Welcome to the latest issue of Cardiology Research Review.

Highlights include an interesting analysis of long-term cardiovascular risk in survivors of Hodgkin’s disease, a 5-year report of the PARTNER trial that should give us confidence in transcatheter aortic valve replacement, and yet more research on the duration of DAPT after stent implantation. A Japanese study reports that major stressful events (in this case the 2011 earthquake) increase the risk of MI, and an Australian study shows that transferring patients to specialised centres post-ACS is worth the effort.

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
john.amerena@researchreview.com.au

Cardiovascular disease after Hodgkin lymphoma treatment: 40-year disease risk

Authors: van Nimwegen F et al.

Summary: This study examined the long-term risk of cardiovascular disease in Hodgkin lymphoma survivors. 2524 Dutch patients who were treated for Hodgkin lymphoma in 1965–1995 and had survived for 5 years after their diagnosis were included. Follow-up data were collected from medical records and general practitioners. During a median follow-up of 20 years, 1713 cardiovascular events (coronary heart disease, valvular heart disease, cardiomyopathy, and congestive heart failure) were identified in 797 patients. After ≥35 years, patients had a 4- to 6-fold increased standardised incidence ratio of coronary heart disease or heart failure compared with the general population. The highest relative risks were seen in patients treated before 25 years of age, but substantial excess risks were also observed in older patients.

Comment: This interesting analysis identifies that long term survivors of Hodgkin’s disease who were treated with the conventional therapy of the time (mediastinal radiotherapy and anthracycline chemotherapy) are at long term increased risk for coronary and valvular heart disease, as well as heart failure, presumably due to the effects of the cancer therapies on the myocardium and coronary arteries. Whether the therapies used today have the same consequences has not been studied.


Abstract

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Abbreviations used in this issue:
ACS = acute coronary syndrome; AMI = acute myocardial infarction; CAD = coronary artery disease; DAPT = dual antiplatelet therapy; MI = myocardial infarction.

This publication is endorsed by ACN according to our Continuing Professional Development Endorsed Course Standards. It has been allocated 1 CPE hour(s) according to the Nursing and Midwifery Board of Australia – Continuing Professional Development Standard.

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5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1)

Authors: Mack M et al.

Summary: This report presented 5-year outcomes of the Placement of Aortic Transcatheter Valves (PARTNER) trial. In the trial, 699 high-risk patients with severe aortic stenosis were randomised to undergo either surgical aortic valve replacement (SAVR) or transcatheter aortic valve replacement (TAVR). At 5 years, the risk of death was 67.8% in the TAVR group and 62.4% in the SAVR group (hazard ratio 1.04; p=NS). There was no structural valve deterioration requiring surgical valve replacement in either group. Moderate or severe aortic regurgitation occurred in 14% of patients in the TAVR group and 1% of patients in the SAVR group (p<0.0001), and was associated with increased 5-year risk of mortality in the TAVR group (72.4% in patients with moderate or severe aortic regurgitation compared with 56.6% in patients with mild aortic regurgitation or less; p=0.003).

Comment: There has been concern as to the durability of valves implanted with TAVR compared to surgically. This 5-year analysis of the PARTNER trial should give us confidence that the Edwards Sapien valve will last at least that long, but it also showed that there was increased risk of aortic insufficiency with TAVR, and that this was associated with worse outcomes. There have been considerable improvements in the valves and implantation techniques since this early study, so this problem has substantially decreased over time.

Reference: Lancet 2015;385(9986):2477-2484

Impact of clinical presentation on ischaemic and bleeding outcomes in patients receiving 6- or 24-month duration of dual-antiplatelet therapy after stent implantation

Authors: Costa F et al.

Summary: This sub-analysis of the PRODIGY trial investigated the impact of clinical presentation on ischaemic and bleeding outcomes in patients receiving 6- or 24-month DAPT after stent implantation. In PRODIGY, 1465 patients with ACS and 505 with stable CAD were randomised to 6- or 24-month DAPT. At 24 months, the composite of death, MI, or cerebrovascular accident (CVA) did not differ between the long- and short-term DAPT arms in either ACS or stable CAD patients. Long-term DAPT was associated with a 75% increase in Bleeding Academic Research Consortium (BARC)-class 2, 3, or 5 bleeding in ACS patients (hazard ratio 1.75; p=0.015) and a 5-fold increase in stable CAD patients (hazard ratio, 5.37; p=0.002). As a result, net adverse cardiovascular events (death, MI, CVA, BARC class 2, 3, or 5 bleeding) were more than doubled in stable CAD patients receiving 24-month DAPT, whereas they did not differ in ACS patients.

Comment: There is ongoing debate about the duration of DAPT after stent implantation. The PRODIGY study and several other small trials have suggested that 6 months is enough, but the DAPT and PEGASUS studies suggest that there is benefit from a longer duration. This sub-analysis of PRODIGY shows that prolonged therapy may be more beneficial in patients who have had stenting for an ACS rather than for stable disease. In the DAPT study there was less stent thrombosis and MI in the non ACS stented patients (75% of subjects) but more bleeding and death in this group. These studies thus suggest that the benefits of prolonged DAPT in non ACS stented patients are not as great as when stents are implanted for ACS, and that a shorter duration could be considered.

Reference: Eur Heart J 2015;36(20):1242-51
Relationship between the seismic scale of the 2011 northeast Japan earthquake and the incidence of acute myocardial infarction

Authors: Tanaka F et al.

Summary: This study examined the influence of the 2011 northeast Japan earthquake on the risk of AMI in people living in the northeast of Iwate prefecture, Japan. Cases were registered from 4 weeks before to 8 weeks after the disaster and in the corresponding periods in 2009 and 2010. The relative risk of AMI was 2.03 for the 4-week period after the disaster compared with the corresponding periods in the preceding years. The number of deaths peaked in the first week after the earthquake before decreasing to levels seen in the preceding years then increasing again after high-magnitude aftershocks. The incidence of AMI was positively correlated with the seismic scale of the earthquake.

Comment: This Japanese study once again shows that there is an increased risk of MI after major stressful events, in this case an earthquake, and that this effect was not extinguished with the repeat stress of aftershocks. This is presumably mediated by sympathetic excess causing plaque rupture, and it would also be interesting to see if there was an increase in Takotsubo cardiomyopathy as well.

Reference: Am Heart J 2015;169(6):861-869

Abstract

Effects of withdrawing vs continuing renin-angiotensin blockers on incidence of acute kidney injury in patients with renal insufficiency undergoing cardiac catheterization

Authors: Baimey K et al., for the CAPTAIN Investigators

Summary: The CAPTAIN trial investigated the impact of withdrawing or continuing angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) prior to coronary angiography on contrast-induced acute kidney injury (AKI). 208 patients taking ACEI/ARBs who had moderate renal insufficiency were randomised to withhold ACEI/ARB treatment ≥24 hours prior to cardiac catheterisation or to continue treatment. The primary outcome was the incidence of AKI (≥0.5 mg/dL increase in serum creatinine from baseline and/or a relative increase of ≥25%) at 48–96 hours post-procedure. The primary outcome occurred in 18.4% of patients who continued ACEI/ARB compared with 10.9% of patients who withheld ACEI/ARB prior to surgery may decrease peri-operative hypotension and renal failure but this has not become commonly adopted. This study shows that contrast-induced nephropathy may be reduced in patients with renal impairment by withholding these agents prior to the angiography, and if this can be reproduced in larger studies, this practice will be incorporated into regular clinical practice.

Comment: There have been reports that withholding ACEI/ARBs >24 hours prior to surgery may decrease peri-operative hypotension and renal failure but this has not become commonly adopted. This study shows that contrast-induced nephropathy may be reduced in patients with renal impairment by withholding these agents prior to the angiography, and if this can be reproduced in larger studies, this practice will be incorporated into regular clinical practice.


Abstract

Long-term mortality following interhospital transfer for acute myocardial infarction

Authors: Ranasinghe I et al.

Summary: This Australian study assessed long-term mortality after interhospital transfer for AMI. 40,482 patients who were admitted to hospitals in NSW with AMI in 2004–2008 were included in the initial cohort. Of these, 8427 patients who were transferred were propensity score matched with 8427 patients who were not transferred. Mortality rates (in-hospital and up to 5.5 years post-discharge) were compared among transferred and non-transferred patients. In the matched cohort, transferred patients were more likely to undergo revascularisation (55.6% vs 13.7%) and had lower mortality at 30 days (3.5% vs 5.7%), 1 year (7.5% vs 12.6%) and at the end of follow-up (15.3% vs 22.5%) than patients who were not transferred.

Comment: Although it is costly, inconvenient and often logistically difficult to transfer patients to specialised centres post ACS (often from regional areas), this study shows that it is worth the effort, in that patients’ short and long term outcomes are much better if transfer is undertaken.

Reference: Heart 2015;101:1032-1040

Abstract

Prognostic significance of peri-procedural myocardial infarction in the era of high sensitivity troponin

Authors: Liu K et al.

Summary: This study validated the joint ACCF/AHA/ESC/WHF Universal Definition of peri-procedural myocardial infarction (PMI) using high sensitivity troponin T (hsTnT). 459 patients who underwent percutaneous coronary interventions in 2001–2013 were included. 76.9% of them were male, and their mean age was 68.6 years. PMI was observed in 4.3% of patients based on the Universal Definition. PMI predictors were chronic kidney disease (odds ratio 3.0), family history of cardiovascular disease (2.7) and use of IIb/IIIa inhibitors (4.2). Major adverse cardiac events (MACE) were reported in 4.4% of patients at 12 months, and were significantly and independently associated with PMI (odds ratio 7.3). Patients with MACE had much higher post-procedural hsTnT levels than those without MACE (156 vs 43 ng/L; p<0.001).

Comment: Periprocedural MI is uncommon but when it occurs, it portends an increased risk of recurrent events in the year after the procedure, with a larger troponin rise being associated with greater risk. This being the case, this type of MI (type 4a) should be included as an end-point in clinical trials, which is often not the case.

Reference: Heart Lung Circ 2015;24(7):673-81

Abstract
Abstract

Comparison of clinical efficacy and cost of a cardiac imaging strategy versus a traditional exercise test strategy for the investigation of patients with suspected stable coronary artery disease

Authors: Demire O et al.

Summary: This study compared the use of a cardiac imaging strategy and a traditional exercise test strategy for the investigation of patients with suspected stable CAD. Data for patients seen in rapid access chest pain clinics at 2 UK hospitals over a 12-month period were reviewed. Hospital A investigated 483 patients using an exercise tolerance test (ETT) and hospital B investigated 295 patients using a cardiac imaging test. Based on the findings of the ETT, hospital A performed invasive coronary angiography (ICA) in 127 (26.3%) patients, and 52 (40.9%) had obstructive CAD. Data for patients seen in rapid access chest pain clinics at 2 UK hospitals.

Comment: Study supports an early imaging strategy (CTCA, stress echo or nuclear) in the diagnosis of symptomatic CAD, and suggests this leads to more accurate diagnosis, less invasive procedures and lower costs. Many hospitals in Australia have adopted this strategy already, so it is reassuring to see that there is now some evidence to support this practice.

Reference: Am J Cardiol 2015;115(12):1631-1635

Abstract

Optimal cutoff levels of more sensitive cardiac troponin assays for the early diagnosis of myocardial infarction in patients with renal dysfunction

Authors: Twerfenbold R et al.

Summary: This study examined the clinical utility of 7 more-sensitive cardiac troponin (cTn) assays in patients with renal dysfunction presenting with symptoms suggestive of AMI. 2813 patients who presented with chest pain (16% with renal dysfunction) were included. In patients with renal dysfunction and elevated baseline cTn levels (>99th percentile), AMI was the most common diagnosis for all assays (range 45%–80%). Diagnostic accuracy in patients with renal dysfunction (quantified by the area under the receiver-operator characteristic curve [AUC]) was 0.87–0.89 at presentation and increased to 0.91–0.96 at 3 hours, with no significant differences between the 7 cTn assays. Overall, the AUC in patients with renal dysfunction was only slightly lower than in patients with normal renal function. The optimal AUC-derived cTn cut-off levels in patients with renal dysfunction were significantly higher than those in patients with normal renal function.

Comment: It is sometimes difficult to determine if a troponin rise in the setting of chest pain with renal impairment is due to ACS or due to decreased excretion. This study shows that high-sensitivity troponin is still accurate for the diagnosis of MI in this context, but suggests that higher cut-offs should be considered for patients with renal dysfunction, although this would have to be formally tested before it could be adopted.

Reference: Circulation 2015;131:2041-2050

Abstract

POST-MI PATIENTS 
REMAIN AT HIGH AND PERSISTENT RISK¹⁻⁴

up to 20% RISK of a recurrent CV event in the first year¹,²

~20% RISK of a recurrent CV event in the subsequent 3 years¹

After a successful intervention, what more can we do to protect them from their subsequent disease?

¹The APOLLO HELICON analysis was a retrospective cohort study that included 108,915 patients from a national Swedish registry with a primary diagnosis of acute MI between July 2006 and June 2011. The primary endpoint was risk for non-fatal MI, non-fatal stroke, or cardiovascular death. The cumulative 1 year incidence of the primary endpoint was 18.3%. In patients who were event free at 1 year, the cumulative incidence of the primary endpoint was 28% after the following 3 years. ²On the basis of pooled data (Framingham Heart Study, Atherosclerosis Risk in Communities Study, and National Heart, Lung, and Blood Institute), the American Heart Association reported that 19% of men and 26% of women aged ≥45 years will die within 1 year after a first MI.³Reference 1. Jernberg T et al. Eur Heart J 2015; doi:10.1093/eurheartj/ehu505. 2. Mozaffarian D et al. Circulation 2015;131(4):434–441. 3. Nakatani D et al. Circ J 2013;77:439–446. 4. Kikkert WJ et al. Am J Cardiol 2014;113:229–235. AstraZeneca Pty Ltd. ABN 54 009 682 311. 5 Alma Road, North Ryde NSW 2113. Medical Information. 1800 805 342; www.astrazeneca.com.au, 406991.022, WL287191, July 2015.