Cardiology Practice Review™

Making Education Easy

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In this issue:

Abbreviations used in this issue:

ACS = acute coronary syndromes;
ATAGI = Australian Technical Advisory Group on Immunisation;
NAFLD = non-alcoholic fatty liver disease; **SCD** = sudden cardiac death;
TGA = Therapeutic Goods Administration.

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Welcome to the 23rd 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, medicolegal issues, 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

Cardiovascular drug interactions with nirmatrelvir/ritonavir in patients with COVID-19

Patients with CVD and symptomatic COVID-19 are often treated with nirmatrelvir-ritonavir (Paxlovid) to prevent progression to severe disease; however, Paxlovid can interact with some previously prescribed medications. This review article examines the potential drug-drug interactions between Paxlovid and commonly used cardiovascular medications.

Paxlovid is an oral antiviral agent for the treatment of symptomatic, non-hospitalised adults with mild to moderate COVID-19 infection who are at high risk for progression to severe disease. Such patients include those with CVD, diabetes, hypertension, and chronic kidney disease. Five of the most important cardiovascular drug interactions with Paxlovid to be aware of include:

- **Antiarrhythmic agents**
  - Plasma levels of many antiarrhythmic drugs such as amiodarone, flecainide and quinidine, may be increased when co-administered with Paxlovid. The exception is sotalol, which is renally cleared and does not interact with Paxlovid. While it may be possible to start Paxlovid after a 2-2.5-day temporary discontinuation of antiarrhythmics, this may not be practical. Alternative COVID-19 therapies should be considered.
- **Antiplatelet agents and anticoagulants**
  - Aspirin and prasugrel are safe to co-administer with Paxlovid. There is an increased risk of blood clots when Paxlovid is given with clopidogrel and an increased risk of bleeding when given with ticagrelor. Consider switching to prasugrel, although this is currently not available in Australia. If prasugrel is contraindicated/unavailable, co-administration of Paxlovid should be avoided and alternative COVID-19 therapies should be considered.
  - Anticoagulants such as warfarin may be co-administered with Paxlovid but require close monitoring of clotting factors. The plasma levels of all direct oral anticoagulants increase when co-administered with Paxlovid, therefore dose adjustment or temporary discontinuation and use of alternative anticoagulants may be required, but administration with rivaroxaban is contraindicated.
- **Certain statins**
  - Co-administration of simvastatin or lovastatin with Paxlovid can lead to increased plasma levels and subsequent myopathy and rhabdomyolysis. These agents should be stopped before starting Paxlovid. Consider dose reduction of atorvastatin and rosuvastatin when co-administered with Paxlovid. Other statins are considered safe when given with Paxlovid.
- **Immunosuppressive agents**
  - The plasma levels of immunosuppressive agents in patients who have undergone heart transplantation rise to toxic levels when co-administered with Paxlovid. Temporary reduction of immunosuppressive agents would require frequent monitoring and be difficult. Therefore, alternative COVID-19 therapies should be considered in these patients. Use with colchicine is also not recommended.

https://tinyurl.com/bdzxzx4w
https://tinyurl.com/4f6347x7

Myocarditis: Review article

This review of myocarditis focuses on epidemiology, causes and pathogenesis, clinical presentation, diagnosis, and therapy. Myocarditis can be caused by viruses, immune-system activation or immune stimulation (e.g., vaccines or cancer therapies), or exposure to toxins and drugs. Genetics may contribute to myocarditis in up to 16% of cases.

In patients with COVID-19 and myocarditis, the mechanisms of cardiac injury may include endothelialitis, myocarditis, myocardial injury due to a mismatch between oxygen supply and demand, microvascular thrombosis, systemic hyperinflammatory response, or myocardial ischaemia.

The main clinical manifestations of myocarditis are chest pain with an otherwise uncomplicated clinical picture (preserved LVEF and no ventricular arrhythmias), new or worsening heart failure, chronic heart failure, life-threatening haemodynamic compromise, and life-threatening arrhythmia or conduction disturbances.

Giant-cell myocarditis should always be suspected in patients with rapidly progressive heart failure or cardiogenic shock, with or without conduction disturbances, that does not respond to usual therapy.

Diagnostic workup includes laboratory testing; electrocardiography, Holter monitoring, and stress testing; functional and structural assessment on cardiac imaging; and tissue characterisation on cardiac MRI. Cardiac MRI has the best sensitivity if performed within 2-3 weeks after the initial clinical presentation.

Endomyocardial biopsy should be reserved for patients with clinically suspected myocarditis and the following findings: cardiogenic shock or acute heart failure requiring inotropic or mechanical circulatory support; ventricular arrhythmias or Mobitz type II second-degree or higher AV block; peripheral eosinophilia or an associated systemic inflammatory disorder; persistent or recurrent release of necrosis markers; or cardiac dysfunction in a patient receiving immune checkpoint inhibitor therapy.

Treatment for myocarditis involves standard treatment of arrhythmias and heart failure. Early administration of immunosuppressive drugs is the standard therapy for eosinophilic myocarditis, giant-cell myocarditis and cardiac sarcoidosis. No specific therapy is available for lymphocytic acute myocarditis, except for the forms associated with systemic diseases and immune checkpoint inhibitors.

https://tinyurl.com/yx3tcrs9

https://tinyurl.com/3c8x4wnz

Myocarditis and myopericarditis cases following COVID-19 mRNA vaccines administered to 12–17-year-olds in Victoria, Australia

This Australian study evaluated myocarditis adverse events after COVID-19 mRNA vaccination in adolescents (Pfizer-BioNTech or Moderna). All myocarditis and myopericarditis events that occurred after COVID-19 mRNA vaccination in adolescents aged 12–17 years that were reported to Surveillance of Adverse Events Following Vaccination in the Community (SAEFVIC) between 22 February 2021 and 22 February 2022 were analysed; most were reported by the practitioner.

Clinical review determined that 75 cases were definite or probable myocarditis (8.3 per 100,000 doses). Cases were predominantly in males (82.7%) and most of them occurred after the second dose (81.3%). Rates were higher in males than females (17.7 vs 3.9 per 100,000; P≤0.001). Presentation was temporally related to the Pfizer-BioNTech vaccine in 84.1% of cases and to the Moderna vaccine in 16.0% of cases.

The most common presenting symptoms were chest pain, dyspnoea and palpitations. Most patients who had a cardiac MRI had abnormalities (n=33, 91.7%). Fifty-one cases (77.1%) required hospitalisation with a median length of stay of two nights. Females were more likely to have ongoing clinical symptoms at 1-month (P=0.02).

https://tinyurl.com/bdz9cfmd

Cardiometabolic outcomes up to 12 months after COVID-19 infection

Following COVID-19, more patients appear to develop diabetes and cardiovascular disease events. This matched cohort study in the UK investigated long-term cardiometabolic outcomes after COVID-19. Using data extracted from the electronic records of 1356 UK family practices, 428,650 patients with COVID-19 but without diabetes or cardiovascular disease were individually matched with 428,650 control patients. The net incidence of diabetes increased in the first 4 weeks after COVID-19 (adjusted rate ratio [RR] 1.81) and remained elevated during weeks 5–12 (RR 1.27), but not beyond 12 weeks. The net incidence of cardiovascular disease also increased in the first 4 weeks after COVID-19 (RR 5.82), mostly driven by pulmonary embolism/deep vein thrombosis and atrial arrhythmia. The incidence of cardiovascular disease declined during weeks 5–12 (RR 1.49) and weeks 13–52 (RR 0.80).

https://tinyurl.com/5n83t5je

ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

The European Society of Cardiology (ESC) has updated their guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. New insights into the epidemiology of sudden cardiac death, new evidence on genetics, imaging, and clinical findings for risk stratification for ventricular arrhythmias and sudden cardiac death, and advances in diagnostics and therapies made this revision necessary.

General aspects

- Increased availability of public access defibrillators and community training in basic life support are key to improving survival of out-of-hospital cardiac arrest victims.
- Patients with genetic cardiomyopathies and arrhythmia syndromes should undergo genetic testing and counselling under the care of a multidisciplinary team.
- A thorough autopsy is recommended in all cases of sudden death under 50 years and should be considered in all cases of sudden death.
- An electrical storm refractory to drug therapy requires advanced catheter ablation techniques, mechanical circulatory support, and autonomic modulation.
- When considering the benefit of ICD therapy, competing risk factors for non-arrhythmic death and the patient's wishes and quality of life need to be taken into account.

Structural heart disease

- Catheter ablation is recommended in coronary artery disease (CAD) patients with recurrent symptomatic sustained monomorphic ventricular tachycardia (SMVT) despite amiodarone therapy and is the recommended first-line treatment for premature ventricular complex-induced cardiomyopathy.
- In patients with hypokinetic non-dilated cardiomyopathy/dilated cardiomyopathy, indication for ICD implantation should not be restricted to an LVEF ≤35% but should also consider cardiac magnetic resonance and genetics.
- Patients with an LMNA mutation require specific risk stratification for sudden cardiac death.
- Patients with arrhythmogenic right ventricular cardiomyopathy have a high rate of ICD interventions which may not be lifesaving.
- A validated risk calculator is useful to examine the risk for sudden cardiac death in hypertrophic cardiomyopathy patients younger than 16 years.
- Myotonic dystrophy patients with palpitations suspected of arrhythmia, syncope or aborted sudden death should be evaluated by invasive electrophysiological study.
- In patients with repaired tetralogy of Fallot and monomorphic VT, catheter ablation is the preferred treatment.

Primary electrical disease

- Nadolol or propranolol are the preferred agent of choice in patients with long QT syndrome and catecholaminergic polymorphic ventricular tachycardia.
- In patients with asymptomatic long QT syndrome the arrhythmic risk may be useful to calculate.
- A type 1 Brugada ECG pattern provoked by sodium channel blocker test in the absence of other findings does not diagnose Brugada syndrome (BrS).
- Sudden cardiac death risk stratification in asymptomatic BrS patients with a spontaneous type 1 pattern remains controversial.
- Routine catheter ablation is not recommended in asymptomatic BrS patients.
- The diagnosis of idiopathic ventricular fibrillation requires ruling out an underlying structural, channelopathic, or metabolic aetiology.
- Early repolarisation pattern can be a benign finding and is distinct from early repolarisation syndrome.
- Left cardiac denervation plays an important role in the management of CPVT and long QT syndrome.

https://tinyurl.com/ybt4h3tb

Management of acute coronary syndromes in older adults

This was a state-of-the-art review on the management of acute coronary syndromes (ACS) in older adults. The effect of ageing on the cardiovascular system includes increased inflammation, increased blood pressure, vascular dysfunction, and increased heart failure. Older patients have unique features that should be considered, including multiple comorbidities, frailty, and cognitive issues, and bleeding risk and poorer renal function. Older women are at increased risk of mortality compared to older men even after adjusting for differences in comorbidities.

Invasive management is preferred regardless of age, sex, or type of ACS. Among older patients with acute MI and shock, a culprit-only PCI approach should be considered over multivessel PCI.

Strategies to reduce bleeding risk include radial access, use of proton pump inhibitors, and utilisation of bleeding risk scores. Of note, systemic anticoagulation and antiplatelet regimens increase bleeding risk without improving mortality.

At hospital discharge, patients should be screened for valvular disease and drug interactions, and referred for outpatient rehabilitation.

https://tinyurl.com/3963ht3x

https://tinyurl.com/yc3kd3av

Non-alcoholic fatty liver disease and risk of new-onset heart failure: An updated meta-analysis of about 11 million individuals

Nonalcoholic fatty liver disease (NAFLD) is associated with an increased long-term risk for new-onset heart failure, according to a recently published systematic review and meta-analysis.

The systematic review identified eligible observational studies in which NAFLD was diagnosed by serum biomarkers/scores, International Classification of Diseases codes, imaging techniques, or liver histology to examine the association between NAFLD and new-onset heart failure.

Eleven longitudinal cohort studies were selected, which included data on just over 11 million individuals and 97,716 cases of incident heart failure over a median of 10 years. There was an association for NAFLD with a moderately higher risk for new-onset heart failure (pooled random-effects HR 1.50), independent of age, sex, ethnicity, adiposity measures, diabetes, hypertension, and other typical cardiovascular risk factors. These results did not change in sensitivity analyses. No significant publication bias was noted.

https://tinyurl.com/ywctj75v

Regulatory News

ATAGI updated guidance on myocarditis and pericarditis after COVID-19 vaccines

The Australian Technical Advisory Group on Immunisation (ATAGI) updated their guidance on myocarditis and pericarditis after COVID-19 vaccines in September. The following has been updated:

- Updated rates of myocarditis and pericarditis following COVID-19 vaccination by age, gender, and dose
- Updated evidence on the long-term outcomes of people with myocarditis or pericarditis following vaccination
- Updated recommendations for revaccination in people with a history of myocarditis or pericarditis following vaccination
- Guidance name changed to include all COVID-19 vaccines (including AstraZeneca and Novavax), not just mRNA.

https://tinyurl.com/5yhhkrvy

TGA – new and extended registrations

Mavacamten (Camzyos) is indicated for the treatment of adults with symptomatic NYHA class II-III obstructive hypertrophic cardiomyopathy. Mavacamten is a selective, allosteric, and reversible cardiac myosin inhibitor.

Rivaroxaban (Xarelto) is now also indicated for the treatment of VTE and prevention of VTE recurrence in term neonates, infants and toddlers, children, and adolescents aged less than 18 years after at least 5 days of initial parenteral anticoagulation treatment.

https://tinyurl.com/bdz69rjz

News in Brief

Associations between dietary fibre intake and cardiovascular risk factors: An umbrella review of meta-analyses of randomised controlled trials

This umbrella meta-analysis evaluated the effects of dietary fibre intake on CVD risk factors. A search of Web of Science, PubMed, Scopus, and the Cochrane Library identified 52 meta-analyses (n=47,197) that were suitable for inclusion. Meta-analysis of the data showed that higher dietary fibre intake was significantly associated with reductions in glycaemic control parameters (e.g., fasting plasma glucose, fasting plasma insulin, insulin resistance, and glycosylated haemoglobin [HbA1c]). Higher dietary fibre intake was also associated with significant reductions in total cholesterol and low-density lipoprotein cholesterol levels, and improved blood pressure levels.

https://tinyurl.com/ywfzk85z

Association of gestational diabetes mellitus with overall and type specific cardiovascular and cerebrovascular diseases

This systematic review and meta-analysis of 15 studies quantified the risk of cardiovascular and cerebrovascular diseases and venous thromboembolism (VTE) in women with a history of gestational diabetes mellitus. Of 513,324 women with gestational diabetes, 9507 had cardiovascular and cerebrovascular disease, with data from about 8 million controls available. Meta-analysis of the data showed that, compared with women without gestational diabetes, women with a history of gestational diabetes were at increased risk for cardiovascular and cerebrovascular diseases (RR 1.45), incident coronary artery disease (RR 1.40), myocardial infarction (RR 1.74), heart failure (RR 1.62), angina pectoris (RR 2.27), cardiovascular procedures (RR 1.87), stroke (RR 1.45), ischaemic stroke (RR 1.49), and VTE (RR 1.28). The results highlight the need for intervention and point out that diabetes in pregnancy is a relevant risk factor for future development of CVD in women.

https://tinyurl.com/2maa7h9d

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

Study Review – Renal decline in non-valvular atrial fibrillation treated with rivaroxaban or warfarin

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