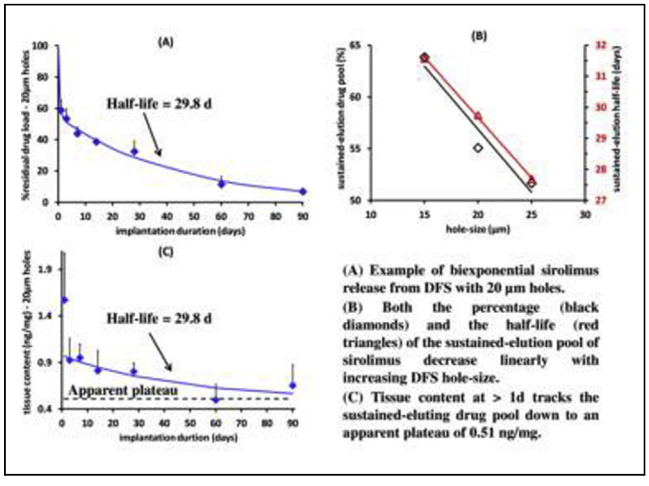
stents (DFS; Medtronic, Santa Rosa CA) however, are a novel platform for polymer-free drug delivery in which the drug is contained in a hollow stent and released through laser drilled holes along the abluminal surface of the stent. We hypothesized that hole-size can modulate in vivo drug release kinetics from DFS.

METHODS Sterilized DFS (96 μg sirolimus/3.0×18 mm) with hole diameters of 15, 20 or 25 μm were mounted on a Microtrac® Stent Delivery System and implanted in non-diseased porcine coronary arteries (target stent-to-artery ratio between 1.10:1 and 1.15:1) for 1 to 90 days (n=6/time point). Explanted stents and arteries were analyzed for sirolimus content using liquid chromatography coupled with ultra violet detection, and liquid chromatography coupled with tandem mass spectrometry detection, respectively. Drug release was fit to a bi-exponential model with zero plateau and tissue content to a mono-exponential model with the same late half-life as late drug release but a positive plateau. Bioequivalence analysis was performed following FDA guidance documentation from 2001 to determine if drug delivery from DFS with different hole-sizes was statistically different. This analysis evaluates the ratio of the geometric least square means of test arms across multiple time points. Test arms are considered bio-equivalent if their geometric ratio is within the bounds of 0.8 - 1.25.

RESULTS Sirolimus release kinetics from DFS were biexponential (Fig A, R2>0.99), speaking to the existence of an easily available and releasable pool of drug that elutes within the first day (first time point) following arterial implantation, plus a pool of sustained-eluting drug with a half-life of 28-32 days. Notably, the fraction of drug load that is sustained-eluting and its half-life of release both decreased with increasing hole-size (Fig B). Tissue content tracked the first order elution of the sustained-eluting drug pool down to an apparent plateau level of 0.51±0.03 ng/mg (Fig C) and was not statistically different for any of the hole sizes evaluated (15, 20, and 25 μm).

CONCLUSIONS Though drug in tissue from DFS with hole-sizes of 15 to 25μm were bioequivalent, hole-size emerged as a design parameter for predictably titrating local tissue retention of DFS eluted drug.



(A) Example of biexponential sirolimus release from DFS with 20 μm holes. (B) Both the percentage (black diamonds) and the half-life (red triangles) of the sustained-elution pool of sirolimus decrease linearly with increasing DFS hole-size. (C) Tissue content at > 1d tracks the sustained-eluting drug pool down to an apparent plateau of 0.51 ng/mg.

CATEGORIES CORONARY: Stents: Drug-Eluting

KEYWORDS Drug-eluting stent, In Vivo, Pharmacokinetics

TCT-555

Impact of Stent Size Selection on Acute and Long-Term Outcomes after Drug-Eluting Stent Implantation in De Novo Coronary Lesions

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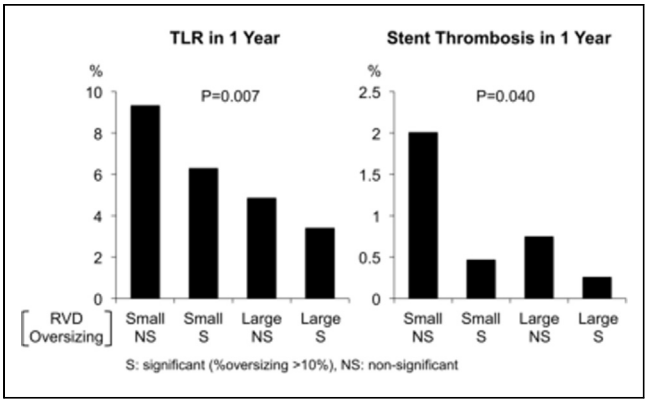
BACKGROUND The advent of bioresorbable scaffolds is redrawing attention to accurate device size selection. While significant undersizing often results in incomplete strut apposition (ISA) or underexpansion, possible impact of oversized stent implantation on arterial wall injury has not been systematically investigated with drug-eluting stents (DES).

METHODS To evaluate the effect of stent oversizing on acute and long-term outcomes, serial (baseline and 6-12 months) coronary angiography and IVUS were performed in 2931 lesions treated with DES (355 sirolimus, 846 paclitaxel, 1387 zotarolimus, and 343 everolimus). The degree of stent oversizing (%SO) to angiographic reference vessel diameter (RVD) was calculated as (nominal stent diameter - RVD) / RVD x 100 (%). Post-procedural stent expansion was calculated by IVUS as minimum stent area divided by the average reference lumen area. Clinical outcomes including target lesion revascularization (TLR) and stent thrombosis were followed for 1 year.

RESULTS Overall, smaller pre-procedural RVD was linearly associated with higher %SO (r=-0.670, p<0.001). Significant stent oversizing (defined as %SO>10%) was found in 82% of small RVD (<2.75 mm) group and 33% of larger RVD (≥2.75 mm) group. The significant oversizing group underwent less post-dilatation (p=0.002), but achieved greater stent expansion (p<0.001) and less ISA (p<0.001) without increase of edge dissection after procedure. When stratified by vessel size and stent oversizing (no difference in DES type among the 4 groups, p=0.525), progressive decreases of angiographic binary restenosis and TLR rates (left figure) were found in favor of larger vessel size and oversized stents. Stent thrombosis was observed the most in the small RVD with low %SO group compared with the other subgroups (p=0.040) (right figure).



CONCLUSIONS In this pooled data analysis, no negative impact of stent oversizing was documented with respect to procedural and long-term clinical outcomes. Clinical adverse events appeared to be primarily related to vessel size itself, rather than the selection of a stent larger than the vessel size. In particular, small vessels treated with a smaller stent were associated with greater adverse events, suggesting that aggressive selection of larger stents with appropriate attention to edge effects may optimize long-term outcomes even in DES implantation.

CATEGORIES CORONARY: Stents: Drug-Eluting

KEYWORDS Drug-eluting stent, Stent implantation

TCT-556

One-year Outcome of a Prospective Trial Stopping Dual Antiplatelet Therapy at 3-Month after Everolimus-eluting Cobalt-chromium Stent Implantation: ShortT and OPtimal duration of Dual AntiPlatelet Therapy after everolimus-eluting cobalt-chromium stent (STOPDAPT) trial

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BACKGROUND Prolonged dual antiplatelet therapy (DAPT) after coronary stent implantation is associated with higher risk for bleeding. Second-generation drug-eluting stents (G2-DES), cobalt-chromium everolimus-eluting stent (CoCr-EES) in particular, are reported to have lower risk for stent thrombosis (ST) compared with first generation DES or bare-metal stents. Therefore, the optimal DAPT duration after CoCr-EES implantation could be shorter than 6-12 months currently recommended in the guidelines. However, there has been no prospective study evaluating DAPT duration shorter than 6 months after CoCr-EES implantation.

METHODS STOPDAPT study is a prospective multicenter single-arm registry enrolling patients who agreed to follow the 3-month DAPT protocol (discontinuation of clopidogrel at 2- to 4-month and aspirin monotherapy thereafter) after successful CoCr-EES implantation. The primary endpoint was a composite of cardiovascular (CV) death, myocardial infarction (MI), stroke, definite ST and TIMI major/minor bleeding at 1-year. As a historical comparison group, we selected the CoCr-EES group in the RESET trial comparing CoCr-EES with sirolimus-eluting stent conducted in 2010, where nearly 90% of patients had continued DAPT at 1-year. With the 6.6% of performance goal based on the event rate of 4.4% in the RESET trial, a total of 1500 patients would yield 95% power at a level of one-sided type 1 error of 0.025.

RESULTS Between September 2012 and October 2013, a total of 1525 patients were enrolled in the study from 58 participating centers across Japan, and 1-year follow-up was completed in 1519 patients (99.6%). Thienopyridine was discontinued within 4-month in 1444 patients (94.7%). The event rates beyond 3-month were very low (CV death: 0.5%, MI: 0.1%, definite/probable ST: 0%, stroke: 0.7%, and TIMI major/minor bleeding: 0.8%). Cumulative 1-year incidence of the primary endpoint was 2.8% (Upper 97.5% confidence interval [CI] 3.6%), which was lower than the pre-defined performance goal of 6.6% (P<0.0001). Compared to CoCr-EES group in the RESET trial, cumulative incidence of the primary endpoint tended to be lower in the STOPDAPT than in the RESET (2.8% versus 4.0%, P=0.06) and adjusted hazard ratio was 0.64 (95%CI 0.42-0.95, P=0.03). The cumulative incidence of definite/probable ST was lower in the STOPDAPT than in the RESET (0 patient [0%] versus 5 patients [0.3%], P=0.03).

CONCLUSIONS Stopping DAPT at 3-month after CoCr-EES implantation was at least as safe as the prolonged DAPT regimen adopted in the previous randomized trial.

CATEGORIES CORONARY: Stents: Drug-Eluting

KEYWORDS Antiplatelet therapy, Dual antiplatelet therapy, Everolimus-eluting stents

TCT-557

New Generation Drug-eluting Stents vs. Bare Metal Stents for Primary Angioplasty in Patients > 75 Years With ST Elevated Myocardial Infarction: The ESTROFA-MI+75 study

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BACKGROUND Primary angioplasty is the best reperfusion treatment in ST elevated myocardial infarction. The prevalence of very elderly patients (> 75 years) undergoing primary angioplasty is progressively increasing as population is ageing. The benefit of the new generation drug-eluting stents over bare metal stents in terms of safety and efficacy is unknown for this important subgroup of patients in this setting.

METHODS Retrospective consecutive registry conducted in 31 centers of patients > 75 years with ST elevation myocardial infarction undergoing primary angioplasty.

RESULTS A total of 3,126 pts have been included, 2,132 (68.2%) treated with BMS and 994 (31.8%) treated with new generation DES. After exclusion of patients presenting with cardiogenic shock or requiring cardiac surgery for mechanical complications (14%) a propensity score matching was performed yielding two comparable groups of 580 patients each with well- balanced baseline clinical or angiographic characteristics. Outcomes at 12 months were: cardiac death and MI 10.2% with BMS and 5.2% with DES (p=0.01), TLR was 3.8% with BMS and 1.5% with DES (p=0.04), definite or probable thrombosis 4.3% with BMS and 2.4% with DES (p=0.06), definite thrombosis 3.7% with BMS and 1.3% with DES (p=0.03) and bleeding BARC > 2 0.7% with BMS and 1.2% with DES (p=0.3).

CONCLUSIONS In this registry of patients over 75 years undergoing primary angioplasty, most were treated with BMS. After propensity score matching clinical outcomes were significantly better in those treated with new DES without significant increase in severe bleeding events in follow up.

CATEGORIES CORONARY: Stents: Drug-Eluting

KEYWORDS Acute myocardial infarction, Drug-eluting stent, Elderly

TCT-558

Simple Versus Complex Stenting in Unprotected Left Main Bifurcation Coronary Intervention: A Comprehensive Meta-analysis

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BACKGROUND Percutaneous intervention of distal bifurcation unprotected left main coronary arteries (UPLMCA) are technically demanding with less favorable outcomes. The optimal treatment strategy to improve long-term outcomes is uncertain.

METHODS Studies comparing simple approach (provisional stenting) versus complex stenting (elective two stent technique) were considered for inclusion. A search strategy using Medline, Embase, Cochrane database and the proceedings of the international meetings were included. Information about study design, inclusion criteria and sample characteristics were extracted. Meta-analysis of pooled event rates was compared between these two stenting approaches.

RESULTS 16 studies including 5978 patients who were treated with simple versus complex bifurcation stenting for UPLMCA bifurcations were analyzed. There were no differences in the rates of myocardial infarction (OR 0.81, CI 0.15-4.2), stent thrombosis (OR 0.8, CI 0.2-1.7), target vessel revascularization (OR 0.4, CI 0.6-2.7) or mortality (OR 0.92, CI 0.3-2.8) between simple versus complex stenting approaches at 1 year. However, at 5 years of follow-up there was a significant difference in the rates of target vessel revascularization (OR 0.4, CI 0.3-0.7, p=0.001) favoring the simple approach. There was no difference in the mortality (OR 0.94, CI 0.75-1.19), stent thrombosis (OR 0.83, 0.32-2.1) or myocardial infarction (OR 1.16, CI 0.7-1.7) using either approach at 5 years of follow-up.

CONCLUSIONS Percutaneous intervention for UPLMCA should favor a simple approach over complex approach to optimize long-term outcomes.

CATEGORIES CORONARY: Stents: Drug-Eluting

KEYWORDS Left main bifurcation, Left main coronary artery, PCI - Percutaneous Coronary Intervention

TCT-559

Long-term Clinical and Angiographic Impact of Stent Fracture on Second Generation Drug-eluting Stent Implantation: Comparison between Xience Everolimus- and Nobori Biolimus-eluting Stents

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BACKGROUND Stent fracture (SF) after drug-eluting stent implantation has been reported to be associated with in-stent restenosis (ISR),