



Comparison of drug-eluting stents for treatment of coronary bifurcation lesions

Evaluation of: Song YB, Hahn JY, Choi SH *et al.*: Sirolimus- versus paclitaxel-eluting stents for the treatment of coronary bifurcations results from the COBIS (Coronary Bifurcation Stenting) registry. *J. Am. Coll. Cardiol.* 55(16), 1743–1750 (2010).

A growing body of head-to-head comparative studies exist evaluating the efficacy and safety of sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES) in lowering major adverse cardiac events (MACEs; e.g., cardiac death, myocardial infarction and target lesion revascularization) in patients with coronary artery disease [1]. These studies have been largely equivocal [2–5], with only a handful of single studies favoring one stent over another, albeit with very little absolute differences and often in selected cohorts, in other words, those with diabetes mellitus [6]. Comparing these two drug-eluting stents in populations with equivalent lesions may remove some of the ambiguity that has resulted.

Song *et al.* recently evaluated the long-term outcome of 1033 patients treated with SES and 562 patients treated with PES for coronary bifurcation lesions (left main disease excluded), with an average follow-up of 22 months [1]. They found that the use of SES versus PES resulted in lower MACEs (5 vs 8.7%; $p < 0.01$). This reduction in MACEs was mainly caused by an absolute risk reduction in target lesion/vessel revascularization, as the differences in hard clinical end points of cardiac death and myocardial infarction were not statistically different. In an attempt to adjust for baseline differences between the groups, propensity-score methodology was applied

and found lower MACEs and target lesion revascularization with SES compared with PES (hazard ratio [HR]: 0.52; 95% CI: 0.30–0.91; $p = 0.02$, and HR: 0.48; 95% CI: 0.25–0.91; $p = 0.02$, respectively). There was an equivalent rate of stent thrombosis between SES and PES (0.7 vs 0.7%; $p = 0.94$), rates that are comparable to other contemporary drug-eluting stent studies.

This study is largely in line with a meta-analysis of 16 studies reported by Schömig *et al.* comparing SES with PES, including a total of 8695 patients with an overall average follow-up of 20 months [7]. Allocation to the SES group was associated with a lower risk of reintervention (HR: 0.74; 95% CI: 0.63–0.87; $p < 0.001$). No significant differences in the rates of myocardial infarction or cardiac death were found between the two stent groups.

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Benefits of statins for patients undergoing PCI intervention

Evaluation of: Zhang F, Dong L, Ge J: Effect of statins pretreatment on periprocedural myocardial infarction in patients undergoing percutaneous coronary intervention: a meta-analysis. *Ann. Med.* 42(3), 171–177 (2010).

It has become increasingly clear that the beneficial effect of HMG–CoA reductase inhibitors extends beyond the long-term improvement in outcomes associated with cholesterol-lowering effects. Two now widely cited randomized controlled trials are notable in demonstrating some of these effects. First, the Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL) study, comparing atorvastatin 80 mg daily initiated within 96 h of unstable angina or non-Q-wave myocardial infarction (MI) with placebo, showed a significantly lower risk of cardiovascular events in the treatment group within the relatively short follow-up period of 16 weeks [1]. Later, the Pravastatin or Atorvastatin Evaluation and Infection Trial – Thrombolysis In Myocardial Infarction 22 (PROVE IT-TIMI 22) study, comparing an intensive statin regime of atorvastatin 80 mg daily and standard therapy with pravastatin 40 mg daily following acute coronary syndrome, showed a benefit at only 30 days [2]. This suggests effects other than cholesterol-lowering, such as alteration of inflammation, improvements in endothelial function and microcirculation and reduction in platelet function and thrombosis, referred to as pleiotropic or plaque stabilizing effects, are an additional benefit of statins [3].

Percutaneous coronary intervention (PCI)-related myocardial injury represented by elevation of cardiac enzymes is a common

occurrence and may have significant prognostic implications [4]. By its very nature, PCI disrupts the vascular endothelium and atheromatous plaque, potentially triggering inflammation, increased thrombosis and disruption of the microcirculation not unlike acute coronary syndrome. The pleiotropic effects of statins may mitigate this associated myocardial injury. The first randomized controlled trial to test this hypothesis was published in 2004. The Antiplatelet Therapy for Reduction of Myocardial Damage During Angioplasty (ARMYDA) trial demonstrated a significantly lower risk (5 vs 18%) of post-PCI creatine kinase-MB (CK-MB) elevation greater than two-times the upper normal limit, 76 patients receiving atorvastatin 40 mg daily for 7 days prior to elective PCI compared with 77 patients receiving placebo, respectively [5].

Zhang *et al.* have pooled six randomized controlled trials involving 2088 statin-naive patients comparing statin pretreatment with placebo in patients undergoing planned PCI with postprocedure myocardial injury documented by enzymes [6]. The dose and duration of statin administration varied widely across the studies. In addition, the definition of MI varied between the trials. One included any elevation of CK-MB greater than twice the normal level while another required chest pain or ischemic ST-segment changes in conjunction with a fivefold elevation of CK-MB. The definition of MI was accepted from each study and CK-MB data were not reanalyzed to reclassify patients. There was consistent adherence to dual antiplatelet therapy with daily aspirin combined with clopidogrel or ticlopidine including loading. Periprocedural MI occurred in 81 of the 1051 (7.7%) statin-treated patients



and 147 of the 1037 (14.2%) placebo-treated patients (odds ratio: 0.51; 95% CI: 0.38–0.67; $p < 0.001$). The rate of death and revascularization at 1-month follow-up was very low, thus the end point of death, Q-wave MI or target vessel revascularization (84 in the statin group vs 159 in the placebo group [odds ratio: 0.48; 95% CI: 0.36–0.64; $p < 0.001$]) was driven mostly by periprocedural MI.

Evidence is mounting that pretreatment with statins should be considered in patients not already taking statins who are undergoing elective PCI. Further randomized controlled trials including longer follow-up for death and major adverse cardiac events will serve to strengthen the evidence to determine the optimal dose and duration of pretreatment therapy.

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Use of bivalirudin in patients receiving clopidogrel at the time of PCI for acute coronary syndromes

Evaluation of: Feldman DN, Minutello RM, Bergman G, Moussa I, Wong SC: Efficacy and safety of bivalirudin in patients receiving clopidogrel therapy after diagnostic angiography for percutaneous coronary intervention in acute coronary syndromes. *Catheter. Cardiovasc. Interv.* DOI: 10.1002/ccd.22546 (2010) (Epub ahead of print).

In the drive to improve outcomes with percutaneous coronary interventions (PCI), there has been an attempt to discover alternative anticoagulation strategies that improve efficacy and safety beyond unfractionated heparin (UFH). In the Randomized Evaluation of PCI Linking Angiomax to Reduced Clinical Events (REPLACE-2)

trial [1] and the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial [2], patients who were to undergo PCI for stable coronary syndromes and non-ST-segment elevation acute coronary syndromes (NSTEMI-ACS) were studied using bivalirudin versus UFH with glycoprotein IIb/IIIa (Gp IIb/IIIa) inhibitors. In the REPLACE-2 trial, approximately 45% of the patients were enrolled with unstable angina or recent (within 1 week) myocardial infarction. In the ACUITY trial, a higher-risk ACS population was studied. In these trials, there were similar efficacy rates among both groups, but the bivalirudin group experienced less bleeding.

However, in these studies, most patients received clopidogrel upstream prior to diagnostic angiography. In contemporary practice, upstream clopidogrel is often withheld



due to a concern for an increased risk of perioperative bleeding if coronary artery bypass graft surgery is undertaken. This paper attempts to address the question of safety and efficacy of bivalirudin if used during PCI without upstream clopidogrel.

In this study, Feldman *et al.* attempt to replicate clinical practice with respect to timing of clopidogrel [3]. The authors retrospectively looked at 980 patients who underwent PCI for NSTEMI-ACS and who did not receive upstream clopidogrel. All patients received clopidogrel loading just prior to or within 30 min of PCI. Patients were then split into two groups, one receiving periprocedural bivalirudin (n = 461; 47%) and the other receiving UFH and Gp IIb/IIIa (n = 519; 53.0%). Clinical parameters were examined. When comparing the bivalirudin group to the UFH with Gp IIb/IIIa group, there was no statistical difference in the rate of in-hospital mortality (0.4 vs 0.2%; p = 0.604), myocardial infarction (6.9 vs 5.4%; p = 0.351) and major adverse cardiac events (7.6 vs 5.8%; p = 0.304). After using a propensity score adjusted multivariate analysis to account for baseline differences in the two groups (as this was not a randomized trial), there was a trend towards less major bleeding (odds ratio: 0.37; 95% CI: 0.10–1.38; p = 0.139), and statistically significantly less minor bleeding (odds ratio: 0.48; 95% CI: 0.31–0.74; p = 0.001) in the bivalirudin group.

The authors acknowledge several limitations to this study. There are inherent limitations in a retrospective analysis that limit

the ability to use the data for prospective decision-making. Although multivariate analysis can attempt to adjust for baseline differences in the study groups, all differences cannot be accounted for. It is possible that physicians chose the anticoagulation strategy according to the overall health of the patient, something that is difficult to quantify and account for. However, in spite of these limitations, this is another interesting paper that supports previous impressions that in NSTEMI-ACS patients, even if clopidogrel is not used upstream, bivalirudin may be used as an alternative to UFH and Gp IIb/IIIa with similar efficacy and fewer bleeding complications.

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Gender and outcome after PCI for acute myocardial infarction

Evaluation of: Woo JS, Kim W, Ha SJ, Kim SJ, Kang WY, Jeong MH: Impact of gender differences on long-term outcomes after successful percutaneous coronary intervention in patients with acute myocardial infarction. *Int. J. Cardiol.* DOI: 10.1016/j.ijcard.2010.02.028 (2010) (Epub ahead of print).

Observational and randomized studies suggest that women have an increased risk of major adverse cardiac events (MACE) and

short-term mortality after acute myocardial infarction following primary percutaneous coronary intervention compared with men. However, many factors need to be taken into consideration when evaluating female gender as an independent predictor of clinical outcome in acute myocardial infarction patients.

Female awareness that heart disease is the leading cause of death in women in the USA is relatively low [1]. Women are more likely to exhibit longer delays in seeking medical care after the development of symptoms



suggestive of acute myocardial infarction [2]. This may be related to the idea that women perceive themselves as caretakers and also the lack of awareness of the high prevalence of heart disease in women.

With this background, Woo *et al.* used the Korea Acute Myocardial Infarction Registry (KAMIR) to evaluate the clinical outcome of 3298 patients (2416 males and 882 females) who had undergone percutaneous coronary intervention with drug-eluting stents [3]. In univariate analysis, in-hospital mortality (odds ratio [OR]: 2.74; 95% CI: 2.08–3.61; $p < 0.001$), 1-month MACEs (OR: 2.30; 95% CI: 1.81–2.92) and 1-year MACEs (OR: 1.64; 95% CI: 1.36–1.97) were significantly higher in women compared with men. However, in multivariate analysis, gender was not found to be an independent predictor of in-hospital mortality (OR: 1.29; 95% CI: 0.84–1.99), 1-month MACEs (OR: 1.09; 95% CI: 0.77–1.58), or 1-year MACEs (OR: 0.99; 95% CI: 0.75–1.29). Women tended to be older with more

comorbidities such as hypertension, diabetes, dyslipidemia and a worse Killip class, which could explain the differences between the two genders with regard to short-term mortality.

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