A RESEARCH REVIEW™
CONFERENCE REVIEW

ACC 67th Annual Scientific Session & Expo 2018

Making Education Easy

Orlando, USA; March 9–12, 2018

In this review:

Abbreviations used in this review
ACS = acute coronary syndrome
ANZACS-QI = All New Zealand Acute Coronary Syndrome Quality Improvement
CMR = cardiac magnetic resonance
CV = cardiovascular
DAPT = dual antiplatelet therapy
EF = ejection fraction
HDL/LDL = high/low-density lipoprotein
HF = heart failure
HR = hazard ratio
LV = left ventricular
MI = myocardial infarction
NSTEMI/STEMI = (non-)ST-segment elevation MI
PAD = peripheral artery disease
PCI = percutaneous coronary intervention
PCSK9 = proprotein convertase subtilisin/kexin type 9
SBP = systolic blood pressure
SGLT-2 = sodium-glucose cotransporter-2
TIMI = thrombolysis in MI.

Welcome

to this review of ACC.18, the 67th Annual Scientific Session & Expo of the American College of Cardiology (ACC), held recently in Orlando, Florida. Dr Mayanna Lund (Middlemore Hospital, Auckland) and Associate Professor Craig Juergens (Liverpool Hospital, New South Wales) attended the prestigious event and have selected ten presentations that we hope you will find informative. Where available, links to published study results have been provided, and the other abstracts can be found on the ACC 2018 website (for registered users) or on the ACC.18 mobile apps.

I hope you find the Conference Review interesting and I look forward to your feedback.

Kind regards

Dr Chris Tofield
christofield@researchreview.co.nz

A cluster-randomized trial of blood-pressure reduction in black barbershops

Authors: Victor R et al.

Summary: Interventional therapy was compared with standard therapy in black barbershop patrons with uncontrolled hypertension in a cluster randomised trial. 319 black men with hypertension who were patrons at 52 black-owned barbershops were assigned to a pharmacist-led intervention (barbers encouraged meetings in barbershops with specialty-trained pharmacists who prescribed antihypertensive drug therapy) or to an active control approach (barbers encouraged lifestyle modification and doctor appointments). Change in SBP at 6 months (primary outcome) was –27.0mm Hg in the intervention group compared with –9.3mm Hg in the standard therapy group (p<0.001).

Comment (ML): Take an undertreated patient group (US black men with hypertension), a frequently visited, trusted community member (the barber), a health professional (the pharmacist), shared stories and standard antihypertensives, and blend. The investigators of this cluster randomised controlled study have previously shown small reductions in blood pressure with the intervention of barbers trained to measure blood pressure, and advising patients to see primary care physicians when indicated. The addition of a prescribing pharmacist visiting the barbershop in the intervention group resulted in a mean 27mm Hg reduction in systolic BP from baseline. There are caveats – the pharmacists were treating to the most recent ACC guidelines and may have targeted lower blood pressures than primary care physicians, and the follow-up was only 6 months. There was also significant resourcing including multiple pharmacist encounters, training of barbers, educational materials, and haircuts. However, there are important lessons here for developing models of care that improve equity through facilitating uptake of proven (and inexpensive) therapies.

Session 408
Reference: N Engl J Med 2018;378:1291-1301; Abstract

Independent commentary by Dr Mayanna Lund MBChB FRACP FCSANZ

Mayanna is a heart failure specialist at Counties Manukau Health and the current Chair of the NZ Heart Failure Working Group. After training in Cardiology at Green Lane Hospital, she undertook fellowships in cardiac transplantation at St Vincent's Hospital in Sydney, and echocardiography and heart failure at Brigham and Women's Hospital in Boston. She is an Honorary Senior Clinical Lecturer for the University of Auckland. Her current interests include the use of big data for quality improvement, the multidisciplinary care of heart failure patients, and cardiac disease in women. Mayanna was on the founding steering group for the NZ Heart Failure Registry, is a former Go Red for Women Ambassador for the NZ Heart Foundation, and is a member of the Heart Foundation Heart Healthcare Specialist Advisory Group.

Independent commentary by Associate Professor Craig Juergens

Associate Professor Craig Juergens is an Interventional Cardiologist at Liverpool Hospital where he is Director of the Cardiac Catheterisation Laboratories. Apart from his interest in Interventional Cardiology, he has a major interest in acute coronary syndromes and has been involved in a large number of multicentre, multinational clinical trials and is author of over 40 peer reviewed papers.

Lower cardiovascular risk associated with SGLT-2i in >400,000 patients: the CVD-REAL 2 study

Authors: Kosiborod M et al.

Summary: The CVD-REAL 2 study examined CV outcomes in patients with type 2 diabetes who were started on SGLT-2 inhibitor therapy compared with other glucose-lowering drugs. New users of SGLT-2 inhibitors and other glucose-lowering drugs were identified via claims, medical records and national registries in South Korea, Japan, Singapore, Israel, Australia and Canada. Dapagliflozin, empagliflozin, ipragliflozin, canagliflozin, tofogliflozin, and luseogliflozin accounted for 75%, 9%, 8%, 4%, 3% and 1% of exposure time in the SGLT-2 inhibitor group. Compared with other glucose-lowering drugs, use of SGLT-2 inhibitors was associated with lower risk of death (HR, 0.51; p<0.001), hospitalisation for HF (0.64; p=0.001), death or hospitalisation for HF (0.60; p<0.001), MI (0.81; p<0.001) and stroke (0.68; p<0.001).

Comment (ML): The increasing prevalence of type 2 diabetes and its cardiovascular complications has changed the profile of heart disease in our communities. Randomised controlled trials of the newer diabetes drug class SGLT-2 inhibitors show consistent reductions in hard CV end-points. The majority of patients in these studies had established CV disease and were recruited from Europe and the US. CVD-REAL 2 used de-identified health records from 6 nations, including 4 in the Asia-Pacific region, to compare CV events in patients commenced on SGLT-2 inhibitors with propensity matched patients commenced on other glucose-lowering drugs. Each group had 235,064 patients, with a total follow-up of over 490,000 patient-years. Essentially, SGLT-2 inhibitor initiation was associated with reduced events across the spectrum of CV disease, with consistent results across countries and ethnicities. While healthcare and societal efforts to prevent development of type 2 diabetes are essential to improve New Zealanders' future CV health, SGLT-2 inhibitors offer a paradigm shift in our management of patients with established diabetes.

Session 407
Reference: J Am Coll Cardiol 2018; published online Mar 11; Abstract

Major adverse limb events in lower extremity peripheral artery disease: COMPASS trial

Authors: Anand S et al.

Summary: This subgroup analysis of the COMPASS trial evaluated the prognosis of patients with lower extremity PAD and a major adverse limb event (MALE). Outcomes in 6391 patients with lower extremity PAD were analysed. A total of 128 patients had an incident MALE (severe limb ischaemia leading to an intervention or major vascular amputation) during a median follow-up of 21 months. The MALE index event significantly increased the risk of subsequent hospitalisation (HR, 7.21; p<0.0001), subsequent amputation (197.5; p<0.0001) and death (3.23; p<0.001). Compared with aspirin alone, the combination of rivaroxaban 2.5mg twice daily plus aspirin significantly reduced the incidence of MALE by 43%, total vascular amputations by 58%, peripheral vascular interventions by 24%, and all peripheral vascular outcomes by 24%.

Comment (ML): This sobering study assessed risk factors and prognosis of MALE. 6391 patients with PAD were enrolled in the COMPASS trial, which randomised patients with stable atherosclerosis to low dose rivaroxaban with aspirin, rivaroxaban alone or aspirin alone for the prevention of CV events. MALE occurred in 128 patients (2%) over 21 months. It was less common in patients randomised to combination rivaroxaban and aspirin compared to aspirin alone. On multivariable analysis, the risks for MALE were related to the severity of the PAD (prior stenting or vascular surgery, prior amputation, Fontaine Class 3 or 4), and randomisation to aspirin. MALE was associated with a subsequent 3-fold risk in mortality. The study is a post hoc analysis, and small numbers of MALE events occurred. Regardless, the subsequent poor prognosis makes prevention an urgent priority.

Session 407
Reference: J Am Coll Cardiol 2018; published online Mar 11; Abstract

Association of hospital performance based on 30-day risk-standardized mortality rate with long-term survival after heart failure hospitalization

Authors: Pandey A et al.

Summary: The long-term clinical implications of hospitalisation for HF at centres defined as high vs low performing based on 30-day risk-standardised mortality rates (RSMR) were assessed in this analysis of data from the Get With The Guidelines-HF registry. 106,304 patients with HF who were admitted to 317 centres in 2005–2013 were included. Hospital-specific 30-day RSMR was calculated using a hierarchical logistic regression model and ranged from 8.6% (quartile 1 [Q1]) to 10.7% (Q4). Hospitals in the low 30-day RSMR group had greater availability of advanced HF therapies, cardiac surgery, and PCI. Patients admitted to hospitals in the high 30-day RSMR group had 14% higher relative risk of 5-year mortality than those admitted to hospitals in the low 30-day RSMR group.

Comment (ML): With increasing prevalence of HF, the associated human toll and healthcare costs continue to rise. Patients hospitalised with HF are at high risk for subsequent adverse events. While early readmission may intuitively be related to quality of care, penalties for higher rates of readmission in the US were associated with higher mortality rates. In this study, over 100,000 patients enrolled in the Get With The Guidelines Registry were studied according to 30-day RSMRs. Hospitals were classified into quartiles based on the 30-day RSMR (low to high). RSMR quartiles continued to predict mortality risk at 1, 3 and 5 years, with the association strongest in patients with reduced LVEF. Hospitals with the lowest mortality rates were more likely to be large, urban, and have advanced therapies available. However, they also performed better on more modifiable quality measures, such as LV function assessment, prescription of evidence-based medical therapies, discharge instructions and a post discharge appointment (metrics collected on the ANZACS-QI NZ Heart Failure Registry brief form). Only patients over 65 years were included, and this has implications for interpreting the study in the NZ context, where Māori and Pacific people with HF present up to 18 years earlier than other ethnicities. However, my take home is that our focus in the care of those hospitalised with HF should continue to be on improved uptake of guideline-directed management.

Session 412

Reference: JAMA Cardiol 2018; published online Mar 12; Abstract

OUTSMART HF: a randomized controlled trial of routine versus selective cardiac magnetic resonance in non-ischemic heart failure (IMAGE-HF project 1B)

Authors: Paterson I et al.

Summary: The OUTSMART-HF trial evaluated whether routine use of CMR yields more specific diagnoses of the underlying aetiology than selective CMR in patients with non-ischaemic HF. 501 patients with non-ischaemic HF from 12 tertiary care centres were randomised to routine or selective CMR. Eligible patients had either recently diagnosed HF or worsening symptoms within the last 12 months. The primary outcome was the aetiology of HF at follow-up as assessed by the treating physician. No differences in the clinical diagnosis of specific HF aetiology were found between routine and selective CMR strategies in patients with non-ischaemic HF. However, more specific HF aetiologies were identified by routine CMR at the time of image assessment.

Comment (ML): Non-ischaemic HF has overtaken ischaemic cardiomyopathy worldwide. Specific therapies may be indicated depending on aetiology. Guideline recommendations to perform CMR imaging in these patients have a level of evidence C. The Canadian OUTSMART investigators compared a strategy of routine CMR vs echo followed by selective CMR (protocol defined) in approximately 500 patients with non-ischaemic cardiomyopathy of unknown subtype. 51 non-protocol CMRs were performed in the selective CMR group. In the intention-to-treat analysis, the primary end-point of a specific clinical diagnosis being reached at 3 months was not met. The secondary end-point of death or CV hospitalisation was not improved by the routine CMR strategy. However, post hoc analysis showed that when a specific diagnosis was made, regardless of randomisation, patients had better event-free survival. This was an important attempt to measure the benefit of routinely adding a CMR to the diagnostic work-up of HF patients. Unfortunately, the level of evidence C stands.

Session 412

Cardiovascular outcomes with alirocumab after acute coronary syndrome

Authors: Steg P et al., for the ODYSSEY Outcomes Investigators

Summary: CV outcome results of the ODYSSEY Outcomes trial of alirocumab in ACS were presented in this special late-breaking clinical trial presentation. The trial randomised 18,924 patients with recent ACS receiving statin therapy up to the maximum tolerated dose and with a residual LDL cholesterol level ≥70 mg/dL, a non-HDL cholesterol level of ≥100 mg/dL or an apolipoprotein B level of ≤80 mg/dL to receive subcutaneous alirocumab 75mg every 2 weeks or matching placebo. The alirocumab dosage was doubled in participants with an LDL cholesterol level ≥50 mg/dL on alirocumab 75mg, and those with two consecutive LDL cholesterol level measurements of <15 mg/dL on alirocumab 75mg were switched to placebo. The trial's primary outcome was time to first occurrence of coronary heart disease death, nonfatal MI, unstable angina requiring hospitalisation or ischaemic stroke. At the time of reporting, it was anticipated that follow-up would be a median of 33 months, with ≥40% of participants followed for ≥36 months. The results were reported at the conference.

Comment (CJ): The ODYSSEY trial represents the second outcomes trial of PCSK9 inhibitors, using alirocumab from Sanofi. This was a large multinational trial including sites in New Zealand, which achieved its primary end-point and in an exploratory analysis reduced total mortality. There were some differences from the Fourier trial including a more recent history of an ACS (average 2.6 months), a run-in period of statin usage, enrollment of patients who were truly statin intolerant (0.9%) and a protocol that allowed down-titration or cessation of the active drug if LDL cholesterol levels were extremely low (<15 mg/dL). The results are exciting but we need to work out how we are going to afford these newer agents, although the investigators highlighted that the greatest absolute benefits were in patients whose baseline LDL cholesterol level was ≥100 mg/dL despite a maximally tolerated dose of statin.

Session 401

Efficacy of a wearable cardioverter-defibrillator after myocardial infarction

Authors: Olgin JE et al.

Summary: VEST (Vest Prevention of Early Sudden Death Trial) randomised patients with acute MI and an EF of ≤35% to receive medical therapy with (n=1524) or without (n=778) a wearable cardioverter-defibrillator vest from hospital discharge. Sudden death at 3 months was the primary outcome, with total and cause-specific mortality, nonfatal ventricular arrhythmias and hospitalisations evaluated as secondary outcomes; both intent-to-treat and on-therapy analyses were planned. Follow-up concluded in August 2017, and findings were reported at the conference.

Comment (CJ): This long-awaited trial failed to reach its primary end-point (sudden cardiac death and death from ventricular arrhythmia), although tantalisingly showed a reduction in total mortality from 4.9% to 3.1% (p=0.04) in the vest group. This may have been related to misclassification of sudden cardiac death or other benefits of wearing the vest, including detecting and treating non-sustained ventricular tachycardias or atrial arrhythmias. Notably due to slow recruitment, the primary end-point was changed, and patients only wore the vest for an average of 14.1 hours a day, and up to 20% of patients assigned to the vest group did not wear it at all. There were 20 appropriate shocks delivered in the vest group, and of these, 14 survived. We await further analysis of what number of subjects died whilst not wearing the vest, but at this point in time the usage of the device should remain as a class IIb indication.

Session 401

Loading doses of atorvastatin versus placebo in patients with acute coronary syndromes and planned revascularization

Authors: Berwanger O et al.

Summary: Patients with ACS suitable for PCI were randomised to receive two loading doses of atorvastatin 80mg (n=2087) or matching placebo (n=2104), administered before and 24 hours after the procedure, and all participants received atorvastatin 40mg for 30 days starting 24 hours later in the SECURE-PCI trial conducted by Brazil-based researchers. 99.3% of participants completed the 30-day follow-up, with 64.7% undergoing PCI, 8% undergoing coronary artery bypass graft surgery and 27.3% receiving medical management only. No significant difference was seen between the atorvastatin and placebo recipients for the 30-day major adverse CV event rate (6.2% vs 7.1%). There were no cases of hepatic failure and three cases of rhabdomyolysis, all in the placebo arm.

Comment (CJ): There are no large studies assessing the benefits of high-dose statin loading prior to planned coronary intervention in an ACS population. This 4191-patient study addressed this gap, in a multicentre, double-blind, placebo-controlled trial from Brazil. Up to 25% of patients had STEMI, and overall 64% of patients underwent PCI. The overall results of the trial did not suggest a reduction in 30-day major adverse CV events by high-dose atorvastatin given between 7 and 9 hours before angiography, but there was a suggestion of benefit in the group who actually underwent PCI (7.0% vs 8.5%), which perhaps should be the focus of future studies. We know giving statins long term in ACS is good, and there appears to be no harm in starting this as soon as possible in this population.

Session 404
Reference: JAMA 2018;319(13):1331-40; Abstract

Carvedilol for prevention of chemotherapy-induced cardiotoxicity

Authors: Avila M et al.

Summary: Patients with HER2-negative breast cancer tumour status and normal LVEF referred for anthracycline therapy were randomised to receive carvedilol or placebo until completion of chemotherapy in the CECCY trial from Brazil. There was no significant difference between the carvedilol and placebo arms for preventing a ≥10% reduction in LVEF at 6 months (primary end-point; 14.5% vs 13.5%) or for change in LVEF or brain natriuretic peptide level, although carvedilol recipients did have a significantly lower troponin I level over time (p=0.003), a significantly lower incidence of diastolic dysfunction (p=0.039) and a trend for a lesser increase in LV end-diastolic diameter (p=0.057).

Comment (CJ): Anthracycline chemotherapy is associated with cardiotoxicity and it is important to find ways to minimise this. This study from Brazil compared carvedilol with placebo in patients with a baseline normal resting EF receiving doxorubicin. Whilst carvedilol did not prevent the incidence of a decrease in EF by ≥10% (15% vs 14%), there was a reduction in biomarker elevation, the significance of which remains to be seen. Interestingly, there were large numbers of patients excluded due to baseline usage of β-blockers and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, which made the study difficult to do, and there was no mention of subtler measures of LV function such as global longitudinal strain. The authors hope to follow patients out to 2 years, which will be of interest.

Session 405
Reference: J Am Coll Cardiol 2018; published online Mar 11; Abstract

6-month versus 12-month or longer dual antiplatelet therapy after percutaneous coronary intervention in patients with acute coronary syndrome (SMART-DATE)

Authors: Hahn J-Y et al.

Summary: Patients with unstable angina and NSTEMI or STEMI scheduled for PCI were randomised to receive 6 months (n=1357) or ≥12 months (n=1355) of DAPT in this trial from South Korea; DAPT included clopidogrel in 79.7% and 81.8% of the respective DAPT arms. Six months of DAPT was found to be noninferior to ≥12 months for the cumulative composite primary end-point event rate (death from any cause, MI or stroke at 18 months; 4.7% vs 4.2% [p=0.03 for non-inferiority]). Of the component end-points, neither the all-cause mortality rate (2.6% vs 2.9%; p=0.90) nor the stroke rate (0.8% vs 0.9%; p=0.84) differed significantly between the two groups, but the MI rate was significantly greater in the 6-month DAPT group (1.8% vs 0.8%; p=0.02). No significant difference was seen between the 6- and 12-month DAPT groups for the stent thrombosis rate or the Bleeding Academic Research Consortium type 2–5 bleeding rate.

Comment (CJ): Current guidelines suggest the use of DAPT for at least 12 months after ACS, but there is interest in reducing this duration in the current era of newer generation drug-eluting stents. This multicentre, randomised, open-label, non-inferiority trial from South Korea sought to compare 6 months with 12 months of therapy. Whilst the trial met non-inferiority, there was a concerning higher rate of MI after 6 months (1.8% vs 0.8%; p=0.02) in the 6-month therapy group, and consistent with other data, close to half of these were in the nonculprit vessel (0.8%). As expected, there was more total bleeding in the 12-month group, but no significant difference in major bleeds. Overall the recommendation of minimum 12-month therapy should remain, particularly in patients at low bleeding risk.

Session 409
Reference: Lancet 2018;391(10127):1274-84; Abstract

SANOFI

Publication of this Conference Review was supported by an educational grant from Sanofi. The content and opinions expressed in this publication do not necessarily reflect the views of Sanofi unless so specified.