Summer 2021

GP Connect

Supporting best practice in cardio-metabolic health

Sydney Cardiology

From the editor – Dr Gunjan Aggarwal

Specialising in general adult cardiology and non-invasive cardiac imaging, particularly echocardiography and cardiac computed tomography (CT).

Welcome to the summer edition of GP Connect. This issue provides updates on nutritional and lifestyle recommendations to reduce cardiovascular risk. There are articles on the nutraceutical red yeast rice for management of statin intolerant patients, dietary and exercise-based strategies for management of hypertriglyceridemia and health benefits of fish consumption.

Dr Rudee Ting, an interventional cardiologist, provides an important summary on the use of antiplatelet drugs in a range of different scenarios including atrial fibrillation, perioperative settings, and post-percutaneous coronary intervention (PCI).

In other exciting news we would like to welcome Dr Tracy Smith, a respiratory physician who will be consulting at our Parramatta rooms. Having had first-hand experience of working collaboratively with Dr Smith in a multidisciplinary breathlessness clinic, I am confident she will be an invaluable addition to the Sydney Cardiology team and provide considerable expertise in the management of your patients with respiratory conditions. Dr Smith writes an excellent article on the respiratory evaluation of a patient with breathlessness in this edition.

The last year has seen unprecedented challenges for the medical profession and community at large. Speaking to GP colleagues, the strain on general practice has been tremendous. There have been immense pressures on general practitioners and their staff from dealing with issues as diverse as changing advice from the government and ATAGI regarding vaccine eligibility, preferred vaccine shortages, patient vaccine hesitation, decreased patient volume and late presentations, aggressive patient encounters and abuse directed at receptionist staff, challenges of implementing infection control measures and appropriate use of PPE to avoiding practice closures, challenges of dealing with patients requesting exemptions, and contending with the risk of contracting and transmitting COVID to their loved ones just to name a few! Despite this, GPs have responded admirably and achieved the incredible task of safely steering the community by guiding the vaccine rollout. Despite bureaucratic missteps contributing to a slow start, Australia is now in an enviable position of achieving a greater than 90% double vaccination rate and is now opening up again. On behalf of Sydney Cardiology, thank you to all our GP colleagues.

I hope you enjoy this edition of GP Connect. We remain open over the Christmas and New Year break to assist you and your patients in any way possible. I hope you and your staff enjoy a well-earned break, and we wish you and your families a festive and merry Christmas and Happy New Year. Hopefully 2022 will mark a new beginning where life will return to some semblance of normality in a post-COVID world! Stay safe.

Sincerely

Dr Gunjan Aggarwal

In this issue

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WISHING YOU A JOYFUL FESTIVE SEASON

Sydney Cardiology

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Over the Christmas period, Sydney Cardiology rooms are open at the following locations. Please call our rooms to make an appointment.

For the on-call cardiologist, please call our pager service on **9966 7700**.

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20 Dec All Locations	**21 Dec** All Locations	**22 Dec** All Locations	**23 Dec** All Locations	**24 Dec** Chatswood Blacktown Bella Vista Parramatta
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Update on antiplatelet agents post coronary stents

Dr Ru-Dee Ting

Specialising in general and interventional cardiology, including cardiac haemodynamic studies and complex coronary intervention.

Why is dual antiplatelet therapy (DAPT) needed?

When drug-eluting stents first came on to the market, there was a very rapid uptake due to the reduced rate of long-term atherosclerotic in-stent restenosis compared to bare metal stents. However, there arose the issue of acute stent thrombosis, which could occur months after stent deployment. This was found to be due to the polymer coating used in drug coated stents, which impaired stent endothelisation. Hence, dual antiplatelets are necessary to prevent this phenomena. It should be noted that newer generation drug-eluting stents have a far lower risk of stent thrombosis, allowing shorter durations of DAPT.

In patients with acute coronary syndromes, the cardiovascular risk remains high beyond the first year, even with successful revascularisation. In this setting, DAPT has been shown to be an effective therapeutic strategy to prevent recurrent ischaemic events compared to aspirin alone.

What is the usual regimen?

DAPT involves aspirin and a P2Y12 inhibitor like clopidogrel or ticagrelor. Since 2020, prasugrel is no longer available in Australia.

Broadly speaking, clopidogrel is used in stable coronary artery disease (CAD) post-stenting, while ticagrelor is used in acute coronary syndromes (ACS). The doses used are as follows:

- Aspirin 300 mg loading dose, 100-150 mg daily
- Clopidogrel 300-600 mg loading dose, 75 mg daily
- Ticagrelor 180 mg loading dose, 90 mg BD

When can the regimen be stopped?

The timing of DAPT is dependent on the risk of bleeding (high vs low) and if the patient has stable CAD vs an ACS (Figure 1).

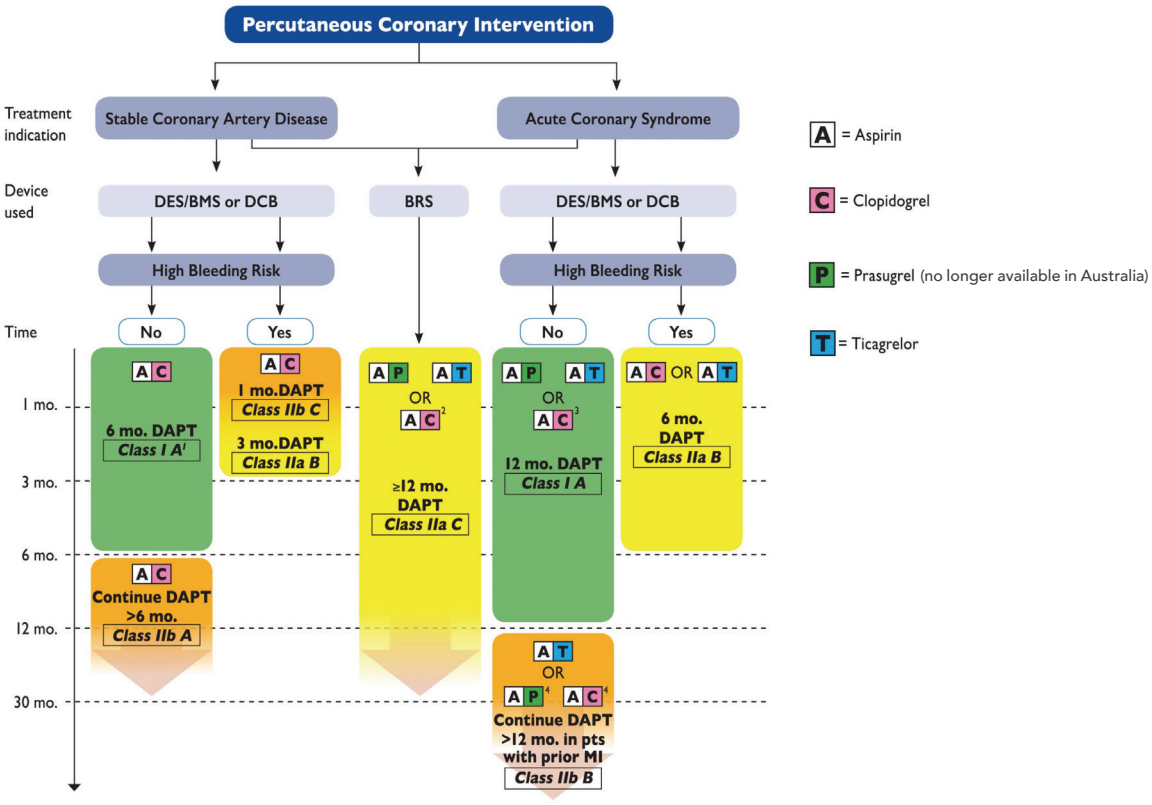

Figure 1. Algorithm for dual antiplatelet therapy (DAPT) in patients treated with percutaneous coronary intervention.

High bleeding risk is considered as an increased risk of spontaneous bleeding during DAPT (e.g., PRECISE-DAPT score ≥25).
Treatments presented within the same line are sorted in alphabetic order, no preferential recommendation unless clearly stated otherwise.
1: After PCI with DCB 6 months. DAPT should be considered (Class IIa B).
2: If patient presents with Stable CAD or, in case of ACS, is not eligible for a treatment with prasugrel or ticagrelor.
3: If patient is not eligible for a treatment with prasugrel or ticagrelor.
4: If patient is not eligible for a treatment with ticagrelor.

BMS = bare-metal stent; BRS = bioresorbable vascular scaffold; DCB = drug-coated balloon; DES: drug-eluting stent.

Update on antiplatelet agents (continued)

In stable CAD, patients who have undergone a percutaneous coronary intervention (PCI) should have 6 months of DAPT, and if no bleeding issues arise, this can be extended up to 30 months.

In stable CAD, patients at high risk of bleeding who have undergone PCI should have 3 months of DAPT. If there is a need for urgent surgery, DAPT can be ceased as early as 1 month.

In ACS patients who have undergone coronary stenting, DAPT should be continued for at least 12 months and if no bleeding issues arise, this can be extended up to 3 years and possible more. The optimal duration of extended DAPT in this circumstance is unclear in ACS patients at high bleeding risk, so DAPT should be continued for 6 months.

4. What if the patient is already on anticoagulation for atrial fibrillation (AF) or other reason?

Unless there is a contraindication, most patients with AF should be on a direct oral anti-coagulant (DOAC) like rivaroxaban, apixaban or dabigatran. In elective PCI, the DOAC is withheld 2 days pre-procedure.

Dual antiplatelet therapy with aspirin and a P2Y12 inhibitor should be given to all patients during the peri-PCI period (up to 1 week after PCI, at the discretion of the treating physician), after which the default strategy is to stop aspirin and continue treatment with a P2Y12 inhibitor, preferably clopidogrel, in combination with a DOAC (i.e., double therapy). In patients at increased thrombotic risk who have an acceptable risk of bleeding, it is reasonable to continue aspirin (i.e., triple therapy) for up to 1 month. Double therapy should be continued for 6-12 months depending on the ischaemic and bleeding risk. In the long-term, patients should discontinue antiplatelet therapy and receive oral anticoagulation alone.

5. What if a patient needs a procedure or an operation?

This is always a complex question balancing the bleeding risk, nature and urgency of the surgery versus the ischaemic risk and time since PCI. Whether DAPT should be continued or discontinued, or if the surgery should be performed, aspirin alone adds a further layer of complexity.

In general, DAPT cessation is likely to be safe 6 months post-PCI and surgery is not recommended in the first month post-PCI. Between 1-5 months, the various factors listed above need to be weighed up.

Wherever possible, surgery should be performed on aspirin. Possible exceptions to this recommendation include intracranial procedures, transurethral prostatectomy, intraocular procedures, and operations with extremely high bleeding risk.

Ticagrelor and clopidogrel should be ceased 3 and 5 days pre-op, respectively. Antiplatelet agents should be recommenced 1-4 days post-op.

1. Valgimigli M, Bueno H, Byrne RA, et al. Eur Heart J 2018;39(3): 213–260.

2. Angiolillo DJ, Bhatt DL, Cannon CP, et al. Circulation. 2021;143:583–596. https://doi.org/10.1161/CIRCULATIONAHA.120.050438

Clinic locations

All clinics have emergency appointment timeslots available for same-day referrals. Contact any of our clinics directly for more assistance.

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Suite 213, Q Central,
10 Norbrik Drive,
Bella Vista NSW 2153

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15-17 Kildare Road,
Blacktown NSW 2148

Tel: 02 9422 6050 | Fax: 02 9676 8900

Chatswood

Suite 901, Level 9, Tower B,
799 Pacific Highway,
Chatswood NSW 2067

Tel: 02 9422 6040 | Fax: 02 9411 1904

Parramatta

Level 5 Suite 501, B1 Tower,
118 Church Street,
Parramatta NSW 2150

Tel: 02 9422 6060 | Fax: 02 9635 1247

Sydney City

Suite 102, Level 1,
37 Bligh Street,
Sydney NSW 2000

Tel: 02 9422 6080 | Fax: 02 9422 6081

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Call (02) 9966 770 for specialist advice

Our team

We have experienced cardiologists in all major sub-specialties to provide the highest quality of patient care. We also have specialists in related fields including endocrinology and respiratory medicine.

Our Sydney Cardiology team includes:

Dr James Wong

Specialising in general cardiology, prevention of coronary artery disease and hypertension.

Dr Abhinav Luhach

Specialising in general adult cardiology, cardiac CT, and preventive cardiology.

Dr Suja Padmanabhan

Specialising in diabetes and general endocrinology with a special interest in diabetes in pregnancy and women's health.

Dr Gunjan Aggarwal

Specialising in general adult cardiology and non-invasive cardiac imaging, particularly echocardiography and cardiac CT.

Dr Andrew Terluk

Specialising in general cardiology with an interest in cardiomyopathy in the setting of cancer.

Dr Tracy Smith

Respiratory and sleep physician specialising in respiratory disease with a special interest in respiratory failure due to lung or heart disease.

Dr Ru-Dee Ting

Specialising in general and interventional cardiology, including cardiac haemodynamic studies and complex coronary intervention.

Dr Fiona Foo

Specialising in general and interventional cardiology with an interest in heart disease affecting women and sports cardiology.

Dr Bill Petrellis

Specialising in general adult cardiology and electrophysiology, including atrial fibrillation and device implantation.

A/Prof Martin Brown

Specialising in advanced heart failure, pulmonary hypertension, and transplant cardiology.

Our Parramatta Clinic is proud to welcome respiratory specialist Dr Tracy Smith

Dr Tracy Smith is Staff Specialist in Respiratory and Sleep Medicine and the lead physician for the Respiratory Integrated Care program at Westmead Hospital. She co-leads a Breathlessness Clinic which aims to help people living with breathlessness enjoy a full and enriching life. Her work in this clinic has earned significant research grant support from a number of funding bodies including HCF, Westmead Hospital Research Education Network, and the NSW Health Translational Research Grant Scheme.

Dr Smith prides herself on delivering comprehensive respiratory assessments and management plans, delivered with compassion and care. She is experienced in all aspects of clinical Respiratory and Sleep Medicine. Her particular clinical interests are COPD and asthma. She is also interested in the assessment and management of people who are breathless but do not yet have a clear diagnosis.

Dr Smith is frequently invited to speak at local, national and international conferences on topics in Respiratory Medicine, especially COPD and breathlessness. She has published a number of research articles and continues to be involved in teaching, with an appointment to the University of Sydney as a Conjoint Clinical Senior Lecturer.

Breathlessness with a focus on COPD, asthma and ILD

Dr Tracy Smith

Specialising in respiratory disease with a special interest in respiratory failure due to lung or heart disease.

Breathlessness

Breathlessness is a common presentation. At times, it will be a medical emergency, but more often breathlessness will be longstanding. This article focuses on the initial assessment of breathlessness which has been present for more than 8 weeks.

COVID has changed everything in life and consults are no exception. As society opens up, and we return to seeing more patients face-to-face, practices will need to consider altering longstanding procedures to consider this differential with all the infection control implications it brings.

Patient history

History of the presenting complaint

Progression of longstanding breathlessness is insidious as changes are gradual and met with increasing accommodation over time. To get at this aspect of the history, ask about changes in exercise tolerance. Some patients will be able to immediately answer this question, others benefit from having this question anchored to an activity in daily life (walking up the stairs, walking the dog, making the bed, mowing the lawn, etc.) and being asked how their breathlessness has changed with this activity over a relatively long period of time (6-12 months). **Example: If you think back to last Christmas, how hard was it to do x activity then? How has it changed?**

In some patients, breathlessness may be more episodic – but again, the timeline is important. Episodic breathlessness over a few days, perhaps weeks, may suggest pulmonary embolism, especially if there are other risk factors present. Breathlessness from asthma is classically episodic and associated with triggers for bronchospasm, though vocal cord dysfunction is an important differential. Patients with underlying respiratory disease may present with breathlessness which appears to be episodic, but is in fact related to exacerbations of chronic obstructive pulmonary disease (COPD) or interstitial lung disease (ILD).

Associated symptoms

Associated symptoms are important in coming to a provisional diagnosis, and will guide selection of further investigations and management. The following is a table with common associated symptoms and differentials to consider.

Table 1. Common symptoms and differentials

Symptom	Differential consideration
Ischemic pain	AMI/angina
Cough and phlegm	Bronchitis Pneumonia Exacerbation of COPD/asthma Bronchiectasis
Dry cough	ILD
Pleuritic pain	Pneumonia Pulmonary embolism Fractured rib
Paroxysmal nocturnal dyspnoea	Congestive heart failure (orthopnoea less specific)
'Funny pain'	Asthma Anxiety Breathing pattern disorder
Expiratory wheeze (heard better with stethoscope than without)	COPD/asthma
'Inspiratory wheeze' (heard best without a stethoscope)	Vocal cord dysfunction
Heamoptysis	Infection Cancer Pulmonary embolism
Unsatisfied inspiration ('I just can't get a good breath in')	ILD Breathing pattern disorder

Past history, smoking, and exposures

A personal history of asthma or eczema in childhood points to asthma as the diagnosis, with a family history of asthma also raising suspicion. A current history of sinusitis or hay fever is also suggestive.

Tobacco smoking is clearly a big issue for respiratory disease. The personal, social, and exposure history is particularly important in a breathless patient. Current smoking is important, including an assessment of pack year history (20 cigs/day for 1 year = 1 pack year). However, understanding pack year history and recency of quitting is equally important and may become more so if computer tomography (CT) scans for cancer screening are approved by Medicare in coming years. Asking about cannabis or shisha smoking and vaping are also important considerations as these contribute to respiratory disease.

The nature of asbestos exposure has changed with increasing regulation. While previously asbestos exposure was associated with working in mining, building, or asbestos board manufacturing, patients who present with asbestos-associated disease are often the children of these workers (who often recall a parent coming home covered in 'white dust') or those exposed as part of DIY home renovations. Silica exposure is still seen occasionally in people who worked in plumbing construction related to digging or blasting Sydney sandstone. There is an evolving epidemic of silicosis in people who work in cutting and installing artificial stone for kitchen and bathroom installation/renovation.

Breathlessness (continued)

Finally, in a multicultural community like Western Sydney, country of birth and year of emigration is important. People from tuberculosis-endemic areas are at risk of reactivation, which appears to be most likely in the 3-5 years following emigration, or if there is significant immunosuppression (particularly renal failure and use of TNF-alpha inhibitors like infliximab).

Physical examination is important in coming to a differential diagnosis. The physical exam will most often confirm what is suspected from the history; however, occasionally a finding will pop up (fine basal crackles → ILD; murmur → mitral regurgitation or aortic stenosis, etc.) which change the complexion of the consultation.

Diagnostic tests in breathlessness

Investigations will be directed by the history and examination findings. In general, full blood count (FBC), electrocardiogram (ECG), chest xray (CXR), and spirometry are a good place to start. Sometimes a CT chest or further cardiac investigations might appropriate. Referral will be required for more sophisticated lung function testing.

Spirometry

If you are confident with spirometry you can skip to Table 2 for a cheat sheet on interpretation.

While many practices will have a spirometer, confidence with conducting and interpreting spirometry is not widespread. In addition, the Medicare rebate is low and it's fiddly/time consuming – if this were not enough, spirometry is an aerosol-generating procedure in the era of COVID which makes it all the more tricky. At the time of publication spirometry can be done on people who have a negative swab for COVID in the last 72 hours. Staff should wear personal protective equipment i.e., mask, gown, goggles and gloves.

Some GPs prefer a trial of treatment with inhaled therapy, particularly in patients with risk factors for COPD (predominantly current or former smoking), rather than undertake spirometry; however studies suggest that ~30% of patients in a general practice population with a label of COPD do not meet diagnostic criteria when spirometry is undertaken.

The National Asthma Council provides detailed instructions on how to conduct and interpret spirometry. Essentially, the patient should be seated for the procedure, take a maximal breath in and exhale until their lungs are completely empty. Contraindications to this procedure exist and include: wounds from recent operations, aneurysms, recent cataract surgeries, etc. Clinicians should offer patients the chance to empty bowels/bladder prior to spirometry.

There are 3 numbers that matter with spirometry.

FEV1: Forced expiratory volume in 1 second.

FVC: Forced vital capacity.

FEV1:FVC ratio.

The FEV1 is the the volume of air forcefully expired from full lungs during the first second of an expiratory manoeuvre.

The FVC is the volume of air exhaled from full inspiration to full expiration. important to note that spirometry is a *FORCED* manoeuvre, and most patients will need significant encouragement to maximally empty their lungs (as a guide, their face should turn a shade of puce. While the FVC is important, it's the FVC percent predicted that matters. We know what a patient's FVC should be based on their age, height, weight, gender and ethnicity. FVC percent predicted is then the patients measured FVC divided by their predicted FVC, usually expressed as a percentage. Modern electronic spirometers will generate this number so long as the inputs are right.

The FEV1:FVC ratio is simple arithmetic. Take the FEV1 in litres and divide by the FVC in litres. This can be expressed either as a decimal or a percentage. Normal is more than 0.7 or 70%, abnormal is less than or equal to 0.7 or 70%. There has been recent discussion of using a lower limit of normal, rather than a fixed ratio, and there are some good reasons for this, but this is a discussion for a future article.

Table 2. Spirometry interpretation

	FEV1:FVC ratio Normal >70%.	FEV1:FVC ratio Reduced ≤70%
FVC – normal ≥80% predicted	Normal	Obstructive
FVC – reduced <80% predicted	Restrictive	Mixed

Look at the ratio. Put the index finger of your right hand in the appropriate box. Next, look at the FVC percent predicted. Put the index finger of your left hand in the appropriate box. Slide your index fingers to where they meet and you have the interpretation of the spirometry.

For patients with obstructive spirometry, it's likely the diagnosis is COPD, though other conditions (active and/or poorly controlled asthma, or bronchiectasis for example). Restrictive spirometry may result from poor effort, any of the fibrosing interstitial lung diseases (e.g., idiopathic pulmonary fibrosis, asbestosis, silicosis, etc.) or neuromuscular disease involving the chest/diaphragm. Mixed spirometry is likely to be COPD, particularly more advanced disease, but there are other potential diagnoses.

Imaging

While the CXR has long been the mainstay of respiratory imaging, it is increasingly replaced by CT scanning. There are 3 basic CT scan options in respiratory medicine (Table 3), each with its own indications and benefits. These are presented with mediastinal 'windows' (lungs look black, can see good detail of nodes/other structures in the mediastinum and pleura) and lung 'windows' (good detail in the lungs, other structures a bit indistinct).

Table 3. CT scan options in respiratory medicine

	Details	Good for	Bad because
Conventional CT chest	Requires contrast. Contrast is seen throughout pulmonary vasculature. Each 'slice' is relatively thick, but 'slices' are close together.	Spotting cancer and infection. Can pick out what is nodes and what is vessels in the mediastinum/ hilum → good for lymphadenopathy.	As each 'slice' is thick, can miss details of interstitium.
High resolution CT (HRCT) chest	No contrast. Each 'slice' is thin, but 'slices' can be far apart.	Interstitium/ fine detail on lung windows. Should include expiratory views (look for gas trapping) and prone views (atelectasis at bases goes away on proning).	May miss small nodules because they fall between slices. Hard to tell nodes from vessels without contrast.
CT pulmonary angiogram (CTPA)	High contrast load. Contrast in pulmonary arteries only.	Good for pulmonary embolism. As a bonus, you get lung windows, but not as good definition as a HRCT.	Volume of contrast → more potential for renal toxicity. Getting contrast 'just right' to get a good scan is tricky.

When to refer, and what to do before you do so

I'm delighted to see any patients with breathlessness, particularly if the patient appears to have a serious cause for their breathlessness or breathlessness appears out of proportion to the clinical findings you have elicited. Things I really value on the referral/prior to referral are:

- A sense of the duration of breathlessness, how many times you've seen the patient and what you have already done
- What you are worried about – cancer, ILD, asthma, progressive breathlessness, etc.
- Up-to-date medication list
- Outcome if they have seen a different specialist (e.g., cardio, renal, endo, etc.)
- Any basic bloods (esp. FBC, EUC, etc.)
- Any relevant imaging
- Spirometry

Summary

- As in all of medicine, clinical history and clinical judgement remain core to caring for patients with breathlessness.
- Elements from the clinical history combine to give a good sense of the underlying diagnosis.
- For the experienced clinician, physical examination most often reveals findings expected from the history, but is essential as unexpected findings may significantly change the direction of the consultation.
- While spirometry isn't as well remunerated as anyone would like, and is frankly a bit of a pain, the gain is ensuring that the right patient gets the right medication, rather than relying on a trial of treatment which may be inappropriate.
- The right CT modality depends on the most likely diagnosis –
  - conventional CT chest if cancer is a concern,
    HRCT is best for interstitial lung disease, and
  - CTPA is great for PE. A sense of what you have done and what you are worried about will help to make the most of the initial consultation to expedite best care.

Our services

Sydney Cardiology is a world class comprehensive cardiology service, delivered with expertise and experience. Using state of the art diagnostic equipment in all five clinic locations, Sydney Cardiology strives to provide exemplary outcomes for long term patient care.

Urgent access

We provide same-day urgent appointments and 24/7 on-call support for GPs with a dedicated phone number, **02 9966 7700**.

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Including stress-echocardiography, echocardiography, holter monitor studies, ambulatory blood pressure studies, coronary calcium score, dobutamine stress echo, electrocardiogram and event monitor recording.

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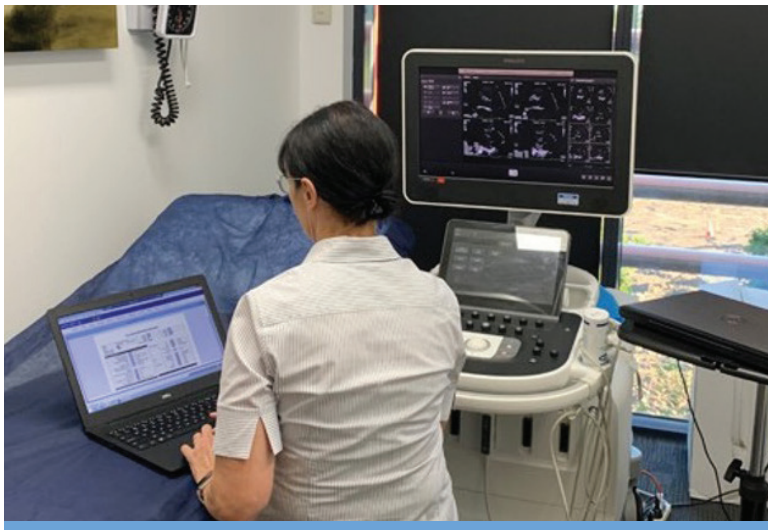
Cardiac procedures

Including coronary angiography, cardiac biopsies, right heart catheterisation, transesophageal echocardiogram and coronary angioplasty.

Including renal and lower limb angioplasty, ankle brachial index and SphygmoCorR central blood pressure testing.



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In-hospital care

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Sydney Adventist Hospital
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Norwest Private Hospital
Bella Vista

Macquarie University Hospital
North Ryde

Northern Beach Hospital
Frenchs Forest

Patient fees

Sydney Cardiology is a private clinic however there are no out of pocket costs for Pensioners and Department of Veterans Affairs patients.

Referrals

To request a referral pad, click here.

Dietary interventions and cardiovascular disease

The following articles first appeared on Australian Doctor's new Cardiology Group that brings GPs and specialists together to discuss hot topics.

Dr Gunjan Aggarwal

Practising at Bella Vista, Blacktown, Parramatta, and Sydney City Cardiology.

Red yeast rice - nutraceutical of promise for statin intolerant patients?

Hypercholesterolemia is an important modifiable risk factor for the development of atherosclerotic plaque. Despite there being a number of effective pharmacologic treatments, a number of patients are either intolerant of therapy such as statins or are not eligible for PCSK9 inhibitors based on current PBS criteria.

There is also an increasing recognition of the importance of inflammation in the development of coronary artery disease and therapies that reduce inflammation have shown some benefit as a therapy for addressing atherosclerosis.

As such, there is growing interest in nutritional non drug approaches to both address hyperlipidemia and also combat systemic inflammation. Red yeast rice (RYR) is such a product that has historically been used in traditional Chinese medicine (xuezhikang). It is created by fermenting yeast (monascus purpureus) in red rice which then gives rise to a complex of substances called monacolins. One of these monacolins is monacolin K which is an inhibitor of HMG-CoA reductase the rate limiting enzyme of cholesterol synthesis. It is structurally very similar to lovastatin.

RYR has demonstrated efficacy when given at a dose of 1200 mg/day and lowers low-density lipoprotein cholesterol (LDL-C) by an average of 1 mmol/L after 8 weeks of therapy. It is equivalent in potency to pravastatin 40 mg daily or lovastatin 20 mg daily. There is some evidence from a Chinese study that it is associated with a reduction in coronary events and mortality post MI in a secondary prevention setting[1].

RYR also has beneficial effects on endothelial function and leads to a reduction in markers of inflammation such as hsCRP by up to 28%[2]. It reduces TNFα by down-regulating the NF-κB activity and reducing the intracellular production of reactive oxygen species in smooth muscle cells by promoting and stabilising the expression of endothelial nitric oxide synthase[3].

Out of all the healthfoods currently marketed in Australia as having beneficial effects on cardiovascular health, RYR is perhaps the one best supported by evidence. It remains a promising option for truly statin intolerant patients who are not candidates for other therapies such as PCSK9 inhibitors and for whom limited other therapeutic options exist.

References: 1. Lu Z, KouW, Du B, et al. Effect of Xuezhikang, an extract fromred yeast Chinese rice, on coronary events in a Chinese population with previous myocardial infarction. Am J Cardiol 2008;101(12):1689-1693. 2. Li JJ, Hu SS, Fang CH, et al. Effects of xuezhikang, an extract of cholestin, on lipid profile and C-reactive protein: a short-term time course study in patients with stable angina. Clin Chim Acta 2005;352(1–2):217-224. 3. Ruscica et al. Impact of nutraceuticals on markers of systemic inflammation: Potential relevance to cardiovascular diseases – A position paper from the International Lipid Expert Panel (ILEP). Progress in Cardiovascular Diseases 67 (2021) 40–52.

Nutritional recommendations for hypertriglyceridemia

For years the cardiology community have focused to a large extent on LDL-C and not paid much attention to triglycerides. There is emerging evidence from mendelian randomisation and epidemiological studies about the importance of elevated triglycerides contributing to atherosclerosis and residual risk of events via an increase in remnant cholesterol and a change in morphology to small dense LDL particles[1].

The American College of Cardiology has recently published an expert consensus statement summarising the Management of ASCVD Risk Reduction in Patients with Persistent Hypertriglyceridemia. They outline the diagnostic evaluation and treatment of elevated triglycerides.

They emphasise the key importance of modification of diet and lifestyle changes as a cornerstone for reducing serum triglycerides. They also summarise the role of improving diabetic control, excluding secondary causes and pharmacologic therapy such as statins, fibrates, and omega-3 fatty acids (especially purified EPA at a dose of 4 g/day).

Their key dietary recommendations depending on the degree of elevation of triglycerides include[2]:

- Recommended weight loss goal of 5-10%.
- Restrict, or preferably abstain, from alcohol consumption.
- 150-minutes of moderate intensity exercise, or 75-minutes of high-intensity exercise a week.
- Alteration in macronutrient profile such as carbohydrate restriction and increased protein in the diet (>30% of total energy). Very low carbohydrate diets (<10% of total energy or calories) are more effective in reducing triglycerides than diets low in fat and higher in carbohydrates.
- Intermittent fasting (alternate day or periodic) and or time restricted feeding can lead to modest weight loss and triglyceride reduction.
- Reduce intake of simple sugars, desserts containing high fructose corn syrup, sugar sweetened beverages, fruit juice.
- Limit intake of fruits with a high glycemic index such as pineapples, mango and watermelon (if triglycerides are more than 5.65 mmol/L)
- Encourage intake of vegetables but limiting intake of vegetables with a high glycaemic index such as potato, yam and parsnip (if triglycerides are more than 5.65 mmol/L)
- Recommend eating more than 2 servings of fatty fish such as salmon, trout or tuna.
- Eliminate sugar sweetened dairy.
- Encourage intake of poultry or lean meats instead of processed meats.
- Replace white grains with fibre rich wholegrains such as brown rice or bread.
- Emphasise tree nuts (almonds and walnuts) and peanuts without added salt.
- Emphasise legumes such as lentils, tofu and chickpeas.
- Encourage olive oil instead of lard, coconut oil or butter (especially if serum cholesterol is also elevated as high saturated fat diets will increase serum LDL-C and LDL-P concentration and increase risk of heart disease).

We would be interested in your clinical experiences. Click here to share lifestyle strategies you have found to work best for your patients with elevated triglycerides.

References 1. Ference et al. Association of Triglyceride-Lowering LPL Variants and LDL-C-Lowering LDLR Variants With Risk of Coronary Heart Disease. JAMA 2019 Jan 29;321(4):364-373. 2. Virani et al. 2021 ACC Expert Consensus Decision Pathway on the Management of ASCVD Risk Reduction in Patients With Persistent Hypertriglyceridemia. JACC. Article in press.

Dietary interventions (continued)

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What is the latest in relation to fish consumption and cardiovascular disease?

For many years health professionals have been advocating fish consumption as part of healthy diet, specifically in relation to reducing the risk of cardiovascular disease. There has also been a multitude of trials examining the role omega-3 fatty acid supplementation has in reducing cardiovascular disease (CVD) burden, as omega-3 fatty acids are not able to be produced naturally by the body.

Unfortunately, despite initial enthusiasm subsequent randomised control trials have shown inconsistent and largely negative results for omega-3 fatty acids supplementation in separate trials involving primary prevention[1], diabetics without established CVD[2] and statin-treated patients at high risk of CVD[3]. In contrast, the REDUCE-IT[4] trial did show a favourable benefit but it used a 2 g of icosapent ethyl twice daily (high dose purified EPA ester) in statin-treated patients with established CVD or risk factors and hypertriglyceridemia.

Local and international guidelines continue to recommend a regular consumption of fish. A recent meta-analysis by Mohan et al,[5] published in JAMA Internal Medicine looked at the association between fish consumption and risk of CVD or mortality.

The authors pooled analysis from 4 international cohort studies of 191 558 people from 58 countries. The main outcome being analysed was mortality and major CV events. The meta-analysis included one very large observational study (PURE) of more than 147 000 patients, most of whom did not have established CVD, and 3 smaller prospective studies where patients had established CVD.

Of the pooled patient data, the mean patient age was 54 years and 48% were male. The median follow up duration was 7.5 years. Patients were divided into quartiles depending on their fish intake, ranging from <50 g/month in the lowest quartile to >350 g/week in the highest quartile.

In the PURE study there was no statistical difference in the rates of major CVD or mortality between the highest and lowest quartiles of fish consumption. However, in the 3 studies looking at patients with established vascular disease, there was a benefit in fish consumption of >175 g/week (~2 servings). A hazard ratio of 0.84 for major CVD and HR of 0.82 of total mortality in favour of fish consumption of >175 g/week compared to <50 g/month was shown. There was no added benefit with fish consumption of >350 g/week. Fish with higher levels of omega-3 were associated with lower risk of CVD, whilst other fish were neutral for their effect.

The authors concluded that a minimum fish intake of 175g/week is associated with a lower risk of major CVD and mortality among patients with prior CVD but not in the general population.

Whilst this study supports fish consumption and is broadly consistent with current recommendations, this is yet to be conclusively established by randomised control trials.

In Australia, the Heart Foundation recommends 2-3 servings of fish per week.

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4. Bhatt D et al. Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia. N Engl J Med 2019; 380:11-22

5. Mohan D et al. Associations of Fish Consumption With Risk of Cardiovascular Disease and Mortality Among Individuals With or Without Vascular Disease From 58 Countries. JAMA Intern Med. 2021;181(5):631-649