Cardiology RESEARCH REVIEW™

Making Education Easy

Issue 107 – 2023

In this issue:

Abbreviations used in this issue

ACS = acute coronary syndrome
CRT = cardiac resynchronisation therapy
HF = heart failure
HR = hazard ratio
LVEF = left ventricular ejection fraction
MI = myocardial infarction
NSTEMI = non-ST-segment elevation MI
PCI = percutaneous coronary intervention
TEER = transcatheter edge-to-edge repair
WHO = World Health Organization

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Welcome to the latest issue of Cardiology Research Review.

In this issue, a meta-analysis confirms that CRT improves outcomes in patients with intraventricular conduction delay but not right bundle branch block, the TRILUMINATE Pivotal trial reports encouraging results for percutaneous tricuspid TEER in patients with severe tricuspid regurgitation, and Spanish investigators show why a policy of medical management and watchful observation is recommended for older patients with frailty and NSTEMI. Also in this issue, a meta-analysis suggests that we should recommend flu vaccinations to patients with coronary artery disease, and US investigators look at the utility of artificial intelligence for the assessment of cardiac function.

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
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Cardiac resynchronization therapy improves outcomes in patients with intraventricular conduction delay but not right bundle branch block

Authors: Friedman DJ et al.

Summary: This meta-analysis of randomised controlled trials investigated the benefits of CRT in patients with differing QRS characteristics. Patient-level data from the pivotal CRT trials (MIRACLE, MIRACLE-ICD, MIRACLE-ICD II, REVERSE, RAFT, BLOCK-HF, COMPANION, and MADIT-CRT) were analysed using Bayesian Hierarchical Weibull survival regression models to assess CRT benefit by QRS morphology and duration. Patients had left bundle branch block (LBBB; n=4549), right bundle branch block (RBBB; n=691), and intraventricular conduction delay (IVCD; n=1024). Overall, 61% of patients received CRT with or without an implantable cardioverter defibrillator. Meta-analysis of the data showed that CRT was associated with a lower risk of HF hospitalisation or death overall (HR 0.73, credible interval [CrI] 0.65–0.84), and in subgroups of patients with QRS ≥150ms and either LBBB (HR 0.56, CrI 0.48–0.66) or IVCD (HR 0.59, CrI 0.39–0.89), but not RBBB (HR 0.97, CrI 0.68–1.34). No significant association of CRT with HF hospitalisation or death was observed when QRS was <150ms, regardless of QRS morphology.

Comment: This meta-analysis of CRT trials has a very clear message. It included 6264 patients and looked mainly at QRS duration and BBB morphology. Outcome was HF hospitalisation or mortality. Patients with a QRS <150ms or RBBB did not demonstrate a benefit in the measured end-points from CRT. On the other hand, LBBB with QRS >150ms (HR 0.56) and IVCD (HR 0.59) benefited from CRT. Nothing really new, but a confirmation.

Reference: Circulation 2023;147(10):812-23
Abstract

Intravascular imaging-guided or angiography-guided complex PCI

Authors: Lee JM et al., for the RENOVATE-COMPLEX-PCI Investigators

Summary: This multicentre, open-label trial in South Korea compared clinical outcomes after intravascular imaging-guided versus angiography-guided PCI for complex coronary artery lesions. 1639 patients with complex coronary artery lesions were randomised 2:1 to undergo either intravascular imaging-guided or angiography-guided PCI; the primary end-point was a composite of death from cardiac causes, target vessel-related MI, or clinically driven target vessel revascularisation. During a median follow-up of 2.1 years, a primary end-point event occurred in 76 patients in the intravascular imaging group and 60 patients in the angiography group (HR 0.64, 95% CI 0.45–0.89; p=0.008). Procedure-related safety events did not differ significantly between groups.

Comment: This is quite a topic especially between cardiologists of different generations … for which patients is PCI with intravascular imaging relevant? Being mindful of longer procedures (here 16.5 min) and current waiting times. This trial implanted specifically biodegradable or biocompatible polymer-coated everolimus-eluting stents in complex lesions. Target vessel failure was less common in patients with imaging-guided PCI (cumulative incidence at 3 years, 7.7% vs 12.3%; p=0.008), as was cardiovascular death (HR 0.47, 95% CI 0.24–0.93). Ostial, left main stem and chronic total occlusion lesions benefited in particular from intracoronary imaging.

Reference: N Engl J Med 2023;388(18):1668-79
Abstract

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Transcatheter repair for patients with tricuspid regurgitation

Authors: Sorajja P et al., for the TRILUMINATE Pivotal Investigators

Summary: This randomised controlled trial investigated the use of percutaneous tricuspid TEER for severe tricuspid regurgitation. 350 patients (mean 78 years, 54.9% female) with symptomatic severe tricuspid regurgitation were enrolled at 65 centres in the US, Canada, and Europe and were randomised 1:1 to receive either TEER or medical therapy (controls). The primary end-point was a hierarchical composite that included death from any cause or tricuspid valve surgery, hospitalisation for HF, and an improvement in quality of life measured by the Kansas City Cardiomyopathy Questionnaire (KCCQ). During the 1-year follow-up, the incidence of death or tricuspid valve surgery and the rate of HF hospitalisations did not differ significantly between groups, but quality of life improved significantly in the TEER group compared with controls (p<0.001).

Comment: A clip to treat tricuspid regurgitation (actually usually two); TEER for the tricuspid valve. 350 patients with functional severe symptomatic tricuspid regurgitation were randomised to control vs TEER. Conventional surgery is often not very promising in these patients. The enrolled patients had comparatively moderate symptoms before the study and the main outcome was a quality of life assessment. The procedure is technically demanding and 87% had a significant reduction in tricuspid regurgitation. Correlating with the degree of tricuspid regurgitation reduction was an increase in the quality of life parameter driving the positive outcome of the study. However, hospitalisation and mortality were not different. It appears that the optimal patient group benefiting from this procedure has not yet been identified, but the results are encouraging.

Reference: N Engl J Med 2023;388(20):1833-42
Abstract

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Effect of routine invasive vs conservative strategy in older adults with frailty and non-ST-segment elevation acute myocardial infarction

Authors: Sanchis J et al.

Summary: This Spanish trial compared 1-year outcomes after invasive versus conservative treatment strategies in frail, older patients with NSTEMI. 167 older adults (≥70 years) with frailty (Clinical Frailty Scale score ≥4) and NSTEMI were randomised to routine invasive (coronary angiography and revascularisation if feasible) or conservative (medical treatment with coronary angiography for recurrent ischaemia) strategies at 13 Spanish hospitals in 2017–2021. The primary end-point was the number of days alive and out of the hospital (DAOH) from discharge to 1 year. Mean DAOH did not differ significantly between groups, but was slightly longer with conservative versus invasive management (312 vs 284 days; p=ns).

Comment: A recurrent theme – how to manage older patients with NSTEMI, in this trial with an emphasis on frailty. Patients over 70 years with NSTEMI were randomised and prospectively included, they had to have 4 or more points on the Clinical Frailty Scale. End-point was 'days alive out of hospital' after 1 year; 167 patients were enrolled and the trial was stopped early. While DAOH was 28 days shorter for invasive management, overall there was no significant difference (p=0.12). There was also no difference regarding cardiac death, reinfarction and revascularisation (p=0.78). Check out the frailty score used – '4' refers to 'vulnerable'. Invasive management in this group of patients would have to be considered with caution.

Reference: JAMA Intern Med 2023;183(5):407-15
Abstract

Influenza vaccination as prevention therapy for stable coronary artery disease and acute coronary syndrome

Authors: Barbetta LMDS et al.

Summary: This meta-analysis investigated the effectiveness of influenza vaccination in patients with ACS and stable coronary artery disease. A search of Cochrane Controlled Register of Trials (CENTRAL), Embase, MEDLINE, www.Clinicaltrials.gov, and the WHO International Clinical Trials Registry Platform from inception to Sep 2021 identified five randomised controlled trials (n=4187) that were suitable for inclusion. Meta-analysis of the data showed that influenza vaccination significantly reduced the risk of all-cause mortality (relative risk [RR] 0.56, 95% CI 0.38–0.84), cardiovascular mortality (RR 0.54, 95% CI 0.37–0.80), major acute cardiovascular events (RR 0.66, 95% CI 0.49–0.88), and ACS (RR 0.63, 95% CI 0.44–0.89), but not the risk of revascularisation, stroke or transient ischaemic attack, or hospitalisation for HF.

Comment: Should you recommend flu vaccinations to patients with coronary artery disease? Here a meta-analysis compared data from 4187 patients in five randomised controlled trials. Across trials, 61–81.4% were men, mean age was around 60. Outcomes showed a reduction in mortality by 44%. Cardiovascular events were reduced by 34%. These effects were mostly seen in patients with previous ACS, not in stable coronary artery disease. Influenza vaccination was shown to be safe 72h after an ACS, and the authors discuss vaccinating ACS patients pre-discharge as a standard procedure.

Reference: Am J Med 2023;136(5):466-75
Abstract

Blinded, randomized trial of sonographer versus AI cardiac function assessment

Authors: He B et al.

Summary: This blinded, non-inferiority clinical trial compared the accuracy of a cardiac sonographer with that of artificial intelligence (AI) for the assessment of LVEF. 3495 transthoracic echocardiograms were randomised 1:1 to be evaluated by AI or one of 25 cardiac sonographers (mean 14.1 years' practise). The echocardiograms were then assessed by one of ten cardiologists (mean 12.7 years' practise). The primary outcome was the change in LVEF between initial AI or sonographer assessment and final cardiologist assessment, defined as the proportion of echocardiograms with substantial (>5%) change. Substantial change between the initial and final assessments occurred in 16.8% of studies in the AI group and 27.2% in the sonographer group (between-group difference, –10.4%; p<0.001 for non-inferiority).

Comment: AI is everywhere. How well does AI compare to sonographers in the assessment of LV function? Controversial for some – I know – the final and reference assessment of LV function was done by cardiologists. 1740 AI studies, 1755 sonographer studies. Blinded and randomised. Outcome was 'substantial change' between initial and final assessment, occurring in 16.8% of the AI and 27.2% of sonographer assessments (p<0.001). Ok, this is a 'Nature' paper. But two-thirds of studies derived LVEF from one plane only. And cardiologists frequently guessed assessment and unblinded the study. And a comparison with a different imaging method for LVEF would make more sense. But I guess it showed that the AI algorithm they used can work.

Reference: Nature 2023;616:520-4
Abstract

Safety, tolerability and efficacy of up-titration of guideline-directed medical therapies for acute heart failure in elderly patients

Authors: Arrigo M et al.

Summary: This subanalysis of the STRONG-HF trial investigated the safety and efficacy of up-titration of guideline-directed medical therapy (GDMT) for acute HF in older patients (>65 years). Patients hospitalised with acute HF who were not receiving optimal GDMT were randomised to high-intensity care (HIC; rapid up-titration of GDMT and close follow-up) or usual care. The effect of HIC on the primary end-point (180-day death or readmission for HF) was numerically higher in younger patients (adjusted HR [aHR] 0.51, 95% CI 0.32–0.82) than older patients (aHR 0.73, 95% CI 0.46–1.15), but did not differ significantly between age-groups after adjustment for COVID-related deaths. HIC induced larger improvements in quality of life to day 90 in younger patients (p=0.032), but was associated with similar rates of adverse events in each age group.

Comment: How fast should we get HF patients to the recommended dose of drugs? Rapid up-titration of HF medication – essentially giving the full dose within 2 weeks (HIC) was compared to usual care of slow deliberate up-titration. Most patients were on some form of treatment before the trial. In this paper, patients aged >65 years were analysed. Mortality was not different between HIC and usual care, nor was the HF readmission rate. And fewer than 20% of patients were older than 75 years. HIC patients had quite an intense follow up as well. This is one of a number of studies that tries to encourage faster titration of HF medication, here even for the elderly. Reassuring to know, but I am not sure how it translates to my daily practise.

Reference: Eur J Heart Fail 2023; published online May 29
Abstract

CONGRATULATIONS TO

Angela Taylor (Specialist Nurse at Nelson Hospital), **Claire Aitken** (Health Provider at Moana House) and **Rohit Bedi** (Dentist at Garden City Dental) **who each were winners of a $200 prezzy card by taking part in our recent Research Review Annual Subscriber Update.**

Five-year follow-up after transcatheter repair of secondary mitral regurgitation

Authors: Stone GW et al., for the COAPT Investigators

Summary: This 5-year follow-up of the COAPT trial compared outcomes after TEER of severe mitral regurgitation compared with guideline-directed medical therapy (GDMT) in patients with HF. 614 patients with HF and moderate-to-severe or severe secondary mitral regurgitation who were symptomatic despite taking maximal doses of GDMT were randomised to undergo TEER plus receive GDMT (device group) or to receive GDMT alone (controls) at 78 sites in the US and Canada. The annualised rate of HF hospitalisations through 5 years was lower in the device group than the control group (33.1% vs 57.2% per year; HR 0.53, 95% CI 0.41–0.68). Five-year all-cause mortality was also lower in the device group (57.3% vs 67.2%; HR 0.72, 95% CI 0.58–0.89), as was 5-year death or hospitalisation for HF (73.6% vs 91.5%; HR 0.53, 95% CI 0.44–0.64). Device-specific safety events occurred in 1.4% of patients, with all events reported within 30 days after the procedure.

Comment: The COAPT trial was one of two trials published in 2018 on TEER – interventionally placing a clip on the commissures of the mitral valve to create a double orifice mitral valve, and reduce the mitral regurgitation. Specifically, patients with severe HF and functional mitral regurgitation were treated. The question for this paper was in particular the durability of the implant and hence this 5-year follow-up paper was highly anticipated. Controls were on GDMT. Mortality was reduced by 28%, hospitalisation for HF by 47%. The survival curves show that the benefits were initially achieved by the procedure and then persisted over time. Unlike other device trials, reintervention was uncommon (11/302). Overall, COAPT confirmed the benefit of TEER in a selective group of patients with functional mitral regurgitation, with the mortality number needed to treat between 5.9 and 7.9.

Reference: N Engl J Med 2023;388:2037-48
Abstract

Family screening for bicuspid aortic valve and aortic dilatation

Authors: Bray JJH et al.

Summary: This meta-analysis investigated the prevalence of bicuspid aortic valve (BAV) and aortic dilatation in first-degree relatives of individuals with BAV. A search of MEDLINE, Embase, and Cochrane CENTRAL identified 23 observational studies involving 2297 index cases and 6054 screened relatives that were suitable for inclusion. Meta-analysis of the data showed that the prevalence of BAV in relatives was 7.3% overall, and 23.6% per family. The prevalence of aortic dilatation in relatives was 9.4% overall, and 29.2% in relatives with BAV. Aortic dilatation alongside tricuspid aortic valves was more common. The prevalence estimate in relatives with tricuspid valves (7.0%) was higher than that reported in the general population.

Comment: Should we do screening echos for family members of BAV patients? This paper tries to guide our decision by summarising data from 23 trials, including data from 2297 BAV patients and 6054 screened relatives. The prevalence of BAV in screened relatives was 7.3% – the key figure of this paper. It is assumed that this prevalence is more than 10-fold higher than that in the general population. In relatives with BAV, 29.2% also had aortic dilatation at the time of screening. The authors critically discuss the role of screening echos, but at least the data give us some evidence when speaking to patients and their families.

Reference: Eur Heart J 2023; published online Jun 8
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. Appointments include being a senior lecturer at Wellington School of Medicine (University of Otago) since 2007, and adjunct Professor at the School of Biological Sciences (Victoria University) Wellington since 2012.

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Remote haemodynamic monitoring of pulmonary artery pressures in patients with chronic heart failure (MONITOR-HF)

Authors: Brugts JJ et al., for the MONITOR-HF Investigators

Summary: The open-label MONITOR-HF trial investigated the utility of remote haemodynamic monitoring of pulmonary artery pressure in patients with chronic HF. At 25 centres in the Netherlands, 348 patients with chronic HF (mean age 69 years, mean LVEF 30%, New York Heart Association class III) and a previous HF hospitalisation were randomised 1:1 to remote haemodynamic monitoring (CardioMEMS-HF system) on top of usual care, or usual care alone. Patients in the monitoring group had a small, wireless, battery-free sensor implanted into the pulmonary artery via the femoral vein. A pressure measurement was taken each morning and readings were sent to a secure website. Physicians accessed the data and set a target pressure for each patient which would indicate the need to review drug treatment. The mean change in the Kansas City Cardiomyopathy Questionnaire (KCCQ) overall summary score at 12 months (primary end-point) was +7.05 in the CardioMEMS group (p=0.0014) and –0.08 in the standard care group (p=ns). During a mean follow-up of 1.8 years there were 117 HF hospitalisations or urgent visits in the monitoring group and 212 in the usual care group, representing a 44% reduction with monitoring (HR 0.56, 95% CI 0.38–0.84; p<0.01).

Comment: How do we monitor HF patients? In this trial, half the patients were randomised to an implanted device that measures pulmonary artery pressure. 348 with quite severe HF (mean LVEF 30%) and at least one previous admission for HF were included. The main outcome was change in KCCQ-measured quality of life; monitoring increased the chances of an improvement in measured quality of life (HR 1.56). However, I note that in the TriClip trial a KCCQ increase of 15 was seen as relevant while in this trial 5 was used as the cut-off. Overall, the trial illustrates a current trend in developing more implantable remote-monitoring devices. And also a trend in using quality of life as the predominant outcome parameter.

Reference: Lancet 2023;401(10394):P2113-23
Abstract