Welcome to issue 22 of Interventional Cardiology Research Review.

In this issue, the MOZART trial researchers have reported that IVUS-guided PCI was safe and associated with a marked reduction in iodine contrast use compared with angiography alone. Other researchers reported that one quarter of their patients with NSTEMI had an occluded culprit coronary artery, and that such patients were more likely to have hypercholesterolaemia, ECG abnormalities, multivessel disease and LV dysfunction. Interesting research from the US found no evidence of adverse outcomes when PCI was performed by operators with acute sleep deprivation due to performing procedures during the previous night, but chronic sleep deprivation did appear to increase bleeding events.

Thank you for your comments, questions and suggestions — please keep them coming.

Kind Regards,

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Second-generation drug-eluting stent implantation followed by 6- versus 12-month dual antiplatelet therapy

Authors: Colombo A et al.

Summary: Patients with stable or unstable angina or silent ischaemia undergoing revascularisation with 2nd second-generation DES were randomised to 6 months (n=682) or 12 months (n=717) of DAPT in the SECURITY noninferiority RCT. The respective 6- and 12-month DAPT groups had: i) similar primary composite endpoint event rates (cardiac death, MI, stroke, definite or probable stent thrombosis or BARC [Bleeding Academic Research Consortium] type 3 or 5 bleeding) at 12 months (4.5% and 3.7% [p<0.05 for noninferiority]); ii) similar main secondary composite endpoint event rates (primary endpoint plus BARC bleeding type 2) at 12 months (5.3% vs. 4.0% [p=0.273]) and during 12–24 months (1.5% vs. 2.2% [p=0.289]); and iii) similar definite or probable stent thrombosis rates at 12 months (0.3% vs. 0.4% [p=0.694]) and during 12–24 months (0.1% vs. 0% [p=0.305]).

Comment: Guidelines recommend DAPT for at least 12 months after DES implantation or for 6–12 months for those not at high risk. Randomised trials have generally shown an increased bleeding risk with no significant reduction in major adverse cardiac events with prolonged therapy. The current study assessed a shorter duration of therapy in patients receiving a second-generation DES. This investigator driven, multicentre international study was stopped early due to logistic and economic constraints. The majority of patients (61.6%) had stable angina and >97% of patients received clopidogrel. Bleeding and major adverse cardiac events were similar, and the study suggested 6 months of therapy was noninferior to 12 months in this low-risk cohort using Endeavour, Nobori, Biomatrix, Promus or Xience stents.

Reference: J Am Coll Cardiol 2014;64(20):2086–97

Abstract
Intravascular ultrasound guidance to minimize the use of iodine contrast in percutaneous coronary intervention

Authors: Mariani J et al.

Summary: The MOZART trial randomised patients undergoing PCI (n=83) to angiographic or IVUS guidance. Compared with angiography, IVUS-guided PCI was associated with a significantly lower median total volume of contrast (20.0 mL vs. 64.5 mL, p<0.001) and a significantly lower median contrast-creatinine clearance ratio (1.0 vs. 0.4, p<0.001), with no between-group difference for in-hospital and 4-month outcomes.

Comment: Contrast-induced acute kidney injury is a potential complication of invasive coronary procedures and is associated with significant morbidity and mortality. The volume of contrast used is a major predictor of contrast-induced acute kidney injury and few studies have attempted to address this issue. This small RCT shows that aggressive use of IVUS can dramatically reduce contrast use. Lessons to be learned to reduce contrast use for routine PCI strategies include rigorous preprocedure planning, use of smaller catheters without side holes and the use of dilute contrast with smaller syringes. All patients had to be suitable for IVUS guidance, the study was not blinded and was not powered for clinical endpoints, but we should consider such strategies in patients at high risk for contrast nephropathy.


Hybrid revascularization for multivessel coronary artery disease

Authors: Gąsior M et al.

Summary: Two hundred patients with multivessel coronary artery disease involving the LAD artery and a >70% lesion in ≥1 other major epicardial vessel who were amenable to both PCI and CABG and referred for conventional surgical revascularisation were randomised 1:1 to undergo hybrid coronary revascularisation or CABG. Among participants assigned to hybrid coronary revascularisation, 93.9% completed the procedure with the remaining 6.1% converted to standard CABG. There was no significant between-group difference at 12 months for mortality, MI, major bleeding or repeat revascularisation, and no cerebrovascular incidents were reported.

Comment: The most advantageous part of CABG is insertion of a LIMA graft to the LAD artery, whilst the long-term efficacy of saphenous vein graft is inferior to DES patency. This prospective, single-centre, randomised, open-label pilot study suggests a hybrid strategy is feasible for patients with multivessel disease (mean Syntax score 23). In the hybrid group, the aim was to perform a minimally invasive direct coronary artery bypass with LIMA to LAD artery followed by PCI to other vessels. This allowed assessment of LIMA graft patency, and antplatelet therapy was started after surgery. Larger studies are needed to confirm this is a viable strategy for routine use.


Non-ST elevation myocardial infarction with occluded artery and its clinical implications

Authors: Soon K et al.

Summary: The prevalences and differences between NSTEMI with occluded versus patent culprit arteries were explored in a retrospective group of 143 patients with NSTEMI who had undergone inpatient coronary angiography and with 12 months of follow-up data. Compared with patients with NSTEMI with a patent culprit artery, those with an occluded culprit artery (n=34) had significantly higher rates of hypercholesterolaemia (85.3% vs. 64.2%, p=0.015), ST-depression abnormality on ECG (52.4% vs. 11.9%, p=0.008), multivessel disease on coronary angiogram (76.5% vs. 48.6%, p=0.004) and LV dysfunction on echocardiogram (77% vs. 48%, p=0.016). A trend for a higher rate of HF within 12 months of discharge was apparent among patients with NSTEMI with an occluded culprit artery, but death, MI, revascularisation, arrhythmia and angina readmission rates did not differ significantly. No correlation was evident between peak creatine kinase level and the timing of percutaneous coronary revascularisation in both groups.

Comment: Generally NSTEMI is thought to be due to incomplete occlusion of the culprit artery as opposed to STEMI where complete occlusion is usually the case. This single-centre, retrospective observational study conducted in a primary PCI centre in Victoria showed that in 24% of NSTEMIs, the culprit artery was in fact occluded. This is consistent with other studies, and clues included ECG changes showing ST depression or T-wave inversion and impaired LV dysfunction. As would be expected, these patients more often had multivessel disease and collaterals present. There was no evidence earlier PCI resulted in less myocardial damage, although the numbers were probably too small to confidently exclude this, and more research is needed to see if this is a viable strategy.

Reference: Heart Lung Circ 2014;23(12):1132–40

AstraZeneca
Prasugrel plus bivalirudin vs. clopidogrel plus heparin in patients with ST-segment elevation myocardial infarction

Authors: Schulz S et al.

Summary: The BRAVE 4 trial randomised patients with STEMI to undergo primary PCI with a prasugrel plus bivalirudin or clopidogrel plus heparin strategy, the trial was terminated early due to slow recruitment after 546 participants had been enrolled. No difference was seen between the prasugrel plus bivalirudin versus clopidogrel plus heparin strategies for the 30-day rate of the primary composite endpoint (death, MI, unplanned revascularisation, stent thrombosis, stroke or bleeding; 15.6% vs. 14.5% [p=0.688]), the composite ischaemic endpoint (death, MI, unplanned revascularisation, stent thrombosis or stroke: 4.8% vs. 5.5% [p=0.589]) or bleeding (14.1% vs. 12.0% [p=0.543]). The results across various subgroups were consistent.

Comment: Recent studies have cast doubt on the benefits of bivalirudin over heparin during primary PCI. This study is another to compare bivalirudin with unfractionated heparin, but with differing antiplatelet agents. Notably the protocol suggested terminating the bivalirudin infusion at the end of the procedure and bailout glycoprotein IIb/IIIa use was low (6.1% clopidogrel and 3.0% prasugrel groups [p=0.074]). The access site was femoral in all but one patient. Whilst the trial was stopped early due to slow recruitment, there were no apparent differences between the treatment arms for composite endpoints. Unlike other bivalirudin STEMI trials, stent thrombosis was similar in both groups (1.1% bivalirudin and 1.5% heparin arms) and bleeding rates were similar. This suggests prasugrel may reduce stent thrombosis but increase bleeding, although the study is underpowered to draw definitive conclusions.


Coronary artery bypass graft surgery versus drug-eluting stents for patients with isolated proximal left anterior descending disease

Authors: Hannam EL et al.

Summary: This research compared outcomes of patients who underwent CABG and received DESs for isolated proximal LAD artery disease over a 3-year period; 5340/6064 patients received DESs, and they were propensity matched into 715 CABG and/or DES pairs to minimise selection bias. No significant difference was seen for mortality alone or mortality, MI, or stroke, but CABG was associated with significantly fewer repeat revascularisations (7.09% vs. 12.98% [p=0.0007]). A Cox proportional analysis confirmed no significant differences in the 3-year mortality rate (adjusted hazard ratio 1.14 [95% CI 0.70–1.85]) and the 3-year mortality, MI, or stroke rate (11.5 [0.76–1.73]), and also confirmed the lower repeat revascularisation rate (0.54 [0.36–0.81]).

Comment: There are at least nine RCTs comparing CABG with PCI in patients with single-vessel LAD artery disease; however, the total number of patients (n=1257) is modest and all but one was before the DES era. This study used New York State’s clinical registries to provide up-to-date comparisons between these two modalities. There appear to be no differences in mortality, MI and stroke between the two groups, but a higher rate of subsequent revascularisation in the stented group. Depending on the perceived difficulty of PCI (chronic total occlusion, complex bifurcation) and quality of the distal vessel for LIMA anastomosis and patient comorbidities, a heart team approach may be ideal in deciding which treatment is best for an individual patient.

Reference: J Am Coll Cardiol 2014;64(25):2717–26

Efficacy of a device to narrow the coronary sinus in refractory angina

Authors: Verheyen S et al.

Summary: This study evaluated a balloon-expandable, coronary sinus-reducing device in 104 patients with CCS (Canadian Cardiovascular Society) class III/IV angina and myocardial ischaemia who were not suitable for revascularisation. The patients were randomised to implantation of the device or to a sham procedure (control group). Compared with controls, a significantly greater proportion of implant recipients had an improvement of ≥2 CCS angina classes at 6 months (35% vs. 15% [p=0.02]). QOL (assessed using the Seattle Angina Questionnaire) also improved significantly in the treatment group compared with the control group (p=0.03).

Comment: The worldwide prevalence of severe angina not amenable to revascularisation is rising, with few therapeutic options available. This small multicentre study randomising patients over 3 years is a proof-of-concept trial examining a novel implantable device in the coronary sinus. The exact mechanism of benefit is unclear, but is felt to be due to recruitment of coronary collateral flow and follows on from a surgical technique described in 1954 that partially occluded the coronary sinus. Whilst this study showed patients subjectively felt better, there was little objective evidence of improvement, and larger studies will be needed to better define the role of this device.


An angiographic tool for risk prediction of side branch occlusion in coronary bifurcation intervention

Authors: Dou K et al.

Summary: These researchers established the RESOLVE scoring system for evaluating the risk of side-branch occlusion using data from 1545 consecutive patients undergoing coronary bifurcation intervention, including 1601 lesions treated with a single-stent technique or main-vessel stenting first strategy; side-branch occlusion occurred in 118 lesions. The risk model and scoring system was constructed, with incremental weights attributed to each component variable according to its estimated coefficients, from 1220 lesions. The remaining 401 lesions were used for validation. Side-branch occlusion after main-vessel stenting was defined as any decrease in TIMI flow grade or absence of side-branch flow after main-vessel stenting. Multivariable analyses revealed six variables independently associated with side-branch occlusion risk (C-statistic 0.80 [95% CI 0.75–0.85] with good calibration); good calibration was confirmed in the validation cohort (0.77 [0.69–0.86]). Side-branch occlusion rates in the validation cohort were 0.0%, 3.8% and 19.8% in low-, intermediate- and high-risk groups, respectively (p<0.001).

Comment: The risk of side-branch occlusion is the most important factor in determining the approach to bifurcation stenting. This study from Fuwai Hospital in Beijing examined a large number of consecutive patients to develop a risk stratification tool to predict the risk of side-branch occlusion. The authors identified six variables, including plaque distribution (same side as side-branch worse), main-vessel TIMI flow before stenting (0 worse), preprocedural diameter stenosis of bifurcation core (≥70° worse), bifurcation angle (≥90° worse), diameter ratio between main vessel/side branch (≥2 worse) and diameter stenosis of side branch before main-vessel stenting (≥90% worse). There is little discussion about using side-branch protection, but the above variables may help to inform decisions around use of such strategies.

Remote ischemic conditioning reduces myocardial infarct size and edema in patients with ST-segment elevation myocardial infarction

Authors: White SK et al.

Summary: Patients with STEMI with TIMI flow grade 0 (n=197) received remote ischemic conditioning with four 5-minute cycles of upper arm cuff inflation/deflation or an uninflated cuff placed on the upper arm for 40 minutes (controls) prior to primary PCI in this RCT. Compared with controls, remote ischemic conditioning was associated with a significant 27% reduction in MI size (18.0% vs. 24.5% [p=0.009]), a lower 24-hour high-sensitivity troponin T level (2296 vs. 2736 ng/L [p=0.037]), and reduced extent of myocardial oedema on T2-mapping cardiac magnetic resonance (28.5% vs. 35.1% [p=0.003]) with lower mean T2 values (68.7 vs. 73.1 msec [p=0.001], precluding the use of cardiac magnetic resonance oedema imaging for estimating the at-risk area. When cardiac magnetic resonance-independent coronary angiography jeopardy scores were used to estimate the at-risk area, remote ischemic conditioning was associated with a significant improvement in the myocardial salvage index (0.42 vs. 0.28 [p=0.03]).

Comment: Despite the increasing prevalence of primary PCI, significant morbidity and mortality of STEMI remains, which may relate to reperfusion injury. Remote ischemic conditioning has emerged as a potential low cost and safe intervention, which may have therapeutic benefit. This randomised single-centre study examined a surrogate MI endpoint and suggested benefit of remote ischemic conditioning. Patients were randomised on arrival to hospital to remote ischemic conditioning or control. The remote ischemic conditioning protocol consisted of a standard blood pressure cuff placed on the upper arm and inflated to 200mm Hg and left inflated for 5 minutes. It was then deflated for 5 minutes and the cycle repeated a total of four times prior to primary PCI. The results are intriguing and a large multicentre RCT powered for hard cardiac endpoints is now needed.


Abstract

Remote ischemic conditioning reduces myocardial infarct size and edema in patients with ST-segment elevation myocardial infarction

Post-MI Patients Remain at High and Persistent Risk

Up to 20% RISK of a recurrent CV event in the first year*1,2

~20% RISK of a recurrent CV event in the subsequent 3 years*

After a successful intervention, what more can we do to protect them from their underlying disease?

*The APOLLO HELICON analysis was a retrospective cohort study that included 108,315 patients from a national Swedish registry with a primary diagnosis of acute MI between July 2006 and June 2011. The primary endpoint was risk for non-fatal MI, non-fatal stroke, or cardiovascular death. The cumulative 1 year incidence of the primary endpoint was 18.3%. In patients who were event free at 1 year, the cumulative incidence of the primary endpoint was 20% after following the subsequent 3 years. On the basis of pooled data (Framingham Heart Study, Atherosclerosis Risk in Communities Study, and National Heart, Lung, and Blood Institute), the American Heart Association reported that 19% of men and 26% of women aged ≥45 years will die within 1 year after a first MI.