ESC Congress 2019 – clinical update from SA experts

Paris, France, 31 August – 4 September 2019

Introduction

During its annual meeting, the European Society of Cardiology (ESC) published guidelines on diabetes, pre-diabetes and cardiovascular disease, supraventricular tachycardia, dyslipidaemia, chronic coronary syndromes and acute pulmonary embolism. These guidelines are available to all at escardio.org/guidelines.

ESC guidelines and clinical trial updates

ESC guidelines

New dyslipidaemia guidelines

The latest ESC dyslipidaemia guidelines recommend lowering LDL-Cholesterol (LDL-C) in very high- and high-risk patients irrespective of baseline concentration. “There is overwhelming evidence from experimental, epidemiological, genetic studies and randomised clinical trials that higher LDL-C is a potent cause of cardiovascular disease and stroke,” according to Professor C Baigent (UK), chairman of the Guideline Committee. In addition, the guidelines recommend that in those most at risk, target LDL-C levels should be achieved together with a minimum 50% LDL-C reduction.

Risk stratification has also been revised; now patients with cardiovascular disease (CVD), diabetes with target organ damage, familial hypercholesterolaemia (FH) and severe chronic kidney disease (CKD) are all categorised as being at very high risk and should be on intensive LDL-C lowering therapy.

These recommendations have been developed with the involvement of the European Atherosclerosis Society and are summarised in a report by Professor Derick Raal (Johannesburg), published recently on the deNovo Medica website, CLICK HERE.

ESC guidelines on diabetic patients and cardiovascular risk

In this updated guidance, new emphasis has been placed on more frequent self-monitoring of blood glucose and blood pressure for patients with diabetes to achieve better control. This is due to new data that implicate glucose variability as a cause of heart disease in diabetes.

In addition, nocturnal hypoglycaemia is associated with deterioration in quality of life – this stresses the importance of not relying only on occasional glucose measurements. Flash technology has been developed, which uses a small sensor worn on the skin, and should be more widely used. These innovations, as they become less expensive, offer major opportunities to improve glucose control.

With regard to treatment, the main new recommendation is that GLP-1 receptor agonists and gliflozins should be used as first-line treatment in type 2 diabetes patients with established CVD. In patients who have poor circulation in the legs, the value of rivaroxaban as a non-vitamin K antagonist is stressed as beneficial for patients with peripheral vascular disease.
New findings from major trials

Heart failure

**DAPA-HF² - SGLT-2 inhibition in patients with heart failure with reduced ejection fraction (HFrEF)**

Dapagliflozin (10mg daily) was compared to placebo in 4,744 randomised patients with HFrEF (<40%), irrespective of diabetic status, with follow-up for 18 months. Exclusion criteria were eGFR <30ml/min/1.73m², hypotension and type 1 diabetes. Cardiovascular death, hospitalisation for heart failure (HF) or an urgent visit relating to HF were reduced from 21.2% (placebo) to 16.2% (dapagliflozin). Dapagliflozin reduced the incidence of both cardiovascular death and worsening kidney function. No adverse safety effects were observed. Results were not influenced by diabetic status.

**PARAGON-HF in heart failure with preserved ejection fraction (HFrEF)**

South Africa recruited 70 of the 4,822 patients with a left ventricular ejection fraction (LVEF) ≥45% and older than 50 years, participating in the global PARAGON-HF trial in 43 countries. Patients were randomised, double-blind, to either the combination of sacubitril/valsartan (97/103mg bd) or valsartan (160mg) only. The primary endpoint was the composite outcome of total HF hospitalisations and cardiovascular death. Fifty-one percent of the patients were female, 2% were black.

Sacubitril/valsartan was not effective in reducing the primary endpoint compared with valsartan. Among secondary endpoints, New York Heart Association Class and renal function were better with sacubitril/valsartan than with valsartan alone. Effective treatment for HFpEF continues to be elusive.

Diabetes and stable coronary disease (THEMIS and THEMIS-PCI)

Ticagrelor protects against cardiovascular events when added to aspirin in acute coronary syndrome (ACS) and in patients with a history of prior myocardial infarction (MI). The THEMIS trial investigated whether patients with diabetes and stable coronary artery disease (CAD), without a history of prior MI or stroke, would benefit from dual antiplatelet therapy (DAPT) - ticagrelor (60mg bd) and low-dose (75-100mg) aspirin - compared to placebo. DAPT was shown to reduce the primary endpoint of cardiovascular death, MI or stroke but at the expense of increased major bleeding. The trialists suggested that DAPT may be beneficial in selected diabetes patients at low risk of bleeding, but with a high risk of ischaemic events.

The THEMIS-PCI study investigated DAPT in a prespecified subgroup of the THEMIS study. Patients with diabetes who had stable CAD and a history of percutaneous coronary intervention (PCI) were included. DAPT provided a favourable net clinical benefit but with increased major bleeding.

The combination of ticagrelor and aspirin did not have a favourable risk benefit ratio among patients with stable ischaemic heart disease and type 2 diabetes. Only in the subgroup that had previously undergone PCI, the risk benefit ratio appeared more favourable. Figure 1 illustrates the THEMIS-PCI results.

Prevention

In the SWEDEHEART registry of risk factors and their relationship with cardiovascular events, insufficient physical activity and current smoking were the strongest predictors of future stroke and HF hospitalisation over a 10-year period. Importantly, for every cardiovascular risk factor treated successfully to target, there was a linear stepwise additional reduction in risk of all outcomes.

A study of the protective effect of a moderate-to-high level of leisure-time physical activity showed an association with a lower risk of instant death in the event of a MI.
The THEMIS trial suggested that DAPT (ticagrelor and low-dose aspirin therapy, 75-100mg) may be beneficial in selected diabetes patients at low risk of bleeding, but with a high risk of ischaemic events.

In an evaluation of older patients (>65 years) from the SPRINT trial, benefits and risks of intensive blood pressure lowering did not differ according to age categories as proposed by the 2018 ESC/ESH guidelines. This study cautions that decision-making surrounding more intensive blood pressure targets among high-risk older patients should be individualised beyond age alone.

Mobile telemonitoring-guided cardiac rehabilitation using smartphones, heart rate monitoring and coaching improved the physical condition of elderly patients who experienced an event/procedure for which cardiac rehabilitation is recommended.

Both blood pressure control and adherence to therapy improved with pharmacist intervention in an Albanian study.

The HOPE-4 study showed that non-professional healthcare workers using an algorithm in a comprehensive model of care, together with the provision of free antihypertensive drugs and a statin, substantially improved CVD risk and blood pressure control.

The PURE study indicates that medium- and low-income countries need to improve healthcare, reduce indoor and outdoor air pollution and increase the emphasis on low-cost proven treatments such as blood pressure and tobacco control to reduce CVD mortality.

The ASCEND Omega-3 trial enrolled 15 480 patients with diabetes but no known CVD, randomised to omega-3 fatty acid 840mg daily versus placebo, followed for 7.4 years. Vascular death, MI and stroke or transient ischaemic attack (TIA) occurred in 8.9% of the omega-3 group compared to 9.2% of the placebo group. No significant differences were detected in all-cause mortality, non-fatal MI, atrial fibrillation (AF) or arrhythmias.

The use of aspirin for primary prevention in a healthy elderly population (>65 years) is not supported by findings from the ASPREE study of 19 114 men and women randomised to either enteric-coated aspirin 100mg daily or placebo, followed for 4.8 years. Although the cumulative incidence of CVD was slightly greater in the placebo-treated patients at around three years, cumulative incidence of major haemorrhage was greater in the aspirin group throughout the follow-up period.

**Figure 1. THEMIS-PCI trial results**

Bhatt DL, Steg PG, Mehta SR., et al., on behalf of the THEMIS Steering Committee and Investigators. Ticagrelor in Patients with Diabetes and Stable Coronary Artery Disease with a History of Previous Percutaneous Coronary Intervention (THEMIS-PCI): a Phase 3, Placebo-controlled, Randomised Trial. Lancet 2019; Sept. 1: [Epub Ahead of Print].

**Conclusion:** In patients with diabetes, stable CAD, and previous PCI, ticagrelor added to aspirin reduced CV death, MI, and stroke, although with increased major bleeding.
**Familial hypercholesterolaemia - lessons from the FH studies collaboration**

The 2017 ESC guidelines recommend primary PCI as the default reperfusion strategy for ST-elevation myocardial infarction (STEMI) patients provided it is performed within recommended time frames. The FAST-MI five-year results, based on French registries, resonate with the South African strategy for acute MI, as reflected by a recent South African guideline recommending immediate management that provides the fastest, safest most effective method of reperfusion therapy i.e. primary PCI or fibrinolysis (Figure 2).

In the FAST-MI trial, 28% of patients with primary PCI were treated beyond the recommended time frames with no improvement between 2005 (27%) and 2010 (29%). A pharmaco-invasive strategy (2/3 pre-hospital) yielded superior five-year survival than primary PCI delivered >120 minutes from diagnostic ECG, and similar survival compared with timely primary PCI. Benefits of a pharmaco-invasive strategy compared to late primary PCI tended to increase with longer follow-up duration, possibly reflecting greater myocardial salvage.

**Acute coronary syndromes**

The only global registry on FH, which includes South African data provided by Professor Derick Raal (Wits) and Professor D Marais (UCT), highlights the need for more intensive therapy to reduce LDL-C in FH patients. Among 42 000 adults with heterozygous FH, only about a half had received a statin at the time of entry to the registry, even though 85% had LDL-C levels above current recommended targets. A key to improved therapy includes screening of relatives after an FH diagnosis.
Importantly, for every CV risk factor at target, there was a linear stepwise additional reduction in risk of all outcomes

Rapid assessment for ACS in the Emergency Unit (ER)

In the RAPID-TnT study, 3,378 patients presenting to the ER with chest pain were randomised to a 0-1 hour assessment of hs troponin T and compared to the standard protocol requiring 0-3 hours assessment. It is important to note that patients were included only when the baseline ECG was not definitive for cardiac ischaemia.

In the rapid rule-out group, patients were admitted if baseline hs troponin T was >52ng/l or if the change over an hour was >5ng/l. Patients were ruled out if the baseline value was <5ng/l, or if the baseline value was <12ng/l and the change over one hour <3ng/l. For patients with baseline values of 13-51ng/l or a change of 3-4ng/l, further observation was undertaken.

In the standard protocol group, patients with values of <29ng/l and no chest pain were discharged. Patients with values >29ng/l, or with known coronary disease or with ongoing chest pain, were admitted.

Death or MI at 30 days occurred in 1% of both groups, and 45% of patients in the rapid rule-out group were discharged from the ER versus 32.3% in the standard care group. A greater percentage of the standard care group underwent functional cardiac testing. There was a greater incidence of procedure-related MI in the rapid rule-out group.

Comparison of the GRACE risk score with standard care in ACS

The Australian GRACE Risk Intervention Study (AGRIS) evaluated the effect of risk stratification using the GRACE risk score in comparison to standard care in 1,403 patients with ACS, followed for 4.5 years. In the risk factor stratification group, there was a higher frequency of coronary angiography and no increase in medication compliance or referral to cardiac rehabilitation. The GRACE risk score did not influence the mean performance outcome.

Antithrombotic regimen in patients undergoing planned PCI

Patients with ACS (41% STEMI, 46% non-STEMI and 12% unstable angina) undergoing early planned invasive therapy were randomised in the ISAR-REACT 5 study to pre-treatment with ticagrelor (180mg loading dose; 90mg bd) or prasugrel given immediately after angiography (60mg loading dose; 10mg od). Prasugrel dose was reduced in patients >75 years or weighing <60kg. Patients with prior stroke, TIA or intracranial haemorrhage were excluded. Of 4,018 patients, 83% underwent PCI, 2% coronary bypass surgery and 14% were treated conservatively and continued their assigned treatment. The primary endpoint of death, MI or stroke at one year occurred in 9.3% with ticagrelor versus 6.9% with prasugrel (P=0.006). Bleeding Academic Research Consortium (BARC) major bleeding was seen in 5.4% with ticagrelor versus 4.8% with prasugrel.

Clopidogrel versus ticagrelor or prasugrel in non-STEMI patients 70 years or older

Of 1,003 patients 70 years or older presenting with non-STEMI, randomised to receive clopidogrel or ticagrelor or prasugrel for 12 months, major and minor bleeding occurred in 17.6% with clopidogrel compared to 23.1% with the more potent P2Y12 inhibitors. Net clinical benefit was assessed as the outcome of death, MI, stroke, TIA or intracranial haemorrhage. Analysis of secondary outcomes showed changes in favour of clopidogrel for major bleeding, fatal bleeding and adherence to therapy. The composite of death, MI or stroke was similar in the two groups.

Culprit-only versus multivessel revascularisation in STEMI

Trial results are conflicting. Figure 3 illustrates the results of the COMPLETE trial, which supports complete revascularisation and demonstrates significant reductions in cardiovascular death or MI; cardiovascular death, MI or revascularisation; and all of the above in addition to unstable angina and HF.
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<th>PRIMARY OUTCOME</th>
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<tr>
<td>CV death or MI %</td>
<td>HR 0.74; 95% CI 0.60 to 0.91, P=0.004</td>
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<td>CV death, MI or ischemia-driven revascularisation %</td>
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<th>SECONDARY OUTCOME</th>
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<tr>
<td>CV death, MI, ischemia-driven PCI, UA or NYHA class IV heart failure %</td>
<td>HR 0.62; 95% CI 0.43 to 0.72</td>
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**Conclusion:** Among patients with STEMI and multivessel CAD, complete revascularisation was superior to culprit-lesion-only PCI in reducing the risk of CV death or MI.


**Figure 3. COMPLETE trial results**

**Early introduction of PCSK9 inhibitor, evolocumab in ACS**

In the large ODYSSEY Outcomes study, the PCSK9 inhibitor, alirocumab, was introduced weeks to months after the occurrence of an ACS. In the much smaller randomised EVOPACS study of 308 patients, evolocumab in addition to atorvastatin 40mg daily was introduced during their hospitalisation for an ACS and compared to atorvastatin 40mg daily only. This strategy was shown to be safe and effective, with a greater reduction in LDL-C in the evolocumab group (-77.1% vs -35.4%), of whom 95.7% achieved an LDL reduction <1.8mmol/l in eight weeks versus 37.6% in the atorvastatin-only group.

**Prophylactic ICD implantation after primary angioplasty for STEMI**

In the DAPA trial, 262 STEMI patients who had undergone primary angioplasty and had an LVEF <30% within four days, a TIMI flow rate <3, primary ventricular fibrillation, or Killip class ≥2, were randomised to ICD implantation 30-60 days after the acute event or standard care. All-cause mortality occurred in 24.4% of the ICD group versus 35.5% of the standard care group (P=0.02).

**Atrial fibrillation**

**Rivaroxaban in patients with stable CAD and AF**

In the AFIRE study, 22,23 2 236 patients (average age 74 years) with stable CAD and AF were randomised to rivaroxaban 15mg daily versus rivaroxaban and antiplatelet therapy (70% aspirin and 27% P2Y12 inhibitor), followed for 24 months. All-cause mortality, MI, stroke, unstable angina requiring revascularisation, or systemic embolism occurred in 4.1% patient-years of the rivaroxaban
monotherapy group compared to 5.8% in the rivaroxaban-plus-antiplatelet group. The rate of major bleeding was 1.6% per patient-year with rivaroxaban and 2.8% per patient-year in the combination group. Reductions in all-cause death and cardiovascular death were significantly impacted with rivaroxaban monotherapy. This study supports several others that have shown the safety and efficacy of NOAC monotherapy in stable CAD.

**PCI in patients with AF**

The ENTRUST-AF PCI24,25 trial evaluated 1,506 AF patients who had recently undergone PCI. Half had presented with ACS, the remainder had stable CAD. Patients were randomised to edoxaban 60mg daily plus clopidogrel 75mg daily for 12 months, or vitamin K antagonist (VKA) plus clopidogrel for 12 months plus aspirin for an average of 66 days. The primary outcome was major or clinically relevant non-major bleeding by 12 months.

The edoxaban/clopidogrel combination was noninferior to VKA plus DAPT, with the primary endpoint reached in 17% of the edoxaban group and 20% of those receiving VKA. There was no significant difference in the secondary endpoint of cardiovascular death, MI, stroke, systemic embolism or definite stent thrombosis. Similar results have been reported with rivaroxaban, dabigatran and apixaban. However, this is the only trial that did not show superiority in the prevention of bleeding.

**Progression of atherosclerosis in patients with AF**

Experimental and clinical data have suggested that non-VKA oral anticoagulants may have an inhibitory effect on atherosclerotic plaque in patients who have undergone catheter ablation for AF, but have no history of CAD. The authors found that VKA-treated patients showed the most progression in atherosclerotic plaque burden, there was less progression in controls, and evidence of minor regression with NOACs. Plaque thickness showed similar directional changes.

**Valvular heart disease**

**Mortality in moderate and severe aortic stenosis**

A large Australian ECG database of 122,809 men and 118,400 women assessed the relationship between the severity of aortic stenosis and survival over 3.3 years. Aortic stenosis was classified as not present (89%), mild (6.7%), moderate (1.4%) or severe (2.6%) by conventional means. Patients with mild aortic stenosis had a prognosis similar to those without aortic stenosis (adjusted five-year mortality: 19%). Adjusted five-year mortality was 43% for moderate aortic stenosis and 53% for severe aortic stenosis; and adjusted five-year mortality risk was very similar, 2.6- and 3.0-fold respectively. The authors concluded that the prognostic impact of moderate aortic stenosis and its management requires re-evaluation.

**Global issues in cardiology and focus on women clinicians and patients**

This year’s ESC meeting was held in collaboration with the World Heart Federation (WHF). The preceding presidents are both women, Professor Barbara Casdei (ESC) and Karen Sliwa (WHF). The ESC reported that of the programme contributors, 68% were men and 32% were women. The WHF committed itself to no further men-only panels at any of their congresses. The programme chairs, Professors Sylvia Priori and Marco Roffi, incorporated the themes of ‘Global
The CREOLE study has shown that in black patients in sub-Saharan Africa, amlodipine plus either hydrochlorothiazide or perindopril was more effective than perindopril plus hydrochlorothiazide at lowering blood pressure at six months.

Global cardiovascular health

At the inaugural meeting, Professor Casedei highlighted that after years of precipitous reductions in cardiovascular deaths, there is now a plateauing of mortality in Europe and, of even more concern, an increase in parts of the Western World and a dramatic increase in low- and middle-income countries (LMICs), including South Africa. There is now a co-existent burden of communicable and non-communicable diseases in South Africa, as opposed to its experiencing a shift from one to the other.

Professor Karen Sliwa reflected on the unique advocacy role of the WHF in improving global health by reducing the burden of CVD. The WHF launched two new roadmaps - HF https://www.worldheart-federation.org/cvd-roadmaps/whf-global-roadmaps/heart-failure/ and CVD prevention in people living with diabetes (in collaboration with the International Diabetes Foundation) https://www.worldheart-federation.org/cvd-roadmaps/whf-global-roadmaps/cvd-diabetes/. The WHF country-level scorecards, which allow stakeholders to assess strengths and gaps in national CVD programmes and policies in order to focus on priority actions, are available at https://www.world-heart-federation.org/cvd-roadmaps/scorecards/about-whf-scorecards/.

Global exchange

A new element at the ESC congress, global exchange sessions, focused on new ways of tackling common problems in CVD and delivering the best care possible. A large focus was on research, with the launch of the Oxford Masters in Clinical Trials https://www.escardio.org/Education/Postgraduate-Programmes/msc-in-clinical-trials - the first postgraduate programme proposed by the European Heart Academy that allows part-time distance learning in running, coordinating and mastering clinical trials. Other focus sessions included medical devices and the navigation of balancing access, safety and innovation; health equity in Africa and closing the gap in healthcare disparities; and leveraging social media, fundraising campaigns and advocacy. These provided new insights into a comprehensive strategy for new cardiovascular practitioners.

The Geoffrey Rose lecture on population sciences

Professor Karen Sliwa spoke on the topic, ‘Heart failure can affect everyone’, with a focus on the Heart of Soweto study and the subsequent 30 studies (Heart of Africa) that have stemmed from this. Publication of the findings of this study in the Lancet was followed by Africa-led studies (IMPI27 and CREOLE28) also being published to wide acclaim in very high-impact journals. She reiterated the relative lack of interest in CVD occurring in LMICs, notably rheumatic heart disease, pulmonary hypertension and peripartum cardiomyopathy, despite their global importance.

Of importance to management and policy is the issue of local context - the CREOLE study has shown that in black patients in sub-Saharan Africa, amlodipine plus either hydrochlorothiazide or perindopril was more effective than perindopril plus hydrochlorothiazide at lowering blood pressure at six months; and IMPI has changed international guidelines for treating pericarditis in HIV-infected patients.

Urbanisation and air pollution

Under-recognised risk factors for CVD were highlighted by Professor Thomas Münzel, who reported that air pollution is now a bigger killer than tobacco and that airborne particulate matter was estimated as the fifth greatest risk factor for cardiovascular disease in ESC member states and affiliated countries, but we will get a truly global view of the challenges for healthcare affecting the entire world.”

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death in 2015. Using an extended risk model, it was demonstrated that almost half of the 790 000 excess deaths per year in Europe due to ambient pollution are related directly to ischaemic heart disease and stroke. This study highlights the key link between medicine and policy - ambient pollution is ultimately a political issue as it is no longer up to the individual only to avoid a particular risk factor. The summary call was for political and social awareness, effective emissions control and environmental quality as a priority for health.

**Women in cardiology: for her, with her, about her**

Professor Roxana Mehran, leading interventional cardiologist and triallist from Mount Sinai, New York, delivered the Andreas Grünitzig lecture on interventional cardiology. With over 120 182 citations, more than 1 000 publications and an H-index of 143, Professor Mehran has spearheaded groundbreaking research and led the development of two coordination centres to support multicentre trials in interventional procedures. She reported that her biggest achievements lay in inspiring women to become interventional cardiologists and she encourages women to join this interesting and rewarding specialty. Professor Mehran spoke of the need to include more women in trials, not only as patients but also as triallists. She used the opportunity to reiterate her ‘Women as One initiative’ and launched the escala-tor awards for talented women in cardiology https://www.womenasone.org/.

Professor Eugene Braunwald spoke about the growing importance and visibility of women in the profession, sharing insights from working with talented women cardiologists and practitioners throughout his career. He regretted the limited role that he and other senior cardiologists had played in not stressing the need for an equitable role for women over the previous decades, and his disappointment with the reputation of cardiology as a hostile environment for women. However, it was clear that both the ESC and global agencies are actively changing and now recruit talented individuals, regardless of sex. He and the moderators expressed hope that this will increase in the future.

Professor Verena Stangl highlighted the fact that although there is increased knowledge of relevant differences between women and men in CVD and the actions of CVD drugs, there is less evidence for recommendations for women; sex-specific differences are often not specifically addressed in current guidelines. Insufficient availability of sex-sensitive evidence and the poor quality thereof is often due to inherent trial design flaws. Of note, the PARADIGM trial had only 21% women, SPRINT 36%, COMPASS 20% and FOURIER 25%. Only PARTNER-2 had >40% (45.8%) women enrolled, yet these results were extrapolated to women and therefore assumed identical results for both women and men.

Professor Carolyn Lam, Singapore, demonstrated a significant increase in CVD in Asian women, with ischaemic heart disease being the major threat, as well as the lean diabetic phenotype of HF, unique to the region. Professor Mayra Guerrero reviewed data on equality for both patients and doctors in the Americas. The higher mortality trends for black and Hispanic women in the US was a major cause for concern - CVD is the top cause of death in US women and kills more than all cancers combined. In addition, 26% of women find CVD embarrassing and only 40% of routine care for women includes a heart risk check. In addition, only 29% of primary care physicians will make CVD a priority for women and only 22% feel prepared to assess CVD risk in women. Of great interest were data showing a statistically significant improvement in outcomes if patients (regardless of sex) were treated by a female doctor, regardless of how sick the patients were. With regard to PCI, women interventional cardiologists treated more STEMI and non-STEMI than male counterparts, with a lower mortality. However only 4% of interventional cardiologists were female and performed only 3% of all PCIs in the >2 million PCI registry.
Quick learnings from other sessions

Lastly, a brief summary of key findings from hotline sessions not dealt with earlier.

**Combined effect of low LDL-C and lower systolic blood pressure on lifetime risk of CVD**

**Key message:** Achievable reductions in LDL-C and systolic blood pressure more than halve the lifetime risk of CVD. Lifelong exposure to lower levels of LDL-C and lower systolic blood pressure was associated with lower cardiovascular risk. However, these findings cannot be assumed to represent the magnitude of benefit achievable from treatment of these risk factors.

**GALACTIC – Goal-directed After Load Reduction in Acute Congestive Cardiac Decompensation: a randomised controlled trial**

**Key message:** In a broad acute HF population, early intensive and sustained vasodilation with nitrates, hydralazine, ACE-inhibitors, ARBs or sacubitril/valsartan using individualised doses was well tolerated, but did not improve 180-day all-cause mortality and AHF rehospitalisation.

**Salt substitution and community-wide reductions in blood pressure and hypertension incidence**

**Key message:** A community-wide salt substitution (potassium chloride replacing 25% of the sodium chloride) intervention trial from Peru showed improved blood pressure and hypertension control. Providing all families, shops, bakeries and restaurants with free salt substitution in exchange for their supply of full-sodium salt for three years reduced blood pressure by an average 1.23/0.72mmHg (P=0.004 and P=0.022, respectively). The effect was greater for the 18% of individuals with hypertension and those ≥60 years old, with significant reductions of 1.92mmHg and 2.17mmHg on average. Cumulative probability of hypertension over the three-year study was reduced 55% compared with controls (P<0.001, using the then-current thresholds of 140mmHg systolic and 90mmHg diastolic).

**BB-meta-HF – Beta-blockers are effective in high-risk HFrEF patients with moderately severe renal dysfunction**

**Key message:** Beta-blockers remain effective for preventing death in HFrEF and sinus rhythm, even in patients with moderate or moderately severe kidney dysfunction.

**Ten-year survival after coronary artery bypass grafting (CABG) versus PCI: The SYNTAX Extended Survival study (SYNTAXES)**

**Key message:** The original SYNTAX study, a landmark multicentre, randomised (1:1) trial of 1 800 patients, examined all-cause mortality (primary outcome) of PCI (n=903) compared to CABG (n=897). This complex cohort included diabetics, as well as patients with left main disease and three-vessel disease with a low-intermediate SYNTAX score. Since its publication, many trials have been published comparing PCI to CABG, usually with reassuring long-term data for CABG.

SYNTAXES is the first large-scale study to provide 10-year outcomes for PCI, albeit mortality only. Notably, 94% completed the 10-year follow up. Results demonstrated *equivalence in the primary endpoint of all-cause mortality* (27% PCI and 23.5% CABG, P=0.092), in spite of the fact that a first-generation paclitaxel-eluting stent was used. Furthermore, contemporary practice using potent antiplatelet agents, physiology or image-guided intervention was not part of the original study design. Long-term follow-up should be the new standard for present-day trials evaluating outcomes in PCI.

**MITRA-FR – two-year follow-up of the MITRA-FR study: a randomised controlled trial evaluating the effectiveness of percutaneous mitral valve repair in secondary mitral regurgitation**

**Key message:** The 24-month results of the MITRA-FR trial confirm that the addition of a percutaneous clip to medical treatment did not decrease the rate of death or unplanned hospitalisation for HF. Next step: Mitra-FR patients followed for up to five years or meta-analysis of individual data.

**DANAMI-2 – 16-year follow-up of the Danish Acute Myocardial Infarction 2 trial – Primary PCI versus fibrinolysis in STEMI**

**Key message:** The benefit of primary PCI over fibrinolysis was maintained at 16-year follow-up. Primary PCI reduced the composite endpoint of death or rehospitalisation for MI, reduced cardiac mortality, and delayed average time to a main event by approximately one year.

**CLARIFY – In stable coronary disease, patients with angina and prior MI have a poor prognosis despite adherence to guideline-recommended therapies. Final five-year results from the CLARIFY study**

**Key message:** This description of the spectrum of chronic coronary syndrome patients shows that, despite high rates of prescription of evidence-based therapies, patients with both angina and prior MI are an easily identifiable high-risk group who may deserve intensive treatment.
A CYP2C19 genotype-guided strategy for selection of oral P2Y12 inhibition in patients with STEMI showed that almost two-thirds of patients could be treated with clopidogrel. Importantly, no differences were seen in thrombotic event rates and the strategy yielded a reduction in bleeding event rates.

**Key message:** The use of secondary-prevention medication after CABG was high early after surgery but decreased significantly over time. RAAS inhibitors were used the least. Platelet inhibitors, statins and beta-blockers were used more and to a similar extent. Continuous treatment with statins, RAAS inhibitors and platelet inhibitors was individually associated with a significant reduction in mortality risk. Beta-blocker treatment was not associated with improved survival after CABG; therefore, these data do not support routine long-term use of beta-blockers after CABG.

As a message for lay persons - CABG is not a definite cure for CAD, which is better viewed as a chronic progressive disease that warrants continuous treatment with secondary-prevention medications to ensure long-term benefits of revascularisation.

**References**

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23. Pandi S, Hellenberg D, Heilig F, Ntsekhe M. Approach to documentation as approved by relevant control authorities.

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