Cardiology Practice Review™

Making Education Easy

Issue 25 - 2023

In this issue:

Abbreviations used in this issue:

AHA = American Heart Association
ACC = American College of Cardiology
CSANZ = Cardiac Society of Australia and New Zealand
EACTS = European Association for Cardio-Thoracic Surgery
ESC = European Society of Cardiology
MBS = Medicare Benefits Schedule
PBS = Pharmaceutical Benefits Scheme

Welcome to the 25th issue of Cardiology Practice Review.

This Review covers news and issues relevant to clinical practice in cardiology. It will bring you the latest updates, both locally and from around the globe, in relation to topics such as new and updated treatment guidelines, changes to medicines reimbursement and licensing, educational, professional body news and more. And finally, on the back cover you will find our COVID-19 resources for Cardiologists and a summary of upcoming local and international educational opportunities including workshops, webinars, and conferences.

We hope you enjoy this Research Review publication and look forward to hearing your comments and feedback.

Kind Regards,

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Editor

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Clinical Practice

ESC/EACTS versus ACC/AHA guidelines for the management of severe aortic stenosis

Aortic stenosis (AS) is a serious and complex condition for which an understanding of current clinical practice guidelines is critical to achieve effective patient care and shared decision-making. This state-of-the-art review was undertaken to compare 2021 ESC/EACTS Guidelines and 2020 ACC/AHA Guidelines recommendations for management of AS based on the evidence to date. The European and American guidelines were found to be generally compatible, except for three key distinctions:

i. Timing of intervention. The European guidelines recommend intervening at a left ventricular ejection fraction of <55%, compared with <60% over serial imaging in the American guidelines for asymptomatic patients.

ii. Valve selection. In the European guidelines, a threshold of age ≥65 years is recommended for surgical bioprosthesis, whereas the American guidelines employ multiple age categories, providing latitude for patient factors and preferences.

iii. Aortic valve replacement criteria. Despite limited evidence, the two guidelines endorse different age cut-offs for transcatheter compared with surgical aortic valve replacement.

The review also discusses trends indicating a declining proportion of mechanical valve replacements and identifies gaps in the literature for transcatheter aortic valve implantation in asymptomatic patients, appropriateness of Ross procedures, concomitant coronary revascularisation with aortic valve replacement, and bicuspid AS.

https://tinyurl.com/ff78m76u

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Coronary atherosclerosis burden and progression to guide clinical decision making: a report from the American College of Cardiology Innovations in Prevention Working Group

This working group report describes a precision heart care approach that emphasises atherosclerosis as the primary disease target for evaluation and treatment, which may represent the first attempt to propose coronary atherosclerosis burden and progression to individualise therapy selection and therapy changes, respectively.

Direct quantification and characterisation of atherosclerosis has the potential to encourage a precision heart care paradigm that improves diagnosis, risk stratification, therapeutic decision making, and longitudinal disease tracking in the context of personalised care. Against this background, the American College of Cardiology Innovations in Prevention Working Group has introduced Atherosclerosis Treatment Algorithms that personalise medical interventions based on atherosclerosis findings from coronary computed tomography angiography and cardiovascular risk factors. The treatment algorithms leverage patient-specific atherosclerosis burden and progression as primary targets for therapeutic intervention by integrating coronary computed tomography angiography-based atherosclerosis evaluation, clinical practice guidelines, and contemporary randomised controlled trial evidence. After defining stages of atherosclerosis severity by coronary computed tomography angiography, the treatment algorithms are described for worsening stages of atherosclerosis for patients with lipid disorders, diabetes, hypertension, obesity, and tobacco use.

The Atherosclerosis Treatment Algorithms are not endorsed by the American College of Cardiology and the algorithms should be not interpreted as a statement of American College of Cardiology policy.

https://tinyurl.com/5h7w58mr

Investigator-reported ventricular arrhythmias and mortality in heart failure with mildly reduced or preserved ejection fraction

Although it is assumed that ventricular arrhythmias are responsible for many or most cases of sudden death in patients with heart failure, there is a deficiency of data on the prevalence or incidence of ventricular tachycardia (VT) and ventricular fibrillation (VF) or their relationship with mortality in heart failure patients with mildly reduced ejection fraction (HFmrEF) or heart failure with preserved ejection fraction (HFpEF).

To investigate the occurrence and consequences of ventricular arrhythmias in patients with HFmrEF and HFpEF, this post hoc analysis assessed the incidence of VT or VF, reported as adverse events, in a large, pooled data set that included four landmark randomised controlled trials (PARAGON-HF, TOPCAT, I-Preserve, CHARM-Preserved). The analysis also assessed the clinical characteristics of patients with these arrhythmias and the variables associated with VT/VF. In 13,609 patients, 146 (1.1%) experienced investigator-reported VT/VF over a follow-up of 3 years (incidence rate 0.3 per 100 person-years). VT/VF was associated with a 3- to 5-fold increase in all-cause and cardiovascular death but not sudden death. Patients with HFmrEF had a higher rate of VT/VF than patients with HFpEF (adjusted HR 2.19, 95% CI: 1.77–2.71).

Although in this post hoc analysis VT and VF were uncommon in patients with HFmrEF and rare in patients with HFpEF, they were strongly associated with mortality and may be a marker of disease severity rather than the risk of sudden death.

https://tinyurl.com/233xkyd8

Gaps in the care of pulmonary hypertension: a cross-sectional patient simulation study among practicing cardiologists and pulmonologists

Diagnosis of pulmonary hypertension (PH) is often delayed or missed, which leads to missed treatment opportunities and disease progression. In this study, 219 board-certified practicing cardiologists and pulmonologists cared for simulated patients presenting with symptoms of chronic dyspnoea and associated signs of potential PH. The investigators scored the clinical quality-of-care decisions made by the physicians in a clinical encounter against predetermined evidence-based criteria. Quality-of-care scores ranged from 18% to 74%. PH, when present, was correctly suspected 49.1% of the time and incorrectly identified in 53.7% of non-PH cases. 2-Dimensional echocardiography was ordered by physicians in just 64.3% of cases. Ordering a 2-dimensional echocardiography in the PH cases was significantly more likely to result in a presumptive diagnosis (61.9% vs 30.7%; p<0.001). Ordering other diagnostic work-up items showed similar results for ventilation/perfusion scan (81.5% vs 51.4%; p=0.005) and high-resolution computed tomography (60.4% vs 43.2%; p=0.001). Physicians who correctly identified PH were significantly more likely to have ordered confirmatory right heart catheterisation or referred to a PH centre (67.3% vs 15.8%; p<0.001). This study revealed a wide range of care in clinical practice in simulated patients presenting with possible PH, specifically in the evaluation and plan for definitive diagnosis of patients with PH. Delay in diagnosis or misdiagnosis of PH was likely attributable to a low clinical suspicion, non-specific symptoms, and underuse of critical diagnostic tests.

https://tinyurl.com/nzcdx6bb

Differences in patient characteristics, clinical practice and outcomes of cardiac implantable electric device therapy between Japan and the USA: a cross-sectional study using data from nationally representative administrative databases

Cardiac implantable electronic devices (CIEDs), which result in improved patient survival, are increasingly being used worldwide. Greater awareness of international differences in patient backgrounds, healthcare systems, and clinical outcomes through examination of large real-world databases is important for higher quality clinical research, which in turn will help to improve healthcare practice across countries. In the apparent absence of any studies directly comparing patient characteristics or clinical outcomes post-CIED implantation among different countries, this cross-sectional study was conducted to identify differences in patient characteristics, clinical practice, and outcomes of CIED therapy between Japan and the US.

Using representative nationwide administrative databases, 107,339 (age range 71–84 years; 48,415 women) and 295,584 (age range 67–83 years; 127,349 women) records of patients hospitalised with first-time implantations of CIEDs were included from Japan and the USA, respectively. Among inpatient defibrillator recipients, the main findings of the study were as follows:

i. The proportions of women and very elderly were lower in Japan compared with the US.
ii. Length of stay post-CIED implantation was significantly longer in Japan than in the US.
iii. In-hospital mortality post-CIED implantation was similar between Japan and the US, except in leadless pacemaker recipients.
iv. 30-day readmission rates were significantly lower in Japan than in the US.

The study investigators recommend additional studies to verify whether the low readmission rate in Japan is related to longer inpatient monitoring post-CIED implantation.

https://tinyurl.com/y527hs8s

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*In **PROVENT** (prophylaxis trial), the 3-month primary analysis (N=5172) demonstrated a 77% risk reduction of developing symptomatic COVID-19 (p<0.001; 95% CI: 46%-90%) vs placebo (incidence of COVID-19: 0.2% of EVUSHELD vs 1% of placebo patients). This increased to 83% risk reduction (95% CI: 66%-91%) vs placebo at the 6.5-month (median) follow-up (incidence of COVID-19: 0.3% of EVUSHELD vs 1.8% of placebo patients).[1,2] In **TACKLE** (treatment trial): EVUSHELD, when given within 7 days of symptom onset (primary analysis, N=822), demonstrated a 50% risk reduction in severe COVID-19 or death from any cause (p=0.010; 95% CI: 15%-71%) vs placebo (incidence: 4% of EVUSHELD vs 9% of placebo patients). When given within 5 days of symptom onset, EVUSHELD demonstrated a 67% risk reduction in severe COVID-19 or death from any cause (p=0.002; CI: 31%-84%) vs placebo (incidence: 4% of EVUSHELD vs 11% of placebo patients). Severe COVID-19 was defined as a minimum of either pneumonia (fever, cough, tachypnoea or dyspnoea, and lung infiltrates) or hypoxaemia (SpO_2 <90% in room air and/or severe respiratory distress), plus a WHO Clinical Progression Scale score of ≥5.[1,3] EVUSHELD was generally well tolerated. The most frequently reported adverse reactions across pre-exposure prophylaxis and treatment of COVID-19 was injection site reaction (1.3% [N=4210] and 2.4% [N=452] respectively).[1] †Based on the incidence of primary endpoint events in the PROVENT trial, the duration of protection was 6 months following a single 300 mg dose of EVUSHELD. The predominant SARS-CoV-2 variants in circulation for the time were Alpha, Beta, Gamma, Epsilon and Delta.[1] Based on the totality of the data for Omicron variant BA.1, the duration of protection was predicted to be up to 6 months following a single 600 mg dose of EVUSHELD (tixagevimab 300 mg / cilgavimab 300 mg).[4]

BEFORE PRESCRIBING PLEASE REVIEW FULL PRODUCT INFORMATION AVAILABLE ON REQUEST FROM ASTRAZENECA ON 1800 805 342 OR www.astrazeneca.com.au/PI

PBS Information: This product is not listed on the PBS.

▼ This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

MINIMUM PRODUCT INFORMATION. EVUSHELD™ (tixagevimab and cilgavimab). THERAPEUTIC INDICATIONS: EVUSHELD has **provisional approval** for the **pre-exposure prophylaxis** of COVID-19 in adults and adolescents aged 12 years and older weighing at least 40 kg, – Who have moderate to severe immune compromise due to a medical condition or receipt of immunosuppressive medications or treatments that make it likely that they will not mount an adequate immune response to COVID-19 vaccination **or** – For whom vaccination with any approved COVID-19 vaccine is not recommended due to a history of severe adverse reaction (e.g., severe allergic reaction) to a COVID-19 vaccine(s) and/or COVID-19 vaccine component(s). **EVUSHELD is not recommended as a substitute for vaccination in individuals for whom COVID-19 vaccination is recommended.** EVUSHELD has **provisional approval** for the **treatment** of COVID-19 in adults who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19. **DOSE AND METHOD OF ADMINISTRATION:** The recommended dose for both, pre-exposure prophylaxis and treatment is 600mg of EVUSHELD (2 cartons), consisting of: • 300 mg of tixagevimab (2 vials). • 300 mg of cilgavimab (2 vials). Administered by a healthcare professional as separate 3.0mL sequential intramuscular (IM) injections at different injection sites, one in each of the gluteal muscles. **Pre-exposure prophylaxis** Repeat doses of 600 mg of EVUSHELD (300 mg of tixagevimab and 300 mg of cilgavimab) is optional and may be given once every 6 months at the discretion of the treating healthcare professional. EVUSHELD has only been studied at the 300 mg dose in clinical studies for the prophylaxis of COVID-19. **Treatment** EVUSHELD should be given as soon as possible after a positive viral test for SARS-CoV-2 and within 7 days after the onset of symptoms of COVID-19. **CONTRAINDICATIONS:** Individuals with a history of severe hypersensitivity reactions, including anaphylaxis, to the active substances or to any of the excipients. **SPECIAL WARNINGS AND PRECAUTIONS FOR USE:** Hypersensitivity including anaphylaxis; Clinically significant bleeding disorders; Breakthrough infection or treatment failure due to antiviral resistance. See full PI for in-vitro neutralisation activity of EVUSHELD against SARS-CoV-2 viral variants. Cardiovascular and thromboembolic events; Pregnancy Category B2 - there are limited data in pregnant women. EVUSHELD should only be used during pregnancy if the potential benefit outweighs the potential risk for the mother and the foetus. Lactation - see full PI. The safety and efficacy of EVUSHELD in children aged <18 years have not been established. No data are available – see full PI. **INTERACTIONS:** EVUSHELD is not renally excreted or metabolised by cytochrome P450 enzymes; therefore, interactions with concomitant medications that are renally excreted or that are substrates, inducers, or inhibitors of cytochrome P450 enzymes are unlikely. Based on PK modelling, COVID-19 vaccination following EVUSHELD administration had no clinically relevant impact on the clearance of EVUSHELD. No data are available on the clearance of EVUSHELD, if administered following vaccination. **ADVERSE EFFECTS:** The overall safety profile in patients who received 300 mg tixagevimab and 300 mg cilgavimab for the treatment of mild to moderate COVID-19 was similar to that reported in participants who received 150 mg tixagevimab and 150 mg cilgavimab in the prophylaxis studies. There is a lack of safety data from clinical studies with repeat dosing of 600 mg Evusheld. Common (≥1/100 to <1/10): Injection site reaction; Hypersensitivity; Headache; Fatigue; Cough; Cardiac disorders. Uncommon (≥1/1,000 to <1/100): Injection related reaction; Thromboembolic events; Cardiac disorders; General disorders and administration site condition. See full PI for uncommon AEs.

CI: confidence interval; SpO_2: oxygen saturation; WHO: World Health Organization.

References: 1. EVUSHELD (tixagevimab and cilgavimab) Product Information. **2.** Levin MJ *et al. N Engl J Med* 2022;386:2188-2200. **3.** Montgomery H *et al. Lancet Respir Med* 2022;10:985-996. **4.** FDA. Emergency Use Authorization (EUA) for EVUSHELD. 24 February 2022. https://www.fda.gov/media/156674/download (accessed December 2022).

Exploring biomarkers in routine diagnostics for the risk stratification of older patients in the chest pain unit: a prospective cohort study

Strategies to combine biomarkers indicative of biological age may help to improve the risk stratification of older patients presenting in the emergency department (ED), due to their objectivity and unambiguous clinical implications. In the context of biomarkers of ageing, three distinct biomarkers, C-reactive protein (CRP), high-sensitive troponin-T (hs-TnT), and haemoglobin (Hb), are often encountered in routine diagnostic procedures.

The purpose of this single-centre, exploratory, prospective cohort study, which was conducted in a chest pain unit (CPU) as part of the cardiological ED of a university hospital, was to estimate the association of the biomarkers, CRP, hs-TnT, and Hb, with older ED patients' all-cause mortality.

A total of 260 cardiological ED patients with a minimum age of 70 years were recruited, of which 63 died during the follow-up period. Positive results in each of the three biomarkers alone as well as the combination were associated with increased all-cause mortality during more than 2 years of follow-up. The biomarkers were, to a certain extent, independently associated with a patient's all-cause mortality. The number of positive results on age-related biomarkers appeared to be strongly indicative of a patient's all-cause mortality, even when controlled for major confounders.

Given that CRP, hs-TnT, and Hb, were strongly associated with an older ED patient's all-cause mortality, the study investigators propose that biomarkers with a clear link to biological ageing processes should be considered as potential candidates to supplement or replace risk stratification approaches.

https://tinyurl.com/2s4845w2

Randomised clinical trial using Coronary Artery Calcium Scoring in Australian Women with Novel Cardiovascular Risk Factors (CAC-WOMEN Trial): study protocol

Traditional risk prediction tools underpredict cardiovascular disease (CVD) risk in women and Indigenous people and do not consider female-specific 'risk-enhancers'. A computerised tomography coronary artery calcium score ('CT-calcium score') can detect calcified atherosclerotic plaque in advance of clinical symptoms. CT-calcium scoring, which is simple, non-invasive, and widely available, may therefore help physicians intensify medical therapy in women with risk-enhancing factors. Furthermore, there have been no trials that have assessed a CT-calcium score-guided approach to preventive care in women with risk-enhancing factors. Also, CT-calcium scoring has been minimally tested in Indigenous populations.

The CAC-WOMEN Trial is a multisite, single-blind, randomised, controlled trial of 700 women that has been designed to assess the effectiveness of a CT-calcium score-guided approach on cardiovascular risk factor control and healthy lifestyle adherence, compared with standard care, in women with risk-enhancing factors. Women without CVD aged 40–65 years (35-65 years for Aboriginal and Torres Strait Islander women) at low-intermediate risk on standard risk calculators and with at least one risk-enhancing factor will be recruited. Aboriginal and Torres Strait Islander women will be actively recruited, aiming for approximately 10% of the sample size.

The CAC-WOMEN Trial will be the first to assess a CT-calcium score-guided approach to CV care and CVD prevention in women with female-specific risk-enhancing factors who would otherwise be considered to be at low-intermediate risk and not qualify for intensive medical therapy. Should it produce positive results, the trial could contribute to the widespread adoption of CT-calcium scores to guide preventive care, leading to a lower burden of CVD in women in Australia.

https://tinyurl.com/2yummsdk

Association of plasma high-density lipoprotein cholesterol level with risk of fractures in healthy older adults

Elevated levels of high-density lipoprotein cholesterol (HDL-C) have been linked to osteoporosis and preclinical research suggests that HDL-C degrades bone mineral density by reducing osteoblast number and function.

Data from the Aspirin in Reducing Events in the Elderly (ASPREE) clinical trial and the ASPREE-Fracture sub-study (which collected data on fractures reported post-randomisation from Australian participants) were included in a post hoc analysis to conduct this observational study assessing the association between HDL-C level at baseline and risk of fracture in individuals randomised to aspirin versus placebo for primary prevention of cardiovascular events. The study cohort included 16,262 healthy participants (age ≥70 years) and analysed 1,659 fractures during 4 years of follow-up. The study found that a higher baseline HDL-C level was associated with a 14% higher risk of fractures, which was independent of other risk factors.

The investigators suggest that the results of their cohort study indicate that higher HDL-C levels may be associated with an increased risk of incident fractures and that an increased fracture risk may be a possible adverse effect of drugs that substantially increase plasma HDL-C levels.

https://tinyurl.com/2p8svnu4

Regulatory News

MBS – Extension of COVID-19 services

A range of COVID-19 health measures are being extended to 31 December 2023. The extension includes Medicare-subsidised telehealth, to determine the eligibility of people with confirmed COVID-19 infection to receive a COVID-19 oral antiviral treatment, and use of cardiac MRI to assist in diagnosing myocarditis associated with mRNA COVID-19 vaccination.

https://tinyurl.com/4zt8xzmd
https://tinyurl.com/5hxkfjnd

News in Brief

Clinical outcomes of telehealth in patients with coronary artery disease and heart failure during the COVID-19 pandemic

Telehealth (TH), primarily by way of telephone encounters, can be safely integrated into ambulatory cardiology practice irrespective of patient age, according to this retrospective observational cohort study that involved adult patients with cardiovascular disease and/or heart failure who were seen by cardiologists in clinics during 6-month periods before and during the initial phase of the COVID-19 pandemic (TH period). TH visits accounted for 0% of visits during the pre-pandemic period versus 68% during the TH period. Telephone visits comprised ≥92% of all TH encounters. Compared with the pre-pandemic period, patients seen during the TH period had fewer overall CV events (adjusted OR 0.78; 95% CI: 0.67–0.90), with similar findings demonstrated in patients aged ≥75 years.

https://tinyurl.com/2p83run2

Invasive management of significant tricuspid regurgitation in clinical practice

Concordance between ESC guidelines recommendations and clinical practice for tricuspid regurgitation (TR) surgical intervention is low, especially in those without concomitant severe left valvular heart disease, according to this sub-study of the ESC Valvular Heart Disease (VHD) II survey performed to evaluate the real-world treatment of TR compared with the clinical ESC guidelines recommendations published in 2012, 2017, and 2021. The results suggest that there is a need to improve further guideline implementation and need for better alternative treatments.

https://tinyurl.com/2nt54aaz

High prevalence of geriatric conditions among older adults with cardiovascular disease

In the field of geriatric cardiology, the combination of older age, multiple comorbidities, polypharmacy, frailty, and adverse non-cardiovascular outcomes presents a challenge for routine clinical practice. The authors of this narrative review, which provides additional evidence of so-called "accelerated aging" in older patients with cardiovascular disease (CVD), conclude that the presence of a high comorbidity burden in older people with CVD suggests that a comprehensive specific approach to caring for this especially vulnerable patient population is essential. The authors also assert that the high prevalence of geriatric conditions associated with CVD emphasises the need for an integrated, multisystem approach.

https://tinyurl.com/yjahxv9d

COVID-19 Resources for Cardiologists

CSANZ https://tinyurl.com/y3xp272
ACC https://tinyurl.com/y68aud3a
ESC https://tinyurl.com/wn3fsts

Conferences, Workshops and CPD

Please click on the links below for upcoming local and international Cardiology meetings, workshops and CPD.

ACRA https://tinyurl.com/y4yj8xb5
CSANZ https://tinyurl.com/3mwt5ttr
Cardiac Skills Australia https://tinyurl.com/zkzlelb
Heart Foundation https://tinyurl.com/y34smdoz
Australian Centre for Heart Health https://tinyurl.com/e2yjcreu
ACC https://tinyurl.com/y2khytpz
AHA https://tinyurl.com/zajc9a7
ESC Congresses and Events https://tinyurl.com/y6ko68yf
ESC Education https://tinyurl.com/y3zkjp3o

Research Review Publications

Acute Coronary Syndrome Research Review with Professor John French

Atrial Fibrillation Research Review with Dr Andre Catanchin

Cardiology Research Review with Associate Professor John Amerena

Heart Failure Research Review with Professor John Atherton, Professor Andrew Coats and Dr Mark Nolan

Interventional Cardiology Research Review with Conjoint Professor Craig Juergens

Educational Series – Transcatheter aortic valve implantation in severe symptomatic aortic stenosis

Lipids Year in Review 2022

Study Review – Long-term evolocumab use in established atherosclerotic cardiovascular disease

