Highlights from the ESC Congress 2019 in Paris

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Even if you were one of the over 30,000 health professionals participating in the annual scientific meeting of the European Society of Cardiology, the vast range of E-seminars, the vast number and diversity of seminars, clinical trials and Late Breaking Science sessions – not to mention the presentation of new guidelines – can be daunting. For this article, the E-Journal invited Prof. Sigmund Silber to provide a short synopsis of what he found of critical interest in coronary heart disease and heart failure.

Topic(s):

Coronary Artery Disease, Acute Coronary Syndromes, Acute Cardiac Care;
Heart Failure;

Introduction

This year, at the annual meeting of the European Society of Cardiology, there were 6,627 scientific contributions in a total of six Hot Line sessions, 13 Late Breaking Science sessions and 3 Late Breaking Basic Science sessions, which makes it particularly difficult to select studies. In addition, five new sets of guidelines were presented:

- Stable coronary heart disease (CHD) – which has now been renamed chronic coronary syndrome (CCS)
- Diabetes mellitus
- Dyslipidaemia
- Supraventricular tachycardia
- Acute pulmonary embolism

I shall focus below on coronary heart disease and heart failure.

Coronary heart disease

ISAR-REACT 5

The ISAR-REACT 5 study, which, as the name suggests, was mainly conducted in Germany, probably attracted the greatest attention. It did what no pharmaceutical company has dared to do, namely a direct head-to-head comparison of ticagrelor versus prasugrel in patients with acute coronary syndrome (ACS). As a reminder, in earlier studies these two drugs demonstrated their benefit always compared to clopidogrel. Approximately 4,000 patients with ACS and planned coronary intervention were randomised. The aim of the study was to prove that ticagrelor is superior to prasugrel. However, the results turned out to be quite different from what was expected: after one year, the primary efficacy endpoint (myocardial infarction, stroke, death) was significantly lower for prasugrel at 6.9% than for ticagrelor at 9.3%. Major bleedings did not differ significantly. There were no relevant differences between STEMI and NSTEMI. Even critics of these results (e.g., PCI was actually performed in only 84% of patients) described it as a "milestone study" that will influence future guidelines.

THEMIS study

On the same day, however, another study was presented that alleviated the "ticagrelor trauma", the THEMIS study, which compared aspirin monotherapy with DAPT (i.e., dual antiplatelet therapy consisting of aspirin with ticagrelor) in patients with stable coronary artery disease (CAD) (which we would now call CCS) and diabetes mellitus without prior myocardial infarction (MI) as regards the occurrence of MI, stroke or death over the course of three years. In nearly 20,000 patients, this combined endpoint was reduced significantly from 7.6% to 6.9% by DAPT with ticagrelor (90 mg twice a day or 60 mg twice a day), especially with regard to MI and stroke. The DAPT increased the rate of major bleeding episodes, as was to be expected, but not the rate of fatal bleeding episodes. So, we see that this study in patients without MI is going in the same direction as the earlier PEGASUS study in patients after MI, with the concept of improving prognosis with more prolonged DAPT, independent of stent implantation.

In this connection, one aspect of the new guidelines on stable CHD (now CCS) may be discussed: prolonged combined antithrombotic therapy with acetylsalicylic acid (ASA) is now recommended for secondary prevention in patients with CCS and sinus rhythm (IIa A) if the ischaemic risk is high but the bleeding risk is low. Regrettably, however, no distinction is made between the individual drugs as potential partners for ASA, that is to say, no distinction between clopidogrel, prasugrel, ticagrelor (PEGASUS, 60 mg twice daily) for DAPT on the one hand or ASA + low-dose rivaroxaban in the vascular dose (COMPASS, 2.5 mg twice daily) on the other. However, at least there is now a recommendation for this new treatment concept for secondary prevention.

In the new CCS guidelines, the prevalence of CAD (defined as the probability of coronary stenosis of over 50%) surprisingly has fallen between 2013 and 2019, at least in Western countries, and indeed dramatically, by about half. This has enormous implications for non-invasive diagnosis before possible cardiac catheterisation as this is now all about a diagnosis of exclusion to avoid unnecessary cardiac catheterisation, which would not have any consequences anyway. In addition to diagnostic imaging of ischaemia with stress echo, myocardial scintigraphy or magnetic resonance imaging, cardiac computed tomography (CT) is playing an

increasingly important role, whether to exclude coronary calcification (Agatston score = 0) or to exclude coronary stenosis of fractional flow reserve (FFR) relevance.

Heart failure

Here too, there were noteworthy new studies.

PARAGON-HF

A still unresolved problem is the treatment of so-called diastolic heart failure. These patients suffer from unexplained effort dyspnoea, but the left ventricular ejection fraction (LVEF) is normal (defined in the guidelines as ≥50%) or only slightly impaired, i.e., 40-49%, in conjunction with LV hypertrophy or an enlarged left atrium, signs of LV diastolic dysfunction and elevated natriuretic peptides. To date, all the studies of this disease have had a negative outcome. The results of the PARAGON-HF study presented here were therefore anticipated all the more eagerly.

About 5,000 such patients worldwide with an LVEF ≥45% were enrolled and randomised either to Entresto or to valsartan. The primary clinical endpoint, a reduction of CV death and hospitalisation because of heart failure, was not reached (however, with a p-value of 0.06). Well, this study might have had a positive outcome if placebo instead of valsartan had been chosen for the control group and, in my opinion, this would even have been acceptable ethically in these patients without a confirmed therapy. But even a near-miss is still a miss.

One must be even more cautious in interpreting the subgroup analyses. With regard to a reduction in hospitalisations because of heart failure, women and patients with slightly impaired LV-EF, that is, between 45 and 50%, had a particular benefit. This still gives some hope in the treatment of diastolic heart failure.

DAPA-HF

Another study on heart failure caused a sensation - the DAPA-HF study with dapagliflozin. We know from previous studies that SGLT-2 inhibitors can prevent or delay the development of heart failure in patients with type 2 diabetes mellitus (DM). This study now investigated whether dapagliflozin can positively influence the clinical course in patients with systolic heart failure (LVEF ≤40%) with and without DM. Nearly 5,000 patients worldwide were randomised in this placebo-controlled study. Dapagliflozin was therefore given not as an antidiabetic drug but as a test drug for heart failure as only just under half of the patients had DM. The primary endpoint after two years, a reduction in CV death, hospitalisation or urgent medical consultation because of heart failure, was reduced highly significantly from about 25% to 20%, that is by about 5% in absolute terms, completely regardless of whether the patients had DM or not and regardless of the cause of the heart failure. Even overall mortality was significantly reduced; the drug was well tolerated – truly remarkable.

This is also reflected in the new diabetes guidelines; SGLT-2 inhibitors have recently been given a level I A recommendation to reduce the risk of hospital referral because of heart failure and also of diabetic nephropathy. However, the glomerular filtration rate (GFR) should be >30.

Metformin is no longer the first step in treatment for patients with type 2 DM and organ damage, e.g., CAD, but an SGLT-2 inhibitor or a GLP-1 receptor agonist should be given from the beginning. If these high-risk patients are already on metformin, an SGLT-2 inhibitor or GLP-1 receptor agonist should be added, even if the HbA1c is well controlled. In addition, the new target for low-density lipoprotein (LDL) cholesterol in these patients and also in all patients with CAD – even without DM, following MI, with CCS, especially after PCI or bypass surgery – is now below 1.4 mmol/l or 55 mg/dl.

Yes indeed, cardiovascular medicine is always full of surprises... for the benefit of our patients.

Conclusion

ISAR-REACT 5 provided an unexpected result. In this randomised trial, performed independently of pharmaceutical companies, against its hypothesis, prasugrel was superior to

ticagrelor in patients with ACS. In THEMIS, comparing ASA monotherapy with DAPT (ASA + ticagrelor) in patients with CCS (stable CAD) without prior myocardial infarction and diabetes mellitus, DAPT was superior to monotherapy. In PARAGON-HF, another study in patients with diastolic heart failure, the comparison of Entresto versus valsartan did not reach the primary endpoint. In DAPA-HF, dapagliflozin reduced clinical events in patients with heart failure - even in those without diabetes mellitus.

Notes to editor

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