Cardiology Practice Review™

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Abbreviations used in this issue:

ESC = European Society of Cardiology
PBS = Pharmaceutical Benefits Scheme

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Welcome to the 27th 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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Clinical Practice

Cardio-oncology recommendations for paediatric oncology patients: An Australian and New Zealand Delphi Consensus

The first-ever guidelines on monitoring children for heart damage during cancer treatment have been published. Heart complications are the second leading cause of death among childhood cancer survivors, after cancer recurrence. Survivors are 15 times more likely to have heart failure and eight times more likely to have heart disease than the general population.

The guidelines were compiled by 29 specialists in paediatric cardiology, oncology, and radiology from Australia and New Zealand. The team was led by researchers from the Murdoch Children's Research Institute, Melbourne. The advice discusses two well-known causes of cardiac issues – inadvertent radiation to the heart and treatment with doxorubicin and other anthracyclines – as well as immunotherapies and targeted biologics that are associated with their own unique cardiovascular risks.

Key recommendations

Drugs acting as inhibitors of VEGF, mTOR, proteasomal, kinases, and immune checkpoints are associated with risk for cardiovascular complications. Then, when these patients are adults, developing metabolic syndrome or kidney disease, and even pregnancy, increase the risk of cardiovascular complications further. Children should be assessed at least once by a cardio-oncologist during treatment, and testing should ideally include a 3-dimensional transthoracic echocardiogram.

The experts made a unanimous recommendation for dexrazoxane, the sole cardio-protective agent used in paediatric oncology for children receiving 250 mg/m^2 or more of doxorubicin or its equivalent.

They also recommend electrocardiograms and troponin I levels within 48 hours of each immune checkpoint inhibitor dose to assess for myocarditis. If myocarditis is suspected, the immunotherapy should be withheld.

In addition, children should be assessed for hypertension within a month of starting a VEGF inhibitor, and for those who receive treatment with an mTOR inhibitor, blood pressure, glucose levels, lipid profiles, and renal function should be evaluated every 6 months.

For patients receiving BCR-Abl tyrosine kinase inhibitors, the initial cardio-oncology assessment should include an electrocardiogram, due to the risk of QT prolongation.

Similarly, the experts call for a review of toxicities at least every 3 months for children who are treated with the Bruton tyrosine kinase inhibitor ibrutinib, with a quick referral to cardiology for any signs of arrhythmia, including palpitations, dizziness, and loss of consciousness.

https://tinyurl.com/3h35x9dk

Myopericarditis after COVID-19 mRNA vaccination among adolescents and young adults

This systematic review and meta-analysis investigated the clinical features and early outcomes associated with myopericarditis after COVID-19 mRNA vaccination in a heterogeneous population of adolescents and young adults. A search of PubMed and EMBASE identified 23 observational studies and case series that described COVID-19 vaccine-associated myopericarditis in a total of 854 individuals aged 12-20 years (90.3% male). The individuals had no history of prior myopericarditis or underlying cardiovascular disease.

Meta-analysis of the data showed that the incidence rate of myopericarditis was higher after the second dose than the first dose, with 74.4% of events occurring after the second dose. The mean interval to onset of myopericarditis post vaccination was 2.6 days (95% CI 1.9-3.3 days). Most patients (84.4%) had preserved LV function. Of the 15.6% with LV systolic dysfunction (LVEF <55%), most were mild; only 1.3% of patients had severe LV systolic dysfunction (LVEF <35%). Cardiac MRI revealed late gadolinium enhancement in 87.2% of patients. Although 92.6% of patients were hospitalised and 23.2% needed ICU admission, inotropes were used in only 1.3% of patients, and none of them died. The authors stress that clinical follow-up of cardiovascular events in patients with vaccine-associated myocarditis is essential.

https://tinyurl.com/4te2shuk

Circulating spike protein detected in post-COVID-19 mRNA vaccine myocarditis

This small prospective study conducted extensive immune profiling of 16 adolescents and young adults hospitalised for myocarditis after SARS-CoV-2 mRNA (Pfizer-BioNTech BNT162b2 or Moderna mRNA-1273) vaccination and compared the results with those of 45 healthy, asymptomatic, age-matched, vaccinated controls. In the postvaccination myocarditis cohort, most patients were male and developed myocarditis after the second dose, with symptom onset occurring within a week after vaccination. The authors found that vaccine-induced immune responses did not differ between individuals who developed myocarditis and those who did not. However, markedly elevated levels of free full-length spike protein, unbound by antibodies, were identified in the postvaccination myocarditis cohort, a finding which was absent in age-matched healthy vaccinated controls (P<0.0001). Larger studies are warranted to understand the immunopathological mechanisms associated with postvaccination myocarditis.

https://tinyurl.com/bdzz4ta5

A stepwise approach to prescribing novel lipid-lowering medications

The following are key points to remember from a review article on a stepwise approach to prescribing novel lipid-lowering therapies:

1. The paper aims to familiarise clinicians with newer lipid-lowering therapies and offers a practical guide for how to prescribe these agents in clinical practice.
2. The article reviews the efficacy and safety of novel lipid-lowering agents, including proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, bempedoic acid, icosapent ethyl, evinacumab, and lomitapide.
3. Pharmacologic therapies with proven benefit are recommended, i.e., statins, ezetimibe, PCSK9 monoclonal antibodies (evolocumab and alirocumab), and icosapent ethyl.
4. Statins are the therapy of choice for initial reduction of LDL-C.
5. Patients with statin intolerance should receive the maximally tolerated statin dose even if ultra-low, rather than discontinue statins.
6. In patients at very high risk of atherosclerotic cardiovascular disease (ASCVD):
   - Ezetimibe should be added if LDL-C is ≥1.8 mmol/L on maximally tolerated statins.
   - A PCSK9 monoclonal antibody should be added if LDL-C remains ≥1.8 mmol/L or non–HDL-C ≥2.6 mmol/L despite ezetimibe and maximally tolerated statin.
     - Bempedoic acid may be considered if concerned about the high cost of a PCSK9 inhibitor.
     - Inclisiran may be considered in patients who prefer less frequent injections.
   - Lomitapide or evinacumab should be considered in patients with homozygous familial hypercholesterolaemia.
7. In patients not at very high risk of ASCVD who are ≤75 years of age:
   - Ezetimibe should be added if LDL-C ≥1.8 mmol/L on maximally tolerated statin.
   - Bempedoic acid should be considered if LDL-C remains ≥1.8 mmol/L despite ezetimibe and maximally tolerated statin.
8. In patients not at very high risk of ASCVD who are >75 years of age, offer moderate-intensity or high-intensity statin, with subsequent intensification if required.
9. Icosapent ethyl should be considered in patients with triglycerides ≥1.5 mmol/L who meet REDUCE-IT criteria.

https://tinyurl.com/48envayp

American College of Cardiology. Five things physicians and patients should question

The American College of Cardiology (ACC) has published a list of five things physicians and patients should question in cardiology as part of the Choosing Wisely campaign. Choosing Wisely has worked with national medical societies like the ACC since 2012 to stimulate conversations between and among clinicians and patients about potentially unnecessary tests, treatments and procedures.

The new ACC Choosing Wisely recommendations include statements regarding heart failure, atrial fibrillation, near-syncope, and atherosclerosis, spanning modalities from invasive haemodynamic assessment and arrhythmia ablation to cardiac imaging. The list, which is based on published national guidelines, includes five recommendations to:

1. Avoid the routine use of invasive haemodynamic monitoring with pulmonary artery catheters in patients with uncomplicated acute decompensated heart failure who are haemodynamically stable and responding to treatment.
2. Avoid performing atrial fibrillation ablation for the sole purpose of discontinuing chronic anticoagulation.
3. Avoid routine imaging stress tests or coronary CT angiography for the workup of palpitations or presyncope.
4. Avoid obtaining a coronary artery calcium score in patients with known clinical atherosclerotic cardiovascular disease.
5. Avoid obtaining routine serial echocardiograms for chronic heart failure if there has been no change in signs, symptoms or management.

https://tinyurl.com/mf9v7uft

Aortic stenosis progression: A systematic review and meta-analysis

Aortic valve stenosis is a progressive disorder with variable progression rates. The factors affecting aortic stenosis (AS) progression remain largely unknown, although elevated Lp(a) has been shown to be a risk factor for accelerated disease progression. This systematic review and meta-analysis involving 24 studies and 5450 patients investigated the progression rate of AS and the impact of sex and baseline AS severity on disease progression.

The pooled annualised progression of mean gradient was +4.10 mm and that of aortic valve area was −0.08 cm^2, which was higher with increasing baseline disease severity. The impact of sex on AS progression was inconclusive as only four studies reported progression stratified by sex, with limited data to perform a meta-analysis.

The study provides progression rates for both haemodynamic and anatomic parameters of AS and highlights the need for more studies to determine whether sex differences affect AS progression.

https://tinyurl.com/fmf3h66s

Regulatory News

Improved access to PBS medicines for pulmonary arterial hypertension

Access to pulmonary arterial hypertension (PAH) PBS medicines has improved as an outcome of the post-market review of PAH medicines. From 1 December 2022, PAH patients with World Health Organization (WHO) Functional Class (FC) III or IV symptoms have access to endothelin receptor antagonist (ERA) and prostanoid medicines for dual therapy. Patients with WHO FC IV symptoms have access to ERA, prostanoid and phosphodiesterase-5 inhibitor medicines for triple therapy.

https://tinyurl.com/yckjy88w

News in Brief

Major global coronary artery calcium guidelines

This state-of-the-art review summarises the framework behind the global guidelines of coronary artery calcium (CAC) screening during atherosclerotic cardiovascular disease risk assessment for applications in both the clinical setting and preventive therapy. There is significant variation in global CAC guidelines, although clinical practice guidelines agree that CAC scoring is vital to up- or down-grade risk in intermediate-risk individuals. The key agreements among global CAC guidelines are to indicate CAC screening for asymptomatic intermediate-risk individuals older than 40 years. Among those having a CAC >100, statin initiation should be considered, whereas those with a CAC = 0 should have the risk downgraded and statins withheld, with screening repeated within 5 to 10 years.

https://tinyurl.com/28dx82er

Renal denervation in the management of hypertension in adults. A clinical consensus statement of the ESC Council on Hypertension and the European Association of Percutaneous Cardiovascular Interventions

Hypertension is a prevalent modifiable cardiovascular risk factor. Based on a review of the available evidence, including high-quality sham-controlled clinical trials, the authors of this clinical consensus statement propose that catheter-based renal denervation (RDN) is an adjunct treatment option for uncontrolled resistant hypertension (confirmed by ambulatory blood pressure measurements) that remains resistant despite best efforts with lifestyle and pharmacological interventions. RDN may also be used in patients who cannot tolerate antihypertensive medications. A shared decision-making process is a key feature of management.

https://tinyurl.com/jhc3d559

Cardiovascular complications of Down syndrome: Scoping review and expert consensus

In individuals with Down syndrome, cardiovascular disease (CVD) significantly contributes to morbidity and mortality. This population has a high incidence of congenital heart disease (up to 50%), pulmonary hypertension, endocrine and metabolic disorders, and risk factors for atherosclerosis, which can negatively impact health outcomes. In addition, disparities in health system-related quality of care and access also contribute to higher rates of CVD mortality. This review and expert consensus provides contemporary insight into the diagnosis, management, and prevalence of CVD in individuals with Down syndrome. The review covers 10 key areas from prenatal diagnosis to disparities in care based on resources.

https://tinyurl.com/43hw7fxk

Metformin can be safely used in patients exposed to contrast media

Metformin is cleared via renal filtration, and concerns of lactic acidosis due to accumulation in acute kidney injury (AKI) have led to restrictions in the use of metformin at the time of contrast application. This systematic review with meta-analysis included seven studies of 2325 individuals. The estimated glomerular filtration rate cut-off used was 30 mL/min/1.73m^2. Results showed no significant association between metformin use and contrast-induced AKI incidence of lactic acidosis. In their conclusion the authors see no reason to discontinue metformin in patients receiving iodine contrast.

https://tinyurl.com/55j7aubc

A systematic review of global autopsy rates in all-cause mortality and young sudden death

This systematic review aimed to quantify the real-world global autopsy rates in either all-cause death or young sudden death (SD) cases. Only 30.3% and 8.2% of the countries reported performing an autopsy in all-cause death (range 0.01% to 83.9%) and young SD (range 5.0% to 100.0%) cases, respectively. Risks of bias included the heterogeneity in reporting clinical versus medicolegal autopsies and the small number of studies overall, which showed a consistent exclusion of low- and middle-income countries. In conclusion, this study demonstrates the low report rate of autopsy globally in the context of either all-cause death or young SD, which makes it difficult to quantify the global burden of disease and address the clinical needs in this area.

https://tinyurl.com/2b333rku

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

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