The year in cardiovascular medicine 2020: heart failure and cardiomyopathies

Héctor Bueno 1,2,3,4,*, Brenda Moura 5,6, Patrizio Lancellotti 7,8, and Johann Bauersachs 9

1Multidisciplinary Translational Cardiovascular Research Group. Centro Nacional de Investigaciones Cardiovasculares (CNIC), Melchor Fernández Almagro, 3, Madrid 28029, Spain; 2Cardiology Department, Hospital Universitario 12 de Octubre and Instituto de Investigación Sanitaria Hospital, 12 de Octubre (imas12), Madrid, Spain; 3Centro de Investigación Biomédica en Red Enfermedades Cardiovasculares (CIBERCV), Madrid, Spain; 4Facultad de Medicina, Universidad Complutense de Madrid, Plaza de Ramón y Cajal, s/n, 28040 Madrid, Spain; 5Cardiology Department, Military Hospital, Av. da Boavista S/N, 4050-115 Porto, Portugal; 6CINTESIS—Center for Health Technology and Services Research, R. Dr. Plácido da Costa, 4200-450 Porto, Portugal. 7Department of Cardiology, CHU SartTilman, University of Liége Hospital, GIGA Cardiovascular Sciences, Avenue de L’Hôpital 1, 4000 Liége, Belgium; 8Cardiology Departments, Gruppo Villa Maria Care and Research, Maria Cecilia Hospital, Cotignola Bari, Italy and Via Corriera, 1, 48033 Cotignola RA, Italy and Anthea Hospital, Via Camillo Rosalba, 35/37, 70124 Bari BA, Italy; and 9Department of Cardiology and Angiology, Hannover Medical School, Carl-Neuberg-Str. 1, 30625 Hannover, Germany

Received 1 October 2020; revised 26 November 2020; editorial decision 10 December 2020; accepted 22 December 2020; online publish-ahead-of-print 3 January 2021

Graphical Abstract

During year 2020, we learned new options to better stratify patients with heart failure and preserved left ventricular ejection fraction (HFrEF) (A), the clinical benefit of three new drugs to improve prognosis of patient with heart failure and reduced left ventricular ejection fraction (HFrEF): empagliflozin, vericiguat and omecamtiv mecarbil (B), the potential benefit of a broader utilization of recommended drugs for HFrEF in patients with left ventricular ejection fraction higher than 40% (C), and the potential added clinical benefit of a comprehensive use of recommended drugs for HFtEF (D) in a year marked by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic (central cartoon). Reprinted or adapted from: (A) Selvaraj et al.,23 (B) Packer et al.,115 Armstrong et al.,126 and Teerlink et al.,132 (C) Böhm et al.,100 (D) Vaduganathan et al.139

* Corresponding author. Tel: (+34) 914 531 200 - Ext 4110; Email: hector.bueno@cnic.es

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author(s) 2021. For permissions, please email: journals.permissions@oup.com.
Introduction
Heart failure (HF) prevalence remains high worldwide with significant sex-related and regional differences in its presentation, management, outcomes. In 2020, advances in biomarkers and imaging techniques were reported for the diagnosis and prognosis of diastolic dysfunction, HF with preserved ejection fraction or monitoring cardiotoxicity; a new definition of HF with recovered left ventricular ejection fraction (LVEF) was released. Benefits of renin–angiotensin–aldosterone system inhibitors and β-blockers may extend to patients with an LVEF up to 55%. Sacubitril–valsartan improved LV remodelling, biomarker levels, and rates of sudden cardiac death. Two studies investigating the sodium-glucose cotransporter 2 inhibitors empagliflozin and sitagliptin in patients with HF were reported: the AFFIRM-AHF trial, intravenous ferric carboxymaltose reduced HF hospitalisations (HFH) in high-risk patients with worsening HF. In the outcome trials VICTORIA and GALACTIC-HF predominantly vericiguat and the myosin activator omecamtiv mecarbil, in the large outcome trials VICTORIA and GALACTIC-HF predominantly reduced HFH in high-risk patients with worsening HF. In the AFFIRM-AHF trial, intravenous ferric carboxymaltose reduced HFH in patients with iron deficiency after an HF decompensation.

Year 2020 will be remembered as the year of coronavirus disease of 2019 (COVID-19). The pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a massive impact on global health and economy. When this article is published, the extraordinary coronavirus 2 (SARS-CoV-2) has caused a massive impact on global health and economy. The pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a massive impact on global health and economy. When this article is published, the extraordinary coronavirus 2 (SARS-CoV-2) has caused a massive impact on global health and economy. When this article is published, the extraordinary coronavirus 2 (SARS-CoV-2) has caused a massive impact on global health and economy. When this article is published, the extraordinary coronavirus 2 (SARS-CoV-2) has caused a massive impact on global health and economy.

Epidemiology
More than 64 million people are living with HF in the world, with an estimated prevalence of 1–2% among adults in developed countries, most often with several comorbidities (Figure 1). The incidence of HF may be stabilizing globally, with decreases in higher-income countries, but increases in lower-income countries, and a shift towards HF with preserved ejection fraction (HFpEF), and increasing due to population ageing and the increase in obesity. Age, traditional risk factors for HF, a sedentary lifestyle, and social deprivation are associated with incident HF. Actually, lifestyle and social determinants of health are attracting more attention in the epidemiology and care of patients with HF. In patients with new-onset HF, the most common first events are cardiac events (36%), recurrent HF (28%), and death (29%).

Non-traditional risk factors, such as pacemaker implantation may play a role in the development of HF: within the first 2 years after implantation in patients without known HF, the incidence of fatal and non-fatal HF is 10.6%, six times higher than for age- and gender-matched individuals without HF and pacemaker. Mortality rates of HF seem to be declining less rapidly than previously in the general population. Among patients with cardiac resynchronization therapy (CRT), a gradual decrease in sudden cardiac death risk has been observed since the early 2000s with implications for the role of implantable defibrillators and the design of comprehensive HF care models.

Significant regional differences in the management of acute HF have been identified, including timing and types of treatments used, and rates and time trends of readmission. However, the importance of distinguishing worsening/chronic HF from new-onset HF in patients with first hospitalization has been highlighted, as patients with worsening/chronic HF have a significantly greater comorbidity burden and higher adjusted risks of mortality and HF readmission.

Clinical aspects
Diagnostics and risk stratification
Imaging
Imaging is pivotal in the diagnosis and risk stratification of patients with HF. The European Society of Cardiology (ESC) Heart Failure Association (HFA) has recently highlighted in a position statement the central role of full echocardiographic examination in patients admitted for acute heart failure (AHF). Once the patient is stabilized, the added value of routine cardiac magnetic resonance (CMR) over echocardiography alone to help diagnose the causes of HF not related to ischaemic heart disease has been questioned. Selective rather than routine CMR for identifying specific HF aetiologies is more cost effective. Noteworthy, CMR could serve to better define HFrEF phenotypes and to select patient specific therapies, such as MRA may be for HFrEF patients with myocardial fibrosis. The diagnosis of HFrEF remains challenging especially in patients with coexisting conditions that account for dyspnoea. Diastolic dysfunction, left atrial enlargement, elevated left atrial pressure, and pulmonary hypertension are common in these patients. The 2016 diastolic dysfunction grading algorithm proposed by the European Association of Cardiovascular Imaging has shown improved prognostic value compared to the 2009 one. However, the high number of patients with doubtful classification renders clinical decision making...
The year in CV Medicine: HF and cardiomyopathies

Biomarkers

Biomarkers are key for diagnosis and prognostic evaluation in patients with HF. Circulating biomarkers related to extracellular matrix regulation were abnormal in patients with HfPcEF, displayed prognostic value, and were influenced favourably by SV in PARAGON-HF. In HF with reduced LVEF (HFrEF), absolute NT-proBNP, hs-TnT, and sST2 levels predict outcomes independent of age, sex, and LVEF category. Differential circulating levels of biomarkers associated with ageing in patients with HF have been reported, with increasing levels of proteins associated with extracellular matrix organization, inflammatory processes, and tumour cell regulation and lower expression of tumour proliferation functions.

In AHF, a specific challenge is to identify infection as a trigger of AHF. Procalcitonin (PCT) has emerged as an alternative for C-reactive protein in diagnosing bacterial infection. In a recent randomized, multicentre, open study, a strategy of PCT-guided initiation of antibiotic therapy was more effective than standard care in improving clinical outcomes. Omics phenotyping is likely the next frontier to unravel disease mechanisms and heterogeneity. As a recent example, incorporating a panel of three metabolite-based biomarkers into a risk score improved the prognostic utility of NT-proBNP by predicting long-term CV death.

Heart failure during the COVID-19 pandemic

The role of the angiotensin-converting enzyme (ACE) receptor 2 in the infection of human cells by SARS-CoV-2 and in the pathophysiology of COVID-19, and the poor prognosis of cardiac patients with COVID-19 raised the concern of a potential deleterious effect of the treatment with ACE inhibitors and angiotensin receptor

Figure 1 Prevalence of heart failure in different world regions as estimated from population-based studies. Reprinted from Groenewegen et al.
Sex and heart failure
Women account for half of patients with HF with a lower incidence rate until the age of 75 years. A higher proportion of HFrEF, probably related to the higher prevalence of obesity and diabetes mellitus. Women with HF present a greater symptom burden and poorer quality of life as compared with men. Significant sex-related differences have been described in Europe in the management of acute and chronic HF including a lower use of guideline-directed medical therapies—which see to be mostly explained by older age and comorbidity rather than by sex itself— with lower crude rates of death and HF hospitalization in women. The lack of sex-related differences in the clinical effect of HF therapies does not justify these differences, although the possibility has been suggested that women with HF might benefit from treatment to a higher level of LVEF than previously considered. A different perspective of the gender gap in HF is the lower proportion of female authors in HF practice guidelines and trials, ranging between 11% and 24% only, with modest increases over time in European and US guidelines references but not in HF trials. Importantly, HF trials with a woman first or senior author are associated with a higher proportion of enrolled female participants.

Peripartum cardiomyopathy
Peripartum cardiomyopathy is the first cause of HF in women during/after pregnancy. The ESC EORP registry on PPCM enrolled >700 women with this condition from 49 countries. It showed that PPCM affects women from any region or ethnicity. Within 6 months after diagnosis, the average rates of maternal mortality, readmission, and neonatal mortality were, respectively, 6%, 10%, and 5%, with marked regional variations. Recovery of LVEF occurred in 46% of women. The management of these patients is reviewed in a recent paper.

HF with recovered left ventricular ejection fraction
This year, a working definition of HF with recovered left ventricular ejection fraction (HFrecEF) has been proposed. This includes: (i) documentation of a decreased LVEF < 40% at baseline; (ii) ≥10% absolute improvement in LVEF; and (iii) a second measurement of LVEF >40%. Reverse LV remodelling is associated with improved myocardial systole and diastole, and better clinical outcomes. However, a significant proportion of patients with HFrecEF develop recurrences of LV dysfunction and HF. Despite improvements in structural and functional abnormalities, many of the multilevel molecular changes occurring during LV remodelling remain dysregulated in reverse remodelled hearts. Therefore, guideline-directed medical and device therapy for patients with HFrecEF should be continued indefinitely with close clinical follow-up.

HF in cancer patients
The role of CV imaging in cancer patients receiving cardiotoxic therapies has been highlighted in a position statement by the HFA and in the European Society for Medical Oncology guidelines. The role of focus echocardiography and CMR has also been recently discussed. In daily practice, caution should, however, be given if using...
late gadolinium enhancement or qualitative T2-weighted STIR imaging-only approach for the exclusion of checkpoint inhibitor-associated myocarditis.83 Imaging is cornerstone for monitoring cardio-toxicity and identifying subtle impairment of myocardial function occurring prior crossing the traditionally defined threshold of LV systolic dysfunction (LVEF < 50%).84,85

**Right ventricular dysfunction (RVD)**

RV and right atrium dysfunction contribute to HFrpEF pathophysi-ology. Also, RV dysfunction (lower RV systolic velocity and RV fractional area change) and impairment in RV-pulmonary artery coupling are more frequently found in HFrpEF patients developing acute lung congestion with exercise.86 Activation of the endothelin and adiponectin neurohormonal pathways is associated with pulmonary haemodynamic derangements, reduced RV functional reserve, reduced cardiac output, and more severe impairment of peak VO2 in HFrpEF patients.87 The most common causes of RVD are left-sided heart diseases (46%), pulmonary thromboembolic disease (18%), chronic lung disease/hypoxia (17%), and pulmonary arterial hypertension (11%). Average 1-year mortality in patients with RVD is high (40%), highest among chronic lung disease patients.88 The presence of RVD at CRT implantation predicts worsening LV remodelling and survival.89

**Pharmacotherapies**

**Angiotensin receptor–neprilysin inhibitors (paragon, paradigm, parallax)**

Angiotensin receptor–neprilysin inhibitor (ARNI) showed, in a sub-analysis of PARADIGM-HF, a reduction in sudden cardiac death risk regardless of the use of implantable cardiac defibrillators.90 Reduction in ventricular volumes and increase in LVEF have been observed with standard echocardiography in patients after 6 months on SV, but improvement in global longitudinal strain is apparent after 3 months.91 In a small cohort of patients with end stage renal disease, SV showed efficacy and safety.91 The LIFE Trial, comparing SV to valsartan in NYHA Class IV HFrpEF patients, although prematurely interrupted because of the COVID-19 pandemic, will still provide information about ARNI as a treatment option for advanced HF patients.90

The PARALLAX trial tested the efficacy of SV vs. optimal individualised background therapy in HFrpEF patients and found a reduction in NT-proBNP from baseline to 12 weeks but no effect on six-minute walk distance from baseline to 24 weeks (presented at ESC 2020—data not published). In the PARAGON Trial in patients with HFrpEF, SV did not result in a lower rate of total hospitalizations for HF and death. Of the 12 pre-specified subgroup analyses, sex and LVEF appeared to modify the effect of SV vs. valsartan on the primary composite outcome. Although no benefit was apparent in men, there was a significant reduction in HF hospitalizations in women.92 Also, patients seemed to derive more benefit from SV when started early after hospitalization.94 Baseline and mean achieved systolic blood pressure of 120–129 mm Hg identified the lowest risk HFrpEF patients, but the blood pressure-lowering effects of SV did not account for its effects on outcomes, regardless of sex.95 Compared with valsartan, SV reduced the risk of renal events and slowed the decline in estimated glomerular filtration rate.96 Reduction in serum uric acid was also associated with improved outcomes.97 A meta-analysis assessing the efficacy of differ-ent renin–angiotensin–aldosterone system (RAAS) antagonists in clinical trials performed in HFrpEF patients (PEP-CHF, CHARMM-preserved, I-PRESERVE, TOPCAT, PARAGON-HF) showed no statistical differ-ence in all-cause and CV mortality among RAAS antagonists and placebo, but a significantly decreased risk in HF hospitalizations in patients allocated to receive ARNI compared with controls (OR, 0.73, 95% CI, 0.61–0.87) and ARB (OR 0.80, 95% CI, 0.71–0.91).98

A patient-level data analysis from the PARADIGM-HF and PARAGON-HF trials (SV vs. enalapril in HFrpEF and SV vs. valsartan in HFrpEF, respectively), and the CHARMM-Alternative and CHARMM-Preserved trials (candesartan vs. placebo) showed that, compared with RAAS inhibitors, SV improved outcomes across the range of LVEF, with a risk reduction (RR) of 0.54 [95% confidence interval (CI) 0.45–0.65] for the recurrent primary endpoint compared with puta-tive placebo (P < 0.001). Treatment benefits were robust in patients with LVEF < 60%, but not in those with LVEF > 60%.99 These results are in line with prior post hoc analyses from the TOPCAT study and β-blocker trials suggesting that the cut-off of LVEF for a beneficial treatment effects is ~55%. These analyses show that in the sparsely studied population of patients with an LVEF of 40–55%, several HF treatments might provide benefit (Figure 2).100

**Sodium-glucose cotransporter 2 inhibitors (EMPEROR-Reduced, DAPA-HF, SOLOIST, VERTIS, SUGAR-DM-HF, EMPA-TROPISM [ATRU-4])**

In patients with type 2 diabetes, the sodium-glucose cotransporter 2 (SGLT-2) inhibitors empagliflozin and dapagliflozin reduce the risk of HF hospitalization regardless of baseline CV risk or history of HF.101,102 In The VERTIS trial, empagliflozin did not significantly reduce CV events, nor the combined endpoint of CV death/HF hospitalization but reduced HF hospitalizations.104

In patients with HFrEF, DAPA-HF has demonstrated a significant reduction in CV mortality and HF events.105,106 This robust effect was analysed in more detail in several seminal papers published in 2020. The benefit of dapagliflozin was independent of the diabetes status, occurring across all levels of HbA1C,107 as well as of baseline renal function or blood pressure, patient age, or background HF ther-apy.108–111 Dapagliflozin improved symptoms, physical function, and quality of life,112 and was shown to be a cost-effective treatment for HFrEF in the UK, German, and Spanish healthcare systems.113 Dapagliflozin also reduces the rate of decline in renal function in HFrEF patients,111 as well as in patients with chronic kidney disease, as shown in the DAPA-CkD trial, where treatment with dapagliflozin reduced the risk of worsening renal function, end-stage kidney disease, or death. This protective effect was observed in patients with or without diabetes.111,114 Empagliflozin also showed marked beneficial effects in HFrEF patients independently from diabetes status (Figure 3), with a significant reduction in the primary composite endpoint of CV death and HF events (hazard ratio (HR), 0.75; 95% CI, 0.65–0.86; P < 0.001), the secondary endpoints of total HF hospitalizations (HR, 0.70; 95% CI, 0.58–0.85; P < 0.001), the annual rate of decline in the estimated glomerular filtration rate (~0.55 vs. -2.28 mL/min/1.73 m² of body-
surface area per year, $P < 0.001$), the risk of serious renal outcomes, and the risk and total number of inpatient and outpatient worsening HF events, which starts early after the initiation of treatment and remains during the duration of treatment. These beneficial effects were also observed to a similar extent in patients pretreated with ARNI and were independent of baseline diabetes status and across the continuum of HbA1c, and in patients with and without CKD and regardless of the severity of kidney impairment at baseline.

In the SUGAR-DM-HF study, empagliflozin reduced LV volumes measured by CV magnetic resonance in patients with HFrEF and type 2 diabetes or prediabetes. The mechanistic trial EMPA-TROPISM (ATRU-4) showed the beneficial effect of empagliflozin in improving LV volumes, LV mass, LV systolic function, functional capacity, and quality of life in non-diabetic patients with HFrEF (ref). Taken the evidence together, SGLT-2 inhibitors reduce all-cause and CV mortality and improve renal outcomes in patients with HFrEF, supporting the role of dapagliflozin and empagliflozin as a new standard of care for patients with HFrEF.

Sotagliflozin, another SGLT-2 inhibitor that displays also gastrointestinal SGLT-1 inhibition and thus reduces intestinal glucose absorption, was investigated in patients with type 2 diabetes after a recent hospitalization for worsening heart failure (SOLOIST-WHF). Patients were included independent of their ejection fraction, and 78% of patients had an ejection fraction $<50\%$. The primary endpoint of CV death, total hospitalizations, and urgent visits for HF was significantly reduced in patients treated with sotagliflozin ($HR, 0.67; 95\% CI, 0.52–0.85; P < 0.001$). The results were consistent among subgroups and especially also in patients with an EF $>50\%$. Sotagliflozin was also investigated in patients with type 2 diabetes, chronic kidney disease, and elevated CV risk (SCORED); primary endpoint (changed during the study to a composite of CV death, total HF hospitalizations and urgent visits for HF) was significantly reduced in patients treated with sotagliflozin ($HR, 0.67; 95\% CI, 0.52–0.85; P < 0.001$). It has to be mentioned that both sotagliflozin trials had to be stopped earlier than planned because of loss of funding from the sponsor.

**Activators of soluble guanylate cyclase**

(\textit{victoria, vitality, capacity})

The activator of soluble guanylate cyclase (\textit{sGC}) vericiguat was investigated in the VICTORIA study in 5050 patients with recently...
Vericiguat significantly reduced the primary outcome of CV death or first HF hospitalisation (HR, 0.90; 95% CI, 0.82–0.98; \( P = 0.02 \)) (Figure 3). While vericiguat significantly reduced HF hospitalisations (HR, 0.90; 95% CI, 0.81–1.00), CV deaths were not significantly diminished. Adverse events were largely similar among the vericiguat and placebo groups. An analysis comparing HRs and absolute RR in three large recent HFrEF trials demonstrated that while the HR suggests a smaller treatment effect in VICTORIA than in the DAPA-HF and PARADIGM-HF trials, a comparison of 12-month event rates for the primary outcome pointed to a comparable benefit across the three trials.127,128 Given the significant interaction of vericiguat effects according to baseline NT-proBNP levels, a post hoc analysis showed an association of vericiguat benefit on the primary outcome in patients with NT-proBNP levels up to 8000 pg/mL, with greatest benefit in patients with NT-proBNP <4000 pg/mL (HR, 0.77, 95% CI, 0.68–0.88).129

Vericiguat was evaluated in HFpEF patients in the VITALITY trial,128 showing no benefit in quality of life and exercise tolerance.130 Similarly, in the CAPACITY trial, the sGC stimulator praliciguat was well-tolerated but did neither affect the primary efficacy endpoint of pVO2 nor other predefined outcome parameters.131

Cardiac myosin activators and inhibitors

Omecantiv mecarbil (GALACTIC-HF, EXPLORER-HCM) Omecantiv mecarbil, a cardiac myosin activator that enhances cardiomyocyte contraction, given twice daily on the basis of plasma levels of the drug, significantly reduced the primary endpoint of HF hospitalisation and CV death in patients with HFrEF and a recent HF event (HR, 0.92; 95% CI, 0.86–0.99; \( P = 0.03 \)) (Figure 3) but had no impact on any of the secondary outcomes (CV death, change in symptom score, first HF hospitalization, and death from any cause).132

A similar compound, danicamtiv, increased stroke volume, improved global longitudinal and circumferential strain, decreased LA minimal volume index, and increased LA function index when compared to placebo in a small phase 2a trial in 40 patients with stable HFrEF.133

Cardiac myosin activators and inhibitors

Omecantiv mecarbil (GALACTIC-HF, EXPLORER-HCM) Omecantiv mecarbil, a cardiac myosin activator that enhances cardiomyocyte contraction, given twice daily on the basis of plasma levels of the drug, significantly reduced the primary endpoint of HF hospitalisation and CV death in patients with HFrEF and a recent HF event (HR, 0.92; 95% CI, 0.86–0.99; \( P = 0.03 \)) (Figure 3) but had no impact on any of the secondary outcomes (CV death, change in symptom score, first HF hospitalization, and death from any cause).132

A similar compound, danicamtiv, increased stroke volume, improved global longitudinal and circumferential strain, decreased LA minimal volume index, and increased LA function index when compared to placebo in a small phase 2a trial in 40 patients with stable HFrEF.133
On the other hand, mavacamten, a myosin inhibitor, significantly improved the combined primary endpoint of increase in peak oxygen consumption (\(p\text{VO}_2\)) and reduction in NYHA class in a phase 3 trial in patients with obstructive hypertrophic cardiomyopathy. Also, outflow tract obstruction and health status were improved.\(^{134}\)

**Other therapies**

**Ferric carboxymaltose (AFFIRM-AHF)**

In iron-deficient patients hospitalized for acute HF (AFFIRM-AHF),\(^{135}\) intravenous ferric carboxymaltose compared to placebo was associated with a trend to reduced total HF hospitalizations and CV death (rate ratio 0.79, 95% CI 0.62–1.01, \(P = 0.059\)). In a pre-specified sensitivity analysis considering the impact of the COVID-19 pandemic, a statistically significant difference in favour of ferric carboxymaltose was reported for the primary endpoint was reported, but not in CV death risk.\(^{136}\)

**MicroRNA-132 inhibition**

In a first clinical trial limited by a small number of HF patients, the antisense oligonucleotide drug directed against miR-132, CDR132L,\(^{137}\) was well tolerated and showed first hints for a cardiac functional improvement.\(^{138}\)

**Comprehensive disease-modifying pharmacological therapies**

Using data from the EMPHASIS-HF, PARADIGM-HF, and DAPA-HF trials lifetime gains in survival have been estimated with comprehensive therapy (SV, \(\beta\)-blocker, MRA, and SGLT-2 inhibitor) vs. RAAS and \(\beta\)-blockers in patients with chronic HFrEF.\(^{11,139}\) The HR for the composite endpoint of CV death or hospitalisation for HF was 0.38 (95% CI 0.30–0.47). Favourable results were also calculated for CV death alone, hospitalization for HF alone, and all-cause mortality. Comprehensive therapy could prolong overall survival 6.3 years in average in a 55-year-old patient. These results support the combination use of SV, \(\beta\)-blockers, mineralocorticoid receptor antagonists, and SGLT-2 inhibitors as a new therapeutic standard.

**Device/interventional therapies**

**Secondary (or functional) mitral regurgitation (COAPT)**

Secondary (or functional) mitral regurgitation (SMR) occurs frequently in HFrEF and is associated with progressive symptoms and worse prognosis. If SMR is treated by edge-to-edge repair, patients with optimal result at discharge and 12-month follow-up displayed best outcomes.\(^{140}\)

**Cardiac resynchronization therapy (STOP-CRT)**

Cardiac resynchronization therapy (STOP-CRT) is an integral part of treatment in patients with HFrEF, especially with left bundle branch block and wide QRS. In a selected cohort of patients with LVEF >50% during CRT and neurohormonal blockade, the STOP-CRT study investigated the feasibility and safety of neurohormonal blocker withdrawal. The incidence of adverse LV remodelling or clinical outcomes was low after discontinuation of betablockade/RAAS inhibition. However, comorbidities prompted the continuation of neurohormonal blockers in many patients.\(^{141}\)

In patients with HFrEF who are ineligible for CRT, baroreflex activation therapy (BAT) may be useful in addition to optimal drug therapy. In the BeAT-HF study, BAT was safe and significantly improved symptoms, quality of life, exercise capacity, and NT-proBNP.\(^{142}\) On the basis of these data, BAT was approved in the USA, while ongoing follow-up in the BeAT-HF study will assess effects on hard outcomes.

**Specific management issues**

**Telemedicine and remote monitoring**

The role of telemedicine and remote monitoring in the management of HF patients is still controversial. An observational study in three European countries showed that pulmonary artery pressure-guided HF management is feasible and safe and associated with better outcomes haemodynamic and clinical outcomes.\(^{143}\) Also, preliminary results testing non-invasive remote physiological monitoring from a wearable sensor showed promising results in the early detection of impending HF rehospitalisation.\(^{144}\) However, different modes of remote monitoring failed to show a benefit in improving treatment, quality of life,\(^{145}\) or clinical outcomes.\(^{146}\) Moreover, remote monitoring with a cardiac implanted electronic device increased clinical activity for patients with HF and AF, with no associated reduction in mortality, and conversely, greater risk of CV hospitalisation amongst patients with persistent/permanent AF.\(^{147}\) In the COVID-19 era, remote monitoring is a useful tool for managing HF patients.\(^{148}\)

**Self-care and palliative care**

Self-care is essential in the management of chronic HF. Practical advice for key activities and priorities for self-care is given in an HFA manuscript.\(^{149}\) At the end of the HF pathway, palliative care should be introduced early, focusing on symptom management,\(^{150}\) regardless of prognosis, but actually only a minority in Europe receive it.\(^{151}\) Providing palliative care substantially reduces hospitalizations, with no clear adverse effect on survival.\(^{152}\)

**Funding**

There was no specific funding for the development of this manuscript. J. Bauersachs is supported by the Deutsche Forschungsgemeinschaft, KFO 311, “Advanced cardiac and pulmonary failure: mechanical unloading and repair”.

**Disclosures:** Dr. Bueno reports grants from Instituto de Salud Carlos III, grants from Sociedad Española de Cardiología, grants from Astra-Zeneca, and personal fees from Bayer; grants and personal fees from BMS, grants and personal fees from Novartis.

Dr. Moura reports personal fees from Astra Zeneca, personal fees from Vifor, personal fees from Servier, personal fees from Novartis, personal fees from Merck Serono, personal fees from Elly-Lilly, personal fees from Boehringer-Ingelheim.
Dr. Bauersachs reports personal fees from Abbott, grants and personal fees from Abiomed, personal fees from Astra Zeneca, personal fees from Bayer, personal fees from BMS, personal fees from Boehringer Ingelheim, grants and personal fees from CviRx, personal fees from Daichi Sankyo, personal fees from Medtronic, personal fees from MSD, personal fees from Novartis, personal fees from Pfizer, personal fees from Servier, grants and personal fees from Vifor, grants from Zoll, personal fees from Abbott, grants and personal fees from Vifor, grants from Zoll, personal fees from Cardior. In addition, Dr. Bauersachs is Board Member of Cardior and has a patent PCT/EP2007/008772 with royalties paid, and a patent PCT/ EP2009/051986 with royalties paid both on microRNA (miRNA) and downstream targets for diagnostic and therapeutic.

Dr Lancellotti has no relevant disclosures.

References


44. Poelmann S. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell 2020;181:270–280.e8.


The year in CV Medicine: HF and cardiomyopathies


Erratum

doi:10.1093/eurheartj/ehaa875

Online publish-ahead-of-print 9 October 2020


Upon the original publication of this article, several errors were noted. The publisher apologises for the following errors that have subsequently been corrected in the online and print versions of the article:

The affiliation footnote ‘7’ should read: “Department of Epidemiology and Population Studies, Institute of Public Health, Jagiellonian University Medical College, ul. Grzegórzecka 20, 31531 Krakow, Poland”.

The “Graphical Abstract” figure should be replaced with the corrected version.

The “Take home” figure should be deleted.

In the “Methods” section, the following text should read: “A summary of the methods and results is shown in the Graphical abstract.”. In addition, two other corrections under the following headings were made:

Under “Derivation data”, the following sentence should read: “Trained nurses performed a personal interview, physical examination and took blood samples. Serum cholesterol was determined by the automated enzymatic method. Past medical and drug history, education, employment, marital status, and physical inactivity were assessed by interview according to standardized questionnaire.”.

Under “External validation data”, the following text should read: “between 2002 and 2011 from 51 045 population-based participants”.

The results in Table 1. should be corrected.

In Table 2., the “Categorical net reclassification improvement (95% CI)” and “Continuous net reclassification improvement (95% CI)” results for “From model 1 (original SCORE) to model 2 (recalibrated SCORE)”, “From model 2 (recalibrated SCORE) to model 3 (HAPIEE SCORE)” and “From model 1 (original SCORE) to model 3 (HAPIEE SCORE)” should be corrected. The results heading for “model 1 (original SCORE) to model 3 (HAPIEE SCORE)” should be: “Predicted 10-year risk (HAPIEE)”. The results for “From model 1 (original SCORE) to model 2 (recalibrated SCORE)” and “From model 2 (recalibrated SCORE) to model 3 (HAPIEE SCORE)” should be corrected. The results heading for “model 1 (original SCORE) to model 3 (HAPIEE SCORE)” should be: “Predicted 10-year risk (HAPIEE)”.

The funding section omitted the following: “the National Science Centre of Poland [2018/29/B/NZ7/02118]”.

In addition, two further corrections have been made to the online version of the article. These are as follows:

The affiliation footnote ‘11’ should read: “Institute of Mathematics and Statistics, University of Tartu, Narva mnt 18, 51009 Tartu, Estonia”.

The funding section omitted the following: “Research Foundation Flanders [1S05916N to O.D.]; Ghent University Special Research Fund [BOF.01P08419 to O.D.]”. 

© The Author(s) 2020. Published by Oxford University Press on behalf of the European Society of Cardiology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted reuse, distribution, and reproduction in any medium, provided the original work is properly cited.