

9:45 a.m.

839FO-6

The Impact of Sirolimus-Eluting Stents in Diabetics: Results From the SIRIUS Trial

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Background: Diabetics after coronary stent implantation manifest more frequent major adverse cardiac events (MACE) and increased restenosis (Res). However, the effects of sirolimus-eluting stents (SES) in diabetics is poorly understood.

Methods: In the randomized double-blind SIRIUS trial (1058 patients), which compared SES vs. control bare stents (CS), 26.4% of patients were diabetic. Within the diabetic subgroup (279 patients), lesion length was 14.5mm and reference vessel diameter was 2.75mm.

Results: Follow-up angiography (@ 8 months) and MACE (up to 9 months) were compared in the SES vs. CS diabetic subgroups (see table). Similar to the overall SIRIUS cohort, diabetics had greater Res and target lesion revascularization (TLR) in the small and medium size vessels (tercile analysis) and a disproportionate contribution to Res within the proximal peri-stent region (48% in SES vs. 27% in CS). Among the diabetics, patients on insulin (n=82), demonstrated reduced angiographic and clinical benefit after SES therapy.

Conclusions: Analysis of the diabetic SIRIUS patients indicates: (1) preserved SES relative treatment effect on Res and TLR, despite higher absolute values; (2) clustering of Res and TLR events in the smaller vessels, due to relatively higher proximal peri-stent late loss; (3) reduced SES efficacy in diabetics on insulin therapy. Further improvement in SES results in diabetics may require increased stent coverage of peri-stent regions (esp. proximal).

Follow-up parameter	SES (n=131)	CS (n=148)	p value
Late loss (mm): in-stent	0.29	1.20	<0.001
Late loss (mm): in-lesion	0.40	1.00	<0.001
Res (%): in-stent	8.3	48.5	<0.001
Res (%): in-lesion	17.6	50.5	<0.001
TLR (%)	7.2	22.9	<0.001
MACE (%)	9.2	25.0	<0.001

POSTER SESSION

1149 Adjunctive Therapies for Percutaneous Coronary Interventions

Tuesday, April 01, 2003, 9:00 a.m.-11:00 a.m.

McCormick Place, Hall A

Presentation Hour: 9:00 a.m.-10:00 a.m.

1149-187

Deferring of Patients With Restenotic Coronary Lesions Based on the Concept of Fractional Flow Reserve Measurement

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Intracoronary pressure measurement is a promising method to invasively quantify the hemodynamic relevance of intermediate coronary lesions. Patients with coronary single vessel-disease and a Fractional Flow Reserve (FFR) ≥ 0.75 across a de-novo coronary lesion have a very low incidence for developing a major adverse cardiac event (MACE) during a follow-up of 24 months and should therefore not receive an intervention. However, it is still unclear if this is also true in restenotic coronary lesions. The aim of the present study was to investigate whether deferring of patients based on the measurement of FFR is also a safe option in restenotic lesions.

Methods: 59 consecutive patients (Pt) (mean age 65 ± 10 ys) with stenoses of angiographically questionable relevance and a FFR ≥ 0.75 were included into the study. Based on the FFR measurement PTCA was avoided in all 47 patients with de-novo lesions (DL) and 12 patients with restenotic lesions (RL). Patients were closely monitored on an outpatient basis. Primary endpoint was the occurrence of major adverse cardiac events (rePTCA, CABG, myocardial infarction, death). Secondary endpoints were the time to revascularization procedures if performed during the follow-up as well as the change in angina status.

Results: Mean follow-up was 492 ± 252 days. The coronary risk profile as well as patient characteristics were similar in both groups. During first year 4 major adverse cardiac events occurred ([DL] PTCA n=1; [RL] PTCA n=3). The risk for the development of major adverse cardiac events during the first year was 2% in the DL-group and 18% in the RL-group (OR 9.0 p<0.05). Time to revascularization procedures was 175 days (DL) and 202 ± 85 days (RL). However, no significant change in angina status was observed.

Conclusion: FFR can accurately identify patients at low risk for the development of major adverse cardiac events in de-novo lesions. If an intended PTCA in a restenotic

lesion is waived, Pts have a 9 fold increased risk for major adverse cardiac events during the following year despite a FFR ≥ 0.75 . However, whether FFR based therapy stratification in these patients requires other cut off values is subject to further investigations.

1149-188

The Importance of Intravascular Ultrasound in Percutaneous Coronary Intervention for Small Coronary Arteries

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Background: Angioplasty of lesions in small coronary arteries remains a significant problem because of the increased risk of restenosis. While we usually use quantitative coronary angiography (QCA) to define small coronary arteries, previous studies reported that QCA for small coronary arteries was not accurate. We studied the difference of restenosis rate between truly small coronary arteries (group1) and falsely small coronary arteries (group2) divided by intravascular ultrasound (IVUS).

Methods: We studied 102 lesions whose reference diameter (RD) were less than 2.8 mm by QCA. These lesions were divided into 2 subgroups according to lumen diameter (LD) by IVUS (group 1: LD 2.5mm). The difference of restenosis rate was evaluated after 6 months follow-up.

Results: Baseline clinical and angiographic characteristics were similar in the two groups. According to IVUS, 43 cases (42.2%) were defined as falsely small coronary arteries (LD > 2.5mm). RD by QCA are similar in two groups (2.31 ± 0.04 vs 2.42 ± 0.04 , p=ns, respectively). The rate of stenting was not significantly different (86.4% vs 95.3%, p=ns, respectively). Post-procedural lumen diameter was significantly larger in falsely small coronary arteries group (2.34 ± 0.07 vs 2.71 ± 0.09 , p<0.001). The angiographic restenosis rate was 44.1% in truly small coronary arteries group, and 20.9% in falsely small coronary arteries group (p<0.05).

Conclusion: Some small coronary arteries defined by QCA have LD more than 2.5mm by IVUS. In these lesions, the restenosis rate was almost similar with lesions more than 3.0 mm. To discuss proper procedures for small coronary arteries, we should define small coronary arteries by IVUS.

1149-189

Chronic Kidney Disease: The Silent Killer After Coronary Angioplasty

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Background: There is evidence that chronic kidney disease (CKD) is associated with increased mortality in patients undergoing PCI. The impact of CKD on quality of life (QOL) in PCI patients is unknown.

Methods: We analyzed a prospective PCI registry where CKD was categorized by creatinine clearance (CrCl) as mild (61-90 ml/min), moderate (31-60 ml/min) and severe (15-30 ml/min) and compared to those with normal CrCl. Patients with CrCl < 15 ml/min or on hemodialysis were excluded. The Seattle Angina Questionnaire (SAQ) was administered at the time of the procedure and at 1 year. Mortality data was obtained from the National Death Index. Univariate and multivariate regression analyses were used.

Results: 1,324 patients with CKD and 232 patients with normal renal function were studied. There was more physical limitation in those with moderate and severe CKD but no difference in angina frequency or QOL at baseline. One-year mortality was 20.3, 5.9, 3.3 and 1.7% for the severe, moderate, mild CKD, and normal renal function patients respectively (p < 0.001). By logistic regression analysis, severe CKD was the strongest independent predictor of death (Table).

	OR for Death (95% CI)	Change QOL
	*P<0.001	P=NS
Severe CKD	8.6 (2.2-33.5) *	33+/-28
Moderate CKD	3.0 (0.9-10)	31+/-24
Mild CKD	2.2 (0.7-7.7)	30+/-26

At follow-up, there was no difference in the angina frequency, physical limitations or QOL among those with and without CKD.

Conclusions: CKD is the most powerful independent predictor of mortality in PCI patients. These data suggest CKD signals a unique state of vascular pathobiology that is silent in terms of QOL measures, but lethal in terms of ultimate outcome.

1149-190

Deceptive Ostial Coronary Lesions: Lack of Relationship Between Imaging and Physiology

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Background: Estimation of ostial lesion severity by angiography has significant limitations due to angulation, branch overlap and artifact. To compare angiography and physiology, ostial diameter stenosis was compared to fractional flow reserve (FFR) in 31 consecutive patients with 38 lesions $\geq 50\%$ diameter narrowing.

Methods: FFR was obtained with a 0.014" pressure guidewire and intracoronary adenosine (30-50 mcg). Two independent observers determined angiographic severity. Patients were divided into two groups by the degree of stenosis ($\geq 70\%$ stenosis and 50-70% stenosis).

Results: The ostial lesions assessed were left main (n=5), anterior descending (n=8), diagonal (n=3), circumflex (n=7), marginal (n=3), right (n=6), posterior descending (n=3), and internal mammary (n=2). For $\geq 70\%$ stenosis, FFR was $0.85 \pm .09$; for ostial lesions between 50-70%, FFR was 0.91 ± 0.03 . In 18 ostial lesions with $\geq 70\%$ stenosis, FFR was ≥ 0.75 in 15 and FFR <0.75 in 3. All 20 ostial lesions with angiographic stenosis between 50-70% had FFR ≥ 0.75 (Yate's p=0.0008, see table)

Conclusion: A significant number of ostial lesions with angiographic stenosis $\geq 70\%$ are associated with a physiologic nonischemic threshold (i.e. FFR ≥ 0.75). Ostial lesions without evidence of ischemia should undergo physiologic testing before interventions.

Ostial Lesions: Angiography vs FFR

	Angiographic stenosis group 1	Angiographic stenosis group 2
FFR	$\geq 70\%$	50-70%
≥ 0.75	15	20
< 0.75	3	0

1149-191 Cutting Balloon Atherotomy Is Associated With Decreased Stent Utilization

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Background: Cutting balloon atherotomy (CBA) achieves luminal gain by creating controlled fissuring of coronary plaques. In a retrospective comparison of CBA to other techniques for treatment of non-intrastent lesions at Barnes-Jewish Hospital, CBA was associated with decreased need for stent implantation (50% vs. 88.4%), greater angiographic and clinical success (99.6% vs. 97.9% and 99.3% vs. 95.9%), and no difference in 1 and 9 month target vessel revascularization (TVR) (1.8% vs. 0.9%, and 15% vs. 12%, respectively). The *Cutting Balloon as Sole Revascularization Trial* compares CBA with conventional balloon angioplasty (POBA) as the primary treatment for non-intrastent lesions. **Methods:** Patients undergoing percutaneous revascularization for native coronary artery lesions are randomized to CBA or POBA as primary treatment. Provisional stenting is indicated for $>35\%$ residual stenosis, grade B or greater dissection, or thrombus. The primary endpoint is stent implantation for sub-optimal results. Secondary endpoints include in-hospital MACE and 1 and 9 month TLR. **Results:** Twenty-two patients have been randomized to the CBA group and 17 patients to the POBA group. Clinical characteristics, vessels treated, and lesion types are similar between the two groups. To date, CBA has achieved greater angiographic success as primary therapy (87.0% vs. 57.7%; $p=0.02$), with fewer dissections (22.2% vs. 45.5%, $p=NS$) compared to conventional angioplasty. CBA is associated with a decreased need for stent implantation (27.8% vs. 81.8%; $p<0.001$). Despite lower stent utilization in the CBA group, there is no difference in final stenosis (14.5% vs. 14.0%).

Conclusions: As primary therapy, CBA appears to achieve greater angiographic success with decreased need for stent implantation compared to POBA. Updated enrollment with cost analysis, 1 month and 9 month outcomes will be presented. A model for comparing cost-benefit of CBA compared to implantation of drug-coated stents will be discussed.

1149-192 Diabetes Does Not Add to the Increased Six-Month Mortality Associated With Increase in CK-MB After Percutaneous Coronary Intervention

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Background: Increased CK-MB release after percutaneous coronary intervention (PCI) is associated with increased mortality. It is not known if the prognosis of diabetic (D) pts with increased CK-MB levels after PCI is different than nondiabetic (ND) pts.

Methods: The GUARDIAN trial contained 2,173 PCI pts who had prospectively acquired baseline clinical and post-PCI CK-MB and ECG data. The incidence and 6-month mortality associated with different levels of CK-MB were compared between 516 D pts and 1,657 ND pts.

Results: The incidence of peak CK-MB elevation in D pts was not greater than in ND pts (table). The D subgroup was older (median age 64.0 vs. 62.0, $p<0.05$); had more females (33.3% vs. 22.7%, $p<0.001$) and fewer whites (86.8% vs. 94.5%, $p<0.001$); was more obese (median body mass index 29.0 vs. 27.3, $p<0.001$); had a higher systolic blood pressure (median 134.0 vs. 130.0, $p<0.001$); and was more likely to have a history of heart failure (15.7% vs. 7.0%, $p<0.001$), cerebrovascular disease (11.4% vs. 8.0%, $p<0.05$), and peripheral vascular disease (18.0% vs. 9.8%, $p<0.001$) than the ND subgroup. The 6-month mortality rates in D were usually slightly greater than in ND at any particular peak CK-MB ratio cutoff, but none were statistically significant (table).

Conclusion: The incidence and magnitude of CK-MB leaks following PCI is no greater in D than in ND. D have a more adverse risk profile than ND, but for any given level of peak CK-MB release post-PCI, diabetes does not significantly elevate 6-month mortality risk.

	Incidence of Peak CK-MB Ratio in PCI Patients (%)					6-Month Mortality in PCI Patients by Peak CK-MB Ratio Cutoffs (%)			
	<1 ULN	≥ 1 ULN	<3 ULN	≥ 3 ULN	≥ 5 ULN	<1 ULN	≥ 3 ULN	≥ 5 ULN	≥ 10 ULN
Diabetic	67.8	21.3	5.0	2.9	2.9	3.1	3.6	6.7	6.7
Non-diabetic	63.9	23.5	5.7	3.7	3.1	1.4	3.8	5.3	5.9
	p=0.57					p=0.06 p=1.00 p=1.00 p=1.00			

1149-193 Long-Term Outcome of Patients With Prior Percutaneous Revascularization Undergoing Repeat Coronary Intervention

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Background: Patients (pts) with a history of prior percutaneous coronary revascularization (PCR) are often excluded from clinical trials. As a result, there is limited data on the outcome of these pts undergoing repeat coronary intervention.

Method: Of 11,282 pts undergoing percutaneous coronary intervention (PCI) in the Prevention of Restenosis with Tranilast and its Outcomes (PRESTO) trial, 3,495 pts had history of prior PCR, 2/3 of whom had prior stent placement. We compared the outcome of these pts with 7,787 pts with de novo lesions.

Results: Mean age was 60 yrs in both groups. Pts with prior PCR were more likely to have DM (26% vs 22%, $P < 0.001$), HTN (70% vs 57%, $p < 0.001$), hypercholesterolemia (66% vs 47%, $p < 0.001$), prior MI (56% vs 31%, $p < 0.001$), and prior CABG (23% vs 9%, $p < 0.001$), and less likely to have new-onset angina (21% vs 26%, $p < 0.001$), significant EKG changes (6% vs 11%, $p < 0.001$), or be current smokers (17% vs 25%, $p < 0.001$). Angiographic features in pts with and without history of PCR, respectively, included: ostial lesions (10% vs 6%, $p < 0.001$), total occlusion (6% vs 10%, $p < 0.001$), ejection fraction (60.9% vs 58.6%, $p < 0.01$), and LAD location (31% vs 41%, $p < 0.001$). IIb/IIIa was used in 39% and 35% respectively ($p < 0.001$). In-hospital rates of cardiac events were low and similar. Kaplan-Meier estimates of events at 9 months are shown (table).

Conclusions: Despite similar in-hospital outcomes, patients with a history of prior PCR have a significantly lower event-free survival at 9-month follow-up.

Kaplan-Meier Estimates of Cardiac Events at 9-month Follow-up

Variable	Prior PCR Estimate (95% CI)	No Prior PCR Estimate (95% CI)	p value
Death	1.7 (1.1-2.2)	1.2 (0.9-1.6)	0.059
MI	2.0 (1.4-2.5)	1.3 (1.0-1.6)	0.018
CABG	7.6 (6.6-8.7)	3.2 (2.7-3.7)	< 0.001
Death or MI	3.4 (2.6-4.1)	2.5 (2.0-2.9)	0.012
Death, MI, or CABG	10.1 (8.9-11.4)	5.4 (4.7-6.0)	< 0.001

1149-194 Rupture of the External Elastic Lamina Increases Plaque Neovascularization After Coronary Angioplasty in the Swine Model

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Background: While plaque neovascularization (NV) is associated with neointimal proliferation after vessel wall injury, rupture of the external elastic lamina (EEL) may increase this angiogenic response. We tested the hypothesis that plaque NV is increased in coronary lesions with EEL rupture after balloon angioplasty in the swine model.

Materials and Methods: Thirty-nine histological sections from ballooned coronary artery angioplasty segments were studied after 6 weeks of barotrauma. Rupture of EEL was defined as extensive tissue interruption along the media-adventitia interface on 40x light microscopy. Neovessels were defined as tubuloluminal anti-vWF positive capillaries recognized in immunostained sections by light microscopy. Morphometric measurements were performed by computerized planimetry.

Results: Plaque NV was increased in lesions with rupture of EEL (Table). Neointimal area was increased and lumen area was decreased in lesions with rupture of EEL (Table). EEL area was similar in both groups. Multiple regression analysis identified rupture of EEL as an independent predictor for plaque NV (RR=19.8; 95% CI=2.4-37).

Conclusion: Neovascularization is increased in coronary plaques with rupture of the external elastic lamina following vessel wall injury. This angiogenic response is associated with increased neointima formation and reduced lumen area. Thus, novel anti-angiogenic therapies may offer an alternative option for the prevention of restenosis.