Interventional Cardiology Research Review™

Making Education Easy

Issue 31 - 2020

In this issue:

Abbreviations used in this issue:

ACS = acute coronary syndrome; **AF** = atrial fibrillation; **CV** = cardiovascular; **DOAC** = direct oral anticoagulant; **HR** = hazard ratio; **IFR** = instantaneous wave-free ratio; **LAA** = left atrial appendage; **MI** = myocardial infarction; **NSTEMI/NSTEACS** = non-ST-segment elevation **MI/ACS**; **PCI** = percutaneous coronary intervention; **PVE** = prosthetic valve endocarditis; **SAVR** = surgical aortic valve replacement; **TAVI/TAVR** = transcatheter aortic valve implantation/replacement.

Welcome to issue 31 of Interventional Cardiology Research Review.

An observational study describing the incidence, causative organisms and outcomes of infective endocarditis in consecutive Swiss registry patients who had undergone TAVR begins this issue. Another observational study has reported long-term clinical outcomes for patients with left main coronary artery stenosis when the IFR (instantaneous wave-free ratio) was used to determine their treatment strategy. Research published in the Lancet has described differences in outcomes for patients aged ≥80 years with NSTEMI treated invasively versus noninvasively. This issue concludes with research reporting no improvement in outcomes and an increased bleeding risk when patients with NSTEACS scheduled for PCI received P2Y12 inhibitor pretreatment.

We hope you enjoy the papers selected for this review of interventional cardiology research. Please feel free to send us your comments and feedback.

Kind Regards,

Professor Craig Juergens
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Infective endocarditis after transcatheter aortic valve replacement

Authors: Stortecky S et al.

Summary: These authors reported on incidence rates, types of microorganisms and outcomes for 149 of 7203 consecutive patients who developed endocarditis during 14,832 patient-years following TAVR in Switzerland. The respective incidences for periprocedural, delayed-early and late endocarditis following TAVR were 2.59, 0.71 and 0.40 events per 100 person-years. In the early endocarditis group, the most frequently isolated microorganisms were *Enterococcus* spp. (30.1%). Nearly half of the patients with periprocedural endocarditis (47.9%) were infected with a pathogen that was not susceptible to the periprocedural antibiotic prophylaxis. Independent predictors of endocarditis were younger age (sub-HR 0.969 [95% CI 0.944–0.994), male sex (1.989 [1.403–2.818), lack of predilatation (1.485 [1.065–2.069]) and treatment in a catheterisation laboratory versus a hybrid operating room (1.648 [1.187–2.287]). A case-control matched analysis revealed that patients who developed endocarditis were at greater risk of death and of stroke (respective HRs 6.55 [95% CI 4.44–9.67] and 4.03 [1.54–10.52]).

Comment: PVE (prosthetic valve endocarditis) affects around 0.3–1% of patients per year after surgical valve replacement, but the impact the growth of TAVR has is not well characterised. This study reports a detailed analysis of the Swiss experience with PVE and TAVR. Whilst there is no direct comparison with a SAVR cohort, the rates of PVE appear to be similar and we do not know how these cases were managed; endocarditis cases had a very high mortality (41%) and stroke risk (3.6%). There are some important lessons to be learned. Given *Enterococci* and *Streptococci* spp. were frequent causes of PVE, we should try and avoid urinary catheterisation and optimise dentition prior to the procedure. Similarly, given the signal that procedures done in catheterisation laboratories were a predictor of PVE, we should take best infection control practices from operating rooms into our catheter labs when doing these and other procedures.

Reference: J Am Coll Cardiol 2020;75:3020–30
Abstract

Left atrial appendage closure versus direct oral anticoagulants in high-risk patients with atrial fibrillation

Authors: Osmancik P et al., on behalf of the PRAGUE-17 Trial Investigators

Summary: The PRAGUE-17 study randomised 402 high-risk patients with nonvalvular AF to receive LAA closure or a DOAC (mostly apixaban) for the prevention of AF-related stroke. After median 19.9 months of follow-up, the respective annual rates of the primary composite outcome (stroke, transient ischaemic attack, systemic embolism, CV-related death, major or nonmajor clinically relevant bleeding or procedure- or device-related complication) in the LAA closure and DOAC groups were 10.99% and 13.42% (p=0.004 for noninferiority). Major LAA closure-related complications occurred in 4.5% of patients.

Comment: Transcatheter LAA closure is a potential alternative to long-term anticoagulation in patients with AF at high bleeding risk, although notably the two landmark randomised trials compared LAA closure in patients who could take warfarin. Subsequently there has been a large-scale shift to the use of DOACs in preference to warfarin in AF patients. The current multicentre, prospective, randomised, noninferiority trial from the Czech Republic provides important contemporary information. Notably, patients were at relatively high bleeding risk and could receive any approved DOAC or LAA closure device (Amulet 61%, Watchman 39%). Following LAA closure, patients received dual antiplatelet therapy for 3 months. The duration of follow-up was relatively short and the benefits of LAA closure are likely to be magnified with time; however, it does not answer the question of whether LAA closure is a better alternative to long-term DOACs in patients at lower bleeding risk.

Reference: J Am Coll Cardiol 2020;75:3122–35
Abstract

Reoperation after transcatheter aortic valve replacement

Authors: Jawitz OK et al.

Summary: These researchers reported on a series of 123 patients (median age 77 years) who underwent surgical reoperation following TAVR, from the US STS (Society of Thoracic Surgeons) database; the respective proportions with predicted STS mortality of <4%, 4–8% and >8% were 17%, 24% and 59%. Reoperations were performed in a median of 2.5 months after TAVR; indications for reoperation included early TAVR device failures such as paravalvular leak (15%), structural prosthetic deterioration (11%), failed repair (11%), sizing or position issues (11%) and PVE (10%). The operative mortality rate was 17.1%. The respective preoperative mortality risk categories of <4%, 4–8% and >8% were associated with observed-to-expected mortality ratios of 5.5, 1.7 and 1.2.

Comment: There has been an explosive growth in the use of TAVR in the treatment of severe aortic stenosis, and whilst there is an excellent knowledge base with respect to redo surgery for SAVR, there are few data on the risks of reoperation after TAVR. The current study reports on patients from the STS Adult Cardiac Surgery Database who underwent SAVR after a failed TAVR. Whilst a rare event (0.3% of TAVR patients), the mean operation time was almost double the published time for redo SAVR, suggesting these are technically challenging cases, resulting in a higher observed than expected mortality rate (greater than 5-fold) and significant morbidity. As TAVR moves into younger patients, we need to ensure that we discuss the long-term implications of TAVR versus SAVR, particularly if an open surgical approach may be necessary in the future.

Reference: JACC Cardiovasc Interv 2020;13:1515–25
Abstract

Safety of revascularization deferral of left main stenosis based on instantaneous wave-free ratio evaluation

Authors: Warisawa T et al.

Summary: Long-term clinical outcomes were reported for patients with left main coronary artery stenosis for whom stenosis was deferred (n=163) or revascularisation was performed (n=151) according to an IFR cutoff of ≤0.89. There was no significant difference between the IFR-based deferral versus revascularisation group for the proportion who had experienced a primary endpoint event by month 30 (composite of death from any cause, nonfatal MI and ischaemia-driven target lesion revascularisation; 14.6% vs. 9.2% [p=0.26]), or for the secondary endpoints of death from any cause (3.7% vs. 4.6%), death from cardiac causes (1.2% vs. 2.0%), nonfatal MI (2.5% vs. 5.3%) and target lesion revascularisation (4.3% vs. 5.3%; p>0.05 for all).

Comment: Angiography is notoriously inaccurate in estimating intermediate-grade left main lesion severity, particularly in ostial lesions, and studies using intravascular ultrasonography have established certain thresholds whereby revascularisation of such lesions can be deferred safely. There are also some data using fractional flow reserve to guide treatment. The current multicentre, observational study reports an IFR threshold of >0.89 as being useful in guiding safe deferral of revascularisation. Notably, there were 100 additional patients who met enrolment criteria in whom the operator chose to override the results and did what they wanted, and importantly these patients did worse than those in whom the protocol was followed. Clearly, large randomised trials are needed, but in the meantime the use of the nonhyperaemic index of IFR may be added to the gestalt in determining the best treatment for these patients.

Reference: JACC Cardiovasc Interv 2020;13:1655–64
Abstract

Coronary angiography and percutaneous coronary intervention after transcatheter aortic valve replacement with Medtronic self-expanding prosthesis

Authors: Khan M et al.

Summary: These authors described the feasibility, challenges, success rates and techniques experienced for coronary angiography and PCI in a retrospective group of 32 patients who had undergone TAVR with a self-expanding prosthesis; there were 46 coronary angiography and 26 PCI procedures analysed. The respective proportions of coronary angiographies and PCIs for which selective left and right coronary angiography using standard catheters could be achieved were 50% and 28%. The PCI success rate was 96%, but 64% required significant technique modification. CT angiography in a subgroup of nine patients revealed that coronary re-access difficulties were the result of a combination of the sealing skirt relationship to coronary ostia and sinotubular junction, as well as commissural post-orientation and significant native leaflet calcification.

Comment: As TAVR is more common and expands to younger, lower-risk patients, future coronary access after TAVR is becoming an important issue. This single-centre study looked at accessing the coronary ostia after deployment of the self-expanding Corevalve and Evolut valves (Medtronic, USA). The median time from TAVR to angiography was 17.4 months. The Mach Voda left (VL) 3.0/3.5 catheter was used when JL catheters were unsuccessful (50%) for the left system and 3DRC and MP catheters were used for the right coronary if JR catheters failed (72%). Of the successful PCIs performed, selective engagement was only achieved in 36% of cases with techniques such as nonselective wiring and railing of the guide or guide extensions with balloon-assisted advancement of the guide. The authors have developed an educational mobile application called TAVRcathAID, which is available for download to help operators in need.

Reference: Int J Cardiol 2020;317:18–24
Abstract

Pulmonary artery denervation for patients with residual pulmonary hypertension after pulmonary endarterectomy

Authors: Romanov A et al.

Summary: Patients with residual chronic thromboembolic pulmonary hypertension despite ≥6 months of medical therapy after pulmonary endarterectomy (mean pulmonary artery pressure ≥25mm Hg or pulmonary vascular resistance >400 dyn•s•cm^{-5}) were randomised to undergo pulmonary artery denervation using remote magnetic navigation for ablation (n=25) or medical therapy with riociguat with a sham procedure (n=25). Compared with the medical therapy group, the pulmonary artery denervation group had experienced a significantly greater reduction in mean pulmonary vascular resistance by month 12 (258 vs. 149 dyn•s•cm^{-5} [p=0.001]) and a significantly greater increase in 6-minute walk distance (470 vs. 399m [p=0.03]). One participant from each group developed a groin haematoma, which resolved without sequelae.

Comment: Surgical pulmonary endarterectomy has emerged as the preferred treatment for chronic thromboembolic pulmonary hypertension, but is not curative in 10–40% of patients. Medical therapy is recommended for these patients, but is expensive and poorly tolerated. This single-centre Russian pilot, randomised, sham-controlled trial reports favourable outcomes for use of pulmonary arterial denervation. The investigators used remote magnetic navigation communicating with a nonfluoroscopic 3D electro-anatomical mapping system (CARTO-RMT, Biosense USA) to perform radiofrequency ablation, encircling the left and right pulmonary arteries and main pulmonary artery trunk. The procedure was safe and effective, but larger multicentre clinical trials are needed to confirm the benefits and whether it translates into improved mortality and potentially is applicable in other causes of pulmonary hypertension.

Reference: J Am Coll Cardiol 2020;76:916–26
Abstract

Invasive versus non-invasive management of older patients with non-ST elevation myocardial infarction (SENIOR-NSTEMI)

Authors: Kaura A et al.

Summary: Survival after invasive versus noninvasive management of NSTEMI within 3 days of peak troponin level was reported for a cohort of 1500 patients aged ≥80 years from routine clinical care; 56% of these patients received noninvasive management. The mortality rate during a median of 3.0 years of follow-up was 41%. Compared with patients managed noninvasively, those who received invasive management had a lower adjusted cumulative 5-year mortality rate (36% vs. 55%; adjusted HR 0.68 [95% CI 0.55–0.84]) and a lower incidence of hospital admission for HF (adjusted rate ratio 0.67 [0.48–0.93]).

Comment: In the routine care of ACS, there is a tendency for older frailer patients to be treated less invasively with angiography and revascularisation, despite studies suggesting the benefits of such a strategy in generally younger populations. This may relate to smaller numbers of patients over 80 years of age enrolled in these studies. The current observational study from five collaborating hospitals in the UK attempts to overcome shortcomings of previous studies using multicentre, routine clinical data encompassing methods to try and overcome the limitations of nonrandomised data. The authors conclude that the benefits of an invasive strategy may extend to those over 80 years of age. Notably, patients with extreme comorbidities were excluded, so the results may not apply to all elderly patients, and we await randomised trials such as SENIOR-RITA for more definitive data, but it would appear reasonable to offer angiography to more elderly patients than we currently do.

Reference: Lancet 2020;396:623-34
Abstract

Effect of genotype-guided oral P2Y12 inhibitor selection vs conventional clopidogrel therapy on ischemic outcomes after percutaneous coronary intervention

Authors: Pereira NL et al.

Summary: Patients with ACS (82%) or stable coronary artery disease (18%) scheduled for PCI were randomised to point-of-care genotype-guided care in which *CYP2C19* loss of function carriers received ticagrelor and noncarriers received clopidogrel (n=2652) or to receive clopidogrel as conventional therapy with genotyping after 12 months (n=2650) in the open-label TAILOR-PCI trial; the trial completion rate was 94%. There were 1849 participants with *CYP2C19* loss of function variants, 85% of whom were assigned to genotype-guided therapy and received ticagrelor; 99% of those assigned to the conventional therapy received clopidogrel. No significant difference was seen between the genotype-guided versus conventional therapy arm for primary endpoint events (composite of CV-related death, MI, stroke, stent thrombosis and severe recurrent ischaemia) at 12 months among *CYP2C19* loss of function carriers (4.0% vs. 5.9%; HR 0.66 [95% CI 0.43–1.02]) or for all participants (4.4% vs. 5.3%; 0.84 [0.65–1.07]), or for 11 prespecified secondary endpoints, including major or minor bleeding, among *CYP2C19* loss of function carriers.

Comment: Large clinical trials have demonstrated the superiority of ticagrelor over clopidogrel when prescribed to all comers with ACS. Ticagrelor overcomes issues of poor metabolisers of clopidogrel due to loss of function alleles, but it is unclear whether tailored prescribing of ticagrelor based on point-of-care genotype testing would be reasonable. In this pragmatic open label, multicentre, randomised trial, patients were randomised within 72 hours of PCI (87% at <24 hours) to a tailored therapy group, whereby those with loss of function alleles were prescribed ticagrelor and the rest clopidogrel, versus a conventional therapy group receiving clopidogrel. There was no overall benefit, although there were strong trends in favour of a genotype-guided strategy with respect to ischaemic endpoints. Unfortunately, the trial does not address the real clinical question of whether a genotype-guided choice of P2Y12 inhibitor therapy versus clopidogrel for all or ticagrelor for all without point-of-care testing is superior, particularly in ACS patients.

Reference: JAMA 2020;324:761–71
Abstract

Aspirin with or without clopidogrel after transcatheter aortic-valve implantation

Authors: Brouwer J et al.

Summary: Patients scheduled for TAVI with no indication for long-term anticoagulation were randomised to receive aspirin with (n=334) or without (n=331) clopidogrel for 3 months; 9.6% and 13.3% of participants from the respective arms received oral anticoagulation during the trial. Compared with aspirin plus clopidogrel, significantly lower proportions of aspirin-only recipients experienced a bleeding event (15.1% vs. 26.6%; risk ratio 0.57 [95% CI 0.42–0.77]), a nonprocedure-related bleeding event (15.1% vs. 24.9%; 0.61 [0.44–0.83]) and a composite of death from CV causes, nonprocedure-related bleeding, stroke or MI (23.0% vs. 31.1%; 0.74 [0.57–0.95]; p<0.001 for noninferiority), but there was no significant difference for a composite of death from CV causes, ischaemic stroke or MI (9.7% vs. 9.9%; 0.98 [0.62–1.55]; p=0.004 for noninferiority).

Comment: TAVI has revolutionised the treatment of severe aortic stenosis, but the choice of which antiplatelet or anticoagulant to use postprocedure is not well studied, despite bleeding and ischaemic complications being a significant cause of morbidity. This multicentre, open-label, investigator-initiated trial from Europe suggests that the use of clopidogrel may be unnecessary. The data only apply to patients who did not have a pre-existing indication for long-term anticoagulation or who had recent coronary stents. This study was powered for bleeding, which drove most of the events, and notably aspirin alone was noninferior but not superior with respect to a composite of thromboembolic events including death from CV causes, ischaemic stroke and MI (9.7% vs. 9.9%). It appears aspirin alone may be reasonable after TAVI, although a larger trial would help clarify this with respect to ischaemic endpoints.

Reference: N Engl J Med 2020;383:1447–57
Abstract

Association of pretreatment with P2Y12 receptor antagonists preceding percutaneous coronary intervention in non-ST-segment elevation acute coronary syndromes with outcomes

Authors: Dworeck C et al.

Summary: Associations of P2Y12 receptor antagonist pretreatment versus no pretreatment with mortality, stent thrombosis and in-hospital bleeding were explored in a prospective cohort of 64,857 patients with NSTEACS undergoing PCI, of whom 92.4% received P2Y12 receptor antagonist pretreatment (43.7% with clopidogrel, 54.5% with ticagrelor and 1.8% with prasugrel). For the entire cohort, the respective 30-day mortality and definite stent thrombosis rates were 1.5% and 0.2%. There was no significant difference between participants who received pretreatment and those who did not for 30-day survival (odds ratio 1.17 [95% CI 0.66–2.11]), 1-year survival (1.34 [0.77–2.34]) or likelihood of stent thrombosis (0.81 [0.42–1.55]), and pretreated patients had a higher likelihood of in-hospital bleeding (1.49 [1.06–2.12]).

Comment: Early treatment of NSTEMI with a P2Y12 receptor antagonist is common practice despite no compelling evidence for its benefit. This large study from the SCARR (Swedish Coronary Angiography and Angioplasty Registry) reports observational data and shows pretreatment was very common (92.4%), but was not associated with improved mortality or stent thrombosis rate, but was associated with increased bleeding. These data are consistent with arguably the only contemporary adequately-powered randomised trial (ACCOAST), which found similar results with the use of prasugrel and calls into question the routine pretreatment of patients with a second antiplatelet before delineation of the coronary anatomy in an NSTEMI population.

Reference: JAMA Netw Open 2020;3:e2018735
Abstract

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Independent commentary by Professor Craig Juergens

Professor Craig Juergens is an Interventional Cardiologist at Liverpool Hospital where he is Head of Cardiology. He established the coronary interventional service at Liverpool hospital which has subsequently become a centre of training for interventional Cardiologists. Apart from his interest in Interventional Cardiology, he has a major interest in acute coronary syndromes and has been involved in a large number of multicentre, multinational clinical trials. He has been author of over 100 peer reviewed papers and he continues as an active clinician in the Department of Cardiology at Liverpool Hospital, as well as providing support for the interventional Cardiology programme at Orange Base hospital.

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