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Cardiology RESEARCH REVIEW™

Making Education Easy

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In this issue:

Abbreviations used in this issue
AF = atrial fibrillation
CABG = coronary artery bypass grafting
FFR = fractional flow reserve
HF = heart failure
HR = hazard ratio
LVEF = left ventricular ejection fraction
MACE = major adverse cardiovascular events
MI = myocardial infarction
PCI = percutaneous coronary intervention
STEMI = ST-segment elevation MI
TAVI = transcatheter aortic valve implantation

Welcome to the latest issue of Cardiology Research Review.

In this issue, a multicentre trial reports that management of STEMI is harder and outcomes are worse in patients with previous TAVI, the results of a Korean study suggest we should initiate rhythm control medication early in patients with AF, and the FLOWER-MI trial compares an FFR-guided strategy with an angiography-guided strategy in STEMI patients undergoing complete revascularisation. Also in this issue, a Canadian study reports the benefits of left atrial appendage closure during cardiac surgery in AF patients, a US study compares 2 dosages of aspirin for secondary prevention (let's all agree on 100mg), and the HOST-EXAM study finds that clopidogrel is superior to aspirin in patients requiring long-term antiplatelet monotherapy after PCI.

I hope you find these and the other selected articles interesting and look forward to receiving any feedback you may have.

Kind regards,
Professor Alexander Sasse
alexandersasse@researchreview.co.nz

ST-segment elevation myocardial infarction following transcatheter aortic valve replacement

Authors: Faroux L et al.

Summary: This multicentre study evaluated the management of STEMI in patients with previous TAVI. 118 patients with STEMI after TAVI were compared with 439 patients with STEMI without previous TAVI. All patients received PCI. Median door-to-balloon time was higher in patients with previous TAVI (40 vs 30 min; p=0.003), as was procedural time, fluoroscopy time, dose-area product, and contrast volume (all p<0.01). PCI failure was more common in patients with previous TAVI (16.5% vs 3.9%; p<0.001). In-hospital and late mortality rates were 25.4% and 42.4%, respectively, in TAVI patients, compared with 20.6% and 38.2%, respectively, in non-TAVI patients.

Comment: TAVI valves are mounted in self- or balloon-expanding wire meshworks in the annulus and aortic sinus; recent trends encourage relatively high implantation to avoid heart block. However, consecutive coronary catheterisation, especially acutely in a STEMI, might be affected. Here 118 patients post TAVI were compared to 439 patients without TAVI in the setting of acute STEMI. PCI failure occurred more frequently in patients with previous TAVI (16.5% vs 3.9%) along with more contrast use and longer door-to-balloon time (40 vs 30 min). Mortality was higher in post-TAVI STEMI though it was difficult to compare to controls. Thrombolysis had not been a factor in this collective of patients.

Reference: J Am Coll Cardiol 2021;77(17):2187-99
Abstract

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Treatment timing and the effects of rhythm control strategy in patients with atrial fibrillation

Authors: Kim D et al.

Summary: This nationwide cohort study in Korea investigated the impact of treatment timing in patients receiving rhythm control for AF. 22,635 patients with AF who were newly treated with rhythm control (antiarrhythmic drugs or ablation) or rate control strategies were followed up for a median 2.1 years. The primary composite outcome was death from cardiovascular causes, ischaemic stroke, hospitalisation for HF, or acute MI. Among patients with early treatment of AF (initiated within 1 year after diagnosis), rhythm control was associated with a lower risk of the primary composite outcome than rate control (HR 0.81, 95% CI 0.71–0.93; p=0.002). No difference in the risk of the primary composite outcome was found between rhythm and rate control strategies in patients with late treatment of AF (initiated >1 year after diagnosis).

Comment: Rate control, sure, but when and if to start rhythm control medication in AF? This large retrospective population-based Korean study looked at outcomes (MACE and hospitalisation) of early (<1 year from onset) compared to late rhythm control in AF. Interestingly, initiating rhythm control early had better outcomes, mostly driven by fewer strokes, HF and MIs. The authors discuss early substrate remodelling or simply more intensive care as potential reasons. Rhythm control >1 year after AF onset was not better than rate control only.

Reference: BMJ 2021;373:n991
Abstract

Comparative effectiveness of aspirin dosing in cardiovascular disease

Authors: Jones WS et al., for the ADAPTABLE Team

Summary: This US study investigated the optimal dose of aspirin for secondary prevention in patients with established atherosclerotic cardiovascular disease. 15,076 patients were randomised to receive aspirin 81mg or 325mg daily and were followed-up for a median 26.2 months. The primary composite outcome (death from any cause or hospitalisation for MI or stroke) occurred in 7.28% of patients taking aspirin 81mg and 7.51% of patients taking aspirin 325mg (HR 1.02, 95% CI 0.91–1.14). Hospitalisation for major bleeding occurred in 0.63% and 0.60% of patients in the respective groups (HR 1.18, 95% CI 0.79–1.77).

Comment: How much aspirin for secondary prevention? The US is still undecided between 81mg and 325mg. The outcome was death, MI or stroke, and the trial ran for about 3 years. 15,076 patients were randomised and got a $US25 remuneration for trial participation. The primary end-point occurred in 7.28% of the 81mg group and 7.51% of the 325mg group. Major bleeds were not different, and long-term adherence to 81mg was better. Can we now all agree on 100mg aspirin?

Reference: N Engl J Med 2021;384(21):1981-90
Abstract

Physical rehabilitation for older patients hospitalized for heart failure

Authors: Kitzman DW et al.

Summary: This randomised controlled trial in the US evaluated a physical rehabilitation intervention for older patients hospitalised with acute decompensated HF. 349 patients were randomised to either the rehabilitation intervention or usual care (controls). The rehabilitation intervention comprised 4 physical-function domains (strength, balance, mobility, and endurance). It was initiated during or soon after hospitalisation and continued for 36 outpatient sessions after discharge. The primary outcome was Short Physical Performance Battery score (lower scores indicating worse physical dysfunction) at 3 months. At baseline, patients in each group had markedly impaired physical function (97% were frail or prefrail). At 3 months, the intervention group had a significantly better score on the Short Physical Performance Battery than the control group (mean 8.3 vs 6.9; p<0.001).

Comment: Older patients (73±8 years) with frailty features were randomised to cardiac rehab after HF presentation. Almost 350 patients, publication made it in the *NEJM*. Patients underwent a progressive rehabilitation intervention that included multiple physical-function domains. Participants of the 12-week rehab programme scored significantly higher on a physical performance test – pretty much across most of the participants. While readmission and mortality were not affected, the message is that even for older patients rehab helps delay frailty and improves physical function.

Reference: N Engl J Med 2021; published online May 16
Abstract

Multivessel PCI guided by FFR or angiography for myocardial infarction

Authors: Puymirat E et al., for the FLOWER-MI Study Investigators

Summary: This analysis of the FLOWER-MI study evaluated whether multivessel PCI guided by FFR is superior to an angiography-guided procedure in patients with STEMI. 1163 patients with STEMI and multivessel disease who had undergone successful PCI of the infarct-related artery were randomised 1:1 to receive complete revascularisation guided by either FFR or angiography. The primary outcome was a composite of death from any cause, nonfatal MI, or urgent revascularisation at 1 year. The mean number of stents placed per patient for nonculprit lesions was 1.01 in the FFR-guided group and 1.50 in the angiography-guided group. During follow-up, a primary outcome event occurred in 5.5% of patients in the FFR-guided group and 4.2% of patients in the angiography-guided group (HR 1.32, 95% CI 0.78–2.23; p=0.31).

Comment: The FLOWER-MI trial investigated FFR- versus angiography-guided revascularisation of non-infarct related coronaries in the context of STEMI. The FFR cut-off for intervention was 0.80. In the angiography group about 96% had an intervention, in the FFR-guided group it was also 96%. The primary outcome was MACE after 1 year, and it was not different between the 2 groups. The authors clearly note the difference between this and other FFR trials, but have no real explanation for the discrepancy.

Reference: N Engl J Med 2021; published online May 16
Abstract

Association of coronary artery bypass grafting vs percutaneous coronary intervention with memory decline in older adults undergoing coronary revascularization

Authors: Whitlock EL et al.

Summary: This retrospective cohort study compared the change in rate of memory decline in older patients undergoing CABG or PCI. 1680 community-dwelling participants in the Health and Retirement Study (HRS) who underwent CABG (n=665; 168 off-pump) or PCI (n=1015) at age ≥65 years were included. In the PCI group, the mean rate of memory decline (assessed by biennial cognitive test scores and proxy cognition reports) was 0.064 memory units/year before the procedure and 0.060 memory units/year after the procedure. In the CABG group, the mean rate of memory decline was 0.049 memory units/year before the procedure and 0.059 memory units/year after the procedure. The between-group difference in memory decline was not significant.

Comment: Cognitive decline following CABG has always been a concern. This trial retrospectively reviewed cognitive test performance in older patients undergoing either PCI or CABG. Patients were part of a large database (HRS) collecting data from 1992 to 2010. Different test formats were normalised. Memory decline over the years was similar in the PCI and CABG groups, the difference between the 2 groups not significant (p=0.98). The secondary end-point of dementia probability was not different between the 2 groups and there was also no significant difference between on- and off-pump CABG. Reassuring, but retrospective data.

Reference: JAMA 2021;325(19):1955-64
Abstract

Statin therapy for primary prevention in the elderly and its association with new-onset diabetes, cardiovascular events, and all-cause mortality

Authors: Lavie G et al.

Summary: This retrospective cohort study in Israel investigated the use of statins for primary prevention in the elderly. 42,767 new users of statins (5970 were aged ≥70 years) without cardiovascular disease or diabetes mellitus were followed up for 5 years for assessment of new-onset diabetes mellitus, MACE and all-cause mortality. Adherence to statins was evaluated according to the proportion of days treated. For the highest (≥75%) and lowest (<25%) proportion of days treated categories, respective incident rates were 16.9% and 16.7% for MACE, 9.4% and 6.3% for all-cause mortality, and 1.7% and 9.4% for new-onset diabetes mellitus. In patients aged ≥70 years, the adjusted HRs for MACE and mortality were significantly decreased in the highest adherence group (0.71 and 0.68, respectively).

Comment: Over 70? Considering statins for primary prophylaxis, what is the evidence? Retrospectively 5970 patients over 70 with no prior cardiovascular events were identified in this study from Israel; outcomes were compared to number of days statins were prescribed (<25%, 25–50%, 50–75%, >75%) during 60 months of observation. With >75% statin prescription, adjusted MACE were reduced, all-cause mortality was non-significantly lower, and there was no indication for higher rates of diabetes. However inconsistent prescription (<75%) was clearly less efficient. If you are prescribing statins for this indication, it will need to be persistent.

Reference: Am J Med 2021;134(5):643-52
Abstract

Independent commentary by Professor Alexander Sasse

Professor Alexander Sasse is Consultant Cardiologist and Clinical Director of the Cardiology Department at Wellington Hospital/CCDHB. His clinical interests include the various modalities of cardiac imaging, structural heart disease and intervention, general cardiology and the prevention of stroke. He went to Medical School in Bonn and did his training at the RWTH Aachen (Germany) and has been a Cardiologist since 2004. In 2007 he moved to Wellington and has been there since. **For full bio CLICK HERE.**

Left atrial appendage occlusion during cardiac surgery to prevent stroke

Authors: Whitlock RP et al., for the LAAOS III Investigators

Summary: This study in Canada investigated the use of left atrial appendage closure (LAAC) during cardiac surgery to prevent stroke in patients with AF. 4770 patients with AF and a CHA_2DS_2-VASc score of ≥2 who were scheduled to undergo cardiac surgery for another indication were randomised to undergo LAAC or no closure (controls) during surgery. All patients were expected to receive usual care, including oral anticoagulation, during a mean 3.8 years of follow-up. Stroke or systemic embolism occurred in 4.8% of patients in the LAAC group and 7.0% of controls during follow-up (HR 0.67, 95% CI 0.53–0.85; p=0.001). The incidence of perioperative bleeding, HF, or death did not differ significantly between groups.

Comment: What is the role of surgical LAAC to reduce the risk of stroke? Important note, the aim was not to replace anticoagulation but to continue standard practise plus LAAC. Patients undergoing cardiac surgery with AF and a CHA_2DS_2-VASc score of at least 2 were 1:1 randomised; surgical technique with or without device was variable, and purse-string closure was not allowed. About 80% of patients remained on oral anticoagulation. 114 in the LAAC group had a stroke or embolism (4.8%) compared to 168 (7.0%) controls. Subgroup analysis confirmed the benefits of LAAC, especially in older, male, hypertensive and HF patients. These are fascinating results – will LAAC during surgery in AF patients become a standard feature?

Reference: N Engl J Med 2021;384:2081-91
Abstract

Aspirin versus clopidogrel for chronic maintenance monotherapy after percutaneous coronary intervention (HOST-EXAM)

Authors: Koo BK et al.

Summary: The HOST-EXAM trial compared the use of long-term monotherapy with aspirin versus clopidogrel after PCI. At 37 sites in South Korea, 5438 patients who received dual antiplatelet therapy (DAPT) without clinical events for 6–18 months after PCI with a drug-eluting stent (DES) were randomised to receive monotherapy with either clopidogrel 75mg once daily or aspirin 100mg once daily for a further 24 months. The primary end-point was a composite of all-cause death, non-fatal MI, stroke, readmission for acute coronary syndrome, and major bleeding. During follow-up, the primary outcome occurred in 152 (5.7%) patients in the clopidogrel group and 207 (7.7%) in the aspirin group (HR 0.73, 95% CI 0.59–0.90; p=0.0035).

Comment: Another permutation of antiplatelets, this time after DES and a course of DAPT; patients were randomised to aspirin or clopidogrel monotherapy. Prospective, randomised, multicentre trial in Korea. The end-point was the usual MACE and bleeding events. And clopidogrel as monotherapy did better, with 5.7% vs 7.7% in the aspirin group reaching an end-point. The authors suggest using long-term clopidogrel instead of aspirin.

Reference: Lancet 2021; published online May 16
Abstract

Long-term clinical outcomes following revascularization in high-risk coronary anatomy patients with stable ischemic heart disease

Authors: Bainey KR et al.

Summary: This Canadian study analysed data from a large angiographic disease-based registry to examine the impact of revascularisation on long-term outcomes in patients with high-risk coronary anatomy and stable ischaemic heart disease (SIHD). 9016 patients with SIHD with high-risk coronary anatomy (3 vessel disease with ≥70% stenosis in all 3 epicardial vessels, or left main disease ≥50% stenosis) were included. 5487 (61.0%) patients received revascularisation with either CABG or PCI, while 3529 (39.0%) patients were managed conservatively. During a median follow-up of 6.2 years, the primary composite end-point of all-cause death or MI occurred less often in patients receiving coronary revascularisation than in patients managed conservatively (HR 0.62, 95% CI 0.58–0.66; p<0.001). No significant differences in risk reduction were seen between PCI and CABG.

Comment: Stenting in SIHD; the ultimate controversy in cardiology. Trial outcomes very much depend on definitions, as well as inclusion and exclusion bias. Canadian registry data of 9016 patients managed with PCI, CABG or conservatively; median follow up 6.2 years. Mortality and MI had a significantly lower risk in the intervention arms (HR 0.62, p<0.001); outcomes were similar for PCI and CABG. Benefits were evident early on and sustained. Included were patients with high-risk coronary anatomy, the word 'FFR' does not feature in the paper. Encouraging data for revascularisation, just mind the definitions.

Reference: J Am Heart Assoc 2021;10:e018104
Abstract

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Effect of implantable vs prolonged external electrocardiographic monitoring on atrial fibrillation detection in patients with ischemic stroke

Authors: Buck BH et al.

Summary: The PER DIEM trial investigated whether 12 months of monitoring with an implantable loop recorder detects more occurrences of AF than 30 days of conventional external loop recorder monitoring in patients with a recent ischaemic stroke. 300 patients without known AF who had an ischaemic stroke within the previous 6 months were randomised to electrocardiographic monitoring with either an implantable loop recorder (12 months) or an external loop recorder (30 days). The primary outcome (definite or highly probable AF) was observed in 15.3% of patients in the implantable loop recorder group and 4.7% of patients in the external loop recorder group (risk ratio 3.29, 95% CI 1.45–7.42; p=0.003).

Comment: How to best screen for AF following an ischaemic stroke? This study compared a 30-day external loop recorder to a 1-year implantable recorder. Definite AF was defined for AF episodes >2 min. Somewhat unsurprisingly the implantable device detected AF in 15.3%, compared to 4.7% in the external device group (HR 3.3, p=0.003); device results were not different when comparing the first 30 days only. Longer monitoring leads to more AF detection, is 24-48h enough then? Does longer monitoring improve outcome? Either way we might have to look harder for AF.

Reference: JAMA 2021;325(21):2160-8
Abstract

Strain-guided management of potentially cardiotoxic cancer therapy

Authors: Thavendiranathan P et al., for the SUCCOUR Investigators

Summary: The SUCCOUR trial investigated whether global longitudinal strain (GLS)-guided cardioprotective therapy (CPT) prevents reduction in LVEF and development of cancer therapy-related cardiac dysfunction (CTRCD) in high-risk patients receiving potentially cardiotoxic chemotherapy. 331 anthracycline-treated patients with an additional risk factor for HF were randomised to receive CPT guided by either ≥12% relative reduction in GLS or >10% absolute reduction of LVEF. Patients were followed for LVEF and CTRCD over 1 year. Change in LVEF did not differ significantly between groups. However, there was significantly greater use of CPT in the GLD-guided group, and fewer patients in the GLD-guided group developed CTRCD (5.8% vs 13.7%; p=0.02).

Comment: Cardiotoxic cancer therapy requires early detection and precise measurement of LV function. GLS measures LV function by quantifying LV wall deformation. In this prospective, controlled trial, anthracycline-treated patients were randomised to GLS- or LVEF-guided initiation of CPT (usually an ACE inhibitor or beta-blocker). The results are a bit difficult to interpret, but essentially GLS was felt to be more sensitive to detect LV dysfunction; 13.7% in the LVEF group developed cardiotoxicity compared to 5.8% in the GLS group. The use of GLS is recommended, but the threshold for CPT is still debated.

Reference: J Am Coll Cardiol 2021;77(4):392-401
Abstract

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CONGRATULATIONS TO

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and **Peter Shapkov** (Breast Surgeon at Waitemata DHB)

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