0 ± 15.4 mm in the EES group and 34.3 ± 13.5 mm in the SES group ($p = 0.85$). Nine-month angiographic follow-up was performed in 80% of the EES group and 81% of the SES group ($p = 0.69$). In-segment late loss as the primary study endpoint was significantly larger in the EES group than in the SES group (0.17 ± 0.41 mm vs. 0.09 ± 0.30 mm, p for noninferiority = 0.96, p for superiority = 0.04). The in-segment binary restenosis rate was also higher in the EES group than in the SES group (7.3% vs. 2.7%, $p = 0.046$). However, in-stent late loss (0.22 ± 0.43 mm vs. 0.18 ± 0.28 mm, $p = 0.29$) and in-stent binary restenosis rate (3.9% vs. 2.7%, $p = 0.53$) were similar among the 2 groups. The incidence of any clinical outcomes (death, myocardial infarction, stent thrombosis, target lesion revascularization, and composite outcomes) was not statistically different between the 2 groups.

Conclusions For patients with long native coronary artery disease, EES implantation was associated with greater angiographic in-segment late loss and higher rates of in-segment restenosis compared with SES implantation. However, clinical outcomes were both excellent and not statistically different. (Percutaneous Treatment of LONG Native Coronary Lesions With Drug-Eluting Stent-III [LONG-DES-III]; NCT01078038) (293).

Vascular Inflammation and Repair: Implications for Re-Endothelialization, Restenosis, and Stent Thrombosis

The cellular and molecular processes that control vascular injury responses after percutaneous coronary intervention involve a complex interplay among vascular cells and progenitor cells that control arterial remodeling, neointimal proliferation, and re-endothelialization. Drug-eluting stents (DES) improve the efficacy of percutaneous coronary intervention by modulating vascular inflammation and preventing neointimal proliferation and restenosis. Although positive effects of DES reduce inflammation and restenosis, negative effects delay re-endothelialization and impair endothelial function. Delayed re-endothelialization and impaired endothelial function are linked to stent thrombosis and adverse clinical outcomes after DES use. Compared with bare-metal stents, DES also differentially modulate mobilization, homing, and differentiation of vascular progenitor cells involved in re-endothelialization and neointimal proliferation. The effects of DES on vascular inflammation and repair directly impact clinical outcomes with these devices and dictate requirements for extended-duration dual antiplatelet therapy (294).

Characterization of Clopidogrel Hypersensitivity Reactions and Management With Oral Steroids Without Clopidogrel Discontinuation

Objectives The purpose of this study was to characterize clopidogrel hypersensitivity and describe its successful management with oral steroids without clopidogrel discontinuation.

Background Hypersensitivity reactions to clopidogrel are poorly understood and present difficulty in management.

Methods Patients diagnosed with clopidogrel hypersensitivity after percutaneous coronary intervention underwent evaluation and received oral prednisone without clopidogrel discontinuation. Cutaneous testing was performed after completion of clopidogrel therapy for diagnosis and assessment of cross-reactivity.

Results Sixty-two patients representing 1.6% of the percutaneous coronary intervention population developed clopidogrel hypersensitivity during the study period. The mean age was 62 ± 11 years, 71% of patients were male, and 35% reported prior adverse drug reaction. Clopidogrel hypersensitivity manifested as generalized exanthema in 79%, localized skin reaction in 16%, and angioedema or urticaria in 5% of patients. Biopsy of affected areas demonstrated a lymphocyte-mediated delayed hypersensitivity reaction. Complete resolution of hypersensitivity reaction was observed in 61 patients (98%) with a short course of oral prednisone. Cutaneous testing confirmed delayed hypersensitivity reaction to clopidogrel in 34 (81%) and immediate hypersensitivity in 3 of 42 patients (7%) tested. Allergenic cross-reactivity was observed for ticlopidine in 10 (24%), prasugrel in 7 (17%), and both ticlopidine and prasugrel in 3 patients (7%). Histological examination showed lymphocyte-mediated hypersensitivity in abnormal patch test areas.

Conclusions Clopidogrel hypersensitivity is manifested as generalized exanthema and is caused by a lymphocyte-mediated delayed hypersensitivity in most patients. This can be managed with oral steroids without clopidogrel discontinuation. Allergenic cross-reactivity with ticlopidine, prasugrel, or both is present in a significant number of patients with clopidogrel hypersensitivity (295).

Percutaneous Coronary Intervention Versus Coronary Artery Bypass Graft Surgery in Left Main Coronary Artery Disease: A Meta-Analysis of Randomized Clinical Data

Objectives The purpose of this study was to determine the safety and efficacy of percutaneous coronary intervention (PCI) compared with coronary artery bypass graft (CABG) in patients with left main coronary artery (LMCA) disease.
Background Previous meta-analyses of PCI versus CABG in LMCA disease mainly included nonprospective, observational studies. Several new randomized trials have recently been reported.
Methods We identified 1,611 patients from 4 randomized clinical trials for the present meta-analysis. The primary endpoint was the 1-year incidence of major adverse cardiac and cerebrovascular events (MACCE), defined as death, myocardial infarction (MI), target vessel revascularization (TVR), or stroke.
Results PCI was associated with a nonsignificantly higher 1-year rate of MACCE compared with CABG (14.5% vs. 11.8%; odds ratio [OR]: 1.28; 95% confidence interval [CI]: 0.95 to 1.72; $p = 0.11$), driven by increased TVR (11.4% vs. 5.4%; OR: 2.25; 95% CI: 1.54 to 3.29; $p < 0.001$). Conversely, stroke occurred less frequently with PCI (0.1% vs. 1.7%; OR: 0.15; 95% CI: 0.03 to 0.67; $p = 0.013$). There were no significant differences in death (3.0% vs. 4.1%; OR: 0.74; 95% CI: 0.43 to 1.29; $p = 0.29$) or MI (2.8% vs. 2.9%; OR: 0.98; 95% CI: 0.54 to 1.78; $p = 0.95$).
Conclusions In patients with LMCA disease, PCI was associated with nonsignificantly different 1-year rates of MACCE, death, and MI, a lower risk of stroke, and a higher risk of TVR compared with CABG (296).

ACCF/AHA Methodology for the Development of Quality Measures for Cardiovascular Technology: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Performance Measures

Consistent with the growing national focus on healthcare quality, the American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) have taken a leadership role over the past decade in developing measures of the quality of cardiovascular care by convening a joint ACCF/AHA Task Force on Performance Measures. The Task Force is charged with identifying the clinical topics appropriate for the development of performance measures and with assembling writing committees composed of clinical and methodological experts in collaboration with appropriate subspecialty societies. The Task Force has also created methodology documents that offer guidance in the development of process, outcome, composite, and efficiency measures. Cardiovascular performance measures using existing ACCF/AHA methodology are based on Class I or Class III guidelines recommendations, usually with Level A evidence. These performance measures, based on evidence-based ACCF/AHA guidelines, remain the most rigorous quality measures for both internal quality improvement and public reporting. However, many of the tools for diagnosis and treatment of cardiovascular disease involve advanced technologies, such as cardiac imaging, for which there are often no underlying guideline documents. Because these technologies affect the quality of cardiovascular care and also have the potential to contribute to cardiovascular health expenditures, there is a need for more critical assessment of the use of technology, including the development of quality and performance measures in areas in which guideline recommendations are absent. The evaluation of quality in the use of cardiovascular technologies requires consideration of multiple parameters that differ from other healthcare processes. The present document describes methodology for development of 2 new classes of quality measures in these situations, appropriate use measures and structure/safety measures. Appropriate use measures are based on specific indications, processes, or parameters of care for which high level of evidence data and Class I or Class III guideline recommendations may be lacking but are addressed in ACCF appropriate use criteria documents. Structure/safety measures represent measures developed to address structural aspects of the use of healthcare technology (e.g., laboratory accreditation, personnel training, and credentialing) or quality issues related to patient safety when there are neither guidelines recommendations nor appropriate use criteria. Although the strength of evidence for appropriate use measures and structure/safety measures may not be as strong as that for formal performance measures, they are quality measures that are otherwise rigorously developed, reviewed, tested, and approved in the same manner as ACCF/AHA performance measures. The ultimate goal of the present document is to provide direction in defining and measuring the appropriate use—avoiding not only underuse but also overuse and misuse—and proper application of cardiovascular technology and to describe how such appropriate use measures and structure/safety measures might be developed for the purposes of quality improvement and public reporting. It is anticipated that this effort will help focus the national dialogue on the use of cardiovascular technology and away from the current concerns about volume and cost alone to a more holistic emphasis on value (297).

Activation and Entrainment Mapping of Hemodynamically Unstable Ventricular Tachycardia Using a Percutaneous Left Ventricular Assist Device

Objectives Our goal was to investigate the effects of percutaneous left ventricular assist device (pLVAD) support during catheter ablation of unstable ventricular tachycardia (VT).

Background Mechanical cardiac support during ablation of unstable VT is being increasingly used, but there is little available information on the potential hemodynamic benefits.
Methods Twenty-three consecutive procedures in 22 patients (ischemic, n = 11) with structural heart disease and hemodynamically unstable VT were performed with either pLVAD support (n = 10) or no pLVAD support (intra-aortic balloon pump counterpulsation, n = 6; no support, n = 7). Procedural monitoring included vital signs, left atrial pressure, arterial blood pressure, cerebral perfusion/oximetry, VT characteristics, and ablation outcomes.
Results The pLVAD group was maintained in VT significantly longer than the non-pLVAD group (66.7 min vs. 27.5 min; p = 0.03) and required fewer early terminations of sustained VT for hemodynamic instability (1.0 vs. 4.0; p = 0.001). More patients in the pLVAD group had at least 1 VT termination during ablation than non-pLVAD patients (9 of 10 [90%] vs. 5 of 13 [38%]; p = 0.03). There were no differences between groups in duration of cerebral deoxygenation, hypotension or perioperative changes in left atrial pressure, brain natriuretic peptide levels, lactic acid, or renal function.
Conclusions In patients with scar-related VT undergoing catheter ablation, pLVAD support was able to safely maintain end-organ perfusion despite extended periods of hemodynamically unstable VT. Randomized studies are necessary to determine whether this enhanced ability to perform entrainment and activation mapping will translate into a higher rate of clinical success (298).

Functional SYNTAX Score for Risk Assessment in Multivessel Coronary Artery Disease

Objectives This study was aimed at investigating whether a fractional flow reserve (FFR)-guided SYNTAX score (SS), termed "functional SYNTAX score" (FSS), would predict clinical outcome better than the classic SS in patients with multivessel coronary artery disease (CAD) undergoing percutaneous coronary intervention (PCI).
Background The SS is a purely anatomic score based on the coronary angiogram and predicts outcome after PCI in patients with multivessel CAD. FFR-guided PCI improves outcomes by adding functional information to the anatomic information obtained from the angiogram.
Methods The SS was prospectively collected in 497 patients enrolled in the FAME (Fractional Flow Reserve versus Angiography for Multivessel Evaluation) study. FSS was determined by only counting ischemia-producing lesions (FFR $\leq$0.80). The ability of each score to predict major adverse cardiac events (MACE) at 1 year was compared.
Results The 497 patients were divided into tertiles of risk based on the SS. After determining the FSS for each patient, 32% moved to a lower-risk group as follows. MACE occurred in 9.0%, 11.3%, and 26.7% of patients in the low-, medium-, and high-FSS groups, respectively (p < 0.001). Only FSS and procedure time were independent predictors of 1-year MACE. FSS demonstrated a better predictive accuracy for MACE compared with SS (Harrell's C of FSS, 0.677 vs. SS, 0.630, p = 0.02; integrated discrimination improvement of 1.94%, p < 0.001).
Conclusions Recalculating SS by only incorporating ischemia-producing lesions as determined by FFR decreases the number of higher-risk patients and better discriminates risk for adverse events in patients with multivessel CAD undergoing PCI. (Fractional Flow Reserve versus Angiography for Multivessel Evaluation [FAME]; NCT00267774) (299).

Strain-Encoded Cardiac Magnetic Resonance During High-Dose Dobutamine Stress Testing for the Estimation of Cardiac Outcomes: Comparison to Clinical Parameters and Conventional Wall Motion Readings

Objectives The purpose of this study was to determine the prognostic value of strain-encoded magnetic resonance imaging (SENC) during high-dose dobutamine stress cardiac magnetic resonance imaging (DS-MRI) compared with conventional wall motion readings.
Background Detection of inducible ischemia by DS-MRI on the basis of assessing cine images is subjective and depends on the experience of the readers, which may influence not only the diagnostic classification but also the risk stratification of patients with ischemic heart disease.
Methods In all, 320 consecutive patients with suspected or known coronary artery disease underwent DS-MRI, using a standard protocol in a 1.5T MR scanner. Wall motion abnormalities (WMA) and myocardial strain were assessed at baseline and during stress, and outcome data including cardiac deaths, nonfatal myocardial infarctions ("hard events"), and revascularization procedures performed >90 days after the MR scans were collected.
Results Thirty-five hard events occurred during a 28 $\pm$ 9 month follow-up period, including 10 cardiac deaths and 25 nonfatal myocardial infarctions, and 32 patients underwent coronary revascularization. Using a series of Cox proportional-hazards models, both resting and inducible WMA offered incremental information for the assessment of hard cardiac events compared to clinical variables (chi-square = 13.0 for clinical vs. chi-square = 26.1 by adding resting WMA, p < 0.001, vs. chi-square = 39.3 by adding inducible WMA, p < 0.001). Adding visual SENC or quantitative strain rate reserve to this model further improved the prediction of outcome (chi-square = 50.7 vs. chi-square = 52.5, p < 0.001 for both). In a subset of patients (n = 175) who underwent coronary angiography, SENC yielded significantly higher sensitivity for coronary artery disease detection (96% vs. 84%, p < 0.02), whereas specificity and accuracy were not significantly different (88% vs. 94% and 93% vs. 88%, p = NS for both).

Conclusions Strain-encoded MRI aids the accurate identification of patients at high risk for future cardiac events and revascularization procedures, beyond the assessment of conventional atherogenic risk factors and resting or inducible WMA on cine images. (Strain-Encoded Cardiac Magnetic Resonance Imaging as an Adjunct for Dobutamine Stress Testing; NCT00758654) (300).

Invasive Acute Hemodynamic Response to Guide Left Ventricular Lead Implantation Predicts Chronic Remodeling in Patients Undergoing Cardiac Resynchronization Therapy

Objectives We evaluated the relationship between acute hemodynamic response (AHR) and reverse remodeling (RR) in cardiac resynchronization therapy (CRT).

Background CRT reduces mortality and morbidity in heart failure patients; however, up to 30% of patients do not derive symptomatic benefit. Higher proportions do not remodel. Multicenter trials have shown echocardiographic techniques are poor at improving response rates. We hypothesized the degree of AHR at implant can predict which patients remodel.

Methods Thirty-three patients undergoing CRT (21 dilated and 12 ischemic cardiomyopathy) were studied. Left ventricular (LV) volumes were assessed before and after CRT. The AHR (maximum rate of left ventricular pressure [LV-dP/dt_{max}]) was assessed at implant with a pressure wire in the LV cavity. Largest percentage rise in LV-dP/dt_{max} from baseline (atrial antibradycardia pacing or right ventricular pacing with atrial fibrillation) to dual-chamber pacing (DDD)-LV was used to determine optimal coronary sinus LV lead position. Reverse remodeling was defined as reduction in LV end systolic volume $\geq$15% at 6 months.

Results The LV-dP/dt_{max} increased significantly from baseline (801 $\pm$ 194 mm Hg/s to 924 $\pm$ 203 mm Hg/s, $p < 0.001$) with DDD-LV pacing for the optimal LV lead position. The LV end systolic volume decreased from 186 $\pm$ 68 ml to 157 $\pm$ 68 ml ($p < 0.001$). Eighteen (56%) patients exhibited RR. There was a significant relationship between percentage rise in LV-dP/dt_{max} and RR for DDD-LV pacing ($p < 0.001$). A similar relationship for AHR and RR in dilated cardiomyopathy and ischemic cardiomyopathy ($p = 0.01$ and $p = 0.006$) was seen.

Conclusions Acute hemodynamic response to LV pacing is useful for predicting which patients are likely to remodel in response to CRT both for dilated cardiomyopathy and ischemic cardiomyopathy. Using AHR has the potential to guide LV lead positioning and improve response rates (301).

Cardiorespiratory Response to Exercise After Renal Sympathetic Denervation in Patients With Resistant Hypertension

Objectives This study sought to investigate the effects of interventional renal sympathetic denervation (RD) on cardiorespiratory response to exercise.

Background RD reduces blood pressure at rest in patients with resistant hypertension.

Methods We enrolled 46 patients with therapy-resistant hypertension as extended investigation of the Symplicity HTN-2 (Renal Denervation With Uncontrolled Hypertension) trial. Thirty-seven patients underwent bilateral RD and 9 patients were assigned to the control group. Cardiopulmonary exercise tests were performed at baseline and 3-month follow-up.

Results In the RD group, compared with baseline examination, blood pressure at rest and at maximum exercise after 3 months was significantly reduced by 31 $\pm$ 13/9 $\pm$ 13 mm Hg ($p < 0.0001$) and by 21 $\pm$ 20/5 $\pm$ 14 mm Hg ($p < 0.0001$), respectively. Achieved work rate increased by 5 $\pm$ 13 W ($p = 0.029$) whereas peak oxygen uptake remained unchanged. Blood pressure 2 min after exercise was significantly reduced by 29 $\pm$ 17/8 $\pm$ 15 mm Hg ($p < 0.001$ for systolic blood pressure; $p = 0.002$ for diastolic blood pressure). Heart rate at rest decreased after RD (4 $\pm$ 11 beats/min; $p = 0.028$), whereas maximum heart rate and heart rate increase during exercise were not different. Heart rate recovery improved significantly by 4 $\pm$ 7 beats/min after renal denervation ($p = 0.009$). In the control group, there were no significant changes in blood pressure, heart rate, maximum work rate, or ventilatory parameters after 3 months.

Conclusions RD reduces blood pressure during exercise without compromising chronotropic competence in patients with resistant hypertension. Heart rate at rest decreased and heart rate recovery improved after the procedure. (Renal Denervation With Uncontrolled Hypertension; [Symplicity HTN-2]; NCT00888433) (302).

10 Years of Intracoronary and Intramyocardial Bone Marrow Stem Cell Therapy of the Heart: From the Methodological Origin to Clinical Practice

Intracoronary and intramyocardial stem cell therapy aim at the repair of compromised myocardium thereby—as a causal treatment—preventing ventricular remodeling and improving overall performance. Since the first-in-human use of bone marrow stem cells (BMCs) after acute myocardial infarction in 2001, a large number of clinical studies have demonstrated their clinical benefit: BMC therapy can be performed with usual cardiac catheterization techniques in the conscious patient as well as also easily during cardiosurgical interventions. New York Heart Association severity degree of patients as well as physical activity improve in addition to ("on top" of) all other therapeutic regimens. Stem cell therapy also represents an ultimate approach in advanced cardiac failure. For acute myocardial infarction and chronic ischemia, long-term mortality after 1 and 5 years, respectively, is significantly reduced. A few studies also indicate beneficial effects for chronic dilated cardiomyopathy. The clinical use of autologous BMC therapy implies no ethical problems, when

unmodified primary cells are used. With the use of primary BMCs, there are no major stem cell-related side effects, especially no cardiac arrhythmias and inflammation. Various mechanisms of the stem cell action in the human heart are discussed, for example, cell transdifferentiation, cell fusion, activation of intrinsic cardiac stem cells, and cytokine-mediated effects. New techniques allow point-of-care cell preparations, for example, within the cardiac intervention or operation theater, thereby providing short preparation time, facilitated logistics of cell transport, and reasonable cost effectiveness of the whole procedure. The 3 main indications are acute infarction, chronic ischemic heart failure, and dilated cardiomyopathy. Future studies are desirable to further elucidate the mechanisms of stem cell action and to extend the current use of intracoronary and/or intramyocardial stem cell therapy by larger and presumably multicenter and randomized trials (303).

Long-Term Outcome of Percutaneous Coronary Intervention for Chronic Total Occlusions

Objectives The aim of this study was to evaluate long-term clinical outcomes after percutaneous coronary intervention (PCI) for chronic total occlusions (CTO).
Background Despite technical advancements, there is a paucity of data on long-term outcomes after PCI of CTO.
Methods We evaluated long-term clinical outcomes in 1,791 patients who underwent PCI of 1,852 CTO at 3 tertiary care centers in the United States, South Korea, and Italy between 1998 and 2007. Median follow-up was 2.9 years (interquartile range: 1.5 to 4.6 years).
Results Procedural success was obtained in 1,226 (68%) patients. Stents were implanted in 1,160 patients (95%); 396 patients (34%) received bare-metal stents (BMS), and 764 patients (66%) received drug-eluting stents (DES). After multivariable analysis, successful CTO PCI was an independent predictor of a lower cardiac mortality (hazard ratio [HR]: 0.40, 95% confidence interval [CI]: 0.21 to 0.75, $p < 0.01$) and reduced need for coronary artery bypass graft surgery (HR: 0.21, 95% CI: 0.13 to 0.40, $p < 0.01$); it also correlated with a strong trend toward lower all-cause mortality (HR: 0.63, 95% CI: 0.40 to 1.00, $p = 0.05$) at 5-year follow-up. Among patients who underwent stent implantation, treatment with DES rather than BMS resulted in less target vessel revascularization at long-term follow-up (17.2% vs. 31.1%, $p < 0.01$); definite/probable stent thrombosis rates were similar (DES 1.7%, BMS 2.3%, $p = 0.58$). Within the DES subgroup, patients treated with paclitaxel-eluting stents and sirolimus-eluting stents had similar clinical outcomes.
Conclusions Successful CTO PCI is associated with reduced long-term cardiac mortality and need for coronary artery bypass graft surgery. Treatment of CTO with DES rather than BMS is associated with a significant reduction in target vessel revascularization with similar rates of stent thrombosis. Paclitaxel-eluting stents and sirolimus-eluting stents had similar long-term safety and efficacy outcomes (304).

Characteristics and In-Hospital Outcomes of Patients With Non–ST-Segment Elevation Myocardial Infarction and Chronic Kidney Disease Undergoing Percutaneous Coronary Intervention

Objectives This study sought to evaluate the characteristics, therapies, and outcomes of patients with chronic kidney disease (CKD) presenting with non–ST-segment elevation myocardial infarction (NSTEMI) and managed with percutaneous coronary intervention (PCI). This specific population has not been evaluated previously.
Background Among patients with acute coronary syndrome, the presence of renal dysfunction is associated with an increased risk of death and major bleeding.
Methods We examined data on 40,074 NSTEMI patients managed with PCI who were captured by the ACTION (Acute Coronary Treatment and Intervention Outcomes Network) registry. Patients were divided according to baseline renal function in 4 groups: no CKD and CKD stages 3, 4, and 5.
Results Overall, 31.1% ($n = 12,045$) of patients with NSTEMI undergoing PCI had CKD. Compared with patients with normal renal function, CKD patients managed with PCI had significantly more history of myocardial infarction, heart failure, and more 3-vessel coronary artery disease. They received fewer antithrombotic therapies but were treated more frequently with bivalirudin. In addition, they had significantly higher rates of in-hospital mortality and major bleeding. CKD stage 4 was associated with the highest risk of adverse events relative to no CKD. The multivariable adjusted odds ratios of in-hospital mortality for CKD stages 3, 4, and 5 relative to no CKD were 2.0, 2.8, and 2.6, respectively (global p value <0.0001), and the analogous adjusted odds ratios of major bleeding were 1.5, 2.8, and 1.8, respectively (global p value <0.0001).
Conclusions CKD patients presenting with NSTEMI and managed with PCI have more comorbidities and receive guideline-recommended therapies less frequently than do patients without CKD. CKD is strongly associated with in-hospital mortality and bleeding in NSTEMI patients undergoing PCI (305).

Time to Significant Gradient Reduction Following Septal Balloon Occlusion Predicts the Magnitude of Final Gradient Response During Alcohol Septal Ablation in Patients With Hypertrophic Obstructive Cardiomyopathy

Objectives The purpose of this study was to investigate whether a relationship exists between an acute reduction in resting left ventricular outflow tract (LVOT) gradient with balloon occlusion and the final invasive gradient response following alcohol septal ablation (ASA).

Background ASA is an alternative therapy to myectomy surgery to reduce the basal septal thickness and decrease the resting and/or provocable LVOT gradient in patients with hypertrophic cardiomyopathy. Patients have a variable gradient response to occlusion of the septal perforator artery before ethanol infusion for ASA.
Methods From November 1998 to November 2008, 120 patients (mean age 60 years [range 16 to 87 years], 50% women) with hypertrophic cardiomyopathy underwent ASA at our institution. The resting LVOT gradient (peak systolic left ventricle [LV] pressure − peak systolic aortic pressure) was measured continuously during the ASA procedure. The time to significant LVOT gradient decrease (defined as >50% decrease from baseline) was recorded following balloon occlusion of the dominant septal perforator coronary artery, which was found to perfuse the basal septum based on contrast echocardiographic studies.
Results The mean baseline resting LVOT gradient was 86 ± 43 mm Hg, and it decreased to 17 ± 11 mm Hg following ASA (−80.2%). The mean time to significant gradient reduction was 3.6 ± 2 min (range 25 s to 11 min). The time to significant LVOT gradient reduction strongly correlated with the final magnitude of gradient reduction following ASA ($r = -0.81$, $p < 0.001$).
Conclusions This study demonstrates a correlation between the time to significant LVOT gradient reduction following septal perforator balloon occlusion and the magnitude of final gradient response after ASA (306).

Long-Term Safety and Effectiveness of Drug-Eluting Stents for the Treatment of Saphenous Vein Grafts Disease: A Population-Based Study

Objectives The purpose of this study was to evaluate the long-term safety and effectiveness of drug-eluting stents (DES) for the treatment of saphenous vein graft (SVG) disease.
Background DES are frequently implanted for SVG interventions, but some studies have shown that they are not effective in reducing target vessel revascularization (TVR) over longer-term follow-up. Some studies suggest there is increased mortality with DES compared with bare-metal stents (BMS).
Methods We performed propensity score matching analysis using a population-based cohort that included 709 well-matched pairs ($n = 1{,}418$) who received DES or BMS for the treatment of SVG disease from 2003 to 2008. Outcomes of interest included repeat TVR, myocardial infarction, and death.
Results The mean age of the propensity-matched cohort was 69 years, 50% had diabetes, and the mean age of SVG was 10.6 years. At 4-year follow-up, the rate of repeat TVR was 21% in the DES group and 27.6% in the BMS group ($p = 0.004$). DES implantation was associated with the largest TVR reduction among patients with diabetes and patients receiving longer stents (≥30 mm) and the number of procedures needed to prevent a TVR at 4 years was 8 and 7, respectively. The composite rate of myocardial infarction or death was not significantly different between DES and BMS at 4 years (27.8% vs. 32.6%, $p = 0.09$).
Conclusions Implantation of DES in the treatment of SVG disease is associated with substantial reduction of repeat revascularization, without evidence of an increased risk of myocardial infarction or death at longer-term follow-up (307).

Surgical Candidacy and Selection Biases in Nonemergent Left Main Stenting: Implications for Observational Studies

Objectives This study sought to characterize reasons for surgical ineligibility in patients undergoing nonemergent unprotected left main (ULM) percutaneous coronary intervention (PCI) and to assess the potential for these reasons to confound comparative effectiveness studies of coronary revascularization.
Background Although both PCI and coronary artery bypass graft surgery are treatments for ULM disease, some patients are not eligible for both treatments, which may result in treatment selection biases.
Methods In 101 consecutive patients undergoing nonemergent ULM PCI, mixed methods were used to determine the prevalence of treatment selection dictated by surgical ineligibility and to identify the reasons cited for avoiding coronary artery bypass graft surgery. We then determined whether these reasons were captured by the ACC–NCDR (American College of Cardiology–National Cardiovascular Data Registry) Cath-PCI dataset to assess the ability of this registry to account for biases in treatment selection. Finally, the association of surgical eligibility with long-term outcomes after ULM PCI was assessed.
Results Treatment selection was dictated by surgical ineligibility in over half the ULM PCI cohort with the majority having reasons for ineligibility not captured by the ACC–NCDR. Surgical ineligibility was a significant predictor of mortality after adjustment for Society of Thoracic Surgeons (hazard ratio [HR]: 5.4, 95% confidence interval [CI]: 1.2 to 25), EuroSCORE (European System for Cardiac Operative Risk Evaluation) (HR: 5.9, 95% CI: 1.3 to 27), or NCDR mortality scores (HR: 6.2, 95% CI: 1.4 to 27).
Conclusions Surgical ineligibility dictating treatment selection is common in patients undergoing nonemergent ULM PCI, occurs on the basis of risk factors not captured by the ACC–NCDR, and is independently associated with worse long-term outcomes after adjusting for standard risk scores (308).

Fundamental Wire Technique and Current Standard Strategy of Percutaneous Intervention for Chronic Total Occlusion With Histopathological Insights

Currently, successful treatment of chronic total occlusion (CTO) seems markedly improved, due to several new

techniques and dedicated device developments. However, this improved success rate is often limited to procedures performed by skilled, highly experienced operators. To improve the overall success rate of percutaneous coronary intervention of CTO from a worldwide perspective, a deeper understanding of CTO histopathology might offer insights into the development of new techniques and procedural strategies. In this review, CTO histopathology and wire techniques are discussed on the basis of the fundamental concepts of antegrade and retrograde approaches. Although details pertaining to wire manipulation are very difficult to explain objectively, we tried to describe this as best as possible in this article. Finally, a systematic review of the current standard CTO strategy is provided. Hopefully, this article will enhance the understanding of this complex procedure and, consequently, promote safe and effective CTO-percutaneous coronary intervention for patients who present with this challenging lesion subset (309).

Long-Term Impact of Chronic Kidney Disease in Patients With ST-Segment Elevation Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention: The HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) Trial

Objectives This study sought to investigate the impact of chronic kidney disease (CKD) in patients undergoing percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI) with different antithrombotic strategies.

Background CKD is associated with increased risk of adverse ischemic and hemorrhagic events after primary PCI for STEMI.

Methods HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trial was a multicenter, international, randomized trial comparing bivalirudin monotherapy or heparin plus a glycoprotein IIb/IIIa inhibitor (GPI) during primary PCI in STEMI. CKD, defined as creatinine clearance <60 ml/min, was present at baseline in 554 of 3,397 patients (16.3%). Patients were followed for 3 years. Net adverse cardiac event (NACE) was defined as the composite of death, reinfarction, ischemia-driven target vessel revascularization (TVR), stroke or non–coronary artery bypass grafting (CABG)-related major bleeding.

Results Patients with CKD compared with patients without had higher rates of NACE (41.4% vs. 23.8%, $p < 0.0001$), death (18.7% vs. 4.4%, $p < 0.0001$), and major bleeding (19.3% vs. 6.7%, $p < 0.0001$). Multivariable analysis identified baseline creatinine as an independent predictor of death at 3 years (hazard ratio: 1.51, 95% confidence interval: 1.21 to 1.87, $p < 0.001$). Patients with CKD randomized to bivalirudin monotherapy versus heparin plus GPI had no significant difference in major bleeding (19.0% vs. 19.6%, $p = 0.72$) or death (19.0% vs. 18.4%, $p = 0.88$) at 3 years. In patients with CKD, there was no difference in the rates of TVR in bare-metal stents (BMS) versus drug-eluting stents (DES) at 3 years (14.1% vs. 15.1%, $p = 0.8$).

Conclusions STEMI patients with CKD have significantly higher rates of death and major bleeding compared with those without CKD. In patients with CKD, there appears to be no benefit of bivalirudin compared with heparin + GPI, or DES versus BMS during primary PCI in improving clinical outcomes (310).

Sirolimus-Eluting Coronary Stents in Octogenarians: A 1-Year Analysis of the Worldwide e-SELECT Registry

Objectives The aim of this study was to identify the worldwide practice of Cypher Select (Cordis Corporation, Bridgewater, New Jersey) or Cypher Select Plus sirolimus-eluting stent (SES) in patients 80 years of age (octogenarian) and to identify clinical outcomes in this patient population.

Background The use of drug-eluting stents in elderly patients may have different features compared with younger patients.

Methods Between 2006 and 2008, 15,147 patients from 320 hospitals in 56 countries were enrolled in a registry. Initial implantation and follow-up outcome information obtained at 1-year follow-up in 675 octogenarian patients were compared with those in 14,472 nonoctogenarian patients.

Results Octogenarians had significantly more comorbidities and had higher Charlson comorbidity index scores (1.5 ± 1.6 vs. 1.0 ± 1.3, $p < 0.001$). Rates of cardiac death (3.3% vs. 0.9%, $p < 0.001$), myocardial infarction (2.3% vs. 1.9%, $p = 0.021$), and definite or probable stent thrombosis (2.3% vs. 0.9%, $p = 0.0002$), and major bleeding (2.0% vs. 0.9%, $p = 0.015$) were significantly higher in octogenarians at 1 year; however, there was no significant difference in the rate of target lesion revascularization between the 2 groups (3.2% vs. 2.2%, $p = 0.12$). In octogenarians, a high Charlson comorbidity index was an independent predictor of death and stent thrombosis up to 360 days from the index procedure (hazard ratio: 1.3, 95% confidence interval: 1.1 to 1.5, $p < 0.001$, and hazard ratio: 1.5, 95% confidence interval: 1.3 to 1.8, $p < 0.001$, respectively).

Conclusions Stenting with SES may be an effective therapeutic option in elderly patients, with acceptable rates of complications and a very low rate of repeat revascularization as demonstrated by this e-SELECT (A Multi-Center Post-Market Surveillance Registry) subgroup analysis (311).

Impact of Intravascular Ultrasound Imaging on Early and Late Clinical Outcomes Following Percutaneous Coronary Intervention With Drug-Eluting Stents

Objectives This study sought to assess the impact of intravascular ultrasound (IVUS)-guided versus angiography-guided drug-eluting stent (DES) implantation.

Background There are limited data on IVUS guidance in the DES era. Therefore, we investigated the impact of IVUS guidance on clinical outcomes in the MATRIX (Comprehensive Assessment of Sirolimus-Eluting Stents in Complex Lesions) registry.
Methods The MATRIX registry prospectively enrolled consecutive, unselected patients treated with sirolimus-eluting stents (SES) (n = 1,504); 631 patients (42%) underwent IVUS-guided stenting, and 873 (58%) had only angiographic guidance. We assessed 30-day, 1-year, and 2-year rates of death/myocardial infarction (MI), major adverse cardiac events (cardiac death, MI, or target vessel revascularization), and definite/probable stent thrombosis in 548 propensity-score matched patient pairs.
Results After matching, baseline and angiographic characteristics were similar in IVUS and no-IVUS groups. Patients in the IVUS group had significantly less death/MI at 30 days (1.5% vs. 4.6%, $p < 0.01$), 1 year (3.3% vs. 6.5%, $p < 0.01$), and 2 years (5.0% vs. 8.8%, $p < 0.01$). Patients in the IVUS group had significantly less major adverse cardiac events at 30 days (2.2% vs. 4.8%, $p = 0.04$) and numerically less major adverse cardiac events at 1 year (9.1% vs. 13.5%, $p = 0.07$) and 2 years (12.9% vs. 16.7%, $p = 0.18$). Rates of MI were significantly lower in the IVUS group at 30 days (1.5% vs. 4.0%, $p < 0.01$), 1 year (1.8% vs. 4.8%, $p < 0.01$), and 2 years (2.1% vs. 5.7%, $p < 0.01$).
Conclusions IVUS-guided stent implantation appears to be associated with a reduction in both early and long-term clinical events. Further investigation in randomized controlled trials is warranted (312).

Myocardium at Risk in ST-Segment Elevation Myocardial Infarction: Comparison of T2-Weighted Edema Imaging With the MR-Assessed Endocardial Surface Area and Validation Against Angiographic Scoring

Objectives The objective of this study was to assess the area at risk (AAR) in ST-segment elevation myocardial infarction with 2 different cardiac magnetic resonance (CMR) imaging methods and to compare them with the validated angiographic Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease Score (APPROACH-score) in a large consecutive patient cohort.
Background Edema imaging with T_2-weighted CMR and the endocardial surface area (ESA) assessed by late gadolinium enhancement have been introduced as relatively new methods for AAR assessment in ST-segment elevation myocardial infarction. However, data on the utility and validation of these techniques are limited.
Methods A total of 197 patients undergoing primary percutaneous coronary intervention in acute ST-segment elevation myocardial infarction were included. AAR (assessed with T_2-weighted edema imaging and the ESA method), infarct size, and myocardial salvage (AAR minus infarct size) were determined by CMR 2 to 4 days after primary angioplasty. Angiographic AAR scoring was performed by use of the APPROACH-score. All measurements were done offline by blinded observers.
Results The AAR assessed by T_2-weighted imaging showed good correlation with the angiographic AAR ($r = 0.87$; $p < 0.001$), whereas the ESA showed only a moderate correlation either to T_2-weighted imaging ($r = 0.56$; $p < 0.001$) or the APPROACH-score ($r = 0.44$; $p < 0.001$). Mean AAR by ESA (20.0 ± 11.7% of left ventricular mass) was significantly ($p < 0.001$) smaller than the AAR assessed by T_2-weighted imaging (35.6 ± 10.9% of left ventricular mass) or the APPROACH-score (27.9 ± 10.5% of left ventricular mass) and showed a significant negative dependence on myocardial salvage index. In contrast, no dependence of T_2-weighted edema imaging or the APPROACH-score on myocardial salvage index was seen.
Conclusions The AAR can be reliably assessed by T_2-weighted CMR, whereas assessment of the AAR by ESA seems to be dependent on the degree of myocardial salvage, thereby underestimating the AAR in patients with high myocardial salvage such as aborted infarction. Thus, assessment of the AAR with the ESA method cannot be recommended. (Myocardial Salvage and Contrast Dye Induced Nephropathy Reduction by N-Acetylcystein [LIPSIA-N-ACC]; NCT00463749) (313).

Physiological Basis for Angina and ST-Segment Change: PET-Verified Thresholds of Quantitative Stress Myocardial Perfusion and Coronary Flow Reserve

Objectives This study aimed to determine the quantitative low-flow threshold for stress-induced perfusion defects with severe angina and/or significant ST-segment depression during dipyridamole hyperemia.
Background Vasodilator stress reveals differences in regional perfusion without ischemia in most patients. However, in patients with a perfusion defect, angina, and/or significant ST-segment depression during dipyridamole stress, quantitative absolute myocardial perfusion and coronary flow reserve (CFR) at the exact moment of definite ischemia have not been established. Defining these low-flow thresholds of angina or ST-segment changes may offer insight into physiological disease severity in patients with atherosclerosis.
Methods Patients underwent rest–dipyridamole stress positron emission tomography (PET) with absolute flow quantification in ml/min/g. Definite ischemia was defined as a new or worse perfusion defect during dipyridamole stress with significant ST-segment depression and/or severe angina requiring pharmacological treatment. Indeterminate clinical features required only 1 of these 3 abnormalities. The comparison group included patients without prior myocardial infarction, or angina or electrocardiographic changes after dipyridamole.

Results In 1,674 sequential PET studies, we identified 194 (12%) with definite ischemia, 840 (50%) studies with no ischemia, and 301 (18%) that were clinically indeterminate. A vasodilator stress perfusion cutoff of 0.91 ml/min/g optimally separated definite from no ischemia with an area under the receiver-operator characteristic curve (AUC) of 0.98 and a CFR cutoff of 1.74 with an AUC = 0.91, reflecting excellent discrimination at the exact moment of definite ischemia.
Conclusions Thresholds of low myocardial vasodilator stress perfusion in ml/min/g and CFR sharply separate patients with angina or ST-segment change from those without these manifestations of ischemia during dipyridamole stress with excellent discrimination. Stress flow below 0.91 ml/min/g in dipyridamole-induced PET perfusion defects causes significant ST-segment depression and/or severe angina. However, when the worst vasodilator stress flow exceeds 1.12 ml/min/g, these manifestations of ischemia occur rarely (314).

Transcatheter Aortic Valve Implantation in Patients With Severe Aortic Stenosis and Small Aortic Annulus

Objectives Valve hemodynamics and clinical outcomes among patients with a small aortic annulus who underwent transcatheter aortic valve implantation (TAVI) were examined.
Background The presence of a small aortic annulus may complicate the surgical management of patients with severe aortic stenosis (AS). TAVI is an alternative to aortic valve replacement (AVR) in high-risk patients, but few data exist on the results of TAVI in patients with a small aortic annulus.
Methods Between 2007 and 2010, 35 patients (mean age 79.2 ± 9.4 years) with severe AS and an aortic annulus diameter <20 mm (mean 18.5 ± 0.9 mm) underwent TAVI with a 23-mm Edwards SAPIEN bioprosthesis (Edwards Lifesciences, Inc., Irvine, California). Echocardiographic parameters and clinical outcomes were assessed prior to discharge and at 6, 12, and 24 months.
Results Procedural success was achieved in 34 patients (97.1%). There was 1 in-hospital death. Peak and mean transaortic gradients decreased from 76.3 ± 33.0 mm Hg and 45.2 ± 20.6 mm Hg at baseline to 21.8 ± 8.4 mm Hg and 11.7 ± 4.8 mm Hg post-procedure, respectively, both $p < 0.0001$. Mean indexed effective orifice area (IEOA) increased from 0.35 ± 0.10 cm^2/m^2 at baseline to 0.90 ± 0.18 cm^2/m^2 post-procedure, $p < 0.0001$. Severe prosthesis–patient mismatch (IEOA <0.65 cm^2/m^2) occurred in 2 patients (5.9%). At a mean follow-up of 14 ± 11 months, gradients remained low and 30 of the 31 remaining survivors were in New York Heart Association functional class I or II.
Conclusions In high-risk patients with severe AS and a small aortic annulus, TAVI is associated with good post-procedural valve hemodynamics and clinical outcomes. TAVI may provide a reasonable alternative to conventional AVR in elderly patients with a small aortic annulus (315).

Renal Function-Based Contrast Dosing to Define Safe Limits of Radiographic Contrast Media in Patients Undergoing Percutaneous Coronary Interventions

Objectives The aim of this study was to evaluate the association between calculated creatinine clearance (CCC)-based contrast dose and renal complications in patients undergoing percutaneous coronary interventions (PCI).
Background Excess volumes of contrast media are associated with renal complications in patients undergoing cardiac procedures. Because contrast media are excreted by the kidney, we hypothesized that a dose estimation on the basis of CCC would provide a simple strategy to define a safe dose of contrast media.
Methods We assessed the association between CCC-based contrast dose and the risk of contrast-induced nephropathy (CIN) and need for in-hospital dialysis in 58,957 patients undergoing PCI and enrolled in the BMC2 (Blue Cross Blue Shield of Michigan Cardiovascular Consortium) registry from 2007 to 2008. Patients receiving dialysis at the time of the procedure were excluded.
Results The risk of CIN and nephropathy requiring dialysis (NRD) was directly associated with increasing contrast volume adjusted for renal function. The risk for CIN and NRD approached significance when the ratio of contrast dose/CCC exceeded 2 (adjusted odds ratio [OR] for CIN: 1.16, 95% confidence interval [CI]: 0.98 to 1.37, adjusted OR for NRD: 1.72, 95% CI: 0.9 to 3.27) and was dramatically elevated in patients exceeding a contrast to CCC ratio of 3 (adjusted OR for CIN: 1.46, 95% CI: 1.27 to 1.66, adjusted OR for NRD: 1.89, 95% CI: 1.21 to 2.94).
Conclusions Our study supports the need for minimizing contrast dose in patients with renal dysfunction. A contrast dose on the basis of estimated renal function with a planned contrast volume restricted to less than thrice and preferably twice the CCC might be valuable in reducing the risk of CIN and NRD (316).

Hospital Variability in the Rate of Finding Obstructive Coronary Artery Disease at Elective, Diagnostic Coronary Angiography

Objectives The purpose of this study was to describe hospital variability in the rate of finding obstructive coronary artery disease (CAD) at elective coronary angiography.
Background A recent national study found that obstructive CAD was found in less than one-half of patients undergoing elective coronary angiography.
Methods We performed a retrospective analysis of 565,504 patients without prior myocardial infarction or revascularization undergoing elective coronary angiography using CathPCI Registry data from 2005 to 2008 to evaluate the rate of finding obstructive CAD (any major epicardial vessel

stenosis ≥50%) at coronary angiography at 691 U.S. hospitals.

Results The rate of obstructive coronary disease found at elective coronary angiography varied from 23% to 100% among hospitals (median 45%; interquartile range: 39% to 52%), and were consistent from year to year and when alternative definitions of coronary stenosis were applied. Sites with lower rates of finding obstructive CAD were more likely to perform procedures on younger patients, those with low Framingham risk (33% in lowest yield quartile vs. 21% in highest yield quartile, $p < 0.0001$); with no or atypical symptoms (73% vs. 58%, $p < 0.0001$); and with a negative, equivocal, or unperformed functional status assessment. Hospitals with lower rates of finding obstructive CAD also less frequently prescribed aspirin, beta-blockers, platelet inhibitors, and statins (all $p < 0.0001$). The CAD rate was lower at facilities with small-volume catheterization laboratories and was not associated with hospital ownership or teaching program status.

Conclusions The rate of finding obstructive CAD at elective coronary angiography varied considerably among reporting centers and was associated with patient selection and pre-procedure assessment strategies. This institutional variation suggests that an important opportunity may exist for quality improvement (317).

The Effect of Age on Clinical Outcomes and Health Status: BARI 2D (Bypass Angioplasty Revascularization Investigation in Type 2 Diabetes)

Objectives The purpose of this study was to determine the extent to which effectiveness of cardiac and diabetes treatment strategies varies by patient age.

Background The impact of age on the effectiveness of revascularization and hyperglycemia treatments has not been thoroughly investigated.

Methods In the BARI 2D (Bypass Angioplasty Revascularization Investigation in Type 2 Diabetes) trial, 2,368 patients with documented stable heart disease and type 2 diabetes were randomized to receive prompt revascularization versus initial medical therapy with deferred revascularization and insulin sensitization versus insulin provision for hyperglycemia treatment. Patients were followed for an average of 5.3 years. Cox regression and mixed models were used to investigate the effect of age and randomized treatment assignment on clinical and health status outcomes.

Results The effect of prompt revascularization versus medical therapy did not differ by age for death (interaction $p = 0.99$), major cardiovascular events (interaction $p = 0.081$), angina (interaction $p = 0.98$), or health status outcomes. After intervention, participants of all ages had significant angina and health status improvement. Younger participants experienced a smaller decline in health status during follow-up than older participants (age by time interaction $p < 0.01$). The effect of the randomized glycemia treatment on clinical and health status outcomes was similar for patients of different ages.

Conclusions Among patients with stable heart disease and type 2 diabetes, the relative beneficial effects of a strategy of prompt revascularization versus initial medical therapy and insulin-sensitizing versus insulin-providing therapy on clinical endpoints, symptom relief, and perceived health status outcomes do not vary by age. Health status improved significantly after treatment for all ages, and this improvement was sustained longer among younger patients. (Bypass Angioplasty Revascularization Investigation in Type 2 Diabetes [BARI 2D]; NCT00006305) (318).

Prognostic Impact of Staged Versus "One-Time" Multivessel Percutaneous Intervention in Acute Myocardial Infarction: Analysis From the HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) Trial

Objectives The purpose of this study was to compare a one-time primary percutaneous coronary intervention (PCI) of the culprit and nonculprit lesions with PCI of only the culprit lesion and staged nonculprit PCI at a later date in patients with ST-segment elevation myocardial infarction (STEMI) and multivessel disease.

Background In patients with STEMI and multivessel disease, it is unknown whether it is safe or even desirable to also treat the nonculprit vessel during the primary PCI procedure.

Methods In the HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trial, 668 of the 3,602 STEMI patients enrolled (18.5%) underwent PCI of culprit and nonculprit lesions for multivessel disease. Patients were categorized into a single PCI strategy ($n = 275$) versus staged PCI ($n = 393$). The endpoints analyzed included the 1-year rates of major adverse cardiovascular events and its components, death, reinfarction, target-vessel revascularization for ischemia, and stroke.

Results Single versus staged PCI was associated with higher 1-year mortality (9.2% vs. 2.3%; hazard ratio [HR]: 4.1, 95% confidence interval [CI]: 1.93 to 8.86, $p < 0.0001$), cardiac mortality (6.2% vs. 2.0%; HR: 3.14, 95% CI: 1.35 to 7.27, $p = 0.005$), definite/probable stent thrombosis (5.7% vs. 2.3%; HR: 2.49, 95% CI: 1.09 to 5.70, $p = 0.02$), and a trend toward greater major adverse cardiovascular events (18.1% vs. 13.4%; HR: 1.42, 95% CI: 0.96 to 2.1, $p = 0.08$). The mortality advantage favoring staged PCI was maintained in a subgroup of patients undergoing truly elective multivessel PCI. Also, the staged PCI strategy was independently associated with lower all-cause mortality at 30 days and at 1 year.

Conclusions A deferred angioplasty strategy of nonculprit lesions should remain the standard approach in patients with STEMI undergoing primary PCI, as multivessel PCI may be associated with a greater hazard for mortality and stent thrombosis. (Harmonizing Outcomes With

Revascularization and Stents in Acute Myocardial Infarction [HORIZONS-AMI]; NCT00433966) (319).

Culprit Vessel Only Versus Multivessel and Staged Percutaneous Coronary Intervention for Multivessel Disease in Patients Presenting With ST-Segment Elevation Myocardial Infarction: A Pairwise and Network Meta-Analysis

Objectives The purposes of this study were to investigate whether, in patients with ST-segment elevation myocardial infarction (STEMI) and multivessel disease (MVD), percutaneous coronary intervention (PCI) should be confined to the culprit or also nonculprit vessels and, when performing PCI for nonculprit vessels, whether it should take place during primary PCI or staged procedures.
Background A significant percentage of STEMI patients have MVD. However, the best PCI strategy for nonculprit vessel lesions is unknown.
Methods Pairwise and network meta-analyses were performed on 3 PCI strategies for MVD in STEMI patients: 1) culprit vessel only PCI strategy (culprit PCI), defined as PCI confined to culprit vessel lesions only; 2) multivessel PCI strategy (MV-PCI), defined as PCI of culprit vessel as well as $\geq$1 nonculprit vessel lesions; and 3) staged PCI strategy (staged PCI), defined as PCI confined to culprit vessel, after which $\geq$1 nonculprit vessel lesions are treated during staged procedures. Prospective and retrospective studies were included when research subjects were patients with STEMI and MVD undergoing PCI. The primary endpoint was short-term mortality.
Results Four prospective and 14 retrospective studies involving 40,280 patients were included. Pairwise meta-analyses demonstrated that staged PCI was associated with lower short- and long-term mortality as compared with culprit PCI and MV-PCI and that MV-PCI was associated with highest mortality rates at both short- and long-term follow-up. In network analyses, staged PCI was also consistently associated with lower mortality.
Conclusions This meta-analysis supports current guidelines discouraging performance of multivessel primary PCI for STEMI. When significant nonculprit vessel lesions are suitable for PCI, they should only be treated during staged procedures (320).

Aspirin Extrusion From Human Platelets Through Multidrug Resistance Protein-4–Mediated Transport: Evidence of a Reduced Drug Action in Patients After Coronary Artery Bypass Grafting

Objectives In this study we investigate: 1) the role of multidrug resistance protein-4 (MRP4), an organic anion unidirectional transporter, in modulating aspirin action on human platelet cyclooxygenase (COX)-1; and 2) whether the impairment of aspirin–COX-1 interaction, found in coronary artery bypass grafting (CABG) patients, could be dependent on MRP4-mediated transport.
Background Platelets of CABG patients present a reduced sensitivity to aspirin despite in vivo and in vitro drug treatment. Aspirin is an organic anion and could be a substrate for MRP4.
Methods Intracellular aspirin concentration and drug COX-1 activity, measured by thrombin-induced thromboxane B2 (TxB2) production, were evaluated in platelets obtained from healthy volunteers (HV) and hematopoietic-progenitor cell cultures reducing or not reducing MRP4-mediated transport. Platelet MRP4 expression was evaluated, in platelets from HV and CABG patients, by dot-blot or by immunogold-electromicrographs or immunofluorescence-microscopy analysis.
Results Inhibition of MRP4-mediated transport by dipyridamole or Mk-571 increases aspirin entrapment and its in vitro effect on COX-1 activity (142.7 $\pm$ 34.6 pg/10^8 cells vs. 343.7 $\pm$ 169.3 pg/10^8 cells TxB2-production). Platelets derived from megakaryocytes transfected with MRP4 small interfering ribonucleic acid have a higher aspirin entrapment and drug COX-1 activity. Platelets from CABG patients showed a high expression of MRP4 whose in vitro inhibition enhanced aspirin effect on COX-1 (349 $\pm$ 141 pg/10^8 cells vs. 1,670 $\pm$ 646 pg/10^8 cells TxB2-production).
Conclusions Aspirin is a substrate for MRP4 and can be extruded from platelet through its transportation. Aspirin effect on COX-1 is little-related to MRP4-mediated aspirin transport in HV, but in CABG patients with MRP4 overexpression, its pharmacological inhibition enhances aspirin action in an efficient way (321).

Incidence of Asymptomatic Intracranial Embolic Events After Pulmonary Vein Isolation: Comparison of Different Atrial Fibrillation Ablation Technologies in a Multicenter Study

Objectives We compared the safety of different devices by screening for subclinical intracranial embolic events after pulmonary vein isolation with either conventional irrigated radiofrequency (RF) or cryoballoon or multielectrode phased RF pulmonary vein ablation catheter (PVAC).
Background New devices specifically designed to facilitate pulmonary vein isolation procedures have recently been introduced.
Methods This prospective, observational, multicenter study included patients with symptomatic atrial fibrillation referred for pulmonary vein isolation. Ablation was performed using 1 of the 3 catheters. Strict periprocedural anticoagulation, with intravenous heparin during ablation to achieve an activated clotting time >300 s, was ensured in all patients. Cerebral magnetic resonance imaging was performed before and after ablation.
Results Seventy-four patients were included in the study: 27 in the irrigated RF group, 23 in the cryoballoon group, and 24 in the PVAC group. Total procedure times were 198 $\pm$ 50 min, 174 $\pm$ 35 min, and 124 $\pm$ 32 min, respectively ($p < 0.001$ for PVAC vs. irrigated RF and cryoballoon).

Findings on neurological examination were normal in all patients before and after ablation. Post-procedure magnetic resonance imaging detected a single new embolic lesion in 2 of 27 patients in the irrigated RF group (7.4%) and in 1 of 23 in the cryoballoon group (4.3%). However, in the PVAC group 9 of 24 patients (37.5%) demonstrated 2.7 ± 1.3 new lesions each ($p = 0.003$ for the presence of new embolic events among the 3 groups).

Conclusions The PVAC is associated with a significantly higher incidence of subclinical intracranial embolic events. Further study of the causes and significance of these emboli is required to determine the safety of the PVAC (322).

Transapical Transcatheter Aortic Valve Implantation in the Presence of a Mitral Prosthesis

Objectives We review our experience with transapical transcatheter aortic valve implantation (AVI) in patients with functioning mitral prostheses, and describe the technical considerations.

Background Transcatheter AVI for aortic stenosis in patients with mitral prostheses is technically challenging.

Methods Ten patients (7 mechanical and 3 bioprosthetic mitral valves) received the Edwards SAPIEN balloon-expandable valve (Edwards Lifesciences, Irvine, California) during 2006 to 2010. All patients were declined conventional surgery and prospectively followed. The mean patient age was 77.6 ± 7.1 years (range: 67 to 88 years). The logistic EuroSCORE and the Society of Thoracic Surgeons–predicted operative mortality were 30.3 ± 18.6% (range: 11.4% to 70.4%), and 9.9 ± 4.8% (range: 4.6% to 18.7%), respectively.

Results All valves were successfully implanted, with no 30-day mortality or mitral prosthetic dysfunction. Nine patients had none to mild residual aortic paravalvular leak. The overall survival was 60% at a mean follow-up of 12.2 ± 10.4 months (range: 2 to 33 months), with 4 nonvalve-related deaths. Seven patients improved to New York Heart Association functional class I to II. The mean transvalvular gradient and effective orifice area improved from 40.0 ± 17.4 mm Hg to 8.2 ± 2.1 mm Hg, and 0.6 ± 0.1 cm^2 to 1.3 ± 0.2 cm^2, respectively ($p < 0.0001$). The mitral bioprosthetic strut predisposes to device "shift" during deployment. An "unfavorable" mechanical mitral prosthetic cage or pivot strut can also cause shifts. Balloon shifts during valvuloplasty warn of a high likelihood of prosthesis shift.

Conclusions This report details the technical lessons learned thus far from our first 10 patients. Excellent procedural success and early outcomes in patients with functioning mitral prosthesis can be achieved (323).

A Multicenter, Randomized Trial Comparing Heparin/Warfarin and Acetylsalicylic Acid as Primary Thromboprophylaxis for 2 Years After the Fontan Procedure in Children

Objectives The purpose of this study was to compare the safety and efficacy of acetylsalicylic acid (ASA) and warfarin for thromboprophylaxis after the Fontan procedure.

Background Fontan surgery is the definitive palliation for children with single-ventricle physiology. Thrombosis is an important complication; the optimal thromboprophylaxis strategy has not been determined.

Methods We performed a multicenter international randomized trial of primary prophylactic anticoagulation after Fontan surgery. Patients were randomized to receive for 2 years either ASA (5 mg/kg/day, no heparin phase) or warfarin (started within 24 h of heparin lead-in; target international normalized ratio: 2.0 to 3.0). Primary endpoint (intention to treat) was thrombosis, intracardiac or embolic (all events adjudicated). At 3 months and 2 years after the Fontan procedure, transthoracic and transesophageal echocardiograms were obtained as routine surveillance. Major bleeding and death were primary adverse outcomes.

Results A total of 111 eligible patients were randomized (57 to ASA, 54 to heparin/warfarin). Baseline characteristics for each group were similar. There were 2 deaths unrelated to thrombosis or bleeding. There were 13 thromboses in the heparin/warfarin group (3 clinical, 10 routine echo) and 12 thromboses in the ASA group (4 clinical, 8 routine echo). Overall freedom from thrombosis 2 years after Fontan surgery was 19%, despite thrombosis prophylaxis. Cumulative risk of thrombosis was persistent but varying and similar for both groups ($p = 0.45$). Major bleeding occurred in 1 patient in each group.

Conclusions There was no significant difference between ASA and heparin/warfarin as primary thromboprophylaxis in the first 2 years after Fontan surgery. The thrombosis rate was suboptimal for both regimens, suggesting alternative approaches should be considered. (International Multi Centre Randomized Clinical Trial Of Anticoagulation In Children Following Fontan Procedures; NCT00182104) (324).

Radiofrequency Ablation of Atrial Fibrillation in Patients With Mechanical Mitral Valve Prostheses: Safety, Feasibility, Electrophysiologic Findings, and Outcomes

Objectives The purpose of this study was to evaluate the feasibility, safety, and outcomes of radiofrequency ablation of atrial fibrillation (AF) in patients with mechanical mitral valve replacement (MVR).

Background The role of ablative therapy in patients with MVR is not yet established, with safety concerns and very few outcome data.

Methods Between January 2003 and December 2008, we followed up 81 patients with MVR undergoing first-time AF ablation (compared with 162 age- and sex-matched controls). Arrhythmia recurrences were identified by symptoms with documentation, event monitoring, Holter monitoring, and electrocardiograms.

Results All MVR and control patients underwent ablation under therapeutic international normalized ratio. No entrapment of catheters or stroke occurred. There were no differences in terms of procedure-related complications between the groups (p = NS). Patients with MVR had larger atria (p < 0.0001), lower left ventricular ejection fractions (p = 0.0001), and more concomitant atrial flutter at baseline (p < 0.0001). Over a 24-month follow-up, they had higher recurrence rates compared with controls (49.4% vs. 27.7% after a single ablation, p = 0.0006). The creation of flutter lines significantly reduced recurrences in patients with any history of atrial flutter (16.7% vs. 60.9%, p = 0.009). At last follow-up, 82.7% of MVR patients had their arrhythmia controlled (69.1% not receiving antiarrhythmic drugs).
Conclusions Radiofrequency ablation is feasible and safe for patients with MVR. It allowed restoration of sinus rhythm in a substantial proportion of patients undergoing ablation. An abnormal atrial substrate underlies recurrences in these patients. The ablation procedure needs to be further refined with a focus on extra pulmonary vein triggers and concomitant flutters to improve outcomes (325).

Association Between IVUS Findings and Adverse Outcomes in Patients With Coronary Artery Disease: The VIVA (VH-IVUS in Vulnerable Atherosclerosis) Study

Objectives The purpose of this study was to determine whether thin-capped fibroatheromata (TCFA) identified by virtual histology intravascular ultrasound (VH-IVUS) are associated with major adverse cardiac events (MACE) on individual plaque or whole patient analysis.
Background Post-mortem studies have identified TCFA as the substrate for most myocardial infarctions. However, little is known about the natural history of individual TCFA and their link with MACE. VH-IVUS provides a method of identifying plaques in vivo that are similar (although not identical) to histologically defined TCFA, and has been validated in human atherectomy and post-mortem studies.
Methods One hundred seventy patients with stable angina or troponin-positive acute coronary syndrome referred for percutaneous coronary intervention (PCI) were prospectively enrolled and underwent 3-vessel VH-IVUS pre-PCI and also post-PCI in the culprit vessel. MACE consisted of death, myocardial infarction, or unplanned revascularization.
Results In all, 30,372 mm of VH-IVUS were analyzed. Eighteen MACE occurred in 16 patients over a median follow-up of 625 days (interquartile range: 463 to 990 days); 1,096 plaques were classified, and 19 lesions resulted in MACE (13 nonculprit lesions and 6 culprit lesions). Nonculprit lesion factors associated with nonrestenotic MACE included VHTCFA (hazard ratio [HR]: 7.53, p = 0.038) and plaque burden >70% (HR: 8.13, p = 0.011). VHTCFA (HR: 8.16, p = 0.007), plaque burden >70% (HR: 7.48, p < 0.001), and minimum luminal area <4 mm^2 (HR: 2.91, p = 0.036) were associated with total MACE. On patient-based analysis, the only factor associated with nonrestenotic MACE was 3-vessel noncalcified VHTCFA (HR: 1.79, p = 0.004).
Conclusions VH-IVUS TCFA was associated with nonrestenotic and total MACE on individual plaque analysis, and noncalcified VHTCFA was associated with nonrestenotic and total MACE on whole-patient analysis, demonstrating that VH-IVUS can identify plaques at increased risk of subsequent events. The preservation of the association between VHTCFA and MACE despite various analyses emphasizes its biological importance (326).

The Pre-Hospital Fibrinolysis Experience in Europe and North America and Implications for Wider Dissemination

Objectives The primary objective of this report was to describe the infrastructures and processes of selected European and North American pre-hospital fibrinolysis (PHL) programs. A secondary objective is to report the outcome data of the PHL programs surveyed.
Background Despite its benefit in reducing mortality in patients with ST-segment elevation myocardial infarction, PHL remained underused in North America. Examination of existing programs may provide insights to help address barriers to the implementation of PHL.
Methods The leading investigators of PHL research projects/national registries were invited to respond to a survey on the organization and outcomes of their affiliated PHL programs.
Results PHL was successfully deployed in a wide range of geographic territories (Europe: France, Sweden, Vienna, England, and Wales; North America: Houston, Edmonton, and Nova Scotia) and was delivered by healthcare professionals of varying expertise. In-hospital major adverse outcomes were rare with mortality of 3% to 6%, reinfarction of 2% to 5%, and stroke of <2%.
Conclusions Combining formal protocols for PHL for some patients with direct transportation of others to a percutaneous coronary intervention hospital for primary percutaneous coronary intervention would allow for tailored reperfusion therapy for patients with ST-segment elevation myocardial infarction. Insights from a variety of international settings may promote widespread use of PHL and increase timely coronary reperfusion worldwide (327).

Saphenous Vein Graft Intervention

Saphenous vein grafts are commonly used conduits for surgical revascularization of coronary arteries but are associated with poor long-term patency rates. Percutaneous revascularization of saphenous vein grafts is associated with worse clinical outcomes including higher rates of in-stent restenosis, target vessel revascularization, myocardial infarction, and death compared with percutaneous coronary

intervention of native coronary arteries. Use of embolic protection devices is a Class I indication according to the American College of Cardiology/American Heart Association guidelines to decrease the risk of distal embolization, no-reflow, and periprocedural myocardial infarction. Nonetheless, these devices are underused in clinical practice. Various pharmacological agents are available that may also reduce the risk of or mitigate the consequences of no-reflow. Covered stents do not decrease the rates of periprocedural myocardial infarction and restenosis. Most available evidence supports treatment with drug-eluting stents in this high-risk lesion subset to reduce angiographic and clinical restenosis, although large, randomized trials comparing drug-eluting stents and bare-metal stents are needed (328).

Impact of Pentoxify: Iline on Platelet Function Profiles in Patients With Type 2 Diabetes Mellitus and Coronary Artery Disease on Dual Antiplatelet Therapy With Aspirin and Clopidogrel

Objectives The aim of this study was to evaluate the impact of the phosphodiesterase (PDE) inhibitor pentoxifylline on platelet function profiles in patients receiving dual antiplatelet therapy (DAPT).

Background Previous studies have shown that, in patients receiving DAPT, the adjunctive use of a PDE inhibitor enhances platelet inhibition, particularly in those presenting with diabetes mellitus (DM). However, the pharmacodynamic (PD) effects of the PDE inhibitor pentoxifylline on platelet function profiles in DM patients receiving DAPT are unknown.

Methods This was a prospective, randomized, double-blind, parallel design study conducted in DM patients with stable coronary artery disease receiving DAPT. Patients were randomly assigned to either pentoxifylline 400 mg or placebo 3 times daily for 14 days. The PD effects were assessed by vasodilator-stimulated phosphoprotein phosphorylation assay, light transmittance aggregometry, VerifyNow P2Y12 assay (Accumetric, Inc., San Diego, California), and multiple electrode aggregometry at baseline and 14 days. The PD effects were also assessed according the presence or absence of high on-treatment platelet reactivity status.

Results A total of 40 patients were available for analysis. At 14 days, there were no differences in the $P2Y_{12}$ reactivity index as assessed by vasodilator-stimulated phosphoprotein phosphorylation between treatment groups (primary endpoint; $p = 0.93$). Intra-group comparisons also failed to show any differences between baseline and 14-day $P2Y_{12}$ reactivity index assessment in the placebo and pentoxifylline arms ($p = 0.61$). There were no significant inter- and intra-group differences in all other PD measures. The PD effects did not vary according the presence or absence of high on-treatment platelet reactivity.

Conclusions Adjunctive treatment with pentoxifylline is not associated with increased platelet inhibitory effects in DM patients with coronary artery disease receiving DAPT (329).

Clinical Experience With Percutaneous Left Ventricular Transapical Access for Interventions in Structural Heart Defects: A Safe Access and Secure Exit

Objectives This study sought to evaluate the safety of percutaneous direct left ventricular access for interventional procedures.

Background Experience with percutaneous access of the left ventricle (LV) for interventional procedures has been limited and associated with a high percentage of major complications. We report our clinical experience with percutaneous direct LV access for interventional procedures.

Methods Between March 2008 and December 2010, there were 32 percutaneous transapical punctures in 28 consecutive patients (16 males, mean age 68.2 ± 10.8 years). The delivery sheath sizes ranged from 5- to 12-F.

Results All transapical punctures were successfully performed, and safe closure of the access sites was achieved. Total procedural time was 153.6 ± 49.4 min for procedures converted from conventional approaches to a transapical approach, 129.5 ± 29.6 min for the transapical approach with trans-septal rail support, and 109.3 ± 41.4 min for the planned transapical approach. Fluoroscopy time was 61.3 ± 26.1 min, 29.7 ± 20.8 min, and 27.4 ± 21.4 min, respectively. Fluoroscopy time for closure of mitral paravalvular leaks was reduced by 35%, from 42.6 ± 29.9 min to 27.4 ± 15.6 min. Complications were observed in 2 patients (7.1%).

Conclusions With meticulous planning, transapical puncture is safe. The transapical access provides a more direct approach to the LV targets for intervention and leads to a significant decrease in the procedural and fluoroscopy times. Device closure of the direct LV access site is a reliable and safe method of hemostasis. Placement of a closure device should be considered if sheaths larger than 5-F are used. Although we used this technique only for paravalvular leak and LV pseudoaneurysm closure, it may have application for other percutaneous structural heart interventions (330).

Clinical Outcomes Using a New Crossover Balloon Occlusion Technique for Percutaneous Closure After Transfemoral Aortic Valve Implantation

Objectives This study sought to evaluate the technical success and clinical outcomes of an adjunctive crossover balloon occlusion technique (CBOT) combined with the 10-F Prostar percutaneous closure device (PCD) on the incidence of vascular and bleeding complications in patients after transfemoral transcatheter aortic valve implantation (TAVI).

Background Vascular closure following large-vessel access has most commonly been performed using a surgical cut-down and repair procedure.

Methods Between November 2008 and September 2010, 58 consecutive patients with severe aortic stenosis underwent TAVI via a retrograde femoral artery approach using the Edwards-SAPIEN transcatheter valve. Among these patients, 56 were treated with a CBOT using the "pre-close" technique and the 10-F Prostar system. The technical success of this new CBOT and the 30-day frequency of clinical events, including all-cause mortality, major vascular complications, and major bleeding (defined according to a modified version of the Valve Academic Research Consortium criteria), were assessed.
Results Successful closure was obtained in all but 3 patients (94.6%). The 30-day frequencies of mortality, major vascular complications, and major bleeding were 7.1%, 14.3%, and 5.4% respectively. No deaths were directly related to access site complications. Fourteen patients (25%) received at least 1 transfusion during the index hospitalization, of which 8 (57.1%) were not related to vascular complications. The mean and median hospital lengths of stay were 7.8 and 6.0 days.
Conclusions This new percutaneous adjunctive CBOT combined with the Prostar PCD resulted in controlled, safe, and successful percutaneous closure in most patients after TAVI (331).

New Insights Into the Coronary Artery Bifurcation: Hypothesis-Generating Concepts Utilizing 3-Dimensional Optical Frequency Domain Imaging

Coronary artery bifurcations are a common challenging lesion subset accounting for approximately 10% to 20% of all percutaneous coronary interventions. The provisional T-stenting approach is generally recommended as the first-line management of most lesions. Carina shift is suggested to be the predominant mechanism of side-branch pinching during provisional T-stenting and has been indirectly inferred from bench work and other intravascular imaging modalities. Offline 3-dimensional (3D) reconstructions of patients studied in the first-in-man trial of the high-frequency (160 frames/s) Terumo optical frequency domain imaging system were undertaken using volume-rendering software. Through a series of 3D reconstructions, several novel hypothesis-generating concepts are presented (332).

2-Year Clinical Follow-Up From the Randomized Comparison of Biolimus-Eluting Stents With Biodegradable Polymer and Sirolimus-Eluting Stents With Durable Polymer in Routine Clinical Practice

Objectives This study sought to investigate safety and efficacy of biolimus-eluting stents (BES) with biodegradable polymer as compared with sirolimus-eluting stents (SES) with durable polymer through 2 years of follow-up.
Background BES with a biodegradable polymer provide similar efficacy and safety as SES with a durable polymer at 9 months. Clinical outcomes beyond the period of biodegradation of the polymer used for drug release and after discontinuation of dual antiplatelet therapy are of particular interest.
Methods A total of 1,707 patients were randomized to unrestricted use of BES (n = 857) or SES (n = 850) in an all-comers patient population.
Results At 2 years, BES remained noninferior compared with SES for the primary endpoint, which was a composite of cardiac death, myocardial infarction, or clinically indicated target vessel revascularization (BES 12.8% vs. SES 15.2%, hazard ratio [HR]: 0.84, 95% confidence interval [CI]: 0.65 to 1.08, $p_{noninferiority} < 0.0001$, $p_{superiority} = 0.18$). Rates of cardiac death (3.2% vs. 3.9%, HR: 0.81, 95% CI: 0.49 to 1.35, p = 0.42), myocardial infarction (6.3% vs. 5.6%, HR: 1.12, 95% CI: 0.76 to 1.65, p = 0.56), and clinically indicated target vessel revascularization (7.5% vs. 8.6%, HR: 0.86, 95% CI: 0.62 to 1.20, p = 0.38) were similar for BES and SES. The rate of definite stent thrombosis through 2 years was 2.2% for BES and 2.5% for SES (p = 0.73). For the period between 1 and 2 years, event rates for definite stent thrombosis were 0.2% for BES and 0.5% for SES (p = 0.42). After discontinuation of dual antiplatelet therapy, no very late definite stent thrombosis occurred in the BES group.
Conclusions At 2 years of follow-up, the unrestricted use of BES with a biodegradable polymer maintained a similar safety and efficacy profile as SES with a durable polymer. (Limus Eluted From a Durable Versus Erodable Stent Coating [LEADERS]; NCT00389220) (333).

Percutaneous Coronary Intervention in Native Arteries Versus Bypass Grafts in Prior Coronary Artery Bypass Grafting Patients: A Report From the National Cardiovascular Data Registry

Objectives This study examined a large registry to determine the frequency, predictors, and outcomes of native coronary artery versus bypass graft percutaneous coronary intervention (PCI) in patients with prior coronary artery bypass graft surgery (CABG).
Background The PCI target vessel and corresponding outcomes in prior CABG patients are poorly studied.
Methods We analyzed the frequency and factors associated with native versus bypass graft PCI in prior CABG patients undergoing PCI between January 1, 2004, and June 30, 2009, in the National Cardiovascular Data Registry (NCDR) CathPCI Registry. Generalized estimating equations logistic regression modeling was used to generate independent variables associated with native versus bypass graft PCI and in-hospital mortality.
Results During the study period, PCI in prior CABG patients represented 17.5% of the total PCI volume (300,902 of 1,721,046). The PCI target was a native coronary artery in 62.5% and a bypass graft in 37.5%: saphenous vein graft (SVG) (104,678 [34.9%]), arterial graft (7,517

[2.5%]), or both arterial graft and SVG (718 [0.2%]). Compared with patients undergoing native coronary artery PCI, those undergoing bypass graft PCI had higher-risk characteristics and more procedural complications. On multivariable analysis, several parameters (including graft stenosis and longer interval from CABG) were associated with performing native coronary PCI, and bypass graft PCI was associated with higher in-hospital mortality (adjusted odds ratio: 1.22, 95% confidence interval: 1.12 to 1.32).

Conclusions Most PCIs performed in prior CABG patients are done in native coronary artery lesions. Compared with native coronary PCI, bypass graft PCI is independently associated with higher in-hospital mortality (334).

Recovery of Microcirculation After Intracoronary Infusion of Bone Marrow Mononuclear Cells or Peripheral Blood Mononuclear Cells in Patients Treated by Primary Percutaneous Coronary Intervention: The Doppler Substudy of the Hebe Trial

Objectives In the present substudy of the Hebe trial, we investigated the effect of intracoronary bone marrow mononuclear cell (BMMC) and peripheral blood mononuclear cell (PBMC) therapy on the recovery of microcirculation in patients with reperfused ST-segment elevation myocardial infarction (STEMI).

Background Several studies have suggested that cell therapy enhances neovascularization after STEMI.

Methods Paired Doppler flow measurements were available for 23 patients in the BMMC group, 18 in the PBMC group, and 19 in the control group. Coronary flow was assessed at 3 to 8 days after primary percutaneous coronary intervention (PCI) and repeated at 4-month follow-up, with intracoronary Doppler flow measurements.

Results At baseline, the coronary flow velocity reserve was reduced in the infarct-related artery and improved over 4 months in all 3 groups. The increase of coronary flow velocity reserve did not significantly differ between the 2 treatment groups and the control group (BMMC group: 2.0 ± 0.5 to 3.1 ± 0.7; PBMC group: 2.2 ± 0.6 to 3.2 ± 0.8; control group: 2.0 ± 0.5 to 3.4 ± 0.9). Additionally, the decrease in hyperemic microvascular resistance index from baseline to 4-month follow-up was not statistically different between the 2 treatment groups and the control group.

Conclusions In STEMI patients treated with primary PCI in the Hebe trial, adjuvant therapy with BMMCs or PBMCs does not improve the recovery of microcirculation. Therefore, our data do not support the hypothesis of enhanced neovascularization after this mode of cell therapy. (Multicenter, randomised trial of intracoronary infusion of autologous mononuclear bone marrow cells or peripheral mononuclear blood cells after primary percutaneous coronary intervention [PCI]; ISRCTN95796863) (335).

1-Year Outcome of TRIAS HR (TRI-Stent Adjudication Study–High Risk of Restenosis): A Multicenter, Randomized Trial Comparing Genous Endothelial Progenitor Cell Capturing Stents With Drug-Eluting Stents

Objectives This study sought to demonstrate the noninferiority of endothelial progenitor cell capturing stents (ECS) relative to drug-eluting stents (DES) regarding target lesion failure (TLF) and the composite of cardiac death, myocardial infarction, and target lesion repeat revascularization within 1 year.

Background A "pro-healing" approach for prevention of in-stent restenosis is theoretically favorable over the use of cytotoxic/cytostatic drugs released from DES to treat coronary artery disease. Promoting accelerated endothelialization of the stent, ECS have shown promising results in studies with patients carrying noncomplex lesions.

Methods We undertook an international, clinical trial in 26 centers planning to randomize 1,300 patients with stable coronary artery disease and with a high risk of restenosis between treatment, with either ECS or DES. After a routine review with 50% of the patients enrolled, early cessation of the trial was recommended by the data and safety monitoring board when TLF in the ECS population was higher and treatment of new patients with an ECS would be unreasonable.

Results At 1 year evaluating 304 patients receiving ECS and 318 receiving DES, TLF occurred in 17.4% of the ECS-treated patients and in 7.0% of the DES-treated patients ($p = 0.98$ for noninferiority).

Conclusions Within 1 year, inhibition of intimal hyperplasia by the ECS is not sufficiently strong to compete with DES in terms of restenosis prevention in patients/lesions with a high risk of restenosis. Furthermore, long-term follow-up is pivotal to fully appreciate the clinical value of ECS, including the effect on late intimal hyperplasia regression (336).

Prognostic Implications of Nonobstructive Coronary Plaques in Patients With Non–ST-Segment Elevation Myocardial Infarction: A Multidetector Computed Tomography Study

Objectives We sought to determine whether the amount of noncalcified plaque (NCP) in nonobstructive coronary lesions as detected by multidetector computed tomography (MDCT) was a predictor of future coronary events.

Background Patients presenting with non–ST-segment elevation myocardial infarction (NSTEMI) frequently have multiple coronary plaques, which may be detected with MDCT.

Methods We included 312 consecutive patients presenting with NSTEMI, who underwent 64-slice MDCT coronary angiography and coronary artery calcium scoring before invasive coronary angiography. All patients were treated according to current guidelines based on an invasive

treatment approach. Quantitative measurements of plaque composition and volume were performed by MDCT in all nonobstructive coronary lesions. The endpoint was cardiac death, acute coronary syndrome, or symptom-driven revascularization.

Results After a median follow-up of 16 months, 23 patients had suffered a cardiac event. Age, male sex, and diabetes mellitus were all associated with an increasing amount of NCP. In a multivariate regression analysis for events, the total amount of NCP in nonobstructive lesions was independently associated with an increased hazard ratio (1.18/100-mm^3 plaque volume increase, $p = 0.01$). Contrary to this, neither Agatston score nor the amount of calcium in nonobstructive lesions was associated with an increased risk.

Conclusions Multidetector computed tomography plaque imaging identified patients at increased risk of recurrent coronary events after NSTEMI by measuring the total amount of NCP in nonobstructive lesions. The amount of calcified plaque was not associated with an increased risk (337).

High On-Treatment Platelet Reactivity After Prasugrel Loading Dose and Cardiovascular Events After Percutaneous Coronary Intervention in Acute Coronary Syndromes

Objectives The aim of this study was to investigate the relationship between platelet reactivity (PR) after a loading dose (LD) of prasugrel and thrombotic events.

Background Post-treatment PR has been shown to be strongly associated with the occurrence of major adverse cardiac events (MACE) after percutaneous coronary intervention (PCI) in the clopidogrel era. Prasugrel is a new $P2Y_{12}$–adenosine diphosphate receptor with a higher potency on PR.

Methods A prospective multicenter study included patients who underwent successful PCI for acute coronary syndromes and received prasugrel therapy. Vasodilator-stimulated phosphoprotein (VASP) index was measured after the prasugrel LD. High on-treatment PR was defined as a VASP index ≥50%. MACE included cardiovascular death, myocardial infarction, and definite stent thrombosis at 1 month.

Results Three hundred one patients were enrolled. The mean VASP index after 60 mg of prasugrel was 34.3 ± 23.1%. High on-treatment PR was observed in 76 patients (25.2%). Patients experiencing thrombotic events after PCI had significantly higher VASP indexes compared with those free of events (64.4 ± 14.4% vs. 33.4 ± 22.7%; range: 51% to 64% and 5% to 47.6%, respectively; $p = 0.001$). Kaplan-Meier analysis comparing good responders and patients with high on-treatment PR demonstrated a significantly higher rate of MACE in patients with suboptimal PR inhibition (log-rank $p < 0.001$). Receiver-operating characteristic curve analysis found a cutoff value of 53.5% of the VASP index to predict thrombotic events at 1 month ($r = 0.86$, $p < 0.001$). Patients with minor or major Thrombolysis In Myocardial Infarction unrelated to coronary artery bypass grafting bleeding and those without had similar VASP indexes (30 ± 17.8% vs. 34.3 ± 23%, $p = 0.70$).

Conclusions Despite the use of prasugrel, a significant number of patients undergoing PCI in the setting of acute coronary syndromes do not achieve optimal PR inhibition. Such patients have a higher risk for MACE after PCI (338).

Prospective Application of Pre-Defined Intravascular Ultrasound Criteria for Assessment of Intermediate Left Main Coronary Artery Lesions: Results From the Multicenter LITRO Study

Objectives This study is a prospective validation of 6 mm^2 as a minimum lumen area (MLA) cutoff value for revascularization of left main coronary artery (LMCA) lesions.

Background Lesions involving the LMCA are prognostically relevant. Angiography has important limitations in the evaluation of LMCA lesions with intermediate severity. An MLA of 6 mm^2 assessed by intravascular ultrasound has been proposed as a cutoff value to determine lesion severity, but there are no large studies evaluating the prospective application and safety of this approach.

Methods We have designed a multicenter, prospective study. Consecutive patients with intermediate lesions in unprotected LMCA were evaluated with intravascular ultrasound. An MLA <6 mm^2 was used as criterion for revascularization.

Results A total of 354 patients were included in 22 centers. LMCA revascularization was performed in 90.5% (152 of 168) of patients with an MLA <6 mm^2 and was deferred in 96% (179 of 186) of patients with an MLA of 6 mm^2 or more. A large scatter was observed between both groups regarding angiographic parameters. In a 2-year follow-up period, cardiac death-free survival was 97.7% in the deferred group versus 94.5% in the revascularized group ($p = 0.5$), and event-free survival was 87.3% versus 80.6%, respectively ($p = 0.3$). In the 2-year period, only 8 (4.4%) patients in the deferred group required subsequent LMCA revascularization, none with an infarction.

Conclusions Angiographic measurements are not reliable in the assessment of intermediate LMCA lesions. An MLA of 6 mm^2 or more is a safe value for deferring revascularization of the LMCA, given the application of the clinical and angiographic inclusion criteria used in this study (339).

A New Risk Scheme to Predict Warfarin-Associated Hemorrhage: The ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation) Study

Objectives The purpose of this study was to develop a risk stratification score to predict warfarin-associated hemorrhage.

Background Optimal decision making regarding warfarin use for atrial fibrillation requires estimation of hemorrhage risk.

Methods We followed up 9,186 patients with atrial fibrillation contributing 32,888 person-years of follow-up on warfarin, obtaining data from clinical databases and validating hemorrhage events using medical record review. We used Cox regression models to develop a hemorrhage risk stratification score, selecting candidate variables using bootstrapping approaches. The final model was internally validated by split-sample testing and compared with 6 published hemorrhage risk schemes.

Results We observed 461 first major hemorrhages during follow-up (1.4% annually). Five independent variables were included in the final model and weighted by regression coefficients: anemia (3 points), severe renal disease (e.g., glomerular filtration rate <30 ml/min or dialysis-dependent, 3 points), age ≥75 years (2 points), prior bleeding (1 point), and hypertension (1 point). Major hemorrhage rates ranged from 0.4% (0 points) to 17.3% per year (10 points). Collapsed into a 3-category risk score, major hemorrhage rates were 0.8% for low risk (0 to 3 points), 2.6% for intermediate risk (4 points), and 5.8% for high risk (5 to 10 points). The *c*-index for the continuous risk score was 0.74 and 0.69 for the 3-category score, higher than in the other risk schemes. There was net reclassification improvement versus all 6 comparators (from 27% to 56%).

Conclusions A simple 5-variable risk score was effective in quantifying the risk of warfarin-associated hemorrhage in a large community-based cohort of patients with atrial fibrillation (340).

6-Month Clinical Outcomes Following Implantation of the Bioresorbable Everolimus-Eluting Vascular Scaffold in Vessels Smaller or Larger Than 2.5 mm

Objectives We investigated the 6-month clinical outcomes after implantation of second-generation 3.0-mm bioresorbable everolimus-eluting vascular scaffolds (BVS) in small coronary vessels (<2.5 mm).

Background BVS are a novel approach to treating coronary lesions and are untested in small vessels.

Methods The ABSORB Cohort B Trial is a multicenter, single-arm, prospective, open-label trial assessing the performance of the second-generation BVS, in which 101 patients were enrolled. The pre-procedural reference vessel diameter (RVD) was assessed by quantitative coronary angiography during post hoc analysis. The vessel size was overestimated, by visual assessment, in 41 patients before implantation of 3.0-mm BVS in vessels with a pre-procedural RVD <2.5 mm. The study population was divided into 2 groups, group I (n = 41) with RVD <2.5 mm and group II (n = 60) with RVD ≥2.5 mm. The composite endpoint of ischemia-driven major adverse cardiac events, defined as ischemia-driven target lesion revascularization, myocardial infarction, or cardiac death, was assessed. Of the 45 patients scheduled for 6-month coronary angiography, 42 patients had the procedure performed, with intravascular ultrasound undertaken in 40 of these patients.

Results At 6 months, no significant differences in ischemia-driven major adverse cardiac events (3 of 41 [7.3%] cases vs. 2 of 60 [3.3%] cases; p = 0.3933) were observed in the small- and large-vessel groups, respectively. No cardiac deaths or episodes of in-scaffold thromboses were seen. Angiographic and intravascular ultrasound follow-up demonstrated no differences in late lumen loss (0.16 ± 0.18 mm vs. 0.21 ± 0.17 mm; p = 0.3525) or percentage lumen area stenosis (17.6 ± 6.0% vs. 19.8 ± 8.5%; p = 0.3643).

Conclusions The second-generation 3.0-mm BVS appears to be safe in small vessels, with similar clinical and angiographic outcomes compared with those of large vessels (341).

Epicardial Ablation of Rotors Suppresses Inducibility of Acetylcholine-Induced Atrial Fibrillation in Left Pulmonary Vein–Left Atrium Preparations in a Beagle Heart Failure Model

Objectives The purpose of this study was to provide direct evidences that rotor ablation suppresses atrial fibrillation (AF) inducibility.

Background Micro–re-entrant wavefronts have been suggested to serve as sources of rapid activations during AF. Whether AF inducibility is suppressed by elimination of rotors remains unknown.

Methods We used optical mapping to study Langendorff-perfused left pulmonary vein (PV)–left atrium (LA) preparations from 13 dogs with pacing-induced heart failure. Atrial arrhythmias were induced by pacing and mapped during acetylcholine infusion (1 μmol/l). Rotors were identified from optical recordings. Epicardial ablation was performed targeting the rotor anchoring sites in preparations with sustained (>10 min) or incessant spontaneous AF. Non-rotor ablation was performed in 4 preparations. Repeated pacing was performed to test the AF inducibility after ablation.

Results Sustained AF (n = 12) and incessant spontaneous AF (n = 1) were induced after acetylcholine infusion. Pulmonary vein focal discharge was found in 9 preparations (9.2 ± 4.2 beats/s), and rotor anchoring was found at the left superior PV-LA junction in 13 preparations (9.1 ± 4.6 beats/s) and at the ligament of Marshall-PV-LA junction in 1 preparation. Epicardial rotor ablation successfully inhibited the inducibility of sustained AF in 12 of 13 preparations (p < 0.01), including 4 with the maximal dominant frequency sites located on the PV-LA junctional rotor zones (direct elimination of mother rotors). The longest AF duration was shortened significantly by rotor ablation (Wilcoxon Z = 3.60, p = 0.002, n = 13), but not by non-rotor ablation (Wilcoxon Z = 1.00, p = 0.317, n = 4).

Conclusions Epicardial ablation of the rotor anchoring sites suppresses AF inducibility. The arrhythmogenicity at the maximal dominant frequency sites is directly/indirectly suppressed by the rotor ablation (342).

Impact of Metabolic Syndrome and Diabetes on Prognosis and Outcomes With Early Percutaneous Coronary Intervention in the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) Trial

Objectives Our purpose was to clarify the clinical utility of identifying metabolic syndrome (MetS) in patients with coronary artery disease (CAD).

Background It is uncertain whether MetS influences prognosis in patients with CAD and whether the risk associated with MetS exceeds the risk associated with the sum of its individual components.

Methods In a post hoc analysis, we compared the incidence of death or myocardial infarction (MI) in stable CAD patients in the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial according to the presence (+) or absence (−) of MetS and diabetes: Group A, −MetS/−diabetes; Group B, +MetS/−diabetes; Group C, −MetS/+diabetes; and Group D, +MetS/+diabetes. We explored which MetS components best predicted adverse outcomes and whether MetS had independent prognostic significance beyond its individual components.

Results Of 2,248 patients, 61% had MetS and 34% diabetes. Risk for death or MI increased from Group A (14%) to Group D (25%, $p < 0.001$). Hypertension (hazard ratio [HR]: 1.30; 95% confidence interval [CI]: 0.98 to 1.71; $p = 0.07$), low high-density lipoprotein cholesterol (HR: 1.26; 95% CI: 1.03 to 1.55; $p = 0.03$), and elevated glucose (HR: 1.17; 95% CI: 0.96 to 1.47; $p = 0.11$) most strongly predicted death or MI. MetS was associated with an increased risk of death or MI (unadjusted HR: 1.41; 95% CI: 1.15 to 1.73; $p = 0.001$). However, after adjusting for its individual components, MetS was no longer significantly associated with outcome (HR: 1.15; 95% CI: 0.79 to 1.68; $p = 0.46$). Allocation to initial percutaneous coronary intervention did not affect the incidence of death or MI within any group.

Conclusions Among stable CAD patients in the COURAGE trial, the presence of MetS identified increased risk for death or MI, but MetS did not have independent prognostic significance after adjusting for its constituent components. The addition of early percutaneous coronary intervention to optimal medical therapy did not significantly reduce the risk of death or MI regardless of MetS or diabetes status. (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation [COURAGE]; NCT00007657) (343).

Stroke Intervention: Catheter-Based Therapy for Acute Ischemic Stroke

The majority (>80%) of the three-quarters of a million strokes that will occur in the United States this year are ischemic in nature. The treatment of acute ischemic stroke is very similar to acute myocardial infarction, which requires timely reperfusion therapy for optimal results. The majority of patients with acute ischemic stroke do not receive any form of reperfusion therapy, unlike patients with acute myocardial infarction. Improving outcomes for acute stroke will require patient education to encourage early presentation, an aggressive expansion of qualified hospitals, and willing providers and early imaging strategies to match patients with their best options for reperfusion therapy to minimize complications (344).

The Impact of Right Coronary Artery Chronic Total Occlusion on Clinical Outcome of Patients Undergoing Percutaneous Coronary Intervention for Unprotected Left Main Disease

Objectives The aim of the present study was to investigate whether right coronary artery chronic total occlusion (CTO) carries prognostic implications in patients undergoing drug-eluting stent–supported percutaneous coronary intervention (PCI) for unprotected left main disease (ULMD).

Background No data exist on the prognostic implication of CTO in patients undergoing PCI for ULMD.

Methods Prospective registry of consecutive patients undergoing PCI for ULMD. Patients with ST-segment elevation myocardial infarction were excluded. Primary endpoints were 6-month and long-term cardiac mortality.

Results From January 2004 to December 2009, 330 patients underwent PCI for ULMD. Of the 330 patients, 78 (24%) had CTO of the right coronary artery, 22 (7%) had CTO of the left anterior descending artery, and 16 (5%) had CTO of the left circumflex artery. Patients with right coronary artery CTO had a higher risk profile compared with patients without right coronary artery CTO. The 6-month mortality rate was 12.8% in patients with right coronary artery CTO, and 3.6% in patients without right coronary artery CTO ($p < 0.002$), and the 3-year cardiac survival rate was $76.4 \pm 6.8\%$ and $89.7 \pm 2.7\%$ ($p < 0.003$), respectively. By multivariable analysis, the only 2 independent predictors of 3-year cardiac mortality were right coronary artery CTO (hazard ratio: 2.15, 95% confidence interval: 1.02 to 4.50; $p = 0.043$) and EuroSCORE (hazard ratio: 1.03, 95% confidence interval: 1.02 to 1.05; $p < 0.001$).

Conclusions Right coronary artery CTO occurs frequently and is a significant predictor of mortality in patients with ULMD undergoing PCI (345).

Dark Regions of No-Reflow on Late Gadolinium Enhancement Magnetic Resonance Imaging Result in Scar Formation After Atrial Fibrillation Ablation

Objectives The aim of this study was to assess acute ablation injuries seen on late gadolinium enhancement (LGE) magnetic resonance imaging (MRI) immediately post-ablation (IPA) and the association with permanent scar 3 months post-ablation (3moPA).

Background Success rates for atrial fibrillation catheter ablation vary significantly, in part because of limited information about the location, extent, and permanence of ablation injury at the time of procedure. Although the amount of scar on LGE MRI months after ablation correlates with procedure outcomes, early imaging predictors of scar remain elusive.
Methods Thirty-seven patients presenting for atrial fibrillation ablation underwent high-resolution MRI with a 3-dimensional LGE sequence before ablation, IPA, and 3moPA using a 3-T scanner. The acute left atrial wall injuries on IPA scans were categorized as hyperenhancing (HE) or nonenhancing (NE) and compared with scar 3moPA.
Results Heterogeneous injuries with HE and NE regions were identified in all patients. Dark NE regions in the left atrial wall on LGE MRI demonstrate findings similar to the "no-reflow" phenomenon. Although the left atrial wall showed similar amounts of HE, NE, and normal tissue IPA (37.7 ± 13%, 34.3 ± 14%, and 28.0 ± 11%, respectively; p = NS), registration of IPA injuries with 3moPA scarring demonstrated that 59.0 ± 19% of scar resulted from NE tissue, 30.6 ± 15% from HE tissue, and 10.4 ± 5% from tissue identified as normal. Paired *t*-test comparisons were all statistically significant among NE, HE, and normal tissue types ($p < 0.001$). Arrhythmia recurrence at 1-year follow-up correlated with the degree of wall enhancement 3moPA ($p = 0.02$).
Conclusions Radiofrequency ablation results in heterogeneous injury on LGE MRI with both HE and NE wall lesions. The NE lesions demonstrate no-reflow characteristics and reveal a better predictor of final scar at 3 months. Scar correlates with procedure outcomes, further highlighting the importance of early scar prediction (346).

Impact of Diabetes Mellitus on the Safety and Effectiveness of Bivalirudin in Patients With Acute Myocardial Infarction Undergoing Primary Angioplasty: Analysis From the HORIZONS-AMI (Harmonizing Outcomes with RevasculariZatiON and Stents in Acute Myocardial Infarction) Trial

Objectives We sought to evaluate the safety and efficacy of bivalirudin compared with glycoprotein IIb/IIIa inhibitors (GPI) in diabetic patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI).
Background Prior studies have demonstrated that GPI are especially beneficial in patients with diabetes with acute coronary syndromes and/or those undergoing PCI.
Methods In the multicenter, prospective HORIZONS-AMI (Harmonizing Outcomes with RevasculariZatiON and Stents in Acute Myocardial Infarction) trial, 3,602 patients with STEMI were randomized to bivalirudin or unfractionated heparin plus a GPI. Clinical outcomes were analyzed at 30 days and 1 year in patients with diabetes.
Results Diabetes mellitus was present in 593 patients (16.5%). The rates of cardiac death were significantly lower in diabetic patients treated with bivalirudin compared with heparin plus GPI (30 days: 2.1% vs. 5.5%, $p = 0.04$; 1 year: 2.5% vs. 7.1%, $p = 0.01$), and bivalirudin resulted in lower 30-day rates of stroke (0% vs. 2%, $p = 0.02$). There were no significant differences among diabetic patients randomized to bivalirudin versus heparin plus GPI in the 1-year rates of major adverse cardiac events (14.2% vs. 16.2%, $p = 0.44$), major bleeding (8.7% vs. 10.7%, $p = 0.42$), or stent thrombosis (4.2% vs. 3.8%, $p = 0.85$). By interaction testing, the relative effects of bivalirudin compared with heparin plus GPI were not significantly different in patients with and without diabetes.
Conclusions In patients with diabetes mellitus presenting with STEMI undergoing primary PCI, anticoagulant therapy with bivalirudin compared with heparin plus GPI is safe and effective and might reduce cardiac mortality at 30 days and 1 year. (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction; NCT00433966) (347).

Angiographic Geometric Changes of the Lumen Arterial Wall After Bioresorbable Vascular Scaffolds and Metallic Platform Stents at 1-Year Follow-Up

Objectives The aim of this study was to compare the angiographic changes in coronary geometry of the bioresorbable vascular scaffolds (BVS) and metallic platform stent (MPS) between baseline and follow-up.
Background Coronary geometry changes after stenting might result in wall shear stress changes and adverse events. The BVS have better conformability, compared with MPS, but still modify artery geometry. It is uncertain whether the BVS resorption can restore the coronary anatomical configuration at midterm follow-up.
Methods All patients of the ABSORB (A Clinical Evaluation of the Bioabsorbable Everolimus Eluting Coronary Stent System [BVS EECSS] in the Treatment of Patients With de Novo Native Coronary Artery Lesions) and SPIRIT (A Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System in the Treatment of Patients With de Novo Native Coronary Artery Lesions) trials treated with a single 3.0 × 18 mm device and imaged at baseline and 6- to 12-month follow-up were eligible. Coronary geometry changes were assessed with quantitative angiography as changes in curvature and angulation. Curvature and angulation changes between systole and diastole were investigated to assess hinging movements of the coronary artery.
Results One hundred sixty-one patients (86 BVS, and 75 MPS) were included. Baseline angiographic characteristics were similar. From post-implantation to follow-up, curvature increased 8.4% ($p < 0.01$) with BVS and decreased 1.9% ($p = 0.54$) with MPS; $p = 0.01$. Angulation increased

11.3% with BVS ($p < 0.01$) and 3.8% with MPS ($p = 0.01$); $p < 0.01$. From pre-implantation to follow-up, BVS decreased 3.4% the artery curvature ($p = 0.05$) and 3.9% the artery angulation ($p = 0.16$), whereas MPS presented with 26.1% decrease in curvature ($p < 0.01$) and 26.9% decrease in angulation ($p < 0.01$), being larger with MPS ($p < 0.01$, both). Hinging movements in curvature from pre-implantation to follow-up decreased 19.7% with BVS and 39.0% with MPS ($p = 0.27$) and decreased 3.9% with BVS and 26.9% with MPS in angulation ($p < 0.01$).

Conclusions At midterm follow-up, the BVS tended to restore the coronary configuration and the systo-diastolic movements to those seen before implantation. The coronary geometry remained similar to that seen at after implantation with MPS. (A Clinical Evaluation of the Bioabsorbable Everolimus Eluting Coronary Stent System [BVS EECSS] in the Treatment of Patients With de Novo Native Coronary Artery Lesions; NCT00856856) (348).

Periprocedural and Short-Term Outcomes of Transfemoral Transcatheter Aortic Valve Implantation With the Sapien XT as Compared With the Edwards Sapien Valve

Objectives The aim of this study was to analyze the short-term outcomes after transcatheter aortic valve implantation with the Edwards Sapien THV (ESV), compared with the Sapien XT THV (SXT) (Edwards Lifesciences, Irvine, California).

Background The SXT has been recently commercialized in Europe, but there are no studies analyzing the efficacy and safety of SXT, compared with ESV.

Methods All consecutive patients ($n = 120$) who underwent transcatheter aortic valve implantation in our center via the transfemoral approach with either ESV ($n = 66$) or SXT ($n = 54$). Valve Academic Research Consortium endpoints were used.

Results Mean age was 80 ± 8 years, and mean Logistic-European System for Cardiac Operative Risk Evaluation was 24.9 ± 17.0. The ilio-femoral artery minimal lumen diameter was smaller in patients treated with the SXT (7.27 ± 1.09 mm vs. 7.94 ± 1.08 mm, $p = 0.002$). Device success was high in both groups (96.3% vs. 92.4%, $p = 0.45$). Major vascular events were 3-fold lower in the SXT group (11.1% vs. 33.3%, relative risk: 0.40, 95% confidence interval: 0.28 to 0.57; $p = 0.004$). Life-threatening and major bleeding events were not significantly different between groups (18.5% vs. 27.3% and 35.2% vs. 40.9%, respectively). The SXT group had a lower 30-day Valve Academic Research Consortium combined safety endpoint (20.4% vs. 45.5%; relative risk: 0.44, 95% confidence interval: 0.24 to 0.80; $p = 0.004$). The 30-day mortality was 1.7% ($n = 2$). At 30 days, mean transaortic gradient was approximately 10 mm Hg in both groups and the aortic regurgitation was mild-to-moderate in 70.2% of SXT and 76.3% of ESV.

Conclusions The new SXT valve has the same short-term performance as the ESV but seems to be associated with a lower risk of major vascular complications and thus has a broader clinical application (349).

Transcatheter Aortic Valve Implantation for Failing Surgical Aortic Bioprosthetic Valve: From Concept to Clinical Application and Evaluation (Part 1)

With an aging population, improvement in life expectancy, and significant increase in the use of bioprosthetic valves, structural valve deterioration will become more and more prevalent. The operative mortality for an elective redo aortic valve surgery is reported to range from 2% to 7%, but this percentage can increase to more than 30% in high-risk and nonelective patients. Because transcatheter aortic valve (TAV)-in-surgical aortic valve (SAV) implantation represents a minimally invasive alternative to conventional redo surgery, it may prove to be safer and just as effective as redo surgery. Of course, prospective comparisons with a large number of patients and long-term follow-up are required to confirm these potential advantages. It is axiomatic that knowledge of the basic construction and dimensions, radiographic identification, and potential failure modes of SAV bioprostheses is fundamental in understanding key principles involved in TAV-in-SAV implantation. The goals of this paper are: 1) to review the classification, physical characteristics, and potential failure modes of surgical bioprosthetic aortic valves; and 2) to discuss patient selection and procedural *techniques relevant to* TAV-in-SAV implantation (350).

Transcatheter Aortic Valve Implantation for Failing Surgical Aortic Bioprosthetic Valve: From Concept to Clinical Application and Evaluation (Part 2)

Objectives This study sought to review the acute procedural outcomes of patients who underwent transcatheter aortic valve (TAV)–in–surgical aortic valve (SAV) implantation at the German Heart Center, Munich, and to summarize the existing literature on TAV-in-SAV implantation ($n = 47$).

Background There are several case reports and small case series describing transcatheter aortic valve implantation for a failing surgical aortic valve bioprosthesis (TAV-in-SAV implantation).

Methods From January 2007 to March 2011, 20 out of 556 patients underwent a TAV-in-SAV implantation at the German Heart Center Munich. Baseline characteristics and clinical outcome data were prospectively entered into a dedicated database.

Results The mean patient age was 75 ± 13 years, and the mean logistic European System for Cardiac Operative Risk Evaluation and Society of Thoracic Surgeons' Risk Model scores were 27 ± 13% and 7 ± 4%, respectively. Of the 20 patients, 14 had stented and 6 had stentless surgical

bioprostheses. Most cases (12 of 20) were performed via the transapical route using a 23-mm Edwards Sapien prosthesis (Edwards Lifesciences, Irvine, California). Successful implantation of a TAV in a SAV with the patient leaving the catheterization laboratory alive was achieved in 18 of 20 patients. The mean transaortic valve gradient was 20.0 ± 7.5 mm Hg. None-to-trivial, mild, and mild-to-moderate paravalvular aortic regurgitation was observed in 10, 6, and 2 patients, respectively. We experienced 1 intraprocedural death following pre-implant balloon aortic valvuloplasty ("stone heart") and 2 further in-hospital deaths due to myocardial infarction.

Conclusions TAV-in-SAV implantation is a safe and feasible treatment for high-risk patients with failing aortic bioprosthetic valves and should be considered as part of the armamentarium in the treatment of aortic bioprosthetic valve failure (351).

Prognostic Significance of Coronary Thrombus in Patients Undergoing Percutaneous Coronary Intervention for Acute Coronary Syndromes: A Subanalysis of the ACUITY (Acute Catheterization and Urgent Intervention Triage strategY) Trial

Objectives The objective of this study is to investigate the incidence and clinical implications of thrombus on baseline angiography among patients presenting with non–ST-segment elevation acute coronary syndromes (ACS) undergoing percutaneous coronary intervention (PCI).

Background Given current advances in the pharmacological and mechanical treatment of ACS patients managed with an early invasive strategy, the incidence and prognostic importance of pre-procedural lesion thrombus is warranted.

Methods In the ACUITY (Acute Catheterization and Urgent Intervention Triage strategY) trial, a total of 3,627 patients with moderate- and high-risk ACS undergoing PCI had their baseline and final post-PCI angiograms analyzed by an independent angiographic core laboratory.

Results Patients with thrombus (n = 530 [15%]) compared with those without thrombus had higher rates of impaired final epicardial coronary flow (final Thrombolysis In Myocardial Infarction [TIMI] flow grade 3: 89.6% vs. 97.1%, $p < 0.0001$). Thrombus was an independent predictor of 30 day death (odds ratio [OR]: 3.16 [95% confidence interval (CI): 1.20 to 8.37], $p = 0.02$), and myocardial infarction (MI) at 30 days (OR: 1.62 [95% CI: 1.17 to 2.24], $p = 0.003$) and at 1 year (OR: 1.56 [95% CI: 1.16 to 2.08], $p = 0.003$). Patients with thrombus had significantly higher rates of stent thrombosis (ST) compared with patients without thrombus at 30 days (2.8% vs. 1.1%, $p = 0.002$) and at 1 year (3.7% vs. 1.8%, $p = 0.003$), and thrombus was an independent predictor of ST at both 30 days (OR: 2.61 [95% CI: 1.38 to 4.91]) and 1 year (OR: 2.98 [95% CI: 1.64 to 5.42]).

Conclusions Pre-procedural thrombus was present in 15% of moderate- and high-risk ACS patients undergoing PCI in the ACUITY trial. Baseline thrombus predicts increased ischemic complications at 30 days including a 3-fold increased risk of death as well as MI up to 1 year. Further evaluation of adjunctive pharmacotherapy is needed in this high-risk population (352).

Optimal Intravascular Ultrasound Criteria and Their Accuracy for Defining the Functional Significance of Intermediate Coronary Stenoses of Different Locations

Objectives We performed this study to determine the optimal intravascular ultrasound (IVUS) criteria and to evaluate their accuracy for defining the functional significance of intermediate coronary stenoses in different locations of the coronary tree.

Background Presence of myocardial ischemia is the most important prognostic factor in patients with coronary artery disease and is determined by both the lesion severity and the amount of myocardium supplied.

Methods IVUS and fractional flow reserve (FFR) measurements were performed in 267 intermediate lesions located at the proximal or mid part of major epicardial coronary arteries. Optimal IVUS criteria and their diagnostic accuracy for functionally significant stenoses (FFR <0.8) were assessed.

Results FFR was <0.8 in 88 lesions (33%). The determinants of FFR were minimum lumen area (MLA) and lesion location. The diagnostic accuracy of MLA was highly variable according to the location of lesions. The best cutoff value of MLA to define the functional significance was 3.0 mm^2 (area under the curve [AUC]: 0.81, 95% confidence interval [CI]: 0.68 to 0.91) for proximal left anterior descending artery (LAD) lesions and 2.75 mm^2 for mid-LAD lesions located before the second diagonal branch (AUC: 0.76, 95% CI: 0.66 to 0.84). However, the appropriate MLA to predict the functional significance of lesions could not be found in other segments.

Conclusions When IVUS parameters are used to determine the functional significance of lesions in patients with intermediate coronary artery stenoses, different criteria should be used according to lesion location. In segments or vessels with anatomic variations, IVUS cannot be used for functional assessment of a stenosis. (Comparison of Fractional Flow Reserve and Intravascular Ultrasound; NCT01133015) (353).

Percutaneous Closure of Congenital Coronary Artery Fistulae: Results and Angiographic Follow-Up

Objectives This study sought to assess clinical and angiographic outcomes in a series of 29 patients who underwent transcatheter closure of coronary artery fistulae (CAF).

Background Transcatheter closure of CAF has become an alternative to surgical closure, but the reported experience is relatively limited.
Methods Medical records of all patients with CAF who underwent transcatheter closure at the Mayo Clinic, Rochester, Minnesota, between 1997 and 2010, were reviewed. Patients with other complex cardiac lesions and those requiring surgery were excluded.
Results Twenty-nine patients with CAF underwent 36 transcatheter closure procedures. The most were women (55%), and the median age at the time of transcatheter closure was 49 years. Twenty-three patients had a single CAF. The most common presenting symptom was chest pain (52%). Thirty devices were deployed antegrade into 1 or more arterial feeders, 3 using an arteriovenous wire loop and 3 retrograde at the fistulous connection. Successful closure occurred immediately in all patients with no residual flow in 89% and with trivial flow in 11%. Four complications occurred including 2 device migrations, 1 coronary spasm, and 1 coronary thrombosis. A follow-up angiogram was obtained in 18 (62%) patients with a median time to follow-up angiography of 1.5 years. Ten patients (56%) of the 18 patients with follow-up angiography had no recanalization of embolized vessel; 4 patients (22%) had trivial recanalization, and 4 patients (22%) had large recanalization. A repeat closure procedure was performed in all 4 patients of the latter.
Conclusions Transcatheter closure of CAF is feasible and should be considered in carefully selected patients. Recanalization of the treated coronary fistulae can occur, so follow-up angiography or other imaging modality should be performed in these patients (354).

Feasibility of Transcatheter Aortic Valve Implantation Without Balloon Pre-Dilation: A Pilot Study

Objectives The purpose of this pilot study was to evaluate the feasibility and safety of transcatheter aortic valve implantation (TAVI) without balloon pre-dilation.
Background Balloon pre-dilation of the stenosed aortic valve is currently believed to be a necessary step for valve preparation before device placement in patients undergoing TAVI and, therefore, is considered an obligatory part of the procedure. However, clear evidence supporting this policy is lacking. In contrast, pre-dilation might be responsible in part for distal embolizations as well as atrioventricular conduction disturbances seen during TAVI procedures.
Methods A total of 60 consecutive patients (mean age 80.1 ± 6.4 years, 53% female, mean logistic EuroScore 23.3 ± 15.2%) undergoing TAVI using the self-expanding Medtronic CoreValve prosthesis (Medtronic, Minneapolis, Minnesota) have been prospectively enrolled at 13 international centers.
Results Pre-procedural mean transaortic valve gradient was 47.8 ± 15.5 mm Hg, mean effective orifice area was 0.67 ± 0.15 cm^2. Technical success rate was 96.7% (58 of 60) of patients. Post-dilation was performed in 16.7% (10 of 60) of patients. Post-procedural mean valve gradient was 4.4 ± 2.0 mm Hg. Circular and noncircular valve configuration was present in 41 and 19 cases (68.3% vs. 31.7%), respectively, with similar effective orifice areas (1.74 ± 0.10 cm^2 vs. 1.71 ± 0.22 cm^2, p = NS). In-hospital mortality, myocardial infarction, stroke, and major vascular complications occurred in 6.7% (4 of 60), 0%, 5%, and 10% of patients. There was no valve embolization. New permanent pacing was needed in 11.7% (7 of 60) of patients.
Conclusions Transcatheter aortic valve implantation without balloon pre-dilation is feasible and safe, resulting in similar acute safety and efficacy as the current standard approach of TAVI with pre-dilation (355).

Impact of Drug Release Kinetics on Vascular Response to Different Zotarolimus-Eluting Stents Implanted in Patients With Long Coronary Stenoses: The LongOCT Study (Optical Coherence Tomography in Long Lesions)

Objectives We assessed the in vivo vascular response to a new generation of zotarolimus-eluting stents (ZES) with prolonged drug release (Resolute ZES-SR, Medtronic Vascular, Santa Rosa, California) compared with ZES with faster kinetics (Endeavor ZES-FR, Medtronic Vascular) by optical coherence tomography.
Background Local drug release kinetics has been implicated with antirestenosis efficacy of drug-eluting stents. However, the impact of different release kinetics on vascular response of diseased human coronary arteries remains to be investigated.
Methods The study population consisted of 43 patients with long lesions in native coronary vessels treated with multiple overlapping ZES. Twenty-one patients treated with ZES-SR were compared with 22 patients treated with ZES-FR from the ODESSA (Optical coherence tomography for DES SAfety) study. The primary endpoint was in-stent neointimal hyperplasia as assessed by optical coherence tomography at 6-month follow-up. Coprimary endpoints were the percentage of uncovered and malapposed struts.
Results Strut-level median neointimal thickness was 0.11 mm (interquartile range [IQR]: 0.07 to 0.15 mm) in ZES-SR and 0.31 mm (IQR: 0.27 to 0.42 mm) in ZES-FR, respectively ($p < 0.001$). The 6-month rate of uncovered struts per patient was 7.38% (IQR: 3.06% to 12.72%) in ZES-SR and 0.00% (IQR: 0.00% to 0.00%) in ZES-FR ($p < 0.001$); rate of malapposed and uncovered struts was 1.47% (IQR: 0.32% to 4.23%) in ZES-SR and 0.00% (IQR: 0.00% to 0.00%) in ZES-FR ($p < 0.001$).
Conclusions This study demonstrated the impact of different release kinetics on human in vivo vascular response to ZES implantation. The new generation of ZES-SR compared with ZES-FR had better suppression of the neointimal response but higher proportion of uncovered and

malapposed struts at 6-month optical coherence tomography follow-up. (Optical Coherence Tomography in Long Lesions [LongOCT]; NCT01133925) (356).

Feasibility and Acute Efficacy of Radiofrequency Ablation of Cavotricuspid Isthmus–Dependent Atrial Flutter Guided by Real-Time 3D TEE

Objectives The aim of this study was to evaluate the feasibility and acute efficacy of real-time 3-dimensional transesophageal echocardiography (RT3DTEE)–guided ablation of the cavotricuspid isthmus (CVTI).

Background The use of RT3DTEE to guide a transcatheter radiofrequency ablation procedure has never been systematically investigated.

Methods Seventy consecutive patients with CVTI-dependent atrial flutter underwent CVTI ablation. Procedural monitoring using RT3DTEE was assigned to patients who requested general anesthesia for the procedure (n = 21 [30%]). In the other 49 patients (the control group), the procedures were monitored using the standard fluoroscopic approach. Procedural time was considered as skin-to-skin electrophysiological procedure duration, not including anesthesia preparation; adequate radiofrequency ablation applications (with fixed temperature and power settings) were considered as lesions lasting $\geq$ 60 s.

Results RT3DTEE allowed visualization of the CVTI and identified related structures in most patients (20 of 21); anatomic features such as long CVTI (n = 11), prominent Eustachian ridge (n = 9), prominent Eustachian valve (n = 6), septal recess (n = 8), and pectinate muscles (n = 10) were frequent. Also, RT3DTEE allowed continuous visualization of ablation catheter movement and contact. Compared with the control group, RT3DTEE was equally effective in achieving CVTI bidirectional block (100% in both groups), and no complications occurred. RT3DTEE shortened procedural time (median 73.0 min, interquartile range [IQR] 60.0 to 90.0 min, vs. median 115.0 min, IQR 85.0 to 133.0 min, $p < 0.001$), reduced radiation exposure (median fluoroscopy time 4.2 min, IQR 3.1 to 8.4 min, vs. median 19.3 min, IQR 12.9 to 36.4 min, $p < 0.001$; median fluoroscopy dose 575.4 cGy · cm^2, IQR 428.5 to 1,299.4 cGy · cm^2, vs. median 3,520.7 cGy · cm^2, IQR 1,700.0 to 6,709.0 cGy · cm^2, $p < 0.001$), and reduced the number of radiofrequency applications to achieve bidirectional block (median 7, IQR 6 to 10, vs. median 12, IQR 10 to 22, $p = 0.007$). A strong learning curve was detected by comparing procedural data between the first and last patients treated using RT3DTEE.

Conclusions RT3DTEE-guided ablation of CVTI was feasible, allowing real-time detailed morphological CVTI characterization as well as continuous visualization of the ablation catheter during radiofrequency ablation. This approach entailed marked reductions in procedural time, radiation exposure, and the number of radiofrequency applications (357).

Assessment of Coronary Atherosclerosis Progression and Regression at Bifurcations Using Combined IVUS and OCT

Objectives The aim of this study was to evaluate the progression of atherosclerotic coronary plaques at bifurcations, using combined intravascular ultrasound–virtual histology (IVUS-VH) and optical coherence tomography (OCT).

Background Pathological findings reveal that atherosclerotic plaques characterized by the presence of large necrotic cores (NCs) with fibrous cap thicknesses < 65 μm are more prone to rupture. Accuracy in the detection of high-risk plaques could be improved by the combined use of IVUS-VH and OCT.

Methods IVUS-VH and OCT are 2 imaging modalities with different lateral resolutions and different depths of penetration. To provide a precise matching of the images, bifurcations were used as landmarks. IVUS-VH and OCT were performed in 56 bifurcations from 24 patients at baseline and at 6-month follow-up. All patients were treated with standard medical therapy. Bifurcations were studied at the proximal, in-bifurcation, and distal regions. Plaques were classified according to their composition as assessed by IVUS-VH and fibrous cap thickness as quantified by OCT.

Results At baseline, 27 NC-rich plaques were found. At 6-month follow-up, 22 (81%) did not show any significant change. Four new NC-rich lesions developed. At both time points, percent NC was higher and the fibrous cap was thinner at the proximal bifurcation rim compared with the distal. There were no significant changes in percent NC and fibrous cap thickness in the 3 bifurcation regions between baseline and follow-up examinations. No major cardiovascular events due to bifurcation lesion progression were observed.

Conclusions The combined use of IVUS-VH and OCT is a reliable tool to serially assess plaque progression and regression, and in the present study it was demonstrated to be safe and feasible. At 6-month follow-up, in this post–percutaneous coronary intervention patient population, most high-risk plaques remained unchanged, retaining their imaging classifications, nevertheless appearing to have remained clinically silent (358).

Randomized Comparison of Everolimus- and Paclitaxel-Eluting Stents: 2-Year Follow-Up From the SPIRIT (Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System) IV Trial

Objectives We sought to determine whether the differences in outcomes present between everolimus-eluting stents (EES) and paclitaxel-eluting stents (PES) in the SPIRIT (Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System) IV trial at 1 year were sustained with longer-term follow-up.

Background In the SPIRIT IV trial, patients undergoing percutaneous coronary intervention who were randomized to

EES compared with PES experienced lower 1-year rates of target lesion failure (cardiac death, target vessel myocardial infarction [MI], or ischemia-driven target lesion revascularization [TLR]), with significant reductions in the individual rates of MI, TLR, and stent thrombosis.

Methods We prospectively randomized 3,687 patients with up to 3 noncomplex previously untreated native coronary artery lesions to EES versus PES at 66 U.S. sites. Follow-up through 2 years is complete in 3,578 patents (97.0%).

Results Treatment with EES compared with PES reduced the 2-year rates of TLF (6.9% vs. 9.9%, p = 0.003), all MI (2.5% vs. 3.9%, p = 0.02), Q-wave MI (0.1% vs. 0.8%, p = 0.002), stent thrombosis (0.4% vs. 1.2%, p = 0.008), and ischemia-driven TLR (4.5% vs. 6.9%, p = 0.004), with nonsignificantly different rates of all-cause and cardiac mortality. Between 1 year and 2 years, there were no significant differences in adverse event rates between the 2 stent types.

Conclusions In the large-scale, prospective, multicenter, randomized SPIRIT IV trial, the benefits of EES compared with those of PES present at 1 year were sustained at 2 years. (Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System; NCT01016041) (359).

2-Year Follow-Up of a Randomized Controlled Trial of Everolimus- and Paclitaxel-Eluting Stents for Coronary Revascularization in Daily Practice: COMPARE (Comparison of the everolimus eluting XIENCE-V stent with the paclitaxel eluting TAXUS LIBERTÉ stent in all-comers: a randomized open label trial)

Objectives The purpose of this study was to compare the safety and efficacy of the Xience V (Abbott Vascular, Santa Clara, California) everolimus-eluting stent (EES) with the Taxus Liberté (Boston Scientific, Natick, Massachusetts) paclitaxel-eluting stent (PES) at 2-year follow-up.

Background COMPARE (Comparison of the everolimus eluting XIENCE-V stent with the paclitaxel eluting TAXUS LIBERTÉ stent in all-comers: a randomized open label trial) demonstrated a superior clinical outcome of EES over PES at 1 year in all comers. Whether this superiority is maintained after discontinuation, at 12 months, of dual antiplatelet therapy is unclear.

Methods Patients undergoing percutaneous coronary intervention with limited exclusion criteria were randomly allocated to EES or PES. The 2-year pre-specified endpoints are composites of safety and efficacy and stent thrombosis.

Results Follow-up was completed in 1,795 of 1,800 patients (99.7%). The groups had similar baseline characteristics. At 2 years, significantly fewer EES patients took dual antiplatelet therapy (11.4% vs. 15.4%, p = 0.02). The primary composite of all death, nonfatal myocardial infarction, and target vessel revascularization occurred in 9.0% of EES patients and 13.7% of PES patients (relative risk [RR]: 0.66; 95% confidence interval [CI]: 0.50 to 0.86) driven by a lower rate of myocardial infarction (3.9% vs. 7.5%; RR: 0.52; 95% CI: 0.35 to 0.77) and target vessel revascularization (3.2% vs. 8.0%; RR: 0.41; 95% CI: 0.27 to 0.62), in parallel with a lower rate of definite or probable stent thrombosis (0.9% vs. 3.9%; RR: 0.23; 95% CI: 0.11 to 0.49). Differences significantly increased between 1- and 2-year follow-up for the primary composite endpoint (p = 0.04), target vessel revascularization (p = 0.02), and definite or probable stent thrombosis (p = 0.02).

Conclusions The substantial clinical benefit of the EES over the PES with regard to measures of both safety and efficacy is maintained at 2 years in real-life practice with an increasing benefit in terms of safety and efficacy between 1 year and 2 years. Comparison of the everolimus eluting XIENCE-V stent with the paclitaxel eluting TAXUS LIBERTÉ stent in all-comers: a randomized open label trial: The COMPARE Trial [COMPARE 1]; NCT01016041) (360).

Bleeding Avoidance Strategies: Consensus and Controversy

Bleeding complications after coronary intervention are associated with prolonged hospitalization, increased hospital costs, patient dissatisfaction, morbidity, and 1-year mortality. *Bleeding avoidance strategies* is a term incorporating multiple modalities that aim to reduce bleeding and vascular complications after cardiovascular catheterization. Recent improvements in the rates of bleeding complications after invasive cardiovascular procedures suggest that the clinical community has successfully embraced specific strategies and improved patient care in this area. There remains controversy regarding the efficacy, safety, and/or practicality of 3 key bleeding avoidance strategies for cardiac catheterization and coronary intervention: procedural (radial artery approach, safezone arteriotomy), pharmacological (multiple agents), and technological (vascular closure devices) approaches to improved access. In this paper, we address areas of consensus with respect to selected modalities in order to define the role of each strategy in current practice. Furthermore, we focus on areas of controversy for selected modalities in order to define key areas warranting cautious clinical approaches and the need for future randomized clinical trials in this area (361).

Impact of Insulin Receptor Substrate-1 Genotypes on Platelet Reactivity and Cardiovascular Outcomes in Patients With Type 2 Diabetes Mellitus and Coronary Artery Disease

Objectives The aim of this study was to assess the association between genetic variants of the insulin receptor substrate (IRS)-1 gene, platelet function, and long-term outcomes in patients with type 2 diabetes mellitus (DM)

and stable coronary artery disease while on aspirin and clopidogrel therapy.

Background The effects of pharmacogenetic determinants on platelet function and cardiovascular outcomes in type DM patients are unknown.

Methods The association between IRS-1 genetic variants, platelet function, and the risk of major adverse cardiac events (MACE) at 2 years was assessed in 187 patients with type 2 DM and stable coronary artery disease on maintenance aspirin and clopidogrel therapy.

Results Seven tag single nucleotide polymorphisms were selected. Individuals with high platelet reactivity were more frequent among carriers of the C allele (GC and CC genotypes; approximately 20% of population) of the rs956115 marker (44.4% vs. 20.5%; odds ratio: 3.1, 95% confidence interval [CI]: 1.44 to 6.67; $p = 0.006$). These patients were at higher risk of MACE (28.0% vs. 10.9%; hazard ratio: 2.90, 95% CI: 1.38 to 6.11; $p = 0.005$). The C allele carriers of the rs956115 marker were more commonly associated with a hyperreactive platelet phenotype. This was confirmed in an external validation cohort of patients with type 2 DM but not in an external validation cohort of patients without DM. Carriers of the C allele of the rs956115 marker also had a significantly higher risk of MACE compared with noncarriers (30.6% vs. 11.4%; hazard ratio: 2.88, 95% CI: 1.35 to 6.14; $p = 0.006$).

Conclusions Type 2 DM patients who are carriers of the C allele of the rs956115 marker of the IRS-1 gene have a hyperreactive platelet phenotype and increased risk of MACE (362).

Prospective Evaluation of On-Clopidogrel Platelet Reactivity Over Time in Patients Treated With Percutaneous Coronary Intervention: Relationship With Gene Polymorphisms and Clinical Outcome

Objectives This study sought to investigate the evolving pattern over time of on-clopidogrel platelet reactivity (PR) and its relationship with genotype and clinical outcomes after percutaneous coronary intervention.

Background Whether on-clopidogrel PR and role of genotype differ over time is unknown.

Methods On-clopidogrel PR before percutaneous coronary intervention, and 1 and 6 months thereafter via VerifyNow P2Y12 (Accumetrics Inc., San Diego, California), *CYP2C19*2, *17, CYP3A5*3*, and *ABCB1* polymorphisms were evaluated in 300 patients. Death, stroke, myocardial infarction, and bleedings were assessed up to 1 year.

Results On-clopidogrel PR varied significantly over time, being higher at baseline than at 1 and 6 months after. From baseline to 1 month, 83 of 300 patients varied their response status. This was mainly due to baseline poor responders becoming full responders (75 of 83). Genotype justifies roughly 18% of this trend. *CYP2C19*2* and **17* influence on PR was consistent over time, whereas that of *ABCB1* appeared of greater impact at baseline. On-clopidogrel PR at 1 month independently best predicts ischemic and bleeding events. We found a therapeutic window (86 to 238 $P2Y_{12}$ reactivity units) with a lower incidence of both ischemic and bleeding complications. A risk score was created by combining genotype (*ABCB1* and *CYP2C19*2*), baseline PR, and creatinine clearance to predict 1-month poor responsiveness and 1-year poor prognosis.

Conclusions In patients at steady state for clopidogrel undergoing percutaneous coronary intervention, PR decreases from baseline to 1 month. Genotype influences ≈18% of this trend. On-clopidogrel PR at 1 month is the strongest predictor of adverse outcomes, and this can be predicted by combining genotype to baseline phenotype and clinical variables (363).

Prognostic Value of the SYNTAX Score in Patients With Acute Coronary Syndromes Undergoing Percutaneous Coronary Intervention: Analysis From the ACUITY (Acute Catheterization and Urgent Intervention Triage StrategY) Trial

Objectives We sought to investigate the predictive value of the SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery) score (SS) for risk assessment of 1-year clinical outcomes in patients with non–ST-segment elevation acute coronary syndromes undergoing percutaneous coronary intervention (PCI).

Background In the SYNTAX trial, the SS was effective in risk-stratifying patients with left main and triple-vessel coronary disease, the majority of whom had stable ischemic heart disease.

Methods The SS was determined in 2,627 patients with non–ST-segment elevation acute coronary syndromes undergoing PCI in the angiographic substudy of the ACUITY (Acute Catheterization and Urgent Intervention Triage StrategY) trial. Patients were stratified according to tertiles of the SS: <7 ($n = 854$), ≥ 7 and <13 ($n = 825$), and ≥ 13 ($n = 948$).

Results Among patients in the first, second, and third SS tertiles, the 1-year rates of mortality were 1.5%, 1.6%, and 4.0%, respectively ($p = 0.0005$); the cardiac mortality rates were 0.2%, 0.9%, and 2.7%, respectively ($p < 0.0001$); the myocardial infarction (MI) rates were 6.3%, 8.3%, and 12.9%, respectively ($p < 0.0001$); and the target vessel revascularization (TVR) rates were 7.4%, 7.0%, and 9.8%, respectively ($p = 0.02$). By multivariable analysis, the SS was an independent predictor of 1-year death (hazard ratio [HR]: 1.04, 95% confidence interval [CI]: 1.01 to 1.07; $p = 0.005$), cardiac death (HR: 1.06, 95% CI: 1.03 to 1.09; $p = 0.0002$), MI (HR: 1.03, 95% CI: 1.02 to 1.05; $p < 0.0001$), and TVR (HR: 1.03, 95% CI: 1.02 to 1.05; $p < 0.0001$). The SS affected death, cardiac death, and MI both within the first 30 days after PCI and between 30 days and 1 year, whereas it affected TVR primarily within the first 30 days. The predictive value of an increased SS was consistent among multiple pre-specified subgroups.

Conclusions In patients with non–ST-segment elevation acute coronary syndromes undergoing PCI, the SS is an independent predictor of the 1-year rates of death, cardiac death, MI, and TVR. (Comparison of Angiomax Versus Heparin in Acute Coronary Syndromes [ACS]; NCT00093158) (364).

Effect of Switching Antithrombin Agents for Primary Angioplasty in Acute Myocardial Infarction: The HORIZONS-SWITCH Analysis

Objectives We investigated the outcomes of switching to bivalirudin after initial administration of heparin in patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention.
Background Unfractionated heparin (UFH) is frequently administered early in ST-segment elevation myocardial infarction. Whether the benefits of bivalirudin documented in the HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trial persist in patients previously administered UFH is unknown.
Methods We analyzed the outcomes of the 2,357 patients from HORIZONS-AMI treated with UFH before enrollment according to their subsequent randomization to bivalirudin (switch group, n = 1,178) or UFH plus a glycoprotein IIb/IIIa inhibitor (control group, n = 1,179).
Results At 30 days, major bleeding occurred in 7.6% of the switch group versus 12.3% of the control group ($p = 0.0001$). Switch patients had lower 30-day rates of cardiac mortality (1.6% vs. 2.9%, $p = 0.04$). At 2-year follow-up, switch patients experienced lower rates of major bleeding (8.4% vs. 13.0%, $p = 0.0003$), cardiac mortality (2.3% vs. 3.8%, $p = 0.04$), and reinfarction (4.0% vs. 7.1%, $p = 0.0002$). Two-year rates of definite/probable stent thrombosis were similar in switch and control patients (3.1% vs. 4.3%, $p = 0.17$).
Conclusions In ST-segment elevation myocardial infarction patients who receive early treatment with UFH, switching to bivalirudin before primary percutaneous coronary intervention results in reduced rates of major bleeding and improved early and late cardiac survival (365).

NIRS and IVUS for Characterization of Atherosclerosis in Patients Undergoing Coronary Angiography

Objectives The aim of this study was to compare the findings of near-infrared spectroscopy (NIRS), intravascular ultrasound (IVUS) virtual histology (VH), and grayscale IVUS obtained in matched coronary vessel segments of patients undergoing coronary angiography.
Background Intravascular ultrasound VH has been developed to add tissue characterization to the grayscale IVUS assessment of coronary plaques. Near-infrared spectroscopy is a new imaging technique able to identify lipid core-containing coronary plaques (LCP).
Methods We performed NIRS and IVUS-VH pullbacks in a consecutive series of 31 patients with a common region of interest (ROI) between 2 side branches. For each ROI, we analyzed the chemogram blocks by NIRS, plaque area and plaque burden by grayscale IVUS, and tissue types by IVUS-VH. The chemogram block is a summary metric of a 2-mm vertical slice of the chemogram. The value ranges from 0 to 1 according to the presence of lipids and represents the probability of LCP with a color scale from red (low probability) through orange and tan to yellow (high probability).
Results Plaque area (mm^2) increases as percentage VH derived-necrotic core (NC) content (4.6 ± 2.7 vs. 7.4 ± 3.5 vs. 8.6 ± 3.4 vs. 7.9 ± 3.3, grouped in percentage NC quartiles, $p < 0.001$) and chemogram block probability color bin thresholds increase (4.9 ± 3.8 red, 7.3 ± 3.6 orange, 8.1 ± 3.4 tan, and 8.7 ± 3.4 yellow, $p < 0.001$). The correlation between the block chemogram detection of lipid core and percentage NC content by VH was weak ($r = 0.149$). Correction for the presence of calcium does not improve this correlation.
Conclusions Larger plaque area by grayscale IVUS was more often associated with either elevated percentage VH-NC or LCP by NIRS; however, the correlation between the detection of LCP by NIRS and necrotic core by VH is weak (366).

Plaque Characteristics of Thin-Cap Fibroatheroma Evaluated by OCT and IVUS

Objectives The purpose of this study was to assess plaque characteristics of optical coherence tomography (OCT)-derived thin-cap fibroatheroma (TCFA) by integrated backscatter intravascular ultrasound (IB-IVUS).
Background Radiofrequency signal-derived IVUS tissue characterization technology has become clinically available and provided objective and quantitative plaque characteristics of the coronary vessel wall. Integrated backscatter IVUS is one of the tissue characterization methods that can possibly provide quantitative plaque characteristics of the OCT-derived TCFA.
Methods Eighty-one coronary lesions with plaque burden >40% were selected and analyzed with both IB-IVUS and OCT. The OCT-derived TCFA was defined as a presence of thin fibrous cap (<65 μm) overlying a signal-poor lesion with diffuse border representing a lipid-rich plaque. By conventional gray-scale IVUS, external elastic membrane (EEM) cross-sectional area (CSA), lumen CSA, plaque plus media (P+M) CSA, plaque burden and remodeling index were measured. By IB-IVUS, plaque characteristics were further classified as fibrosis, dense fibrosis, calcification, or lipid pool.
Results Optical coherence tomography identified 40 TCFAs (49%) and 41 non-TCFAs. The EEM CSA, P+M CSA, plaque burden, and remodeling index were significantly larger in OCT-derived TCFA than non-TCFA. By IB-IVUS, percentage lipid pool area (= lipid pool area/

P+M CSA × 100) was significantly higher (62.4 ± 12.8% vs. 38.4 ± 13.1%, $p < 0.0001$) and percentage fibrosis area (= fibrosis area/P+M CSA × 100) was significantly lower (34.6 ± 11.4% vs. 50.5 ± 8.7%, $p < 0.0001$) in OCT-derived TCFA than non-TCFA. By receiver-operator characteristic curve analysis, percentage lipid pool area ≥55%, percentage fibrosis area ≤41%, and remodeling index ≥1.0 were predictors of OCT-derived TCFA.

Conclusions The OCT-derived TCFA had larger plaque burden and positive remodeling with predominant lipid component and less fibrous plaque assessed by IB-IVUS (367).

Impact of Bleeding on Mortality After Percutaneous Coronary Intervention: Results From a Patient-Level Pooled Analysis of the REPLACE-2 (Randomized Evaluation of PCI Linking Angiomax to Reduced Clinical Events), ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy), and HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) Trials

Objectives This study sought to develop a risk score predictive of bleeding in patients undergoing percutaneous coronary intervention (PCI) and to investigate the impact of bleeding on subsequent mortality.

Background Bleeding complications after PCI have been independently associated with early and late mortality.

Methods This study represents a patient-level pooled analysis including 17,034 patients undergoing PCI from 3 large, randomized trials of bivalirudin versus heparin plus glycoprotein IIb/IIIa inhibitors, including the REPLACE-2 (Randomized Evaluation of PCI Linking Angiomax to Reduced Clinical Events), ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy), and HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trials. We developed a risk score to predict non-coronary artery bypass graft (CABG)–related TIMI (Thrombolysis In Myocardial Infarction) major bleeding and evaluated the impact of various types of bleeding on 1-year mortality.

Results A non-CABG–related TIMI major bleed occurred within 30 days in 267 patients (1.6%), and death occurred in 497 patients (2.9%) within 1 year. A risk score was developed to predict the bleeding risk of patients undergoing PCI, consisting of 7 variables (serum creatinine, age, sex, presentation, white blood cell count, cigarette smoking, and randomized treatment). The TIMI major bleeding rates increased by bleeding risk score groups: from 0.4% for those in the lowest to 5.8% for those in the highest risk group. Non-CABG–related TIMI major bleeding and the occurrence of myocardial infarction within 30 days were independent predictors of subsequent mortality, with respective hazard ratios of 4.2 and 2.9, each $p < 0.001$. Ranked in order of severity, TIMI major bleeding, blood transfusion without TIMI bleed, TIMI minor bleeding requiring blood transfusion, and TIMI minor bleeding not requiring blood transfusion were independent predictors of subsequent mortality with hazard ratios of 4.89, 2.91, 2.73, and 1.66, respectively. Isolated hematomas were not predictive of subsequent mortality.

Conclusions Non-CABG–related bleeding within 30 days is strongly associated with an increased risk of subsequent mortality at 1 year in patients undergoing PCI for all indications. A risk score was established to calculate the bleeding risk for patients undergoing PCI, allowing therapeutic decision making to minimize the incidence of bleeding (368).

Total Ischemic Time: The Correct Focus of Attention for Optimal ST-Segment Elevation Myocardial Infarction Care

Currently accepted standards for gauging quality of care in the treatment of ST-segment elevation myocardial infarction (STEMI) mainly focus on shortening the time to treatment after the patient arrives at the hospital. But this narrow focus fails to consider the substantial duration of myocardial ischemia that exists prior to hospital arrival, and the large number of deaths that occur during the pre-hospital period. The time from symptom onset until reperfusion occurs is one estimate of total ischemic time. Several experimental studies and now human clinical studies have confirmed that infarct size and mortality are strongly correlated with the total ischemic time, and much less so with its subintervals like door-to-balloon time. This review will discuss the importance of total ischemic time in STEMI (369).

Validation of Minimal Luminal Area Measured by Intravascular Ultrasound for Assessment of Functionally Significant Coronary Stenosis: Comparison With Myocardial Perfusion Imaging

Objectives This study sought to evaluate the ability of minimal luminal area (MLA) measured by intravascular ultrasound (IVUS) to assess the functional significance of coronary artery disease.

Background The use of IVUS to determine the functional significance of coronary artery lesions remains a matter for debate.

Methods From our prospective IVUS imaging database, between July 2009 and April 2010, 170 coronary lesions in 150 patients who underwent stress myocardial single-photon emission computed tomography (SPECT) performed within 1 month of IVUS evaluation were identified and analyzed. MLA and other parameters were measured by IVUS and compared with the results of myocardial SPECT.

Results Overall, 45 lesions had positive SPECT, and 125 lesions had negative SPECT. The MLA of lesions with positive SPECT was smaller than the MLA of those with

negative SPECT (1.7 ± 0.5 mm^2 vs. 2.3 ± 1.1 mm^2, $p < 0.001$). By logistic regression analysis, MLA (odds ratio: 3.1 by decrease of 1 mm^2, 95% confidence interval [CI]: 1.75 to 5.5, $p < 0.01$) was an independent predictor of the positive SPECT. Using receiver-operator characteristic curve analysis, the best cutoff value of MLA was ≤2.1 mm^2 with an 86.7% sensitivity, a 50.4% specificity, a 38.6% positive predictive value, and a 91.3% negative predictive value versus lesions with a positive SPECT (area under the curve: 0.690, 95% CI: 0.615 to 0.759, $p < 0.01$).

Conclusions The best cutoff value of MLA measured by IVUS to predict myocardial ischemia was 2.1 mm^2. The IVUS-measured MLA appeared to play a limited role in detecting functionally significant lesions assessed by myocardial SPECT (370).

Percutaneous Coronary Intervention of Unprotected Left Main Coronary Artery Disease as Culprit Lesion in Patients With Acute Myocardial Infarction

Objectives This study sought to evaluate short- and long-term outcomes of patients undergoing emergency percutaneous coronary intervention (PCI) for acute myocardial infarction due to a culprit lesion in an unprotected left main coronary artery.

Methods In this retrospective, 2-center, international observational study, 5,261 patients were admitted between February 2005 and December 2008 with acute myocardial infarction and treated with PCI; of these, 1,277 were ST-segment elevation myocardial infarction and 3,984 non–ST-segment elevation myocardial infarction. We identified 48 patients among this cohort who underwent emergency PCI to an unprotected left main coronary artery culprit lesion.

Results Mean age was 70 ± 12.5 years, and 45% of the patients presented with ST-segment elevation myocardial infarction or new left bundle branch block. Cardiogenic shock was present in 45%, and distal left main coronary artery disease was present in 71% of patients. Angiographic procedural success was achieved in 92% of patients. Overall in-hospital mortality was 21%, due in all cases to refractory, multiorgan failure. Twenty-five percent experienced major adverse cardiac events, defined as death, myocardial infarction, stent thrombosis, and target vessel revascularization. In patients presenting in cardiogenic shock, in-hospital mortality was 32%. At 1-year follow-up, in-hospital survivors had a mortality rate of 10.5%, whereas 18.4% experienced subsequent major adverse cardiac events. Long-term prognosis was excellent in hospital survivors with a 1-year survival rate of 89.5%.

Conclusions Patients with acute myocardial infarction and thrombosis of the unprotected left main coronary artery are a high-risk subgroup with a substantial mortality, particularly if they present in cardiogenic shock. We demonstrate that in these patients, PCI is a feasible treatment option associated with reasonably good outcomes. Long-term prognosis is excellent in hospital survivors with an 89.5% survival rate at 1 year (371).

Comparison of Titanium-Nitride-Oxide–Coated Stents With Zotarolimus-Eluting Stents for Coronary Revascularization: A Randomized Controlled Trial

Objectives This study sought to compare the efficacy of passive stent coating with titanium-nitride-oxide (TiNO) with drug-eluting stents releasing zotarolimus (ZES) (Endeavor, Medtronic, Minneapolis, Minnesota).

Background Stent coating with TiNO has been shown to reduce restenosis compared with bare-metal stents in experimental and clinical studies.

Methods In an assessor-blind noninferiority study, 302 patients undergoing percutaneous coronary intervention were randomized to treatment with TiNO or ZES. The primary endpoint was in-stent late loss at 6 to 8 months, and analysis was by intention to treat.

Results Both groups were well balanced with respect to baseline clinical and angiographic characteristics. The TiNO group failed to reach the pre-specified noninferiority margin for the primary endpoint (in-stent late loss: 0.64 ± 0.61 mm vs. 0.47 ± 0.48 mm, difference: 0.16, upper 1-sided 95% confidence interval [CI]: 0.26; $p_{noninferiority} = 0.54$), and subsequent superiority testing was in favor of ZES ($p_{superiority} = 0.02$). In-segment binary restenosis was lower with ZES (11.1%) than with TiNO (20.5%; $p_{superiority} = 0.04$). A stratified analysis of the primary endpoint found particularly pronounced differences between stents among diabetic versus nondiabetic patients (0.90 ± 0.69 mm vs. 0.39 ± 0.38 mm; $p_{interaction} = 0.04$). Clinical outcomes showed a similar rate of death (0.7% vs. 0.7%; $p = 1.00$), myocardial infarction (5.3% vs. 6.7%; $p = 0.60$), and major adverse cardiac events (21.1% vs. 18.0%, hazard ratio: 1.19, 95% CI: 0.71 to 2.00; $p = 0.50$) at 1 year. There were no differences in rates of definite or probable stent thrombosis (0.7% vs. 0%; $p = 0.51$) at 1 year.

Conclusions Compared with TiNO, ZES was superior with regard to late loss and binary restenosis. The concept of passive stent coating with TiNO remains inferior to drug-eluting stent technology in reducing restenosis. ([TIDE] Randomized Trial Comparing Titan Stent With Zotarolimus-Eluting Stent: NCT00492908) (372).

Randomized Comparison of Pre-Hospital–Initiated Facilitated Percutaneous Coronary Intervention Versus Primary Percutaneous Coronary Intervention in Acute Myocardial Infarction Very Early After Symptom Onset: The LIPSIA-STEMI Trial (Leipzig Immediate Prehospital Facilitated Angioplasty in ST-Segment Myocardial Infarction)

Objectives This multicenter trial sought to assess the merits of facilitated percutaneous coronary intervention (PCI) versus primary PCI in an ST-segment elevation

myocardial infarction (STEMI) network with long transfer distances in patients presenting early after symptom onset.

Background Facilitated PCI with fibrinolysis might be beneficial in specific high-risk STEMI situations to prevent myocardial necrosis expansion.

Methods Patients with STEMI (<3 h after symptom onset) were randomized to either pre-hospital–initiated facilitated PCI using tenecteplase (Group A; n = 81) or primary PCI (Group B; n = 81) plus optimal antithrombotic comedication. The primary endpoint was infarct size assessed by delayed-enhancement magnetic resonance imaging. Secondary endpoints were microvascular obstruction and myocardial salvage, early ST-segment resolution, and a composite of death, repeated myocardial infarctions, and congestive heart failure within 30 days.

Results The median time from symptom onset to randomization was 64 min (interquartile range [IQR]: 42 to 103 min) in Group A versus 55 min in Group B (IQR: 27 to 91 min; p = 0.26). Despite better pre-interventional TIMI (Thrombolysis In Myocardial Infarction) flow in Group A (71% vs. 35% TIMI flow grade 2 or 3; p < 0.001), the infarct size tended to be worse in Group A versus Group B (17.9% of left ventricle [IQR: 8.4% to 35.0%] vs. 13.7% [IQR: 7.5% to 24.0%]; p = 0.10). There was also a strong trend toward more early and late microvascular obstruction, (p = 0.06 and 0.09) and no difference in ST-segment resolution (p = 0.26). The combined clinical endpoint showed a trend toward higher event rates in Group A (19.8% vs. 13.6%; p = 0.13, relative risk: 0.52, 95% confidence interval: 0.23 to 1.18).

Conclusions In STEMI patients presenting early after symptom onset with relatively long transfer times, a fibrinolytic-based facilitated PCI approach with optimal antiplatelet comedication does not offer a benefit over primary PCI with respect to infarct size and tissue perfusion. ([LIPSIA-STEMI] The Leipzig Immediate Prehospital Facilitated Angioplasty in ST-Segment Myocardial Infarction; NCT00359918) (373).

A Patient-Level Pooled Analysis Assessing the Impact of the SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) Score on 1-Year Clinical Outcomes in 6,508 Patients Enrolled in Contemporary Coronary Stent Trials

Objectives This study sought to assess the impact of the SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score (SXscore) on clinical outcomes in patients undergoing percutaneous coronary intervention.

Background The SXscore has been demonstrated to have an ability to predict clinical outcomes in patients undergoing percutaneous revascularization. Current studies are limited by the relatively small number of patients in each SXscore group.

Methods Patient-level data from 7 contemporary coronary stent trials were pooled by an independent academic research organization (Cardialysis, Rotterdam, the Netherlands). Analysis was performed on a cohort of 6,508 patients treated with drug-eluting stents and who had calculated SXscores. Clinical outcomes in terms of death, myocardial infarction (MI), repeat revascularization, and major adverse cardiac events (MACE, a composite of death, MI, and repeat revascularization) were subsequently stratified according to SXscore quartiles: $SXscore_{Q1} \leq 8$ (n = 1,702); $8 < SXscore_{Q2} < 15$ (n = 1,528); $15 \leq SXscore_{Q3} < 23$ (n = 1,620); and $SXscore_{Q4} \geq 23$ (n = 1,658).

Results One-year outcomes were available in 6,496 patients (99.8%). At 1-year follow-up, all clinical outcomes including mortality, MI, repeat revascularization, MACE, and definite and any stent thrombosis were all significantly higher in patients in the highest SXscore quartile. Similar trends were observed in a subgroup of 2,093 patients (32.2%) who presented with an ST- or non–ST-segment elevation MI. The rate of MACE among patients with an SXscore >32 and ≤32 was 24.9% and 14.0%, respectively (p < 0.001). The SXscore was identified as an independent predictor of all clinical outcomes including mortality, MACE, and stent thrombosis (p < 0.001 for all).

Conclusions This study confirms the consistent ability of the SXscore to identify patients who are at highest risk of adverse events (374).

Clinical and Angiographic Predictors and Prognostic Value of Failed Thrombus Aspiration in Primary Percutaneous Coronary Intervention

Objectives This study sought to investigate which factors are associated with failure of thrombus aspiration (TA) and if this has prognostic implications.

Background The pathophysiological mechanism and clinical benefit of TA during primary percutaneous coronary intervention for acute ST-segment elevation myocardial infarction is still in debate.

Methods Between August 2001 and October 2007, TA was attempted in 1,399 patients. Failure of TA was defined as the inability to reach and/or cross the occlusion with the aspiration catheter for effective thrombus removal. In addition, we analyzed patients in which no material could be obtained. We examined baseline clinical and angiographic variables related to failure of TA or to the lack of aspirate. Follow-up on vital status was obtained at 1 year.

Results In 144 (10.3%) patients, the aspiration catheter failed to cross the lesion. After multivariable adjustment, marked proximal tortuosity (odds ratio [OR]: 2.88, 95% confidence interval [CI]: 1.92 to 4.31, p < 0.001), the presence of a calcified lesion (OR: 2.70, 95% CI: 1.77 to 4.13, p < 0.001), and a bifurcation lesion (OR: 1.97, 95% CI: 1.15 to 3.37, p = 0.013) were independent predictors of failed TA. Age over 60 years and the circumflex as infarct-related artery were associated with the lack of aspirate. Mortality rates at 1 year were 6.2% in patients with failed

TA and 6.4% with successful TA (hazard ratio: 0.98, 95% CI: 0.49 to 1.95, p = 0.95).

Conclusions The presence of marked proximal tortuosity of the infarct-related artery, a calcified lesion, and a bifurcation lesion are independent predictors of failure of thrombus aspiration. We found that unsuccessful TA did not affect 1-year mortality (375).

Safety of Contemporary Percutaneous Peripheral Arterial Interventions in the Elderly: Insights From the BMC2 PVI (Blue Cross Blue Shield of Michigan Cardiovascular Consortium Peripheral Vascular Intervention) Registry

Objectives This study sought to evaluate the effect of age on procedure type, periprocedural management, and in-hospital outcomes of patients undergoing lower-extremity (LE) peripheral vascular intervention (PVI).

Background Surgical therapy of peripheral arterial disease is associated with significant morbidity and mortality in the elderly. There are limited data related to the influence of advanced age on the outcome of patients undergoing percutaneous LE PVI.

Methods Clinical presentation, comorbidities, and in-hospital outcomes of patients undergoing LE PVI in a multicenter, multidisciplinary registry were compared between 3 age groups: <70 years, between 70 and 80 years, and ≥80 years (elderly group).

Results In our cohort, 7,769 patients underwent LE PVI. The elderly patients were more likely to be female and to have a greater burden of comorbidities. Procedural success was lower in the elderly group (74.2% for age ≥80 years vs. 78% for age 70 to <80 years and 81.4% in patients age <70 years, respectively; p < 0.0001). Unadjusted rates of procedure-related vascular access complications, post-procedure transfusion, contrast-induced nephropathy, amputation, and major adverse cardiac events were higher in elderly patients. After adjustment for baseline covariates, the elderly patients were more likely to experience vascular access complications; however, advanced age was not found to be associated with major adverse cardiac events, transfusion, contrast-induced nephropathy, or amputation.

Conclusions Contemporary PVI can be performed in elderly patients with high procedural and technical success with low rates of periprocedural complications including mortality. These findings may support the notion of using PVI as a preferred revascularization strategy in the treatment of severe peripheral arterial disease in the elderly population (376).

Primary Percutaneous Coronary Intervention for Unprotected Left Main Disease in Patients With Acute ST-Segment Elevation Myocardial Infarction: The AMIS (Acute Myocardial Infarction in Switzerland) Plus Registry Experience

Objectives This study sought to assess outcomes in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention (PCI) for unprotected left main (LM) disease.

Background Limited data are available on outcomes in patients with ST-segment elevation myocardial infarction undergoing LM PCI.

Methods Of 9,075 patients with ST-segment elevation myocardial infarction enrolled in the AMIS (Acute Myocardial Infarction in Switzerland) Plus registry between 2005 and June 30, 2010, 6,666 underwent primary PCI. Of them, 348 (5.2%; mean age: 63.5 ± 12.6 years) underwent LM PCI, either isolated (n = 208) or concomitant to PCI for other vessel segments (n = 140). They were compared with 6,318 patients (94.8%; mean age: 61.9 ± 12.5 years) undergoing PCI of non-LM vessel segments only.

Results The LM patients had higher rates of cardiogenic shock (12.2% vs. 3.5%; p < 0.001), cardiac arrest (10.6% vs. 6.3%; p < 0.01), in-hospital mortality (10.9% vs. 3.8%; p < 0.001), and major adverse cardiac and cerebrovascular events (12.4% vs. 5.0%; p < 0.001) than non-LM PCI. Rates of mortality and major adverse cardiac and cerebrovascular events were highest for concurrent LM and non-LM PCI (17.9% and 18.6%, respectively), intermediate for isolated LM PCI (6.3% and 8.3%, respectively), and lowest for non-LM PCI (3.8% and 5.0%, respectively). Rates of mortality and major adverse cardiac and cerebrovascular events for LM PCI were higher than for non-LM multivessel PCI (10.9% vs. 4.9%, p < 0.001, and 12.4% vs. 6.4%, p < 0.001, respectively). LM disease independently predicted in-hospital death (odds ratio: 2.36; 95% confidence interval: 1.34 to 4.17; p = 0.003).

Conclusions Emergent LM PCI in the context of acute myocardial infarction, even including 12% cardiogenic shock, appears to have a remarkably high (89%) in-hospital survival. Concurrent LM and non-LM PCI has worse outcomes than isolated LM PCI (377).

The V2 Transition Ratio: A New Electrocardiographic Criterion for Distinguishing Left From Right Ventricular Outflow Tract Tachycardia Origin

Objectives We sought to develop electrocardiography (ECG) criteria for distinguishing left ventricular outflow tract (LVOT) from right ventricular outflow tract (RVOT) origin in patients with idiopathic outflow tract ventricular tachycardia (OTVT) and lead V_3 R/S transition.

Background Several ECG criteria have been proposed for differentiating left from right OTVT origin; ventricular tachycardias (VTs) with left bundle branch block and V_3 transition remain a challenge.

Methods We analyzed the surface ECG pattern of patients with OTVT with a precordial transition in lead V_3 who underwent successful catheter ablation. Sinus and VT QRS morphologies were measured in limb and precordial leads with electronic calipers. The V_2 and V_3 transition ratios were calculated by computing the percentage R-wave during VT

$(R/R+S)_{VT}$ divided by the percentage R-wave in sinus rhythm $(R/R+S)_{SR}$.

Results We retrospectively analyzed ECGs from 40 patients (mean age 44 ± 14 years, 21 female) with outflow tract premature ventricular contractions (PVCs)/VT. Patients with structural heart disease, paced rhythms, and bundle branch block during sinus rhythm were excluded. The V_2 transition ratio was significantly greater for LVOT PVCs compared with RVOT PVCs (1.27 ± 0.60 vs. 0.23 ± 0.16; $p < 0.001$) and was the only independent predictor of LVOT origin. In 21 prospective cases, a V_2 transition ratio ≥0.60 predicted an LVOT origin with 91% accuracy. A PVC precordial transition occurring later than the sinus rhythm transition excluded an LVOT origin with 100% accuracy.

Conclusions The V_2 transition ratio is a novel electrocardiographic measure that reliably distinguishes LVOT from RVOT origin in patients with lead V_3 precordial transition. This measure might be useful for counseling patients and planning an ablation strategy (378).

The Impact of Patient and Lesion Complexity on Clinical and Angiographic Outcomes After Revascularization With Zotarolimus- and Everolimus-Eluting Stents: A Substudy of the RESOLUTE All Comers Trial (A Randomized Comparison of a Zotarolimus-Eluting Stent With an Everolimus-Eluting Stent for Percutaneous Coronary Intervention)

Objectives The aim of this study was to investigate the impact of patient and lesion complexity on outcomes with newer-generation zotarolimus-eluting stents (ZES) and everolimus-eluting stents (EES).

Background Clinical and angiographic outcomes of newer-generation stents have not been described among complex patients.

Methods Patients enrolled in the RESOLUTE All Comers trial (A Randomized Comparison of a Zotarolimus-Eluting Stent With an Everolimus-Eluting Stent for Percutaneous Coronary Intervention) were stratified into "complex" and "simple."

Results Of 2,292 patients, 1,520 (66.3%) were complex and treated with ZES (n = 764) or EES (n = 756). Event rates were higher among complex patients, and results did not differ between ZES and EES, regardless of complexity. At 1 year, target lesion failure was 8.9% in ZES- and 9.7% in EES-treated complex patients ($p = 0.66$) and 6.8% in ZES- and 5.7% in EES-treated simple patients ($p = 0.55$). Rates of cardiac death (1.3% vs. 2.2%, $p = 0.24$), target-vessel myocardial infarction (4.3% vs. 4.4%, $p = 0.90$), and clinically indicated target lesion revascularization (4.4% vs. 4.0%, $p = 0.80$) were similar for both stent types among complex patients. Definite or probable stent thrombosis occurred in 20 (1.3%) complex patients with no difference between ZES (1.7%) and EES (0.9%, $p = 0.26$). Angiographic follow-up showed similar results for ZES and EES in terms of in-stent percentage diameter stenosis (22.2 ± 15.4% vs. 21.4 ± 15.8%, $p = 0.67$) and in-segment binary restenosis (6.6% vs. 8.0%, $p = 0.82$) in the complex group.

Conclusions In this all-comers randomized trial, major adverse cardiovascular events were more frequent among complex than simple patients. The newer-generation ZES and EES proved to be safe and effective, regardless of complexity, with similar clinical and angiographic outcomes for both stent types through 1 year. (RESOLUTE-III All Comers Trial: A Randomized Comparison of a Zotarolimus-Eluting Stent With an Everolimus-Eluting Stent for Percutaneous Coronary Intervention; NCT00617084) (379).

Long-Term Comparison of Everolimus-Eluting and Sirolimus-Eluting Stents for Coronary Revascularization

Objectives This study sought to compare the unrestricted use of everolimus-eluting stents (EES) with sirolimus-eluting stents (SES) in patients undergoing percutaneous coronary intervention.

Background It is unclear whether there are differences in safety and efficacy between EES and SES during long-term follow-up.

Methods Using propensity score matching, clinical outcome was compared among 1,342 propensity score–matched pairs of patients treated with EES and SES. The primary outcome was a composite of death, MI, and target vessel revascularization.

Results The median follow-up was 1.5 years with a maximum of 3 years. The primary outcome occurred in 14.9% of EES- and 18.0% of SES-treated patients up to 3 years (hazard ratio [HR]: 0.83, 95% confidence interval [CI]: 0.68 to 1.00, $p = 0.056$). All-cause mortality (6.0% vs. 6.5%, HR: 0.92, 95% CI: 0.68 to 1.25, $p = 0.59$) was similar, risks of myocardial infarction (MI) (3.3% vs. 5.0%, HR: 0.62, 95% CI: 0.42 to 0.92, $p = 0.017$), and target vessel revascularization (7.0% vs. 9.6%, HR: 0.75, 95% CI: 0.57 to 0.99, $p = 0.039$) were lower with EES than SES. Definite stent thrombosis (ST) (HR: 0.30, 95% CI: 0.12 to 0.75, $p = 0.01$) was less frequent among patients treated with EES. The reduced rate of MI with EES was explained in part by the lower risk of definite ST and the corresponding decrease in events associated with ST (HR: 0.25, 95% CI: 0.08 to 0.75, $p = 0.013$).

Conclusions The unrestricted use of EES appears to be associated with improved clinical long-term outcome compared with SES. Differences in favor of EES are driven in part by a lower risk of MI associated with ST (380).

Complexity of Atherosclerotic Coronary Artery Disease and Long-Term Outcomes in Patients With Unprotected Left Main Disease Treated With Drug-Eluting Stents or Coronary Artery Bypass Grafting

Objectives The aim of this study was to compare treatment effects of drug-eluting stents (DES) or coronary artery

bypass grafting (CABG) for left main coronary artery (LMCA) disease according to the complexity of atherosclerotic disease burden.

Background Limited information is available on the relationships between the extent of coronary atherosclerosis and very long-term outcomes of surgical or percutaneous LMCA revascularization.

Methods A total of 1,146 patients with unprotected LMCA disease who received DES (n = 645) or underwent CABG (n = 501) were evaluated. The extent of atherosclerotic disease burden was measured using the SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery) score; a low-risk score was defined as ≤22, an intermediate-risk score as 23 to 32, and a high-risk score as ≥33.

Results After multivariate adjustment with the inverse-probability-of-treatment weighting method, the 5-year risks for death (6.1% for DES vs. 16.2% for CABG; hazard ratio [HR]: 0.52; 95% confidence interval [CI]: 0.21 to 1.28; p = 0.15) and the composite of death, Q-wave myocardial infarction, or stroke (6.4% vs. 16.2%; HR: 0.54; 95% CI: 0.22 to 1.34; p = 0.18) favored DES in patients with low-risk SYNTAX scores; in contrast, the 5-year risks for death (26.9% vs. 17.8%; HR: 1.46; 95% CI: 0.92 to 2.30; p = 0.11) and the composite outcome (27.6% vs. 19.5%; HR: 1.36; 95% CI: 0.87 to 2.12; p = 0.18) favored CABG in patients with high-risk SYNTAX scores (interaction p = 0.047 for death, interaction p = 0.08 for composite outcome). Patients undergoing CABG consistently had lower rates of target vessel revascularization.

Conclusions According to the complexity of concomitant coronary disease, there were differential treatment effects on long-term mortality in patients with unprotected LMCA disease who received DES or underwent CABG (381).

Incidence, Predictive Factors, and Prognostic Value of Myocardial Injury Following Uncomplicated Transcatheter Aortic Valve Implantation

Objectives This study sought to: 1) determine the incidence, degree, and timing of the rise in serum cardiac markers of myocardial injury associated with uncomplicated transcatheter aortic valve implantation (TAVI); and 2) evaluate the predictive factors and prognostic value of myocardial injury associated with TAVI.

Background Very few data exist on the occurrence and clinical relevance of myocardial injury during TAVI procedures.

Methods A total of 101 patients who underwent successful TAVI (transfemoral [TF] approach, n = 38; transapical [TA] approach, n = 63) were included. Creatine kinase-MB (CK-MB) and cardiac troponin T (cTnT) levels were determined at baseline and at 6 to 12, 24, 48, and 72 h following TAVI.

Results TAVI was associated with some degree of myocardial injury in 99% of the patients (TF: 97%, TA: 100%) as determined by a rise in cTnT (maximal value, 0.48 μg/l, interquartile range [IQR]: 0.24 to 0.82 μg/l) and in 77% of the patients (TF: 47%, TA: 95%) as determined by a rise in CK-MB (maximal value, 18.6 μg/l; IQR: 11.0 to 27.4 μg/l). TA approach and baseline renal dysfunction were associated with a higher increase in biomarkers of myocardial injury (p < 0.01 for both). A larger myocardial injury was associated with a smaller improvement of left ventricular ejection fraction (LVEF) (p < 0.01). The degree of rise in cTnT was an independent predictor of cardiac mortality at 9 ± 10 months of follow-up (hazard ratio: 1.14 per each increase of 0.1 μg/l, 95% confidence interval: 1.02 to 1.28, p = 0.028).

Conclusions TAVI was systematically associated with some degree of myocardial injury, with TA approach and baseline renal dysfunction determining a higher increase in biomarkers of myocardial injury. A greater degree of myocardial injury was associated with less improvement in LVEF and a higher cardiac mortality at follow-up (382).

Promoting Global Cardiovascular Health: Ensuring Access to Essential Cardiovascular Medicines in Low- and Middle-Income Countries

On May 13, 2010, a resolution passed at the United Nations for a high-level meeting with heads of state on noncommunicable chronic diseases (NCDs), catapulting NCDs atop the political and health agendas. This meeting on NCDs, slated for September 2011, provides the rare political moment to commit to scaling up international, regional, and national efforts to prevent and treat NCDs, giving the issue the priority it deserves. An analogous high-profile meeting transpired in 2001 on human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS), effectively serving as the nucleating event for a vigorous global and political movement towards universal prevention and treatment. As was the case at the HIV/AIDS meeting, a key priority area in the new NCD movement remains ensuring universal access to reliable, affordable essential medicines to prevent and treat NCDs. The upcoming meeting, therefore, provides the perfect opportunity to capitalize on the increased political and social awareness of NCDs and to apply the lessons learned from the HIV/antiretroviral experience in order to improve access to essential medicines for NCDs. Social mobilization and political advocacy, used in tandem with technical solutions, is an important lesson from the HIV experience, and will likely be important to ensure access to essential medicines for NCDs, including cardiovascular disease. Here, we use cardiovascular disease as a specific case study to examine the issue, outlining early solutions while drawing parallels and analogies to the HIV experience (383).

Intraluminal Thrombus in Facilitated Versus Primary Percutaneous Coronary Intervention: An Angiographic Substudy of the ASSENT-4 PCI (Assessment of the Safety and Efficacy of a New Treatment Strategy With Percutaneous Coronary Intervention) Trial

Objectives This study investigated the occurrence of intraluminal thrombus and its potential implications with facilitated percutaneous coronary interventions (fPCIs).

Background The effect of fPCI on the presence and consequences of intraluminal thrombus is unknown.

Methods Thrombolysis In Myocardial Infarction (TIMI) flow grade, frame count, and thrombus grade; distal embolization; and slow flow in the infarct-related artery were assessed in a blinded fashion on coronary angiograms in 1,342 patients from the ASSENT-4 PCI (Assessment of the Safety and Efficacy of a New Treatment Strategy With Percutaneous Coronary Intervention) trial. Residual TIMI thrombus grade $\geq$2 and/or distal embolization and/or slow flow, reflecting thrombus burden (TB), following PCI were correlated with ST-segment resolution, epicardial blood flow, and clinical outcome. The clinical composite endpoint was death, congestive heart failure, or shock.

Results In the fPCI group, more TIMI flow grade 2/3 in the infarct-related artery at the first angiogram (73.7% vs. 33.4%, $p < 0.001$) and a higher TB following PCI (19.7% vs. 13.4%, $p = 0.002$) were found in comparison with the primary PCI group. Post-PCI TIMI thrombus grade was significantly associated with ST-segment resolution ($p < 0.001$) and TIMI frame count ($p < 0.0001$) in both groups. In the fPCI group, the presence of post-PCI thrombus was associated with a significantly worse outcome at 90 days (clinical composite endpoint: 32.1% vs. 18.6%, $p = 0.023$). Multivariable logistic regression showed that facilitation with tenecteplase ($p = 0.005$) and TB (odds ratio: 2.43, 95% confidence interval: 1.30 to 4.51, $p = 0.0052$) were independent predictors of 90-day mortality.

Conclusions In ASSENT-4 PCI, despite more patency, residual TB was significantly higher in fPCI patients and was associated with less efficient tissue reperfusion and worse clinical outcomes. (A Trial Evaluating the Efficacy and Safety of Tenecteplase Together With Unfractionated Heparin Prior to Early Percutaneous Coronary Intervention [PCI] as Compared to Standard Primary PCI in Patients With Acute Myocardial Infarction [ASSENT-4 PCI]; NCT00168792) (384).

The Incidence of Bradyarrhythmias and Clinical Bradyarrhythmic Events in Patients With Acute Coronary Syndromes Treated With Ticagrelor or Clopidogrel in the PLATO (Platelet Inhibition and Patient Outcomes) Trial: Results of the Continuous Electrocardiographic Assessment Substudy

Objectives The aim of this study was to determine whether ticagrelor increased the risk of ventricular pauses compared with clopidogrel and whether these pauses were associated with any clinical bradycardic events in patients presenting with acute coronary syndromes.

Background Ticagrelor, an oral reversibly binding $P2Y_{12}$ inhibitor, provides more potent and consistent inhibition of platelet aggregation than clopidogrel but in a phase II study was associated with increased risk for ventricular pauses. A prospective continuous electrocardiographic (cECG) assessment was therefore performed within the PLATO (Platelet Inhibition and Patient Outcomes) study comparing ticagrelor and clopidogrel in patients hospitalized with acute coronary syndromes.

Methods Patients in the cECG assessment had planned 7-day cECG recording initiated at the time of randomization (week 1), which was within 24 h of symptom onset, and then repeated at 1 month after randomization during the convalescent phase. The principal safety endpoint was the incidence of ventricular pauses lasting at least 3 s. Investigators also reported symptomatic bradycardic adverse events during the entire study duration (median 277 days).

Results A total of 2,908 patients were included in the cECG assessment, of whom 2,866 (98.5%) had week 1 recordings, 1,991 (68.4%) had 1-month recordings, and 1,949 (67.0%) had both. During the first week after randomization, ventricular pauses $\geq$3 s occurred more frequently in patients receiving ticagrelor than clopidogrel (84 [5.8%] vs. 51 [3.6%]; relative risk: 1.61; $p = 0.006$). At 1 month, pauses $\geq$3 s occurred overall less frequently and were similar between treatments (2.1% vs. 1.7%). Most were ventricular pauses, and the greatest excess associated with ticagrelor were asymptomatic, sinoatrial nodal in origin (66%), and nocturnal. There were no differences between ticagrelor and clopidogrel in the incidence of clinically reported bradycardic adverse events, including syncope, pacemaker placement, and cardiac arrest.

Conclusions In the PLATO cECG assessment, more patients treated with ticagrelor compared with clopidogrel had ventricular pauses, which were predominantly asymptomatic, sinoatrial nodal in origin, and nocturnal and occurred most frequently in the acute phase of acute coronary syndromes. There were no apparent clinical consequences related to the excess in ventricular pauses in patients assigned to ticagrelor. (A Comparison of AZD6140 and Clopidogrel in Patients With Acute Coronary Syndrome [PLATO]; NCT00391872) (385).

The Relationship Between Volumetric Plaque Components and Classical Cardiovascular Risk Factors and the Metabolic Syndrome: A 3-Vessel Coronary Artery Virtual Histology–Intravascular Ultrasound Analysis

Objectives The aim of this study was to analyze volumetric plaque composition of the coronary arterial tree according to the classical cardiovascular risk factors and metabolic

syndrome (MS) using virtual histology–intravascular ultrasound (VH-IVUS).

Background It remains unclear how the cardiovascular risk factors correlate with the histological components of coronary plaques.

Methods "Whole vessel" VH-IVUS analysis was performed in 189 vessels of 63 patients. The components of atherosclerotic plaques were classified as fibrous, fibrofatty, necrotic core (NC), and dense calcium. Quantitative assessment of these plaque components and the presence of VH-IVUS–derived thin-cap fibroatheroma in the coronary arterial trees were compared with cardiovascular risk factors.

Results There was a significantly larger mean plaque-plus-media burden in patients with diabetes mellitus (DM) (47 ± 5% vs. 39 ± 7% in non-DM patients, $p < 0.001$) and MS (47 ± 4% vs. 39 ± 7% in non-MS patients, $p < 0.001$). DM patients had a significantly larger %NC (17.8 ± 5.6% vs. 12.5 ± 6.1%, $p = 0.003$) compared with non-DM patients; and MS patients had a significantly larger %NC (17.3 ± 5.8% vs. 12.8 ± 6.2%, $p = 0.016$) as compared to non-MS patients. Finally, VH-IVUS–derived thin-cap fibroatheromas were more frequent in DM patients (3.4 ± 2.0 vs. 2.1 ± 1.7 in non-DM patients, $p = 0.016$) and in MS patients (4.1 ± 2.1 vs. 1.9 ± 1.4 in non-MS patients, $p = 0.001$).

Conclusions Three-vessel VH-IVUS analysis showed that DM and MS patients, compared to patients without DM or MS, had a larger plaque-plus-media burden, larger amount of NC, and more frequent VH-IVUS–derived thin-cap fibroatheromas in coronary arterial trees, implying greater plaque vulnerability in DM and MS patients (386).

The Relationship Between Attenuated Plaque Identified by Intravascular Ultrasound and No-Reflow After Stenting in Acute Myocardial Infarction: The HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) Trial

Objectives The aim of this study was to understand the impact of attenuated plaque on distal embolization during stent implantation in patients with acute myocardial infarction (AMI).

Background Attenuated plaques identified by grayscale intravascular ultrasound (IVUS) might predict transient deterioration in coronary flow and/or no-reflow during percutaneous coronary intervention (PCI).

Methods We analyzed clinical, angiographic, and IVUS data from 364 patients (n = 364 infarct-related arteries) enrolled in the randomized HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trial. No-reflow was final Thrombolysis In Myocardial Infarction (TIMI) flow grade ≤2 in the absence of mechanical obstruction. Attenuated plaque was hypoechoic or mixed atheroma with ultrasound attenuation without calcification. A mean attenuation score was created by measuring the angle of attenuation each 1 mm, scoring the angle as 1 to 4 (corresponding to <90°, 90° to 180°, 180° to 270°, or 270° to 360°, respectively), summing the scores, and normalizing for analysis length.

Results Overall, 284 (78.0%) patients had attenuated plaques; no-reflow occurred in 37 (10.2%). Patients with no-reflow had a higher mean attenuation score (median [interquartile range] 2.2 [0.0 to 2.8] vs. 1.3 [0.7 to 1.8], $p < 0.001$), lower baseline left ventricular ejection fraction (52.8% [43.2% to 61.5%] vs. 61.4% [52.2% to 68.1%], $p = 0.002$), and more baseline angiographic thrombus (89.2% vs. 74.1%, $p = 0.043$) with no differences in post-PCI stent expansion versus patients without no-reflow. Multivariate analysis indicated that mean attenuation score was the strongest predictor of no-reflow. The mean attenuation score that best predicted no-reflow was ≥2 points (90° to 180°, sensitivity of 81.5%, and specificity of 80.5%).

Conclusions Attenuated plaque was present in three-quarters of patients with AMI. The amount of attenuated plaque strongly correlated with no-reflow; the larger the attenuated plaque, the greater the likelihood of no-reflow. (Dual Arm Factorial Randomized Trial in Patients w/ST Segment Elevation AMI to Compare the Results of Using Anticoagulation With Either Unfractionated Heparin + Routine GP IIb/IIIa Inhibition or Bivalirudin + Bail-out GP IIb/IIIa Inhibition; and Primary Angioplasty with stent implantation with Either a Slow Rate-release Paclitaxel-eluting Stent [TAXUS™] or Uncoated Bare Metal Stent [EXPRESS2™]; NCT00433966) (387).

Assessment of Echo-Attenuated Plaque by Optical Coherence Tomography and its Impact on Post-Procedural Creatine Kinase-Myocardial Band Elevation in Elective Stent Implantation

Objectives This study examined morphological characteristics of echo-attenuated plaques by optical coherence tomography (OCT) and evaluated their influence on creatine kinase-myocardial band (CK-MB) elevation after percutaneous coronary intervention (PCI) in patients with elective stent implantation.

Background Recent intravascular ultrasound studies have described atherosclerotic plaques with echo attenuation (EA) without associated bright echoes that are correlated with no-reflow phenomenon after PCI.

Methods We studied 135 native de novo culprit coronary lesions in 135 patients with normal pre-PCI CK-MB levels (28 with unstable angina; 107 with stable angina) who underwent intravascular ultrasound and OCT examinations before elective stent implantation. The lesions were divided into 2 groups based on the presence or absence of EA, and OCT findings were compared. We then determined predictors of post-PCI CK-MB elevation.

Results EA was found in 47 (34.8%) lesions and was associated with the presence of OCT-derived thin-capped fibroatheroma, ruptured plaques, greater lipid content,

intravascular ultrasound–derived large reference and plaque area, lesion eccentricity, and microcalcification. Elevated CK-MB levels were observed in 36 (26.7%) lesions, and significantly more frequently in lesions with EA than without. In multivariable analysis, EA (odds ratio [OR]: 3.49; 95% confidence interval [CI]: 1.53 to 7.93; p = 0.003) and OCT-derived ruptured plaque (OR: 2.92; 95% CI: 1.21 to 7.06; p = 0.017) were independent predictors of post-PCI CK-MB elevation.

Conclusions Atherosclerotic plaques with EA were associated with characteristics considered to be high risk or unstable. OCT examination showed an additive predictive value to the presence of EA for post-PCI CK-MB elevation (388).

Early and Long-Term Outcomes After Combined Percutaneous Revascularization in Patients With Carotid and Coronary Artery Stenoses

Objectives This study sought to evaluate the 30-day and long-term clinical outcomes of patients with carotid obstructive disease (COD) and concomitant coronary artery disease (CAD) undergoing a combined percutaneous revascularization, in 4 high-volume centers skilled for the treatment of multilevel vascular disease.

Background The optimal management of patients with COD and concomitant CAD remains controversial. A variety of therapeutic strategies, including coronary artery bypass grafting, alone or in combination with carotid artery revascularization, have been reported.

Methods Between January 2006 and April 2010, 239 consecutive patients with COD (symptomatic carotid stenosis in 20.5%) and concomitant CAD were treated with staged or simultaneous carotid artery stenting and percutaneous coronary intervention, and enrolled in this prospective registry. The primary endpoint was the incidence of major cardiac and cerebrovascular events, including any death, myocardial infarction, or stroke occurring between the first revascularization procedure and 30 days after treatment of the second vascular territory affected.

Results The incidence of the primary endpoint at 30 days was 4.2% (95% confidence interval [CI]: 2.02 to 7.56). The rate of death, myocardial infarction, and stroke at long-term follow-up (median 520 days) was 4.2%, 2.1%, and 3.8%, respectively. At long-term follow-up, patients with previous cardiovascular disease had significantly higher rates of major cardiac and cerebrovascular events than did patients with a first clinical episode (17% vs. 6%, hazard ratio: 3.34; 95% CI: 1.46 to 7.63; p = 0.004).

Conclusions In patients with COD and concomitant CAD, a combined percutaneous treatment compares favorably with previous surgical or hybrid experiences. Such strategy may be particularly suited to complex patients at high surgical risk (389).

The Impact of Pravastatin Pre-Treatment on Periprocedural Microcirculatory Damage in Patients Undergoing Percutaneous Coronary Intervention

Objectives This study evaluated the effect of pravastatin pre-treatment on post-procedural index of microcirculatory resistance (IMR) values that are introduced for assessing the status of the microcirculation independently of the epicardial area.

Background Pre-treatment with statins decreased the incidence of cardiac enzyme increase after percutaneous coronary intervention (PCI). However, 2 different etiologies, distal embolization of atheroma or ischemia caused by side-branch occlusion, cannot be differentiated by measuring cardiac enzyme levels.

Methods Eighty patients with stable angina were randomly assigned to either pravastatin treatment (20 mg/day, n = 40) or no treatment (n = 40) 4 weeks before elective PCI. An intracoronary pressure/temperature sensor-tipped guidewire was used. Thermodilution curves were obtained during maximal hyperemia. The IMR was calculated from the ratio of the mean distal coronary pressure at maximal hyperemia to the inverse of mean hyperemic transit time. Creatine kinase-myocardial band and troponin I values were measured at baseline and at 8 and 24 h after PCI.

Results Post-PCI troponin I levels tended to be lower in patients with pravastatin treatment (median: 0.13 [interquartile range (IQR): 0.10 to 0.31] vs. 0.22 [IQR: 0.10 to 0.74] ng/ml, p = 0.1). However, patients with pravastatin treatment had significantly lower IMR than did patients without pravastatin treatment (median: 12.6 [IQR: 8.8 to 18.0] vs. 17.6 [IQR: 9.7 to 33.9], p = 0.007). Multivariate analysis revealed that the lack of pravastatin pre-treatment was the only independent predictor of post-PCI impaired IMR (p = 0.03).

Conclusions Post-PCI measurement of the IMR confirmed that pre-treatment with pravastatin was associated with reduced microvascular dysfunction induced by PCI regardless of side branch occlusions. These data suggest that pre-treatment with statin is desired in patients undergoing elective PCI. (The Impact of Pravastatin Pretreatment on Periprocedural Microcirculatory Damage After Percutaneous Coronary Intervention; UMIN000002885) (390).

Long-Term Safety and Efficacy of Paclitaxel-Eluting Stents: Final 5-Year Analysis From the TAXUS Clinical Trial Program

Objectives These studies sought to evaluate the clinical outcomes of the slow-release Taxus paclitaxel-eluting stent (PES) versus an otherwise identical bare-metal stent (BMS).

Background Prior studies were not individually powered to generate reliable estimates of low-frequency safety endpoints or to characterize the long-term safety and efficacy profile of PES.

Methods The completed 5-year databases from the prospective, randomized, double-blind TAXUS I, II, IV, and V trials were pooled for a patient-level analysis.
Results The study population comprised 2,797 randomized patients (1,400 PES and 1,397 BMS). At the end of the 5-year study period, PES compared with BMS significantly reduced the rate of ischemia-driven target lesion revascularization (12.3% vs. 21.0%, $p < 0.0001$), with consistent reductions across high-risk subgroups and in patients with and without routine angiographic follow-up. There were no significant differences between the stent types in the 1-year or cumulative 5-year rates of death or myocardial infarction (MI). However, cardiac death or MI between 1 and 5 years was increased with PES (6.7% vs. 4.5%, $p = 0.01$), as was stent thrombosis (protocol definition: 0.9% vs. 0.2%, $p = 0.007$; ARC definition: 1.4% vs. 0.9%, $p = 0.18$).
Conclusions In this pooled patient-level analysis from the prospective, randomized, double-blind TAXUS trials, PES compared with BMS resulted in a durable 47% reduction in the 5-year rate of ischemia-driven target lesion revascularization in simple and complex lesions, with nonsignificant differences in the cumulative 5-year rates of death or MI. Between 1 and 5 years, however, the rates of cardiac death or MI and protocol-defined stent thrombosis were increased with PES (391).

Troponin T Levels and Infarct Size by SPECT Myocardial Perfusion Imaging

Objectives To evaluate the relationship between serial cardiac troponin T (cTnT) levels with infarct size and left ventricular ejection fraction by gated single-photon emission computed tomography myocardial perfusion imaging (SPECT-MPI) in patients with acute myocardial infarction (AMI).
Background Current guidelines recommend the use of cTnT as the biomarker of choice for the diagnosis of AMI. Data relating cTnT to SPECT-MPI in patients with AMI are limited.
Methods A subset of patients with their first AMI participating in a community-based cohort of AMI in Olmsted County, Minnesota, were prospectively studied. Serial cTnT levels were evaluated at presentation, <12 h and 1, 2, and 3 days after onset of pain. Peak cTnT was defined as the maximum cTnT value.
Results A total of 121 patients (age, 61 ± 13 years; 31% women) with AMI underwent gated SPECT-MPI at a median (25th percentile, 75th percentile) of 10 (5, 15) days post-AMI. The type of infarct was non–ST-segment elevation myocardial infarction in 61%, and 13% were anterior in location. The median infarct size was 1% (0%, 11%) and the median gated left ventricular ejection fraction was 54% (47%, 60%). Fifty-nine patients (49% of the population) had no measurable infarction by SPECT-MPI. Independent predictors of measurable SPECT-MPI infarct size included cTnT at days 1, 2, and 3 and peak cTnT, but not at presentation or <12 h. In receiver-operator characteristic analysis, the area under the curve was highest at day 3. Receiver-operator characteristic analysis demonstrated a cutoff of 1.5 ng/ml for peak cTnT for the detection of measurable infarct size.
Conclusions In a community-based cohort of patients with their first AMI, independent predictors of measurable SPECT-MPI infarct size included cTnT at days 1, 2, and 3 and peak cTnT. In contrast, cTnT level at presentation and <12 h was not an independent predictor of myocardial infarction size as assessed by SPECT-MPI. Receiver-operator characteristic analysis demonstrated a cutoff value peak cTnT of 1.5 ng/ml for the detection of measurable infarct (392).

Clinical Evaluation of the Resolute Zotarolimus-Eluting Coronary Stent System in the Treatment of De Novo Lesions in Native Coronary Arteries: The RESOLUTE US Clinical Trial

Objectives The RESOLUTE US (R-US) trial is a prospective, observational study designed to evaluate the clinical effectiveness of the Resolute zotarolimus-eluting stent (R-ZES) in a U.S. population.
Background The R-ZES releases zotarolimus over a 6-month period in order to achieve optimal clinical effectiveness and safety.
Methods The R-US trial recruited patients with de novo native coronary lesions suitable for 1- or 2-vessel treatment with stents from 2.25 to 4.0 mm in diameter. In the main analysis cohort (2.5- to 3.5-mm stents and single-lesion treatment), the primary endpoint was 12-month target lesion failure (TLF) defined as the composite of cardiac death, myocardial infarction (MI), and clinically-driven target lesion revascularization (TLR), compared with data from Endeavor zotarolimus-eluting stent (E-ZES) trials, adjusting for baseline covariates through propensity scores.
Results Overall, 1,402 patients were enrolled with a mean reference vessel diameter of 2.59 ± 0.47 mm and diabetes prevalence of 34.4%. In the main analysis cohort, TLF was 3.7% at 12 months compared with historical E-ZES results (TLF = 6.5%). The R-ZES met the 3.3% margin of non-inferiority (rate difference = −2.8%, upper 1-sided 95% confidence interval: −1.3%, $p < 0.001$). The overall TLF rate was 4.7%, and rates of cardiac death, MI, and TLR were 0.7%, 1.4%, and 2.8%, respectively. The 12-month rate of stent thrombosis was 0.1%.
Conclusions The R-ZES achieved a very low rate of clinical restenosis while maintaining low rates of important clinical safety events such as death, MI, and stent thrombosis at 1-year follow-up. (The Medtronic RESOLUTE US Clinical Trial [R-US]; NCT00726453) (393).

Pericardial Fat Is Associated With Atrial Fibrillation Severity and Ablation Outcome

Objectives The aim of this study was to characterize the relationship between pericardial fat and atrial fibrillation (AF).

Background Obesity is an important risk factor for AF. Pericardial fat has been hypothesized to exert local pathogenic effects on nearby cardiac structures above and beyond that of systemic adiposity.
Methods One hundred ten patients undergoing first-time AF ablation and 20 reference patients without AF underwent cardiac magnetic resonance imaging for the quantification of periatrial, periventricular, and total pericardial fat volumes using a previously validated technique. Together with body mass index and body surface area, these were examined in relation to the presence of AF, the severity of AF, left atrial volume, and long-term AF recurrence after ablation.
Results Pericardial fat volumes were significantly associated with the presence of AF, AF chronicity, and AF symptom burden (all p values <0.05). Pericardial fat depots were also predictive of long-term AF recurrence after ablation ($p = 0.035$). Finally, pericardial fat depots were also associated with left atrial volume (total pericardial fat: $r = 0.46$, $p < 0.001$). Importantly, these associations persisted after multivariate adjustment and additional adjustment for body weight. In contrast, however, systemic measures of adiposity, such as body mass index and body surface area, were not associated with these outcomes in multivariate-adjusted models.
Conclusions Pericardial fat is associated with the presence of AF, the severity of AF, left atrial volumes, and poorer outcomes after AF ablation. These associations are both independent of and stronger than more systemic measures of adiposity. These findings are consistent with the hypothesis of a local pathogenic effect of pericardial fat on the arrhythmogenic substrate supporting AF (394).

A Prospective, Randomized Evaluation of a Novel Everolimus-Eluting Coronary Stent: The PLATINUM (A Prospective, Randomized, Multicenter Trial to Assess an Everolimus-Eluting Coronary Stent System [PROMUS Element] for the Treatment of up to Two De Novo Coronary Artery Lesions) Trial

Objectives We sought to evaluate the clinical outcomes with a novel platinum chromium everolimus-eluting stent (PtCr-EES) compared with a predicate cobalt chromium everolimus-eluting stent (CoCr-EES) in patients undergoing percutaneous coronary intervention (PCI).
Background Randomized trials have demonstrated an excellent safety and efficacy profile for the CoCr-EES. The PtCr-EES uses the identical antiproliferative agent and polymer but with a novel platinum chromium scaffold designed for enhanced deliverability, vessel conformability, side-branch access, radiopacity, radial strength, and fracture resistance.
Methods A total of 1,530 patients undergoing PCI of 1 or 2 de novo native lesions were randomized at 132 worldwide sites to CoCr-EES ($n = 762$) or PtCr-EES ($n = 768$). The primary endpoint was the 12-month rate of target lesion failure (TLF), the composite of target vessel-related cardiac death, target vessel-related myocardial infarction (MI), or ischemia-driven target lesion revascularization (TLR) in the per-protocol population (patients who received ≥ 1 assigned study stent), powered for noninferiority.
Results The 12-month rate of TLF in the per-protocol population occurred in 2.9% versus 3.4% of patients assigned to CoCr-EES versus PtCr-EES, respectively (difference: 0.5%, 95% confidence interval: −1.3% to 2.3%, $p_{noninferiority} = 0.001$, $p_{superiority} = 0.60$). By intention-to-treat, there were no significant differences between CoCr-EES and PtCr-EES in the 12-month rates of TLF (3.2% vs. 3.5%, $p = 0.72$), cardiac death or MI (2.5% vs. 2.0%, $p = 0.56$), TLR (1.9% vs. 1.9%, $p = 0.96$), or Academic Research Consortium definite or probable stent thrombosis (0.4% vs. 0.4%, $p = 1.00$).
Conclusions In this large-scale, prospective, single-blind randomized trial, a novel PtCr-EES was noninferior to the predicate CoCr-EES for TLF, with nonsignificant differences in measures of safety and efficacy through 12-month follow-up after PCI. (A Prospective, Randomized, Multicenter Trial to Assess an Everolimus-Eluting Coronary Stent System [PROMUS Element] for the Treatment of up to Two De Novo Coronary Artery Lesions: NCT00823212) (395).

2-Year Follow-Up of Patients Undergoing Transcatheter Aortic Valve Implantation Using a Self-Expanding Valve Prosthesis

Objectives The purpose of this study was to evaluate the safety, device performance, and clinical outcome up to 2 years for patients undergoing transcatheter aortic valve implantation (TAVI).
Background The role of TAVI in the treatment of calcific aortic stenosis evolves rapidly, but mid- and long-term results are scarce.
Methods We conducted a prospective, multicenter, single-arm study with symptomatic patients undergoing TAVI for treatment of severe aortic valve stenosis using the 18-F Medtronic CoreValve (Medtronic, Minneapolis, Minnesota) prosthesis.
Results In all, 126 patients (mean age 82 years, 42.9% male, mean logistic European System for Cardiac Operative Risk Evaluation score 23.4%) with severe aortic valve stenosis (mean gradient 46.8 mm Hg) underwent the TAVI procedure. Access was transfemoral in all but 2 cases with subclavian access. Retrospective risk stratification classified 54 patients as moderate surgical risk, 51 patients as high-risk operable, and 21 patients as high-risk inoperable. The overall technical success rate was 83.1%. Thirty-day all-cause mortality was 15.2%, without significant differences in the subgroups. At 2 years, all-cause mortality was 38.1%, with a significant difference between the moderate-risk group and the combined high-risk groups (27.8% vs. 45.8%, $p = 0.04$). This difference was mainly attributable to an increased risk of

noncardiac mortality among patients constituting the high-risk groups. Hemodynamic results remained unchanged during follow-up (mean gradient: 8.5 ± 2.5 mm Hg at 30 days and 9.0 ± 3.4 mm Hg at 2 years). Functional class improved in 80% of patients and remained stable over time. There was no incidence of structural valve deterioration.

Conclusions The TAVI procedure provides sustained clinical and hemodynamic benefits for as long as 2 years for patients with symptomatic severe aortic stenosis at increased risk for surgery (396).

Relation Between Hyperinsulinemia and Nonculprit Plaque Characteristics in Nondiabetic Patients With Acute Coronary Syndromes

Objectives We sought to assess whether hyperinsulinemia is associated with percentage lipid and coronary plaque burden in nondiabetic patients with acute coronary syndromes (ACS).

Background Hyperinsulinemia carries an increased risk of cardiovascular disease even in pre-diabetic patients, but the precise mechanisms of its effects remain unclear.

Methods Nonculprit coronary lesions associated with mild-to-moderate stenosis in 82 nondiabetic patients with ACS were examined by integrated backscatter intravascular ultrasound (IB-IVUS), using a 40-MHz intravascular catheter. Conventional IVUS and IB-IVUS measurements from the worst 10-mm segment (1-mm intervals) were calculated. All patients underwent a 75-g oral glucose tolerance test (OGTT) to calculate the area under the insulin concentration-time curve (AUC insulin) from 0 to 120 min.

Results Patients in the high tertile of AUC insulin had a significantly greater percentage lipid area and absolute lipid volume than did patients in the intermediate and low tertiles (tertile 3 vs. tertile 2 vs. tertile 1; 37.6 ± 16.6% vs. 25.8 ± 11.9% vs. 27.5 ± 14.7%, $p < 0.01$ by analysis of variance [ANOVA], and 29.9 ± 22.6 mm^3 vs. 15.3 ± 12.6 mm^3 vs. 17.7 ± 12.7 mm^3, $p < 0.01$ by ANOVA, respectively) and a smaller percentage fibrosis area (55.0 ± 11.5% vs. 61.7 ± 9.4% vs. 60.7 ± 9.4%, $p = 0.03$ by ANOVA). Multiple regression analysis showed that the high tertile of AUC insulin was independently associated with an increased percentage lipid area ($p < 0.05$). On conventional IVUS analysis, external elastic membrane cross-sectional area was significantly increased with greater plaque volume in patients in the high tertile of AUC insulin (both $p < 0.05$ by ANOVA).

Conclusions Hyperinsulinemia is associated with an increased lipid content and a greater plaque volume of nonculprit intermediate lesions in nondiabetic patients with ACS, suggesting that plaque vulnerability is increased in this subgroup of patients (397).

Multidetector Computed Tomography in Transcatheter Aortic Valve Implantation

Aortic stenosis is a common disorder. Aortic valve replacement is indicated in symptomatic patients with severe aortic stenosis, as the prognosis of untreated patients is poor. Nevertheless, many patients pose a prohibitively high surgical risk and are not candidates for surgical valve replacement. Transcatheter aortic valve implantation (TAVI) is a novel method to treat selected high-risk patients with aortic stenosis. Patient screening and anatomic measurements of the aortic root are of great importance to ensure procedural success and appropriate patient selection. Multidetector computed tomography (CT) is playing an increasingly important role in patient screening protocols before TAVI, provides detailed anatomic assessment of the aortic root and valve annulus, assesses the suitability of iliofemoral access, and determines appropriate coaxial angles to optimize the valve implantation procedure. Additionally, CT is providing a greater understanding of medium-term valve durability and integrity. This review outlines an evolving role for CT angiography in support of a TAVI program and describe step by step how CT can be used to enhance the procedure and provide a practical guide for the utilization of CT angiography in support of a transcatheter aortic valve program (398).

Synchronicity of LV Contraction as a Determinant of LV Twist Mechanics: Serial Speckle-Tracking Analyses in WPW Syndrome Before and After Radiofrequency Catheter Ablation

Objectives This study set out to investigate the isolated impact of synchronous patterns of left ventricular (LV) contraction (i.e., LV synchronicity) on LV twist behavior.

Background Although the relationships between LV loading status/LV contractility and twist are well-established, no data are available regarding the relation between LV twist and LV synchronicity, without any interference by changes in LV pre-load, afterload, and contractility. Serial assessment of patients with Wolff-Parkinson-White syndrome before and after radiofrequency catheter ablation (RFCA) allows this to be explored.

Method Of the 40 Wolff-Parkinson-White patients initially screened, 34 were enrolled. Two-dimensional and Doppler echocardiography along with speckle tracking-derived LV twist mechanics, apical-basal rotation delay, and left ventricular dyssynchrony index (LVdys) were obtained before and after RFCA. The LVdys was defined as the maximal delay in time-to-peak radial strain of different LV segments at the papillary muscle level.

Results Overall, no significant changes were demonstrated in LV volumes, systolic and diastolic function, and end-systolic wall stress before versus after RFCA. After RFCA, median value of LVdys was attenuated from 33.5 (interquartile range [IQR]: 14.0 to 84.3) to 14.0 (IQR: 11.5 to 21.8) ($p = 0.002$), which was accompanied by a reduction in apical-basal rotation delay from 9.7% (IQR: 3.5 to 23.7) to 3.3% (IQR: 1.3 to 8.0) ($p = 0.004$). In contrast, LV twist

increased from 14.2° (IQR: 9.1° to 18.4°) before to 19.7° (IQR: 15.0° to 22.6°) after RFCA (p = 0.002). Delta LV twist pre- to post-RFCA displayed a significant inverse correlation with changes in apical-basal rotation delay ($r = -0.42$, p = 0.01) and Delta LVdys ($r = -0.39$, p = 0.02).

Conclusions The LV synchronous contraction is significantly related to LV twist (399).

Platelet Inhibition by Adjunctive Cilostazol Versus High Maintenance-Dose Clopidogrel in Patients With Acute Myocardial Infarction According to Cytochrome P450 2C19 Genotype

Objectives The aim of this study was to assess the degree of platelet inhibition by adjunctive cilostazol in patients with acute myocardial infarction (AMI) according to hepatic cytochrome P450 *2C19* (*CYP2C19)* genotype.

Background Although adjunctive cilostazol intensifies platelet inhibition in AMI patients, it is not established whether this regimen can be free from the effect of *CYP2C19* loss-of-function variants (*2/*3).

Methods We randomly assigned 126 AMI patients with available *CYP2C19* genotyping to receive adjunctive cilostazol (triple group; n = 64) or high maintenance-dose (MD) clopidogrel of 150 mg/day (high-MD group; n = 62). Using conventional aggregometry and VerifyNow (Accumetrics Inc., San Diego, California), platelet reactivity was measured at pre-discharge and 30-day follow-up. Primary endpoint was change in maximal platelet aggregation (ΔAgg_{max}) between pre-discharge and 30-day follow-up. High on-treatment platelet reactivity (HPR) was defined as 20 μmol/l adenosine diphosphate–induced maximal platelet aggregation (Agg_{max}) >59%.

Results In noncarriers, despite numerically greater inhibition by adjunctive cilostazol, changes in platelet measures and the rate of HPR did not significantly differ between the 2 groups. In carriers, ΔAgg_{max} after 5 and 20 μmol/l adenosine diphosphate stimuli was significantly higher in the triple (n = 39) versus high-MD group (n = 38) (21.8 ± 13.9% vs. 9.0 ± 13.3%, p < 0.001, and 24.2 ± 17.2% vs. 7.7 ± 15.5%, p < 0.001, respectively). Likewise, changes in late platelet aggregation and P2Y12 reaction unit were consistently greater in the triple versus high-MD group. Fewer patients in the triple group met the criteria of HPR at 30-day follow-up than in the high-MD group (15.4% vs. 44.7%, p = 0.005).

Conclusions Compared with high-MD clopidogrel, adjunctive cilostazol significantly enhances platelet inhibition and reduces the rate of HPR, especially in AMI patients with *CYP2C19* loss-of-function variants. (Adjunctive Cilostazol Versus High Maintenance-Dose Clopidogrel in Acute Myocardial Infarction (AMI) Patients According to *CYP2C19* Polymorphism [ACCE-LAMI2C19]; NCT00915733) (400).

High Doses of Clopidogrel to Overcome Genetic Resistance: The Randomized Crossover CLOVIS-2 (Clopidogrel and Response Variability Investigation Study 2)

Objectives This study sought to determine whether the pharmacokinetic (PK) and pharmacodynamic (PD) responses to high or standard clopidogrel loading doses (LDs) differ according to *CYP2C19*2* allele.

Background *CYP2C19* loss-of-function alleles are associated with reduced responsiveness to standard clopidogrel doses.

Methods Young post-myocardial infarction patients heterozygous (wild type [wt]/*2, n = 43) or homozygous (*2/*2, n = 8) for the *CYP2C19*2* genetic variant were matched with patients not carrying the variant (wt/wt, n = 58). All patients were randomized to a 300- or 900-mg clopidogrel LD. The relative reduction in residual platelet aggregation (RR-RPA, %) and the area under the plasma concentration time curve of active metabolite from baseline to 6 h after loading (AUC_{0-6}) were compared according to both LD and *CYP2C19*2* carriage.

Results The 300-mg LD led to a gene-dose effect for RR-RPA (−65.7% ± 35.9% in wt/wt vs. −48.0% ± 38.4% in wt/*2 vs. −14.6% ± 32.4% in *2/*2; overall p value = 0.003, p = 0.03 for wt/wt versus wt/*2, p = 0.04 for wt/*2 versus *2/*2) with minor effect in *2/*2 carriers. After the 900-mg LD, the effect of the *CYP2C19*2* variant on platelet inhibition was fully compensated in wt/*2 carriers but not in *2/*2 carriers (−83.6% ± 25.8% in wt/wt vs.−77.2% ± 26.9% in wt/*2 vs. −29.5% ± 26.8% in *2/*2; overall p value = 0.0003, p = 0.20 for wt/wt versus wt/*2, p < 0.001 for wt/*2 versus *2/*2). A similar pattern was observed for the active metabolite AUC_{0-6} according to carriage of *CYP2C19*2* for both LDs. There was a significant correlation between PK and PD responses irrespective of the LD.

Conclusions Carriers of *CYP2C19*2* display significantly lower responses to clopidogrel with a gene-dose effect. Clopidogrel resistance can be overcome by increasing the dose in heterozygous carriers but not in homozygous carriers. (Clopidogrel and Response Variability Investigation Study 2 [CLOVIS-2]; NCT00822666) (401).

Trends, Predictors, and Outcomes of Cerebrovascular Events Related to Percutaneous Coronary Intervention: A 16-Year Single-Center Experience

Objectives We sought to determine trends, predictors, in-hospital and long-term outcomes of cerebrovascular events (CVE) related to percutaneous coronary intervention (PCI) over a 16-year period.

Background Despite a temporal increase in patient risk profile and procedural complexity, rates of PCI-related mortality and myocardial infarction have decreased. Temporal trends, characterization, and outcomes after PCI-related CVE in the contemporary era remain unknown.

Methods We performed a retrospective study of 24,126 PCI hospitalizations in 19,165 unique patients, between January 1, 1994, and December 31, 2009, and compared those who suffered an in-hospital PCI-CVE with the remaining control population who did not.
Results The incidence of CVE was 0.37% (n = 89), of which 22% were transient ischemic attacks. Temporal analysis showed no significant trend in incidence over 16 years (p = 0.47). Multiple clinical and angiographic predictors of PCI-CVE were identified. Multivariate logistic regression analyses revealed age, female sex, myocardial infarction within 7 days before PCI, and history of prior CVE as independent predictors of PCI-CVE, with a 19-fold increase in incidence in patients over 80 with a prior CVE history. In-hospital mortality was 19% after PCI-CVE versus 2% in controls (p < 0.001). Those who survived PCI-CVE exhibited a markedly higher risk of mortality over the subsequent 10 years (p < 0.001).
Conclusions The incidence of PCI-related CVE has remained steady over a 16-year period, despite an increase in the baseline risk profile. Age and prior history of CVE were the strongest independent demographic predictors. PCI-CVE had a markedly adverse impact on early and late outcomes (402).

Randomized Comparison of a Polymer-Free Sirolimus-Eluting Stent Versus a Polymer-Based Paclitaxel-Eluting Stent in Patients With Diabetes Mellitus: The LIPSIA Yukon Trial

Objectives The objective of the study was to assess non-inferiority of the polymer-free sirolimus-eluting Yukon Choice stent (Translumina GmbH, Hechingen, Germany) compared with the polymer-based Taxus Liberté stent (Boston Scientific, Natick, Massachusetts) with regard to the primary endpoint, in-stent late lumen loss, at 9 months in patients with diabetes mellitus.
Background The Yukon Choice stent has been evaluated in several randomized controlled trials before, albeit to date, there has been no trial that exclusively enrolled patients with diabetes mellitus.
Methods Patients with diabetes mellitus undergoing percutaneous coronary intervention for clinically significant de novo coronary artery stenosis were randomized 1:1 to receive either the polymer-free sirolimus-eluting Yukon Choice stent or the polymer-based paclitaxel-eluting Taxus Liberté stent.
Results A total of 240 patients were randomized. Quantitative coronary angiography was available for 79% of patients. Mean in-stent late lumen loss was 0.63 ± 0.62 mm for the Yukon Choice stent and 0.45 ± 0.60 mm for the Taxus Liberté stent. Based on the pre-specified margin, the Yukon Choice stent failed to show noninferiority for the primary endpoint. During follow-up, there were no significant differences between groups regarding death, myocardial infarction, stent thrombosis, target lesion revascularization, target vessel revascularization, or nontarget vessel revascularization.
Conclusions Compared with the Taxus Liberté stent, the polymer-free sirolimus-eluting Yukon Choice stent failed to show noninferiority with regard to the primary endpoint, in-stent late lumen loss, in patients with diabetes mellitus after 9-month follow-up. Both stents showed comparable clinical efficacy and safety. (Yukon Choice Versus Taxus Liberté in Diabetes Mellitus; NCT00368953) (403).

First-in-Human Evaluation of a Novel Robotic-Assisted Coronary Angioplasty System

Objectives We aimed to evaluate the safety and feasibility of a robotic angioplasty system in delivery and manipulation of coronary guidewires, balloons, and stents in patients undergoing elective percutaneous coronary intervention (PCI).
Background A remote-control, robotic-assisted angioplasty system is under development to address some of the procedural challenges and occupational hazards associated with traditional PCI.
Methods Patients with coronary artery disease and clinical indication for elective PCI were enrolled. The coronary angioplasty procedure was performed with the CorPath 200 robotic system (Corindus, Inc., Natick, Massachusetts). The system consists of a remote interventional cockpit and a multicomponent bedside unit that enables the operator to advance, retract, and rotate guidewires and rapid exchange catheters. The primary endpoint was device clinical success (≤30% residual stenosis) without in-hospital major adverse cardiac events. Technical success was defined as the ability of the system to complete all the planned angioplasty steps on the basis of procedural segments. Patients were followed up to 30 days after angioplasty procedure.
Results A total of 8 patients were enrolled in the study. The primary endpoint was achieved in all patients (100%). The technical success of the robotic system was 97.9% in completing 47 of 48 planned steps. There were no device- or procedure-related complications and no in-hospital or 30-day major adverse cardiac events. The operators rated the robotic system performances as equal to or better than manual procedures in 97.5% of the cases. The operator radiation exposure was 97% lower than the levels found at the standard table position.
Conclusions Early clinical experience with a robotic-assisted angioplasty system demonstrated feasibility, safety, and procedural effectiveness comparable to manual operation. In addition, the total operator exposure to radiation was significantly low. A larger study is warranted to verify the safety and effectiveness of robotic-assisted percutaneous coronary intervention (404).

Impact of Bleeding on Subsequent Early and Late Mortality After Drug-Eluting Stent Implantation

Objectives The aim of this study was to assess the impact of early and late bleeding on subsequent mortality after drug-eluting stent (DES) implantation.

Background Little is known about the impact of late bleeding after DES implantation.
Methods With a time-updated Cox model, the impact of bleeding and myocardial infarction (MI) on 3-year mortality was analyzed in 3,148 consecutive patients who underwent DES implantation for coronary disease.
Results Bleeding, defined according to STEEPLE (Safety and Efficacy of Enoxaparin in PCI Patients, an International Randomized Evaluation) minor or major criteria, occurred in 6.5% of patients over 3 years. Patients with bleeding were older; were more likely to be female; had higher rates of diabetes mellitus, hypertension, and extensive coronary disease and lower ventricular function; and underwent more complex procedures than those without bleeding. The 3-year adjusted hazard ratios (HRs) for mortality were 5.81 (95% confidence interval [CI]: 3.92 to 8.60; $p < 0.001$) for patients with bleeding and 2.53 (95% CI: 1.62 to 3.96; $p < 0.001$) for patients with MI. When the timings of events were separated, the HRs for mortality were 4.89 (95% CI: 3.08 to 7.78; $p < 0.001$) and 7.81 (95% CI: 4.39 to 13.89; $p < 0.001$) for patients with bleeding within and after 30 days, respectively. By contrast, the HRs for mortality were 1.85 (95% CI: 1.09 to 3.14, $p = 0.022$) and 10.33 (95% CI: 4.91 to 21.75, $p < 0.001$) for patients with MI within and after 30 days, respectively.
Conclusions Bleeding is closely associated with mortality during both the early and late periods after DES implantation. Therefore, in addition to carefully assessing bleeding after stenting, evidence-based treatment should be implemented to offer the best balance of benefit and harm (405).

The Prognostic Utility of the SYNTAX Score on 1-Year Outcomes After Revascularization With Zotarolimus- and Everolimus-Eluting Stents: A Substudy of the RESOLUTE All Comers Trial

Objectives This study assessed the ability of the SYNTAX score (SXscore) to stratify risk in patients treated with percutaneous coronary intervention (PCI) using zotarolimus-eluting or everolimus-eluting stents.
Background The SXscore can identify patients treated with PCI who are at highest risk of adverse events.
Methods The SXscore was calculated prospectively in 2,033 of the 2,292 patients enrolled in the RESOLUTE All Comers study (RESOLUTE III All Comers Trial: A Randomized Comparison of a Zotarolimus-Eluting Stent With an Everolimus-Eluting Stent for Percutaneous Coronary Intervention). Clinical outcomes in terms of a patient-oriented composite endpoint (POCE) of all-cause death, myocardial infarction (MI), and repeat revascularization; the individual components of POCE; target lesion failure (TLF) (a composite of cardiac death, target-vessel MI, and clinically driven target lesion revascularization); and stent thrombosis were subsequently stratified according to SXscore tertiles: $SXscore_{LOW} \leq 9$ ($n = 698$), $9 < SXscore_{MID} \leq 17$ ($n = 676$); $SXscore_{HIGH} > 17$ ($n = 659$).
Results At 12-month follow-up, rates of POCE, MI, repeat revascularization, TLF, and the composite of death/MI were all significantly higher in patients in the highest SXscore tercile. Rates of stent thrombosis were all highest in the $SXscore_{HIGH}$ tertile ($p > 0.05$). After multivariate adjustment, the SXscore was identified as an independent predictor of POCE, MI, repeat revascularization, and TLF ($p < 0.05$ for all). At 12-month follow-up, the SXscore, ACEF score, and Clinical SXscore had C-statistics of 0.57, 0.78, and 0.67, respectively, for mortality and of 0.62, 0.56, 0.63, respectively, for POCE. No significant between-stent differences were observed for TLF or POCE in any of the SXscore tertiles.
Conclusions The SYNTAX score is able to stratify risk amongst an all-comers population treated with PCI with second-generation drug-eluting stents (DES); however, improvements can be made with the inclusion of clinical variables. (RESOLUTE III All Comers Trial: A Randomized Comparison of a Zotarolimus-Eluting Stent With an Everolimus-Eluting Stent for Percutaneous Coronary Intervention; NCT00617084) (406).

Clopidogrel and Proton Pump Inhibitors: Influence of Pharmacological Interactions on Clinical Outcomes and Mechanistic Explanations

Dual antiplatelet therapy with aspirin and clopidogrel is associated with a significant reduction in vascular ischemic events; however, gastrointestinal bleeding events are a major concern in high-risk and older patients. Clinical practice guidelines recommend combination therapy with proton pump inhibitors (PPI) and dual antiplatelet therapy to attenuate gastrointestinal bleeding risk. In addition, high on-treatment platelet reactivity has been associated with recurrent ischemic events. Whether or not the pharmacological interaction between clopidogrel and PPI, which results in diminished antiplatelet effect, adversely influences clinical efficacy is highly controversial and the subject of debate. Based on largely anecdotal post-hoc analyses, the U.S. Federal Drug Administration's and European Medicines Agency's recommendations discourage PPI use (particularly omeprazole) in patients treated with clopidogrel. However, many American College of Cardiology/American Heart Association/Society for Cardiovascular Angiography and Interventions experts do not support change in clinical practice guidelines recommendations without adequately powered, prospective, randomized clinical trial data (407).

Prasugrel Overcomes High On-Clopidogrel Platelet Reactivity Post-Stenting More Effectively Than High-Dose (150-mg) Clopidogrel: The Importance of CYP2C19*2 Genotyping

Objectives The primary aim of the study was to determine the antiplatelet effects of prasugrel versus high-dose

clopidogrel in patients with high on-treatment platelet reactivity (HTPR) after percutaneous coronary intervention (PCI) and, secondarily, their relation to cytochrome (CYP) 2C19*2 carriage.

Background High on-treatment platelet reactivity after clopidogrel administration after PCI is linked to the loss-of-function *CYP2C19*2* allele and accompanied by an increased risk of adverse events.

Methods We performed a prospective, randomized, single-blind, crossover study of platelet inhibition by prasugrel 10 mg/day versus high-dose 150 mg/day clopidogrel in 71 (of 210 screened; 33.8%) post-PCI patients with HTPR. Platelet function was assessed by the VerifyNow assay (Accumetrics, San Diego, California), and real-time polymerase chain reaction genotyping was performed for *CYP2C19*2* carriage.

Results The primary endpoint of platelet reactivity (measured in platelet reactivity units) at the end of the 2 treatment periods was lower after prasugrel compared with clopidogrel (least-squares estimates 129.4, 95% confidence interval [CI]: 111.1 to 147.7 versus 201.7, 95% CI: 183.2 to 220.2; $p < 0.001$). The least-squares mean difference between the 2 treatments was −122.9 (95% CI: −166.7 to −79.2, $p < 0.001$), and −47.5 (95% CI: −79.5 to −15.4, $p = 0.004$), in carriers and noncarriers of at least 1 mutant allele, respectively. The HTPR rates were lower for prasugrel than for clopidogrel, in all patients (7.5% vs. 35.8%, $p < 0.001$), in carriers (5.3% vs. 47.4%, $p = 0.007$), and in noncarriers (8.8% vs. 29.4%, $p = 0.005$), respectively.

Conclusions In patients with HTPR after PCI, prasugrel is more effective compared with high clopidogrel in reducing platelet reactivity, particularly in *CYP2C19*2* carriers. Genotyping guidance might be helpful only in case an increased clopidogrel maintenance dose is considered. (Prasugrel Versus High Dose Clopidogrel in Clopidogrel Resistant Patients Post Percutaneous Coronary Intervention (PCI); NCT01109784) (408).

Enhanced Prediction of Mortality After Percutaneous Coronary Intervention by Consideration of General and Neurological Indicators

Objectives This study sought to improve methodology for predicting post–percutaneous coronary intervention (PCI) mortality.

Background Recently, an increased proportion of post-PCI deaths caused by noncardiac causes has been suggested, often in rapidly triaged patients resuscitated from sudden cardiac death or presenting with cardiogenic shock. Older risk adjustment algorithms may not adequately reflect these issues.

Methods Consecutive patients undergoing PCI from 2000 to 2009 were randomly divided into training ($n = 8,966$) and validation ($n = 8,891$) cohorts. The 2010 ACC-NCDR (American College of Cardiology–National Cardiovascular Data Registry) mortality algorithm was applied to the training cohort and its highest risk decile, separately. Variables describing general and neurological status at admission were then tested for their additional predictive capability and new algorithms developed. These were tested in the validation cohort, using receiver-operator characteristic curve, Hosmer-Lemeshow, and reclassification measures as principal outcome measures.

Results In-hospital mortality was 1.0%, of which 52.2% had noncardiac causes or major contributions. Baseline model C-statistics for the total and upper decile training cohorts were 0.904 and 0.830. The Aldrete score (addressing consciousness, respiration, skin color, muscle function, and circulation) and neurology scores added incremental information, resulting in improved validation cohort C-statistics (entire group: 0.883 to 0.914, $p < 0.001$; high-risk decile: 0.829 to 0.874, $p < 0.001$). Reclassification of the ACC-NCDR <90th and ≥90th risk percentiles by the new score yielded improved mortality prediction ($p < 0.001$ and $p = 0.033$, respectively).

Conclusions Half of in-hospital deaths in this series were of noncardiac causation. Prediction of in-hospital mortality after PCI can be considerably improved over conventional models by the inclusion of variables describing general and neurological status (409).

Stent Thrombosis and Bleeding Complications After Implantation of Sirolimus-Eluting Coronary Stents in an Unselected Worldwide Population: A Report From the e-SELECT (Multi-Center Post-Market Surveillance) Registry

Objectives The aim of this study was to ascertain the 1-year incidence of stent thrombosis (ST) and major bleeding (MB) in a large, unselected population treated with sirolimus-eluting stents (SES).

Background Stent thrombosis and MB are major potential complications of drug-eluting stent implantation. Their relative incidence and predisposing factors among large populations treated worldwide are unclear.

Methods The SES were implanted in 15,147 patients who were entered in a multinational registry. We analyzed the incidence of: 1) definite and probable ST as defined by the Academic Research Consortium; and 2) MB, with the STEEPLE (Safety and efficacy of Enoxaparin in PCI) definition, together with their relation to dual antiplatelet therapy (DAPT) and to 1-year clinical outcomes.

Results The mean age of the sample was 62 ± 11 years, 30.4% were diabetic, 10% had a Charlson comorbidity index ≥3, and 44% presented with acute coronary syndrome or myocardial infarction. At 1 year, the reported compliance with DAPT as recommended by the European Society of Cardiology guidelines was 86.3%. Adverse event rates were: ST 1.0%, MB 1.0%, mortality 1.7%, myocardial infarction 1.9%, and target lesion revascularization

2.3%. Multivariate analysis identified 9 correlates of ST and 4 correlates of MB. Advanced age and a high Charlson index were associated with an increased risk of both ST and MB. After ST, the 7-day and 1-year all-cause mortality was 30% and 35%, respectively, versus 1.5% and 10% after MB. Only 2 of 13,749 patients (0.015%) experienced both MB and ST during the entire 1-year follow-up period.

Conclusions In this worldwide population treated with ≥1 SES, the reported compliance with DAPT was good, and the incidence of ST and MB was low. Stent thrombosis and MB very rarely occurred in the same patient. (The e-SELECT Registry: a Multicenter Post-Market Surveillance; NCT00438919) (410).

Composition of Coronary Thrombus in Acute Myocardial Infarction

Objectives We sought to analyze the composition of coronary thrombus in vivo in ST-segment elevation myocardial infarction (STEMI) patients.

Background The dynamic process of intracoronary thrombus formation in STEMI patients is poorly understood.

Methods Intracoronary thrombi (n = 45) were obtained by thromboaspiration in 288 consecutive STEMI patients presenting for primary percutaneous intervention, and analyzed using high-definition pictures taken with a scanning electron microscope. Plasma biomarkers (TnI, CRPus, IL-6, PAI-1, sCD40 ligand, and TNF-α) and plasma fibrin clot viscoelastic properties were measured simultaneously on peripheral blood.

Results Thrombi were mainly composed of fibrin (55.9 ± 18%) with platelets (16.8 ± 18%), erythrocytes (11.5 ± 9%), cholesterol crystals (5.2 ± 8.4%), and leukocytes (1.3 ± 2.0%). The median ischemic time was 175 min (interquartile range: 140 to 297). Ischemic time impacted thrombi composition, resulting in a positive correlation with intracoronary thrombus fibrin content, r = 0.38, p = 0.01, and a negative correlation with platelet content, r = −0.34, p = 0.02. Thus, fibrin content increased with ischemic time, ranging from 48.4 ± 21% (<3 h) up to 66.9 ± 9% (>6 h) (p = 0.02), whereas platelet content decreased from 24.9 ± 23% (<3 h) to 9.1 ± 6% (>6 h) (p = 0.07). Soluble CD40 ligand was positively correlated to platelet content in the thrombus (r = 0.40, p = 0.02) and negatively correlated with fibrin content (r = −0.36; p = 0.04). Multivariate analysis indicated that ischemic time was the only predictor of thrombus composition, with a 2-fold increase of fibrin content per ischemic hour (adjusted odds ratio: 2.00 [95% confidence interval: 1.03 to 3.7]; p = 0.01).

Conclusions In acute STEMI, platelet and fibrin contents of the occlusive thrombus are highly dependent on ischemia time, which may have a direct impact on the efficacy of drugs or devices used for coronary reperfusion (411).

Incidence, Predictors, Treatment, and Long-Term Prognosis of Patients With Restenosis After Drug-Eluting Stent Implantation for Unprotected Left Main Coronary Artery Disease

Objectives The aim of this study was to evaluate the incidence, predictors, and long-term outcomes of patients with in-stent restenosis (ISR) after percutaneous coronary intervention (PCI) with drug-eluting stents (DES) for unprotected left main coronary artery (LMCA) disease.

Background Few data on the clinical course and management of patients experiencing restenosis after DES treatment for unprotected LMCA disease have appeared.

Methods Between February 2003 and November 2007, 509 consecutive patients with unprotected LMCA disease underwent DES implantation, with 402 (80.1%) undergoing routine surveillance or clinically driven angiographic follow-up. A major adverse cardiac event was defined as the composite of death, myocardial infarction (MI), or target-lesion revascularization.

Results The overall incidence of angiographic ISR in LMCA lesions was 17.6% (71 of 402 patients, 57 with focal-type and 14 with diffuse-type ISR. Forty patients (56.3%) underwent repeated PCI, 10 (14.1%) underwent bypass surgery, and 21 (29.6%) were treated medically. During long-term follow-up (a median of 31.7 months), there were no deaths, 1 (2.2%) MI, and 6 (9.5%) repeated target-lesion revascularization cases. The incidence of major adverse cardiac event was 14.4% in the medical group, 13.6% in the repeated PCI group, and 10.0% in the bypass surgery group (p = 0.91). Multivariate analysis showed that the occurrence of DES-ISR did not affect the risk of death or MI.

Conclusions The incidence of ISR was 17.7% after DES stenting for LMCA. The long-term clinical prognosis of patients with DES-ISR associated with LMCA stenting might be benign, given that these patients were optimally treated with the clinical judgment of the treating physician (412).

Severe Renal Impairment and Stroke Prevention in Atrial Fibrillation: Implications for Thromboprophylaxis and Bleeding Risk

The prevalence of atrial fibrillation (AF) in end-stage renal failure is high, with an increased risk of stroke among these patients with AF compared with the AF population without severe renal impairment. Many trials have shown the net clinical benefit of oral anticoagulation therapy for primary and secondary prevention of stroke in patient populations with AF. However, current stroke risk stratification schemes are based on studies that have deliberately excluded patients with severe renal impairment. Indeed, there are no large randomized controlled trials that assess the real risk/benefit of full intensity anticoagulation in

patients with severe renal impairment. Also, rates of major bleeding episodes in anticoagulated hemodialysis patients with AF are high. These data are influenced by the lack of appropriate monitoring, the difficulties in maintaining the international normalized ratio target (variable between the studies), and an inaccurate bleeding classification. Thus, the limited available data may be difficult to apply to such a heterogeneous patient population, characterized by both an increased risk of bleeding and a hypercoagulability state, as seen in the patient population with severe renal impairment (413).

The Pathology of Neoatherosclerosis in Human Coronary Implants: Bare-Metal and Drug-Eluting Stents

Objectives Human coronary bare-metal stents (BMS) and drug-eluting stents (DES) from autopsy cases with implant duration >30 days were examined for the presence of neointimal atherosclerotic disease.

Background Neointimal atherosclerotic change (neoatherosclerosis) after BMS implantation is rarely reported and usually occurs beyond 5 years. The incidence of neoatherosclerosis after DES implantation has not been reported.

Methods All available cases from the CVPath stent registry (n = 299 autopsies), which includes a total of 406 lesions—197 BMS, 209 DES (103 sirolimus-eluting stents [SES] and 106 paclitaxel-eluting stents [PES])—with implant duration >30 days were examined. Neoatherosclerosis was recognized as clusters of lipid-laden foamy macrophages within the neointima with or without necrotic core formation.

Results The incidence of neoatherosclerosis was significantly greater in DES lesions (31%) than BMS lesions (16%; $p < 0.001$). The median stent duration with neoatherosclerosis was shorter in DES than BMS (DES, 420 days [interquartile range [IQR]: 361 to 683 days]; BMS, 2,160 days [IQR: 1,800 to 2,880 days], $p < 0.001$). Unstable lesions characterized as thin-cap fibroatheromas or plaque rupture were more frequent in BMS (n = 7, 4%) than in DES (n = 3, 1%; $p = 0.17$), with relatively shorter implant durations for DES (1.5 ± 0.4 years) compared to BMS (6.1 ± 1.5 years). Independent determinants of neoatherosclerosis identified by multiple logistic regression included younger age ($p < 0.001$), longer implant durations ($p < 0.001$), SES usage ($p < 0.001$), PES usage ($p = 0.001$), and underlying unstable plaques ($p = 0.004$).

Conclusions Neoatherosclerosis is a frequent finding in DES and occurs earlier than in BMS. Unstable features of neoatherosclerosis are identified for both BMS and DES with shorter implant durations for the latter. The development of neoatherosclerosis may be yet another rare contributing factor to late thrombotic events (414).

Can Differences in Corrected Coronary Opacification Measured With Computed Tomography Predict Resting Coronary Artery Flow?

Objectives A proof-of-concept study was undertaken to determine whether differences in corrected coronary opacification (CCO) within coronary lumen can identify arteries with abnormal resting coronary flow.

Background Although computed tomographic coronary angiography can be used for the detection of obstructive coronary artery disease, it cannot reliably differentiate between anatomical and functional stenoses.

Methods Computed tomographic coronary angiography patients (without history of revascularization, cardiac transplantation, and congenital heart disease) who underwent invasive coronary angiography were enrolled. Attenuation values of coronary lumen were measured before and after stenoses and normalized to the aorta. Changes in CCO were calculated, and CCO differences were compared with severity of coronary stenosis and Thrombolysis In Myocardial Infarction (TIMI) flow at the time of invasive coronary angiography.

Results One hundred four coronary arteries (n = 52, mean age = 60.0 ± 9.5 years; men = 71.2%) were assessed. Compared with normal arteries, the CCO differences were greater in arteries with computed tomographic coronary angiography diameter stenoses ≥50%. Similarly, CCO differences were greater in arteries with TIMI flow grade <3 (0.406 ± 0.226) compared with those with normal flow (TIMI flow grade 3) (0.078 ± 0.078, $p < 0.001$). With CCO differences, abnormal coronary flow (TIMI flow grade <3) was identified with a sensitivity and specificity, positive predictive value, and negative predictive value of 83.3% (95% confidence interval [CI]: 57.7 to 95.6%), 91.2% (95% CI: 75.2% to 97.7%), 83.3% (95% CI: 57.7% to 95.6%), and 91.2% (95% CI: 75.2% to 97.7%), respectively. Accuracy of this method was 88.5% with very good agreement (kappa = 0.75, 95% CI: 0.55 to 0.94).

Conclusions Changes in CCO across coronary stenoses seem to predict abnormal (TIMI flow grade <3) resting coronary blood flow. Further studies are needed to understand its incremental diagnostic value and its potential to measure stress coronary blood flow (415).

A Randomized, Double-Blind, Multicenter Comparison Study of Triple Antiplatelet Therapy With Dual Antiplatelet Therapy to Reduce Restenosis After Drug-Eluting Stent Implantation in Long Coronary Lesions: Results From the DECLARE-LONG II (Drug-Eluting Stenting Followed by Cilostazol Treatment Reduces Late Restenosis in Patients with Long Coronary Lesions) Trial

Objectives The purpose of this study was to determine whether cilostazol reduces intimal hyperplasia in patients undergoing long zotarolimus-eluting stent implantation

(stent length: ≥30 mm) for native long coronary lesions (length: ≥25 mm).

Background Restenosis after drug-eluting stent implantation remains a significant clinical problem in long coronary lesions.

Methods Patients (n = 499) were assigned randomly to triple (aspirin, clopidogrel, and cilostazol, triple group: n = 250) or dual antiplatelet therapy (aspirin and clopidogrel and placebo, dual group: n = 249) for 8 months after long zotarolimus-eluting stent implantation. The primary end point was in-stent late loss at the 8-month angiography according to the intention-to-treat principle.

Results The 2 groups had similar baseline characteristics. The in-stent (0.56 ± 0.55 mm vs. 0.68 ± 0.59 mm, p = 0.045) and in-segment (0.32 ± 0.54 mm vs. 0.47 ± 0.54 mm, p = 0.006) late loss were significantly lower in the triple versus dual group, as were 8-month in-stent restenosis (10.8% vs. 19.1%, p = 0.016), in-segment restenosis (12.2% vs. 20.0%, p = 0.028), and 12-month ischemic-driven target lesion revascularization (5.2% vs. 10.0%, p = 0.042) rates. At 12 months, major adverse cardiac events including death, myocardial infarction, and ischemic-driven target lesion revascularization tended to be lower in the triple group than the dual group (7.2% vs. 12.0%, p = 0.07). Percent intimal hyperplasia volume by volumetric intravascular ultrasound analysis was reduced from 27.1 ± 13.2% for the dual group to 22.1 ± 9.9% for the triple group (p = 0.017).

Conclusions Patients receiving triple antiplatelet therapy after long zotarolimus-eluting stent implantation had decreased extent of late luminal loss, percent intimal hyperplasia volume, and angiographic restenosis, resulting in a reduced risk of 12-month target lesion revascularization compared with patients receiving dual antiplatelet therapy. (Triple Versus Dual Antiplatelet Therapy after ABT578-Eluting Stent; NCT00589927) (416).

Clopidogrel–Drug Interactions

Multidrug therapy increases the risk for drug–drug interactions. Clopidogrel, a prodrug, requires hepatic cytochrome P450 (CYP) metabolic activation to produce the active metabolite that inhibits the platelet $P2Y_{12}$ adenosine diphosphate (ADP) receptor, decreasing platelet activation and aggregation processes. Atorvastatin, omeprazole, and several other drugs have been shown in pharmacodynamic studies to competitively inhibit CYP activation of clopidogrel, reducing clopidogrel responsiveness. Conversely, other agents increase clopidogrel responsiveness by inducing CYP activity. The clinical implications of these pharmacodynamic interactions have raised concern because many of these drugs are coadministered to patients with coronary artery disease. There are multiple challenges in proving that a pharmacodynamic drug–drug interaction is clinically significant. To date, there is no consistent evidence that clopidogrel–drug interactions impact adverse cardiovascular events. Statins and proton pump inhibitors have been shown to decrease adverse clinical event rates and should not be withheld from patients with appropriate indications for therapy because of concern about potential clopidogrel–drug interactions. Clinicians concerned about clopidogrel–drug interactions have the option of prescribing either an alternative platelet $P2Y_{12}$ receptor inhibitor without known drug interactions, or statin and gastro-protective agents that do not interfere with clopidogrel metabolism (417).

Efficacy of Post-Operative Clopidogrel Treatment in Patients Revascularized With Coronary Artery Bypass Grafting After Myocardial Infarction

Objectives The objective of this study was to examine the clinical efficacy of clopidogrel treatment on death and recurrent myocardial infarction (MI) among MI patients revascularized by coronary artery bypass graft surgery (CABG).

Background The benefit from post-operative clopidogrel in CABG-treated MI patients is largely unknown.

Methods All patients admitted with first-time MI between 2002 and 2006, treated with CABG within 180 days after admission, were identified by nationwide administrative registers. Clopidogrel treatment was determined by claimed prescriptions after discharge from surgery. Risk of death or recurrent MI, and of a combined end point of the 2, were assessed by cumulative incidence and Cox proportional hazards model. A propensity score-matched subgroup analysis was done.

Results We included 3,545 patients, and of these, 957 (27.0%) were treated with clopidogrel after CABG. Mean follow-up was 466 ± 144 days. Among patients treated with clopidogrel, 39 (4.1%) died or experienced a recurrent MI, whereas that occurred in 203 (7.8%) patients without clopidogrel (log-rank p = 0.0003). Hazard ratio was 0.59 (95% confidence interval [CI]: 0.42 to 0.85) for patients treated with clopidogrel, with no-clopidogrel as reference. By propensity score, of 945 patients with or without clopidogrel treatment who were matched, death or recurrent MI occurred in 38 (4.0%) patients with clopidogrel and 57 (6.0%) without clopidogrel (log-rank p = 0.05). Corresponding hazard ratio was 0.67 (95% CI: 0.44 to 1.00) for clopidogrel users, with no-clopidogrel as reference.

Conclusions Among MI patients revascularized by CABG, only 27% received clopidogrel after discharge. Clopidogrel-treated patients had a lower risk of the combined end point of death or recurrent MI. Focus on discharge clopidogrel treatment of these patients should be made (418).

Efficacy and Safety of Glycoprotein IIb/IIIa Inhibitors During Elective Coronary Revascularization: A Meta-Analysis of Randomized Trials Performed in the Era of Stents and Thienopyridines

Objectives The purpose of this study was to investigate the efficacy and safety of glycoprotein IIb/IIIa inhibitors (GPIs) during elective percutaneous coronary intervention (PCI).

Background Studies have documented that GPIs are useful during PCI; however, much of this research was conducted before the routine use of coronary stents and thienopyridines.

Methods We searched the MEDLINE, Cochrane clinical trials, and ClinicalTrials.gov databases from inception for studies that randomly assigned patients undergoing elective PCI to a GPI versus control. Trials were included if stents and thienopyridines were used routinely and clinical outcomes were reported. Outcomes were assessed within 30 days. A DerSimonian-Laird model was used to construct random effects summary risk ratios (RRs) and 95% confidence intervals (CIs).

Results Our search yielded 22 studies with 10,123 patients. The incidence of nonfatal myocardial infarction was 5.1% with GPI versus 8.3% with control (RR: 0.66, 95% CI: 0.55 to 0.79, $p < 0.0001$). Major bleeding was 1.2% versus 0.9% (RR: 1.37, 95% CI: 0.83 to 2.25, $p = 0.22$), minor bleeding was 3.0% versus 1.7% (RR: 1.70, 95% CI: 1.28 to 2.26, $p < 0.0001$), and mortality was 0.3% versus 0.5% (RR: 0.70, 95% CI: 0.36 to 1.33, $p = 0.27$), respectively.

Conclusions In the current era of elective PCI performed with stents and thienopyridines, GPIs provide clinical benefit. These agents reduce nonfatal myocardial infarction without a notable increase in major bleeding; however, they increase the risk of minor bleeding. All-cause mortality is not reduced (419).

Effects of Aspirin Responsiveness and Platelet Reactivity on Early Vein Graft Thrombosis After Coronary Artery Bypass Graft Surgery

Objectives The purpose of this study was to determine if an incomplete response to or inadequate antiplatelet effect of aspirin, or both, contribute to saphenous vein graft (SVG) occlusion after coronary artery bypass graft (CABG) surgery.

Background Thrombosis is the predominant cause of early SVG occlusion. Aspirin, which inhibits cyclooxygenase-1 activity and thromboxane generation in platelets, reduces early SVG occlusion by one-half.

Methods Aspirin responsiveness and platelet reactivity were characterized 3 days and 6 months after coronary artery bypass graft surgery in 229 subjects receiving aspirin monotherapy by platelet aggregation to arachidonic acid, adenosine diphosphate, collagen and epinephrine, Platelet Function Analyzer-100 (Siemens Healthcare Diagnostics, Newark, Delaware) closure time (CT) using collagen/epinephrine agonist cartridge and collagen/adenosine diphosphate (CADP) agonist cartridge, VerifyNow Aspirin assay (Accumetrics, Inc., San Diego, California), and urine levels of 11-dehydro-thromboxane B_2 ($UTXB_2$). SVG patency was determined 6 months after surgery by computed tomography coronary angiography.

Results Inhibited arachidonic acid-induced platelet aggregation, indicative of aspirin-mediated cyclooxygenase-1 suppression, occurred in 95% and >99% of subjects 3 days and 6 months after surgery, respectively. Despite this, 73% and 31% of subjects at these times had elevated $UTXB_2$. Among tested parameters, only $UTXB_2$ and CADP CT measured 6 months after surgery correlated with outcome. By multivariate analysis, CADP CT of ≤88 s (odds ratio: 2.85, $p = 0.006$), target vessel diameter of ≤1.5 mm (odds ratio: 2.38, $p = 0.01$), and $UTXB_2$ of ≥450 pg/mg creatinine (odds ratio: 2.59, $p = 0.015$) correlated with SVG occlusion. CADP CT and $UTXB_2$ in combination further identified subjects at particularly high and low risk for SVG occlusion.

Conclusions Aspirin-insensitive thromboxane generation measured by $UTXB_2$ and shear-dependent platelet hyperreactivity measured by Platelet Function Analyzer-100 CADP CT are novel independent risk factors for early SVG thrombosis after coronary artery bypass graft surgery (420).

The Valve-in-Valve Technique for Treatment of Aortic Bioprosthesis Malposition: An Analysis of Incidence and 1-Year Clinical Outcomes From the Italian CoreValve Registry

Objectives We appraised the incidence and clinical outcomes of patients who were treated with the valve-in-valve (ViV) technique for hemodynamically destabilizing paraprosthetic leak (PPL).

Background Device malpositioning causing severe PPL after transcatheter aortic valve implantation is not an uncommon finding. It occurs after release of the prosthesis, leading to hemodynamic compromise. It can be managed successfully in selected cases with implantation of a second device inside the malpositioned primary prosthesis (ViV technique).

Methods Consecutive patients (n = 663) who underwent transcatheter aortic valve implantation with the 18-F CoreValve ReValving System (Medtronic, Inc., Minneapolis, Minnesota) at 14 centers across Italy were included in this prospective web-based registry. We identified patients treated with the ViV technique for severe PPL and analyzed their clinical and echocardiographic outcomes. Primary end points were major adverse cerebrovascular and cardiac events and prosthesis performance at the 30-day and midterm follow-up.

Results Overall procedural success was obtained in 650 patients (98.0%). The ViV technique was used in 24 (3.6%) of 663 patients. The 30-day major adverse cerebrovascular and cardiac event rates were 7.0% and 0% in patients undergoing the standard procedure and ViV technique,

respectively (p = 0.185); the mortality rates were 5.6% versus 0% in patients undergoing the standard procedure and ViV technique, respectively (p = 0.238). There was an improvement in the mean transaortic gradient in all patients without significant difference between the 2 groups (from 52.1 ± 17.1 mm Hg and 45.4 ± 14.8 mm Hg [p = 0.060] to 10.1 ± 4.2 mm Hg and 10.5 ± 5.2 mm Hg, respectively [p = 0.838]). At 12 months, the major adverse cerebrovascular and cardiac event rates in the standard procedure and ViV technique groups were 4.5% and 14.1%, respectively (p = 0.158), and the mortality rates were 4.5% versus 13.7%, respectively (p = 0.230).

Conclusions This large, multicenter registry provides important information about the feasibility, safety, and efficacy of the ViV technique with the third-generation CoreValve ReValving System. The clinical and echocardiographic end points compare favorably with those of patients undergoing the standard procedure. The ViV technique offers a viable therapeutic option in patients with acute significant PPL without recourse to emergent surgery (421).

Contrast-Enhanced C-Arm CT Evaluation of Radiofrequency Ablation Lesions in the Left Ventricle

Objectives The purpose of this study was to evaluate use of cardiac C-arm computed tomography (CT) in the assessment of the dimensions and temporal characteristics of radiofrequency ablation (RFA) lesions. This imaging modality uses a standard C-arm fluoroscopy system rotating around the patient, providing CT-like images during the RFA procedure.

Background Both cardiac magnetic resonance (CMR) and CT can be used to assess myocardial necrotic tissue. Several studies have reported visualizing cardiac RFA lesions with CMR; however, obtaining CMR images during interventional procedures is not common practice. Direct visualization of RFA lesions using C-arm CT during the procedure may improve outcomes and circumvent complications associated with cardiac ablation procedures.

Methods RFA lesions were created on the endocardial surface of the left ventricle of 9 swine using a 7-F RFA catheter. An electrocardiographically gated C-arm CT imaging protocol was used to acquire projection images during iodine contrast injection and after the injection every 5 min for up to 30 min, with no additional contrast. Reconstructed images were analyzed offline. The mean and SD of the signal intensity of the lesion and normal myocardium were measured in all images in each time series. Lesion dimensions and area were measured and compared in pathologic specimens and C-arm CT images.

Results All ablation lesions (n = 29) were visualized and lesion dimensions, as measured on C-arm CT, correlated well with postmortem tissue measurements (linear dimensions: concordance correlation = 0.87; area: concordance correlation = 0.90. Lesions were visualized as a perfusion defect on first-pass C-arm CT images with a signal intensity of 95 HU lower than that of normal myocardium (95% confidence interval: −111 HU to −79 HU). Images acquired at 1 and 5 min exhibited an enhancing ring surrounding the perfusion defect in 24 lesions (83%).

Conclusions RFA lesion size, including transmurality, can be assessed using electrocardiographically gated cardiac C-arm CT in the interventional suite. Visualization of RFA lesions using cardiac C-arm CT may facilitate the assessment of adequate lesion delivery and provide valuable feedback during cardiac ablation procedures (422).

Global Risk Classification and Clinical SYNTAX (Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery) Score in Patients Undergoing Percutaneous or Surgical Left Main Revascularization

Objectives The aim of this study was to investigate the ability to predict cardiac mortality of the Global Risk Classification (GRC) and the Clinical SYNTAX (Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery) score (CSS) in left main (LM) patients undergoing percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG).

Background There is a renewed interest in combining clinical and angiographic information to define the risk of patients undergoing LM revascularization.

Methods The GRC and CSS were assessed in patients undergoing LM PCI (n = 400) or CABG (n = 549). Stand-alone clinical (ACEF [age, creatinine, ejection fraction]), EuroSCORE (European System for Cardiac Operative Risk Evaluation) and angiographic (SYNTAX score) risk scores were also investigated.

Results The GRC (Hosmer-Lemeshow statistic 0.357, p = 0.550; area under the curve 0.743) and the ACEF (Hosmer-Lemeshow 0.426, p = 0.514; area under the curve 0.741) showed the most balanced predictive characteristics in the PCI and CABG cohorts, respectively. In PCI patients, the CSS used fewer data to achieve similar discrimination but poorer calibration than the GRC. Propensity-adjusted outcomes were comparable between PCI and CABG patients with low, intermediate, or high EuroSCORE, ACEF, GRC, and CSS and those with low or intermediate SYNTAX score. Conversely, in the group with the highest SYNTAX score, the risk of cardiac mortality was significantly higher in PCI patients (hazard ratio: 2.323, 95% confidence interval: 1.091 to 4.945, p = 0.029).

Conclusions In LM patients undergoing PCI, combined scores improve the discrimination accuracy of clinical or angiographic stand-alone tools. In LM patients undergoing CABG, the ACEF score has the best prognostic accuracy compared with other stand-alone or combined scores. The good predictive ability for PCI along with the poor

predictive ability for CABG make the SYNTAX score the preferable decision-making tool in LM disease (423).

Clinical Determinants of Radiation Dose in Percutaneous Coronary Interventional Procedures: Influence of Patient Size, Procedure Complexity, and Performing Physician

Objectives The Objectives of this work were to establish the primary clinical determinants of patient radiation dose associated with percutaneous coronary interventional (PCI) and to identify opportunities for dose reduction.

Background Use of X-ray imaging and associated radiation dose is a necessary part of PCI. Potential adverse consequences of radiation dose include skin radiation injury and predicted increase in lifetime cancer risk.

Methods Cumulative skin dose (CSD) (measured in gray [Gy] units) was selected as a measurement of patient radiation burden. Several patient-, disease-, and treatment-related variables, including 15 performing physicians, were analyzed in a multiple linear regression statistical model with cumulative skin dose CSD as the primary end point. The model results provide an estimate of the relative CSD increase (decrease) attributable to each variable.

Results Percutaneous coronary interventions performed on 1,287 male and 540 female patients were included. Median patient age was 68.6 years, median body mass index was 29.7 kg/m^2, and median weight was 88 kg. Median CSD was 1.64 Gy per procedure for male and 1.15 Gy for female patients. Increasing body mass index, patient sex, lesion complexity, lesion location, and performing physician were significantly associated with CSD. Physicians who performed more procedures were associated with lower CSD.

Conclusions Several primary determinants of patient radiation dose during PCI were identified. Along with physician development of radiation-sparing methods and skills, pre-procedure dose planning is proposed to help minimize radiation dose for PCI (424).

Plasma High-Mobility Group Box 1 Levels Predict Mortality After ST-Segment Elevation Myocardial Infarction

Objectives We evaluated the potential association between plasma high-mobility group box 1 (HMGB1) levels and outcome in patients with ST-segment elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention.

Background The positive effect of reperfusion after STEMI may be compromised by ischemic/reperfusion injury. HMGB1 is released by necrotic cells and, in preclinical studies, has been implicated to play a role in myocardial ischemic/reperfusion injury.

Methods The study included 141 STEMI patients, with acute occlusion of the left anterior descending coronary artery successfully treated with percutaneous coronary intervention. Plasma HMGB1 levels were measured by enzyme-linked immunoadsorbent assay at admission. Forty-two healthy individuals served as control subjects.

Results After a median of 10 months of follow-up, 13 STEMI patients died. There were no significant differences with regard to baseline variables between the group of patients who survived and those who died. Baseline HMGB1 levels were increased in STEMI patients when compared with control subjects. Furthermore, the STEMI patients who died had higher HMGB1 levels than those who survived. After adjusting for age, sex, troponin I, and creatine kinase-myocardial band, we found that a doubling of HMGB1 concentrations increased the risk of mortality by 75% (hazard ratio: 1.75; 95% confidence interval: 1.1 to 2.8).

Conclusions Plasma HMGB1 levels are elevated in STEMI patients compared with healthy control subjects. Furthermore, after a follow-up period of 10 months, plasma HMGB1 levels are shown to be independently associated with increased mortality in STEMI patients treated with PCI. These data suggest that plasma HMGB1 may be used as a new prognostic biomarker in STEMI patients (425).

Radial Artery Access as a Predictor of Increased Radiation Exposure During a Diagnostic Cardiac Catheterization Procedure

Objectives We sought to determine whether radial artery access is associated with increased radiation exposure during cardiac catheterization and whether this relationship differs between operators, after adjustment for clinical and patient characteristics associated with greater radiation exposure.

Background Although previous studies have demonstrated a relationship between radial access and increased radiation exposure to the patient during fluoroscopy-guided cardiac procedures, such studies did not account for differences in operator technique or clustering of patients, procedure complexity, or patient size. Those studies included data from few operators.

Methods Data were collected prospectively on 5,954 diagnostic cardiac catheterizations performed at a tertiary cardiac center. A multilevel regression analysis was used to determine the relationship between radial artery access and radiation exposure.

Results After adjustment for multiple factors, radial access was associated with increased exposure (beta = 0.22, $p < 0.0001$) when compared with the use of femoral access, as measured using the logarithmically transformed air kerma (LogAK). On average, radial access accounted for a 23% increase in measured AK. This was consistent between operators. There were observed differences in the mean LogAK between operators ($p = 0.0158$), as well as substantial variation in measured

LogAK between patients within each operator's practice ($p < 0.001$).

Conclusions Radial artery access cardiac catheterization was associated with increased radiation exposure to the patient when compared with femoral access. The measured AK was still far below the threshold for deterministic effects in most patients studied. Observed variations in AK between and within operators may point to better opportunities to reduce exposure (426).

Off-Hour Primary Percutaneous Coronary Angioplasty Does Not Affect Outcome of Patients With ST-Segment Elevation Acute Myocardial Infarction Treated Within a Regional Network for Reperfusion: The REAL (Registro Regionale Angioplastiche dell'Emilia-Romagna) Registry

Objectives This study aims to evaluate whether results of "off-hours" and "regular-hours" primary angioplasty (primary percutaneous coronary intervention [pPCI]) are comparable in an unselected population of patients with ST-segment elevation acute myocardial infarction treated within a regional network organization.

Background Conflicting results exist on the outcome of off-hours pPCI.

Methods We analyzed in-hospital and 1-year cardiac mortality among 3,072 consecutive ST-segment elevation myocardial infarction (STEMI) patients treated with pPCI between January 1, 2004, and June 30, 2006, during regular-hours (weekdays 8:00 AM to 8:00 PM) and off-hours (weekdays 8:01 PM to 7:59 AM, weekends, and holidays) within the STEMI Network of the Italian Region Emilia-Romagna (28 hospitals: 19 spoke and 9 hub interventional centers).

Results Fifty-three percent of patients were treated off-hours. Baseline findings were comparable, although regular-hours patients were older and had more incidences of multivessel disease. Median pain-to-balloon (195 min, interquartile range [IQR]: 140 to 285 vs. 186 min, IQR: 130 to 280 min; $p = 0.03$) and door-to-balloon time (88 min, IQR: 60 to 122 vs. 77 min, IQR: 48 to 116 min; $p < 0.0001$) were longer for off-hours pPCI. However, unadjusted in-hospital (5.8% off-hours vs. 7.2% regular-hours, $p = 0.11$) and 1-year cardiac mortality (8.4% off-hours vs. 10.3% regular-hours, $p = 0.08$) were comparable. At multivariate analysis, off-hours pPCI did not predict an adverse outcome either for the overall population (odds ratio [OR]: 0.70, 95% confidence interval [CI]: 0.49 to 1.01) or for patients directly admitted to the interventional center (OR: 0.79, 95% CI: 0.52 to 1.20).

Conclusions When pPCI is performed within an efficient STEMI network focused on reperfusion, the clinical effectiveness of either off-hours or regular-hours pPCI is comparable (427).

5-Year Follow-Up of Polytetrafluoroethylene-Covered Stents Compared With Bare-Metal Stents in Aortocoronary Saphenous Vein Grafts: The Randomized BARRICADE (Barrier Approach to Restenosis: Restrict Intima to Curtail Adverse Events) Trial

Objectives We sought to evaluate the utility of the JOSTENT polytetrafluoroethylene (PTFE) stent-graft (Jomed GmbH, Rangendingen, Germany) in patients with diseased saphenous vein grafts (SVGs) undergoing percutaneous coronary intervention (PCI).

Background Prior trials of the JOSTENT stent-graft did not mandate high-pressure implantation or prolonged dual antiplatelet therapy, and were limited by short-term follow-up.

Methods A total of 243 patients at 47 centers with 1 to 2 discrete lesions in SVGs were prospectively randomized to JOSTENT implantation ($\geq$18 atm.) versus bare-metal stents (BMS). The JOSTENT patients were treated with aspirin indefinitely and clopidogrel for $\geq$8 months. Routine angiographic follow-up was performed at 8 months, and all patients were followed for 5 years.

Results The primary end point of in-lesion binary restenosis occurred in 31.8% of lesions treated with the JOSTENT versus 28.4% of lesions treated with BMS (relative risk: 1.12, 95% confidence interval [CI]: 0.72 to 1.75, $p = 0.63$). At 9 months, the major secondary end point of target vessel failure (death, myocardial infarction, or clinically driven target vessel revascularization) occurred in 32.2% of patients treated with the JOSTENT versus 22.1% of patients treated with BMS (hazard ratio: 1.54, 95% CI: 0.94 to 2.53, $p = 0.08$). During long-term follow-up, significantly more events accrued in the JOSTENT arm such that by 5 years target vessel failure had occurred in 68.3% of JOSTENT patients versus 51.8% of BMS patients (hazard ratio: 1.59, 95% CI: 1.13 to 2.23, $p = 0.007$).

Conclusions The long-term prognosis for diseased SVGs requiring PCI is dismal. The JOSTENT PTFE stent-graft results in inferior outcomes compared with BMS, despite high-pressure implantation and prolonged dual antiplatelet therapy, a finding that becomes more evident with longer-term follow-up (428).

Acute Stroke Intervention

This review summarizes the current state-of-the-art regarding the endovascular management of acute ischemic stroke. Beginning with intravenous tissue plasminogen activator, this paper traces the gradual shift of systemic thrombolysis from a competing to complementary treatment modality. Intra-arterial thrombolysis, mechanical thrombectomy with the Merci (Concentric Medical, Mountain View, California) and Penumbra (Penumbra, Inc., Alameda, California) systems, angioplasty, primary intracranial stenting, and emerging stentriever devices are sequentially

reviewed. Ultimately, this paper lays the foundation for current endovascular stroke management and considers future areas of progress and research (429).

5-Year Follow-Up of Coronary Revascularization in Diabetic Patients With Multivessel Coronary Artery Disease: Insights From ARTS (Arterial Revascularization Therapy Study)-II and ARTS-I Trials

Objectives We compared the 5-year outcomes of diabetic patients with multivessel disease treated with sirolimus-eluting stents (SES), bare-metal stents (BMS), and coronary artery bypass graft surgery (CABG) enrolled in the ARTS (Arterial Revascularization Therapy Study) I and II studies.

Background Diabetes is an established risk factor for major adverse cardiac events after revascularization. Recent trials suggest that revascularization with drug-eluting stents has equivalent safety to CABG up to 2 years.

Methods The ARTS I and II studies included 367 diabetic patients (SES: 159, CABG: 96, and BMS: 112) compared with respect to 5-year clinical outcomes.

Results The rate of major adverse cardiovascular and cerebrovascular events was significantly higher in patients treated with BMS (BMS 53.6% vs. CABG 23.4% vs. SES 40.5%; log-rank, $p < 0.01$ for SES vs. BMS and SES vs. CABG). There was no significant difference in mortality among all 3 groups. There was, however, a statistically significant difference in the myocardial infarction rate between BMS and CABG arms (BMS 11.0%, CABG 5.2%, SES 4.8%, $p = 0.04$ for SES vs. BMS and $p = 0.76$ for SES vs. CABG). The rate of repeat revascularization was significantly lower in patients treated with CABG compared with SES (SES 33.2% vs. CABG 10.7%, $p < 0.001$). Revascularization rate of patients treated with SES at 5 years approached that of patients treated with BMS although remained significantly lower. This "catch-up" phenomenon was not apparent in the nondiabetic population.

Conclusions At 5-year follow-up, CABG has comparable safety and superior efficacy compared with BMS and SES in the treatment of diabetic patients with multivessel disease (430).

Prospective Randomized Comparison of Sirolimus- or Everolimus-Eluting Stent to Treat Bifurcated Lesions by Provisional Approach

Objectives This study sought to compare the procedural performance and the acute angiographic result on side-branch ostium obtained using 2 different drug-eluting stents (DES) to treat patients with bifurcated coronary lesions.

Background Drug-eluting stents are routinely used in percutaneous coronary interventions (PCI) of bifurcated coronary lesions. Different DES types have major technical differences that may influence the procedural and clinical performance in bifurcation PCI.

Methods Consecutive patients with bifurcated lesions undergoing DES implantation using a systematic provisional-stenting strategy were randomized to sirolimus-eluting stent (SES) or everolimus-eluting stent (EES) before intervention. The procedural details for PCI were prospectively recorded to assess the occurrence of any trouble in the side-branch (SB) management (primary end point). Post-PCI angiographic result (primary end point: minimal lumen diameter at SB ostium) was evaluated offline by 3-dimensional reconstruction and quantitative coronary analysis. Clinical outcome was prospectively recorded up to 18 months to assess the occurrence of target bifurcation failure.

Results A total of 150 patients were enrolled in the study (29% diabetics, 17% unprotected left main). The stent was successfully implanted according to randomization in all cases. Procedural performance was not significantly different between the 2 kinds of DES. Three-dimensional reconstruction and quantitative coronary analysis showed similar post-PCI results in the main vessel and better results in the SB with EES than with SES (minimal lumen diameter at SB ostium: 1.94 ± 0.72 mm vs. 1.64 ± 0.62 mm; $p = 0.013$). At 18 months, target bifurcation failure occurred in 7 (9.0%) of SES-treated patients versus 8 (10.7%) of EES patients ($p = 0.57$).

Conclusions In patients with bifurcated lesions treated by provisional stenting technique, EES compared with SES is associated with similar procedural performance and better 3-dimensional reconstruction and quantitative coronary analysis result in the SB. Both DES are associated with low rates of major adverse events and angiographic failure. (Sirolimus Versus Everolimus-Eluting Stent Randomized Assessment in Bifurcated Lesions and Clinical Significance of Residual Side-Branch Stenosis [SEA-SIDE]; NCT00697372) (431).

Impact of Lesion Sets on Mid-Term Results of Surgical Ablation Procedure for Atrial Fibrillation

Objectives The objective of this study was to evaluate the effects of different lesion sets of ablation in patients undergoing mitral surgery plus maze.

Background The role of lesion sets on outcome after maze is poorly defined.

Methods A total of 141 patients were prospectively followed up. Two different lesion sets were prepared: 32 patients underwent a radiofrequency left atrial lesion set of maze ("limited"), and 109 had combined left and right atrial lesion sets of maze ± ganglionic plexi isolation ("extensive"). A longitudinal observational study assessed the role of "extensive" versus "limited" ablation on atrial fibrillation (AF), New York Heart Association (NYHA) functional class II/III, treatment with antiarrhythmic drugs, follow-up recovery of the ratio of E- to A-wave (E/A), and survival and time to hospitalization (overall and for heart failure).

Results The prevalence of AF over time was lower in the "extensive" arm (adjusted relative risk [RR]: 0.10; 95% confidence interval [CI]: 0.03 to 0.31; $p < 0.001$), with

significantly lower prevalence at discharge, 3 months, and 18 months. The prevalence of patients in NYHA functional class II/III over time was lower in the "extensive" arm (adjusted RR: 0.11; 95% CI: 0.03 to 0.34; $p < 0.001$), with significant differences at any assessment (except the third month). The differences in E/A recovery and use of antiarrhythmic drugs were less marked, with an RR of 1.55 (95% CI: 0.99 to 2.42; $p = 0.05$) and RR of 0.76 (95% CI: 0.54 to 1.06; $p = 0.11$), respectively, with a significantly lower prevalence of antiarrhythmic drugs in the "extensive" ablation arm at 12, 18, and 24 months. Rates of hospitalization for heart failure, overall hospitalization, and the combined event death/hospitalization were lower in the "extensive" arm ($p = 0.11$, $p = 0.003$, and $p = 0.002$, respectively).

Conclusions The addition of right-sided ablation improves clinical and electrophysiologic results after maze procedure (432).

Improvement in Mortality Risk Prediction After Percutaneous Coronary Intervention Through the Addition of a "Compassionate Use" Variable to the National Cardiovascular Data Registry Cath: PCI Dataset: A Study From the Massachusetts Angioplasty Registry

Objectives This study investigated the impact of adding novel elements to models predicting in-hospital mortality after percutaneous coronary interventions (PCIs).

Background Massachusetts mandated public reporting of hospital-specific PCI mortality in 2003. In 2006, a physician advisory group recommended adding to the prediction models 3 attributes not collected by the National Cardiovascular Data Registry instrument. These "compassionate use" (CU) features included coma on presentation, active hemodynamic support during PCI, and cardiopulmonary resuscitation at PCI initiation.

Methods From October 2005 through September 2007, PCI was performed during 29,784 admissions in Massachusetts nonfederal hospitals. Of these, 5,588 involved patients with ST-segment elevation myocardial infarction or cardiogenic shock. Cases with CU criteria identified were adjudicated by trained physician reviewers. Regression models with and without the CU composite variable (presence of any of the 3 features) were compared using areas under the receiver-operator characteristic curves.

Results Unadjusted mortality in this high-risk subset was 5.7%. Among these admissions, 96 (1.7%) had at least 1 CU feature, with 69.8% mortality. The adjusted odds ratio for in-hospital death for CU PCIs (vs. no CU criteria) was 27.3 (95% confidence interval: 14.5 to 47.6). Discrimination of the model improved after including CU, with areas under the receiver-operating characteristic curves increasing from 0.87 to 0.90 ($p < 0.01$), while goodness of fit was preserved.

Conclusions A small proportion of patients at extreme risk of post-PCI mortality can be identified using pre-procedural factors not routinely collected, but that heighten predictive accuracy. Such improvements in model performance may result in greater confidence in reporting of risk-adjusted PCI outcomes (433).

A Randomized Clinical Study Comparing Double Kissing Crush With Provisional Stenting for Treatment of Coronary Bifurcation Lesions: Results From the DKCRUSH-II (Double Kissing Crush versus Provisional Stenting Technique for Treatment of Coronary Bifurcation Lesions) Trial

Objectives The present study aimed to investigate the difference in major adverse cardiac events (MACE) at 12 months in patients with coronary bifurcation lesions after double kissing double crush (DK crush) or provisional stenting (PS) techniques.

Background Provisional side branch (SB) stenting is preferable to DK crush because it has been associated with fewer complications. It is unknown which strategy would provide the best results.

Methods From April 2007 to June 2009, 370 unselected patients with coronary bifurcation lesions from 7 Asian centers were randomly assigned to either the DK or the PS group. Additional SB stenting in PS was required if final results were suboptimal. The primary end point was the occurrence of MACE at 12 months, including cardiac death, myocardial infarction, or target vessel revascularization (TVR). Secondary end point was the angiographic restenosis at 8 months.

Results There were 3 procedural occlusions of SB in the PS group. At 8 months, angiographic restenosis rates in the main vessel and SB were significantly different between the DK (3.8% and 4.9%) and the PS groups (9.7% and 22.2%, $p = 0.036$ and $p < 0.001$, respectively). Additional SB stenting in the PS group was required in 28.6% of lesions. TVR was 6.5% in the DK group, occurring significantly less often than in the PS group (14.6%, $p = 0.017$). There were nonsignificant differences in MACE and definite stent thrombosis between the DK (10.3% and 2.2%) and PS groups (17.3%, and 0.5%, $p = 0.070$ and $p = 0.372$, respectively).

Conclusions DK crush was associated with a significant reduction of TLR and TVR in this unselected patient population. However, there was no significant difference in MACE between DK and the PS groups. (Randomized Study on DK Crush Technique Versus Provisional Stenting Technique for Coronary Artery Bifurcation Lesions; ChicTR-TRC-00000015) (434).

Prevalence and Predictors of Concomitant Carotid and Coronary Artery Atherosclerotic Disease

Objectives The purpose of this research was to evaluate the relationship between coronary and carotid atherosclerotic disease using current guidelines for the definition of carotid artery stenosis (CAS).

Background The reported prevalence of concomitant coronary and carotid atherosclerotic disease has varied among studies due to differences in study populations and methodologies used.
Methods We performed a retrospective analysis of prospectively collected data obtained between January 2007 and May 2009 from consecutive patients undergoing same-day coronary angiography and carotid Doppler studies. Spearman correlations and multinomial logistic regression models were used to identify independent correlates of CAS.
Results The study included 1,405 patients (age 65 ± 11 years, 77.2% male), of whom 12.8% had significant CAS (peak systolic velocity [PSV] >125 cm/s) and 4.6% had severe CAS (PSV >230 cm/s). Mild CAS (PSV <125 cm/s and the presence of a sonographic atherosclerotic lesion) was present in 58%. The severity of CAS and the extent of coronary artery disease (CAD) were significantly correlated ($r = 0.255$, $p < 0.001$). Independent predictors of severe CAS defined by PSV were the presence of left-main or 3-vessel CAD, increasing age, a history of stroke, smoking status, and diabetes mellitus.
Conclusions The degree of internal carotid artery (ICA) stenosis is related to the extent of CAD, though the prevalence of clinically significant ICA stenosis is lower in specific CAD subsets than previously reported (435).

High Versus Standard Clopidogrel Maintenance Dose After Percutaneous Coronary Intervention and Effects on Platelet Inhibition, Endothelial Function, and Inflammation: Results of the ARMYDA-150 mg (Antiplatelet Therapy for Reduction of Myocardial Damage During Angioplasty) Randomized Study

Objectives This study was done to compare effects of high versus standard clopidogrel maintenance doses on platelet inhibition, inflammation, and endothelial function in patients undergoing percutaneous coronary intervention.
Background Previous data suggested that clopidogrel has various biological actions in addition to antiplatelet effects.
Methods Fifty patients were randomly assigned 1 month after intervention (T-0) to receive standard (75 mg/day; n = 25) or high (150 mg/day; n = 25) clopidogrel maintenance dose for 30 days (until T-1); at this time-point, cross-over was performed, and the assigned clopidogrel maintenance regimen was switched and continued for a further 30 days (until T-2). Platelet reactivity (expressed as $P2Y_{12}$ reaction units by the point-of-care VerifyNow assay [Accumetrics, San Diego, California]), endothelial function (evaluated by flow-mediated vasodilation), and high-sensitivity C-reactive protein levels were measured at T-0, T-1, and T-2.
Results Patients in the 150-mg/day arm had higher platelet inhibition (50 ± 20% vs. 31 ± 20% in the 75-mg/day group; $p < 0.0001$), better flow-mediated vasodilation (16.9 ± 12.6% vs. 7.9 ± 7.5%; $p = 0.0001$), and lower high-sensitivity C-reactive protein levels (3.6 ± 3.0 mg/l vs. 7.0 ± 8.6 mg/l; $p = 0.016$). Higher clopidogrel dose was associated with decreased proportion of patients with $P2Y_{12}$ reaction units ≥240 (12% vs. 32%; $p = 0.001$), flow-mediated vasodilation <7% (16% vs. 58%; $p = 0.0003$), and high-sensitivity C-reactive protein levels >3 mg/l (46% vs. 64%; $p = 0.07$).
Conclusions For patients undergoing percutaneous coronary intervention, the 150-mg/day clopidogrel maintenance dose is associated with stronger platelet inhibition, improvement of endothelial function, and reduction of inflammation, compared with the currently recommended 75-mg/day regimen; those effects might have a role in the clinical benefit observed with clopidogrel and may provide the rationale for using the higher maintenance regimen in selected patients (436).

Clinical Characteristics, Management, and Outcomes of Patients Diagnosed With Acute Pulmonary Embolism in the Emergency Department: Initial Report of EMPEROR (Multicenter Emergency Medicine Pulmonary Embolism in the Real World Registry)

Objectives In a large U.S. sample, this study measured the presentation features, testing, treatment strategies, and outcomes of patients diagnosed with pulmonary embolism (PE) in the emergency department (ED).
Background No data have quantified the demographics, clinical features, management, and outcomes of outpatients diagnosed with PE in the ED in a large, multicenter U.S. study.
Methods Patients of any hemodynamic status were enrolled from the ED after confirmed acute PE or with a high clinical suspicion prompting anticoagulation before imaging for PE. Exclusions were inability to provide informed consent (where required) or unavailability for follow-up.
Results A total of 1,880 patients with confirmed acute PE were enrolled from 22 U.S. EDs. Diagnosis of PE was based upon positive results of computerized tomographic pulmonary angiogram in most cases (n = 1,654 [88%]). Patients represented both sexes equally, and racial and ethnic composition paralleled the overall U.S. ED population. Most (79%) patients with PE were employed, and one-third were older than age 65 years. The mortality rate directly attributed to PE was 20 in 1,880 (1%; 95% confidence interval [CI]: 0% to 1.6%). Mortality from hemorrhage was 0.2%, and the all-cause 30-day mortality rate was 5.4% (95% CI: 4.4% to 6.6%). Only 3 of 20 patients with major PE that ultimately proved fatal had systemic anticoagulation initiated before diagnostic confirmation, and another 3 of these 20 received a fibrinolytic agent.
Conclusions Patients diagnosed with acute PE in U.S. EDs have high functional status, and their mortality rate is low. These registry data suggest that appropriate initial medical management of ED patients with severe PE with

anticoagulation is poorly standardized and indicate a need for research to determine the appropriate threshold for empiric treatment when PE is suspected before diagnostic confirmation (437).

With the "Universal Definition," Measurement of Creatine Kinase-Myocardial Band Rather Than Troponin Allows More Accurate Diagnosis of Periprocedural Necrosis and Infarction After Coronary Intervention

Objectives We aimed to assess the differential implications of creatine kinase-myocardial band (CK-MB) and troponin measurement with the universal definition of periprocedural injury after percutaneous coronary intervention.

Background Differentiation between definitions of periprocedural necrosis and periprocedural infarction has practical, sociological, and research implications. Troponin is the recommended biomarker, but there has been debate about the recommended diagnostic thresholds.

Methods Thirty-two patients undergoing multivessel percutaneous coronary intervention and late gadolinium enhancement (LGE) cardiac magnetic resonance (CMR) imaging in a prospective study had cardiac troponin I, CK-MB, and inflammatory markers (C-reactive protein, serum amyloid A, myeloperoxidase, tumor necrosis factor alpha) measured at baseline, 1 h, 6 h, 12 h, and 24 h after the procedure. Three "periprocedural injury" groups were defined with the universal definition: G1: no injury (biomarker <99th percentile); G2: periprocedural necrosis (1 to 3 × 99th percentile); G3: myocardial infarction (MI) type 4a (>3 × 99th percentile). Differences in inflammatory profiles were analyzed.

Results With CK-MB there were 17, 10, and 5 patients in groups 1, 2, and 3, respectively. Patients with CK-MB–defined MI type 4a closely approximated patients with new CMR-LGE injury. Groups defined with CK-MB showed progressively increasing percentage change in C-reactive protein and serum amyloid A, reflecting increasing inflammatory response ($p < 0.05$). Using cardiac troponin I resulted in 26 patients defined as MI type 4a, but only a small minority had evidence of abnormality on CMR-LGE, and only 3 patients were defined as necrosis. No differences in inflammatory response were evident when groups were defined with troponin.

Conclusions Measuring CK-MB is more clinically relevant for diagnosing MI type 4a, when applying the universal definition. Current troponin thresholds are oversensitive with the arbitrary limit of 3 × 99th percentile failing to discriminate between periprocedural necrosis and MI type 4a. (Myocardial Injury following Coronary Artery bypass Surgery versus Angioplasty: a randomised controlled trial using biochemical markers and cardiovascular magnetic resonance imaging; ISRCTN25699844) (438).

Long-Term Prevention of Stroke: A Modern Comparison of Current Carotid Stenting and Carotid Endarterectomy

Objectives This study sought to evaluate long-term outcomes of carotid stenting (CAS) versus carotid endarterectomy (CEA) based on physician-guided indications.

Background The issue regarding long-term outcome of CAS versus CEA in patients with carotid stenosis is clinically relevant but remains unsettled.

Methods Consecutive patients (71% men, mean age 71.3 years) treated by CEA (n = 1,118) or CAS (n = 1,084) after a training phase were reviewed. Selection of treatment was based on better-suitability characteristics (morphology and clinical). Data were adjusted with propensity score analysis and stratified by symptoms, age, and sex.

Results Thirty-day stroke/death rates were similar: 2.8% in CAS and 2.0% in CEA ($p = 0.27$). The risk was higher in symptomatic (3.5%) versus asymptomatic (2.0%) patients ($p = 0.04$) but without significant difference between CAS and CEA groups. Five-year survival rates were 82.0% in CAS and 87.7% in CEA ($p = 0.05$). Kaplan-Meier estimates of the composite of any periprocedural stroke/death and ipsilateral stroke at 5 years after the procedure were similar in all patients (4.7% vs. 3.7%; $p = 0.4$) and the subgroups of symptomatic (8.7% vs. 4.9%; $p = 0.7$) and asymptomatic (2.5% vs. 3.3%; $p = 0.2$) patients in CEA versus CAS, respectively. Cox analysis, adjusted by propensity score, identified statin treatment ($p = 0.016$) and symptomatic disease ($p = 0.003$) associated with the composite end point. There were no sex- or age-related significant outcome differences.

Conclusions When physicians use their clinical judgment to select the appropriate technique for carotid revascularization CAS can offer efficacy and durability comparable to CEA with benefits persisting at 5 years (439).

Ticagrelor Versus Clopidogrel in Patients With Acute Coronary Syndromes Undergoing Coronary Artery Bypass Surgery: Results From the PLATO (Platelet Inhibition and Patient Outcomes) Trial

Objectives The purpose of this study is to evaluate the efficacy and safety of ticagrelor and clopidogrel in patients with acute coronary syndrome undergoing coronary artery bypass graft surgery (CABG), as a post-randomization strategy.

Background Ticagrelor is a novel, reversibly binding, oral, direct-acting $P2Y_{12}$-receptor antagonist. In the PLATO (Platelet Inhibition and Patient Outcomes) trial, which randomized 18,624 patients with acute coronary syndromes, ticagrelor compared with clopidogrel significantly reduced the risk of the primary composite end point of cardiovascular (CV) death, myocardial infarction, or stroke (hazard ratio [HR]: 0.84; 95% confidence interval [CI]: 0.77 to 0.92; $p < 0.001$). This report investigated the outcomes of patients treated with CABG during the trial.

Methods In total, 1,899 patients underwent CABG post-randomization. The protocol recommended ticagrelor/placebo to be withheld for 24 to 72 h and clopidogrel/placebo for 5 days preoperatively. In all, 1,261 patients underwent CABG and were receiving study drug treatment <7 days before surgery. The statistical analysis was based on events occurring from the CABG procedure until the end of the study, excluding 3 patients with CABG after study end.

Results In the 1,261 patient cohort, the relative reduction of primary composite end point at 12 months (10.6% [66 of 629] with ticagrelor versus 13.1% [79 of 629] with clopidogrel; HR: 0.84; 95% CI: 0.60 to 1.16; $p = 0.29$) was consistent with the results of the whole trial. Total mortality was reduced from 9.7% (58 of 629) to 4.7% (29 of 629; HR: 0.49; 95% CI: 0.32 to 0.77; $p < 0.01$), CV death from 7.9% (47 of 629) to 4.1% (25 of 629; HR: 0.52; 95% CI: 0.32 to 0.85; $p < 0.01$), and non-CV death numerically from 2.0% to 0.7% ($p = 0.07$). There was no significant difference in CABG-related major bleeding between the randomized treatments.

Conclusions In the subgroup of patients undergoing CABG within 7 days after the last study drug intake, ticagrelor compared with clopidogrel was associated with a substantial reduction in total and CV mortality without excess risk of CABG-related bleeding (440).

Endocardial Radiofrequency Ablation for Hypertrophic Obstructive Cardiomyopathy: Acute Results and 6 Months' Follow-Up in 19 Patients

Objectives The purpose of this study was to examine the efficacy and safety of endocardial radiofrequency ablation of septal hypertrophy (ERASH) for left ventricular outflow tract (LVOT) gradient reduction in hypertrophic obstructive cardiomyopathy (HOCM).

Background Anatomic variability of the vessels supplying the obstructing septal bulge can limit the efficacy of transcoronary ablation of septal hypertrophy in HOCM. Previous studies showed that inducing a local contraction disorder without reducing septal mass results in effective gradient reduction. We examined an alternative endocardial approach to transcoronary ablation of septal hypertrophy by using ERASH.

Methods Nineteen patients with HOCM were enrolled; in 9 patients, the left ventricular septum was ablated, and in 10 patients, the right ventricular septum was ablated. Follow-up examinations (echocardiography, 6-min walk test, bicycle ergometry) were performed 3 days and 6 months after ERASH.

Results After 31.2 ± 10 radiofrequency pulses, a significant and sustained LVOT gradient reduction could be achieved (62% reduction of resting gradients and 60% reduction of provoked gradients, $p = 0.0001$). The 6-min walking distance increased significantly from 412.9 ± 129 m to 471.2 ± 139 m after 6 months, $p = 0.019$); and New York Heart Association functional class was improved from 3.0 ± 0.0 to 1.6 ± 0.7 ($p = 0.0001$). Complete atrioventricular block requiring permanent pacemaker implantation occurred in 4 patients (21%); 1 patient had cardiac tamponade.

Conclusions ERASH is a new therapeutic option in the treatment of HOCM, allowing significant and sustained reduction of the LVOT gradient as well as symptomatic improvement with acceptable safety by inducing a discrete septal contraction disorder. It may be suitable for patients not amenable to transcoronary ablation of septal hypertrophy or myectomy (441).

Genetic Warfarin Dosing: Tables Versus Algorithms

Objectives The aim of this study was to compare the accuracy of genetic tables and formal pharmacogenetic algorithms for warfarin dosing.

Background Pharmacogenetic algorithms based on regression equations can predict warfarin dose, but they require detailed mathematical calculations. A simpler alternative, recently added to the warfarin label by the U.S. Food and Drug Administration, is to use genotype-stratified tables to estimate warfarin dose. This table may potentially increase the use of pharmacogenetic warfarin dosing in clinical practice; however, its accuracy has not been quantified.

Methods A retrospective cohort study of 1,378 patients from 3 anticoagulation centers was conducted. Inclusion criteria were stable therapeutic warfarin dose and complete genetic and clinical data. Five dose prediction methods were compared: 2 methods using only clinical information (empiric 5 mg/day dosing and a formal clinical algorithm), 2 genetic tables (the new warfarin label table and a table based on mean dose stratified by genotype), and 1 formal pharmacogenetic algorithm, using both clinical and genetic information. For each method, the proportion of patients whose predicted doses were within 20% of their actual therapeutic doses was determined. Dosing methods were compared using McNemar's chi-square test.

Results Warfarin dose prediction was significantly more accurate (all $p < 0.001$) with the pharmacogenetic algorithm (52%) than with all other methods: empiric dosing (37%; odds ratio [OR]: 2.2), clinical algorithm (39%; OR: 2.2), warfarin label (43%; OR: 1.8), and genotype mean dose table (44%; OR: 1.9).

Conclusions Although genetic tables predicted warfarin dose better than empiric dosing, formal pharmacogenetic algorithms were the most accurate (442).

Randomized Comparison of Percutaneous Coronary Intervention With Sirolimus-Eluting Stents Versus Coronary Artery Bypass Grafting in Unprotected Left Main Stem Stenosis

Objectives The purpose of this randomized study was to compare sirolimus-eluting stenting with coronary artery

bypass grafting (CABG) for patients with unprotected left main (ULM) coronary artery disease.

Background CABG is considered the standard of care for treatment of ULM. Improvements in percutaneous coronary intervention (PCI) with use of drug-eluting stents might lead to similar results. The effectiveness of drug-eluting stenting versus surgery has not been established in a randomized trial.

Methods In this prospective, multicenter, randomized trial, 201 patients with ULM disease were randomly assigned to undergo sirolimus-eluting stenting (n = 100) or CABG using predominantly arterial grafts (n = 101). The primary clinical end point was noninferiority in freedom from major adverse cardiac events, such as cardiac death, myocardial infarction, and the need for target vessel revascularization within 12 months.

Results The combined primary end point was reached in 13.9% of patients after surgery, as opposed to 19.0% after PCI ($p = 0.19$ for noninferiority). The combined rates for death and myocardial infarction were comparable (surgery, 7.9% vs. stenting, 5.0%; noninferiority $p < 0.001$), but stenting was inferior to surgery for repeat revascularization (5.9% vs. 14.0%; noninferiority $p = 0.35$). Perioperative complications including 2 strokes were higher after surgery (4% vs. 30%; $p < 0.001$). Freedom from angina was similar between groups ($p = 0.33$).

Conclusions In patients with ULM stenosis, PCI with sirolimus-eluting stents is inferior to CABG at 12-month follow-up with respect to freedom from major adverse cardiac events, which is mainly influenced by repeated revascularization, whereas for hard end points, PCI results are favorable. A longer follow-up is warranted. (Percutaneous Coronary Intervention [PCI] With Drug-Eluting Stents [DES] Versus Coronary Artery Bypass Graft [CABG] for Patients With Significant Left Main Stenosis; NCT00176397) (443).

Long-Term Prognostic Value of Dobutamine Stress CMR

Objectives The aim of this study was to assess the long-term value of high-dose dobutamine cardiac magnetic resonance (DCMR) for the prediction of cardiac events in a large cohort of patients with known or suspected coronary artery disease.

Background High-dose DCMR has been shown to be a useful technique for diagnosis and intermediate-term prognostic stratification.

Methods Clinical data and DCMR results were analyzed in 1,463 consecutive patients undergoing DCMR between 2000 and 2004. Ninety-four patients were lost to follow-up. The remaining 1,369 patients were followed up for a mean of 44 ± 24 months. Cardiac events, defined as cardiac death and nonfatal myocardial infarction, were related to clinical and DCMR results.

Results Three-hundred fifty-two patients underwent early revascularization (≤3 months of DCMR) and were excluded from analysis. Of the remaining 1,017 patients, 301 patients (29.6%) experienced inducible wall motion abnormalities (WMA). Forty-six cardiac events were reported. In those with and without inducible WMA, the proportion of patients with cardiac events was 8.0% versus 3.1%, respectively, $p = 0.001$ (hazard ratio: 3.3; 95% confidence interval: 1.8 to 5.9 for the presence of inducible WMA; $p < 0.001$). A DCMR without inducible WMA carried an excellent prognosis, with a 6-year cardiac event-free survival of 96.8%. In all 1,369 patients in the patient group with stress-inducible WMA, those patients with medical therapy demonstrated a trend to a higher cardiac event rate (8.0%) than those with early revascularization (5.4%) ($p = 0.234$). Patients with normal DCMR and medical therapy or early revascularization demonstrated similar cumulative cardiac event rates (3.1% vs. 3.2%, $p = 0.964$).

Conclusions In a large cohort of patients, DCMR has an added value for predicting cardiac events during long-term follow-up, improving the differentiation between high-risk and low-risk patients. Patients with inducible WMA and following early revascularization, demonstrate lower cardiac event rates than patients with medical therapy alone (444).

Usefulness of TEE as the Primary Imaging Technique to Guide Transcatheter Transapical Aortic Valve Implantation

Objectives The aim of this study was to: 1) determine the usefulness of transesophageal echocardiography (TEE) as the primary technique to guide transapical (TA) transcatheter aortic valve implantation (TAVI); and 2) to compare TEE with angiography as the primary imaging modality for TA-TAVI guidance.

Background TEE has been routinely used as an adjunct to angiography during TA-TAVI procedures, but very few data exist on the use of TEE as the primary imaging technique guiding TA-TAVI.

Methods One hundred consecutive high-risk patients (mean age 79 ± 9 years, mean logistic EuroSCORE: 25.8 ± 17.6%) who underwent TA-TAVI in our center were included. The Edwards valve was used in all cases, and all procedures were performed in an operating room without hybrid facilities. The TA-TAVI was primarily guided by angiography in the first 25 patients (A-TAVI group) and by TEE in the last 75 patients (TEE-TAVI group). Procedural, 30-day, and follow-up results were evaluated.

Results No differences were observed between groups at baseline except for a higher ($p = 0.001$) prevalence of moderate or severe mitral regurgitation in the TEE-TAVI group. The procedure was successful in 97.3% and 100% of the patients in the TEE-TAVI and A-TAVI groups, respectively ($p = 1.0$), and a lower contrast volume was used

in the TEE-TAVI group (12 [5 to 20] ml vs. 40 [20 to 50] ml, $p < 0.0001$). There were no differences between groups in the occurrence of valve malposition needing a second valve (TEE-TAVI: 5.3%; A-TAVI: 4%; $p = 1.0$) or valve embolization (TEE-TAVI: 1.3%; A-TAVI: 4%; $p = 0.44$). The results regarding post-procedural valve hemodynamic status and aortic regurgitation were similar between groups. The survival rates at 30-day and 1-year follow-up were 87% and 75% in the TEE-group and 88% and 84% in the A-TAVI group, respectively (log-rank = 0.49).

Conclusions TEE-TAVI was associated with similar acute and midterm results as A-TAVI and significantly reduced contrast media use during the procedures. These results suggest the feasibility and safety of performing TA-TAVI procedures in an operating room without hybrid facilities, but larger studies are needed to confirm these findings (445).

Quantification of Coronary Arterial Stenoses by Multidetector CT Angiography in Comparison With Conventional Angiography: Methods, Caveats, and Implications

Multidetector computed tomography (MDCT) is a rapidly evolving technology for performing noninvasive coronary angiography. Despite good sensitivity and specificity for detecting significant coronary artery disease in patients, disagreement on individual coronary arterial stenosis severity is common between MDCT and the current gold standard, conventional angiography. The reasons for such disagreement are numerous, but are at least partly inherent to MDCT's modest spatial and temporal resolution at present. Less well acknowledged, however, is the fact that MDCT and conventional angiography are fundamentally different technologies, rendering good agreement on the degree of lumen narrowing rather unrealistic, given both of their respective limitations. Discrepant stenosis assessment by MDCT and conventional angiography receives remarkable attention, whereas its significance for patient outcome is less certain. On the other hand, the ability to noninvasively assess coronary arterial plaque characteristics and composition in addition to lumen obstruction shows strong promise for improved risk assessment and may at last enable us to move beyond mere coronary stenosis assessment for the management of patients with coronary artery disease (446).

Noninvasive Evaluation of Coronary Reperfusion by CT Angiography in Patients With STEMI

Objectives The aim of this study was to determine whether 64-slice multidetector computed tomography (MDCT) can differentiate coronary reperfusion with Thrombolysis In Myocardial Infarction (TIMI) flow grade 3 from TIMI flow grade ≤2 after ST-segment elevation myocardial infarction (STEMI).

Background Multidetector computed tomography has become a popular modality for noninvasive coronary artery imaging. Recently, 64-slice MDCT has been applied to evaluate coronary arteries in acute coronary artery disease.

Methods The presence or absence of distal reperfusion in infarct-related arteries (IRA) was visualized with 64-slice MDCT during the acute phase in 87 non–high-risk patients after STEMI. To differentiate TIMI flow grade 3 from TIMI flow grade 2, we calculated the computed tomography (CT) number ratio by dividing the CT number of the contrast-enhanced coronary lumen at the most distal IRA by that at the proximal site to the culprit lesion in patients with reperfusion on MDCT. The MDCT findings were compared with TIMI flow grade with invasive coronary angiography (ICA) performed 20 ± 5 min later.

Results According to ICA, 58 patients had TIMI flow grade 0 or 1, 17 had TIMI flow grade 2, and 12 had TIMI flow grade 3, whereas distal reperfusion was evident on MDCT in 28 of the 29 patients with TIMI flow grade ≥2 and absent in 55 of the 58 with TIMI flow grade ≤1. The CT number ratio was significantly higher in TIMI flow grade 3 than in TIMI flow grade ≤2 (0.64 ± 0.11 vs. 0.37 ± 0.12; $p < 0.0001$). The sensitivity, specificity, and accuracy of a diagnosis of TIMI flow grade 3 on the basis of a CT number ratio of ≥0.54 that was an optimal cutoff value determined by receiver-operator characteristic curve analysis were 92%, 97%, and 97%, respectively.

Conclusions Visualization of the IRA by 64-slice MDCT enables noninvasive differentiation of angiographic TIMI flow grade 3 from TIMI flow grade ≤2 coronary reperfusion during the acute phase in patients with STEMI (447).

Prospective Validation of Standardized, 3-Dimensional, Quantitative Coronary Computed Tomographic Plaque Measurements Using Radiofrequency Backscatter Intravascular Ultrasound as Reference Standard in Intermediate Coronary Arterial Lesions: Results From the ATLANTA (Assessment of Tissue Characteristics, Lesion Morphology, and Hemodynamics by Angiography With Fractional Flow Reserve, Intravascular Ultrasound and Virtual Histology, and Noninvasive Computed Tomography in Atherosclerotic Plaques) I Study

Objectives This study sought to determine the accuracy of 3-dimensional, quantitative measurements of coronary plaque by computed tomography angiography (CTA) against intravascular ultrasound with radiofrequency backscatter analysis (IVUS/VH).

Background Quantitative, 3-dimensional coronary CTA plaque measurements have not been validated against IVUS/VH.

Methods Sixty patients in a prospective study underwent coronary X-ray angiography, IVUS/VH, and coronary

CTA. Plaque geometry and composition was quantified after spatial coregistration on segmental and slice-by-slice bases. Correlation, mean difference, and limits of agreement were determined.

Results There was significant correlation for all prespecified parameters by segmental and slice-by-slice analyses ($r = 0.41$ to 0.84; all $p < 0.001$). On a segmental basis, CTA underestimated minimal lumen diameter by 21% and overestimated diameter stenosis by 39%. Minimal lumen area was overestimated on CTA by 27% but area stenosis was only underestimated by 5%. Mean difference in noncalcified plaque volume and percent and calcified plaque volume and percent were 38%, −22%, 104%, and 64%. On a slice-by-slice basis, lumen, vessel, noncalcified-, and calcified-plaque areas were overestimated on CTA by 22%, 19%, 44%, and 88%. There was significant correlation for percentage of atheroma volume (0.52 vs. 0.54; $r = 0.51$; $p < 0.001$). Compositional analysis suggested that high-density noncalcified plaque on CTA best correlated with fibrous tissue and low-density noncalcified plaque correlated with necrotic core plus fibrofatty tissue by IVUS/VH.

Conclusions This is the first validation that standardized, 3-dimensional, quantitative measurements of coronary plaque correlate with IVUS/VH. Mean differences are small, whereas limits of agreement are wide. Low-density noncalcified plaque correlates with necrotic core plus fibrofatty tissue on IVUS/VH (448).

Influence of Site and Operator Characteristics on Carotid Artery Stent Outcomes: Analysis of the CAPTURE 2 (Carotid ACCULINK/ACCUNET Post Approval Trial to Uncover Rare Events) Clinical Study

Objectives The aim of this study was to analyze the CAPTURE 2 (Carotid ACCULINK/ACCUNET Post Approval Trial to Uncover Rare Events) study for physician- or site-related variables associated with differential outcomes for carotid artery stenting (CAS).

Background The CAPTURE 2 trial is an ongoing, prospective, nonrandomized, independently adjudicated, multicenter clinical study enrolling high-surgical-risk patients undergoing CAS.

Methods In this assessment of the CAPTURE 2 study, the American Heart Association carotid endarterectomy guideline limits were used to define acceptable site and physician CAS outcomes; therefore, the resulting population of nonoctogenarian, asymptomatic subjects in this analysis is confined to 3,388 (of the total 5,297) subjects treated at 180 U.S. hospitals by 459 operators between March 2006 and January 2009.

Results The rates of death, stroke, and myocardial infarction and death and stroke (DS) at 30 days were 3.5% and 3.3%, respectively, for the full CAPTURE 2 study cohort and 2.9% and 2.7%, respectively, for the asymptomatic, nonoctogenarian subgroup. In this subgroup, two-thirds of sites (118 of 180, 66%) had no DS events. Within the remaining sites, an inverse relationship between event rates and hospital patient volume as well as between event rates and individual operator volume was observed. The DS rates trended lower for interventional cardiologists compared with other specialties.

Conclusions Outcomes from the largest prospectively gathered, independently adjudicated, multicenter CAS study indicate that CAS can be safely performed in a variety of hospital settings by physicians with various specialties. The most important determinant of perioperative CAS outcomes was both site and operator CAS volume. A threshold of 72 cases was found to be necessary for consistently achieving a DS rate below 3% in this later-phase single arm study; background era and non-study operator experience will affect this determination. (Second Phase of "Carotid RX ACCULINK/RX ACCUNET Post-Approval Trial to Uncover Unanticipated or Rare Events"; NCT00302237) (449).

Incidence, Prognostic Impact, and Influence of Antithrombotic Therapy on Access and Nonaccess Site Bleeding in Percutaneous Coronary Intervention

Objectives The aim of this study was to evaluate the relative frequency of access and nonaccess site bleeding, the association of these events with 1-year mortality, and the impact of randomized antithrombotic therapy.

Background Post-percutaneous coronary intervention (PCI) bleeding has been strongly associated with subsequent mortality. The extent to which access versus nonaccess site bleeding contributes to this poor prognosis and the role of antithrombotic therapies remains poorly understood.

Methods The incidence and impact of Thrombolysis In Myocardial Infarction (TIMI) major/minor 30-day bleeding and randomized antithrombotic therapy were examined in a combined dataset from the REPLACE-2 (Randomized Evaluation in PCI Linking Angiomax to Reduced Clinical Events), Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY), and HORIZONS-AMI (Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction) trials in 17,393 PCI patients.

Results The TIMI major/minor bleeding occurred in 5.3% of patients, 61.4% of which (3.3%) were nonaccess site bleeds. After multivariable adjustment, TIMI bleeding was associated with an increased risk of 1-year mortality (hazard ratio [HR]: 3.17, 95% confidence interval [CI]: 2.51 to 4.00, $p < 0.0001$). The HR of a nonaccess site bleed was approximately 2-fold that of an access site bleed: HR: 3.94, 95% CI: 3.07 to 5.15, $p < 0.0001$ versus HR: 1.82, 95% CI: 1.17 to 2.83, $p = 0.008$, respectively. Randomization to bivalirudin versus heparin + a glycoprotein IIb/IIIa inhibitor resulted in

38% and 43% relative reductions in TIMI major/minor and TIMI major bleeding, respectively ($p < 0.0001$ for both), with significant reductions in both access and nonaccess site bleeding.

Conclusions Nonaccess site bleeding after PCI is common, representing approximately two-thirds of all TIMI bleeding events, and is associated with a 4-fold increase in 1-year mortality. Use of bivalirudin rather than heparin + a glycoprotein IIb/IIIa inhibitor significantly decreases both nonaccess site as well as access site bleeding events by approximately 40% (450).

The SPIRIT V Study: A Clinical Evaluation of the XIENCE V Everolimus-Eluting Coronary Stent System in the Treatment of Patients With De Novo Coronary Artery Lesions

Objectives The SPIRIT V (A Clinical Evaluation of the XIENCE V Everolimus-Eluting Coronary Stent System in the Treatment of Patients With De Novo Coronary Artery Lesions) study is a post-market surveillance experience of the XIENCE V (Abbott Vascular, Santa Clara, California) everolimus-eluting stent (EES) in patients with higher-risk coronary anatomy.

Background Previous pre-approval studies have shown the safety and efficacy of EES in highly selected groups of patients.

Methods The SPIRIT V trial is a prospective, open label, single arm, multicenter study. Two thousand seven hundred patients with multiple de novo coronary artery lesions suitable for treatment with a planned maximum of 4 EES were enrolled at 93 centers in Europe, Asia Pacific, Canada, and South Africa. Lesions had a reference vessel diameter between 2.25 and 4.0 mm and a length of $\leq$28 mm by visual estimation. An independent clinical events committee adjudicated all end point-related events. The primary end point was the composite rate of all death, myocardial infarction (MI), and target vessel revascularization at 30 days. Secondary end points included stent thrombosis and acute success (clinical device and procedure success).

Results At 30 days, the primary composite end point of all death, MI, and target vessel revascularization was 2.7%. At 1 year, rates of cardiac death, overall MI, and target lesion revascularization were 1.1%, 3.5%, and 1.8%, respectively. The cumulative rate of definite and probable stent thrombosis was low at 0.66% at 1 year.

Conclusions Use of EES in patients with multiple, complex de novo lesions yielded 1-year major adverse cardiac events, stent thrombosis, and target lesion revascularization rates that are comparable to those of the more controlled SPIRIT II and SPIRIT III trials—which included patients with restricted inclusion/exclusion criteria—and other all-comer population, physician-initiated studies like the X-SEARCH (Xience Stent Evaluated At Rotterdam Cardiology Hospital) and COMPARE (A Randomized Controlled Trial of Everolimus-eluting Stents and Paclitaxel-eluting Stents for Coronary Revascularization in Daily Practice) trials (451).

The STAT-MI (ST-Segment Analysis Using Wireless Technology in Acute Myocardial Infarction) Trial Improves Outcomes

Objectives The goal of this study was to evaluate the impact of the STAT-MI (ST-Segment Analysis Using Wireless Technology in Acute Myocardial Infarction) network on outcomes in the treatment of patients presenting with ST-segment elevation myocardial infarction (STEMI).

Background Shortening door-to-balloon (D2B) time remains a national priority for the treatment of STEMI. We previously reported a fully automated wireless network (STAT-MI) for transmission of electrocardiograms (ECGs) for suspected STEMI from the field to offsite cardiologists, allowing early triage with shortening of subsequent D2B times. We now report the impact of the STAT-MI wireless network on infarct size, length of hospital stay (LOS), and mortality.

Methods A fully automated wireless network (STAT-MI) was developed to enable automatic 12-lead ECG transmission and direct communication between emergency medical services personnel and offsite cardiologists that facilitated direct triage of patients to the cardiac catheterization laboratory. Demographic, laboratory, and time interval data of STAT-MI network patients were prospectively collected over a 33-month period and compared with concurrent control patients who presented with STEMI through non–STAT-MI pathways.

Results From June 2006 through February 2009, 92 patients presented via the STAT-MI network, and 50 patients presented through non–STAT-MI pathways (control group). Baseline clinical and demographic variables were similar in both groups. Overall, compared with control subjects, STAT-MI patients had significantly shorter D2B times (63 [42 to 87] min vs. 119 [96 to 178] min, $U = 779.5$, $p < 0.00004$), significantly lower peak troponin I (39.5 [11 to 120.5] ng/ml vs. 87.6 [38.4 to 227] ng/ml, $U = 889.5$, $p = 0.005$) and creatine phosphokinase-MB (126.1 [37.2 to 280.5] ng/ml vs. 290.3 [102.4 to 484] ng/ml, $U = 883$, $p = 0.001$), higher left ventricular ejection fractions (50% [35 to 55] vs. 35% [25 to 52], $U = 1{,}075$, $p = 0.004$), and shorter LOS (3 [2 to 4] days vs. 5.5 [3.5 to 10.5] days, $U = 378$, $p < 0.001$).

Conclusions A fully automated, field-based, wireless network that transmits ECGs automatically to offsite cardiologists for the early evaluation and triage of patients with STEMI shortens D2B times, reduces infarct size, limits ejection fraction reduction, and shortens LOS (452).

Predicting Successful Guidewire Crossing Through Chronic Total Occlusion of Native Coronary Lesions Within 30 Minutes: The J-CTO (Multicenter CTO Registry in Japan) Score as a Difficulty Grading and Time Assessment Tool

Objectives This study sought to establish a model for grading lesion difficulty in interventional chronic total occlusion (CTO) treatment.

Background Owing to uncertainty of success of the procedure and difficulties in selecting suitable cases for treatment, performance of interventional CTO remains infrequent.

Methods Data from 494 native CTO lesions were analyzed. To eliminate operator bias, the objective parameter of successful guidewire crossing within 30 min was set as an end point, instead of actual procedural success. All observations were randomly assigned to a derivation set and a validation set at a 2:1 ratio. The J-CTO (Multicenter CTO Registry of Japan) score was determined by assigning 1 point for each independent predictor of this end point and summing all points accrued. This value was then used to develop a model stratifying all lesions into 4 difficulty groups: easy (J-CTO score of 0), intermediate (score of 1), difficult (score of 2), and very difficult (score of $\geq$3).

Results The set end point was achieved in 48.2% of lesions. Independent predictors included calcification, bending, blunt stump, occlusion length >20 mm, and previously failed lesion. Easy, intermediate, difficult, and very difficult groups, stratified by J-CTO score, demonstrated stepwise, proportioned, and highly reproducible differences in probability of successful guidewire crossing within 30 min (87.7%, 67.1%, 42.4%, and 10.0% in the derivation set and 92.3%, 58.3%, 34.8%, and 22.2% in the validation set, respectively). Areas under receiver-operator characteristic curves were comparable (derivation: 0.82 vs. validation: 0.76).

Conclusions This model predicted the probability of successful guidewire crossing within 30 min very well and can be applied for difficulty grading (453).

Circadian Variation in Coronary Stent Thrombosis

Objectives We sought to determine the circadian, weekly, and seasonal variation of coronary stent thrombosis.

Background Other adverse cardiovascular events such as acute myocardial infarction are known to have higher incidences during the early morning hours, Mondays, and winter months.

Methods The Mayo Clinic Percutaneous Coronary Intervention Registry was searched for patients admitted to our center who underwent repeat percutaneous coronary intervention in a previously stented coronary artery segment. Stent thrombosis was confirmed by angiographic review, and date and time of symptom onset were obtained from medical records.

Results We identified 124 patients with definite stent thrombosis and known date and time of symptom onset. In these patients, onset of stent thrombosis was significantly associated with time of day ($p = 0.006$), with a peak incidence around 7:00 AM. When patients were subdivided into early stent thrombosis (0 to 30 days; $n = 49$), late stent thrombosis (31 to 360 days; $n = 30$), and very late stent thrombosis (>360 days; $n = 45$), only early stent thrombosis remained significantly associated with time of day ($p = 0.030$). No association with the day of the week was found ($p = 0.509$); however, onset of stent thrombosis did follow a significant seasonal pattern, with higher occurrences in the summer ($p = 0.036$).

Conclusions Coronary stent thrombosis occurs more often in the early morning hours. Early stent thrombosis follows a circadian rhythm with a peak at 7:00 AM. This pattern was not significant in late and very late stent thrombosis. Occurrences throughout the week were equally distributed, but stent thrombosis was more likely to occur in the summer months (454).

Long-Term Outcomes After the Percutaneous Treatment of Drug-Eluting Stent Restenosis

Objectives This study sought to evaluate the long-term angiographic and clinical outcomes after the treatment of drug-eluting stent in-stent restenosis (DES-ISR) based on the angiographic pattern of restenosis.

Background Long-term outcomes after percutaneous treatment of DES-ISR are unclear.

Methods This study performed a retrospective analysis of 481 consecutive de novo DES-ISR lesions ($n = 392$) treated percutaneously between August 2002 and July 2007. The lesions were divided based on the pattern of restenosis: focal (305; 63.4%), diffuse (120; 24.9%), and occlusive (56; 11.6%).

Results The majority (65%) of patients had angina or ischemia on presentation and 13% had an acute coronary syndrome. Angiographic follow-up after treatment of DES-ISR was available in 65.5% of lesions. A second angiographic restenosis occurred in 29.1% of the focal group, 45.8% ($p = 0.007$) of the diffuse, and 65.6% ($p < 0.0001$) of the occlusive. The pattern of DES-ISR predicted the pattern of recurrence: occlusive reoccluded in 66.7%; diffuse recurred as diffuse or occlusive in 57.9%; focal as focal in 67.2%. During a median follow-up of 2.97 years (interquartile range: 2.37 to 3.89), major adverse cardiac events occurred in 32.8% of patients with no significant differences among the focal, diffuse, and occlusive groups (30.9%, 38.7%, 31.1%; $p = 0.38$). Diffuse restenosis was associated with a significantly higher target lesion revascularization rate compared with focal (27.1% vs. 15.8%; $p = 0.008$). A disparity between restenosis (65.6%) and target lesion revascularization (18.5%) rates for occlusive DES-ISR suggests that as many recurrent restenoses were occlusive, they were not retreated.

Conclusions DES-ISR identifies a high-risk cohort that is at an increased risk of events, in particular repeat revascularization, during long-term follow-up. The initial pattern of

restenosis is the most important predictor of recurrent restenosis or the need for subsequent reintervention (455).

Dynamic 3-Dimensional Stress Cardiac Magnetic Resonance Perfusion Imaging: Detection of Coronary Artery Disease and Volumetry of Myocardial Hypoenhancement Before and After Coronary Stenting

Objectives The aim of this study was to establish a new, dynamic 3-dimensional cardiac magnetic resonance (3D-CMR) perfusion scan technique exploiting data correlation in k-space and time with sensitivity-encoding and to determine its value for the detection of coronary artery disease (CAD) and volumetry of myocardial hypoenhancement ($VOLUME_{hypo}$) before and after percutaneous coronary stenting.

Background Dynamic 3D-CMR perfusion imaging might improve detection of myocardial perfusion deficits and could facilitate direct volumetry of myocardial hypoenhancement.

Methods In 146 patients with known or suspected CAD, a 3.0-T CMR examination was performed including cine imaging, 3D-CMR perfusion under adenosine stress and at rest followed by delayed enhancement imaging. Quantitative invasive coronary angiography defined significant CAD (≥50% luminal narrowing). Forty-eight patients underwent an identical repeat CMR examination after percutaneous stenting of at least 1 coronary lesion. The 3D-CMR perfusion scans were visually classified as pathologic if ≥1 segment showed an inducible perfusion deficit in the absence of delayed enhancement. The $VOLUME_{hypo}$ was measured by segmentation of the area of inducible hypoenhancement and normalized to left-ventricular myocardial volume (%$VOLUME_{hypo}$).

Results The 3D-CMR perfusion resulted in a sensitivity, specificity, and diagnostic accuracy of 91.7%, 74.3%, and 82.9%, respectively. Before and after coronary stenting, % $VOLUME_{hypo}$ averaged to 14.2 ± 9.5% and 3.2 ± 5.2%, respectively, with a relative $VOLUME_{hypo}$ reduction of 79.4 ± 25.4%. Intrareader and inter-reader reproducibility of $VOLUME_{hypo}$ measurements was high (Lin's concordance correlation coefficient, 0.96 and 0.96, respectively).

Conclusions The 3D-CMR stress perfusion provided high image quality and high diagnostic accuracy for the detection of significant CAD. The $VOLUME_{hypo}$ measurements were highly reproducible and allowed for the assessment of the treatment effect achievable by percutaneous coronary stenting (456).

Calcium-Channel Blockers Do Not Alter the Clinical Efficacy of Clopidogrel After Myocardial Infarction: A Nationwide Cohort Study

Objectives The purpose of this study was to determine the risk of adverse cardiovascular events associated with concomitant use of clopidogrel and calcium-channel blockers (CCBs) in patients with myocardial infarction (MI).

Background CCBs inhibit a variety of cytochrome P-450 enzymes, some of which contribute to clopidogrel metabolic activation. This interaction may diminish the efficacy of clopidogrel.

Methods All patients surviving 30 days after a first-time MI in the period 2000 to 2006 in Denmark were identified by individual-level linkage of nationwide administrative registers. The cohort was divided into patients treated with and without clopidogrel and followed for 1 year after discharge. The risk of a composite of cardiovascular death, MI, or stroke and the risk of the individual components of the composite end point and all-cause death associated with CCBs were analyzed with multivariable Cox proportional hazard models and in univariate propensity score-matched models.

Results A total of 56,800 patients were included, of whom 24,923 were treated with clopidogrel and 13,380 with CCBs. In the Cox analyses, the risk of the composite end point associated with CCBs was increased in both patients treated and not treated with clopidogrel, with a hazard ratio of 1.15 (95% confidence interval [CI]: 1.07 to 1.24) and 1.05 (95% CI: 1.01 to 1.11), respectively. The increased risk was independent of clopidogrel use; the hazard rate ratio was 1.08 (95% CI: 0.99 to 1.18). Analyses of all additional adverse end points and propensity score–matched models provided similar results.

Conclusions The clinical efficacy of clopidogrel in patients with a recent MI is not modified by concomitant CCB treatment. This potential drug interaction is unlikely to have clinical significance (457).

Cardiovascular Mortality in Chronic Kidney Disease Patients Undergoing Percutaneous Coronary Intervention Is Mainly Related to Impaired P2Y12 Inhibition by Clopidogrel

Objectives We sought to determine whether low platelet response to the $P2Y_{12}$ receptor antagonist clopidogrel as assessed by vasodilator-stimulated phosphoprotein flow cytometry test (VASP-FCT) differentially affects outcomes in patients with or without chronic kidney disease (CKD) undergoing percutaneous coronary intervention (PCI).

Background Although both CKD and impaired platelet responsiveness to clopidogrel are strong predictors of unfavorable outcome after PCI, the impact of their association is unknown. The platelet VASP-FCT assay is specific for the $P2Y_{12}$ ADP receptor pathway. In this test, platelet activation is expressed as the platelet reactivity index (PRI).

Methods Four-hundred forty unselected patients (CKD: 126, estimated glomerular filtration rate [eGFR] <60 ml/min/1.73 m^2), no-CKD: 314 eGFR >60 ml/min/1.73 m^2) undergoing urgent (n = 336) or planned (n = 104) PCI were prospectively enrolled. In each subgroup, patients were

classified as low-responders (LR: PRI ≥61%) or responders (R: PRI <61%) to clopidogrel.

Results At a mean follow-up of 9 ± 2 months, all-cause mortality, cardiac death, and possible stent thrombosis were higher in CKD than in no-CKD patients. Within the CKD group, the LR status was associated with higher rates of all-cause mortality (25.5% vs. 2.8%, $p < 0.001$), cardiac death (23.5% vs. 2.8%, $p < 0.001$), all stent thrombosis (19.6% vs. 2.7%, $p = 0.003$), and MACE (33.3% vs. 12.3%, $p = 0.007$). Conversely, in no-CKD patients, the LR status did not affect outcomes. Multivariate analysis identified Killip class ≥3, drug-eluting stent implantation, and the interaction between LR and CKD (hazard ratio: 11.96, 95% confidence interval: 1.22 to 116.82; $p = 0.033$) as independent predictors of cardiac death.

Conclusions In CKD patients, the presence of low platelet response to clopidogrel is associated with worse outcomes after PCI (458).

Left Atrial Strain Predicts Reverse Remodeling After Catheter Ablation for Atrial Fibrillation

Objectives The purpose of this study was to assess left atrial (LA) strain during long-term follow-up after catheter ablation for atrial fibrillation and to find predictors for LA reverse remodeling.

Background The association between LA reverse remodeling and improvement in LA strain after catheter ablation has not been investigated thus far.

Methods In 148 patients undergoing catheter ablation for atrial fibrillation, LA volumes and LA strain were assessed with echocardiography at baseline and after a mean of 13.2 ± 6.7 months of follow-up. The study population was divided according to LA reverse remodeling at follow-up: responders were defined as patients who exhibited 15% or more reduction in maximum LA volume at long-term follow-up. Left atrial systolic (LAs) strain was assessed with tissue Doppler imaging.

Results At follow-up, 93 patients (63%) were classified as responders, whereas 55 patients (37%) were nonresponders. At baseline, LAs strain was significantly higher in the responders as compared with the nonresponders (19 ± 8% vs. 14 ± 6%; $p = 0.001$). Among the responders, a significant increase in LAs strain was noted from baseline to follow-up (from 19 ± 8% to 22 ± 9%; $p < 0.05$), whereas no change was noted among the nonresponders. LAs strain at baseline was an independent predictor of LA reverse remodeling (odds ratio: 1.813; 95% confidence interval: 1.102 to 2.982; $p = 0.019$).

Conclusions In the present study, 63% of the patients exhibited LA reverse remodeling after catheter ablation for atrial fibrillation, with a concomitant improvement in LA strain. LA strain at baseline was an independent predictor of LA reverse remodeling (459).

Door-to-Balloon Times Under 90 Min Can Be Routinely Achieved for Patients Transferred for ST-Segment Elevation Myocardial Infarction Percutaneous Coronary Intervention in a Rural Setting

Objectives The purpose of this study was to demonstrate the feasibility of routine transfer of ST-segment elevation myocardial infarction (STEMI) patients to achieve percutaneous coronary intervention (PCI) in less than 90 min from presentation.

Background Many PCI hospitals have achieved routine door-to-balloon times under 90 min for patients with STEMI presenting *directly* to the hospital. However, few patients transferred from a non-PCI center undergo PCI within 90 min of presentation.

Methods Our rural PCI hospital implemented a program in 2005 for rapid triage, transfer, and treatment of STEMI patients and made additional improvements in 2006 and 2007. Intervals between milestones in the STEMI triage/transfer/treatment process were assessed before and after implementation of the program.

Results During the 5-year study period, 676 patients with 687 STEMIs were transferred from 19 community hospitals and underwent PCI. Median door-to-balloon time decreased from 189 min to 88 min ($p < 0.001$). The time intervals reflecting efficiency of the referring hospitals, transfer services, and PCI hospital all significantly improved. In 2008, median door-to-balloon times were <90 min for 6 of the 7 most frequently referring hospitals. Delays during off-hours presentation in 2004 were abolished after the program was implemented in 2005. In-hospital mortality decreased from 6% before to 3% after implementation of the program. In multivariate modeling, presentation before initiation of the STEMI program predicted increased risk of in-hospital mortality (odds ratio: 3.74, 95% confidence interval: 1.22 to 11.51, $p = 0.021$).

Conclusions A program of rapid triage, transfer, and treatment of STEMI patients presenting to non-PCI hospitals can reduce in-hospital mortality and produce progressive improvements in door-to-balloon time such that median door-to-balloon times under 90 min are feasible (460).

Multicenter Randomized Trial Evaluating the Efficacy of Cilostazol on Ischemic Vascular Complications After Drug-Eluting Stent Implantation for Coronary Heart Disease: Results of the CILON-T (Influence of CILostazol-based triple antiplatelet therapy ON ischemic complication after drug-eluting stenT implantation) Trial

Objectives We aimed to test whether cilostazol has beneficial effects in the real-world patients treated with intracoronary drug-eluting stents (DES).

Background The addition of cilostazol on the conventional dual antiplatelet therapy has been reported to reduce platelet

reactivity and to improve clinical outcomes after percutaneous coronary intervention in previous studies.

Methods In a randomized multicenter trial, we enrolled 960 patients who received DES. They were randomized to receive either dual antiplatelet therapy (DAT) (aspirin and clopidogrel) or triple antiplatelet therapy (TAT) (aspirin, clopidogrel, and cilostazol) for 6 months. Primary end point was the composite of cardiac death, nonfatal myocardial infarction, ischemic stroke, or target lesion revascularization (TLR). Secondary end points were $P2Y_{12}$ reaction unit (PRU) measured with the VerifyNow P2Y12 assay (Accumetrics, San Diego, California) at discharge and at 6 months after the index procedure. All-cause death, stent thrombosis, and each component of the primary end point at 6 months were other secondary end points. Analysis was done on an intention-to-treat basis.

Results At 6 months' follow-up, there was no difference in the primary end point between the 2 groups (8.5% in TAT vs. 9.2% in DAT, $p = 0.74$). In secondary end point analysis, the TAT group achieved lower PRU levels than the DAT group both at discharge (206.6 ± 90.3 PRU vs. 232.2 ± 80.3 PRU, $p < 0.001$) and at 6 months (210.7 ± 87.9 PRU vs. 255.7 ± 73.7 PRU, $p < 0.001$). In the Cox proportional hazards analysis, lesion length (≥28 mm, hazard ratio [HR]: 2.10, 95% confidence interval [CI]: 1.25 to 3.52), and PRU level at discharge (every increase in tertile, HR: 1.61, 95% CI: 1.16 to 2.25) were predictors of the primary end point, but not the use of cilostazol (HR: 0.90, 95% CI: 0.54 to 1.52).

Conclusions Despite the greater reduction of platelet reactivity by addition of cilostazol to conventional DAT, TAT did not show superiority in reducing the composite of adverse cardiovascular outcomes after DES implantation. (The Efficacy of CILostazol ON Ischemic Complications After DES Implantation [CILON-T]; NCT00776828) (461).

Standardized Endpoint Definitions for Transcatheter Aortic Valve Implantation Clinical Trials: A Consensus Report From the Valve Academic Research Consortium

Objectives To propose standardized consensus definitions for important clinical endpoints in transcatheter aortic valve implantation (TAVI), investigations in an effort to improve the quality of clinical research and to enable meaningful comparisons between clinical trials. To make these consensus definitions accessible to all stakeholders in TAVI clinical research through a peer reviewed publication, on behalf of the public health.

Background Transcatheter aortic valve implantation may provide a worthwhile less invasive treatment in many patients with severe aortic stenosis and since its introduction to the medical community in 2002, there has been an explosive growth in procedures. The integration of TAVI into daily clinical practice should be guided by academic activities, which requires a harmonized and structured process for data collection, interpretation, and reporting during well-conducted clinical trials.

Methods and Results The Valve Academic Research Consortium established an independent collaboration between Academic Research organizations and specialty societies (cardiology and cardiac surgery) in the USA and Europe. Two meetings, in San Francisco, California (September 2009) and in Amsterdam, the Netherlands (December 2009), including key physician experts, and representatives from the U.S. Food and Drug Administration (FDA) and device manufacturers, were focused on creating consistent endpoint definitions and consensus recommendations for implementation in TAVI clinical research programs. Important considerations in developing endpoint definitions included: 1) respect for the historical legacy of surgical valve guidelines; 2) identification of pathophysiological mechanisms associated with clinical events; 3) emphasis on clinical relevance. Consensus criteria were developed for the following endpoints: mortality, myocardial infarction, stroke, bleeding, acute kidney injury, vascular complications, and prosthetic valve performance. Composite endpoints for TAVI safety and effectiveness were also recommended.

Conclusions Although consensus criteria will invariably include certain arbitrary features, an organized multidisciplinary process to develop specific definitions for TAVI clinical research should provide consistency across studies that can facilitate the evaluation of this new important catheter-based therapy. The broadly based consensus endpoint definitions described in this document may be useful for regulatory and clinical trial purposes (462).

Catheter Ablation for Atrial Fibrillation: Are Results Maintained at 5 Years of Follow-Up?

Objectives This study describes 5-year follow-up results of catheter ablation for atrial fibrillation (AF).

Background Long-term efficacy following catheter ablation of AF remains unknown.

Methods A total of 100 patients (86 men, 14 women), age 55.7 ± 9.6 years, referred to our center for a first AF ablation (63% paroxysmal; 3.5 ± 1.4 prior ineffective antiarrhythmic agents) were followed for 5 years. Complete success was defined as absence of any AF or atrial tachycardia recurrence (clinical or by 24-h Holter monitoring) lasting ≥30 s.

Results Arrhythmia-free survival rates after a single catheter ablation procedure were 40%, 37%, and 29% at 1, 2, and 5 years, respectively, with most recurrences over the first 6 months. Patients with long-standing persistent AF experienced a higher recurrence rate than those with paroxysmal or persistent forms (hazard ratio [HR]: 1.9, 95% confidence interval [CI]: 1.0 to 3.5; $p = 0.0462$). In all, 175 procedures were performed, with a median of 2 per patient. Arrhythmia-free survival following the last catheter ablation procedure was 87%, 81%, and 63% at 1, 2, and 5 years, respectively. Valvular heart disease (HR: 6.0, 95% CI: 2.0 to

17.6; p = 0.0012) and nonischemic dilated cardiomyopathy (HR: 34.0, 95% CI: 6.3 to 182.1; p < 0.0001) independently predicted recurrences. Major complications (cardiac tamponade requiring drainage) occurred in 3 patients (3%).
Conclusions In selected patients with AF, a catheter ablation strategy with repeat intervention as necessary provides acceptable long-term relief. Although most recurrences transpire over the first 6 to 12 months, a slow but steady decline in arrhythmia-free survival is noted thereafter (463).

Association of Mortality With Years of Education in Patients With ST-Segment Elevation Myocardial Infarction Treated With Fibrinolysis

Objectives The purpose of this study was to examine the association between lower socioeconomic status (SES), as ascertained by years of education, and outcomes in patients with acute ST-segment elevation myocardial infarction (STEMI).
Background Previous studies have shown an inverse relationship between SES and coronary heart disease and mortality. Whether a similar association between SES and mortality exists in STEMI patients is unknown.
Methods We evaluated 11,326 patients with STEMI in the GUSTO-III (Global Use of Strategies to Open Occluded Coronary Arteries) trial study from countries that enrolled >500 patients. We evaluated clinical outcomes (adjusted using multivariate regression analysis) according to the number of years of education completed.
Results One-year mortality was inversely related to years of education and was 5-fold higher in patients with <8 years compared with those with >16 years of education (17.5% vs. 3.5%, p < 0.0001). The strength of the relationship between education and mortality varied among different countries. Nonetheless, years of education remained an independent correlate of mortality at day 7 (hazard ratio per year of increase in education: 0.86; 95% confidence interval: 0.83 to 0.88) and also between day 8 and 1 year (hazard ratio per year of increase in education: 0.96; 95% confidence interval: 0.94 to 0.98), even after adjustment for baseline characteristics and country of enrollment.
Conclusions When the number of years of education was used as a measure of SES, there was an inverse relationship such that significantly higher short-term and 1-year mortality existed beyond that accounted for by baseline clinical variables and country of enrollment. Future studies should account for and investigate the mechanisms underlying this link between SES and cardiovascular disease outcomes (464).

Long-Term Comparison of Drug-Eluting Stents and Coronary Artery Bypass Grafting for Multivessel Coronary Revascularization: 5-Year Outcomes From the Asan Medical Center-Multivessel Revascularization Registry

Objectives We performed the long-term (5-year) follow-up of a large cohort of patients who underwent drug-eluting stent (DES) or coronary artery bypass graft (CABG) surgery for multivessel revascularization.
Background Limited information is available on very long-term outcomes after multivessel DES treatment relative to CABG.
Methods We evaluated 3,042 patients with multivessel disease who received DES (n = 1,547) or underwent CABG (n = 1,495) between January 2003 and December 2005, and for whom complete follow-up data were available for a median 5.6 years (interquartile range: 4.6 to 6.3 years). We compared adverse outcomes (death; a composite outcome of death, myocardial infarction, or stroke; and repeat revascularization).
Results After adjustment for differences in baseline risk factors, 5-year risk of death (hazard ratio [HR]: 1.00; 95% confidence interval [CI]: 0.76 to 1.32, p = 0.99) and the combined risk of death, myocardial infarction, or stroke (HR: 0.97; 95% CI: 0.76 to 1.24, p = 0.81) were similar between the DES group and the CABG group. However, the rates of revascularization were significantly higher in the DES group (HR: 2.93; 95% CI: 2.20 to 3.90, p < 0.001). Similar results were obtained in comparisons of DES with CABG for high-risk clinical and anatomic subgroups with diabetes mellitus, abnormal ventricular function, age 65 years or more, and 3-vessel and left main disease. However, mortality benefit with DES implantation relative to CABG was noted in patients with 2-vessel disease (HR: 0.57; 95% CI: 0.36 to 0.92, p = 0.02).
Conclusions For patients with multivessel disease, DES treatment, compared with CABG, showed similar rates of mortality and of the composite safety outcomes, but higher rates of revascularization up to 5 years (465).

Comparative Validation of a Novel Risk Score for Predicting Bleeding Risk in Anticoagulated Patients With Atrial Fibrillation: The HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly) Score

Objectives The purpose of this study was to investigate predictors of bleeding in a cohort of anticoagulated patients and to evaluate the predictive value of several bleeding risk stratification schemas.
Background The risk of bleeding during antithrombotic therapy in patients with atrial fibrillation (AF) is not homogeneous, and several clinical risk factors have been incorporated into clinical bleeding risk stratification schemas. Current risk stratification schemas for bleeding during anticoagulation therapy have been based on complex scoring systems that are difficult to apply in clinical practice, and few have been derived and validated in AF cohorts.
Methods We investigated predictors of bleeding in a cohort of 7,329 patients with AF participating in the SPORTIF (*S*troke Prevention Using an ORal Thrombin Inhibitor in Atrial Fibrillation) III and V clinical trials and

evaluated the predictive value of several risk stratification schemas by multivariate analysis. Patients were anticoagulated orally with either adjusted-dose warfarin (target international normalized ratio 2 to 3) or fixed-dose ximelagatran 36 mg twice daily. Major bleeding was centrally adjudicated, and concurrent aspirin therapy was allowed in patients with clinical atherosclerosis.

Results By multivariate analyses, significant predictors of bleeding were concurrent aspirin use (hazard ratio [HR]: 2.10; 95% confidence interval [CI]: 1.59 to 2.77; $p < 0.001$); renal impairment (HR: 1.98; 95% CI: 1.42 to 2.76; $p < 0.001$); age 75 years or older (HR: 1.63; 95% CI: 1.23 to 2.17; $p = 0.0008$); diabetes (HR: 1.47; 95% CI: 1.10 to 1.97; $p = 0.009$), and heart failure or left ventricular dysfunction (HR: 1.32; 95% CI: 1.01 to 1.73; $p = 0.041$). Of the tested schemas, the new HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly) score performed best, with a stepwise increase in rates of major bleeding with increasing HAS-BLED score ($p_{trend} < 0.0001$). The c statistic for bleeding varied between 0.50 and 0.67 in the overall entire cohort and 0.68 among patients naive to warfarin at baseline ($n = 769$).

Conclusions This analysis identifies diabetes and heart failure or left ventricular dysfunction as potential risk factors for bleeding in AF beyond those previously recognized. Of the contemporary bleeding risk stratification schemas, the new HAS-BLED scheme offers useful predictive capacity for bleeding over previously published schemas and may be simpler to apply (466).

Multiple Biomarkers at Admission Significantly Improve the Prediction of Mortality in Patients Undergoing Primary Percutaneous Coronary Intervention for Acute ST-Segment Elevation Myocardial Infarction

Objectives We investigated whether multiple biomarkers improve prognostication in ST-segment elevation myocardial infarction (STEMI) patients undergoing primary percutaneous coronary intervention.

Background Few data exist on the prognostic value of combined biomarkers.

Methods We used data from 1,034 STEMI patients undergoing primary percutaneous coronary intervention in a high-volume percutaneous coronary intervention center in the Netherlands and investigated whether combining N-terminal pro-brain natriuretic peptide, glucose, C-reactive protein, estimated glomerular filtration rate, and cardiac troponin T improved the prediction of mortality. A risk score was developed based on the strongest predicting biomarkers in multivariate Cox regression. The additional prognostic value of the strongest predicting biomarkers to the established prognostic factors (age, body weight, diabetes, hypertension, systolic blood pressure, heart rate, anterior myocardial infarction, and time to treatment) was assessed in multivariable Cox regression.

Results During follow-up (median, 901 days), 120 of the 1,034 patients died. In Cox regression, glucose, estimated glomerular filtration rate, and N-terminal pro-brain natriuretic peptide were the strongest predictors for mortality ($p < 0.05$, for all). A risk score incorporating these biomarkers identified a high-risk STEMI subgroup with a significantly higher mortality when compared with an intermediate- or low-risk subgroup ($p < 0.001$). Addition of the 3 biomarkers to established prognostic factors significantly improved prediction for mortality, as shown by the net reclassification improvement (0.494, $p < 0.001$) and integrated discrimination improvement (0.0295, $p < 0.01$).

Conclusions Our data suggest that addition of a multimarker to a model including established risk factors improves the prediction of mortality in STEMI patients undergoing primary percutaneous coronary intervention. Furthermore, the use of a simple risk score based on these biomarkers identifies a high-risk subgroup (467).

Cerebral Embolism Following Transcatheter Aortic Valve Implantation: Comparison of Transfemoral and Transapical Approaches

Objectives The objective of this study was to compare the incidence of cerebral embolism (CE) as evaluated by diffusion-weighted magnetic resonance imaging (DW-MRI) following transapical (TA) transcatheter aortic valve implantation (TAVI) versus transfemoral (TF) TAVI.

Background The TA-TAVI approach avoids both the manipulation of large catheters in the aortic arch/ascending aorta and the retrograde crossing of the aortic valve, and this avoidance might lead to a lower rate of CE.

Methods This was a prospective multicenter study including 60 patients who underwent cerebral DW-MRI the day before and within the 6 days following TAVI (TF approach: 29 patients; TA approach: 31 patients). Neurologic and cognitive function assessments were performed at DW-MRI time points.

Results The TAVI procedure was performed with the Edwards valve and was successful in all cases but one (98%). A total of 41 patients (68%) had 251 new cerebral ischemic lesions at the DW-MRI performed 4 ± 1 days after the procedure, 19 patients in the TF group (66%) and 22 patients in the TA group (71%; $p = 0.78$). Most patients (76%) with new ischemic lesions had multiple lesions (median number of lesions per patient: 3, range 1 to 31). There were no differences in lesion number and size between the TF and TA groups. No baseline or procedural factors were found to be predictors of new ischemic lesions. The occurrence of CE was not associated with a measurable impairment in cognitive function, but 2 patients (3.3%) had a clinically apparent stroke within the 24 h following the procedure (1 patient in each group).

Conclusions TAVI is associated with a high rate of silent cerebral ischemic lesions as evaluated by DW-MRI, with no differences between the TF and TA approaches. These results provide important novel insight into the mechanisms of CE associated with TAVI and support the need for further research to both reduce the incidence of CE during these procedures and better determine their clinical relevance (468).

The Aging Heart and Post-Infarction Left Ventricular Remodeling

Aging is a risk factor for heart failure, which is a leading cause of death world-wide. Elderly patients are more likely than young patients to experience a myocardial infarction (MI) and are more likely to develop heart failure following MI. The poor clinical outcome of aging in cardiovascular disease is recapitulated on the cellular level. Increase in stress exposure and shifts in signaling pathways with age change the biology of cardiomyocytes. The progressive accumulation of metabolic waste and damaged organelles in cardiomyocytes blocks the intracellular recycling process of autophagy and increases the cell's propensity toward apoptosis. Additionally, the decreased cardiomyocyte renewal capacity in the elderly, due to reduction in cellular division and impaired stem cell function, leads to further cardiac dysfunction and maladaptive responses to disease or stress. We review the cellular and molecular aspects of post-infarction remodeling in the aged heart, and relate them to the clinical problem of post-infarction remodeling in elderly patients (469).

5-Year Follow-Up After Primary Percutaneous Coronary Intervention With a Paclitaxel-Eluting Stent Versus a Bare-Metal Stent in Acute ST-Segment Elevation Myocardial Infarction: A Follow-Up Study of the PASSION (Paclitaxel-Eluting Versus Conventional Stent in Myocardial Infarction With ST-Segment Elevation) Trial

Objectives The purpose of this study was to evaluate the long-term outcomes of the PASSION (Paclitaxel-Eluting Versus Conventional Stent in Myocardial Infarction with ST-Segment Elevation) trial.

Background In primary percutaneous coronary intervention for acute ST-segment elevation myocardial infarction (STEMI), the use of drug-eluting stents (DES) is still controversial. Several randomized controlled trials of DES, compared with bare-metal stents (BMS), with short-term follow-up showed a reduction in target lesion revascularization (TLR), but no differences in rates of cardiac death or recurrent myocardial infarction. Moreover, the occurrence of (very) late stent thrombosis (ST) continues to be of major concern, and, therefore, long-term follow-up results are needed.

Methods We randomly assigned 619 patients presenting with STEMI to a paclitaxel-eluting stent (PES) or the similar BMS. The primary end point was the composite of cardiac death, recurrent myocardial infarction, or TLR. We performed clinical follow-up at 5 years.

Results At 5 years, the occurrence of the composite of cardiac death, recurrent myocardial infarction, or TLR was comparable at 18.6% versus 21.8% in PES and BMS, respectively (hazard ratio [HR]: 0.82, 95% confidence interval [CI]: 0.58 to 1.18, p = 0.28). The incidence of definite or probable ST was 12 (4.2%) in the PES group and 10 (3.4%) in the BMS group (HR: 1.19, 95% CI: 0.51 to 276, p = 0.68).

Conclusions In the present analysis of PES compared with BMS in primary percutaneous coronary intervention for STEMI, no significant difference in major adverse cardiac events was observed. In addition, no difference in the incidence of definite or probable ST was seen, although very late ST was almost exclusively seen after the use of PES. (Paclitaxel-Eluting Versus Conventional Stent in Myocardial Infarction with ST-Segment Elevation [PASSION]; ISRCTN65027270) (470).

Very Late Stent Thrombosis After Primary Percutaneous Coronary Intervention With Bare-Metal and Drug-Eluting Stents for ST-Segment Elevation Myocardial Infarction: A 15-Year Single-Center Experience

Objectives The purpose of this study was to assess the frequency of very late stent thrombosis (VLST) after stenting with bare-metal stents (BMS) and drug-eluting stents (DES) for ST-segment elevation myocardial infarction (STEMI).

Background Stent thrombosis occurs more frequently after stenting for STEMI than after elective stenting, but there are little data regarding VLST.

Methods Consecutive patients (n = 1,463) who underwent stenting for STEMI were prospectively enrolled in our database. BMS were implanted exclusively from 1995 to 2002, and DES and BMS were implanted from 2003 to 2009. Follow-up was obtained at 1 to 15 years.

Results BMS patients (n = 1,095) were older and had more shock, whereas DES patients (n = 368) had more diabetes and smaller vessels. Stent thrombosis occurred in 107 patients, of which 42 were VLST (>1 year). Stent thrombosis continued to increase to at least 11 years with BMS and to at least 4.5 years with DES. Stent thrombosis rates with BMS versus DES were similar at 1 year (5.1% and 4.0%, respectively) but increased more with DES after the first year (1.9%/year vs. 0.6%/year, respectively). Landmark analysis (>1 year) found DES had a higher frequency of VLST (p < 0.001) and reinfarction (p = 0.003). DES was the only significant independent predictor of VLST (hazard ratio: 3.79, 95% confidence interval: 1.64 to 8.79, p = 0.002).

Conclusions VLST after primary PCI for STEMI occurs with relatively high frequency to at least 11 years with BMS

and to at least 4.5 years with DES. Very late stent thrombosis and reinfarction (>1 year) were more frequent with DES. New strategies are needed to manage this problem (471).

Incidence, Predictors, Management, Immediate and Long-Term Outcomes Following Grade III Coronary Perforation

Objectives The aim of this study was to evaluate the incidence, predictors, management, and clinical outcomes in patients with grade III coronary perforation during percutaneous coronary intervention.
Background Grade III coronary perforation is a rare but recognized complication associated with high morbidity and mortality.
Methods From 24,465 patients undergoing percutaneous coronary intervention from May 1993 to December 2009, 56 patients had grade III coronary perforation.
Results Most lesions were complex: 44.6% type B2, 51.8% type C, and 28.6% chronic total occlusions, and within a small vessel (≤2.5 mm) in 32.1%. Glycoprotein IIb/IIIa inhibitors were administered in 17.9% of patients. The device causing perforation was intracoronary balloon in 50%: 53.6% compliant, 46.4% noncompliant; intracoronary guidewire in 17.9%; rotablation in 3.6%; and directional atherectomy in 3.6%. Following perforation, immediate treatment and success rates, respectively, were prolonged balloon inflation 58.9%, 54.5%; covered stent implantation 46.4%, 84.6%; coronary artery bypass graft surgery (CABG) and surgical repair 16.0%, 44.4%; and coil embolization 1.8%, 100%. Multiple methods were required in 39.3%. During the procedure (n = 56), 19.6% required cardiopulmonary resuscitation and 3.6% died. In-hospital (n = 54), 3.7% required CABG, 14.8% died. The combined procedural and in-hospital myocardial infarction rate was 42.9%, and major adverse cardiac event rate was 55.4%. At clinical follow-up (n = 46) (median: 38.1 months, range 7.6 to 122.8), 4.3% had a myocardial infarction, 4.3% required CABG, and 15.2% died. The target lesion revascularization rate was 13%, with target vessel revascularization in 19.6%, and major adverse cardiac events in 41.3%.
Conclusions Grade III coronary perforation is associated with complex lesions and high acute and long-term major adverse cardiac event rates (472).

Late Restenosis Following Sirolimus-Eluting Stent Implantation

Objectives This serial angiographic study evaluated the incidence and predictors of late restenosis after sirolimus-eluting stent (SES) implantation.
Background Previous studies showed late restenosis (i.e., late catch-up phenomenon) after implantation of 7-hexanoyltaxol-eluting stents and nonpolymeric, paclitaxel-eluting stents.
Methods Between August 2004 and December 2006, SES implantation was performed in 1,393 patients with 2,008 lesions, in whom 8-month and 2-year follow-up coronary angiography were planned.
Results Of 2,008 lesions, 1,659 (83%) underwent 8-month follow-up angiography (8.3 ± 2.2 months). Restenosis was observed in 122 lesions (7.4%). Coronary angiography 2 years (1.9 ± 0.4 years) after SES deployment was performed in 1,168 lesions (74% of lesions without restenosis at 8-month follow-up angiography). Late restenosis was observed in 83 lesions (7.1%). There was significant decrease in minimum luminal diameter (MLD) between 8-month and 2-year follow-up (2.56 ± 0.56 mm vs. 2.35 ± 0.71 mm, $p < 0.001$). Multivariate analysis showed in-stent restenosis before SES implantation and MLD at 8-month follow-up as independent predictors of late restenosis.
Conclusions Between 8-month and 2-year follow-up after SES implantation, MLD decreases, which results in late restenosis in some lesions. In-stent restenosis before SES implantation and MLD at 8-month follow-up are independent predictors of late restenosis (473).

Persistent Coronary No Flow After Wire Insertion Is an Early and Readily Available Mortality Risk Factor Despite Successful Mechanical Intervention in Acute Myocardial Infarction: A Pooled Analysis From the STRATEGY (Single High-Dose Bolus Tirofiban and Sirolimus-Eluting Stent Versus Abciximab and Bare-Metal Stent in Acute Myocardial Infarction) and MULTISTRATEGY (Multicenter Evaluation of Single High-Dose Bolus Tirofiban Versus Abciximab With Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction Study) Trials

Objectives These studies sought to investigate the impact on mortality of coronary flow after passage of the wire through the culprit vessel in patients with ST-segment elevation myocardial infarction (STEMI) undergoing mechanical reperfusion.
Background Reduced spontaneous coronary flow before percutaneous coronary intervention influences mortality in patients with STEMI. Response to vessel wiring in patients with an occluded coronary artery before intervention might further discriminate outcomes irrespective of pre- and post-intervention coronary flow.
Methods Data from the STRATEGY (Single High-Dose Bolus Tirofiban and Sirolimus-Eluting Stent Versus Abciximab and Bare-Metal Stent in Acute Myocardial Infarction) and MULTISTRATEGY (Multicenter Evaluation of Single High-Dose Bolus Tirofiban Versus Abciximab With Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction Study) trials were pooled: of 919 index procedures, 902 films (98%) were technically adequate for core laboratory TIMI (Thrombolysis In Myocardial Infarction) flow determination.

Results TIMI flow grade 0 was present before percutaneous coronary intervention in 59% of infarct vessels, TIMI flow grade 1 to 2 was found in 21%, whereas the remainder of infarct arteries presented with TIMI flow grade 3. In 49% of patients who showed persistent TIMI flow grade 0 after wire insertion (AWI), mortality was higher at 30 days (5.3%) and 1 year (9.4%) compared with patients in whom TIMI flow grade before percutaneous coronary intervention was either >0 (0.8%; $p < 0.003$ and 3.6%, $p < 0.008$) or improved from 0 AWI (1.5%, $p < 0.04$ and 3.6%, $p < 0.02$). After correcting for multiple imbalances, including baseline and final flow, persistent TIMI flow grade 0 AWI remained associated at 30 days to 2-fold (risk ratio [RR]: 2.1, 95% confidence interval [CI]: 1.08 to 5.00; $p = 0.038$) and at 1 year to almost 3-fold increases of mortality (RR: 2.7, 95% CI: 1.3 to 5.6; $p = 0.008$).

Conclusions STEMI patients displaying persistent no-flow AWI have a lower survival rate despite an apparently successful mechanical intervention. As an early marker for high residual mortality risk, persistent no-flow AWI may qualify STEMI patients for dedicated pharmacomechanical treatment strategies (474).

Four-Year Follow-Up of TYPHOON (Trial to Assess the Use of the CYPHer Sirolimus-Eluting Coronary Stent in Acute Myocardial Infarction Treated With BallOON Angioplasty)

Objectives The aim of this study was to assess the long-term safety and efficacy of the CYPHER (Cordis, Johnson and Johnson, Bridgewater, New Jersey) sirolimus-eluting coronary stent (SES) in percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI).

Background Concern over the safety of drug-eluting stents implanted during PCI for STEMI remains, and long-term follow-up from randomized trials are necessary. TYPHOON (Trial to assess the use of the cYPHer sirolimus-eluting stent in acute myocardial infarction treated with ballOON angioplasty) randomized 712 patients with STEMI treated by primary PCI to receive either SES ($n = 355$) or bare-metal stents (BMS) ($n = 357$). The primary end point, target vessel failure at 1 year, was significantly lower in the SES group than in the BMS group (7.3% vs. 14.3%, $p = 0.004$) with no increase in adverse events.

Methods A 4-year follow-up was performed. Complete data were available in 501 patients (70%), and the survival status is known in 580 patients (81%).

Results Freedom from target lesion revascularization (TLR) at 4 years was significantly better in the SES group (92.4% vs. 85.1%; $p = 0.002$); there were no significant differences in freedom from cardiac death (97.6% and 95.9%; $p = 0.37$) or freedom from repeat myocardial infarction (94.8% and 95.6%; $p = 0.85$) between the SES and BMS groups. No difference in definite/probable stent thrombosis was noted at 4 years (SES: 4.4%, BMS: 4.8%, $p = 0.83$). In the 580 patients with known survival status at 4 years, the all-cause death rate was 5.8% in the SES and 7.0% in the BMS group ($p = 0.61$).

Conclusions In the 70% of patients with complete follow-up at 4 years, SES demonstrated sustained efficacy to reduce TLR with no difference in death, repeat myocardial infarction or stent thrombosis. (The Study to Assess AMI Treated With Balloon Angioplasty [TYPHOON]; NCT00232830) (475).

Prediction of 1-Year Clinical Outcomes Using the SYNTAX Score in Patients With Acute ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention: A Substudy of the STRATEGY (Single High-Dose Bolus Tirofiban and Sirolimus-Eluting Stent Versus Abciximab and Bare-Metal Stent in Acute Myocardial Infarction) and MULTISTRATEGY (Multicenter Evaluation of Single High-Dose Bolus Tirofiban Versus Abciximab With Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction Study) Trials

Objectives This study sought to evaluate the impact of SYNTAX score (SXscore), and compare its performance in isolation and combination with the PAMI (The Primary Angioplasty in Myocardial Infarction Study) score, for the prediction of 1-year clinical outcomes in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention.

Background Patients with STEMI were excluded from the original SYNTAX score (SXscore) algorithm. Therefore, the utility of using the SXscore in this patient group remains undefined.

Methods SXscore was calculated retrospectively in 807 patients with STEMI enrolled in the randomized STRATEGY (Single High-Dose Bolus Tirofiban and Sirolimus-Eluting Stent Versus Abciximab and Bare-Metal Stent in Acute Myocardial Infarction) and MULTISTRATEGY (Multicenter Evaluation of Single High-Dose Bolus Tirofiban Versus Abciximab With Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction Study) clinical trials. Clinical outcomes of all-cause death, reinfarction, and clinically driven target vessel revascularization were subsequently stratified according to SXscore tertiles: $SX_{LOW} \leq 9$ ($n = 311$), $9 < SX_{MID} \leq 16$ ($n = 234$), $SX_{HIGH} > 16$ ($n = 262$).

Results At 1-year follow-up, all clinical outcomes including mortality, mortality/reinfarction, major adverse cardiac events (MACE) (a composite of all-cause death, reinfarction and target vessel revascularization), and definite, definite/probable, and any stent thrombosis were all significantly higher in patients in the highest SXscore tertile. SXscore was identified as an independent predictor of mortality, MACE, and stent thrombosis out to 1-year

follow-up. The combination SYNTAX-PAMI score led to a net reclassification improvement of 15.7% and 4.6% for mortality and MACE, respectively. The C-statistics for the SXscore, PAMI score, and the combined SYNTAX-PAMI score were 0.65, 0.81, and 0.73 for 1-year mortality, and 0.68, 0.64, and 0.69 for 1-year MACE, respectively.

Conclusions SXscore does have a role in the risk stratification of patients with STEMI having primary percutaneous coronary intervention; however, this ability can be improved through a combination with clinical variables. (Multicentre 2×2 Factorial Randomised Study Comparing Tirofiban Versus Abciximab and SES Versus BMS in AMI; NCT00229515) (476).

Drug-Eluting Introducer Sheath Prevents Local Peripheral Complications: Pre-Clinical Evaluation of Nitric Oxide–Coated Sheath

Objectives This study evaluated the protective effect of nitric oxide–coating of introducer sheath on the local complications in juvenile porcine femoral arteries with similar size to human radial arteries.

Background Insertion of an introducer sheath induces vasospasm and transient or permanent vessel occlusion of radial arteries.

Methods Nitric oxide–coated or control introducer sheaths with or without spasmolytic cocktail (control + C-sheath) were inserted into porcine femoral arteries, followed by percutaneous coronary intervention (PCI). The diameter of the femoral artery at the puncture site, distally and proximally, was measured by quantitative angiography. Histopathological and histomorphometric parameters of the femoral arteries were analyzed 1 h or 1 week after PCI.

Results Insertion of femoral sheath led to mild or severe spasms, with significantly higher vessel diameter at the access site (2.69 ± 0.81 mm vs. 1.77 ± 0.77 mm and 1.85 ± 0.66 mm, $p < 0.001$), and proximal and distal to it, during PCI in the nitric oxide–sheath group versus the control-sheath and control + C-sheath groups, respectively. Immediately following PCI, significantly less luminal thrombosis (12% vs. 33% and 31% of all analyzed segments, $p < 0.001$) was observed in the nitric oxide–sheath arteries. At 1 week, lower intimal inflammation score (0.43 ± 11 vs. 1.03 ± 0.35 and 1.04 ± 0.32, $p < 0.05$), less luminal thrombosis (8% vs. 21% and 30% $p < 0.05$), and smaller intimal hyperplasia (0.31 ± 0.31 mm^2 vs. 0.47 ± 1.00 mm^2 and 0.86 ± 0.82 mm^2, $p < 0.05$) were observed in NO-sheath arteries at the injury site.

Conclusions Nitric oxide coating on the introducer sheath prevents local complications during PCI and results in less vascular thrombosis and inflammation at the access site, contributing to patency of the access vessel with similar size to the radial artery (477).

Survival of Patients Undergoing Rescue Percutaneous Coronary Intervention: Development and Validation of a Predictive Tool

Objectives This study sought to develop a tool for predicting an individual's risk of mortality following rescue percutaneous coronary intervention (PCI).

Background Although fibrinolytic therapy is appropriate and improves survival for certain ST-segment elevation myocardial infarction patients, a substantial proportion suffer ongoing myocardial ischemia, a class I indication for emergent percutaneous coronary intervention (rescue PCI).

Methods Using the National Cardiovascular Data Registry (NCDR), rescue PCI was defined as nonelective PCI following failed fibrinolysis in patients with continuing or recurrent myocardial ischemia. Multivariable logistic regression was used to determine mortality predictors and the C-statistic for model discrimination. The NCDR-RESCUE (Real-World Estimator of Survival in Catheterized STEMI Patients Following Unsuccessful Earlier Fibrinolysis) score was developed using a shortened list of 6 pre-angiographic variables and 70% of the cohort; performance was subsequently validated against the remaining 30%.

Results Among 166,516 PCI procedures on patients with an admission diagnosis of ST-segment elevation myocardial infarction, 8,007 (4.8%) represented rescue PCI. In-hospital mortality occurred in 464 (5.8%). Factors in the final model were age, glomerular filtration rate, history of congestive heart failure, insulin-treated diabetes, cardiogenic shock, and salvage status. The NCDR-RESCUE score effectively segregated individuals into 6 clinically meaningful risk categories, with 0.4% (0.0% to 1.3%), 1.6% (0.9% to 2.4%), 7.6% (5.3% to10.4%), 27.5% (20.7% to 35.1%), 64.2% (49.8% to 76.9%), or 100% (59.0% to 100.0%) risk, respectively, of in-hospital mortality (mean ± 95% confidence interval, C-index = 0.88, Hosmer-Lemeshow p = 0.898).

Conclusions In-hospital mortality risk among individuals undergoing rescue PCI varies from minimal to extreme and can be easily calculated using the NCDR-RESCUE score. This information can be of value in counseling patients, families, and referring caregivers (478).

Difference of Culprit Lesion Morphologies Between ST-Segment Elevation Myocardial Infarction and Non–ST-Segment Elevation Acute Coronary Syndrome: An Optical Coherence Tomography Study

Objectives The aim of this study was to investigate the difference of culprit lesion morphologies assessed by optical coherence tomography (OCT) between ST-segment elevation myocardial infarction (STEMI) and non–ST-segment elevation acute coronary syndrome (NSTEACS).

Background Autopsy studies have reported that rupture of a thin-cap fibroatheroma and subsequent thrombus

formation is the most important mechanism leading to acute coronary syndrome (ACS). Optical coherence tomography is a high-resolution imaging modality that is capable of investigating detailed coronary plaque morphology in vivo.

Methods We examined the culprit lesion morphologies by OCT in 89 consecutive patients with acute coronary syndrome (STEMI = 40; NSTEACS = 49).

Results The incidence of plaque rupture, thin-cap fibroatheroma, and red thrombus was significantly higher in STEMI compared with NSTEACS (70% vs. 47%, $p = 0.033$, 78% vs. 49%, $p = 0.008$, and 78% vs. 27%, $p < 0.001$, respectively). Although the lumen area at the site of plaque rupture was similar in the both groups (2.44 ± 1.34 mm^2 vs. 2.96 ± 1.91 mm^2, $p = 0.250$), the area of ruptured cavity was significantly larger in STEMI compared with NSTEACS (2.52 ± 1.36 mm^2 vs. 1.67 ± 1.37 mm^2, $p = 0.034$). Furthermore, the ruptured plaque of which aperture was open-wide against the direction of coronary flow was more often seen in STEMI compared with NSTEACS (46% vs. 17%, $p = 0.036$).

Conclusions The present OCT study demonstrated the differences of the culprit lesion morphologies between STEMI and NSTEACS. The morphological feature of plaque rupture and the intracoronary thrombus could relate to the clinical presentation in patients with acute coronary disease (479).

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