ESC Congress 2022 Conference Review™

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In this review:

Abbreviations used in this review:

BP = blood pressure; **CABG** = coronary artery bypass graft; **CV** = cardiovascular; **DAPT** = dual antiplatelet therapy; **HF** = heart failure; **LV/LVEF** = left ventricular (ejection fraction); **MI** = myocardial infarction; **PCI** = percutaneous coronary intervention; **SGLT-2** = sodium-glucose cotransporter-2.

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Welcome to this review of the 2022 ESC (European Society of Cardiology) Conference held in Barcelona.

The ESC was delighted to host the 2022 conference onsite in Barcelona this year, where more than 14,500 cardiology professionals from around the world gathered both in-person and online to explore the latest developments in CV medicine and patient care. This review covers ten interesting presentations that were featured at the conference, including a number of important trials in cardiology, such as ADVOR (intravenous acetazolamide for acute decompensated HF), REVIVED (multivessel PCI versus optimal medical therapy for ischaemic LV dysfunction), PACIFIC-AMI (asundexian added to DAPT in patients undergoing PCI for acute MI) and more.

We hope you enjoy this Conference Review, and we invite your comments and feedback.

Kind Regards,

Professor John French

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ADVOR: acetazolamide in acute heart failure

Speaker: Dr W Mullens (Genk, Belgium)

Summary: Eligible patients hospitalised with acute decompensated HF (mean age 78 years; 37.4% female) were randomised to receive intravenous acetazolamide 500mg (n=259) or placebo (n=260) each day in the ADVOR trial; participants were administered double the oral maintenance dose of intravenous oral loop diuretics over split doses, and acetazolamide or placebo was administered each day with the first dose. At a mean follow-up of 3 months, a greater proportion of participants in the acetazolamide arm achieved successful decongestion within 3 days of randomisation (primary outcome) than in the placebo arm (42.2% vs. 30.5% [p<0.001]), and this group also had a shorter mean duration of hospitalisation (8.8 vs. 9.9 days [p=0.016]). No significant between-group difference was observed for rehospitalisation for HF or mortality, a combined renal safety endpoint, hypokalaemia or hypotension.

Comment: Acetazolamide, a diuretic that reduces sodium resorption in the proximal tubule via carbonic anhydrase inhibition, has been available for decades but without a clear role in HF treatment. The ADVOR trial, which randomised patients with acute decompensated HF to 500mg daily of acetazolamide intravenously or matching placebo, showed a higher rate of successful treatment of congestion within 3 days, with no apparent adverse effects. There were significantly more patients discharged free of congestion. This supports a routine role for acetazolamide in patients with acute HF. While no socioeconomic analysis was presented, length of stay was reduced by 1 day, so routine adoption of this additional diuretic in acute HF treatment is likely to reduce the burden on hospitals.

Session: Hot Line Session 2

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Independent commentary by Professor John French.

Independent commentary by Professor John French, Director of Coronary 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 Wellcome 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 was on the steering committees of the SHOCK, OAT, HERO-2 and CRISP-AMI trials. Professor French has served on the clinical endpoints committees of several major trials. Professor French's current major research interests include the acute coronary syndromes especially ST elevation MI, and cardiac biomarkers, especially high-sensitivity troponins.

REVIVED: percutaneous revascularization for ischemic left ventricular dysfunction

Speaker: Prof. D Perera (London, UK)

Summary: These researchers compared revascularisation by PCI with optimal medical therapy in patients with LVEF ≤35%, extensive coronary artery disease and evidence of myocardial viability in this randomised open-label trial. Participants were randomised to receive either multivessel PCI (n=347) or optimal medical therapy (n=353). At follow-up of 3.4 years, there was no evidence that multivessel PCI improved LVEF or event-free survival. All-cause hospitalisation or mortality for HF (primary outcome) occurred in 37.1% and 38.0% of the PCI and optimal medical therapy groups, respectively (p=0.96); similar findings were observed in all subgroups. There was no significant between-group difference for all-cause mortality, acute MI or 12-month LVEF.

Comment: Since the CASS trial 4 decades ago (when there was little medical therapy), CABG has been shown to improve survival in patients undergoing CABG with severe LV impairment, a mortality benefit of CABG confirmed on 10-year follow-up of the STICH trial, which randomised patients in the 2000s to CABG in addition to optimal medical therapy or the latter alone. However, registries report PCI continues to be the more common revascularisation procedure used in ischaemic cardiomyopathy. To attempt to provide data to support such practice, the REVIVED trial randomised patients with ischaemic cardiomyopathy with a large (viable) ischaemic burden on nuclear scanning to PCI or optimal medical therapy, and reported no difference in late mortality from any cause or hospitalisation for HF; there were no reductions in individual components. The REVIVED trial raises many questions including the study population ('only' 700 patients were randomised in 6.6 years from 40 UK centres), the role of viability studies in directing management, and the prognostic role of PCI in chronic coronary syndromes. Larger randomised trials, such as STICH-3, are needed to clarify treatment of patients with multivessel disease and significant LV impairment comparing CABG to PCI, on a background of currently optimal multiagent medical therapies.

Session: Hot Line Session 3

Genotype-guided oral P2Y12 inhibitor therapy reduces cumulative ischemic events following percutaneous coronary intervention – a prespecified secondary analysis of the TAILOR-PCI randomised trial

Presenter: Dr B Ingraham (Rochester, US)

Summary/comment: This prespecified secondary analysis from the TAILOR-PCI trial addressed the related questions: did identification of loss of function *CYP2C19* allele carriers and thus altering P2Y12 therapy reduce ischaemic outcomes? Among the 1849/5276 (35%) of patients with loss of function alleles in TAILOR-PCI, there was a 40% reduction in cumulative events, ischaemic and bleeding, at 12 months, among those randomised to genotype-guided therapy, with the major separation in the Kaplan-Meier curves occurring in the first ~90 days; there were no differences in any component either ischaemic or bleeding. These results have applications for practice in Australia, as 82% of patients had an acute coronary syndrome as the indication for randomisation. Thus, in places that use clopidogrel rather than ticagrelor for patients with an acute coronary syndrome, it could be argued that loss of function *CYP2C19* allele testing should occur if PCI is performed.

Session: Late-Breaking Science – Innovations in drug treatment

A pre-specified meta-analysis of DELIVER and EMPEROR-Preserved

Presenter: Dr M Vaduganathan (Boston, US)

Summary/comment: While the SGLT-2 inhibitors dapagliflozin and empagliflozin have recently been shown to improve clinical outcomes in HF, their role in patients with preserved LV function warranted clarification. Among >12,000 patients, mean age 72 years (44% female) and mean LVEF 54%, included in this meta-analysis, the primary endpoint of CV death or first HF hospitalisation was 20% lower among those randomised to SGLT-2 inhibitors; quality of life measures were also improved. Indeed among the almost 4000 patients with LVEF ≥60%, the benefit of SGLT-2 inhibitors was the same, confirming the role of these agents in HF therapy irrespective of LVEF.

Session: Hot Line Session 4

PACIFIC-AMI – efficacy and safety of factor XIa inhibitor asundexian on top of dual antiplatelet therapy after acute myocardial infarction

Presenter: Prof. J Alexander (Durham, US)

Summary/comment: For 3 decades, in addition to conceptual advantages, there has been evidence that 'antithrombin therapies' reduce ischaemic events in patients with acute MI. However, the key clinical question has been finding the 'sweet spot' of particular drug doses, especially in combination with antiplatelet therapies, which has often remained elusive as increased bleeding has tended to counter reductions in ischaemic events. In PACIFIC-AMI, a dose-ranging trial of the factor XIa inhibitor asundexian in patients with acute MI undergoing PCI, this agent on top of DAPT did not cause increased bleeding at any dose, although the trial was under-powered to examine major clinical outcomes. Whether this agent will find a place in the postacute MI therapeutic regimen, especially when aspirin is often now ceased earlier, awaits further trial evidence.

Session: Hot Line Session 5

ALL-HEART – allopurinol and cardiovascular outcomes in ischaemic heart disease

Presenter: Prof. I Mackenzie

Summary/comment: The idea that therapeutic suppression of levels of oxygen radicals has long been considered conceptually attractive by some (including this commentator). At least for the prevention of CV disease by the xanthine oxidase inhibitor allopurinol, this hypothesis has been refuted. Among people aged 60 years or more without gout, patients randomised to allopurinol had no difference in rates of nonfatal MI, nonfatal stroke or CV death. Of note, more than half those randomised to allopurinol, discontinued during the 4.8 years of follow-up, and a much higher rate in this group withdrew from the trial. Of note, the most common dosage of allopurinol was 600mg daily, potentially explaining the high withdrawal rate.

Session: Hot Line Session 3

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A polypill strategy in secondary prevention: results of the SECURE trial

Presenter: Dr V Fuster (New York, US)

Summary: In this phase 3 randomised controlled trial, patients who had experienced an MI within the preceding 6 months were assigned to either a polypill-based strategy consisting of aspirin100mg, ramipril 2.5mg, 5mg or 10mg and atorvastatin 20mg or 40mg (n=1237) or usual care (n=1229). Patient-reported adherence to treatment was higher in the polypill group than in the usual care group. Fewer primary outcome events (CV death, nonfatal type 1 MI, nonfatal ischaemic stroke, urgent revascularisation) and secondary outcome events (CV death, nonfatal type 1 MI, nonfatal ischaemic stroke) occurred in the polypill group than in the usual care group (9.5% vs. 12.7% [p=0.02] and 8.2% vs. 11.7% [p=0.005], respectively). Adverse events were similar in both groups.

Comment: The use of the polypill has conceptual advantages, especially when there are barriers (potential or real) to adherence to evidence-based secondary prevention therapies. In this trial, patients aged 65 years or more with at least one additional (high-) risk factor randomised to polypills containing aspirin 100mg, atorvastatin (20mg or 40mg) and ramipril (2.5mg, 5mg or 10mg), versus 'usual care', had 25% lower rates of the primary CV endpoint (including urgent revascularisation). The rate of the 'hard' major secondary endpoint of CV death, MI or stroke was 24% lower. While the polypill strategy does not require finessing lipid-modifying or BP therapies to targets, clearly usual care was suboptimal in achieving these targets. These results will apply to patients where circumstances mean usual care doesn't regularly achieve multiple evidence-based therapies.

Session: Hot Line Session 1

PERSPECTIVE – sacubitril/valsartan and cognitive function in HFmrEF and HFpEF

Presenter: Prof. J McMurray

Summary/comment: As neprilysin is involved in the proteolytic cleavage of β-amyloid peptides, including in the brain, there has been concern that sacubitril/valsartan, a neprilysin inhibitor therapy for HF, may allow accumulation of β-amyloid in the brain, and thus be associated with cognitive decline. The PERSPECTIVE trial randomised patients with HF (mean age 72.5 years) almost half of whom had atrial fibrillation and/or diabetes to sacubitril/valsartan or valsartan alone. The primary endpoint of cognitive function at 3 years was similar in each group, and interestingly, there was PET evidence of less β-amyloid plaques in brains in the sacubitril/valsartan group, adding to the list of clinical trials where a mechanistically hypothesised adverse (or beneficial) therapeutic effect has not been trial-confirmed.

Session: Hot Line Session 1

TIME – the treatment in morning versus evening study

Presenter: Prof. T MacDonald (Dundee, UK)

Summary: These researchers compared the impact of morning (6.00am to 10.00am) versus evening (8.00pm to midnight) dosing of BP medications in 21,104 hypertensive patients. At 5-year follow-up, there was no significant difference observed between evening versus morning dosing for vascular death, MI or stroke. In general, BP was found to be higher in the morning among patients who received morning dosing, and higher in the evening in those who received evening dosing.

Comment: As BP varies over a 24-hour cycle, and some patients find compliance with therapy easier at different times of the day, morning or night, whether it matters when antihypertensive therapy is taken is of potential prognostic significance. However, the TIME trial definitively found timing doesn't matter. Among >20,000 patients randomised to either morning or evening antihypertensive therapy and followed for at least 5 years, rates of vascular death, stroke or MI were similar. Among this low-risk cohort with event rates <1% per year, timing of BP treatment did not matter, implying that what time is best for patient compliance should be recommended.

Session: Hot Line Session 1

Routine stress testing after high-risk PCI – POST-PCI trial

Presenter: Prof. D Park (Seoul, Korea)

Summary: These researchers compared the efficacy of routine functional testing with standard care alone, as follow-up strategies to improve clinical outcomes among high-risk patients who have undergone PCI. At 1 year post-PCI, patients with high-risk anatomical or clinical characteristics were randomly assigned to either functional testing (nuclear stress testing, exercise electrocardiography or stress echocardiography; n=849) or standard care (n=857). At 24-month follow-up, a primary outcome event (all-cause mortality, MI or hospitalisation for unstable angina) had occurred in 5.5% of the functional testing group and 6.0% of the standard care group (p=0.62); there were no significant between-group differences for the secondary outcomes of invasive coronary angiography and repeat revascularisation.

Comment: Since the publication from the Cleveland Clinic in the 1990s showing residual ischaemia on sestamibi scanning after otherwise successful CABG was associated with worse late outcomes, there has been a popular vogue by extrapolation post-PCI to undertake routine exercise stress testing including with imaging. This trial from Korea reported, among patients undergoing high risk PCI and randomised to routine exercise stress testing (the use of imaging was recommended) or ischaemia guided-testing, that rates of the primary endpoint of death from any cause, MI or hospitalisation for unstable angina, were similar. Overall event rates were low despite the use of various high risk criteria required such as left main stenosis, multivessel PCI and chronic total occlusion(s), so whether these data apply to populations that have even higher late event rates is uncertain.

Session: Latest science – Hot topic

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