Cardiology RESEARCH REVIEW™

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Issue 113 – 2024

In this issue:

Abbreviations used in this issue
ACS = acute coronary syndrome
AF = atrial fibrillation
COVID-19 = coronavirus disease 2019
HFpEF = heart failure with preserved ejection fraction
HR = hazard ratio
LVEF = left ventricular ejection fraction
MI = myocardial infarction
NSTEMI = non-ST-elevation MI
PCI = percutaneous coronary intervention

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Welcome to the latest issue of Cardiology Research Review.

In this issue, a Danish cohort study reports an increasing lifetime risk of AF, the STEP-HFpEF DM trial finds that semaglutide is effective in patients with obesity-related heart failure and type 2 diabetes, and investigators in Israel remind us to consider cardiac sarcoidosis in middle-aged adults presenting with unexplained high-grade atrioventricular block. Also in this issue, US investigators highlight a potential drug interaction between diltiazem and rivaroxaban, and the PHOSP-COVID study finds an increased risk of long COVID in patients with cardiovascular disease.

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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Temporal trends in lifetime risks of atrial fibrillation and its complications between 2000 and 2022

Authors: Vinter N et al.

Summary: This nationwide cohort study in Denmark examined temporal trends in the lifetime risk of AF and its complications. 3.5 million individuals (51.7% female) aged ≥45 years who did not have AF were followed up until incident AF, migration, death, or end of follow-up, whichever came first. All 362,721 individuals with incident AF but no prevalent complications were further followed up until incident heart failure, stroke, or MI. The lifetime risks of AF and its complications were compared over two prespecified periods (2000–10 and 2011–22). The lifetime risk of AF increased from 24.2% in 2000–10 to 30.9% in 2011–22. The most frequent complication after AF was heart failure (lifetime risk of 42.9% in 2000–10 and 42.1% in 2011–22). The lifetime risks of stroke and MI after AF decreased slightly between the two periods; from 22.4% to 19.9% for stroke, and from 13.7% to 9.8% for MI. There were no differential decreases between males and females.

Comment: AF is a major contributor to cardiovascular burden of disease, and is associated with an excess in mortality. Residual lifetime risk measures the cumulative risk for developing a disease over the remaining lifespan. This study in Denmark – in some respects a similar health system when compared to NZ – assessed patients over 45 years (>3.5 million) for their lifetime AF risk by following them over the years until AF, death or reaching age 95. The main outcome, the lifetime AF risk over the last 20 years, was 27.7%. However this risk increased to 30.9% after 2011, a figure worth remembering. Once you have AF, the lifetime risk of heart failure is 41% and the lifetime risk of a stroke is 21.3%. The paper also identifies a long list of risk factors for lifetime AF risk, too long for this review to quote. AF is common and will become more common, and it has very relevant complications.

Reference: BMJ 2024;385:e077209
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. **For full bio CLICK HERE.**

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Semaglutide in patients with obesity-related heart failure and type 2 diabetes

Authors: Kosiborod MN et al., for the STEP-HFpEF DM Trial Committees and Investigators

Summary: The STEP-HFpEF DM trial investigated the efficacy of semaglutide in patients with type 2 diabetes and obesity-related heart failure. 616 patients with HFpEF, body mass index ≥30, and type 2 diabetes were randomised to receive once-weekly injections of semaglutide 2.4mg or placebo for 52 weeks. The primary end-points were the change from baseline in the Kansas City Cardiomyopathy Questionnaire clinical summary score (KCCQ-CSS) and the change from baseline in body weight. At 52 weeks, KCCQ-CSS had decreased by 13.7 points with semaglutide and 6.4 points with placebo (p<0.001), and the mean percentage change in body weight was –9.8% with semaglutide and –3.4% with placebo (p<0.001). Serious adverse events were reported in 17.7% of patients in the semaglutide group and 28.8% in the placebo group.

Comment: Semaglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist, and related studies seem to be appearing in a large number with multiple permutations. Here, obese patients with diabetes and manifest HFpEF received weekly semaglutide or placebo injections for 1 year. The aim was to assess the clinical status using the KCCQ-CSS, with clinical end-points assessed as secondary. KCCQ-CSS score improved in both groups but more so in the treatment group (difference 7.3 points). Weight loss was 6.4% more with semaglutide. Secondary clinical end-points including C-reactive protein and B-type natriuretic peptide levels, 6-min walk test and heart failure admissions were lower in the treatment group, but the study was clearly not powered or long enough to measure mortality or long-term heart failure effects. There were more serious adverse events in the placebo group; the drug seemed to be generally well tolerated. So another piece in the puzzle to show the effects of GLP-1 receptor agonists on obesity and heart failure.

Reference: N Engl J Med. 2024;390(15):1394–1407
Abstract

Prevalence of cardiac sarcoidosis in middle-aged adults diagnosed with high-grade atrioventricular block

Authors: Maizels L et al.

Summary: This study in Israel investigated the prevalence and clinical characteristics of cardiac sarcoidosis in middle-aged patients with unexplained high-grade atrioventricular block. Thirty patients aged 18–65 years who presented with unexplained high-grade atrioventricular block and were referred for cardiac magnetic resonance imaging (MRI), positron emission tomography (PET)-computed tomography, or both, prior to pacemaker implantation were evaluated. 37% of patients had suspected cardiac sarcoidosis based on imaging findings; this was confirmed by tissue biopsy in 33% of patients. Compared with patients with idiopathic high-grade atrioventricular block, all cardiac sarcoidosis patients were male (100% vs 60%; p=0.029), were more likely to present with heart failure symptoms (50% vs 10%; p=0.047), had thicker interventricular septum on echocardiography (12.2 vs 9.45mm; p=0.002), and were more likely to present with right ventricular dysfunction (33% vs 10%; p=0.047).

Comment: This paper reflects a development we have been seeing, especially with doing more cardiac MRI – we have probably been underestimating cardiac sarcoidosis. This study used MRI and/or PET to assess patients presenting with heart block and pacemaker indication aged 18–65 years, something we have been trying to do as well. Just a small group of 30 patients, and 33% were diagnosed with cardiac sarcoidosis. In this small group, all cardiac sarcoid patients were male, had more often heart failure, and tended to have a thicker interventricular septum (12mm) when compared to non-sarcoid patients. A small descriptive study only, but it raises awareness to look out for cardiac sarcoidosis in this group of patients.

Reference: Am J Med. 2024;137(4):358–65
Abstract

Deep learning to estimate cardiovascular risk from chest radiographs

Authors: Weiss J et al.

Summary: This risk prediction study developed and tested a deep-learning model (CXR CVD-Risk) to estimate 10-year risk of major adverse cardiovascular events (MACE) from a routine chest radiograph (CXR) and compared its performance with that of the traditional atherosclerotic cardiovascular disease (ASCVD) risk score. The CXR CVD-Risk model used data from patients screened in 2010–11 and was validated in outpatients with unknown ASCVD risk score (n=8869) or known ASCVD risk score (n=2132). Among outpatients with unknown ASCVD risk, those with a risk of ≥7.5% as predicted by CXR CVD-Risk had higher 10-year risk for MACE after adjustment for confounding factors (adjusted HR 1.73, 95% CI 1.47–2.03). In outpatients with known ASCVD risk, the CXR CVD-Risk model predicted MACE beyond the traditional ASCVD risk score (adjusted HR 1.88, 95% CI 1.24–2.85).

Comment: Artificial intelligence (AI) in cardiology. Mostly a proof of concept study to raise the idea. The study used CXR images from 8869 individuals that had the CXR for cancer screening in 2010–2011 and no background of established cardiovascular disease; for comparison there were 2132 patients with established elevated cardiovascular risk. Primary outcome was incident MACE after 10 years. The first component was a calibration of the CXR assessment with cardiovascular risk, then the attempt of discrimination of the CXR information and finally using the CXR as a prognostic tool. It is pretty much trying to establish if patients would be statin eligible. The observed MACE rate was 2.2 times higher in patients characterised by the CXR tool. The CXR also identified patients with higher risk in those with established cardiovascular risk. Bottom line: cardiovascular risk prediction can be supported by AI algorithms from 10-year-old chest x-rays.

Reference: Ann Intern Med. 2024;177(4):409–17
Abstract

Ticagrelor alone versus ticagrelor plus aspirin from month 1 to month 12 after percutaneous coronary intervention in patients with acute coronary syndromes (ULTIMATE-DAPT)

Authors: Ge Z et al., for the ULTIMATE-DAPT Investigators

Summary: This randomised controlled trial investigated the safety and efficacy of oral ticagrelor alone or in combination with aspirin from month 1 to 12 after PCI. 3400 patients who underwent PCI after ACS and who had no major ischaemic or bleeding events after 1 month of dual antiplatelet therapy (DAPT) with ticagrelor 90mg twice daily and aspirin 100mg once daily were randomised to continue with DAPT or switch to ticagrelor plus placebo for a further 11 months. Between months 1 and 12 after PCI, clinically relevant bleeding occurred in 2.1% of patients in the ticagrelor plus placebo group and in 4.6% of patients in the DAPT group (HR 0.45, 95% CI 0.30–0.66; p<0.0001). Major adverse cardiovascular or cerebrovascular events (MACCE) occurred in 3.6% and 3.7% of patients in the respective groups (p=ns).

Comment: Ticagrelor studies were usually done with aspirin as baseline therapy, where the stronger antiplatelet effect reduced ischaemic outcomes, but often at the expense of bleeding events. This study randomised 3400 ACS patients to ticagrelor alone or ticagrelor + aspirin – after an initial 1 month on the dual combination. The outcome after 12 months is quite clear. MACCE rates were similar in both groups: 3.6% and 3.7%, but bleeding events were pretty much twice as high in the ticagrelor + aspirin group (HR 0.45; p<0.0001). Yet another permutation of the post-ACS DAPT algorithm, but maybe one to look at.

Reference: Lancet 2024;403(10439):1866–78
Abstract

Serious bleeding in patients with atrial fibrillation using diltiazem with apixaban or rivaroxaban

Authors: Ray WA et al.

Summary: This retrospective cohort study compared bleeding risk in new users of apixaban or rivaroxaban who were also taking diltiazem or metoprolol for AF. 204,155 US Medicare beneficiaries (mean age 76.9 years, 52.7% female) who initiated apixaban or rivaroxaban were included; 53,275 were also taking diltiazem and 150,880 were taking metoprolol. Study participants had 90,927 person-years of follow-up (median 120 days). The primary outcome was a composite of bleeding-related hospitalisation and death with recent evidence of bleeding. Compared with metoprolol, patients taking diltiazem were at higher risk for the primary outcome (HR 1.21, 95% CI 1.13–1.29) and its individual components of bleeding-related hospitalisation (HR 1.22, 95% CI 1.13–1.31) and death with recent evidence of bleeding (HR 1.19, 95% CI 1.05–1.34). The risk associated with diltiazem doses >120 mg/day (HR 1.29, 95% CI 1.19–1.39) was greater than that for lower doses (HR 1.13, 95% CI 1.04–1.24).

Comment: This paper is a reminder that drug interactions do matter. 200,000+ patients on rivaroxaban or apixaban were also taking diltiazem or metoprolol. Primary outcome was bleeding and death. Mean age was 77 years, 50–59% were female. Compared to the metoprolol group, the patients taking diltiazem – about one-quarter of all patients – had a significantly higher risk of bleeding (HR 1.21) and death from recent bleeding (HR 1.19). Patients taking more than 120 mg/day of diltiazem had a further 14% higher risk. So there is a clear message: be careful with diltiazem and rivaroxaban. Verapamil and dabigatran were not studied in this paper and no comments are made.

Reference: JAMA 2024;331(18):1565–75
Abstract

Direct oral anticoagulants for stroke prevention in patients with device-detected atrial fibrillation: A study-level meta-analysis of the NOAH-AFNET 6 and ARTESiA trials

Authors: McIntyre WF et al.

Summary: This meta-analysis investigated the efficacy and safety of direct oral anticoagulants for stroke prevention in patients with device-detected AF. A search of MEDLINE and Embase identified two randomised controlled trials that compared oral anticoagulation with antiplatelet or no antithrombotic therapy in adults with device-detected AF: the NOAH-AFNET 6 trial of edoxaban (n=2536) and the ARTESiA trial of apixaban (n=4012). Meta-analysis of the data from these two trials demonstrated that oral anticoagulation with edoxaban or apixaban significantly reduced the risk of ischaemic stroke (relative risk [RR] 0.68, 95% CI 0.50–0.92). Oral anticoagulation also reduced a composite of cardiovascular death, all-cause stroke, peripheral arterial embolism, MI, or pulmonary embolism (RR 0.85, 95% CI 0.73–0.99), but did not reduce cardiovascular or all-cause mortality. Oral anticoagulation was associated with an increase in major bleeding (RR 1.62, 95% CI 1.05–2.50).

Comment: This trial is labelled as a meta-analysis, although it essentially merges two trials. Your patient has a device such as a pacemaker and the pacemaker check detects AF. How about anticoagulation? When AF was detected, the initiation of anticoagulation reduced cardiovascular events by 15% (RR 0.85). Stroke was reduced by 32%. Mortality was not reduced. But how much AF was detected? – a median of 2.8h and 1.5h in each study. The paper more or less skilfully avoids the question of how much AF has to be detected to start anticoagulation. But it concludes that AF detection with devices can reduce stroke risk, with an elevated bleeding risk in keeping with what we know about anticoagulants.

Reference: Circulation 2024;149(13):981–8
Abstract

Long COVID and cardiovascular disease

Authors: Lawson CA et al., on behalf of the PHOSP-COVID Study Collaborative Group

Summary: This prospective cohort study investigated recovery after COVID-related hospitalisation in patients with cardiovascular risk factors or cardiovascular disease. 2545 patients (38.8% women) who were hospitalised with COVID-19 were included; 472 (18.5%) had cardiovascular disease and 1355 (53.2%) had cardiovascular risk factors. Compared with 718 controls, patients with cardiovascular disease or cardiovascular risk factors were older and more likely to have had severe COVID-19. Full recovery was significantly poorer at 12 months in patients with cardiovascular disease (adjusted odds ratio [aOR] 0.62, 95% CI 0.43–0.89) and cardiovascular risk factors (aOR 0.66, 95% CI 0.50–0.86) than in controls.

Comment: COVID is still around and causing trouble. This study did not look at all-comers with COVID but rather at patients that were hospitalised. 2545 patients in UK hospitals in 2020–21. 1827 patients had cardiovascular risk factors or cardiovascular disease, and 718 were controls. Recovery from COVID was faster and to a higher degree in controls than in those with cardiovascular risk, this included cognitive parameters as well. Overall only one in three patients with cardiovascular risk had made a full recovery after 1 year following a COVID admission. Patients with elevated troponin during the admission were at particular risk. While the UK certainly had a different COVID experience compared to NZ, these outcomes highlight the risk of patients with cardiovascular risk or established disease and COVID.

Reference: Open Heart 2024;11(1):e002662
Abstract

Invasive vs. conservative management of older patients with non-ST-elevation acute coronary syndrome

Authors: Kotanidis CP et al.

Summary: This meta-analysis compared outcomes after invasive versus conservative management of NSTEMI in older patients. A search of MEDLINE, Web of Science and Scopus identified six randomised controlled trials (n=1479) that investigated routine invasive and conservative strategies in patients aged >70 years with NSTEMI and were suitable for inclusion. Meta-analysis of individual participant data from the trials showed that 24.5% of participants who received invasive management compared with 28.9% who received conservative management achieved the composite primary end-point of all-cause mortality or MI at 1 year (p=ns).

Comment: A UK study of older patients presenting with NSTEMI. In this case, old means 70 and older. It's a meta-analysis of six trials, 1479 patients and median age in the end was 84 years. 48% were female. Half for invasive, half for medical management. Different statistical models were used, but there was no difference in the combined end-point of mortality or MI recurrence after 1 year, occurring in about 25%. However MI alone was less common (38%) in the invasive group – with no effect on mortality alone. The MI result was the only major outcome difference reported in the study, and the authors conclude that it justifies a more liberal approach to invasive management in the elderly. Bleeding risk was not consistently reported in the analysed trials hence the meta-analysis has no conclusion on this outcome. The recommendation is a "balanced approach to individualized treatment strategy".

Reference: Eur Heart J. 2024;45(23):2052–62
Abstract

Catheter ablation for persistent atrial fibrillation: Patterns of recurrence and impact on quality of life and health care utilisation

Authors: Crowley R et al.

Summary: This post hoc analysis of the CAPLA study evaluated patterns of AF recurrence after catheter ablation for persistent AF. 333 patients with symptomatic persistent AF were randomised to pulmonary vein isolation plus posterior wall isolation or pulmonary vein isolation alone. 154 (46.2%) of them (median age 67.3 years, 28% female) had AF recurrence in the 12 months after catheter ablation. Recurrence was paroxysmal in 63% of patients and persistent in 37% and did not differ between randomisation groups. Patients with persistent AF recurrence had lower baseline LVEF (p<0.001), larger left atrial volume (p=0.008), and greater median AF burden (27.4% vs 0.9%; p<0.001) than patients with paroxysmal AF recurrence. Healthcare utilisation was significantly higher in patients with persistent versus paroxysmal AF recurrence (78.9% vs 46.4%; p<0.001) and lowest in those without AF recurrence (9.5%; p<0.001). Patients without AF recurrence had greater improvements in quality of life than those with either paroxysmal or persistent AF recurrence.

Comment: An Australian, UK and Canadian study, published as a fast track in the EHJ. Persistent AF (>7 days, <3 years), ablation, and monitoring with implanted device in some. Patients were randomised to two different ablation techniques, so no medical control. Female and older patients had a higher chance of AF recurrence, as did patients with large left atrial volume and low LVEF. The ablation method made no difference. Persistent AF had more AF when compared to paroxysmal AF, but still a markedly reduced burden of AF, much shorter AF and fewer hospital visits than before ablation. The authors conclude that this should be considered when offering ablation for persistent AF – although follow up of the study was only 12 months.

Reference: Eur Heart J. 2024; published online May 17
Abstract

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