

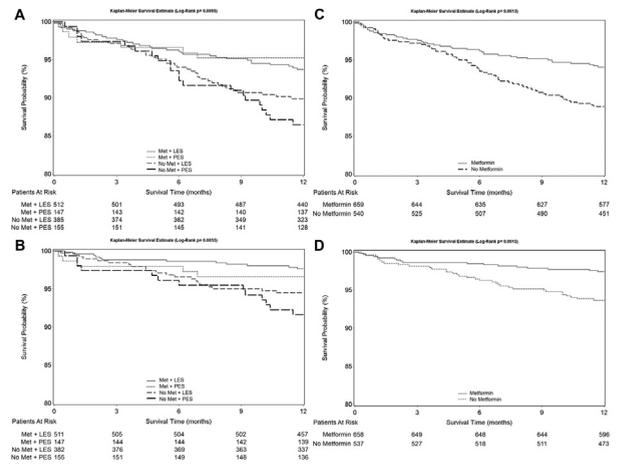
Clopidogrel is a prodrug that requires activation by CYP2C19 and other isoenzymes of the cytochrome P450 system. Carriers of a loss-of-function CYP2C19 allele have lower levels of the active metabolite, resulting in reduced platelet inhibition and a potentially higher rate of adverse cardiovascular events. As PPI are competitive inhibitors of CYP2C19, coadministration with Clopidogrel can further reduce the latter's antiplatelet activity.

The COGENT randomised trial which enrolled predominantly white Caucasian males did not demonstrate any adverse interaction between Clopidogrel and Omeprazole use. However, this interaction may be significant in Asian patients as up to 55% of Asians carry a loss-of-function CYP2C19 allele as compared to 30% of Caucasians. We hypothesize that Asian patients taking both Clopidogrel and the PPI Omeprazole are at higher risk of adverse cardiovascular events post-PCI.

Methods: This retrospective cohort study in a 1300-bed tertiary hospital in Singapore included all patients from 1st January to 31st December 2011 who had PCI and received either Omeprazole or a H2RA, together with 12 months of Aspirin and Clopidogrel. Prescription and outcome data were retrieved from electronic medical records. The primary outcome was the incidence of cardiovascular complications within 12 months of the initial PCI. Cardiovascular complication is defined as cardiovascular death, non-fatal myocardial infarction, need for urgent target vessel revascularisation and ischemic stroke.

Results: We identified 933 patients, of which 614 patients met the criteria for inclusion. The primary outcome occurred in 27 of 296 patients (9.1%) from the Omeprazole group and 13 of 318 patients (4.1%) from the H2RA group ($p = 0.014$). The difference remained statistically significant after adjustment for baseline differences in cardiovascular risk factors in both groups ($p = 0.042$).

Conclusions: Using Omeprazole rather than a H2RA was associated with a significantly greater incidence of cardiovascular complications in Asian patients on Clopidogrel after PCI. Larger studies are required to further evaluate this observation.



Chronic Total Occlusion

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Metformin Does Not Adversely Impact Outcome Following Percutaneous Coronary Intervention in Patients with Diabetes Mellitus

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Background: The use of metformin in patients with non-insulin-dependent diabetes mellitus (NIDDM) has been associated with improved cardiovascular outcomes. However, recent studies raise concern that use of metformin may inhibit endothelialization following limus-eluting stent (LES) placement and increase the risk of stent thrombosis. Therefore, we set out to study the impact of metformin on stent thrombosis and major adverse cardiovascular events in patients that received drug-eluting stents (DES).

Methods: We evaluated consecutive patient with NIDDM discharged on oral anti-hyperglycemic agents that underwent DES placement at our institution from 2003 through 2012. We assessed stent thrombosis, major adverse cardiovascular events (MACE), target lesion revascularization, myocardial infarction, and all-cause mortality at one year and analyzed the impact of metformin use and stent type on these outcomes.

Results: We included 1,201 patients with a mean age of 66 ± 10 years, 64.1% were male, 63.5% had ACS, 74.8% received LES, 25.2% received paclitaxel-eluting stents (PES), and 55% were taking Metformin. There was no difference in stent thrombosis, regardless of stent type or metformin use. Whether or not patients received LES or PES did not significantly impact MACE (Figure 1A) or all-cause mortality (Figure 1B). Patients taking metformin had a significant reduction in MACE ($p=0.002$) and all-cause mortality ($p=0.002$) compared with patients not taking metformin (Figure 1C and Figure 1D, respectively). However, multivariate analysis demonstrated that stent type and metformin use were not significantly associated with MACE or all-cause mortality.

Conclusion: In patients with NIDDM, the use of metformin following placement of DES did not increase the risk of stent thrombosis and MACE, regardless of the type of stent placed.

Rationale of the Decision-Making of Treatment in Chronic Total Occlusion Lesions in a University Hospital

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Background: The presence of a chronic total occlusion (CTO) in up to 30% of routine angiograms emphasizes the importance to select an optimal treatment strategy effectiveness of its treatment and its implication in future clinical events.

Objective: We assessed the rationale for decision-making in treatment of CTO at our institution.

Methods: From June 2010 to December 2012 we evaluated all consecutive patients in our catheterization laboratory in which at least one CTO was diagnosed. Data were prospectively collected on treatment decisions (medical vs. surgery vs. percutaneous coronary intervention <PCI>), PCI indications and subsequent cardiac events through time.

Results: 711 patients with at least one CTO in the basal coronary angiogram were included. Two groups were made according to programmed to PCI (PPCI)=189 patients and non-programmed to PCI (NPPCI)=522 patients. There was a statistical difference among basal characteristics in patients PPCI vs. NPPCI with less acute myocardial infarction (AMI) 16(13,6%) vs. 81(15,5%) $p=0.016$; less involvement of 3-vessel disease 56(29,6%) vs. 224 (42,9%) $p=0.002$; and less presence of coronary left-main disease 12 (6,4%) vs. 72 (13,8%) $p=0.007$. There was also a difference between age ($62,6 \pm 10,4$ years vs. $68,3 \pm 10,7$ years; $p < 0.0001$); ejection fraction (EF) ($47,1 \pm 13,8\%$ vs. $44,9 \pm 13,9\%$; $p=0.017$) and creatinine clearance ($70,8 \pm 28,6$ ml/min vs. $62 \pm 23,1$, ml/min; $p < 0.001$). The multivariate analysis demonstrated that the following variables in predicting no PCI as first step approach in CTO lesions: AMI, number of diseased vessels, left main lesion and age. There was a trend to be treated by PCI as first step approach in patients with positive ischemia by a stress test.

Conclusion: In a large all comer CTO lesion population, in a University hospital; the first step approach of revascularization is dictated by clinical factors as age, comorbidity (EF and creatinine clearance), AMI; anatomical factors such as left-main disease and 3-vessel disease. On the other hand, at our institution the choice of PCI as first step

approach is in the global context of less patient fragility and the positivity of an ischemia test.

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Retrograde Recanalization of Chronic Total Occlusions in Europe: Procedural and In-Hospital Outcomes from the Multicenter Ercto Registry

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Objective: The aim of this study was to describe the five-year European experience of retrograde percutaneous coronary interventions (PCI) revascularization for complex chronic total occlusions (CTOs) of coronary arteries.

Background: Retrograde approach increases the success rate of percutaneous recanalization of complex CTOs of coronary arteries.

Methods: Demographic data, procedural outcomes and in-hospital clinical events were collected on 1582 consecutive lesions of 1395 patients enrolled between January 2008 and December 2012 having retrograde CTO PCI at 44 European medical centers by 45 experienced interventionalist operators. A revision of J-CTO score proposed for antegrade lesions was used to better describe success according to lesion difficulty.

Results: Patients mean age was 62.0±10.4 years, 88.5% were men, 17.6% had prior coronary artery bypass surgery. The CTO target vessel was the right coronary artery (70.4%), circumflex (7.8%), left anterior descending artery (20.3%), and left main artery or by-pass graft (1.5%). The retrograde approach was used after prior failed attempt in 43.5% of cases. During the procedure the retrograde approach was used as first line strategy in 76.2% of cases, while immediately after antegrade failed approach in 23.8% of cases. Retrograde collateral vessels were septal (62.7%), epicardial (13.4%), by-pass graft (3.9%) or missing information (20.0%). Technical success was 75.3% (n=1.191). The mean contrast volume and fluoroscopy time were 396.3±171.3 ml and 69.8±34.1 mins, respectively. A major complication occurred in 16 patients (1.0%). In multivariable analysis, age of the patient (per 10-year increase), lower operator volume (<50, 50-100, >100), increased J-CTO score were significantly associated with increased technical failure, (p=0.01, p<0.001, p<0.001), respectively.

Conclusion: In Europe among selected centers dedicated to CTO revascularization, retrograde approach was performed over a 5-year period in 16.5% of these patients. The number of retrograde procedures were exponentially increasing during the last 2 years and were associated with high success and low major complications rates.

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Myocardial Perfusion in Patients with Total Occlusion of a Single Coronary Artery with and without Collateral Circulation

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Background: Previous studies that investigated the effects of coronary collateral circulation on myocardial perfusion were compromised by inclusion of patients with multivessel coronary artery disease, incomplete occlusion, prior myocardial infarction, or a combination of these.

Aim of work: In this study we will investigate the relationship between angiographic collateral circulation and myocardial perfusion in patients with total occlusion of a

single coronary artery, in the absence of myocardial infarction or significant stenosis in the other coronary arteries supplying the same myocardial territory.

Methods and Results: Forty patients underwent stress myocardial single photon emission computed tomography within 90 days of angiography. Collateral circulation was present in 24 patients (group A) and absent in 16 patients (group B). Reversible perfusion defects were present in 22(91.7%) patients in group A and in 12(75%) in group B, comparison between both groups came back statistically insignificant (p-value = NS). Group A included 4(18.2%) patients with a small size defect (<5%), 9(40.9%) patients with a moderate perfusion defect (5-10%) and 9(40.9%) patients with a large perfusion defect (>10%); while group B had 2(16.6%) patients with small perfusion defect, 5(41.6%) patients with a moderate perfusion defect and also 5(41.6%) patients with a large perfusion defect, comparison between both groups came back statistically insignificant (p-value = NS). The mean exercise time for patients in group A was 6.9 ±0.92 minutes and their mean achieved peak METs was 7.35±0.35 METs. On the other hand; the mean exercise time for patients in group B was 6.9 ±0.83 minutes and their mean peak METs was 7.23±0.25 METs. Comparison between both groups also appeared to be statistically insignificant (p-value = NS).

Conclusion: In patients with a single-vessel total coronary occlusion and without myocardial infarction, stress-induced myocardial ischemia is almost always present, irrespective of presence or absence of angiographic collaterals. These data suggest that coronary collaterals do not appear to protect against stress-induced perfusion defects. Nevertheless collaterals in our study did not have any positive impact on the functional capacity of patients, predicted by the analysis of exercise duration and achieved peak METs.

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Restenotic Stented Versus De Novo Chronic Total Occlusion Outcomes Following Successful Intervention with Drug-eluting Stents

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Background: There are limited data comparing angiographic and clinical outcomes of re-stenotic stented chronic total occlusive (CTO) lesion successfully revascularized with drug-eluting stents (DESs) with those of de novo CTO lesion.

Methods: The study population consisted of consecutive 269 CTO patients (pts) who successfully treated with DESs between January 2004 and June 2010. A total 249 pts with de novo CTO lesion and 20 pts with re-stenotic stented CTO lesion were included for analysis. The 6-to-9 month angiographic and 2-year clinical outcomes were compared between the 2 groups.

Results: The baseline clinical characteristics were similar between the two groups except prior myocardial infarction, LDL-cholesterol level, number of total implanted stent and use of cilostazol. Angiographic outcomes at 6-to-9 months were similar between the two groups. At 2-year follow-up, the incidence of major clinical outcomes including all death, any myocardial infarction, any revascularization, target lesion and vessel revascularization (TLR and TVR) and major adverse cardiac events (MACEs) were similar between the two groups (Table). Further, even after adjustment of baseline differences with multivariate analysis adjusted by age, gender, dyslipidemia, LVEF, Lefevre classification, all the major clinical outcomes were similar between the two groups.

Conclusion: In our study, there were no difference in 6-to-9 month angiographic and 2-year clinical outcomes between pts with stented and de novo CTO lesions once the CTO pts were successfully treated with DESs.