

# Cardiology Research Review™

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Issue 146 - 2022

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### Abbreviations used in this issue:

ACS = acute coronary syndrome; AF = atrial fibrillation;  
ASCVD = atherosclerotic cardiovascular disease;  
BARC = Bleeding Academic Research Consortium; BP = blood pressure;  
CAGS = coronary artery graft surgery; COVID-19 = coronavirus disease 2019;  
DAPT = dual antiplatelet therapy;  
HFpEF = heart failure with preserved ejection fraction; HR = hazard ratio;  
OR = odds ratio.

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## Welcome to the latest issue of Cardiology Research Review.

In this issue, a UK study demonstrates an association between troponin positivity and short-term mortality in patients hospitalised with COVID-19, a prespecified subanalysis of the EAST-AFNET4 trial finds that patients with AF and higher comorbidity burden are more likely to benefit from early rhythm control, and the findings of an open-label trial in Poland suggest that cardioneuroablation may be a promising adjunct for reflex syncope. Also in this issue, an economic evaluation demonstrates the cost-effectiveness of wearable devices for AF screening, and the findings of a US study support recommendations for antibiotic prophylaxis before invasive dental procedures in individuals at high risk for infective endocarditis.

We hope you find these and the other selected studies interesting, and welcome your feedback.

Kind Regards,

**Associate Professor John Amerena**

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### Troponin and short-term mortality in hospitalised patients with COVID-19 infection

**Authors:** Shyam-Sundar V et al.

**Summary:** This retrospective study at an inner-city London hospital investigated the association between troponin positivity and mortality in patients hospitalised with COVID-19. 402 adults admitted to Homerton University Hospital with COVID-19 between Feb 4 and April 30, 2020, were included. Troponin positivity was defined as greater than the upper limit of normal (>15.5 ng/L for females and >34 ng/L for males), and the primary outcome was mortality within 28 days of hospital admission. A chi-squared test showed that survival of patients with COVID-19 was significantly better in those with negative versus positive troponin. Multivariate logistic regression analysis showed that lung disease, age, troponin positivity and continuous positive airway pressure were all significantly associated with death (area under the curve 0.889, sensitivity 0.886, and specificity 0.629). Within this model, troponin positivity was independently associated with short-term mortality (OR 2.97, 95% CI 1.34–6.61;  $p=0.008$ ).

**Comment:** It is known that COVID can cause myocarditis, and in fact the risk of myocarditis with an acute COVID infection is much higher than the risk of getting it from the mRNA vaccines. This interesting analysis shows that elevated troponin with acute COVID is associated with increased death at 28 days. Whether this rise is due to myocarditis, subclinical ischaemia or the systemic illness is not clear, but it suggests that troponin should be measured in all patients who contract COVID to identify a high-risk group.

**Reference:** *BMJ Open* 2022;12(8):e061426

[Abstract](#)



## Cardiology Research Review™

### Independent commentary by Associate Professor John Amerena

Associate Professor John Amerena trained in Melbourne before spending four years in the United States at the University of Michigan. Over that period of time he worked in the fields of hypertension and hyperlipidemia, before returning to Australia where he is now a Cardiologist at Barwon Health. He currently has a joint appointment in the Department of Clinical and Biomedical Sciences at the University of Melbourne and the Department of Epidemiology and Preventive Medicine at Monash University. He is the director of the Geelong Cardiology Research Unit, which is currently involved in many phase II-III clinical trials. While still actively researching in hypertension, his focus has changed to research in antithrombotic/antiplatelet therapies, particularly in the context of acute coronary syndromes and atrial fibrillation. Heart failure is also a major interest, and he is also the Director of the Heart Failure Programme at Barwon Health. He is well published in these areas, as well as in many other areas of cardiovascular medicine.

## Early rhythm control in patients with atrial fibrillation and high comorbidity burden

**Authors:** Rillig A et al.

**Summary:** This prespecified subanalysis of the EAST-AFNET4 trial evaluated the efficacy and safety of early rhythm control according to comorbidity burden in patients with recently diagnosed AF. 1093 EAST-AFNET4 participants had a CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\geq 4$  (mean 74.8 years, 61% female) and 1696 had a CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $< 4$  (mean 67.4 years, 37% female). Early rhythm control reduced the composite primary efficacy outcome (cardiovascular death, stroke, or hospitalisation for worsening heart failure or ACS) compared with usual care in patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\geq 4$  (HR 0.64, 95% CI 0.51–0.81;  $p < 0.001$ ) but not in patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $< 4$  (HR 0.93, 95% CI 0.73–1.19;  $p = 0.56$ ). The primary safety outcome (death, stroke, or serious adverse events of rhythm control therapy) did not differ significantly between treatment groups in patients with higher comorbidity burden, but occurred more often with early rhythm control versus usual care in patients with CHA<sub>2</sub>DS<sub>2</sub>-VASc scores  $< 4$  (HR 1.39, 95% CI 1.05–1.82;  $p = 0.019$ ).

**Comment:** Several large clinical trials have suggested that an early rhythm control approach in patients with recent onset AF is associated with better outcomes. This early rhythm control approach is generally with ablation rather than pharmacotherapy, but in many places in Australia access to AF ablation is limited or waiting times are long, making an early rhythm control strategy not feasible. This study showed that patients with AF and CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\geq 4$  were the most likely to benefit, so perhaps these patients should be given preference for ablation, given the limited resources.

**Reference:** *Circulation* 2022;146(11):836-47

[Abstract](#)

## Cardioneuroablation for reflex syncope: Efficacy and effects on autonomic cardiac regulation

**Authors:** Piotrowski R et al.

**Summary:** This open-label trial in Poland evaluated the effects of cardioneuroablation (CNA) on syncope recurrence in patients with vasovagal syncope. 48 patients with symptomatic cardioinhibitory vasovagal syncope (or mixed vasovagal syncope and positive atropine test) were randomised to CNA or optimal non-pharmacological therapy (controls). Patients in the CNA group received radiofrequency ablation of the ganglionated plexi from the left and right atrium. During 2 years' follow-up, 2 (8%) patients in the CNA group and 13 (54%) patients in the control group had syncope recurrence ( $p = 0.0004$ ). Quality of life improved significantly after 2 years in the CNA group ( $p = 0.0001$  vs baseline) but remained stable in the control group.

**Comment:** Cardioinhibitory vasovagal syncope can cause significant impairment of quality of life for patients who have it. Lifestyle changes and increasing fluid intake, or pharmacological treatment (beta-blockers, ivabradine, midodrine, selective serotonin re-uptake inhibitors and fludrocortisone) often give inadequate control of symptoms and a permanent pacemaker is inserted as the last resort. This neuromodulatory therapy ablating atrial ganglionic plexi, which seems to dampen autonomic activity, is conceptually appealing and will be a useful adjunct to current therapy if larger trials confirm its benefit.

**Reference:** *JACC Clin Electrophysiol* 2022; published online Aug 28

[Abstract](#)

## Left atrial appendage occlusion versus oral anticoagulation in atrial fibrillation

**Authors:** Chew DS et al.

**Summary:** This study used a Markov model to determine whether left atrial appendage (LAA) occlusion or oral anticoagulation is the optimal strategy for stroke prevention in patients with AF. Evidence from published literature was used to inform model inputs. Patients with nonvalvular AF without prior stroke were the target population, and the primary end-point was clinical benefit (measured in quality-adjusted life-years). Baseline risks for stroke and bleeding determined whether LAA occlusion was preferred over anticoagulants in patients with AF. The combined risks favoured LAA occlusion for higher bleeding risk, but the benefit of LAA occlusion became less certain at higher stroke risks.

**Comment:** LAA occlusion is an attractive option for patients with AF who cannot take oral anticoagulants (e.g. previous intracerebral haemorrhage) or cannot tolerate them due to recurrent bleeding. This study suggests that there is benefit in high bleeding risk patients, particularly in patients at lower stroke risk (CHA<sub>2</sub>DS<sub>2</sub>-VASc score 2), but as stroke risk increases the benefits decline. Despite this, LAA occlusion should be considered in patients with high CHA<sub>2</sub>DS<sub>2</sub>-VASc scores if anticoagulation can't be used given the high risk of stroke, as there is no other option.

**Reference:** *Ann Intern Med* 2022;175(9):1230-39

[Abstract](#)

## Association of dual antiplatelet therapy with ticagrelor with vein graft failure after coronary artery bypass graft surgery

**Authors:** Sandner S et al.

**Summary:** This systematic review and meta-analysis compared the risks of vein graft failure and bleeding associated with ticagrelor DAPT or ticagrelor monotherapy versus aspirin in patients undergoing CAGS. A search of MEDLINE, Embase, and Cochrane Library databases identified 4 randomised controlled trials ( $n = 1316$ ) that compared the effects of ticagrelor DAPT or ticagrelor monotherapy versus aspirin on saphenous vein graft failure. Compared with aspirin, ticagrelor DAPT was associated with a significantly lower incidence of saphenous vein graft failure per graft (11.2% vs 20%; OR 0.51, 95% CI 0.35–0.74;  $p < 0.001$ ) and per patient (OR 0.51, 95% CI 0.35–0.74;  $p < 0.001$ ), but a significantly higher incidence of BARC type 2, 3, or 5 bleeding events (22.1% vs 8.7%; OR 2.98, 95% CI 1.99–4.47;  $p < 0.001$ ). Ticagrelor monotherapy was not significantly associated with saphenous vein graft failure or BARC type 2, 3, or 5 bleeding events compared with aspirin.

**Comment:** DAPT after CAGS is not commonly used in Australia, unless the surgery is done proximate to an ACS. This study shows less saphenous vein graft failure rate if DAPT is used routinely after surgical coronary revascularisation, but at the risk of increased bleeding. Thus, DAPT should be considered post CAGS in low bleeding risk patients with multiple saphenous vein grafts, but whether this applies to arterial grafts is not known, as their failure rate is generally lower than veins.

**Reference:** *JAMA* 2022;328(6):554-62

[Abstract](#)

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## Cost-effectiveness of screening for atrial fibrillation using wearable devices

**Authors:** Chen W et al.

**Summary:** This study used a microsimulation decision-analytic model to evaluate the cost-effectiveness of screening for AF using wrist-worn wearable devices. 30 million simulated individuals with an age, sex, and comorbidity profile matching the US population (aged  $\geq 65$  years) were included in the model. Eight AF screening strategies (6 wrist-worn wearable devices and 2 traditional modalities – pulse palpation and 12-lead electrocardiogram) were compared with no screening. All 6 wrist-worn wearable devices were estimated to be more effective than no screening and were associated with greater relative benefit than traditional modalities. Compared with no screening, screening via wrist-worn wearable devices was associated with a reduction in stroke incidence (by 20–23 per 100,000 person-years), but an increase in major bleeding (by 20–44 per 100,000 person-years). The overall preferred strategy was wearable photoplethysmography, followed by wearable electrocardiography with patch monitor confirmation.

**Comment:** Recent technological advances have allowed AF screening by non-traditional means. Smart phone apps allow rhythm recording continuously or when symptomatic, and increase AF detection rates and appropriate anticoagulation, albeit at the risk of increased bleeding, particularly in older patients. This study using a simulation model suggests this is a cost-effective strategy that reduces stroke, making it reasonable to recommend this technology for patients at high risk of AF and stroke.

**Reference:** *JAMA Health Forum* 2022;3(8):e222419  
[Abstract](#)

## Effectiveness of standard vs enhanced self-measurement of blood pressure paired with a connected smartphone application

**Authors:** Pletcher MJ et al.

**Summary:** This randomised controlled trial compared the use of self-measured BP (SMBP) paired with a connected smartphone app versus standard SMBP in patients with uncontrolled BP. 2101 patients (mean age 58 years, 56.7% female) who had uncontrolled BP at their last clinic visit were randomised to SMBP with a device that paired with a connected smartphone app (enhanced group) or a standard device (standard group). Participants received their device in the mail, along with web-based educational materials and phone-based support as needed. The primary outcome (reduction in systolic BP from baseline at 6 months) did not differ significantly between groups:  $-10.8$  mm Hg in the enhanced group versus  $-10.6$  mm Hg in the standard group ( $p=ns$ ).

**Comment:** This study showed that in patients with poorly controlled clinic BP, self measurement at home with a device linked to a smartphone app did not improve control compared to self measurement without the app support. Home BP measurement is being used more frequently as devices are inexpensive, reliable and durable, and feedback from better control gives patients positive reinforcement to continue with their lifestyle and medication.

**Reference:** *JAMA Intern Med* 2022; published online Aug 15  
[Abstract](#)

## Autoimmune diseases and cardiovascular risk: A population-based study on 19 autoimmune diseases and 12 cardiovascular diseases in 22 million individuals in the UK

**Authors:** Conrad N et al.

**Summary:** This population-based study in the UK investigated the association between autoimmune diseases and cardiovascular disease. Data were extracted from the Clinical Practice Research Datalink (CRPD;  $n=22,009,375$ ), GOLD and Aurum datasets to assemble a cohort of 446,449 individuals who were diagnosed with any of 19 autoimmune diseases in 2000–2017, were aged  $<80$  years at diagnosis, and were free of cardiovascular disease up to 12 months after diagnosis. A matched cohort of 2,102,830 controls without autoimmune disease who were free of cardiovascular disease up to 12 months after study entry was also assembled. 15.3% of patients with autoimmune disease and 11.0% of controls developed incident cardiovascular disease during a median 6.2 years of follow-up. The incidence of cardiovascular disease was 23.3 events per 1000 patient-years among patients with autoimmune disease and 15.0 events per 1000 patient-years among controls (HR 1.56, 95% CI 1.52–1.59). The risk of cardiovascular disease increased progressively with the number of autoimmune diseases present.

**Comment:** The link between cardiovascular disease and chronic inflammation has been established, and several anti-inflammatory treatments have improved outcomes in patients with elevated C-reactive protein levels and ASCVD (canakinumab) and chronic coronary artery disease (colchicine). This study shows that chronic systemic inflammatory disorders such as systemic sclerosis and systemic lupus erythematosus are associated with an increased risk of cardiovascular disease, and that the risk increases with the number of inflammatory diseases present. Therefore cardiovascular risk assessment and aggressive risk factor management should be undertaken in these individuals to try and prevent development of cardiovascular disease and events.

**Reference:** *Lancet* 2022;400(10354):733-43  
[Abstract](#)

## Antibiotic prophylaxis against infective endocarditis before invasive dental procedures

**Authors:** Thornhill MH et al.

**Summary:** This US study evaluated the efficacy of antibiotic prophylaxis against infective endocarditis in patients undergoing invasive dental procedures. 7,951,972 individuals were included in a case-crossover analysis and cohort study. For those at high risk of infective endocarditis, case-crossover analysis demonstrated a significant temporal association between infective endocarditis and invasive dental procedures in the preceding 4 weeks (OR 2.00, 95% CI 1.59–2.52;  $p=0.002$ ). This relationship was strongest for dental extractions and oral-surgical procedures. Antibiotic prophylaxis was associated with a significant reduction in the incidence of infective endocarditis after invasive dental procedures (OR 0.49, 95% CI 0.29–0.85;  $p=0.01$ ). The cohort study confirmed the associations between infective endocarditis and extractions or oral surgical procedures in patients at high risk for infective endocarditis, and the benefit of antibiotic prophylaxis in these patients.

**Comment:** This is the first study to definitively prove there is a link between dental procedures and infective endocarditis in patients at high risk (prosthetic heart valve, previous endocarditis etc), and that this risk can be reduced by use of prophylactic antibiotics in the perioperative period. Whether this is true for low-to-medium risk patients is not clear, and whether antibiotics would prevent endocarditis in lower risk patients undergoing dental procedures has not been shown, but there is no reason to think they would not be effective. Good dental hygiene is also a factor, and may be more important in the long term than prophylactic antibiotics at the time of procedures.

**Reference:** *J Am Coll Cardiol* 2022;80(11):1029-41  
[Abstract](#)

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## Dapagliflozin for heart failure according to body mass index: The DELIVER trial

**Authors:** Adamson C et al.

**Summary:** This analysis of the DELIVER trial investigated the efficacy and safety of dapagliflozin according to body mass index (BMI) in patients with HFpEF. Patients were categorised as having normal weight (21.5%), overweight (33.1%), class I obesity (25.2%), class II obesity (12.8%), and class III obesity (6.6%). Compared with placebo, dapagliflozin reduced the risk of the primary outcome to a similar extent across all of the BMI categories: HRs were 0.89 (95% CI 0.69–1.15), 0.87 (95% CI 0.70–1.08), 0.74 (95% CI 0.58–0.93), 0.78 (95% CI 0.57–1.08), and 0.72 (95% CI 0.47–1.08), respectively. The placebo-corrected changes in Kansas City Cardiomyopathy Questionnaire total symptom score with dapagliflozin at 8 months were 0.9, 2.5, 1.9, 2.7, and 8.6 points, respectively (p-interaction=0.03), and the placebo-corrected change in weight at 12 months was -0.88, -0.65, -1.42, -1.17, and -2.50kg, respectively (p-interaction=0.002).

**Comment:** The DELIVER trial studying dapagliflozin in HFpEF showed a significant benefit over placebo on top of background therapy. This was driven primarily by a reduction in hospitalisation for heart failure and urgent heart failure visits, with no effect on cardiovascular or all-cause mortality. We know from clinical practice that many patients with HFpEF are overweight/obese and this subanalysis confirms this, as well as identifying that obese patients are at increased risk of hospitalisation for heart failure and are more symptomatic than those with lower weight. The benefit of dapagliflozin was not affected by weight, but quality of life and symptoms improved more in the obese patients.

**Reference:** *Eur Heart J* 2022; published online Aug 27  
[Abstract](#)

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