Spring 2021

GP Connect

Supporting best practice in cardio-metabolic health

Sydney Cardiology are an essential service, and we operate as a COVID-safe business. All clinic locations remain open and fully operational.

Sydney Cardiology

From the editor – Dr Gunjan Aggarwal

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

Click here to learn more about Dr Aggarwal

Welcome to the spring edition of GP Connect. This issue focuses on the importance of accurately evaluating cardiovascular risk by using diagnostic tools such as calcium scoring and implementing novel evidence based strategies to reduce residual cardiovascular risk.

Newer strategies for lowering residual risk covered in this issue include the concept of dual pathway inhibition which combines antiplatelet drugs with lower doses of direct acting oral anticoagulants (rivaroxaban at a dose of 2.5 mg bd) for patients with either polyvascular disease, cardiovascular disease or peripheral vascular disease with additional risk factors.

There are also several classes of drugs, such as SGLT2 inhibitors and GLP 1 agonists, that simultaneously reduce the risk of secondary cardiovascular events and ameliorate the advance of renal disease. The result has been a paradigm shift in the management of cardio-renal-metabolic conditions such as diabetes. Their use in diabetic and obese patients is nicely summarised in an article by Dr Padmanabhan, an endocrinologist with Sydney Cardiology.

Although GPs have successfully been using these drugs for some time, cardiologists will also now need to be familiar with using SGLT2 inhibitors as this revolutionary class of drugs is proving to be a game changer in the management of patients with heart failure with reduced ejection fraction (HFrEF) by producing remarkable additional reductions in mortality and heart failure hospitalizations. In other exciting news the EMPEROR – Preserved trial that tested the efficacy of empagliflozin in patients with heart failure with preserved ejection fraction (HFpEF) with an EF >40% has reported a positive result in terms of significantly reducing the rate of cardiovascular death or hospitalization by 21%. This will potentially meet an enormous unmet need that exists currently in the treatment of heart failure by providing the first ever effective therapy for HFpEF, thus broadening access to thousands of patients for whom currently limited treatments exist.

In this issue

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I hope you enjoy this edition of GP Connect. I would also like to take this opportunity to thank you and your frontline staff for your hard work and dedication in steering the community safely through the Covid-19 pandemic by continuing to provide ongoing care in these challenging and unprecedented times. I am hopeful that 2022 will represent a new beginning, and we will emerge stronger having survived this difficult period. Stay safe.

Sincerely

Dr Gunjan Aggarwal

SGLT2 inhibitors and GLP1 agonists in the management of type 2 diabetes

Dr Suja Padmanabhan

Endocrinologist (Parramatta Rooms)

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

Click here to learn more about Dr Padmanabhan

The last 5 years have seen a number of new and exciting treatments available for the management of type 2 diabetes, with benefits beyond optimisation of glycaemic control. SGLT2 inhibitors and GLP1 agonists offer opportunity for weight loss, reduction in cardiovascular risk and mortality and delaying progression to chronic kidney disease. Thus the choice of agents for the treatment of type 2 diabetes should be dictated by an individual's risk factor profile in addition to HbA1C.

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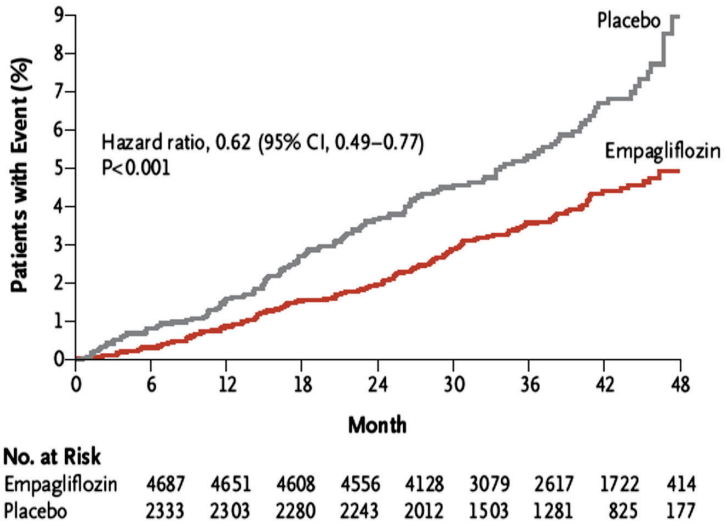

Figure 1: *Mortality benefit in patients treated with SGLT2 inhibitor*

SGLT2 inhibitors

How do they work?

SGLT2 inhibitors are oral agents taken once a day with or without food, and are available alone or in combination with Metformin or a DPP4 inhibitor (Table 1). The mechanism of action is through inhibition of the SGLT2 glucose transporter in the proximal renal tubule which reabsorbs 90% of filtered glucose.

What are the benefits to your patients?

- Decrease in HbA1c of 0.5-1.0% (more with higher baseline HbA1c)
- 30% reduction in heart failure hospitalisation
- 30-40% reduction in all cause and cardiovascular mortality*
- 15% reduction in cardiovascular events*
- 30-50% reduction in progression of renal disease
- 2-3 kg weight loss
- 6 mmHg BP reduction

* Only empagliflozin studies showed a significant reduction in cardiovascular events and mortality (Figure 1). Additionally these benefits may not be generalisable to patients without type 2 diabetes or an established history of cardiovascular disease.

What should you warn patients of?

- Increased risk of urinogenitary infection
- Increased polyuria
- Dizziness and dehydration (may need to reduce dose of other medications e.g. diuretics)
- Euglycemic DKA (highest risk with surgery, fasting or GI illness)

GLP1 agonists

How do they work?

GLP1 agonists are injectable therapies which stimulate the GLP1 receptor enhancing oral glucose stimulated insulin secretion "the incretin effect". In addition to insulin secretion GLP1 agonists decrease glucagon concentrations, slow gastric emptying, increase satiety and decrease free fatty acid concentrations making them beneficial for weight loss (Figure 2).

What are the benefits to your patients?

- Decrease in HbA1c of up to 1.5% (more with higher baseline HbA1c)
- Weight loss 3-6.5 kg over 1 year
- 10-25% reduction in the composite risk of a cardiovascular event, mortality or non-fatal stroke (driven primarily by reduction in stroke)
- Small reductions in BP and Lipids

What should you warn patients of?

- Gastrointestinal side effects such as nausea, vomiting and diarrhoea are most common and usually settle after a few weeks. Starting at low doses and increasing slowly reduces the risk
- Rarely pancreatitis, gall stones and worsening diabetic retinopathy can occur

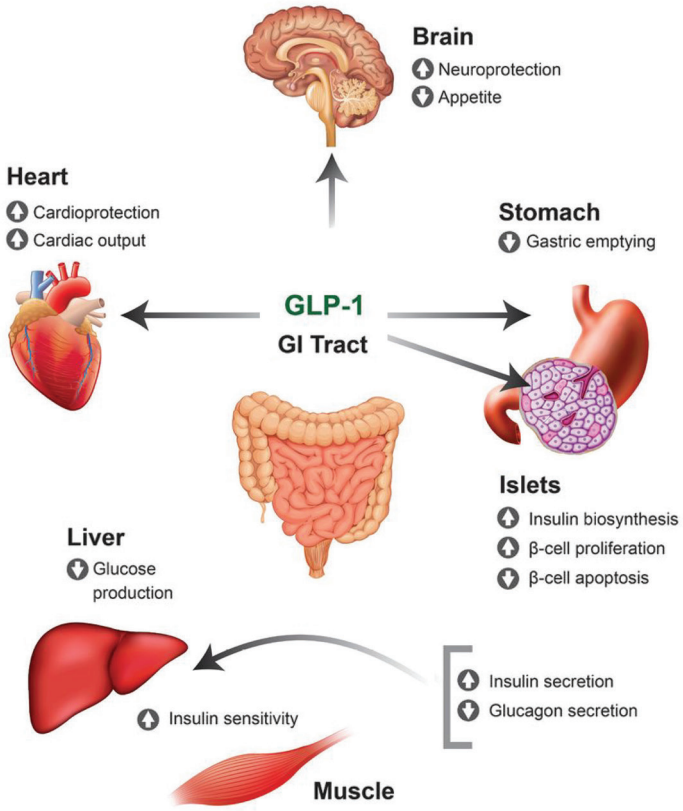

Figure 2: Mechanism of action GLP1 Agonists

Table 1: Current PBS Listed Indications for SGLT2 Inhibitors and GLP1 Agonists available in Australia

	Dose	Combinations	PBS Indication
SGLT2 I			
Empagliflozin (Jardiance)	10-25mg daily	(Jardiamet, Glyxambi)	Add on to 1. Metformin and / or Sulphonylurea 2. Insulin AND HbA1c > 7% **Not PBS subsidised for monotherapy or use with GLP1 agonist*
Dapagliflozin (Forxiga)	5-10mg daily	(XigDuo, Qtern)	
Ertugliflozin (Steglatro)	5-15mg daily	(Segluromet, Steglujan)	As above but not subsidised for use with Insulin
GLP1 agonists			
Exenetide	BD	-	Add on to 1. Metformin and Sulphonylurea (or just Metformin if Sulphonylurea not tolerated) 2. Insulin AND HbA1c > 7%
Dulaglitide	weekly	-	
Semeglutide	weekly	-	As above

Case Study: Raj*

56-year-old man with type 2 diabetes

HbA1c: 8.6%

Body mass index: 31 (with central adiposity)

Raj was diagnosed with diabetes 10 years ago, and he has a past history of myocardial infarction 2 years ago. He is currently treated with metformin 2 grams daily and leads a sedentary lifestyle. He has tried Gliclazide in the past, but this was not well tolerated.

What changes would you make to Raj's treatment to help him lower his HbA1c?

Raj needs to address his lifestyle risk factors – particularly his low activity levels. Changes also need to be made to his pharmacotherapy. He is at significant and ongoing risk of cardiovascular disease and his HbA1c needs to be lowered. On this basis, Raj would benefit from the addition of empagliflozin, an SGLT2 inhibitor which has been shown to significantly reduce cardiovascular events and mortality, in addition to lowering HbA1c.

6 months later, Raj has made significant improvements – he is incorporating exercise into his daily routine in the form of walks in the morning before work, and he is taking steps to improve his diet. His lifestyle changes, coupled with the addition of empagliflozin to his treatment, has resulted in a lower HbA1c, but his latest result is still above target at 7.8% and he is finding it difficult to lose weight.

What changes would you make to Raj's treatment to help him attain a target HbA1c <7%?

The addition of a GLP1 agonist such as dulaglitide or semaglutide once weekly may help to reduce his HbA1c further. Additional benefits of adding a GLP1 agonist are a reduction in appetite and weight loss. At this time, GLP1 inhibitors are not reimbursed in combination with SGLT2 inhibitor, so Raj would be prescribed the GLP1 agonist and continue the SGLT2 inhibitor on a private script (which would be significantly cheaper than the GLP1 agonist). If Raj is unable to pay for a private script or is not keen to commence injectable therapy, a DPP4 could be added to the SGLT2 in one of the available combination medications (Glyxambi) which would be more cost effective.

* Image is not a real patient. Name has been changed to preserve anonymity.

References: Zinman et al. Empagliflozin Cardiovascular Outcomes and Mortality in Type 2 Diabetes. NEJM 2015, Hinen D. Glucagon like peptide 1 receptor agonists for type 2 diabetes. Diabetes Spectrum 2017.

Our Team

We have experienced cardiologists in all major sub specialties to provide the highest quality of patient care.
Our Sydney Cardiology team includes:

Dr James Wong

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

Learn more...

Dr Bill Petrellis

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

Learn more...

Dr Fiona Foo

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

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Dr Gunjan Aggarwal

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

Learn more...

Dr Abhinav Luhach

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

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A/Prof Martin Brown

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

Learn more...

Dr Ru-Dee Ting

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

Learn more...

Dr Andrew Terluk

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

Learn more...

Dr Suja Padmanabhan

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

Learn more...

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**.

Non-invasive testing

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

Echo, ABP, and holter monitor-only referral services

We provide echo-only, ABP-only, and holter monitor-only referral services, with a summary report on any adverse findings.

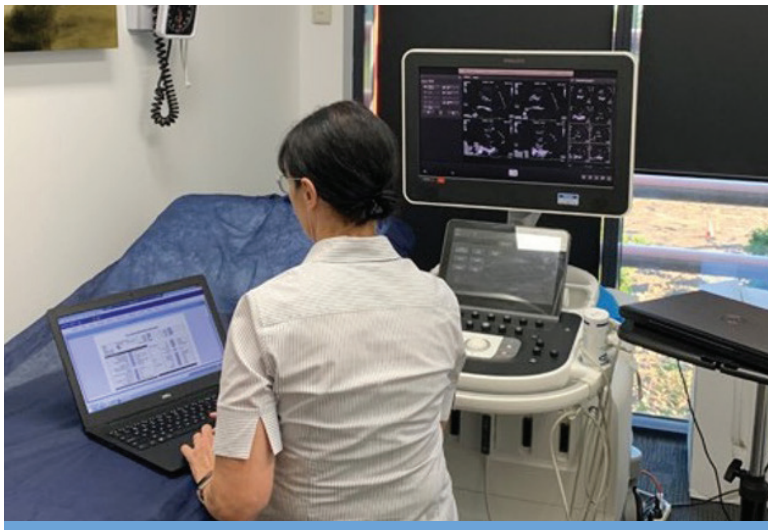
Electrophysiology

Including diagnostic electrophysiology studies, ablation of cardiac arrhythmias, cardiac device implantation, pacemakers and defibrillators, and follow up of implanted cardiac devices.

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.



ECG fax service

For urgent advice, 12-lead ECGs can be faxed to our locations.

Bella Vista - Fax: 02 9672 6214

Blacktown - Fax: 02 9676 8900

Chatswood - Fax: 02 9411 1904

Parramatta - Fax: 02 9635 1247

Sydney City - Fax: 02 9422 6081

Peripheral vascular services

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

In-hospital care

All patients with appropriate private health coverage undergoing hospital procedures, do not incur any out-of-pocket costs. Sydney Cardiology has access to leading private hospitals, including:

Sydney Adventist Hospital
Wahroonga

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

Opinion: Coronary Artery Calcium scoring (CAC)

Dr Abhinav Luhach

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

Click here to learn more about Dr Luhach

Cardiovascular risk assessment is an integral part of our daily clinical practice, for both GPs and physicians. There are a number of risk calculators that are available which rely on parameters such as age, sex lipids, BP, presence of diabetes and smoking status.

In Australia, the Absolute Cardiovascular Risk Calculator is recommended. It provides a 5-year risk estimate of cardiovascular events. It important to bear in mind that the calculator is used in a primary prevention setting and therefore does not apply to patients who have already had cardiovascular events, or those who already are known to have certain high-risk conditions (e.g., Familial Hypercholestrolaemia). It also excludes a number of cardiovascular risk factors (such as family history, ethnicity), and some comorbidities' known to increase CV risk (renal impairment, chronic inflammatory conditions) and biomarkers.

In some of these cases, a CAC can be of value in primary prevention and as a tool in appropriate settings in conjunction with traditional risk factor calculators. Recently, the National Heart Foundation published a statement on the use of CAC, which is worth reading.[1]

CAC can be used in selected, asymptomatic people deemed to be at intermediate risk using the risk factor calculator, where it may lead to a change in management. It can also be considered in patients who appear to be at low risk using the risk factor calculator, but are also known to have conditions that may lead to their risk being underestimated by the calculator.

It is important to consider issues such as radiation exposure and cost (it is not reimbursable by Medicare) when ordering a CAC and discussing with the patient. It is also worth bearing in mind that there is limited data from an Australian context, with overseas recommendations and data used to guide our approach locally. Furthermore, to date there is limited trial data to indicate using CAC to guide treatment leads to improved CV outcomes. This is still an area that requires further research.

The main benefit of CAC is that in some patients, it may reclassify their CV risk as being either low (if CAC is zero) or high. A high risk on the basis of CAC can be either because of the absolute CAC score being elevated, or alternatively the age and gender matched percentile (>75th percentile used as cut-off for high risk). Patients reclassified as high risk should then be managed according to their new risk stratification, including considering appropriate medical therapies.

It is also worth remembering that the process of coronary artery calcification does not begin until middle age in males, and about a decade later in females. Younger patients can still have coronary artery plaque, but it will likely be non-calcified in which their case may have a CAC of zero, so it could falsely reassure a patient in this context and needs to be interpreted with caution.

1. Jennings, et, al. National Heart Foundation of Australia: position statement on coronary artery calcium scoring for the primary prevention of cardiovascular disease in Australia. The MJA 2021.

Clinic locations

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

Bella Vista

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

Tel: 02 9422 6000 | Fax: 02 9672 6214

Blacktown

Suite 4,
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 Cardiology

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

Tel: 02 9422 6080 | Fax: 02 9422 6081

Sydney Cardiology offers a free after-hours consult service for GPs

Call (02) 9966 770 for specialist advice

Dr Gunjan Aggarwal

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

Empagliflozin - A new exciting treatment for heart failure with preserved ejection fraction (HFpEF).

Heart failure with preserved Left Ventricular Ejection fraction (LVEF) more than 50% (HFpEF) is an enormous clinical problem that accounts for around half of total heart failure cases. It is becoming more prevalent in our society due to an aging population and increased prevalence of comorbid conditions such as diabetes, obesity, hypertension and chronic kidney disease.

There is a paucity of effective treatments for HFpEF with a number of clinical trials for multiple drugs having failed in the past to show any substantial clinical benefit. That has now changed with the advent of SGLT2 inhibitors such as empagliflozin.

Data from the EMPEROR-Reduced[1] and DAPAHF[2] trials have already shown these drugs to be of substantial benefit in patients with Heart failure with reduced ejection fraction (LVEF <40%) (HFrEF) with or without diabetes in preventing heart failure hospitalization and cardiovascular mortality. A number of new heart failure clinical guidelines from multiple societies around the world have already incorporated SGLT2 inhibitors as essential therapy for patients with HFrEF along with the traditional drugs such as sacubitril/valsartan, beta blockers and spironolactone.

The EMPEROR-Preserved and Deliver trials are currently evaluating the utility of empagliflozin and dapagliflozin compared with placebo in patients with HFpEF with a primary endpoint of cardiovascular death or heart failure hospitalization.

The EMPEROR-Preserved results presented a few days ago has confirmed that the trial met its primary endpoint, establishing empagliflozin as the first therapy to significantly reduce the relative risk of the composite of cardiovascular death or hospitalisation for heart failure in adults, with or without diabetes, who live with heart failure with preserved ejection fraction (LVEF>40%) by a significant 21%. There was a nonsignificant 9% relative risk reduction in the incidence of cardiovascular death and most of the benefit was driven by a 27% significant reduction in the incidence of heart failure hospitalization[3].

The definition of HFpEF used in this trial (LVEF>40%) however differed slightly from its actual definition (LVEF>50%) and thus included patients in the mid range EF (40-50%). Empagliflozin did not produce a benefit in terms of heart failure hospitalisation however if LVEF was greater than 60-65%.

Empagliflozin is nevertheless a potential game changer and once approved by PBS will help meet an enormous clinical need that currently exists in the treatment of patients with HFpEF.

References: 1. Packer et al. Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure. N Engl J Med 2020; 383:1413-1424. **2.** McMurray et al. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. N Engl J Med 2019; 381:1995-2008. **3.** Anker et al. Empagliflozin in Heart Failure with a Preserved Ejection Fraction. N Engl J Med August 27, 2021.

Dual pathway inhibition – exciting new approach for reducing residual risk

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

There is an unmet need for strategies to further lower residual risk of vascular events in patients with established cardiovascular disease. Traditional approaches to reduce risk of cardiovascular events have included more aggressive management of risk factors such as hyperlipidemia (focusing on LDL-C, non-HDL-C, apo B and triglycerides), hypertension, hyperglycemia (using newer agents such as SGLT2 inhibitors and GLP 1 agonists) and targeting residual inflammation (hsCRP).

Novel strategies include targeting thrombotic risk with additional antithrombotic therapy. Single antiplatelet therapy with either aspirin or clopidogrel (if aspirin intolerant) is currently used in patients with established chronic cardiovascular disease for secondary prevention. Dual antiplatelet therapy is used with aspirin and either clopidogrel or ticagrelor in patients with recent acute coronary syndrome for up to 12 months and for at least 6 months following percutaneous coronary intervention (PCI).

Dual pathway inhibition refers to strategies that include single antiplatelet therapy such as aspirin at a dose of 100 mg daily with novel oral anticoagulants such as rivaroxaban at a lower dose of 2.5 mg bd.

A number of trials including COMPASS[1] (in a mixed population of patients with chronic coronary artery disease, peripheral artery disease or cerebrovascular disease aged more than 65 or less than 65 with 2 additional risk factors such as diabetes, active smoking, congestive cardiac failure or chronic kidney disease) and VOYAGER PAD[2] (in patients following lower extremity revascularisation for peripheral vascular disease) compared a combination of aspirin 100 mg and rivaroxaban 2.5 mg bd to aspirin 100 mg alone and have shown impressive reductions in mortality, ischemic stroke, myocardial infarction and limb amputation of around 25-50%.

Based on these results rivaroxaban 2.5 mg bd in combination with aspirin 100 mg daily is now available on the PBS as an authority script using the code 11013. The criteria for using this regimen is complex and somewhat different from the inclusion criteria in the COMPASS trial, but include patients with multivessel coronary disease (requiring previous PCI or CABG) or peripheral vascular disease (requiring surgery or stent) with one additional risk factor either diabetes, congestive cardiac failure (LVEF 30-50%) or chronic kidney disease (eGFR 15-60 ml/min). Additional information is available on the PBS website https://www.pbs.gov.au/medicine/item/12197Y and the initial prescription requires consultation with a cardiologist or physician.

Contraindications include active or high risk of bleeding, recent ischemic stroke within 1-month, previous hemorrhagic stroke, severe heart failure with EF less than 30% or eGFR less than 15 ml/min. Patients that need dual antiplatelet therapy (for recent acute coronary syndrome or PCI) or full dose anticoagulation (such as for atrial fibrillation) are excluded. Patients need to be monitored closely for bleeding which typically occurs in the first year and is usually from the gastrointestinal tract.

These new treatments will help guide an unmet need for additional risk lowering in our highest risk patients with polyvascular disease.

References: 1. Eikelboom JW, Connolly SJ, Bosch J, Dagenais GR, Hart RG, Shestakovska O, Diaz R, Alings M, Lonn EM, Anand SS, et al.; COMPASS Investigators. Rivaroxaban with or without aspirin in stable cardiovascular disease. N Engl J Med. 2017; 377:1319–1330. doi: 10.1056/NEJMoa1709118. 2. Bonaca et al. Rivaroxaban in Peripheral Artery Disease after Revascularization. N Engl J Med 2020; 382:1994-2004.

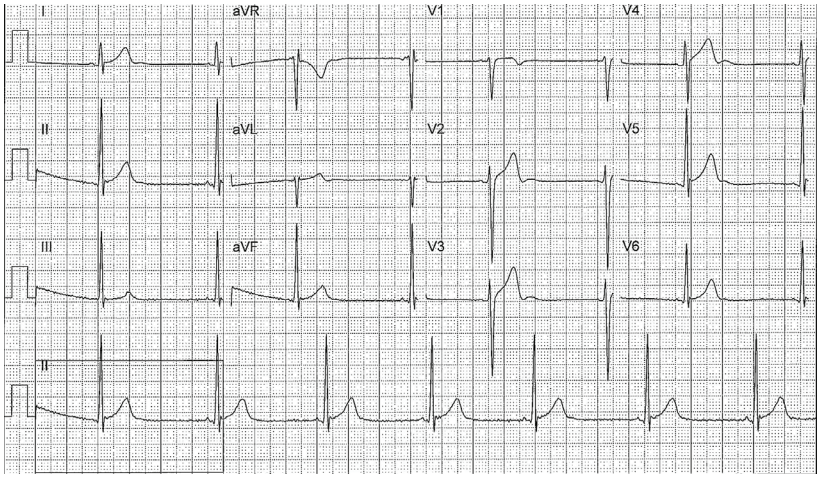
ECG: Test your knowledge

Dr Abhinav Luhach

Practicing at Bella Vista, Blacktown, Chatswood, Parramatta and Sydney City Cardiology

Question: A 36-year-old male has a pre-employment ECG. What does it show?

Answer: The patient is in sinus bradycardia. U waves are present.



A U wave is an uncommon finding on ECG. They occur after the T wave and are best seen in leads V2 and V3. They are usually only seen if the heart rate is <60bpm.

It can be a normal finding in some situations if it is upright and small (generally <1mm in amplitude or <25% the height of the preceding T wave). Some causes of U waves include prominent bradycardia, hypokaleamia and raised intracranial pressure. U waves can sometimes also be seen in the setting of digoxin use or certain antiarrhythmics.

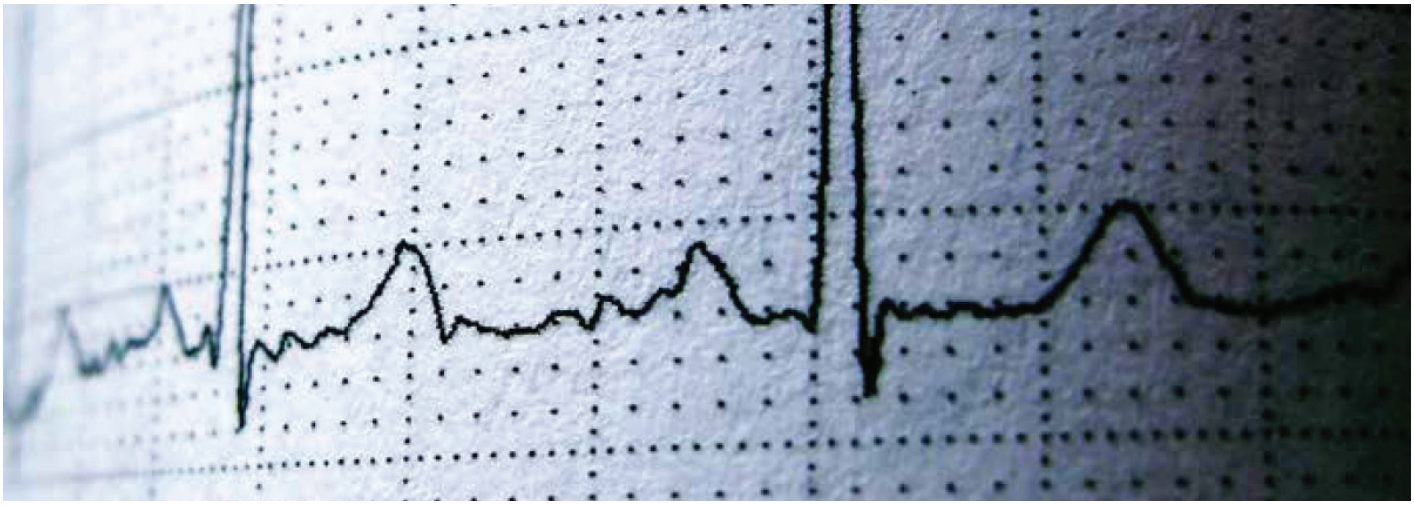
A large amplitude U wave or a U wave that is inverted (associated with an upright T wave) is abnormal. The latter can signify coronary artery or other cardiac pathology.

In this case, the patient was asymptomatic. History revealed the patient participates in competition level athletic events which explains his sinus bradycardia and associated U wave.

Australian Doctor How to Treat:

ECG Interpretation

Dr James Wong



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