

Cardiology Research Review™

Making Education Easy

Issue 158 - 2023

In this issue:

- > ANGPTL3 might be a suitable target for triglyceride and cholesterol lowering
- > Complete vs culprit-only PCI in older patients with MI
- > Catheter ablation reduces psychological distress in patients with AF
- > Outcomes of thrombus aspiration during PCI for STEMI
- > Benefits of lipid-lowering therapy for primary prevention in the elderly
- > Outcomes after PCI in patients with ischaemic LV dysfunction
- > Prognostic significance of ventricular ectopic beats during exercise
- > Ten-year cardiovascular risk in patients with newly diagnosed type 2 diabetes
- > Impact of smoking status on cardiovascular outcomes after PCI

Abbreviations used in this issue:

AF = atrial fibrillation; ANGPTL3 = angiotensin-like protein 3;
ASCVD = atherosclerotic cardiovascular disease; HDL = high-density lipoprotein;
HR = hazard ratio; LDL = low-density lipoprotein;
LVEF = left ventricular ejection fraction; MI = myocardial infarction;
NSTEMI = non-STEMI; PCI = percutaneous coronary intervention;
STEMI = ST-elevation MI; TIMI = Thrombolysis in Myocardial Infarction.

Welcome to the latest issue of Cardiology Research Review.

In this issue, a first-in-human trial supports ANGPTL3 as a potential therapeutic target in the management of ASCVD, the REMEDIAL trial shows that catheter ablation improves symptoms of anxiety and depression more so than medical therapy alone in patients with symptomatic AF, and an analysis of Victorian Cardiac Outcomes Registry data finds that intracoronary thrombus aspiration + PCI in patients with STEMI does not improve mortality outcomes more than PCI alone. Also in this issue, a Danish cohort study reports that LDL cholesterol reduction for primary prevention is equally beneficial in elderly (≥ 70 years) and younger individuals.

We hope you find the selected studies interesting, and welcome your feedback.

Kind Regards,

Associate Professor John Amerena

john.amerena@researchreview.com.au

RNA interference targeting ANGPTL3 for triglyceride and cholesterol lowering: Phase 1 basket trial cohorts

Authors: Watts GF et al.

Summary: ARO-ANG3 is an RNA interference therapy that targets ANGPTL3, a regulator of lipoprotein metabolism. This first-in-human trial investigated the effects of ARO-ANG3 in four cohorts of healthy individuals (n=52) and one cohort of patients with hepatic steatosis (n=9). Systemic absorption of ARO-ANG3 in healthy individuals was rapid and sustained, and the drug was generally well tolerated. In these participants, ARO-ANG3 reduced ANGPTL3 levels by a mean 45–78% when measured 85 days post-dose. Corresponding reductions in triglycerides (median –34% to –54%) and non-HDL cholesterol levels (mean –18% to –29%) were seen with the three highest doses.

Comment: Elevated triglycerides are an underappreciated risk factor for ASCVD, and have not received much attention until recently. Fibrates (fenofibrate and gemfibrozil) had no benefit in outcome trials, although subgroup analysis from FIELD and ACCORD studies showed that diabetic patients with atherogenic dyslipidaemia (low HDL and high triglycerides) did benefit. More recently, icosapent ethyl (a highly purified fish oil) improved outcomes in patients with ASCVD and elevated triglycerides (with and without diabetes) in the REDUCE-IT study, but the benefit was mainly due to increased icosapent ethyl rather than reduction in triglycerides on mediation analysis. The compound ANGPTL3 seems to lower triglycerides quite effectively and appears to be well tolerated and safe, but whether reducing triglycerides and non-HDL cholesterol is beneficial will need outcome trials.

Reference: *Nat Med.* 2023;29:2216–23

[Abstract](#)

Claim CPD/CME points [Click here](#) for more info.



Cardiology Research Review™

Independent commentary by Associate Professor John Amerena

Associate Professor John Amerena trained in Melbourne before spending four years in the United States at the University of Michigan. Over that period of time he worked in the fields of hypertension and hyperlipidemia, before returning to Australia where he is now a Cardiologist at Barwon Health. He currently has a joint appointment in the Department of Clinical and Biomedical Sciences at the University of Melbourne and the Department of Epidemiology and Preventive Medicine at Monash University. He is the director of the Geelong Cardiology Research Unit, which is currently involved in many phase II-III clinical trials. While still actively researching in hypertension, his focus has changed to research in antithrombotic/antiplatelet therapies, particularly in the context of acute coronary syndromes and atrial fibrillation. Heart failure is also a major interest, and he is also the Director of the Heart Failure Programme at Barwon Health. He is well published in these areas, as well as in many other areas of cardiovascular medicine.

RESEARCH REVIEW™ Australia's Leader in Specialist Publications

www.researchreview.com.au

a RESEARCH REVIEW publication

Complete or culprit-only PCI in older patients with myocardial infarction

Authors: Biscaglia S et al., for the FIRE Trial Investigators

Summary: The multicentre FIRE trial investigated the benefits of complete versus culprit-only revascularisation in older patients (≥ 75 years) with MI and multivessel disease. 1445 patients aged 77–84 years with MI and multivessel disease who were undergoing PCI of the culprit lesion were randomised to receive either physiology-guided complete revascularisation of nonculprit lesions or to receive culprit lesion revascularisation only. The primary outcome was a composite of death, MI, stroke, or any revascularisation at 1 year. A primary outcome event occurred in 15.7% of patients in the complete-revascularisation group compared with 21.0% in the culprit lesion-only group (HR 0.73, 95% CI 0.57–0.93; $p=0.01$); cardiovascular death or MI occurred in 8.9% and 13.5% of patients in the respective groups (HR 0.64, 95% CI 0.47–0.88). The safety outcome (a composite of contrast-associated acute kidney injury, stroke, or bleeding) did not differ significantly between groups.

Comment: The COMPLETE trial showed that complete rather than culprit-only revascularisation improved outcomes in patients with STEMI. This study is important as it looked at older patients who had both STEMI and NSTEMI, and showed that physiology-guided complete revascularisation at the time of the index procedure was beneficial 1 year after the index event. Although there are some concerns about the accuracy of fractional flow reserve (FFR) in the context of an acute MI, this study shows we should have a low threshold for FFR of nonculprit lesions when performing angiography on patients with MI, especially as there is a likelihood that FFR will be funded next year in Australia.

Reference: *N Engl J Med.* 2023;389(10):889–98

[Abstract](#)

Atrial fibrillation catheter ablation vs medical therapy and psychological distress

Authors: Al-Kaisey AM et al.

Summary: The REMEDIAL study investigated whether AF catheter ablation is associated with greater improvements in psychological distress than medical therapy alone. At two AF centres in Australia, 100 patients (mean age 59 years, 32% female) with symptomatic AF were randomised to receive AF catheter ablation or medical therapy alone. The primary outcome was Hospital Anxiety and Depression Scale (HADS) score at 12 months. Successful pulmonary vein isolation was achieved in all patients in the ablation group. The combined HADS score was lower in the ablation group than the medical therapy group at 6 months (8.2 vs 11.9; $p=0.006$) and 12 months (7.6 vs 11.8; $p=0.005$). The prevalence of severe psychological distress (HADS score >15) was also significantly lower in the ablation group at 6 and 12 months, as were the anxiety HADS score, the depression HADS score, and the Beck Depression Inventory-II score. Median AF burden in the ablation group was lower than that in the medical therapy group (0% vs 15.5%; $p<0.001$).

Comment: We know that AF is a considerable cause of stress in patients with paroxysmal AF, as there is usually no trigger for a paroxysm, which can be very disruptive for patients who are symptomatic, even if they do not need to attend hospital. We know that AF ablation reduces AF burden much more effectively than medical therapy, so it is not surprising that less psychological stress was seen in patients who had a successful ablation. This is yet another reason to consider early ablation in younger patients with paroxysmal AF.

Reference: *JAMA* 2023;330(10):925–33

[Abstract](#)

Outcomes of thrombus aspiration during primary percutaneous coronary intervention for ST-elevation myocardial infarction

Authors: Rajakariar K et al.

Summary: This study investigated the use of intracoronary thrombus aspiration as an adjunct to primary PCI in patients with STEMI. Data from 6270 consecutive patients undergoing primary PCI for STEMI in Melbourne in 2007–2018 were analysed. 26% of patients underwent PCI + thrombus aspiration and 74% underwent PCI alone. Patients undergoing thrombus aspiration were more likely to have complex lesions (83% vs 66%; $p<0.01$) with TIMI 0 flow (77% vs 56%; $p<0.01$), and were more likely to be male (81% vs 78%), younger (61 vs 63 years), using glycoprotein IIb/IIIa inhibitors (76% vs 58%), and current smokers (40% vs 36%). No significant between-group differences in post-procedural TIMI flow, stroke, 30-day or long-term mortality were seen. Multivariable analysis demonstrated a reduction in 30-day major adverse cardiovascular and cerebrovascular events (HR 0.75, CI 0.63–0.89; $p<0.01$) in the thrombus aspiration group, but this had no impact on long-term mortality.

Comment: This Australian analysis of the Victorian Cardiac Outcomes Registry data was consistent with the large clinical trials that did not show any benefit of thrombus aspiration in the setting of STEMI compared with PCI alone. Although there was a short-term benefit, there was no mortality benefit at 1 year. It may be tempting to aspirate if there is a large thrombus burden on initial imaging, but this study and the global data would suggest that thrombus aspiration has no major benefit over PCI alone.

Reference: *Intern Med J.* 2023;53(8):1376–82

[Abstract](#)

LDL-C reduction with lipid-lowering therapy for primary prevention of major vascular events among older individuals

Authors: Andersson NW et al.

Summary: This Danish cohort study evaluated the use of lipid-lowering therapy for primary prevention in elderly individuals. 65,190 individuals aged ≥ 50 years who had commenced lipid-lowering therapy in 2008–2017 and had no history of ASCVD were included. The risk of major vascular events among elderly individuals (≥ 70 years) was compared with that in younger individuals (<70 years). In both age-groups the median LDL cholesterol reduction was 1.7 mmol/L. Each 1mmol/L decrease in LDL cholesterol in older individuals was associated with a 23% lower risk of major vascular events (HR 0.77, 95% CI 0.71–0.83), which was comparable to that seen in younger participants (HR 0.76, 95% CI 0.71–0.80).

Comment: We know that age is a strong risk factor for cardiovascular events, but the benefits of LDL reduction with statins in the elderly for primary prevention has not been studied in detail. This observational study suggests that the beneficial effects of statins in primary prevention in the elderly are the same as in younger populations. A larger Australian randomised controlled trial (STAREE) is currently underway looking at statin versus placebo in older patients without clinical cardiovascular disease, which should add more information regarding the benefits of lipid lowering in this group of patients whose numbers are rapidly expanding.

Reference: *J Am Coll Cardiol.* 2023;82(14):1381–91

[Abstract](#)

World-first clinical trials begin for promising new anti-clotting stroke drug

Stroke is a leading cause of death and disability globally, with limited emergency treatment options. The Heart Research Institute has made a breakthrough 25 years in the making, identifying and developing a new anti-clotting drug that shows great promise to treat stroke – and have now launched Phase II clinical trials in 80 stroke patients in six leading hospitals across Australia.



RESEARCH REVIEW™

Australia's Leader in Specialist Publications

FOR AUSTRALIAN HEALTHCARE PROFESSIONALS

GSK

IF YOU COULD HELP PREVENT SHINGLES, WHY WOULDN'T YOU?¹

HELP PREVENT
SHINGLES AND
PHN in your adult
patients at increased
risk of shingles, with
SHINGRIX¹

Not a real patient, for illustrative purposes only.
Not representative of every patient's experience.
PHN=post-herpetic neuralgia.

Indication¹: SHINGRIX is indicated for the prevention of herpes zoster (HZ) and post-herpetic neuralgia in:

- adults 50 years of age or older;
- adults 18 years of age or older at increased risk of HZ.

Dosing¹: The primary vaccination schedule consists of two doses; an initial dose, followed by a second dose 2 to 6 months later. For subjects who are immunodeficient, immunosuppressed or likely to become immunosuppressed due to known disease or therapy, and who would benefit from a shorter vaccination schedule, the second dose can be given 1-2 months after the initial dose.

Safety¹: Very common (≥10%) solicited local adverse reactions and solicited general adverse events were pain, redness, and swelling at the injection site; and myalgia, fatigue, headache, shivering, fever, and gastrointestinal symptoms, respectively.

PBS Information:
This product is not listed on the PBS or the
National Immunisation Program (NIP).



Please review full Product Information before prescribing. Product Information can be accessed at www.gsk.com.au/shingrix or by scanning the QR code.

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

HZ=herpes zoster

Reference: 1. SHINGRIX Approved Product Information.

For information on GSK products or to report an adverse event involving a GSK product, please contact GSK Medical Information on 1800 033 109. Trade marks are owned by or licensed to the GSK group of companies. © 2023 GSK group of companies or its licensors. GlaxoSmithKline Australia Pty Ltd, Melbourne, VIC. ABN 47 100 162 481. PM-AU-SGX-ADVT-230003. Date of approval: February 2023.



SHINGRIX
Recombinant Varicella Zoster Virus glycoprotein E antigen
(AS01_B adjuvanted vaccine)

Arrhythmia and death following percutaneous revascularization in ischemic left ventricular dysfunction

Authors: Perera D et al., for the REVIVED-BCIS2 Investigators

Summary: This prespecified analysis of the REVIVED-BCIS2 trial investigated whether percutaneous revascularisation improves survival outcomes in patients with ischaemic LV dysfunction. At 40 centres across the UK, 700 patients with severe LV dysfunction (median LVEF 28%) and extensive coronary artery disease were randomised to undergo either PCI + optimal medical and device therapy (OMT) or OMT alone. Just over half the patients (53.1%) had an implantable cardioverter defibrillator (ICD) inserted prior to randomisation or during follow-up. The composite primary outcome of all-cause death or aborted sudden death (i.e. an appropriate ICD discharge or a resuscitated cardiac arrest) occurred in 41.6% of patients in the PCI group and 40.2% in the OMT group during 2 years of follow-up ($p=ns$).

Comment: Outside the setting of acute coronary syndrome, PCI has not been shown to improve cardiovascular or all-cause mortality, but does reduce symptoms and tablet burden. PCI is sometimes performed in patients with ischaemic cardiomyopathy if there are good targets, with the presumption that there will be an improvement in LV function and perhaps less arrhythmia. This study shows that PCI + OMT is no better than OMT alone in reducing the risk of serious arrhythmia in patients with severe ischaemic cardiomyopathy (mean LVEF 28%), so PCI should be reserved for symptom relief rather than mortality benefit.

Reference: *Circulation* 2023;148(11):862–71

[Abstract](#)

Prognostic significance of different ventricular ectopic burdens during submaximal exercise in asymptomatic UK Biobank subjects

Authors: van Duijvenboden S et al.

Summary: This study used UK Biobank data to investigate the association between premature ventricular contractions (PVCs) during submaximal exercise and major adverse cardiovascular events (MACE) and all-cause mortality in middle-aged and older individuals. PVCs from ECGs recorded during exercise (6-min) and recovery (1-min) were analysed for 48,315 asymptomatic participants (mean 56.8 years, 51.1% female). Even low PVC counts during exercise and recovery were associated with increased risk of MACE (MI, heart failure and life-threatening ventricular arrhythmia) during a median follow-up of 12.6 years, and the risk increased with higher PVC count. A similar trend was observed for all-cause mortality, although associations were only significant for high PVC burdens. Complex PVC rhythms were associated with a higher risk of MACE and mortality than PVC count alone.

Comment: It is not unusual to see ventricular ectopy or short runs of non-sustained ventricular tachycardia in patients performing stress testing, even if the stress test is negative for ischaemia. This study shows that this type of exercise-induced ventricular ectopy is probably not benign, and the more ectopics the greater the subsequent risk. It suggests that this ectopic activity may indicate subclinical cardiomyopathy, so a stress echo may be helpful in this situation to assess LV function at rest and see what happens with exercise.

Reference: *Circulation* 2023; published online Oct 19

[Abstract](#)

10-Year cardiovascular risk in patients with newly diagnosed type 2 diabetes mellitus

Authors: Gyldenkerne C et al.

Summary: This Danish cohort study investigated sex- and age-specific 10-year cardiovascular disease risk in patients with newly diagnosed type 2 diabetes (T2D) compared with the general population. 142,587 Danish patients who were diagnosed with T2D in 2006–2013 and 388,410 sex- and age-matched individuals from the general population were included; none of them had a history of ASCVD. Compared with the general population, the 10-year risk of cardiovascular disease (MI, stroke, and fatal cardiovascular disease) was higher in patients with T2D in both sexes and across all age groups. Patients aged 40–49 years had the largest difference in 10-year cardiovascular disease risk compared with the general population (6.1% vs 3.3%).

Comment: It has traditionally been thought that T2D was a “coronary risk equivalent” based on historical observational data, but this has been challenged. This study shows that T2D does impart a significant cardiovascular risk, and that cardiovascular disease occurs 12 years earlier in patients with T2D compared with their nondiabetic counterparts, and that the earlier the age of diagnosis, the greater the risk. This argues strongly for aggressive risk factor management as soon as T2D is diagnosed to try and delay the development of cardiovascular disease for as long as possible.

Reference: *J Am Coll Cardiol.* 2023;82(16):1583–94

[Abstract](#)



30 NOV – 1 DEC 2023



STEM-ming cardiovascular disease:

Improving patient care through multidisciplinary approaches

REGISTER NOW!
www.sydneycvsymposium.org.au

Venue: Susan Wakil Health Building, The University of Sydney

Princesses' Lecture: Prof David Kaye,
Baker Heart & Diabetes Institute

Sydney CV Symposium Lecture: Prof Alta Schutte,
The George Institute for Global Health



Smoking and cardiovascular outcomes after percutaneous coronary intervention

Authors: Ki Y-J et al.

Summary: This Korean study used data from the National Health Insurance System to investigate the impact of smoking and its cessation on cardiovascular outcomes after PCI. 74,471 patients undergoing PCI in 2009–2016 were classified as non-, ex-, or current smokers based on their smoking status at the first health check-up within 1 year after PCI. The primary outcome was major adverse cardiovascular and cerebrovascular events (MACCE; a composite of all-cause death, MI, coronary revascularisation, and stroke). During 4 years of follow-up after PCI, current smokers had a 19.8% higher rate of MACCE than non-smokers (adjusted HR 1.198; 95% CI 1.137–1.263), whereas ex-smokers and non-smokers tended to have comparable rates. Among patients who stopped smoking after PCI, those with cumulative smoking exposure of <20 pack-years tended to have a MACCE rate comparable to that of non-smokers, whereas those with cumulative exposure of ≥20 pack-years had a MACCE rate comparable to that of persistent smokers.

Comment: We know that smoking is a major risk factor for cardiovascular events, and that smoking cessation reduces the risk of subsequent events. This study quantitates the extent of risk of ongoing smoking post PCI, showing that ongoing smoking was associated with a 20% increased risk of a recurrent event, and that giving up smoking tended to reduce events (if smoking history was <20 pack-years). This emphasises the importance of smoking cessation counselling in patients with coronary artery disease, and active referral to a smoking cessation clinic (or prescribing nicotine replacement therapy or antismoking drugs) should be encouraged.

Reference: *Eur Heart J.* 2023; published online Sep 26

[Abstract](#)

Kindly Supported by



RACP MyCPD participants can claim **the time spent reading and evaluating research reviews** as CPD in the online **MyCPD program**.

Please contact MyCPD@racp.edu.au for any assistance.



Follow Research Review Australia on LinkedIn

linkedin.com/company/research-review-australia/



Australian Research Review subscribers can claim CPD/CME points for time spent reading our reviews from a wide range of local medical and nursing colleges. Find out more on our [CPD page](#).

Research Reviews are prepared with an independent commentary from relevant specialists. To become a reviewer please email geoff@researchreview.com.au.

Research Review Australia Pty Ltd is an independent Australian publisher. Research Review receives funding from a variety of sources including Government depts., health product companies, insurers and other organisations with an interest in health. Journal content is created independently of sponsor companies with assistance from leading local specialists. **Privacy Policy:** Research Review will record your email details on a secure database and will not release them to anyone without your prior approval. Research Review and you have the right to inspect, update or delete your details at any time. **Disclaimer:** This publication is not intended as a replacement for regular medical education but to assist in the process. The reviews are a summarised interpretation of the published study and reflect the opinion of the writer rather than those of the research group or scientific journal. It is suggested readers review the full trial data before forming a final conclusion on its merits.

Research Review publications are intended for Australian health professionals.

