Cardiology Research Review™

Making Education Easy

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In this issue:

Abbreviations used in this issue:

ACS = acute coronary syndrome; **BMI** = body mass index; **CABG** = coronary artery bypass graft; **CV** = cardiovascular; **DAPT** = dual antiplatelet therapy; **HR** = hazard ratio; **MI** = myocardial infarction; **PCI** = percutaneous coronary intervention.

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Welcome to the latest issue of Cardiology Research Review.

In this issue, an analysis of the NutriNet-Santé cohort finds that high consumption of ultra-processed foods is associated with CV disease, a UK Biobank study reports that habitual use of glucosamine supplements to relieve osteoarthritis pain is associated with a reduction in CV disease events, and a meta-analysis demonstrates that postoperative cognitive impairment and delirium are major issues in CABG patients. Swedish researchers report that stress-related disorders increase the risk of CV disease, a French cohort study questions the benefits of statins for primary prevention in the elderly, and the STEP-IN-AMI trial shows that intensive psychotherapy improves long term outcomes after acute MI.

We hope you find these and the other selected studies interesting, and look forward to receiving any feedback you may have.

Kind Regards,

Associate Professor John Amerena

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Ultra-processed food intake and risk of cardiovascular disease

Authors: Srour B et al.

Summary: This analysis of the NutriNet-Santé cohort determined the association between consumption of ultra-processed foods and risk of CV disease. 105,159 participants recorded their dietary intake of ultra-processed foods using repeated 24-hour dietary records. During a median follow-up of 5.2 years, incidence rates for high vs low consumers of ultra-processed foods were 277 vs 242 per 100,000 person-years for overall CV disease, 124 vs 109 per 100,000 person-years for coronary heart disease, and 163 vs 144 per 100,000 person-years for cerebrovascular disease. The findings remained significant after adjustment for nutritional quality of the diet.

Comment: The old adage "you are what you eat" is likely to be true based on the results of this analysis. Although it is an observational study there were a large number of participants and the statistics are robust. Adopting a diet based on more natural food would therefore seem reasonable but there is not enough evidence to make this a public health policy yet.

Reference: BMJ 2019;365:l1451

Abstract

Association of habitual glucosamine use with risk of cardiovascular disease

Authors: Ma H et al.

Summary: This analysis of UK Biobank data assessed the association between habitual glucosamine use and risk of CV disease events. 466,039 participants without CV disease at baseline who completed a questionnaire on supplement use were included. During a median 7-year follow-up, there were 10,204 CV disease events, 3060 CV disease deaths, 5745 coronary heart disease events, and 3263 stroke events. After adjusting for confounding factors, glucosamine use was found to be associated with a significantly lower risk of CV disease events (HR, 0.85), CV disease deaths (HR, 0.78), coronary heart disease (HR, 0.82), and stroke (HR, 0.91).

Comment: These are reassuring data given the common use of glucosamine ± chondroitin in our society to relieve arthritic pains. Although there is little evidence that glucosamine is any better than placebo in relieving arthritis pain, many patients seem to derive benefit and swear by it. This study suggests there are no harmful effects, and perhaps even benefits, possibly mediated by increased physical activity in the individuals who took it. Thus we should not discourage patients from taking glucosamine if they think it helps, even if this is due to a placebo-like effect.

Reference: BMJ 2019;365:l1628
Abstract

Cognitive outcomes following coronary artery bypass grafting

Authors: Greaves D et al.

Summary: This meta-analysis examined cognitive outcomes after CABG surgery. A search of four databases identified 215 studies (n=91,829) that reported the prevalence of cognitive impairment before and after CABG surgery. Meta-analysis of the data found that 19% of patients had pre-surgical cognitive impairment. Approximately 43% of patients had cognitive impairment acutely after CABG surgery, and nearly 40% of patients had long-term cognitive impairment (up to 5 years postoperatively). 18% of CABG patients had postoperative delirium and 7% had postoperative dementia.

Comment: Cognitive impairment after open heart surgery is not uncommon but is much less frequent than in the past. Although occasional patients develop delirium, most make a good functional recovery and long-term cognitive impairment is very uncommon in this era. Subtle abnormalities may be able to be picked up with neurocognitive testing before and after surgery, but this is seldom a clinically relevant issue. Patients with impaired or borderline cognitive function prior to surgery would seem to be at increased risk, so careful evaluation in these situations is important preoperatively to establish baseline cognitive function.

Reference: Int J Cardiol 2019;289:43-9
Abstract

Stress related disorders and risk of cardiovascular disease

Authors: Song H & Fang F

Summary: This sibling-controlled cohort study in Sweden determined the association between stress-related disorders and subsequent risk of CV disease. 136,637 patients in the Swedish National Patient Register with stress-related disorders in 1987–2013 were compared with 171,314 unaffected full siblings and 1,366,370 matched unexposed individuals from the general population. During up to 27 years of follow-up, the crude incidence rate of any CV disease was 10.5, 8.4, and 6.9 per 1000 person-years in patients with stress-related disorders, their unaffected full siblings, and the matched unexposed individuals. In sibling-based comparisons, the hazard ratio for any CV disease was 1.64 during the first year after diagnosis of a stress-related disorder, decreasing to 1.29 beyond the first year. Stress-related disorders were more strongly associated with early onset (age <50 years) CV diseases than later onset CV diseases. Comparisons with the population-matched cohort yielded similar results.

Comment: We know from the INTERHEART study that psychosocial factors were strongly associated with CV disease in a post-ACS population. This paper confirms that stress is related to CV disease, particularly in the first year after diagnosis, but extending for many years onwards. This could indicate that stress may be a trigger for an early event and perhaps in the long-term stress could be associated with poor lifestyle choices that increase the risk of future CV disease.

Reference: BMJ 2019;365:l1255
Abstract

Real-life benefits of statins for cardiovascular prevention in elderly subjects

Authors: Bezin J et al.

Summary: This population-based cohort study in France evaluated the benefits of statins in the elderly. 3642 new users of statins (aged ≥75 years) were matched 1:1 to statin nonusers for age, sex, numbers of different drugs dispensed, medical consultations, and cardiovascular history. Patients were classified into 3 cardiovascular risk groups: secondary prevention, primary prevention with modifiable risk factors (diabetes or cardiovascular medications), and primary prevention without modifiable risk factors. During a median follow-up of 4.7 years, cumulative use of statins was associated with a lower risk of outcomes in the primary prevention with modifiable risk factors group (adjusted HR, 0.93 per year of use; p<0.01) and in the secondary prevention group (HR, 0.75; p<0.01), but not in the primary prevention without modifiable risk factors group.

Comment: The benefit of statins for primary prevention in the elderly has been questioned, and the evidence for secondary prevention in this age group is scarce as they were not included in most of the pivotal trials that showed benefit. This observational study suggests that statins are not beneficial for primary prevention in subjects aged 75 years of age unless there are modifiable risk factors, but that the benefits in secondary prevention are maintained. This suggests that starting statins in the healthy elderly is unlikely to be advantageous, but this will be explored in the STAREE study which is about to start in Australia.

Reference: Am J Med 2019;132(6):740-48
Abstract

Short-term psychotherapy in acute myocardial infarction (STEP-IN-AMI) trial

Authors: Pristipino C et al.

Summary: The STEP-IN-AMI trial examined whether short-term psychotherapy enhances long-term clinical outcomes after acute MI (AMI). 94 patients aged ≤70 years were randomised within 1 week of their AMI to short-term ontopsychological psychotherapy plus routine medical therapy, or to routine medical therapy only. The primary composite outcome comprised new cardiovascular events (re-infarction, death, stroke, revascularisation, life-threatening ventricular arrhythmias, and the recurrence of clinically significant angina) and clinically significant new comorbidities. At the 5-year follow-up, psychotherapy patients had a lower incidence of the primary outcome relative to controls (19% absolute risk reduction). The benefit was attributed to a lower incidence of new comorbidities and clinically significant angina. Improvements among psychotherapy patients relative to controls occurred mainly in the first year and were maintained for the following 4 years.

Comment: We know that depression is quite common post MI, and that it is associated with a worse long-term outcome. Despite this, several studies using antidepressant therapy after MI have been unable to demonstrate an improvement in CV outcomes, despite patients feeling better. This study suggests that intensive psychotherapy post MI improves long term outcomes in these patients but needs to be proven in larger studies. If this does indeed prove to be a successful strategy, it will create major logistical issues, as psychiatric services are already overburdened with acute psych issues, let alone providing psychotherapy to depressed post-MI patients.

Reference: Am J Med 2019;132(5):639-46
Abstract

Understanding the consequences of education inequality on cardiovascular disease

Authors: Carter A et al.

Summary: This study investigated the role of BMI, systolic blood pressure (SBP), and smoking in the effect of education on the risk of CV disease. Mendelian randomisation analysis of UK Biobank and international genome-wide association study data found that each additional standard deviation of education (3.6 years) was associated with a 37% lower risk of coronary heart disease. BMI, SBP and smoking were estimated to mediate 18%, 21% and 34%, respectively, of the effect of education on coronary heart disease, and all 3 risk factors combined were estimated to mediate 36% of the total risk reduction. Similar results were obtained when investigating the risk of stroke, MI, and CV disease.

Comment: Poor education achievement is generally, but not always, associated with lower socioeconomic status, which we know is a risk factor for CV disease. This study suggests that BMI, smoking and blood pressure mediate up to 50% of this increase in risk with poor education, but the contribution of elevated lipids and exercise was not reported. We know that these conventional risk factors increase the risk of CV events, and that exercise, good diet and moderation of alcohol consumption decrease risk, but family history is almost certainly a contributor to excess CV events in these patients. I wonder if there is a clustering of harmful genes in this population and that the inability to achieve good educational achievement is linked phylogenetically to adverse CV risk factors.

Reference: BMJ 2019;365:l1855
Abstract

Effect of 1-month dual antiplatelet therapy followed by clopidogrel vs 12-month dual antiplatelet therapy on cardiovascular and bleeding events in patients receiving PCI

Authors: Watanabe H et al.

Summary: The open-label STOPDAPT-2 trial compared the use of very short duration DAPT versus 12-month DAPT after PCI. 3045 patients who underwent PCI at 90 hospitals in Japan in 2015–2017 were randomised 1:1 to receive 1 month of DAPT followed by clopidogrel monotherapy, or to 12 months of DAPT with aspirin and clopidogrel. The primary end-point was a composite of CV death, MI, ischaemic or haemorrhagic stroke, stent thrombosis, or major or minor bleeding at 12 months. One-month DAPT was superior to 12-month DAPT for the primary end-point (2.36% vs 3.70%; HR, 0.64). Major or minor bleeding occurred in 0.41% of patients in the 1-month DAPT group compared with 1.54% of patients in the 12-month DAPT group (HR, 0.26; p=0.004).

Comment: With the evolution of second and third generation drug-eluting stents, the risk of stent thrombosis has diminished markedly, so that shorter and shorter duration of DAPT after PCI is being explored. Most guidelines would still recommend 12 months' DAPT after ACS ± PCI or at least 6 months after elective stenting. This study shows that early cessation of aspirin at 1 month may be safe and certainly reduces bleeding compared with DAPT but this should only be considered if there was unmanageable bleeding and clopidogrel would have to be used as ticagrelor is only reimbursed for use with aspirin.

Reference: JAMA 2019;321(24):2414-27
Abstract

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Independent commentary by Associate Professor John Amerena, FRACP, FACC, FCSANZ, Dept. of Clinical and Biomedical Science, University of Melbourne (Geelong). Full biography here.

Association of statin adherence with mortality in patients with atherosclerotic cardiovascular disease

Authors: Rodriguez F et al.

Summary: This retrospective cohort study determined the association between statin adherence and mortality in patients with atherosclerotic CV disease. 347,104 adults with atherosclerotic CV disease who had stable statin prescriptions and who were treated within the Veterans Affairs Health System in 2013–2014 were included. Statin adherence was determined by the medication possession ratio (MPR); adherence was defined as an MPR ≥80%. Patients taking moderate-intensity statin therapy were more adherent than patients taking high-intensity statin therapy (odds ratio [OR], 1.18); women and minority groups were less adherent. Younger and older patients were less likely to be adherent than adults aged 65–74 years. During a mean follow-up of 2.9 years, 85,930 patients (24.8%) died. Compared with the most adherent patients (MPR ≥90%), hazard ratios for death were 1.30, 1.21 and 1.08 in patients with MPR <50%, 50–69% and 70–89%, respectively.

Comment: It is not surprising that non-adherence to statins in patients with CV disease increases the risk of subsequent events and death. Access to medical advice and medication may be an issue in the US but although this is not so much of a problem here, adherence to statins post CV events is less than ideal in Australia. Education in conjunction with timely and affordable medical review in patients with CV disease would almost certainly increase compliance with medication in this context. Cardiac rehab could also play an important role in this situation, although the traditional model is to only provide rehab in a secondary prevention setting.

Reference: JAMA Cardiol 2019;4(3):206-13
Abstract

Cardiovascular disease burden from ambient air pollution in Europe reassessed using novel hazard ratio functions

Authors: Lelieveld J et al.

Summary: This study used a Global Exposure Mortality Model to estimate excess CV mortality attributed to air pollution in Europe and the 28 countries of the European Union (EU-28). The annual excess mortality rate from ambient air pollution was calculated to be 790,000 in Europe and 659,000 in the EU-28 (40–80% of the excess deaths were due to CV events). It was estimated that air pollution reduces the mean life expectancy in Europe by 2.2 years.

Comment: Increasing data suggest that air pollution is associated with adverse CV and respiratory outcomes. These data indicate that there is a real risk with increasing levels of air pollution, and that reducing pollution by transferring to renewable energy sources will reduce risk. However, even if this is implemented it will take many years for the effects to become evident.

Reference: Eur Heart J 2019;40(20):1590-96
Abstract

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