Welcome to this review of the European Society of Cardiology (ESC) Congress held recently in Barcelona.

The ESC Congress is the world’s largest and most influential cardiovascular event, with over 500 experts sessions and more than 4,500 abstracts contributing to the advancement of cardiovascular medicine worldwide. Professor John French attended the Congress and selected the presentations included in this review. Many high profile studies were reported at the Congress and a number of them were published simultaneously in major journals. Where possible we have included the link to the published article. Otherwise abstracts and presentations can be reached via the ESC365 application on the ESC website (http://compess365.escardio.org/).

We hope you enjoy these selections and look forward to your comments and feedback.

Kind Regards,

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Rivaroxaban with or without aspirin in stable cardiovascular disease
Presenter: John Eikelboom (Hamilton, Canada)

Summary: The double-blind COMPASS trial evaluated the use of rivaroxaban with or without aspirin in stable cardiovascular disease. 27,395 patients with stable atherothrombotic cardiovascular disease were randomised to receive rivaroxaban 2.5mg twice daily plus aspirin 100mg once daily, rivaroxaban 5mg twice daily alone, or aspirin 100mg once daily. The primary outcome (a composite of cardiovascular death, stroke, or MI) occurred in fewer patients in the rivaroxaban plus aspirin group than in the aspirin alone group (4.1% vs 5.4%; hazard ratio, 0.76; p<0.001), but major bleeding events occurred in more patients in the rivaroxaban plus aspirin group (3.1% vs 1.9%; hazard ratio, 1.7; p<0.001). Rivaroxaban 5mg twice daily did not result in better cardiovascular outcomes than aspirin alone and was associated with more major bleeding events. The study was stopped for superiority of the rivaroxaban plus aspirin group after a mean follow-up of 23 months.

Comment: COMPASS was presented as a late breaking clinical trial and published in NEJM. The trial found that rivaroxaban 2.5mg twice daily and aspirin was superior to aspirin alone in patients with stable coronary heart disease. These findings are congruent with previous trials, including ATLAS-TIMI 51 and PIONEER-AF, which showed that this low dose of rivaroxaban was beneficial in patients treated with dual antiplatelet therapy, either post-MI or those with AF undergoing PCI. The approach of targeting both antiplatelet and Factor 10 pathways is conceptually attractive. However, whether this rivaroxaban dose will translate into clinical practice in Australia, and what the best combination of antiplatelet therapy in post-MI patients is, remains to be determined.

Reference: New Engl J Med 2017; published online Aug 27

Abstract

COMPASS-PAD: cardiovascular outcomes for people using anticoagulation strategies trial: results in patients with peripheral arterial disease
Presenter: Sonia Anand (Hamilton, Canada)

Summary: This analysis of the COMPASS trial evaluated the use of rivaroxaban with or without aspirin in patients with PAD. 7470 patients with PAD were enrolled in COMPASS, of whom 4129 had symptomatic PAD limbs, 1919 had carotid disease, and 1422 had coronary artery disease and low ankle-brachial index. Patients were randomised to 1 of 3 groups: rivaroxaban 2.5mg twice daily plus aspirin 100mg daily; rivaroxaban 5mg twice daily alone; or aspirin 100 mg daily alone. Results in the PAD subgroup showed significant benefits of the combination arm on both major adverse cardiovascular events and major adverse limb events. The combination increased the risk of major bleeding but did not increase the risk of fatal or critical organ bleeding, and most major bleeds were reversible.

Comment: This COMPASS additional presentation addressed the randomised treatment of patients with PAD with rivaroxaban 2.5mg twice daily. In several prior trials of other agents (e.g. clopidogrel) in patients with both coronary and PAD, putatively beneficial agents have been less effective in the latter group of patients compared with patients with coronary artery disease. Thus, given the paucity of data suggesting benefit of agents other than statins and aspirin in this group of PAD patients, the approximately 50% reduction in events (including amputation) among those randomised to rivaroxaban 2.5mg twice daily in this study should lead to its adoption in Australia for this indication.

Session: Hot Line: Late Breaking Clinical Trials 1; ESC Congress 2017
Dual antithrombotic therapy with dabigatran after PCI in atrial fibrillation

Presenter: Christopher Cannon (Boston, USA)

Summary: The RE-DUAL trial examined the use of dual antithrombotic therapy with dabigatran after PCI in patients with AF. 2725 patients with AF who had undergone PCI were randomised to receive triple therapy with warfarin plus a P2Y12 inhibitor (clopidogrel or ticagrelor) and aspirin (for 1–3 months) or dual therapy with dabigatran 110mg or 150mg plus a P2Y12 inhibitor. The risk of bleeding was lower in patients who received dual therapy with dabigatran and a P2Y12 inhibitor than in those who received triple therapy. Dual therapy was noninferior to triple therapy with respect to the risk of thromboembolic events.

Comment: This trial randomised patients to either triple therapy (warfarin plus dual antiplatelet therapy) or dual therapy with dabigatran and a P2Y12 inhibitor. The rates of the primary composite efficacy end-point of thromboembolic events (MI, stroke, or systemic embolism), death, or unplanned revascularisation was 13.7% with dual therapy compared with 13.4% with triple therapy. While the trial design is somewhat different from that of the PIONEER AF-PCI trial (ivaroxaban was used as the oral anticoagulant in the experimental arms), these results are enabling in terms of using dabigatran compared to using warfarin. However, whether dabigatran will become the direct oral anticoagulant of choice when one is needed post-PCI remains to be determined.

Reference: New Engl J Med 2017; published online Aug 27

Apixaban vs conventional therapy in anticoagulation-naive patients with atrial fibrillation undergoing cardioversion: The EMANATE Trial

Presenter: Michael Ezekowitz (Villanova, USA)

Summary: The EMANATE trial compared the rates of stroke and bleeding with apixaban versus usual care (heparin and warfarin) in anticoagulation-naive patients with AF randomised for elective cardioversion. 1,500 patients were randomly allocated to apixaban 5mg twice daily or parental heparin with warfarin prior to cardioversion. Patients treated with apixaban had fewer strokes and similar bleeding to those receiving usual care. There were no strokes reported in the apixaban group and 6 strokes reported in the usual care group (p=0.01). No systemic embolic events were reported in either group. Major bleeds occurred in 3 and 6 patients in the apixaban and usual care groups, respectively, while clinically significant non-major bleeding occurred in 11 and 13 patients in the respective groups.

Comment: The cardioversion of patients with AF remains concerning regarding the risk of thromboembolism due predominantly to clot formation in the left atrial appendage (LAA). In this trial, apixaban therapy was compared to conventional therapy with heparin and vitamin K antagonist (usually warfarin) in patients with AF undergoing direct current (DC) cardioversion. It showed somewhat reassuringly that although thrombus was detected on occasions on transoesophageal echocardiography (TOE), this generally didn’t result in a systemic embolism, at least one that was clinically detected. Also, in each randomisation arm, repeat TOE at approximately 5 weeks showed a 50–60% reduction in LAA thrombus. Whether a TOE is required, based on these data or one can wait about 5 weeks on apixaban therapy and then perform DC cardioversion remains debatable, however this seems a cost-effective strategy.

Session: Hot Line: Late-Breaking Clinical Trials 2; ESC Congress 2017

Catheter ablation versus standard conventional treatment in patients with left ventricular dysfunction and atrial fibrillation: the CASTLE-AF trial

Presenter: Nassir Marrouche (Salt Lake City, USA)

Summary: The CASTLE-AF trial compared catheter ablation and standard treatment in patients with LV dysfunction and AF. 363 patients with LVEF ≤35% and AF were randomised 1:1 to catheter ablation or conventional treatment and were followed up for a median 37.8 months. The primary end-point of death or hospitalisation for heart failure occurred in 28.5% of patients in the catheter ablation group compared with 44.6% of patients in the conventional treatment group (p=0.007).

Comment: The successful DC cardioversion of AF to sinus rhythm has been a longstanding cardiology procedure. However there is evidence that among patients with heart failure and AF, improved survival and/or reduced hospitalisation for heart failure occurred after ablation of AF by pulmonary vein isolation compared to conventional therapy. The CASTLE-AF study showed that, among a relatively small number of randomised patients, there were reductions of >40% in AF frequency with catheter ablation compared to conventional therapy. This correlated with the reduction in both LV dysfunction and in fact survival. The extent of outcome improvements implies practice should be changed in this subgroup of AF patients with LV dysfunction.

Session: Hot Line: Late-Breaking Clinical Trials 1; ESC Congress 2017

Clinical outcomes of state-of-the-art percutaneous coronary revascularization in patients with de novo three vessel disease: results of the SYNTAX II trial

Presenter: Javier Escaned (Madrid, Spain)

Summary: The SYNTAX II trial investigated whether recent technical and procedural developments in PCI significantly influence outcomes in patients with 3-vessel coronary artery disease. The new and improved PCI strategy required use of the SYNTAX II score to guide Heart Team decisions on myocardial revascularisation and guideline-directed medical therapy. SYNTAX II enrolled 454 patients at 22 European centres and the primary end-point was a composite of major adverse cardiac and cerebrovascular events (MACCE) at 1 year. Outcomes were compared with those in the SYNTAX I trial. The 1-year results showed a significantly lower rate of MACCE in SYNTAX II versus SYNTAX I PCI patients (10.6% vs 17.4%; p=0.006), as well as lower rates of MI (1.4% vs 4.8%; p=0.007), any repeat revascularisation (8.2% vs 13.7%; p=0.015), and definite stent thrombosis (0.7% vs 2.7%; p=0.045).

Comment: SYNTAX II recruited 454 patients in 22 European Countries and aimed to determine if the use of physiological assessment (a hybrid of instantaneous fractional reserve [iFR] and fractional flow reserve [FFR]) and the use of 6 clinical variables in the SYNTAX II score improved outcomes compared to the PCI and coronary artery bypass graft (CABG) arms in SYNTAX I. Of note, the addition of physiological assessment lowered the number of stents used in SYNTAX II, though the median SYNTAX score was slightly lower. MACCE rates after PCI were lower in SYNTAX II than SYNTAX I, and similar to those in patients in SYNTAX I randomised to CABG.

Session: Late-Breaking Science in PCI 1; ESC Congress 2017

Have we reached the bottom line in mortality after acute myocardial infarction?

Presenter: Nicolas Danchin (Paris, France)

Summary: This study assessed changes over 20 years in patient characteristics, management, and 6-month outcomes in patients admitted to intensive coronary care units for STEMI or NSTEMI in France. Data were analysed from 5 nationwide French surveys (the FAST-MI programme) that have been undertaken every 5 years since 1995. The surveys included all adult patients admitted to a coronary care unit or an intensive care unit within 48 hours of acute STEMI or NSTEMI onset over a 5-year period. Mortality rates in all STEMI and NSTEMI patients reduced from 17.2% to 5.3%, and for NSTEMI reduced from 17.2% to 6.3%. Indeed, over every 5-year period mortality improved including after adjustment for other factors and in patients who had no reperfusion as well. Compared to 1995, the adjusted mortality hazard ratio in all STEMI patients in 2015 was 0.32.

Session: Late-Breaking Science in PCI 2; ESC Congress 2017
Unexplained breathlessness or fatigue...
...could it be Pulmonary Arterial Hypertension (PAH)?

ACT EARLY
BEFORE MORE DAMAGE IS DONE


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Antinflammatory therapy with canakinumab for atherosclerotic disease

Presenter: Paul Ridker (Boston, USA)

Summary: The CANTOS trial evaluated the use of antinflammatory therapy with the monoclonal antibody canakinumab in patients with atherosclerosis. 10,061 patients with previous MI and a high-sensitivity C-reactive protein (hs-CRP) level >2 mg/L were randomised to placebo or 1 or 3 canakinumab doses (50mg, 150mg, and 300mg) subcutaneously every 3 months. The primary efficacy end-point was nonfatal MI, nonfatal stroke or cardiovascular death. At a median follow-up of 3.7 years, the incidence rate for the primary end-point (per 100 person-years) was 4.50 in the placebo group compared with 4.11, 3.86 and 3.90 in the canakinumab 50mg, 150mg, and 300mg groups, respectively. Hazard ratios compared with placebo were 0.93 (p=0.30), 0.85 (p=0.027) and 0.86 (p=0.031) in the respective groups. Canakinumab dose-dependently reduced hs-CRP levels from baseline without affecting lipid levels.

Comment: The hypothesis that inflammation in the blood vessel wall may contribute to clinical events in patients with atherosclerosis has been attractive for a few decades. However, proof of this concept has not been achieved until the results of the CANTOS trial were reported. The study found that patients with prior coronary heart disease and a hs-CRP level >2 fared better when randomised to receive specific antinflammatory therapy with the monoclonal antibody canakinumab. These patients had fewer late events. The results of this trial are provocative and may lead to further investigations of targets in the inflammatory milieu. Just what are the desired therapeutic targets and are they as well as, or instead of, further aggressive reduction in LDL cholesterol levels?

Reference: New Engl J Med 2017; published online Aug 27

Abstract

Oxygen therapy in suspected acute myocardial infarction

Presenter: Robin Hofmann (Stockholm, Sweden)

Summary: The registry-based DETO2X-AMI trial examined the use of routine oxygen therapy in patients with suspected acute MI. 6629 patients with suspected MI and an oxygen saturation <90% were randomised to receive either supplemental oxygen (6 L/min for 6–12 hours, delivered via an open face mask) or ambient air. The median duration of oxygen therapy was 11.6h, and the median oxygen saturation at the end of the treatment period was 99% in patients assigned to oxygen and 97% in patients assigned to ambient air. Hypoxaemia developed in 1.9% and 7.7% in patients assigned to ambient air. Hypoxaemia developed in 1.9% and 7.7% in the respective groups. Canakinumab dose-dependently reduced hs-CRP levels from baseline without affecting lipid levels.

Comment: Oxygen supplementation therapy has been routinely applied for decades in ambulances and emergency departments in patients with suspected acute MI, and has been supported by clinical guidelines. However, oxygen supplementation therapy has recently been questioned with suspected acute MI and has been supported by clinical guidelines. The DETO2X-AMI registry-based randomised trial, using the national SWEDHEART registry, found the routine use of oxygen supplementation was not useful, though also not harmful, in patients with suspected MI.

Reference: New Engl J Med 2017; published online Aug 27

Abstract

Catheter-based renal denervation in patients with uncontrolled hypertension in the absence of antihypertensive medications (SPYRAL HTN-OFF MED)

Presenter: Michael Böhm (Homburg/Saar, Germany)

Summary: The sham-controlled SPYRAL HTN-OFF MED study evaluated the effects of renal denervation on blood pressure in the absence of antihypertensive medications. 80 patients with uncontrolled hypertension who were drug-naive or discontinued their antihypertensive medications were enrolled at 21 centres in the USA, Europe, Japan, and Australia. Patients underwent renal angiography before being randomly assigned to renal denervation or a sham control group. The primary end-point was change in 24-h blood pressure at 3 months. Office and 24-h ambulatory blood pressure decreased significantly from baseline to 3 months in the renal denervation group but no significant changes were seen in the sham-control group.

Comment: The issue as to whether renal artery denervation can achieve an improvement in blood pressure which is sustainable has been the topic of intensive investigation and contradictory results thus far. The SPYRAL hypertension trial has been a further attempt to clarify this issue. Patients with hypertension were removed from other agents during the investigation and randomised to renal artery denervation with a newer device allowing more complete renal artery coverage, or a sham control. There was a resulting reduction in both 24-h and office blood pressure (the latter by 10mmHg). Whether this study will proceed to further investigations and whether there is a future for this technique in clinical practice remains to be seen.

Reference: Lancet 2017; published online Aug 28

Abstract

Efficacy of beta-blockers in heart failure according to left ventricular ejection fraction: an individual patient level analysis of double-blind randomised trials

Presenter: Dipak Kotecha (Birmingham, England)

Summary & comment: The issue as to whether beta-blockers improve late mortality after acute MI has been the subject of much discussion recently. Debate increased following the National Heart Foundation (NHF) and Cardiac Society of Australia and New Zealand (CSANZ) 2016 acute coronary syndrome guidelines that suggested discontinuation of these agents in low risk patients. While a heart failure cohort is different, this meta-analysis of several trials has shown mortality benefit of beta-blockers in those with LVEF <50%; the numbers with higher LVEF were too small to be confident about outcomes. This report implies that, in a post-MI population predominantly beta-blockers should be trialled in those with LVEF >50%.

Session: Late-Breaking Science in Heart Failure; ESC Congress 2017

Independent commentary by Professor John French. Director of Cororary Care and Cardiovascular Research at Liverpool Hospital, Sydney, and conjoint Professor at the University of New South Wales. After basic physician training he undertook a PhD at the University of Adelaide, further cardiology training at Greenlane Hospital, Auckland, New Zealand, and a Welcome Trust Postdoctoral Fellowship at University College London, UK. Prior to his current position Professor French was appointed to Greenlane Hospital and the University of Auckland from 1992-2003. Professor French has been an investigator and co-investigator in numerous randomised controlled trials, and has shown mortality benefit of beta-blockers in those with LVEF <50%; the numbers with higher LVEF were too small to be confident about outcomes. This report implies that, in a post-MI population predominantly beta-blockers should be trialled in those with LVEF >50%.

24-h and office blood pressure (the latter by 10mmHg). Whether this study will proceed to further investigations and whether there is a future for this technique in clinical practice remains to be seen.

Reference: Lancet 2017; published online Aug 28

Abstract

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