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Cardiology Research Review™

Making Education Easy

Issue 57 – 2015

In this issue:

Abbreviations used in this issue
AF = atrial fibrillation
CAD = coronary artery disease
CT = computed tomography
DAPT = dual antiplatelet therapy
MI = myocardial infarction
PCI = percutaneous coronary intervention
STEMI = ST segment elevation MI

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Cardiology Research Review

Welcome to the June edition of NZ Cardiology Research Review, covering the wonderful world of new publications in April and May.

There has been a cluster of papers on ways you might consider lowering your risk of cardiovascular mortality or morbidity including:

- moderation of alcohol consumption (http://eurheartj.oxfordjournals.org/content/36/15/939)
- moderation of jogging (http://content.onlinejacc.org/article.aspx?articleID=2108914)
- taking saunas (http://archinte.jamanetwork.com/article.aspx?articleid=2130724) and
- avoiding divorce (http://circoutcomes.ahajournals.org/content/8/3/244).

I have stuck to reviewing the one factor that is largely immune to confounding and also to modification (height). Other issues reviewed include the initial assessment of chest pain with an anatomical rather than a physiological test (or is a biomarker sufficient at least in the initial phase?), the value of searching for asymptomatic AF, health hazards faced by our interventional colleagues, whether thrombolysis isn't quite dead yet and how long to continue DAPT. For our electrician colleagues, there is an update on the safety of exercise in those with long QT and on the developing technology of leadless pacemakers. Finally there's one for the surgeons on the choice of technology for valve replacement. Feedback is always welcome.

Kind regards,

Associate Professor Stewart Mann
stewartmann@researchreview.co.nz

Short measures all round

Authors: Nelson C et al., for the CARDIoGRAM+C4D Consortium

Summary: This study determined the association between adult height and the risk of CAD. The impact of a 1-SD (6.5cm) change in height on CAD risk was assessed in 65,066 cases and 128,383 controls. The risk of CAD associated with the presence of various numbers of height-associated alleles was also assessed, using genotype data for 18,249 individuals. The risk of CAD was found to increase by 13.5% for every 1-SD decrease in height ($p<0.001$). Individuals with an increased number of height-raising variants had a reduced risk of CAD (odds ratio for height quartile 4 vs 1, 0.74; $p<0.001$). Genetically determined height was shown to be significantly associated with low-density lipoprotein cholesterol and triglyceride levels.

Comment: Having now two cardiology colleagues whom I can defiantly outstare straight in the umbilicus, I'm only too aware of my position in the higher-archy although can gloat when it comes to comfort factors using a Skycouch or even an ordinary airline seat. The association of shorter stature with higher cardiovascular risk has been known for some time but assumed to have some relationship to environmental factors such as nutrition. This analysis corrects for these issues and shows that there are direct genetic associations between height and lipid levels. Perhaps this is yet another risk factor to add to the recently announced New Zealand cardiovascular disease risk equation.

Reference: Genetically determined height and coronary artery disease. N Engl J Med 2015;372:1608-1618
Abstract

Cardiology Research Review

Independent commentary by Stewart Mann, Associate Professor of Cardiovascular Medicine at the University of Otago, Wellington.

For full bio CLICK HERE.

CONGRATULATIONS TO **Jacqui Adair** who won the iPad mini 3 by taking part in our recent Subscriptions Update promotion. Jacqui is a Clinical Nurse Specialist at Middlemore Hospital in Auckland.

Broken PROMISE of the Duke with 10,000 recruits

Authors: Douglas P et al., for the PROMISE Investigators

Summary: This study compared the use of anatomical and functional diagnostic testing in patients with symptoms suggestive of CAD. 10,003 symptomatic patients were randomised to a strategy of initial anatomical testing with the use of CT coronary angiography (CTCA) or to functional testing (exercise electrocardiography, nuclear stress testing, or stress echocardiography). The composite primary end-point was death, MI, hospitalisation for unstable angina, or major procedural complication. During a median follow-up period of 25 months, 3.3% of patients in the CTCA group and 3.0% of patients in the functional-testing group had a primary end-point event (p=NS). CTCA was associated with fewer catheterisations showing no obstructive CAD (3.4% vs 4.3%; p=0.02), but more patients in the CTCA group underwent catheterisation within 90 days after randomisation (12.2% vs 8.1%).

Comment: Duke University recruited 10,000 subjects to march them initially up one of two hills, one leading to the CT scanner, the other to the treadmill. One hope for CTCA was that it might dissociate the processes of diagnosis and intervention while also outlining intramural vulnerable plaque that was much more likely to become a culprit lesion in an occlusion. Nevertheless, the oculostenotic driver still held sway in this trial with more in the CT group going on to invasive angiography and intervention, with no benefit to the primary end-points of death, MI, unstable angina or major procedural complication. Due to a low rate of this end-point (3% as against the expected 9%) and lack of difference between groups the trial was abandoned by its NIH funder due to the low likelihood of it ever reaching a clinically relevant distinction. This left the recruits neither up nor down. The result has not stopped the advocates of CTCA advocating for an upgrade in its place in the guidelines.

Reference: Outcomes of anatomical versus functional testing for coronary artery disease. N Engl J Med 2015;372:1291-1300
Abstract

GOMER faster at APACE

Authors: Reichlin T et al.

Summary: This study prospectively validated a novel 1-hour algorithm using high-sensitivity cardiac troponin T measurement for early rule-out and rule-in of acute MI. 1320 patients who presented to the emergency department with suspected acute MI were included. The high-sensitivity cardiac troponin T 1-hour algorithm (incorporating baseline values as well as absolute changes within the first hour) was validated against the final diagnosis. Acute MI was the final diagnosis in 17.3% of patients. Using the algorithm, 59.5% of patients were classified as "rule-out," 16.4% were classified as "rule-in" and 24.1% were classified to the "observational zone." The 1-hour algorithm provided significantly higher negative and positive predictive values than the standard interpretation of high-sensitivity cardiac troponin T using a single cut-off level.

Comment: The House of God's somewhat pejorative exhortation ("Get Out of My Emergency Room") has lately been adopted by governments advocating targets for swift triage of acute cases. The majority of patients presenting with chest discomfort do not have an acute coronary syndrome but excluding this has traditionally taken a few hours. The advent of high sensitivity troponin tests has enabled progressive speeding up of the process using a number of similar protocols that incorporate clinical, electrocardiographic and biomarker factors. Use of this one in the APACE trial and a follow-up study yet to be published (TRAPID) has enabled around 60% of patients with chest pain to be assigned within 1 hour to a safe rapid discharge group (99–100% specificity).

Reference: Prospective validation of a 1-hour algorithm to rule-out and rule-in acute myocardial infarction using a high-sensitivity cardiac troponin T assay. CMAJ 2015; published online April 13
Abstract

You may not know it but you 'af AF

Authors: Svennberg E et al.

Summary: This Swedish study examined the prevalence of untreated AF in the elderly. 7173 individuals aged 75–76 years were invited to be screened for AF using intermittent ECG recordings over 2 weeks. Oral anticoagulant (OAC) treatment was offered to those who had AF detected. 3.0% of participants were found to have previously unknown AF, and 9.3% had a prior diagnosis of AF (total AF prevalence 12.3%). 2.1% of those with a prior diagnosis of AF were not taking OAC treatment. In total, 5.1% of the screened population had untreated AF; screening resulted in initiation of OAC treatment in 3.7% of participants. Most of the individuals with previously undiagnosed AF accepted initiation of OAC treatment.

Comment: I have previously been concerned about undue efforts at identifying short periods of asymptomatic AF and wondered what relevance if any they had to stroke. However, some while ago data emerged from patients with implantable devices showing that those with such episodes were indeed at increased risk of stroke. This current study gave patients in their mid-seventies (who automatically have a CHA_2DS_2VASc risk of ≥2 if they have evidence of AF) a hand-held ECG recording device and found a small number with evidence of asymptomatic AF. These patients were offered oral anticoagulation. Presumably with the usual Swedish registry data in place we will eventually learn if this leads to the expected benefit in outcomes.

Reference: Mass screening for untreated atrial fibrillation: the STROKESTOP study. Circulation 2015; published online April 24
Abstract

Hazards of plumbing

Authors: Klein L et al., on behalf of the SCAI

Summary: This study by the Society for Cardiovascular Angiography and Interventions (SCAI) evaluated occupational health hazards in interventional cardiologists and staff. SCAI members were contacted via email and questioned about age, years of invasive practice, and diagnostic and interventional cases per year. They were also asked to report any orthopaedic and radiation-associated problems. 314 members responded. Responders were generally busy and experienced, performing a mean 380 diagnostic and 200 interventional cases annually. 6.9% of them reported having to limit their caseload because of radiation exposure, 9.3% reported a health-related period of absence, and 49.4% reported at least one orthopaedic injury (24.7% cervical spine, 34.4% lumbar spine, and 19.6% hip, knee or ankle joint problems). Age and annual total caseload were significantly correlated with orthopaedic problems. There was a small but substantial incidence of cancer.

Comment: Not all hazards encountered in the cath lab are bad outcomes for the patient. Those who choose to spend a fair proportion of their working lives in this environment may pay a price in their health. The current trend for staff to be instantly available 24/7 may itself create hazards before they even reach the lab. This analysis concentrates on orthopaedic and radiation-related issues but others (e.g. exposure to infectious body fluids) may be shared with surgical colleagues and cousins in the wider world of plumbing. Radiation may lead to an increased incidence of cancer with worryingly higher rates of cerebral tumours on the side nearest the radiation source. Another study (http://interventions.onlinejacc.org/article.aspx?articleid=2276897) shows increased subclinical carotid-intima-media thickness (again more preponderant on the left side) and more shortening of telomeres in lab staff with high long-term exposures.

Reference: Occupational health hazards of interventional cardiologists in the current decade: results of the 2014 SCAI membership survey. Cathet Cardiovasc Intervent 2015; published online Mar 24
Abstract

Drug-assisted intervention in STEMI may enhance outcomes downstream

Authors: Gershlick A et al.

Summary: This study assessed the impact of time delay on outcomes in patients randomised to a pharmacoinvasive strategy (PI) or primary PCI (p-PCI) after STEMI. 30-day clinical outcomes were examined according to PCI-related delay (P-RD), which was categorised as ≤55 min, >55–97 min and >97 min. The composite end-point of death/congestive heart failure/cardiogenic shock/MI did not differ significantly between treatment arms across the P-RD spectrum. Outcomes did not worsen for the PI arm as the P-RD increased, but did for the P-PCI arm (p trend=0.038). For P-RD ≤55 min, fewer events tended to occur with P-PCI than PI. However, as P-RD increased to >55 min, PI was associated with better outcomes than P-PCI. Continuous analysis of P-RD showed that for every 10-min increment there was a trend towards benefit in the PI arm.

Comment: Early trials of a "pharmacoinvasive" strategy (boosting reperfusion in STEMI with thrombolysis before transfer to a PCI centre) were not persuasive but utilised a variety of different protocols. The previously published STREAM trial suggested that a short time between initial contact and PCI favoured a direct strategy but once this delay exceeded an hour or so, use of thrombolysis at the time of initial contact before rapid transfer for PCI began to show advantages. The initially specified subgroups of time delay did not show significant differences but this analysis grading relative benefits of each strategy by time delay intervals of 10 minutes shows an impressive progressive likelihood of benefit once the delay to PCI exceeds an hour.

Reference: Impact of a pharmacoinvasive strategy when delays to primary PCI are prolonged. Heart 2015;101:692-698
Abstract

Ticagrelor takes off on a winged horse

Authors: Bonaca M et al., for the PEGASUS-TIMI 54 Steering Committee and Investigators

Summary: The PEGASUS-TIMI 54 trial investigated the long-term efficacy and safety of ticagrelor in patients with acute coronary syndrome. 21,162 patients who had had an MI 1–3 years earlier were randomised 1:1:1 in a double-blind design to receive ticagrelor 90mg twice daily, ticagrelor 60mg twice daily, or placebo in addition to low-dose aspirin for a median 33 months. Compared with placebo, both ticagrelor dosages reduced the rate of the primary efficacy end-point (a composite of cardiovascular death, MI, or stroke). Kaplan-Meier rates at 3 years were 7.85% in the 90mg twice daily group, 7.77% in the 60mg twice daily group, and 9.04% in the placebo group. Hazard ratios compared with placebo were 0.85 for the 90mg dose (p=0.008) and 0.84 for the 60mg dose (p=0.004). Rates of Thrombolysis in Myocardial Infarction (TIMI) major bleeding were higher with both ticagrelor doses than with placebo (both p<0.001).

Comment: The ideal duration of DAPT after MI with or without stenting has been a conundrum investigated in a number of different trials. A recent meta-analysis (http://www.bmj.com/content/350/bmj.h1618) of randomised trials of DAPT after drug-eluting stent insertion (mainly using aspirin and clopidogrel) showed little benefit in extending treatment for as much as a year, let alone longer and suggested a higher all-cause death rate with prolonged therapy. Undoubtedly, there is a trade-off between reduction of ischaemic events and bleeding problems. The PEGASUS trial of ticagrelor was enriched with patients at high risk of ischaemic events and examined the continuation of DAPT beyond a year in doses of either 60mg or 90mg twice daily. This proved beneficial with only a slight increase in bleeding. The equation may of course not be quite the same for patients with a lower risk of recurrent ischaemic events or higher risk of bleeding and it will be important to tailor strategies to individuals rather than have a blanket policy.

Reference: Long-term use of ticagrelor in patients with prior myocardial infarction. N Engl J Med 2015;372:1791-1800
Abstract

Iron man events for ion channel problems?

Authors: Aziz P et al.

Summary: This retrospective study examined the prevalence and outcomes of sports participation in children with long QT syndrome (LQTS). 212 genotype-positive patients referred for evaluation and management of LQTS at the Children's Hospital of Philadelphia were reviewed. 103 of the children (mean follow-up 7.1 years, mean QTc 468ms) participated in competitive (n=26) or recreational (n=77) sports. All of them were treated with beta-blockers. No LQTS symptoms occurred during sports participation during 775 patient-years of follow-up. 5 appropriate implantable cardioverter-defibrillator (ICD) shocks occurred in 2 patients, but they were not related to sports participation.

Comment: Sudden death during sports events is very dramatic, especially during live television. Controversy continues about the need for screening of athletes at various levels, including school sports, to exclude conditions associated with such risk such as hypertrophic cardiomyopathy and electrophysiological abnormalities such as LQTS. This analysis of such patients generally treated with beta-blockers showed a complete absence of significant events during recreational sport although some patients with ICDs had appropriate shocks unconnected with sporting competition. However, more serious athletes might have problems with taking beta-blockers and their effect on performance.

Reference: Sports participation in genotype positive children with long QT syndrome. JACCCEP 2015;1(1):62-70
Abstract

Time spent reading this publication has been approved for CME for Royal New Zealand College of General Practitioners (RNZCGP) General Practice Educational Programme Stage 2 (GPEP2) and the Maintenance of Professional Standards (MOPS) purposes, provided that a Learning Reflection Form is completed. Please **CLICK HERE** to download your CPD MOPS Learning Reflection Form. One form per review read would be required.

Time spent reading this publication has been approved for CNE by The College of Nurses Aotearoa (NZ) for RNs and NPs. For more information on how to claim CNE hours please **CLICK HERE**

Unleaded pacing?

Authors: Knops R et al.

Summary: This study reported the complication incidence, electrical performance, and rate response characteristics within the first year in patients implanted with a leadless cardiac pacemaker (LCP). One-year follow-up data were available for 31 of 33 patients (mean age 76 years) from the LEADLESS trial cohort who had an indication for single-chamber pacing and received an LCP. No pacemaker-related adverse events were reported during follow-up. The pacing performance results at 6- and 12-months' follow-up were: mean pacing threshold (at a 0.4-ms pulse width), 0.40 and 0.43V, respectively; R-wave amplitude, 10.6 and 10.3mV; and impedance, 625 and 627Ω. At the 12-month follow-up, the rate response sensor was activated in 61% of patients, with an adequate rate response observed in all patients.

Comment: Pacing systems don't tend to use much lead (/'led'/) but most tend to need a lead (/'li:d/) although this can be the most mechanically vulnerable part of the system. Pacing systems without the lead (/'li:d/) exist but are mainly suitable only for single chamber pacing. The systems still involve a right ventricular endocardial implant and, despite this small trial suggesting good performance and safety over 1 year, several perforations (some fatal) were reported in Europe by last year so further development was suspended. Long-term performance with respect to thrombogenicity, infection and extractability issues also needs to be established. Another device under development provides left ventricular stimulation potentially allowing leadless cardiac resynchronisation therapy (CRT) but this has also been associated with some important adverse events so the technology is still very much in its development phase.

Reference: Chronic performance of a leadless cardiac pacemaker: 1-year follow-up of the LEADLESS Trial. J Am Coll Cardiol 2015;65(15):1497-1504
Abstract

Would you opt for pig, calf or pyrolytic carbon?

Authors: Chikwe J et al.

Summary: This study examined morbidity and mortality outcomes in patients undergoing mitral valve replacement with bioprosthetic or mechanical valves. Outcomes for 3433 patients aged 50–69 years who underwent primary isolated mitral valve replacement using bioprosthetic or mechanical valves in 1997–2007 were reviewed. Survival rates did not differ between groups during a median follow-up period of 8.2 years. Mechanical valve replacement was associated with a higher 15-year cumulative incidence of stroke (14.0% vs 6.8%), a lower 15-year cumulative incidence of reoperation (5.0% vs 11.1%), and a higher 15-year cumulative incidence of a bleeding event (14.9% vs 9.0%) than bioprosthetic valve replacement.

Comment: Technological developments continue to improve both bioprosthetic and mechanical heart valves. Choice is usually between longevity (mechanical win) and avoidance of the need for anticoagulants (bio win). This creates a problem for interpretation of long-term trials as by the time of analysis the technology of both types of new implants has evolved considerably. Patients aged between 50 and 69 years (who clearly fall into the category of "middle-aged") were analysed in matched pairs in this retrospective study. While there was the predictably higher stroke and bleeding rate with mechanical prostheses and higher rate of reoperation in the bioprosthetic group, survival rates to 15 years were similar.

Reference: Survival and outcomes following bioprosthetic vs mechanical mitral valve replacement in patients aged 50 to 69 years. JAMA 2015;313(14):1435-1442
Abstract