ESC HEART FAILURE
ESC Heart Failure 2022; **9**: 3667–3693
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.14257

REVIEW

Heart failure: an update from the last years and a look at the near future

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Abstract

In the last years, major progress occurred in heart failure (HF) management. Quadruple therapy is now mandatory for all the patients with HF with reduced ejection fraction. Whilst verciguat is becoming available across several countries, omecamtiv mecarbil is waiting to be released for clinical use. Concurrent use of potassium-lowering agents may counteract hyperkalaemia and facilitate renin–angiotensin–aldosterone system inhibitor implementations. The results of the EMPagliflozin outcomE tRial in Patients With chrOnic heaRt Failure With Preserved Ejection Fraction (EMPEROR-Preserved) trial were confirmed by the Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction (DELIVER) trial, and we now have, for the first time, evidence for treatment of also patients with HF with preserved ejection fraction. In a pre-specified meta-analysis of major randomized controlled trials, sodium–glucose co-transporter-2 inhibitors reduced all-cause mortality, cardiovascular (CV) mortality, and HF hospitalization in the patients with HF regardless of left ventricular ejection fraction. Other steps forward have occurred in the treatment of decompensated HF. Acetazolamide in Acute Decompensated Heart Failure with Volume Overload (ADVOR) trial showed that the addition of intravenous acetazolamide to loop diuretics leads to greater decongestion vs. placebo. The addition of hydrochlorothiazide to loop diuretics was evaluated in the CLOROTIC trial. Torasemide did not change outcomes, compared with furosemide, in TRANSFORM-HF. Ferric derisomaltose had an effect on the primary outcome of CV mortality or HF rehospitalizations in IRONMAN (rate ratio 0.82; 95% confidence interval 0.66–1.02; $P = 0.070$). Further options for the treatment of HF, including device therapies, cardiac contractility modulation, and percutaneous treatment of valvulopathies, are summarized in this article.

Keywords Heart failure; HFmrEF; HFpEF; HFrEF; Diagnosis; Prognosis; Treatment; SGLT2 inhibitors; Acute HF

Received: 19 November 2022; Accepted: 21 November 2022
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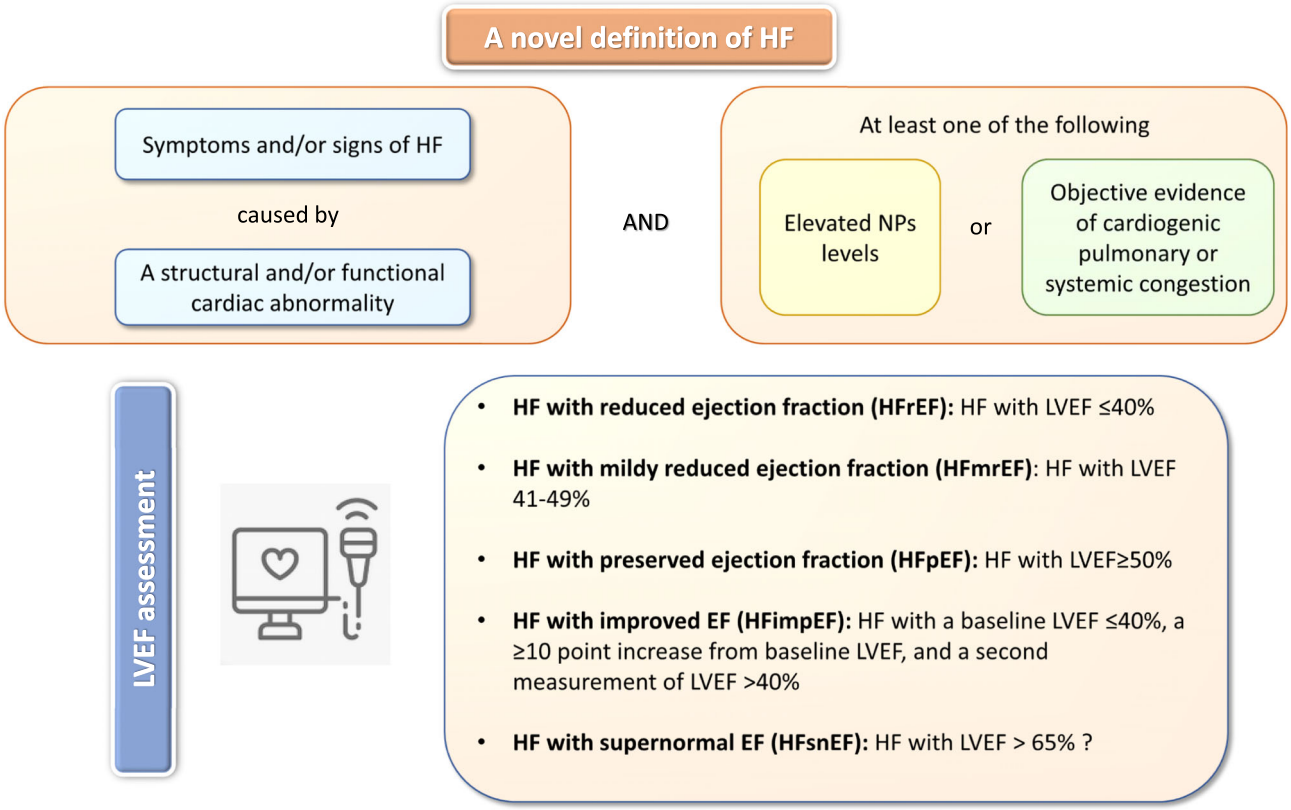
Introduction

Heart failure (HF) is a major health and economic challenge worldwide. In this article, we aim to summarize the most recent findings and advances in the field of HF.

Universal definition of heart failure

The Heart Failure Society of America (HFSA), the Heart Failure Association (HFA) of the European Society of Cardiology (ESC), and the Japanese Heart Failure Society (JHFS) proposed the universal definition of HF. HF is a clinical syndrome with symptoms and/or signs caused by a structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide (NP) levels and/or objective evidence of pulmonary or systemic congestion.[1] According to left ventricular (LV) ejection fraction (EF) (LVEF), patients with HF are classified into those with reduced EF (HFrEF, EF $\leq$ 40%), mildly reduced EF (HFmrEF, EF 41–49%), preserved EF (HFpEF, EF $\geq$ 50%), and improved EF (HFimpEF, baseline EF $\leq$ 40%, a $\geq$10-point increase in EF, and a second EF $>$ 40%)[1–3] (*Figure 1*).

Figure 1 A novel definition of heart failure (HF) (modified from Bozkurt *et al.*[1]). LVEF, left ventricular ejection fraction; NPs, natriuretic peptides.



Epidemiology

Due to population growth and ageing, the total number of HF patients continues to rise. It is estimated that 64.3 million people live with HF worldwide. In developed countries, the prevalence of known HF is generally estimated at 1–2% of the general adult population.[2,4] Groenewegen *et al*. estimated a more realistic prevalence of 4.2% with HF that remains undetected in over half of the cases.[2,4]

An alarming rise in relatively young people and in countries with low socio-demographic index is probably related to an increase in risk factors.[5,6] In addition, there has been a clear transition towards HFpEF due to an improvement in the recognition of the disorder but also its relationship to obesity and the ageing of the population.[4,7–10] HF is still burdened by high morbidity and mortality.[11–13]

Sex differences

Sex-based differences exist among patients with HF.[14–19] Women with known or suspected coronary artery disease are at a higher risk of new-onset HF,[20] but they are generally older than men at the time of diagnosis, more frequently develop HFpEF, and seem to have a better prognosis than men, even after age adjustment.[21,22] A systematic review of randomized controlled trials, including 183 097 patients with HFrEF, showed that women were under-enrolled in most of the studies, representing about a quarter of the patients.[23] Several studies investigated interactions between sex and treatment effects.[15,24–26]

Diagnosis and prognosis

Electrolytes

Both hypokalaemia and hyperkalaemia have been associated with worse prognosis.[27,28] Cooper *et al*. showed a U-shaped relationship between serum potassium levels and mortality risk in 13 015 patients with HFrEF from the Swedish Heart Failure Registry.[29] Hyperkalaemia (together with elevated plasma volume) is a sign of instability after a recent hospitalization,[30] and it is a frequent cause of renin–angiotensin–aldosterone system inhibitor (RAASi) discontinuation.[31] However, an analysis from the ESC–HFA–EURObservational Research Programme (EORP) Heart Failure Long-Term Registry showed that hyperkalaemia was no lon-

ger associated with mortality after adjusting for RAASi discontinuation, suggesting that hyperkalaemia may be a risk marker for RAASi discontinuation rather than a risk factor for worse outcomes.[32,33] These data were then confirmed in the Observational study from the Stockholm CREAtinine Measurements (SCREAM) project 2006–18.[34] About half of the HF patients also present hyperuricaemia, a prognostic ominous factor in HFrEF.[35] In the Prospective Comparison of ARNI with ARB Global Outcomes in HF With Preserved Ejection Fraction (PARAGON-HF) trial, serum uric acid (UA) was an independent predictor of poor outcome also in HFpEF. Sacubitril/valsartan reduced serum UA levels and the need for UA-related drugs with an improvement of outcomes.[36] Similarly, in the Dapagliflozin and Prevention of Adverse-outcomes in Heart Failure trial (DAPA-HF), compared with placebo, dapagliflozin reduced UA and improved outcomes irrespective of UA concentration.[37]

Biomarkers

Biomarkers are needed for the management of patients with HF.[38–42] Brain natriuretic peptide (BNP) and N-terminal pro-BNP (NT-proBNP) are related with left intracardiac filling pressures and pulmonary capillary wedge pressures (PCWP).[43] Cardiac troponin (Tn) has a central role in the prognostic evaluation of HF patients.[44] In the Empagliflozin Outcome Trial in Patients with Chronic Heart Failure and a Reduced Ejection Fraction (EMPEROR-Reduced), increasing levels of high-sensitivity cardiac Tn T were associated with higher rates of comorbidities [i.e. diabetes mellitus (DM) and atrial fibrillation (AF)], more advanced New York Heart Association (NYHA) functional class, decreased renal function, higher concentrations of NP, and worse clinical course.[45] The combination of NT-proBNP and cardiac Tn improves HF risk prediction in overweight and obese individuals.[46]

Several other biomarkers are under study and have already demonstrated a diagnostic and prognostic role, including soluble suppression of tumourigenesis-2 (sST2), galectin-3, and GDF-15, markers that are associated with inflammatory disease and fibrosis,[47] bio-adrenomedullin (bio-ADM), a possible marker of congestion,[48,49] circulating dipeptidyl peptidase 3 (cDPP3),[50,51] a protease involved in angiotensin II and enkephalin degradation,[52] carboxy-terminal propeptide of procollagen type I (PICP),[53] fibroblast growth factor 23 (FGF23),[54] antigen carbohydrate 125 (CA125),[55,56] cystatin C,[47] serum and urine neutrophil gelatinase-associated lipocalin (NGAL),[57] and urine peptides.[58]

Imaging

The role of imaging in the management of HF is well established.[59–63] The Copenhagen City Heart Study investigated the prognostic value of two-dimensional speckle tracking echocardiography in the general population. Overall, 4013 citizens were included. Whole wall and epi-myocardial global longitudinal strain (GLS) were found to be detrimental in differentiating between ischaemic and non-ischaemic aetiology[64] to assess diastolic function[65] and to be significant predictors of outcome [a composite of incident HF or cardiovascular (CV) death] in males, whereas no GLS parameter was useful in females,[66] and also able to improve diagnosis. In a larger cohort of 117 275 subjects being followed up with echocardiography, even modest LVEF changes over time had a significant impact on prognosis with an increase from 12% to 29% of 5 year all-cause mortality among subjects with the smallest to the largest decrease in LVEF (from <5 to >30 units).[67] Several ultrasound methods allow the detection of elevated intracardiac pressures and/or fluid overload, including imaging of the heart, lungs (B-lines), kidneys (intrarenal venous flow), and venous system (inferior vena cava and internal jugular vein diameter).[68] Among 238 subjects with at least one risk factor for HF, subclinical congestion assessed by inferior vena cava diameter, jugular vein distensibility ratio, and the number of B-lines at lung ultrasound was detected in 30%.[69] LVEF remains a major determinant of prognosis.[63] Systolic time intervals can be reliably quantified by conventional echocardiography. Patients with HFrEF displayed shorter LV ejection times reflecting an impairment in LV contractility.[70] Longer systolic ejection times were independently associated with improved outcome in HFrEF but not in HFpEF patients.[71,72]

'Atrial disease', also referred as atrial failure or myopathy, represents an intersection of subclinical structural, electrophysiological, and functional changes that affect the atria and has an important diagnostic and prognostic role, above all in patients with HFpEF.[2,73,74] Left atrial (LA) reservoir and pump strain are associated with LV filling pressure and may contribute to the limitation of exercise capacity in the patients with HF.[75,76] LA size predicted 4 year mortality also in HF patients with mitral regurgitation (MR) treated by percutaneous repair.[77]

Machine learning and risk prediction

Machine learning procedures have been successfully used to guide diagnosis,[78] therapeutic strategies,[79] and prognosis.[80] Using a machine learning algorithm, Adler *et al*. proposed a novel mortality risk score that was then successfully validated across the LVEF categories.[81,82] A machine learning approach was also useful to stratify patients, namely, those with HFpEF, into different clusters with different outcomes.[38,81–85]

Treatment of heart failure with reduced ejection fraction

Pharmacological therapies

Pharmacotherapy is the cornerstone of treatment for HFrEF and is based on combined administration of drugs acting through different pathways.[2,86–88] However, implementation of the so-called guidelines directed medical treatment (GDMT) remains suboptimal in a large proportion of patients.[14,89–95] In a multinational observational study, using healthcare databases in Sweden, the United Kingdom, and the United States, among new users of HFrEF drugs, over 12 month follow-up, target doses of angiotensin-converting enzyme inhibitors (ACEis), angiotensin receptor blockers (ARBs), beta-blockers, and angiotensin receptor–neprilysin inhibitors (ARNIs) were achieved in 15%, 10%, 12%, and 30% of patients, respectively. Treatment discontinuation was frequently observed occurring in 55% of the patients on ACEi, 33% of those on ARB, 40% of those on mineralocorticoid receptor antagonist (MRA), and, importantly as ACEi/ARB discontinuation might have been related to the initiation of ARNI, 27% of those on ARNI.[96] Another recent analysis of Medicare beneficiaries in the United States showed that 34% did not have an active sacubitril/valsartan prescription at Day 180 after its initiation with Black race, comorbidities, and the start early after a hospitalization as factors increasing the likelihood of early discontinuation.[97] Several strategies have been proposed for the implementation of GDMT, including rapid sequencing and patient profiling.[98–102]

Neurohormonal modulators

The interaction between different drugs has therefore a major role for their tolerance and the implementation of GDMT. Use of sacubitril/valsartan (when compared with enalapril) did not lead to greater discontinuation or dose down-titration of other key GDMT and promoted sustained MRA use in follow-up.[101] Initiation of sacubitril/valsartan as first-line therapy in *de novo* HF patients was safe.[103] Further benefits of ARNI on liver function have been highlighted.[104] On the other hand, sacubitril/valsartan failed to improve exercise capacity compared with enalapril in two small randomized controlled trials, the ACTIVITY-HF and OUTSTEP-HF trials.[105–107] In 2021, the results of PARADISE-MI trial were published.[108–111] Sacubitril/valsartan did not significantly reduce the rate of CV death or incident HF in patients with LVEF $\leq$ 40% and/or pulmonary congestion following acute myocardial infarction (AMI), compared with ramipril.[111] However, in a *post hoc* analysis of the PARADISE-MI trial using the win ratio, sacubitril/valsartan was superior to ramipril among high-risk survivors of AMI.[112]

Finerenone is a novel nonsteroidal, selective MRA.[113,114] FIDELIO-DKD and FIGARO-DKD trials demonstrated that finerenone improved CV and kidney outcomes in patients with chronic kidney disease (CKD) and type 2 DM.[114–118] These positive results have been recently confirmed in the FIDELITY pooled analysis.[118] Further evidence on the efficacy and safety of finerenone compared with placebo in patients with HF and LVEF of 40% or greater is expected from the ongoing Finerenone Trial to Investigate Efficacy And Safety Superior to Placebo in Patients With Heart Failure (FINEARTS-HF) study, which is currently recruiting (NCT04435626).

Sodium–glucose co-transporter-2 inhibitors

Sodium–glucose co-transporter-2 (SGLT2) inhibitors have a central role in the prevention and treatment of HF.[119–128] A recent meta-analysis of major randomized clinical trials (RCTs), including 71 553 participants with HF, CKD, or high-risk type 2 DM, showed that SGLT2 inhibitors reduced the risk of HF hospitalization by 31% and the composite outcome of CV death or HF hospitalization by 24%. Results were consistent across the broad spectrum of cardio-renal-metabolic risk, although those with established HF had the greatest absolute benefit.[129] Data from the Swedish Heart Failure Registry showed similar results with SGLT2i administration, leading to a 30% reduction of CV death/first HF hospitalization.[130] SGLT2 inhibitors reduced CV events regardless of several baseline characteristics, including NT-proBNP concentrations, body mass index (BMI), ischaemic vs. non-ischaemic aetiology, or the presence of chronic obstructive pulmonary disease.[131–136] Data on improvement in exercise capacity are still debated.[137] Tomasoni *et al*. reviewed growing evidence that support the early, upfront initiation of SGLT2is in both acute and chronic HF patients due to early benefits, with clinically meaningful reductions in clinical events that reach statistical significance within days to weeks, safety, and tolerability.[100,154,342,343]

Potassium-lowering agents

The DIAMOND trial, enrolling 1642 patients with HFrEF and current or a history of RAASi-related hyperkalaemia, showed that the use of patiromer was associated with significantly lower serum potassium levels at follow-up, fewer hyperkalaemia episodes, concurrent use of high doses of MRAs, and overall higher RAASi use compared with placebo.[138,139]

Soluble guanylate cyclase stimulators

Vericiguat, soluble guanylate cyclase stimulators, reduced the risk of CV death or HF hospitalization in patients with HFrEF and recently decompensated HF.[140,141] Benefits were consistent in those with and without AF and across the full range of estimated glomerular filtration rate (eGFR).[142,143] Vericiguat treatment was associated with reduction in inflammatory- and oxidative stress-related markers, such as high-sensitivity C-reactive protein and UA.[144]

Myosin activators

New insights from the Global Approach to Lowering Adverse Cardiac outcomes Through Improving Contractility in HF (GALACTIC-HF) trial show the efficacy and safety of the selective cardiac myosin activator omecamtiv mecarbil in patients with severe systolic HF and with systolic blood pressure (BP) ≤100 mmHg.[145–150] In Multicenter Exercise Tolerance Evaluation of Omecamtiv Mecarbil Related to Increased Contractility in Heart Failure (METEORIC-HF) trial, omecamtiv mecarbil did not improve functional capacity in patients with HFrEF over 20 weeks.[151] This drug remains therefore indicated to improve patients' outcomes.[2] Danicamtiv is another selective myosin activator capable of improving LV and atrial contractility in experimental models and in a Phase 2a trial in patients with HFrEF.[152]

Possible future options

Transient receptor potential vanilloid 4 (TRPV4) channel regulates fluid exchange in the lungs. A novel transient TRPV4 antagonist (GSK2798745) was tested in a pilot randomized, placebo-controlled trial aimed at the reduction of lung water content.[153] The new drug was well tolerated and showed a trend towards improved gas transfer.[154] Mesenchymal autologous stem-cell therapy has had promising results in ischaemic cardiomyopathy and HF.[155,156] The Phase II CONCERT-HF trial demonstrated that the combination of mesenchymal stem cells and c-kit-positive cardiac cells was associated with further improvement in clinical outcome and quality of life (QoL).[157] Target therapies focusing on miRNA and plasma proteome may become a future perspective.[158,159]

Non-pharmacological therapies

Dietary interventions and exercise training

Dietary interventions are related to HF incidence and outcome.[160–162] A meta-analysis, including 122 RCTs and 176 097 participants, summarized and confirmed the impact of nutritional and dietary interventions on HF-related outcomes. Coenzyme Q10 was associated with lower all-cause mortality, whereas Mediterranean diet was related with a lower risk of developing HF.[162,163] A high-protein diet resulted in greater reductions in cardiometabolic risks relative to a standard-protein diet.[164] Ergoreflex is a cardiorespiratory reflex activated during physical effort. HF patients often develop skeletal myopathy, which is associated with increasing ergoreflex sensitivity and dyspnoea on effort. Exercise training represents a valuable strategy to reduce such sensitivity and increase exercise tolerance.[165–167]

Implantable defibrillator therapy

Sudden cardiac death (SCD) is a complication of HF.[168] Docherty *et al*. developed a risk model for SCD in ischaemic cardiomyopathy using data from the Effect of Carvedilol on Outcome After Myocardial Infarction in Patients With Left Ventricular Dysfunction trial (CAPRICORN) and the Valsartan in Acute Myocardial Infarction Trial (VALIANT). This SCD risk score was superior to LVEF alone and might be useful in identifying patients for future trials testing treatments to prevent SCD early after AMI.[169] Current guidelines advise implantation of an implantable cardiac defibrillator (ICD) for SCD prevention in patients with a life expectancy of >1 year. An analysis, including 17 901 US veterans with HFrEF receiving a new ICD placement, showed that 1 year mortality was around 13%, suggesting the need of a better selection of patients. Age at implant was associated with higher rates of mortality.[170]

Cardiac resynchronization therapy

Cardiac resynchronization therapy (CRT) improves cardiac function and symptoms and reduces morbidity and mortality in an appropriately selected group of HF patients.[2,171] It may be a feasible treatment that can offer short-term and long-term clinical benefits for NYHA Class IV HF patients.[172] Nevertheless, up to two thirds of eligible patients are not referred for CRT.[173,174] A joint position statement from three ESC Associations, HFA, European Heart Rhythm Association (EHRA), and European Association of Cardiovascular Imaging (EACVI), aimed at overcoming CRT under-utilization, improving patient selection, and implementing dedicated post-implant CRT care pathways.[174]

Cardiac contractility modulation

Cardiac contractility modulation (CCM) may improve functional capacity and reduce CV and HF hospitalizations.[175,176] A comprehensive meta-analysis of individual patient data from all known randomized trials has shown that CCM provides statistically significant and clinically meaningful benefits in measures of functional capacity and HF-related QoL.[177] Long-term effects of CCM were evaluated in a European prospective registry including 503 patients. CCM improved QoL, functional status, and LVEF. Furthermore, HF hospitalizations were reduced compared with before treatment.[178]

Percutaneous treatment of mitral regurgitation

Valvular heart disease is a major determinant of outcome in patients with HF.[74,179–183] Moderate-to-severe functional MR has a prevalence up to 41% in patients with worsening chronic or new-onset acute HF from the BIOSTAT-CHF study.[179] MR severity may dynamically change after a dedicated period of GDMT optimization.[184] Moreover, GDMT prescription is associated with higher 2 year survival after transcatheter edge-to-edge mitral valve repair (M-TEER) in HFrEF patients with functional MR.[185] M-TEER using a MitraClip device should be considered in selected HFrEF patients with secondary MR, not eligible for surgery, who fulfil the Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation (COAPT) selection

criteria.[182,186,187] Residual MR 1+ after MitraClip was associated with reduced risk of 1 year mortality, compared with residual MR 2+ and 3/4+.[188,189] LA enlargement is a strong and independent predictor of adverse long-term outcome after M-TEER.[77,190] Among 221 patients with HFrEF and MR $\geq$ 3+ successfully treated with M-TEER, 40% had an improvement in right ventricular (RV) function, and this finding was independently associated with lower risk of death or heart transplantation (HTx) [hazard ratio (HR) 0.52; 95% confidence interval (CI) 0.29–0.94; P = 0.030].[191] In another cohort, more than one third of patients with secondary MR, undergoing successful M-TEER, experienced an improvement in tricuspid regurgitation (TR). A TR $\leq$ 2+ at short-term follow-up was independently associated with long-term mortality, whereas pre-procedural TR was not. Optimal M-TEER result and a small LA were among factors associated with a higher likelihood of TR $\leq$ 2+ after M-TEER.[192] Finally, mitral valve repair with MitraClip has positive clinical and echocardiographic impact in patients with functional MR 1 year after implantation. Preserved GLS and global constructive work values appeared to be associated with LV reverse remodelling post-intervention.[193]

In-hospital mortality after MitraClip procedure did not differ according to centre procedural volume, although patients treated in high-volume centres had a higher risk profile.[194] Novel percutaneous treatments of functional MR are currently studied.[195,196]

Percutaneous treatment of tricuspid regurgitation

Tricuspid regurgitation can be the cause or the consequence of RV dysfunction and HF.[2,197] In a large database of almost half-million US patients with HF, both prevalent TR and incident TR were independently associated with an increased risk of mortality at a median follow-up of 1.5 years.[180] Tricuspid valve surgery is recommended in patients with severe TR requiring left-sided cardiac surgery. It should be also considered in patients with moderate TR and tricuspid annulus dilatation requiring left-sided cardiac surgery and in symptomatic patients with isolated severe TR.[2] However, surgery in isolated TR is burdened by high in-hospital mortality. A new risk score for in-hospital mortality prediction after isolated tricuspid valve surgery, the TRI-SCORE, has been proposed.[198]

Transcatheter tricuspid valve repair (TTVR) for severe TR was found to be safe and effective in different studies.[197,199,200] TTVR improved nutritional status, QoL, and outcome.[201] Actually, four devices have received the CE mark, that is, TriClip, PASCAL, TricValve, and Cardioband, addressing different mechanisms underlying TR.[197] Unterhuber *et al*. showed that outcome after TTVR was associated with pre-procedural cardiac index in a bimodal fashion with increased mortality for both patients in a low and high cardiac output (CO) state and highest overall mortality for patients with a high CO state phenotype.[202]

Heart failure with preserved ejection fraction

Epidemiology, clinical phenotypes, and pathophysiology

Heart failure with preserved ejection fraction is a heterogeneous syndrome with multiple aetiologies and phenotypes and accounts for more than half of the HF hospitalizations.[84,85,203–207] Kammerlander *et al*. investigated the prevalence of HFpEF following left-sided valve repair. Among 673 patients included, 67.4% fulfilled all criteria of HFpEF according to current guideline recommendations.[208] Three phenogroups of HFpEF were described among the participants to the TOPCAT trial.[85] Using unsupervised cluster analysis based on circulating biomarkers, Woolley *et al*. identified four distinct clusters of HFpEF with remarkable differences in clinical characteristics and outcomes, potentially reflecting different underlying pathophysiology.[84]

The role of DM and obesity in the pathogenesis of HFpEF has drawn significant attention in recent years.[203,209–213] CV effects of obesity may be driven by the distribution of fat, which can accumulate in the epicardial, visceral, and subcutaneous compartments.[214–216] Via adipokine-mediated inflammatory mechanisms, epicardial obesity might cause adverse myocardial remodelling in HF that was independently related with diastolic dysfunction, worse haemodynamic and metabolic profile, and worse survival.[217–219] However, also sarcopenia was an independent predictor of 1 year mortality in both HFpEF and HFrEF.[220]

Other mechanisms involved in the pathogenesis of HFpEF are venous dysfunction, endothelium-independent microvascular dysfunction, and subclinical inflammation.[221–224]

Diagnosis and prognosis

The diagnosis of HFpEF remains challenging.[225] The H_2FPEF and HFA-PEFF scores have been proposed and validated to solve the clinical dilemma of diagnosing HFpEF.[205,226–230] These scores also provided a prognostic significance.[231–233] Tomasoni *et al*. investigated the diagnostic and prognostic value of H_2FPEF and HFA-PEFF scores in patients with HFpEF caused by cardiac amyloidosis (CA). The HFA-PEFF score has a higher diagnostic utility compared with H_2FPEF score and holds independent prognostic value for all-cause mortality.[234] Exercise testing has also a central role to confirm the diagnosis of HFpEF.[235] Cardiopulmonary exercise test and echocardiographic parameters (i.e. LA size and function) allow the risk stratification of HFpEF patients.[60,73,74,76,236–239] Cardiac magnetic resonance (CMR) has a major role in the detection and quantification of myocardial fibrosis and adipose tissue,

two major determinants of the phenotype and outcomes of patients with HFpEF.[214,218]

Treatment

Sodium–glucose co-transporter-2 inhibitors

The EMPagliflozin outcomE tRial in Patients With chrOnic heaRt Failure With Preserved Ejection Fraction (EMPEROR-Preserved) trial was the first trial proving benefits on major clinical endpoints in HFpEF. Empagliflozin reduced the composite endpoint of CV death or HF hospitalization in patients with LVEF $>$ 40% and NYHA Class II–IV, irrespective of DM history (HR 0.79; 95% CI 0.69–0.90; $P < 0.001$).[240] When compared with prior trials in HFpEF, the EMPEROR-Preserved cohort has a somewhat higher burden of comorbidities, lower LVEF, higher median NT-proBNP, and greater use of MRAs at baseline.[241] In a smaller randomized trial, enrolling 324 patients with HFpEF, dapagliflozin improved symptoms, QoL, and functional capacity compared with placebo.[242] In 2022, the results of the Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction (DELIVER) trial have been published.[243,244] Dapagliflozin reduced the combined risk of worsening HF or CV death among patients with symptoms and signs of HF, elevated concentrations of NT-proBNP, evidence of structural heart disease, and LVEF $>$ 40% compared with placebo (HR 0.82; 95% CI 0.73–0.92; $P < 0.001$).[244] Importantly, no appreciable difference was found in benefit among patients with an LVEF of 60% or more and those with an LVEF of $<$60%.

Vaduganathan *et al*. performed a pre-specified meta-analysis of DELIVER and EMPEROR-Preserved and subsequently included trials that enrolled patients with reduced LVEF (DAPA-HF and EMPEROR-Reduced) and those admitted to hospital with worsening HF, irrespective of LVEF (SOLOIST-WHF).[123] Among 12 251 participants from DELIVER and EMPEROR-Preserved, SGLT2 inhibitors reduced the composite endpoint of CV death or first hospitalization for HF (HR 0.80 [95% CI 0.73–0.87]) with consistent reductions in both components: CV death (0.88 [0.77–1.00]) and first hospitalization for HF (0.74 [0.67–0.83]). Among the 21 947 participants of five major trials, SGLT2is reduced the risk of CV death or HF hospitalization (0.77 [0.72–0.82]), CV death (0.87 [0.79–0.95]), first hospitalization for HF (0.72 [0.67–0.78]), and all-cause mortality (0.92 [0.86–0.99]). So, SGLT2 inhibitors reduced the risk of CV death and hospitalisations for HF in a broad range of patients with HF, supporting their role as a foundational therapy for HF, irrespective of LVEF or care setting.[123]

Other drugs

Inorganic nitrite improves peripheral and pulmonary components of oxygen (O_2) uptake during exercise in patients with HFpEF, including skeletal muscle conductance, peripheral O_2 kinetics, and lung gas diffusion.[245] HFpEF frequently coexists in patients with symptomatic AF and preserved EF. Dronedarone is associated with reduced CV events in patients with paroxysmal or persistent AF/atrial flutter and HF across the spectrum of LVEF, including those with HFpEF and HFmrEF.[246] Restoration and maintenance of sinus rhythm in patients with comorbid AF and HFpEF improve haemodynamic parameters, BNP, and symptoms associated with HFpEF.[247]

Device-based percutaneous treatments

The use of devices capable of creating interatrial shunts, to reduce LA pressure, represents a promising therapeutic option in patients with HFpEF. Most of the early trials demonstrate feasibility, safety, and effectiveness in reducing PCWP and improving patients' symptoms and QoL.[248–250] Of note, the Atrial shunt device for heart failure with preserved and mildly reduced ejection fraction (REDUCE-LAP II), a randomized, blinded, sham-controlled trial, including patients with symptomatic HF, LVEF $\geq$ 40%, and PCWP during exercise of at least 25 mmHg, failed to demonstrate difference between groups for the primary hierarchical composite endpoint (win ratio 1.0 [95% CI 0.8–1.2]; $P = 0.85$).[251]

Splanchnic nerve modulation

Approximately 60–70% of blood volume resides in the venous circulation, and up to 20–50% is in the high capacitance, highly innervated, veins of the splanchnic compartment. Sympathetic stimulation causes their constriction or shifting blood to the heart with a rise in intracardiac pressure. Splanchnic nerve modulation is proposed to inhibit such effect.[252,253] In a first series of patients with HFpEF, its favourable effects on exercise PCWP and an improvement in QoL are reported.[254–256]

Heart failure with supranormal ejection fraction

Left ventricular EF may have a U-shaped relationship with outcome, with patients with supranormal (sn) EF (HFsnEF) having a higher risk of events.[19,257–259] Overall, 2.5% of patients enrolled in the RELAX-AHF-2 trial had an LVEF $\geq$ 65%. These patients with HFsnEF, compared with HFpEF patients, were more often women, with higher prevalence of non-ischaemic HF, had lower levels of NPs and higher blood urea nitrogen plasma levels, and were less likely to be treated with beta-blockers. All-cause mortality was not statistically different between groups, although patients with HFsnEF had the highest numerical rate.[258] Another study investigated the prognostic implication of snLVEF as assessed by CMR and its inter-relationship with stroke volume. LVEF in the sn range was associated with a higher risk of adverse CV outcomes, particularly in those with lower stroke volume.[260]

Comorbidities

In a systematic review of HF trials, Khan *et al*. found that only 51% of HFrEF and 27% of HFpEF trials reported baseline comorbidities.[261] Cardiac and non-cardiac comorbidities, including ischaemic cardiomyopathy, AF, hypertension, hyperlipidaemia, DM, CKD, anaemia, and frailty, may influence the management of HF patients and are associated with outcome.[163,262–269] The FRAGILE-HF study was a prospective multicentre study investigating the prevalence, overlap, and prognostic implications of physical and social frailties and cognitive dysfunction in patients hospitalized with HF. Patients with a greater number of frailty domains had higher mortality and HF rehospitalization.[270] Furthermore, up to 30% of HF patients suffer from depression and even more have depressive symptoms.[271]

Anaemia and iron deficiency

Anaemia and iron deficiency (ID) are common in HF and are associated with prognosis.[272–274] Ferric carboxymaltose (FCM) has proven to improve QoL and outcome in patients with HF and ID.[275–277] However, data from the Swedish Heart Failure Registry showed that ID was screened only in about a quarter of the patients and only one in five patients received FCM when indicated.[278] Accurate diagnosis of ID remains controversial and not well established.[279] Sierpinski *et al*. quantified bone marrow iron stores in 30 patients with ischaemic HF and LVEF $\leq$ 45% and in 10 healthy subjects. They found that depleted iron stores in bone marrow have been found in most of patients with ischaemic HF with LVEF $\leq$ 45% (80%), regardless of concomitant anaemia. High serum soluble transferrin receptors reflecting depleted iron stores in bone marrow were the most accurate biomarker measured in peripheral blood, which strongly predicted increased mortality in this subset of patients.[280] In HFpEF, ID impacts prognosis but less exercise capacity.[275] Secondary analysis of DAPA-HF and EMPEROR-Reduced trials suggested that SGLT2i increased haematocrit and haemoglobin levels and reduced the rates of anaemia, compared with placebo likely through their anti-inflammatory effects.[281–283]

The effects of iron therapy in patients with ID were further evaluated in Effectiveness of Intravenous iron treatment vs. standard care in patients with heart failure and iron deficiency (IRONMAN), a prospective multicentre open-label, blinded-endpoint trial conducted across 70 UK hospitals enrolling 1137 adults with HF, LVEF $<$ 45%, and ID, only 14% hospitalized. Patients were assigned to intravenous (i.v.) ferric derisomaltose or not, in addition to standard HF care. Additional iron administrations were allowed if ID returned. During a median follow-up of 2.7 years, the primary outcome of HF hospitalisations and CV death occurred in 22.4 vs. 27.5 per 100 patient-years in the ferric derisomaltose vs. the usual care group [rate ratio (RR) 0.82; 95% CI 0.66–1.02; P = 0.070].[284] Consistently with AFFIRM-AHF, statistical significance was reached in a pre-specified COVID-19 sensitivity analysis (RR 0.76; 95% CI 0.58–1.00; P = 0.047), the reduction in the primary endpoint was driven by a reduction in HF hospitalizations, and QoL was also improved. Safety of iron therapy was also confirmed with fewer serious cardiac adverse events and no increase in infections or other untoward events with ferric derisomaltose. Compared with AFFIRM-AHF, these data were obtained with a longer follow-up and mainly in outpatients; no interaction with HF aetiology was found, differently from AFFIRM-AHF.[276,277,284]

Pulmonary hypertension

Patients with HF often present pulmonary hypertension (PH), which is mainly post-capillary. Some of them also develop a pre-capillary component, leading to a combined pre- and post-capillary PH.[285,286] RV dysfunction and PH are confirmed as major determinants of the poor prognosis of HF patients, including those with HFpEF.[287–291] In HFpEF and PH, diffuse RV fibrosis was described.[292]

COVID-19

The recent coronavirus disease 2019 (COVID-19) pandemic had a catastrophic impact on health systems worldwide.[293,294] Hospitalizations due to acute CV causes showed a significant reduction in the first pandemic period, leading to an increase in case severity and in-hospital mortality.[295–299]

A history of HF was associated with an increased risk of adverse outcome in COVID-19 patients.[300–302] The RAAS plays a key role in the pathophysiology of HF, and the angiotensin-converting enzyme 2 (ACE2) is the receptor for severe acute respiratory distress syndrome coronavirus 2 (SARS-CoV-2). An increased susceptibility to COVID-19 infection has been hypothesized in patients treated with these drugs due to a higher expression of ACE2 mRNA.[303] However, real-world data did not support such hypothesis.[304] In a 1.4 million cohort from the Swedish National Patient Registry, use of RAASi was not associated with increased risk of hospitalization for or death from COVID-19.[305]

Nevertheless, COVID-19 infection may favour HF through several mechanisms that cause direct or indirect cardiac damage (i.e. fever, tachycardia, adrenergic stimulation, exaggerated inflammatory response, endotheliitis, and myocarditis).[301,306,307] In a large Spanish cohort of COVID-19 patients, NT-proBNP was frequently elevated even in the absence of clinical criteria for the diagnosis of HF. Moreover, NT-proBNP was independently associated with mortality after adjusting for relevant confounders, including chronic

HF and acute HF.[308–310] Lassen *et al*. compared echocardiographic findings in 91 consecutive patients hospitalized for COVID-19 with sex- and age-matched COVID-19-free subjects. Tn and NT-proBNP plasma levels and parameters of RV function were abnormal during hospitalization but improved during follow-up, whereas LV GLS remained abnormal also during follow-up.[311]

It has been hypothesized that COVID-19 might induce an HFpEF-like syndrome.[312] Hadzibegovic *et al*. showed that patients hospitalized for COVID-19 had a higher likelihood of presenting HFpEF, assessed by the HFA-PEFF score, compared with subjects with similar age, sex, and comorbidity status and without COVID-19.[313] Vascular and endothelial dysfunction, similar to that reported in untreated hypertensive patients, was observed at 4 month follow-up after COVID-19.[314]

Solid organ-transplanted recipients suffering from SARS-CoV-2 were reported to have up to 25% increased risk of death compared with matched controls.[315] Vaccines to prevent COVID-19 may have a reduced efficacy in immunocompromised patients. Among 42 HTx recipients, only 15% showed the presence of anti-spike immunoglobulin G (IgG) antibodies after the first dose of vaccine, and 36% of those who did not respond to the first dose of vaccine became anti-spike IgG seropositive after the second vaccination.[316]

Practical guidance was published in order to aid clinicians in the diagnosis and management of CV disease during COVID-19 pandemic.[317–319]

Advanced heart failure

Definition and prognosis

Many patients with HF progress into a phase of advanced HF, characterized by persistent symptoms despite maximal therapy.[320] The HFA-ESC advanced HF definition has been recently validated. The Italian HELP-HF registry enrolled consecutive patients with HF and at least one high-risk 'I NEED HELP' marker. Out of 4753 patients with HF screened, 1149 (24.3%) patients had at least one high-risk 'I NEED HELP' marker, and among them, 193 (16.8%) patients met the HFA-ESC advanced HF definition. The HFA-ESC advanced HF definition was associated with a higher risk of all-cause mortality or first HF hospitalization (adjusted HR 1.98; 95% CI 1.57–2.50; $P < 0.001$).[321] The efficacy and tolerability of GDMT in patients with the most advanced stages of HFrEF often remain unsettled.[150,322,323]

Therapy

Advanced therapeutic strategies including HTx, mechanical circulatory support (MCS) implantation, intermittent inotropes, and also end-of-life cares are often required in these patients.[324] Age and shock severity predict mortality in cardiac intensive care unit.[325]

Heart transplantation remains a limited therapeutic option due to the disproportion between donors and possible candidates needing the transplantation. The first case of genetically modified porcine-to-human cardiac xenotransplantation has been recently reported.[326]

Long-term MCS is a valid alternative in patients non-eligible to HTx or in those deteriorating while waiting for transplantation. However, MCS implantation is burdened by high costs and adverse events, limiting its use, and requiring restrictive clinical criteria as well.[327] The SweVAD study will compare survival, medium-term benefits, costs, and potential hazards with LV assist device (LVAD) vs. GDMT as destination therapy strategy in patients with advance HF ineligible for HTx.[328] The MOMENTUM 3 pivotal trial established superiority of the HeartMate 3 (HM3) LVAD, a fully magnetically levitated centrifugal-flow pump, over the HeartMate II axial-flow pump.[329] The primary results of accumulating HM3 LVAD experience suggest a lower adverse event burden and similar survival compared with the pivotal MOMENTUM 3 trial.[330] Conflicting data on fibrotic changes after LVAD support were reported.[331] A recent study showed that cardiac fibrosis was strongly increased in most failing hearts and even significantly increased during mechanical unloading.[332]

Sacubitril/valsartan initiation in patients with continuous-flow LVAD implant effectively reduces mean arterial pressure, a factor related to adverse events.[333]

Infections are common following LVAD implantation and predict adverse events.[334] The ARIES HM3 trial is an international, RCT to test the hypothesis that aspirin may be removed safely from the antithrombotic regimen with the HM3 LVAD to reduce bleeding risk.[335]

Palliative care

Quality of life is clinically relevant in patients with HF and has become a major endpoint for HF studies.[167,203,336–339] QoL in end-stage HF is even more important. As a consequence, the management of end-stage HF needs to include palliative care.[150,340] Sahlollbey *et al*. performed a meta-analysis of 10 RCTs showing that palliative care, compared with usual care, was associated with a reduction in HF hospitalization, with no clear adverse effect on survival, and a modest, though significant, improvement in QoL and symptoms in patients with advanced HF.[341]

Acute heart failure

Acute HF remains a life-threatening condition, burdened by high mortality.[9,342–345] A novel classification of acute HF has been provided in the latest ESC guidelines.[2] A study conducted in Australia and New Zealand showed that 1

out of 10 patients died within 30 days of their last HF hospitalization and 25% of patients required an unplanned rehospitalization.[346] In the BIOSTAT-CHF cohorts, acute HF inpatients displayed a higher 6 month mortality, compared with chronic outpatients with worsening HF (12.3% vs. 4.7%).[347]

Biomarkers, decongestion, and renal function

Higher levels of NT-proBNP at discharge, or an inadequate decline during hospitalization, confer higher risk of readmission and/or death within 180 days.[39,43] A practical approach would consider changes >30% of NT-proBNP as clinically relevant.[43] Also, high levels of bio-ADM levels at discharge are strongly associated with residual congestion in patients with acute HF.[48,348] An early re-evaluation (>10 days) with CA-125 measurement after an acute HF hospitalization may be useful in patient management.[55,56]

Other biomarkers are emerging. cDPP3 is a protease involved in angiotensin II and enkephalin degradation.[51] In patients with cardiogenic shock (CS), higher baseline cDPP3 levels were associated with increased short-term mortality and more severe organ dysfunction, and its rapid decrease within 24 h predicted a favourable outcome.[52] DPP3 administration in a mouse model induced myocardial depression and renal impairment, whereas DPP3 inhibition by a specific antibody normalized cardiac and kidney function with reduction in oxidative stress and inflammation.[50] Wettersten *et al*. evaluated the prognostic significance of serum and urine NGAL in 927 patients with acute HF. Serum NGAL outperformed urine NGAL but neither was superior to admission or peak serum creatinine for predicting adverse events.[57]

In an analysis of the RELAX-AHF-2 trial, worsening renal function (WRF), defined as a rise in serum creatinine ≥0.3 mg/dL, occurred in 28.2% of patients within the first 5 days of an acute HF hospitalization, with a higher incidence in those with a higher LVEF.[349] Measurement of natriuresis in patients hospitalized for acute HF early identifies high-risk patients with a poor diuretic response.[350] The Pragmatic Urinary Sodium-based treatment algoritHm in Acute Heart Failure (PUSH-AHF) is a randomized, open-label controlled study aiming to enrol 310 acute HF patients in order to assess the efficacy of natriuresis-guided diuretic therapy. Patients will be randomized to either natriuresis-driven therapy or standard care, and the co-primary endpoints are 24 h urinary sodium excretion and 6 month all-cause mortality or first HF rehospitalization.[351]

Treatment

The prehospital patient pathway and healthcare organization play a significant role in the management of acute HF.[344,352] In 2022, the positive results of the Acetazolamide in Acute Decompensated Heart Failure with Volume Overload (ADVOR) trial have been published. The addition of acetazolamide (500 mg/day, i.v.) to loop diuretic therapy in patients with acute decompensated HF resulted in a greater incidence of successful decongestion, without differences in WRF, hypokalaemia, hypotension, and adverse event vs. placebo.[353] The addition of hydrochlorothiazide to loop diuretics was evaluated in the CLOROTIC trial.[354] Torasemide did not change outcomes, compared with furosemide, in TRANSFORM-HF[355,356] (*Figure 2*).

The EMPULSE trial randomized 530 patients hospitalized for acute HF, when clinically stable, to receive empagliflozin 10 mg once daily or placebo for up to 90 days. Empagliflozin provided a clinical benefit, defined as a hierarchical composite of death from any cause, number of HF events and time to first HF event, or a 5-point or greater difference in change from baseline in the Kansas City Cardiomyopathy Questionnaire Total Symptom Score at 90 days, as assessed using a win ratio (stratified win ratio 1.36; 95% CI 1.09–1.68; P = 0.0054).[357] In the EMPA-RESPONSE-AHF trial, empagliflozin increased fractional glucose excretion and plasma osmolality, without changes in fractional sodium and chloride excretion and urinary osmolality, and caused a temporary decline in eGFR.[358] An improvement in early decongestion has been confirmed in another study.[359] Optimization of treatment before or shortly after discharge remains a major goal in order to improve post-discharge outcomes in patients hospitalized for acute HF.[95,100,103,343,360] An intensive treatment strategy of rapid up-titration of GDMT and close follow-up after an acute HF admission reduced symptoms, improved QoL, and reduced the risk of 180 day all-cause death or HF readmission compared with usual care.[361]

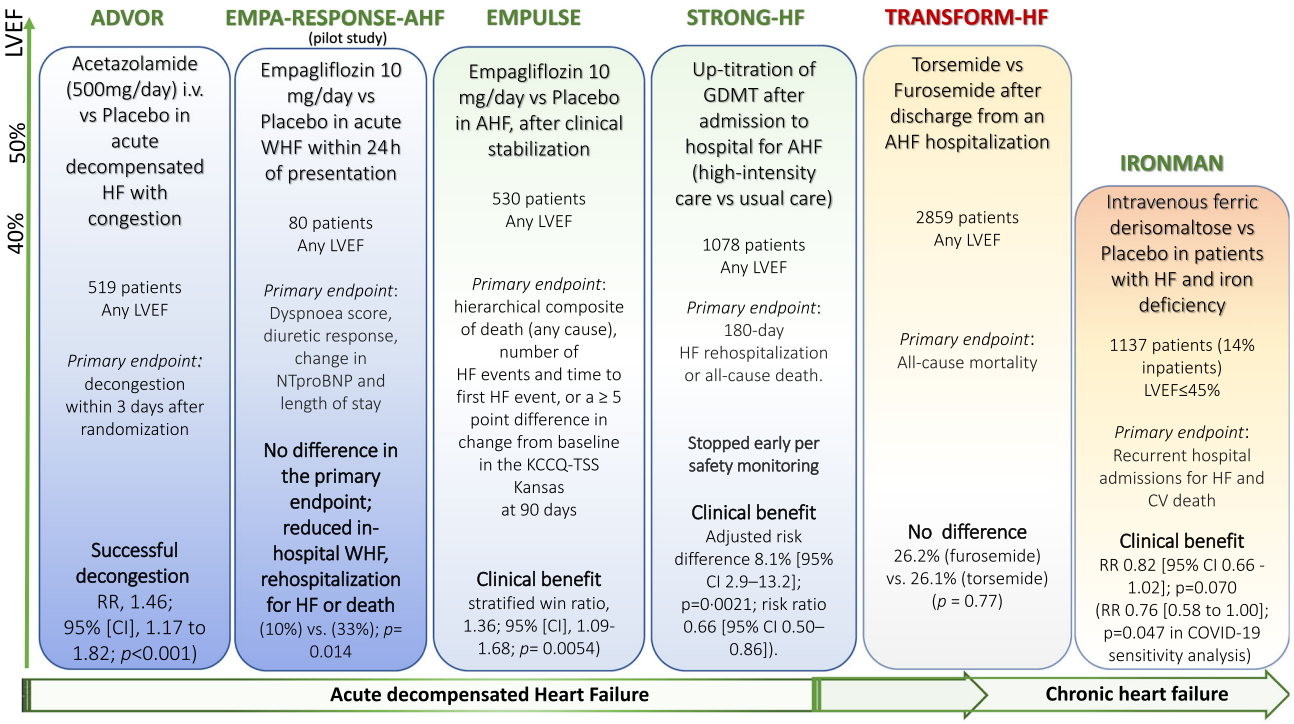
In a meta-analysis of six RCTs, including 11 359 patients treated with i.v. serelaxin or placebo within the first 16 h of acute HF admission, serelaxin administration was associated with a reduction in 5 day worsening HF, markers of renal dysfunction, NT-proBNP and Tn, and a favourable outcome.[362] In patients hospitalized for acute HF with reduced LVEF, a 24 h infusion of istaroxime improved parameters of diastolic and systolic cardiac function without major cardiac adverse effects.[363] The Phase 2a SEISMIC study, including patients with pre-CS, istaroxime improved BP and echocardiography measures related to HF (i.e. cardiac index, LA area, and LV end-systolic volume) and was well tolerated.[364]

Procalcitonin-guided initiation of antibiotic therapy did not improve clinical outcomes compared with standard of care in 742 patients admitted for acute HF.[365]

Cardiogenic shock

Cardiogenic shock is still burdened by an extremely poor prognosis.[366,367] Data from the Nationwide Readmis-

Figure 2 Recent completed trials in patients with heart failure (HF) [focusing on acute HF (AHF)]. CI, confidence interval; CV, cardiovascular; GDMT, guideline-directed medical therapy; KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire Total Symptom Score; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-brain natriuretic peptide; RR, rate ratio; WHF, worsening heart failure.



sions Database showed that a regional 'hub-and-spoke' triage system, with direct admission to CS hubs or transfer to hubs, is associated with a lower mortality.[368] MCS may be useful in the management of CS. However, data from RCTs seem not to reflect real-world practice. Enrolment criteria from the main RCTs on MCS were applied to 1305 patients with CS admitted to a tertiary care hospital between 2009 and 2019. Only one third of this real-world population with CS was eligible for any trial. This was mostly due to the exclusion of CS not secondary to AMI, but even in a post-AMI CS scenario, only 65.4% of patients were eligible.[369]

Remote monitoring, telemedicine, and rehabilitation

Telemedicine and telemonitoring for HF patients have grown great interest, also driven by the need to find new management solutions in the era of COVID-19 pandemic.[317,370,371] Patients with depression have been excluded in most telemedicine studies. However, in a pre-specified analysis of the Telemedical Interventional Monitoring in Heart Failure (TIM-HF) trial, telemedicine significantly improved symptoms of depression and QoL over a period of 12 months in patients with chronic HF and moderate depression.[372] Available options to telemonitor patients include patient self-managed testing, wearable devices, technologies integrated into pacemakers and defibrillators, or arrhythmia monitoring systems.[160,373–375] Recently, implantable devices that can monitor pulmonary artery pressure have shown safety and have succeeded in reducing hospitalization rates in symptomatic HF patients.[376–378]

Cardiac rehabilitation (CR) is defined as a multidisciplinary programme that includes exercise training, cardiac risk factor modification, psychosocial assessment, and outcomes assessment. CR resulted in a reduction of HF-related hospitalizations and significant improvements in QoL, functional capacity, and exercise performance.[167,379,380] In the REHAB-HF trial, in a diverse population of older patients who were hospitalized for acute HF, an early, transitional, tailored, progressive rehabilitation intervention that included multiple physical function domains resulted in greater improvement in physical function than usual care.[380] Several devices may be useful to monitor physical activity.[381]

Specific causes of heart failure

Cancer treatment

Cancer and HF have common pathways including inflammation, cellular metabolic changes, genetic predisposition, clonal haematopoiesis, and angiogenesis.[382–384] In a prospective study, patients with cancer, compared with healthy controls, were more likely to present premature ventricular contractions and non-sustained ventricular tachycardia.[385] HF can develop as a consequence of the toxic effects of anti-cancer therapy (cardiotoxicity).[383,386–388] In patients treated with immune checkpoint inhibitors (ICIs), pharmacovigilance data analysis reported an incidence of 4.2% of cardiac events, including myocarditis, which was often burdened by a high mortality.[389,390] The incidence of cardiac events was higher in those patients with dual ICI therapy. For this reason, a grading system for ICI myocarditis, based on endomyocardial biopsy, was developed.[391] New guidelines on cardio-oncology have been recently issued by the ESC.[392]

Cardiomyopathies

Cardiomyopathies are a heterogeneous cause of HF.[393–395] Electrocardiogram or clinical red flags can help identify specific forms.[396,397] Over the last years, improvement in survival was observed in patients with dilated cardiomyopathy (DCM), thanks to the efficacy of treatment and its implementation.[398] Withdrawal of HF drugs in patients with recovered DCM was associated with relapses in 44% of patients and with early ventricular remodelling, increase in myocardial mass, and decrease in GLS.[399,400]

Novel treatment strategies are being developed for hypertrophic cardiomyopathy, including mavacamten, a modulator of cardiac β-myosin, causing reversible inhibition of actin–myosin cross bridging, which now adds to septal reduction techniques, biventricular pacing, mitral valve surgical or percutaneous repair, and gene-based therapies.[401]

Cardiac amyloidosis

Increasing prevalence of CA is due to greater awareness and advances in diagnosis. Easily available echocardiographic red flags, when combined together, demonstrated good diagnostic accuracy.[402] CA often coexists with aortic stenosis (AS)[403–406] but also with mitral and tricuspid stenosis.[407] About 8–16% of patients with severe AS undergoing transcatheter aortic valve replacement have CA.[404]

Several measures, including a quantitation of disease severity by clinical and functional endpoints, biomarkers, imaging, and electrocardiographic parameters, should be used to detect disease progression and should be performed in a relatively short time frame (6–12 months) after diagnosis.[408,409] In a multicentre study including patients with immunoglobulin light chain (AL) or transthyretin (TTR) CA, both peak oxygen consumption (VO_2) $\leq$13 mL/kg/min and NT-proBNP $\geq$ 1800 ng/L were independently associated with a two-fold higher risk of the primary endpoint (death or HF hospitalization).[410]

Recent years saw the introduction of promising targeted therapies, which aim to interfere with the deposition of misfolded TTR at various stages of the cascade underlying TTR-CA progression. These include TTR tetramer stabilizers (tafamidis, diflunisal, and epigallocatechin-3-gallate), TTR silencers (inotersen and patisiran), and fibril disruptors (monoclonal antibodies, doxycycline, and tauroursodeoxycholic acid).[411–415]

Myocarditis

Acute myocarditis is an acute-onset inflammatory heart disease with heterogeneous clinical presentation, varying from chest pain, life-threatening ventricular arrhythmias, to CS.[416] Viral infections may be the cause of acute myocarditis with typical prodromic symptoms/signs (i.e. fever, flu-like symptoms, and sore throat).[417,418] The role of viral detection and immunomodulation in patients with acute lymphocytic myocarditis has been reviewed.[419] In an RCT, i.v. immunoglobulin did not improve systolic function or functional status in patients with parvovirus B19-related DCM compared with placebo.[420] Modulation of the acute defence reaction by eplerenone prevents cardiac disease progression in viral myocarditis.[421]

Conclusions

In recent years, there has been great progress in the treatment of HF. The 2021 ESC guidelines for the management of HF established the four pillars of HFrEF treatment with ACEis/ARNIs, beta-blockers, MRAs, and SGLT2is. These drugs should be started as soon as possible. The DIAMOND trial established the role of novel potassium binders, namely, patiromer, for the treatment of hyperkalaemia in order to reduce the rate of RAASi discontinuation. A major clinical need has been met in the last 2 years. With the results of

the EMPEROR-Preserved and DELIVER trials, SGLT2 inhibitors are the first class of drugs that demonstrated to improve prognosis in patients with HF and mildly reduced or preserved LVEF.

Conflict of interest

The authors declare no conflicts of interest as regard this article.

References

1. Bozkurt B, Coats AJS, Tsutsui H, Abdelhamid CM, Adamopoulos S, Albert N, Anker SD, Atherton J, Bohm M, Butler J, Drazner MH, Michael Felker G, Filippatos G, Fiuzat M, Fonarow GC, Gomez-Mesa JE, Heidenreich P, Imamura T, Jankowska EA, Januzzi J, Khazanie P, Kinugawa K, Lam CSP, Matsue Y, Metra M, Ohtani T, Francesco Piepoli M, Ponikowski P, Rosano GMC, Sakata Y, Seferovic P, Starling RC, Teerlink JR, Vardeny O, Yamamoto K, Yancy C, Zhang J, Zieroth S. Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure: endorsed by the Canadian Heart Failure Society, Heart Failure Association of India, Cardiac Society of Australia and New Zealand, and Chinese Heart Failure Association. *Eur J Heart Fail*. 2021; **23**: 352–380.
2. Authors/Task Force Members, McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Bohm M, Burri H, Butler J, Celutkiene J, Chioncel O, Cleland JGF, Coats AJS, Crespo-Leiro MG, Farmakis D, Gilard M, Heymans S, Hoes AW, Jaarsma T, Jankowska EA, Lainscak M, Lam CSP, Lyon AR, McMurray JJV, Mebazaa A, Mindham R, Muneretto C, Francesco Piepoli M, Price S, Rosano GMC, Ruschitzka F, Kathrine Skibelund A, Group ESCSD. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: developed by the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure of the European Society of Cardiology (ESC). With the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail*. 2022; **24**: 4–131.
3. Abraham WT, Psotka MA, Fiuzat M, Filippatos G, Lindenfeld J, Mehran R, Ambardekar AV, Carson PE, Jacob R, Januzzi JL, Jr., Konstam MA, Krucoff MW, Lewis EF, Piccini JP, Solomon SD, Stockbridge N, Teerlink JR, Unger EF, Zeitler EP, Anker SD, O'Connor CM. Standardized definitions for evaluation of heart failure therapies: scientific expert panel from the Heart Failure Collaboratory and Academic Research Consortium. *Eur J Heart Fail*. 2020; **22**: 2175–2186.
4. Groenewegen A, Rutten FH, Mosterd A, Hoes AW. Epidemiology of heart failure. *Eur J Heart Fail*. 2020; **22**: 1342–1356.
5. Liew D, Audehm RG, Haikerwal D, Piazza P, Neville AM, Lim K, Parsons RW, Sindone AP. Epidemiology of heart failure: Study of Heart failure in the Australian Primary carE setting (SHAPE). *ESC Heart Fail*. 2020; **7**: 3871–3880.
6. Bragazzi NL, Zhong W, Shu J, Abu Much A, Lotan D, Grupper A, Younis A, Dai H. Burden of heart failure and underlying causes in 195 countries and territories from 1990 to 2017. *Eur J Prev Cardiol*. 2021; **28**: 1682–1690.
7. Seferovic PM, Jankowska E, Coats AJS, Maggioni AP, Lopatin Y, Milinkovic I, Polovina M, Lainscak M, Timmis A, Huculeci R, Vardas P, Task Force of the HFAA, the Esc Atlas of Cardiology leadership dicwtNHFSotESCm, countries ESCam. The Heart Failure Association Atlas: rationale, objectives, and methods. *Eur J Heart Fail*. 2020; **22**: 638–645.
8. Seferovic PM, Vardas P, Jankowska EA, Maggioni AP, Timmis A, Milinkovic I, Polovina M, Gale CP, Lund LH, Lopatin Y, Lainscak M, Savarese G, Huculeci R, Kazakiewicz D, Coats AJS, National Heart Failure Societies of the ESCmc. The Heart Failure Association Atlas: heart failure epidemiology and management statistics 2019. *Eur J Heart Fail*. 2021; **23**: 906–914.
9. Sulo G, Igland J, Overland S, Egeland GM, Roth GA, Vollset SE, Tell GS. Heart failure in Norway, 2000–2014: analysing incident, total and readmission rates using data from the Cardiovascular Disease in Norway (CVDNOR) Project. *Eur J Heart Fail*. 2020; **22**: 241–248.
10. Li L, Liu R, Jiang C, Du X, Huffman MD, Lam CSP, Patel A, Hillis GS, Anderson CS, Ma C, Zhao X, Wang X, Li L, Dong J. Assessing the evidence–practice gap for heart failure in China: the Heart Failure Registry of Patient Outcomes (HERO) study design and baseline characteristics. *Eur J Heart Fail*. 2020; **22**: 646–660.
11. Velagaleti RS, Larson MG, Enserro D, Song RJ, Vasan RS. Clinical course after a first episode of heart failure: insights from the Framingham Heart Study. *Eur J Heart Fail*. 2020; **22**: 1768–1776.
12. Butt JH, Fosbol EL, Gerds TA, Andersson C, McMurray JJV, Petrie MC, Gustafsson F, Madelaire C, Kristensen SL, Gislason GH, Torp-Pedersen C, Kober L, Schou M. Readmission and death in patients admitted with new-onset versus worsening of chronic heart failure: insights from a nationwide cohort. *Eur J Heart Fail*. 2020; **22**: 1777–1785.
13. Ishigami J, Trevisan M, Lund LH, Jernberg T, Coresh J, Matsushita K, Carrero JJ. Acceleration of kidney function decline after incident hospitalization with cardiovascular disease: the Stockholm CREAtinine Measurements (SCREAM) project. *Eur J Heart Fail*. 2020; **22**: 1790–1799.
14. Lainscak M, Milinkovic I, Polovina M, Crespo-Leiro MG, Lund LH, Anker SD, Laroche C, Ferrari R, Coats AJS, McDonagh T, Filippatos G, Maggioni AP, Piepoli MF, Rosano GMC, Ruschitzka F, Simic D, Asanin M, Eicher JC, Yilmaz MB, Seferovic PM, European Society of Cardiology Heart Failure Long-Term Registry Investigators G. Sex- and age-related differences in the management and outcomes of chronic heart failure: an analysis of patients from the ESC HFA EORP Heart Failure Long-Term Registry. *Eur J Heart Fail*. 2020; **22**: 92–102.
15. Ibrahim NE, Pina IL, Camacho A, Bapat D, Felker GM, Maisel AS, Butler J, Prescott MF, Abbas CA, Solomon SD, Januzzi JL, Jr., Prospective Study of Biomarkers SI, Ventricular Remodeling During Entresto Therapy for Heart Failure Study I. Sex-based differences in biomarkers, health status, and reverse cardiac remodelling in patients with heart failure with reduced ejection fraction treated with sacubitril/valsartan. *Eur J Heart Fail*. 2020; **22**: 2018–2025.
16. Suthahar N, Meems LMG, Ho JE, de Boer RA. Sex-related differences in contemporary biomarkers for heart failure: a review. *Eur J Heart Fail*. 2020; **22**: 775–788.
17. Rossello X, Ferreira JP, Pocock SJ, McMurray JJV, Solomon SD, Lam CSP, Girerd N, Pitt B, Rossignol P, Zannad F. Sex differences in mineralocorticoid receptor antagonist trials: a pooled analysis of three large clinical trials. *Eur J Heart Fail*. 2020; **22**: 834–844.
18. Stretti L, Zippo D, Coats AJS, Anker MS, von Haehling S, Metra M, Tomasoni D. A year in heart failure: an update of recent findings. *ESC Heart Fail*. 2021; **8**: 4370–4393.

19. Stewart S, Playford D, Scalia GM, Currie P, Celermajer DS, Prior D, Codde J, Strange G, Investigators N. Ejection fraction and mortality: a nationwide register-based cohort study of 499 153 women and men. *Eur J Heart Fail*. 2021; **23**: 406–416.
20. Nunez J, Lorenzo M, Minana G, Palau P, Monmeneu JV, Lopez-Lereu MP, Gavara J, Marcos-Garces V, Rios-Navarro C, Perez N, de Dios E, Nunez E, Sanchis J, Chorro FJ, Bayes-Genis A, Bodi V. Sex differences on new-onset heart failure in patients with known or suspected coronary artery disease. *Eur J Prev Cardiol*. 2021; **28**: 1711–1719.
21. Taylor CJ, Ordonez-Mena JM, Jones NR, Roalfe AK, Lay-Flurrie S, Marshall T, Hobbs FDR. National trends in heart failure mortality in men and women, United Kingdom, 2000–2017. *Eur J Heart Fail*. 2021; **23**: 3–12.
22. Yamamoto E, Kato T, Yaku H, Morimoto T, Inuzuka Y, Tamaki Y, Ozasa N, Kitai T, Taniguchi R, Iguchi M, Kato M, Takahashi M, Jinnai T, Ikeda T, Himura Y, Nagao K, Kawai T, Komasa A, Nishikawa R, Kawase Y, Morinaga T, Kawato M, Seko Y, Toyofuku M, Furukawa Y, Nakagawa Y, Ando K, Kadota K, Shizuta S, Ono K, Sato Y, Kuwahara K, Kimura T, Investigators KS. Sex differences in patients with acute decompensated heart failure in Japan: observation from the KCHF registry. *ESC Heart Fail*. 2020; **7**: 2485–2493.
23. Whitelaw S, Sullivan K, Eliya Y, Alruwayeh M, Thabane L, Yancy CW, Mehran R, Mamas MA, Van Spall HGC. Trial characteristics associated with under-enrolment of females in randomized controlled trials of heart failure with reduced ejection fraction: a systematic review. *Eur J Heart Fail*. 2021; **23**: 15–24.
24. Wang N, Evans J, Sawant S, Sindone J, Lal S. Sex-specific differences in the efficacy of heart failure therapies: a meta-analysis of 84,818 patients. *Heart Fail Rev*. 2022.
25. Blumer V, Gayowsky A, Xie F, Greene SJ, Graham MM, Ezekowitz JA, Perez R, Ko DT, Thabane L, Zannad F, Van Spall HGC. Effect of patient-centered transitional care services on patient-reported outcomes in heart failure: sex-specific analysis of the PACT-HF randomized controlled trial. *Eur J Heart Fail*. 2021; **23**: 1488–1498.
26. Dewan P, Jackson A, Lam CSP, Pfeffer MA, Zannad F, Pitt B, Solomon SD, McMurray JJV. Interactions between left ventricular ejection fraction, sex and effect of neurohumoral modulators in heart failure. *Eur J Heart Fail*. 2020; **22**: 898–901.
27. Ferreira JP, Mogensen UM, Jhund PS, Desai AS, Rouleau JL, Zile MR, Rossignol P, Zannad F, Packer M, Solomon SD, McMurray JJV. Serum potassium in the PARADIGM-HF trial. *Eur J Heart Fail*. 2020; **22**: 2056–2064.
28. Lombardi CM, Carubelli V, Peveri G, Inciardi RM, Pagnesi M, Ravera A, Tomasoni D, Garafa E, Oriecuia C, Specchia C, Metra M. Prognostic significance of serum potassium in patients hospitalized for acute heart failure. *ESC Heart Fail*. 2022; **9**: 2357–2366.
29. Cooper LB, Benson L, Mentz RJ, Savarese G, DeVore AD, Carrero JJ, Dahlstrom U, Anker SD, Lainscak M, Hernandez AF, Pitt B, Lund LH. Association between potassium level and outcomes in heart failure with reduced ejection fraction: a cohort study from the Swedish Heart Failure Registry. *Eur J Heart Fail*. 2020; **22**: 1390–1398.
30. Rossignol P, Fay R, Girerd N, Zannad F. Daily home monitoring of potassium, creatinine, and estimated plasma volume in heart failure post-discharge. *ESC Heart Fail*. 2020; **7**: 1257–1263.
31. Volterrani M, Perrone V, Sangiorgi D, Giacomini E, Iellamo F, Degli Esposti L, on the behalf of a LSG. Effects of hyperkalaemia and non-adherence to renin–angiotensin–aldosterone system inhibitor therapy in patients with heart failure in Italy: a propensity-matched study. *Eur J Heart Fail*. 2020; **22**: 2049–2055.
32. Rossignol P, Lainscak M, Crespo-Leiro MG, Laroche C, Piepoli MF, Filippatos G, Rosano GMC, Savarese G, Anker SD, Seferovic PM, Ruschitzka F, Coats AJS, Mebazaa A, McDonagh T, Sahuquillo A, Penco M, Maggioni AP, Lund LH. Unravelling the interplay between hyperkalaemia, renin–angiotensin–aldosterone inhibitor use and clinical outcomes. Data from 9222 chronic heart failure patients of the ESC-HFA-EORP Heart Failure Long-Term Registry. *Eur J Heart Fail*. 2020; **22**: 1378–1389.
33. Rossignol P, Duarte K, Girerd N, Karoui M, McMurray JJV, Swedberg K, van Veldhuisen DJ, Pocock S, Dickstein K, Zannad F, Pitt B. Cardiovascular risk associated with serum potassium in the context of mineralocorticoid receptor antagonist use in patients with heart failure and left ventricular dysfunction. *Eur J Heart Fail*. 2020; **22**: 1402–1411.
34. Trevisan M, Fu EL, Xu Y, Savarese G, Dekker FW, Lund LH, Clase CM, Sjolander A, Carrero JJ. Stopping mineralocorticoid receptor antagonists after hyperkalaemia: trial emulation in data from routine care. *Eur J Heart Fail*. 2021; **23**: 1698–1707.
35. Tedeschi A, Agostoni P, Pezzuto B, Corra U, Scrutinio D, La Gioia R, Raimondo R, Passantino A, Piepoli MF. Role of comorbidities in heart failure prognosis Part 2: chronic kidney disease, elevated serum uric acid. *Eur J Prev Cardiol*. 2020; **27**: 35–45.
36. Selvaraj S, Claggett BL, Pfeffer MA, Desai AS, Mc Causland FR, McGrath MM, Anand IS, van Veldhuisen DJ, Kober L, Janssens S, Cleland JGF, Pieske B, Rouleau JL, Zile MR, Shi VC, Lefkowitz MP, McMurray JJV, Solomon SD. Serum uric acid, influence of sacubitril–valsartan, and cardiovascular outcomes in heart failure with preserved ejection fraction: PARAGON-HF. *Eur J Heart Fail*. 2020; **22**: 2093–2101.
37. McDowell K, Welsh P, Docherty KF, Morrow DA, Jhund PS, de Boer RA, O'Meara E, Inzucchi SE, Kober L, Kosiborod MN, Martinez FA, Ponikowski P, Hammarstedt A, Langkilde AM, Sjostrand M, Lindholm D, Solomon SD, Sattar N, Sabatine MS, McMurray JJV. Dapagliflozin reduces uric acid concentration, an independent predictor of adverse outcomes in DAPA-HF. *Eur J Heart Fail*. 2022; **24**: 1066–1076.
38. Vidula MK, Orlenko A, Zhao L, Salvador L, Small AM, Horton E, Cohen JB, Adusumalli S, Denduluri S, Kobayashi T, Hyman M, Fiorilli P, Magro C, Singh B, Pourmussa B, Greczylo C, Basso M, Ebert C, Yarde M, Li Z, Cvijic ME, Wang Z, Walsh A, Maranville J, Kick E, Luettgen J, Adam L, Schafer P, Ramirez-Valle F, Seiffert D, Moore JH, Gordon D, Chirinos JA. Plasma biomarkers associated with adverse outcomes in patients with calcific aortic stenosis. *Eur J Heart Fail*. 2021; **23**: 2021–2032.
39. Moura B, Aimo A, Al-Mohammad A, Flammer A, Barberis V, Bayes-Genis A, et al. Integration of imaging and circulating biomarkers in heart failure: a consensus document by the Biomarkers and Imaging Study Groups of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2021; **23**: 1577–1596.
40. Henkens M, Remmelzwaal S, Robinson EL, van Ballegooijen AJ, Barandiaran Aizpurua A, Verdonschot JAJ, et al. Risk of bias in studies investigating novel diagnostic biomarkers for heart failure with preserved ejection fraction. A systematic review. *Eur J Heart Fail*. 2020; **22**: 1586–1597.
41. Kuan WS, Ibrahim I, Chan SP, Li Z, Liew OW, Frampton C, et al. Mid-regional pro-adrenomedullin outperforms N-terminal pro-B-type natriuretic peptide for the diagnosis of acute heart failure in the presence of atrial fibrillation. *Eur J Heart Fail*. 2020; **22**: 692–700.
42. Januzzi JL, Tan X, Yang L, Brady JE, Yang M, Banka P, et al. N-terminal pro-B-type natriuretic peptide testing patterns in patients with heart failure with reduced ejection fraction. *ESC Heart Fail*. 2022; **9**: 87–99.
43. Nunez J, de la Espriella R, Rossignol P, Voors AA, Mullens W, Metra M, et al. Congestion in heart failure: a circulating biomarker-based perspective. A review from the Biomarkers Working Group of the Heart Failure

Association, European Society of Cardiology. *Eur J Heart Fail*. 2022; **24**: 1751–1766.
44. Ferreira JP, Ouwerkerk W, Tromp J, Ng L, Dickstein K, Anker S, et al. Cardiovascular and non-cardiovascular death distinction: the utility of troponin beyond N-terminal pro-B-type natriuretic peptide. Findings from the BIOSTAT-CHF study. *Eur J Heart Fail*. 2020; **22**: 81–89.
45. Packer M, Januzzi JL, Ferreira JP, Anker SD, Butler J, Filippatos G, et al. Concentration-dependent clinical and prognostic importance of high-sensitivity cardiac troponin T in heart failure and a reduced ejection fraction and the influence of empagliflozin: the EMPEROR-Reduced trial. *Eur J Heart Fail*. 2021; **23**: 1529–1538.
46. Suthahar N, Meems LMG, Groothof D, Bakker SJL, Gansevoort RT, van Veldhuisen DJ, et al. Relationship between body mass index, cardiovascular biomarkers and incident heart failure. *Eur J Heart Fail*. 2021; **23**: 396–402.
47. Meijers WC, Bayes-Genis A, Mebazaa A, Bauersachs J, Cleland JGF, Coats AJS, et al. Circulating heart failure biomarkers beyond natriuretic peptides: review from the Biomarker Study Group of the Heart Failure Association (HFA), European Society of Cardiology (ESC). *Eur J Heart Fail*. 2021; **23**: 1610–1632.
48. Pandhi P, Ter Maaten JM, Emmens JE, Struck J, Bergmann A, Cleland JG, et al. Clinical value of pre-discharge bio-adrenomedullin as a marker of residual congestion and high risk of heart failure hospital readmission. *Eur J Heart Fail*. 2020; **22**: 683–691.
49. Ter Maaten JM, Kremer D, Demissei BG, Struck J, Bergmann A, Anker SD, et al. Bio-adrenomedullin as a marker of congestion in patients with new-onset and worsening heart failure. *Eur J Heart Fail*. 2019; **21**: 732–743.
50. Deniau B, Rehfeld L, Santos K, Dienelt A, Azibani F, Sadoune M, et al. Circulating dipeptidyl peptidase 3 is a myocardial depressant factor: dipeptidyl peptidase 3 inhibition rapidly and sustainably improves haemodynamics. *Eur J Heart Fail*. 2020; **22**: 290–299.
51. Boorsma EM, Ter Maaten JM, Damman K, van Veldhuisen DJ, Dickstein K, Anker SD, et al. Dipeptidyl peptidase 3, a marker of the antagonist pathway of the renin–angiotensin–aldosterone system in patients with heart failure. *Eur J Heart Fail*. 2021; **23**: 947–953.
52. Takagi K, Blet A, Levy B, Deniau B, Azibani F, Feliot E, et al. Circulating dipeptidyl peptidase 3 and alteration in haemodynamics in cardiogenic shock: results from the OptimaCC trial. *Eur J Heart Fail*. 2020; **22**: 279–286.
53. Raafs AG, Verdonschot JAJ, Henkens M, Adriaans BP, Wang P, Derks K, et al. The combination of carboxy-terminal propeptide of procollagen type I blood levels and late gadolinium enhancement at cardiac magnetic resonance provides additional prognostic information in idiopathic dilated cardiomyopathy—a multilevel assessment of myocardial fibrosis in dilated cardiomyopathy. *Eur J Heart Fail*. 2021; **23**: 933–944.
54. Stohr R, Brandenburg VM, Heine GH, Maeder MT, Leibundgut G, Schuh A, et al. Limited role for fibroblast growth factor 23 in assessing prognosis in heart failure patients: data from the TIME-CHF trial. *Eur J Heart Fail*. 2020; **22**: 701–709.
55. Lourenco P, Cunha FM, Elias C, Fernandes C, Barroso I, Guimaraes JT, et al. CA-125 variation in acute heart failure: a single-centre analysis. *ESC Heart Fail*. 2022; **9**: 1018–1026.
56. Nunez J, de la Espriella R, Minana G, Santas E, Llacer P, Nunez E, et al. Antigen carbohydrate 125 as a biomarker in heart failure: a narrative review. *Eur J Heart Fail*. 2021; **23**: 1445–1457.
57. Wettersten N, Horiuchi Y, van Veldhuisen DJ, Mueller C, Filippatos G, Nowak R, et al. Short-term prognostic implications of serum and urine neutrophil gelatinase-associated lipocalin in acute heart failure: findings from the AKINESIS study. *Eur J Heart Fail*. 2020; **22**: 251–263.
58. He T, Mischak M, Clark AL, Campbell RT, Delles C, Diez J, et al. Urinary peptides in heart failure: a link to molecular pathophysiology. *Eur J Heart Fail*. 2021; **23**: 1875–1887.
59. Tayal U, Wage R, Newsome S, Manivarmane R, Izgi C, Muthumala A, et al. Predictors of left ventricular remodelling in patients with dilated cardiomyopathy—a cardiovascular magnetic resonance study. *Eur J Heart Fail*. 2020; **22**: 1160–1170.
60. Yamanaka S, Sakata Y, Nochioka K, Miura M, Kasahara S, Sato M, et al. Prognostic impacts of dynamic cardiac structural changes in heart failure patients with preserved left ventricular ejection fraction. *Eur J Heart Fail*. 2020; **22**: 2258–2268.
61. Nauta JF, Hummel YM, Tromp J, Ouwerkerk W, van der Meer P, Jin X, et al. Concentric vs. eccentric remodelling in heart failure with reduced ejection fraction: clinical characteristics, pathophysiology and response to treatment. *Eur J Heart Fail*. 2020; **22**: 1147–1155.
62. Smiseth OA, Morris DA, Cardim N, Cikes M, Delgado V, Donal E, et al. Multimodality imaging in patients with heart failure and preserved ejection fraction: an expert consensus document of the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging*. 2022; **23**: e34–e61.
63. Janwanishstaporn S, Feng S, Teerlink J, Metra M, Cotter G, Davison BA, et al. Relationship between left ventricular ejection fraction and cardiovascular outcomes following hospitalization for heart failure: insights from the RELAX-AHF-2 trial. *Eur J Heart Fail*. 2020; **22**: 726–738.
64. Vachalcova M, Valocik G, Kurecko M, Grapsa J, Taha VA, Michalek P, et al. The three-dimensional speckle tracking echocardiography in distinguishing between ischaemic and non-ischaemic aetiology of heart failure. *ESC Heart Fail*. 2020; **7**: 2297–2304.
65. Hansen S, Brainin P, Sengelov M, Jorgensen PG, Bruun NE, Olsen FJ, et al. Prognostic utility of diastolic dysfunction and speckle tracking echocardiography in heart failure with reduced ejection fraction. *ESC Heart Fail*. 2020; **7**: 147–157.
66. Skaarup KG, Lassen MCH, Johansen ND, Sengelov M, Marott JL, Jorgensen PG, et al. Layer-specific global longitudinal strain and the risk of heart failure and cardiovascular mortality in the general population: the Copenhagen City Heart Study. *Eur J Heart Fail*. 2021; **23**: 1819–1827.
67. Strange G, Playford D, Scalia GM, Celermajer DS, Prior D, Codde J, et al. Change in ejection fraction and long-term mortality in adults referred for echocardiography. *Eur J Heart Fail*. 2021; **23**: 555–563.
68. Pellicori P, Platz E, Dauw J, Ter Maaten JM, Martens P, Pivetta E, et al. Ultrasound imaging of congestion in heart failure: examinations beyond the heart. *Eur J Heart Fail*. 2021; **23**: 703–712.
69. Cuthbert JJ, Pellicori P, Flockton R, Kallvikbacka-Bennett A, Khan J, Rigby AS, et al. The prevalence and clinical associations of ultrasound measures of congestion in patients at risk of developing heart failure. *Eur J Heart Fail*. 2021; **23**: 1831–1840.
70. Alhakak AS, Teerlink JR, Lindenfeld J, Bohm M, Rosano GMC, Biering-Sorensen T. The significance of left ventricular ejection time in heart failure with reduced ejection fraction. *Eur J Heart Fail*. 2021; **23**: 541–551.
71. Patel PA, Ambrosy AP, Phelan M, Alenezi F, Chiswell K, Van Dyke MK, et al. Association between systolic ejection time and outcomes in heart failure by ejection fraction. *Eur J Heart Fail*. 2020; **22**: 1174–1182.
72. Alhakak AS, Sengelov M, Jorgensen PG, Bruun NE, Johnsen C, Abildgaard U, et al. Left ventricular systolic ejection time is an independent predictor of all-cause mortality in heart failure with reduced ejection fraction. *Eur J Heart Fail*. 2021; **23**: 240–249.
73. Khan MS, Memon MM, Murad MH, Vaduganathan M, Greene SJ, Hall M, et al. Left atrial function in heart failure with preserved ejection fraction: a systematic review and meta-analysis. *Eur J Heart Fail*. 2020; **22**: 472–485.
74. Tamargo M, Obokata M, Reddy YNV, Pislaru SV, Lin G, Egbe AC, et al. Func-

tional mitral regurgitation and left atrial myopathy in heart failure with preserved ejection fraction. *Eur J Heart Fail*. 2020; **22**: 489–498.
75. Inoue K, Khan FH, Remme EW, Ohte N, Garcia-Izquierdo E, Chetrit M, et al. Determinants of left atrial reservoir and pump strain and use of atrial strain for evaluation of left ventricular filling pressure. *Eur Heart J Cardiovasc Imaging*. 2021; **23**: 61–70.
76. Sugimoto T, Barletta M, Bandera F, Generati G, Alfonzetti E, Rovida M, et al. Central role of left atrial dynamics in limiting exercise cardiac output increase and oxygen uptake in heart failure: insights by cardiopulmonary imaging. *Eur J Heart Fail*. 2020; **22**: 1186–1198.
77. Iliadis C, Baldus S, Kalbacher D, Boekstegers P, Schillinger W, Ouarrak T, et al. Impact of left atrial diameter on outcome in patients undergoing edge-to-edge mitral valve repair: results from the German TRAnscatheter Mitral valve Interventions (TRAMI) registry. *Eur J Heart Fail*. 2020; **22**: 1202–1210.
78. Konig S, Pellissier V, Hohenstein S, Bernal A, Ueberham L, Meier-Hellmann A, et al. Machine learning algorithms for claims data-based prediction of in-hospital mortality in patients with heart failure. *ESC Heart Fail*. 2021; **8**: 3026–3036.
79. Rocon C, Tabassian M, Tavares de Melo MD, de Araujo Filho JA, Grupi CJ, Parga Filho JR, et al. Biventricular imaging markers to predict outcomes in non-compaction cardiomyopathy: a machine learning study. *ESC Heart Fail*. 2020; **7**: 2431–2439.
80. Ju C, Zhou J, Lee S, Tan MS, Liu T, Bazoukis G, et al. Derivation of an electronic frailty index for predicting short-term mortality in heart failure: a machine learning approach. *ESC Heart Fail*. 2021; **8**: 2837–2845.
81. Adler ED, Voors AA, Klein L, Macheret F, Braun OO, Urey MA, et al. Improving risk prediction in heart failure using machine learning. *Eur J Heart Fail*. 2020; **22**: 139–147.
82. Greenberg B, Adler E, Campagnari C, Yagil A. A machine learning risk score predicts mortality across the spectrum of left ventricular ejection fraction. *Eur J Heart Fail*. 2021; **23**: 995–999.
83. Segar MW, Khan MS, Patel KV, Vaduganathan M, Kannan V, Willett D, et al. Incorporation of natriuretic peptides with clinical risk scores to predict heart failure among individuals with dysglycaemia. *Eur J Heart Fail*. 2022; **24**: 169–180.
84. Woolley RJ, Ceelen D, Ouwerkerk W, Tromp J, Figarska SM, Anker SD, et al. Machine learning based on biomarker profiles identifies distinct subgroups of heart failure with preserved ejection fraction. *Eur J Heart Fail*. 2021; **23**: 983–991.
85. Segar MW, Patel KV, Ayers C, Basit M, Tang WHW, Willett D, et al. Phenomapping of patients with heart failure with preserved ejection fraction using machine learning-based unsupervised cluster analysis. *Eur J Heart Fail*. 2020; **22**: 148–158.
86. Ouwerkerk W, Teng TK, Tromp J, Tay WT, Cleland JG, van Veldhuisen DJ, et al. Effects of combined renin–angiotensin–aldosterone system inhibitor and beta-blocker treatment on outcomes in heart failure with reduced ejection fraction: insights from BIOSTAT-CHF and ASIAN-HF registries. *Eur J Heart Fail*. 2020; **22**: 1472–1482.
87. Ameri P, Bertero E, Maack C, Teerlink JR, Rosano G, Metra M. Medical treatment of heart failure with reduced ejection fraction: the dawn of a new era of personalized treatment? *Eur Heart J Cardiovasc Pharmacother*. 2021; **7**: 539–546.
88. Tomasoni D, Adamo M, Lombardi CM, Metra M. Highlights in heart failure. *ESC Heart Fail*. 2019; **6**: 1105–1127.
89. Packer M, Metra M. Guideline-directed medical therapy for heart failure does not exist: a non-judgmental framework for describing the level of adherence to evidence-based drug treatments for patients with a reduced ejection fraction. *Eur J Heart Fail*. 2020; **22**: 1759–1767.
90. Giovinazzo S, Carmisciano L, Toma M, Benenati S, Tomasoni D, Sormani MP, et al. Sacubitril/valsartan in real-life European patients with heart failure and reduced ejection fraction: a systematic review and meta-analysis. *ESC Heart Fail*. 2021; **8**: 3547–3556.
91. Savarese G, Kishi T, Vardeny O, Adamsson Eryd S, Bodegard J, Lund LH, et al. Heart failure drug treatment—inertia, titration, and discontinuation: a multinational observational study (EVOLUTION HF). *JACC Heart Fail*. 2022.
92. Bhatt AS, Varshney AS, Nekoui M, Moscone A, Cunningham JW, Jering KS, et al. Virtual optimization of guideline-directed medical therapy in hospitalized patients with heart failure with reduced ejection fraction: the IMPLEMENT-HF pilot study. *Eur J Heart Fail*. 2021; **23**: 1191–1201.
93. Butler J, Yang M, Sawhney B, Chakladar S, Yang L, Djatche LM. Treatment patterns and clinical outcomes among patients <65 years with a worsening heart failure event. *Eur J Heart Fail*. 2021; **23**: 1334–1342.
94. Gupta P, Voors AA, Patel P, Lane D, Anker SD, Cleland JGF, et al. Non-adherence to heart failure medications predicts clinical outcomes: assessment in a single spot urine sample by liquid chromatography-tandem mass spectrometry (results of a prospective multicentre study). *Eur J Heart Fail*. 2021; **23**: 1182–1190.
95. Carubelli V, Lombardi C, Specchia C, Peveri G, Oriecuia C, Tomasoni D, et al. Adherence and optimization of angiotensin converting enzyme inhibitor/angiotensin II receptors blockers and beta-blockers in patients hospitalized for acute heart failure. *ESC Heart Fail*. 2021; **8**: 1944–1953.
96. Savarese G, Bodegard J, Norhammar A, Sartipy P, Thuresson M, Cowie MR, et al. Heart failure drug titration, discontinuation, mortality and heart failure hospitalization risk: a multinational observational study (US, UK and Sweden). *Eur J Heart Fail*. 2021; **23**: 1499–1511.
97. Bhatt AS, Vaduganathan M, Solomon SD, Schneeweiss S, Lauffenburger JC, Desai RJ. Sacubitril/valsartan use patterns among older adults with heart failure in clinical practice: a population-based cohort study of >25 000 Medicare beneficiaries. *Eur J Heart Fail*. 2022; **24**: 1506–1515.
98. Rosano GMC, Moura B, Metra M, Bohm M, Bauersachs J, Ben Gal T, et al. Patient profiling in heart failure for tailoring medical therapy. A consensus document of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2021; **23**: 872–881.
99. Packer M, McMurray JJV. Rapid evidence-based sequencing of foundational drugs for heart failure and a reduced ejection fraction. *Eur J Heart Fail*. 2021; **23**: 882–894.
100. Tomasoni D, Fonarow GC, Adamo M, Anker SD, Butler J, Coats AJS, et al. Sodium–glucose co-transporter 2 inhibitors as an early, first-line therapy in patients with heart failure and reduced ejection fraction. *Eur J Heart Fail*. 2022; **24**: 431–441.
101. Bhatt AS, Vaduganathan M, Claggett BL, Liu J, Packer M, Desai AS, et al. Effect of sacubitril/valsartan vs. enalapril on changes in heart failure therapies over time: the PARADIGM-HF trial. *Eur J Heart Fail*. 2021; **23**: 1518–1524.
102. Seferovic PM, Polovina M, Adlbrecht C, Belohlavek J, Chioncel O, Goncalvesova E, et al. Navigating between Scylla and Charybdis: challenges and strategies for implementing guideline-directed medical therapy in heart failure with reduced ejection fraction. *Eur J Heart Fail*. 2021; **23**: 1999–2007.
103. Senni M, Wachter R, Witte KK, Straburzynska-Migaj E, Belohlavek J, Fonseca C, et al. Initiation of sacubitril/valsartan shortly after hospitalisation for acutely decompensated heart failure in patients with newly diagnosed (*de novo*) heart failure: a subgroup analysis of the TRAN-

SITION study. *Eur J Heart Fail*. 2020; **22**: 303–312.
104. Suzuki K, Claggett B, Minamisawa M, Packer M, Zile MR, Rouleau J, et al. Liver function and prognosis, and influence of sacubitril/valsartan in patients with heart failure with reduced ejection fraction. *Eur J Heart Fail*. 2020; **22**: 1662–1671.
105. Halle M, Schobel C, Winzer EB, Bernhardt P, Mueller S, Sieder C, et al. A randomized clinical trial on the short-term effects of 12-week sacubitril/valsartan vs. enalapril on peak oxygen consumption in patients with heart failure with reduced ejection fraction: results from the ACTIVITY-HF study. *Eur J Heart Fail*. 2021; **23**: 2073–2082.
106. Piepoli MF, Hussain RI, Comin-Colet J, Dosantos R, Ferber P, Jaarsma T, et al. OUTSTEP-HF: randomised controlled trial comparing short-term effects of sacubitril/valsartan versus enalapril on daily physical activity in patients with chronic heart failure with reduced ejection fraction. *Eur J Heart Fail*. 2021; **23**: 127–135.
107. Edelmann F, Jaarsma T, Comin-Colet J, Schorr J, Ecochard L, Hussain RI, et al. Rationale and study design of OUTSTEP-HF: a randomised controlled study to assess the effect of sacubitril/valsartan and enalapril on physical activity measured by accelerometry in patients with heart failure with reduced ejection fraction. *Eur J Heart Fail*. 2020; **22**: 1724–1733.
108. Jering KS, Claggett B, Pfeffer MA, Granger C, Kober L, Lewis EF, et al. Prospective ARNI vs. ACE inhibitor trial to DetermIne Superiority in reducing heart failure Events after Myocardial Infarction (PARADISE-MI): design and baseline characteristics. *Eur J Heart Fail*. 2021; **23**: 1040–1048.
109. Docherty KF, Campbell RT, Brooksbank KJM, Dreisbach JG, Forsyth P, Godeseth RL, et al. Effect of neprilysin inhibition on left ventricular remodeling in patients with asymptomatic left ventricular systolic dysfunction late after myocardial infarction. *Circulation*. 2021; **144**: 199–209.
110. Docherty KF, Campbell RT, Brooksbank KJM, Godeseth RL, Forsyth P, McConnachie A, et al. Rationale and methods of a randomized trial evaluating the effect of neprilysin inhibition on left ventricular remodelling. *ESC Heart Fail*. 2021; **8**: 129–138.
111. Pfeffer MA, Claggett B, Lewis EF, Granger CB, Kober L, Maggioni AP, et al. Angiotensin receptor–neprilysin inhibition in acute myocardial infarction. *N Engl J Med*. 2021; **385**: 1845–1855.
112. Berwanger O, Pfeffer M, Claggett B, Jering KS, Maggioni AP, Steg PG, et al. Sacubitril/valsartan versus ramipril for patients with acute myocardial infarction: win-ratio analysis of the PARADISE-MI trial. *Eur J Heart Fail*. 2022; **24**: 1918–1927.
113. Agarwal R, Kolkhof P, Bakris G, Bauersachs J, Haller H, Wada T, et al. Steroidal and non-steroidal mineralocorticoid receptor antagonists in cardiorenal medicine. *Eur Heart J*. 2021; **42**: 152–161.
114. Bakris GL, Agarwal R, Anker SD, Pitt B, Ruilope LM, Rossing P, et al. Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes. *N Engl J Med*. 2020; **383**: 2219–2229.
115. Filippatos G, Bakris GL, Pitt B, Agarwal R, Rossing P, Ruilope LM, et al. Finerenone reduces new-onset atrial fibrillation in patients with chronic kidney disease and type 2 diabetes. *J Am Coll Cardiol*. 2021; **78**: 142–152.
116. Pitt B, Filippatos G, Agarwal R, Anker SD, Bakris GL, Rossing P, et al. Cardiovascular events with finerenone in kidney disease and type 2 diabetes. *N Engl J Med*. 2021; **385**: 2252–2263.
117. Filippatos G, Anker SD, Agarwal R, Ruilope LM, Rossing P, Bakris GL, et al. Finerenone reduces risk of incident heart failure in patients with chronic kidney disease and type 2 diabetes: analyses from the FIGARO-DKD trial. *Circulation*. 2022; **145**: 437–447.
118. Agarwal R, Filippatos G, Pitt B, Anker SD, Rossing P, Joseph A, et al. Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis. *Eur Heart J*. 2022; **43**: 474–484.
119. Seferovic PM, Coats AJS, Ponikowski P, Filippatos G, Huelsmann M, Jhund PS, et al. European Society of Cardiology/Heart Failure Association position paper on the role and safety of new glucose-lowering drugs in patients with heart failure. *Eur J Heart Fail*. 2020; **22**: 196–213.
120. Seferovic PM, Fragasso G, Petrie M, Mullens W, Ferrari R, Thum T, et al. Heart Failure Association of the European Society of Cardiology update on sodium–glucose co-transporter 2 inhibitors in heart failure. *Eur J Heart Fail*. 2020; **22**: 1984–1986.
121. Seferovic PM, Fragasso G, Petrie M, Mullens W, Ferrari R, Thum T, et al. Sodium–glucose co-transporter 2 inhibitors in heart failure: beyond glycaemic control. A position paper of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2020; **22**: 1495–1503.
122. Butler J, Handelsman Y, Bakris G, Verma S. Use of sodium–glucose co-transporter-2 inhibitors in patients with and without type 2 diabetes: implications for incident and prevalent heart failure. *Eur J Heart Fail*. 2020; **22**: 604–617.
123. Vaduganathan M, Docherty KF, Claggett BL, Jhund PS, de Boer RA, Hernandez AF, et al. SGLT-2 inhibitors in patients with heart failure: a comprehensive meta-analysis of five randomised controlled trials. *Lancet*. 2022; **400**: 757–767.
124. Verma S, Dhingra NK, Butler J, Anker SD, Ferreira JP, Filippatos G, et al. Empagliflozin in the treatment of heart failure with reduced ejection fraction in addition to background therapies and therapeutic combinations (EMPEROR-Reduced): a post-hoc analysis of a randomised, double-blind trial. *Lancet Diabetes Endocrinol*. 2022; **10**: 35–45.
125. Anker SD, Khan MS, Shahid I, Filippatos G, Coats AJS, Butler J. Sodium–glucose co-transporter 2 inhibitors in heart failure with preserved ejection fraction: reasons for optimism. *Eur J Heart Fail*. 2021; **23**: 1250–1255.
126. McEwan P, Darlington O, McMurray JJV, Jhund PS, Docherty KF, Bohm M, et al. Cost-effectiveness of dapagliflozin as a treatment for heart failure with reduced ejection fraction: a multinational health-economic analysis of DAPA-HF. *Eur J Heart Fail*. 2020; **22**: 2147–2156.
127. Herrington WG, Savarese G, Haynes R, Marx N, Mellbin L, Lund LH, et al. Cardiac, renal, and metabolic effects of sodium–glucose co-transporter 2 inhibitors: a position paper from the European Society of Cardiology ad-hoc task force on sodium–glucose co-transporter 2 inhibitors. *Eur J Heart Fail*. 2021; **23**: 1260–1275.
128. Pagnesi M, Baldetti L, Aimo A, Inciardi RM, Tomasoni D, Vizzardi E, et al. Prognostic benefit of new drugs for HFrEF: a systematic review and network meta-analysis. *J Clin Med*. 2022; **11**: 348.
129. Bhatia K, Jain V, Gupta K, Bansal A, Fox A, Qamar A, et al. Prevention of heart failure events with sodium–glucose co-transporter 2 inhibitors across a spectrum of cardio-renal-metabolic risk. *Eur J Heart Fail*. 2021; **23**: 1002–1008.
130. Becher PM, Schrage B, Ferrannini G, Benson L, Butler J, Carrero JJ, et al. Use of sodium–glucose co-transporter 2 inhibitors in patients with heart failure and type 2 diabetes mellitus: data from the Swedish Heart Failure Registry. *Eur J Heart Fail*. 2021; **23**: 1012–1022.
131. Zelniker TA, Morrow DA, Mosenzon O, Goodrich EL, Jarolim P, Murphy SA, et al. Relationship between baseline cardiac biomarkers and cardiovascular death or hospitalization for heart failure with and without sodium–glucose co-transporter 2 inhibitor therapy in DECLARE-TIMI 58. *Eur J Heart Fail*. 2021; **23**: 1026–1036.
132. Januzzi JL Jr, Zannad F, Anker SD, Butler J, Filippatos G, Pocock SJ, et al. Prognostic importance of NT-proBNP

and effect of empagliflozin in the EMPEROR-Reduced trial. *J Am Coll Cardiol*. 2021; **78**: 1321–1332.
133. Adamson C, Jhund PS, Docherty KF, Belohlavek J, Chiang CE, Diez M, et al. Efficacy of dapagliflozin in heart failure with reduced ejection fraction according to body mass index. *Eur J Heart Fail*. 2021; **23**: 1662–1672.
134. Sama IE, Woolley RJ, Nauta JF, Romaine SPR, Tromp J, Ter Maaten JM, et al. A network analysis to identify pathophysiological pathways distinguishing ischaemic from non-ischaemic heart failure. *Eur J Heart Fail*. 2020; **22**: 821–833.
135. Butt JH, Nicolau JC, Verma S, Docherty KF, Petrie MC, Inzucchi SE, et al. Efficacy and safety of dapagliflozin according to aetiology in heart failure with reduced ejection fraction: insights from the DAPA-HF trial. *Eur J Heart Fail*. 2021; **23**: 601–613.
136. Dewan P, Docherty KF, Bengtsson O, de Boer RA, Desai AS, Drozdz J, et al. Effects of dapagliflozin in heart failure with reduced ejection fraction and chronic obstructive pulmonary disease: an analysis of DAPA-HF. *Eur J Heart Fail*. 2021; **23**: 632–643.
137. Abraham WT, Lindenfeld J, Ponikowski P, Agostoni P, Butler J, Desai AS, et al. Effect of empagliflozin on exercise ability and symptoms in heart failure patients with reduced and preserved ejection fraction, with and without type 2 diabetes. *Eur Heart J*. 2021; **42**: 700–710.
138. Butler J, Anker SD, Siddiqi TJ, Coats AJS, Dorigotti F, Filippatos G, et al. Patiromer for the management of hyperkalaemia in patients receiving renin–angiotensin–aldosterone system inhibitors for heart failure: design and rationale of the DIAMOND trial. *Eur J Heart Fail*. 2022; **24**: 230–238.
139. Butler J, Anker SD, Lund LH, Coats AJS, Filippatos G, Siddiqi TJ, et al. Patiromer for the management of hyperkalemia in heart failure with reduced ejection fraction: the DIAMOND trial. *Eur Heart J*. 2022.
140. Armstrong PW, Pieske B, Anstrom KJ, Ezekowitz J, Hernandez AF, Butler J, et al. Vericiguat in patients with heart failure and reduced ejection fraction. *N Engl J Med*. 2020; **382**: 1883–1893.
141. Lombardi CM, Cimino G, Pagnesi M, Dell'Aquila A, Tomasoni D, Ravera A, et al. Vericiguat for heart failure with reduced ejection fraction. *Curr Cardiol Rep*. 2021; **23**: 144.
142. Voors AA, Mulder H, Reyes E, Cowie MR, Lassus J, Hernandez AF, et al. Renal function and the effects of vericiguat in patients with worsening heart failure with reduced ejection fraction: insights from the VICTORIA (Vericiguat Global Study in Subjects with HFrEF) trial. *Eur J Heart Fail*. 2021; **23**: 1313–1321.
143. Ponikowski P, Alemayehu W, Oto A, Bahit MC, Noori E, Patel MJ, et al. Vericiguat in patients with atrial fibrillation and heart failure with reduced ejection fraction: insights from the VICTORIA trial. *Eur J Heart Fail*. 2021; **23**: 1300–1312.
144. Kramer F, Voss S, Roessig L, Igl BW, Butler J, Lam CSP, et al. Evaluation of high-sensitivity C-reactive protein and uric acid in vericiguat-treated patients with heart failure with reduced ejection fraction. *Eur J Heart Fail*. 2020; **22**: 1675–1683.
145. Teerlink JR, Diaz R, Felker GM, McMurray JJV, Metra M, Solomon SD, et al. Cardiac myosin activation with omecamtiv mecarbil in systolic heart failure. *N Engl J Med*. 2021; **384**: 105–116.
146. Teerlink JR, Diaz R, Felker GM, McMurray JJV, Metra M, Solomon SD, et al. Effect of ejection fraction on clinical outcomes in patients treated with omecamtiv mecarbil in GALACTIC-HF. *J Am Coll Cardiol*. 2021; **78**: 97–108.
147. Teerlink JR, Diaz R, Felker GM, McMurray JJV, Metra M, Solomon SD, et al. Omecamtiv mecarbil in chronic heart failure with reduced ejection fraction: GALACTIC-HF baseline characteristics and comparison with contemporary clinical trials. *Eur J Heart Fail*. 2020; **22**: 2160–2171.
148. Felker GM, Solomon SD, Claggett B, Diaz R, McMurray JJV, Metra M, et al. Assessment of omecamtiv mecarbil for the treatment of patients with severe heart failure: a post hoc analysis of data from the GALACTIC-HF randomized clinical trial. *JAMA Cardiol*. 2022; **7**: 26–34.
149. Metra M, Pagnesi M, Claggett BL, Diaz R, Felker GM, McMurray JJV, et al. Effects of omecamtiv mecarbil in heart failure with reduced ejection fraction according to blood pressure: the GALACTIC-HF trial. *Eur Heart J*. 2022.
150. Tomasoni D, Vishram-Nielsen JKK, Pagnesi M, Adamo M, Lombardi CM, Gustafsson F, et al. Advanced heart failure: guideline-directed medical therapy, diuretics, inotropes, and palliative care. *ESC Heart Fail*. 2022; **9**: 1507–1523.
151. Lewis GD, Voors AA, Cohen-Solal A, Metra M, Whellan DJ, Ezekowitz JA, et al. Effect of omecamtiv mecarbil on exercise capacity in chronic heart failure with reduced ejection fraction: the METEORIC-HF randomized clinical trial. *JAMA*. 2022; **328**: 259–269.
152. Voors AA, Tamby JF, Cleland JG, Koren M, Forgosh LB, Gupta D, et al. Effects of danicamtiv, a novel cardiac myosin activator, in heart failure with reduced ejection fraction: experimental data and clinical results from a phase 2a trial. *Eur J Heart Fail*. 2020; **22**: 1649–1658.
153. Ciccarelli M, Sorriento D, Fiordelisi A, Gambardella J, Franco A, Del Giudice C, et al. Pharmacological inhibition of GRK2 improves cardiac metabolism and function in experimental heart failure. *ESC Heart Fail*. 2020; **7**: 1571–1584.
154. Stewart GM, Johnson BD, Sprecher DL, Reddy YNV, Obokata M, Goldsmith S, et al. Targeting pulmonary capillary permeability to reduce lung congestion in heart failure: a randomized, controlled pilot trial. *Eur J Heart Fail*. 2020; **22**: 1641–1645.
155. Mathiasen AB, Qayyum AA, Jorgensen E, Helqvist S, Kofoed KF, Haack-Sorensen M, et al. Bone marrow-derived mesenchymal stromal cell treatment in patients with ischaemic heart failure: final 4-year follow-up of the MSC-HF trial. *Eur J Heart Fail*. 2020; **22**: 884–892.
156. Bartunek J, Terzic A, Davison BA, Behfar A, Sanz-Ruiz R, Wojakowski W, et al. Cardiopoietic stem cell therapy in ischaemic heart failure: long-term clinical outcomes. *ESC Heart Fail*. 2020.
157. Bolli R, Mitrani RD, Hare JM, Pepine CJ, Perin EC, Willerson JT, et al. A Phase II study of autologous mesenchymal stromal cells and c-kit positive cardiac cells, alone or in combination, in patients with ischaemic heart failure: the CCTRN CONCERT-HF trial. *Eur J Heart Fail*. 2021; **23**: 661–674.
158. Berulava T, Buchholz E, Elerdashvili V, Pena T, Islam MR, Lbik D, et al. Changes in m6A RNA methylation contribute to heart failure progression by modulating translation. *Eur J Heart Fail*. 2020; **22**: 54–66.
159. Garg A, Foinquinos A, Jung M, Janssen-Peters H, Biss S, Bauersachs J, et al. MiRNA-181a is a novel regulator of aldosterone–mineralocorticoid receptor-mediated cardiac remodelling. *Eur J Heart Fail*. 2020; **22**: 1366–1377.
160. Jaarsma T, Hill L, Bayes-Genis A, La Rocca HB, Castiello T, Celutkiene J, et al. Self-care of heart failure patients: practical management recommendations from the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2021; **23**: 157–174.
161. Kaluza J, Levitan EB, Michaelsson K, Wolk A. Anti-inflammatory diet and risk of heart failure: two prospective cohort studies. *Eur J Heart Fail*. 2020; **22**: 676–682.
162. Khan MS, Khan F, Fonarow GC, Sreenivasan J, Greene SJ, Khan SU, et al. Dietary interventions and nutritional supplements for heart failure: a systematic appraisal and evidence map. *Eur J Heart Fail*. 2021; **23**: 1468–1476.
163. Bielecka-Dabrowa A, Ebner N, Dos Santos MR, Ishida J, Hasenfuss G, von Haehling S. Cachexia, muscle wasting, and frailty in cardiovascular disease. *Eur J Heart Fail*. 2020; **22**: 2314–2326.

164. Evangelista LS, Jose MM, Sallam H, Serag H, Golovko G, Khanipov K, et al. High-protein vs. standard-protein diets in overweight and obese patients with heart failure and diabetes mellitus: findings of the Pro-HEART trial. *ESC Heart Fail*. 2021; **8**: 1342–1348.
165. Aimo A, Saccaro LF, Borrelli C, Fabiani I, Gentile F, Passino C, et al. The ergoreflex: how the skeletal muscle modulates ventilation and cardiovascular function in health and disease. *Eur J Heart Fail*. 2021; **23**: 1458–1467.
166. Nijholt KT, Sanchez-Aguilera PI, Voorrips SN, de Boer RA, Westenbrink BD. Exercise: a molecular tool to boost muscle growth and mitochondrial performance in heart failure? *Eur J Heart Fail*. 2022; **24**: 287–298.
167. von Haehling S, Arzt M, Doehner W, Edelmann F, Evertz R, Ebner N, et al. Improving exercise capacity and quality of life using non-invasive heart failure treatments: evidence from clinical trials. *Eur J Heart Fail*. 2021; **23**: 92–113.
168. Abdelhamid M, Rosano G, Metra M, Adamopoulos S, Bohm M, Chioncel O, et al. Prevention of sudden death in heart failure with reduced ejection fraction: do we still need an implantable cardioverter-defibrillator for primary prevention? *Eur J Heart Fail*. 2022; **24**: 1460–1466.
169. Docherty KF, Ferreira JP, Sharma A, Girerd N, Gregson J, Duarte K, et al. Predictors of sudden cardiac death in high-risk patients following a myocardial infarction. *Eur J Heart Fail*. 2020; **22**: 848–855.
170. Fudim M, Carlisle MA, Devaraj S, Ajam T, Ambrosy AP, Pokorney SD, et al. One-year mortality after implantable cardioverter-defibrillator placement within the Veterans Affairs Health System. *Eur J Heart Fail*. 2020; **22**: 859–867.
171. Moubarak G, Viart G, Anselme F. Acute correction of electromechanical dyssynchrony and response to cardiac resynchronization therapy. *ESC Heart Fail*. 2020; **7**: 1302–1308.
172. Lee SS, Kwon HJ, Park KM, On YK, Kim JS, Park SJ. Cardiac resynchronization therapy in New York Heart Association class-IV patients dependent on intravenous drugs or invasive supportive treatments. *ESC Heart Fail*. 2020; **7**: 3109–3118.
173. Glikson M, Nielsen JC, Kronborg MB, Michowitz Y, Auricchio A, Barbash IM, et al. 2021 ESC guidelines on cardiac pacing and cardiac resynchronization therapy. *Eur Heart J*. 2021; **42**: 3427–3520.
174. Mullens W, Auricchio A, Martens P, Witte K, Cowie MR, Delgado V, et al. Optimized implementation of cardiac resynchronization therapy: a call for action for referral and optimization of care: a joint position statement from the Heart Failure Association (HFA), European Heart Rhythm Association (EHRA), and European Association of Cardiovascular Imaging (EACVI) of the European Society of Cardiology. *Eur J Heart Fail*. 2020; **22**: 2349–2369.
175. Anker SD, Borggrefe M, Neuser H, Ohlow MA, Roger S, Goette A, et al. Cardiac contractility modulation improves long-term survival and hospitalizations in heart failure with reduced ejection fraction. *Eur J Heart Fail*. 2019; **21**: 1103–1113.
176. Tschope C, Kherad B, Klein O, Lipp A, Blaschke F, Gutterman D, et al. Cardiac contractility modulation: mechanisms of action in heart failure with reduced ejection fraction and beyond. *Eur J Heart Fail*. 2019; **21**: 14–22.
177. Giallauria F, Cuomo G, Parlato A, Raval NY, Kuschyk J, Stewart Coats AJ. A comprehensive individual patient data meta-analysis of the effects of cardiac contractility modulation on functional capacity and heart failure-related quality of life. *ESC Heart Fail*. 2020; **7**: 2922–2932.
178. Kuschyk J, Falk P, Demming T, Marx O, Morley D, Rao I, et al. Long-term clinical experience with cardiac contractility modulation therapy delivered by the Optimizer Smart system. *Eur J Heart Fail*. 2021; **23**: 1160–1169.
179. Pagnesi M, Adamo M, Sama IE, Anker SD, Cleland JG, Dickstein K, et al. Impact of mitral regurgitation in patients with worsening heart failure: insights from BIOSTAT-CHF. *Eur J Heart Fail*. 2021; **23**: 1750–1758.
180. Messika-Zeitoun D, Verta P, Gregson J, Pocock SJ, Boero I, Feldman TE, et al. Impact of tricuspid regurgitation on survival in patients with heart failure: a large electronic health record patient-level database analysis. *Eur J Heart Fail*. 2020; **22**: 1803–1813.
181. Chen S, Redfors B, Crowley A, Ben-Yehuda O, Summers M, Hahn RT, et al. Impact of recent heart failure hospitalization on clinical outcomes in patients with severe aortic stenosis undergoing transcatheter aortic valve replacement: an analysis from the PARTNER 2 trial and registries. *Eur J Heart Fail*. 2020; **22**: 1866–1874.
182. Senni M, Adamo M, Metra M, Alfieri O, Vahanian A. Treatment of functional mitral regurgitation in chronic heart failure: can we get a 'proof of concept' from the MITRA-FR and COAPT trials? *Eur J Heart Fail*. 2019; **21**: 852–861.
183. Packer M. Disproportionate functional mitral regurgitation: a new therapeutic target in patients with heart failure and a reduced ejection fraction. *Eur J Heart Fail*. 2020; **22**: 23–25.
184. Gill H, Chehab O, Allen C, Patterson T, Redwood S, Rajani R, et al. The advantages, pitfalls and limitations of guideline-directed medical therapy in patients with valvular heart disease. *Eur J Heart Fail*. 2021; **23**: 1325–1333.
185. Higuchi S, Orban M, Adamo M, Giannini C, Melica B, Karam N, et al. Guideline-directed medical therapy in patients undergoing transcatheter edge-to-edge repair for secondary mitral regurgitation. *Eur J Heart Fail*. 2022.
186. Seferovic PM, Ponikowski P, Anker SD, Bauersachs J, Chioncel O, Cleland JGF, et al. Clinical practice update on heart failure 2019: pharmacotherapy, procedures, devices and patient management. An expert consensus meeting report of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2019; **21**: 1169–1186.
187. Coats AJS, Anker SD, Baumbach A, Alfieri O, von Bardeleben RS, Bauersachs J, et al. The management of secondary mitral regurgitation in patients with heart failure: a joint position statement from the Heart Failure Association (HFA), European Association of Cardiovascular Imaging (EACVI), European Heart Rhythm Association (EHRA), and European Association of Percutaneous Cardiovascular Interventions (EAPCI) of the ESC. *Eur Heart J*. 2021; **42**: 1254–1269.
188. Bedogni F, Popolo Rubbio A, Grasso C, Adamo M, Denti P, Giordano A, et al. Italian Society of Interventional Cardiology (GIse) registry Of Transcatheter treatment of mitral valve regurgitaTiOn (GIOTTO): impact of valve disease aetiology and residual mitral regurgitation after MitraClip implantation. *Eur J Heart Fail*. 2021; **23**: 1364–1376.
189. Reichart D, Kalbacher D, Rubsamen N, Tigges E, Thomas C, Schirmer J, et al. The impact of residual mitral regurgitation after MitraClip therapy in functional mitral regurgitation. *Eur J Heart Fail*. 2020; **22**: 1840–1848.
190. Iliadis C, Kalbacher D, Lurz P, Petrescu AM, Orban M, Puscas T, et al. Left atrial volume index and outcome after transcatheter edge-to-edge valve repair for secondary mitral regurgitation. *Eur J Heart Fail*. 2022; **24**: 1282–1292.
191. Caiffa T, De Luca A, Biagini E, Lupi L, Bedogni F, Castrichini M, et al. Impact on clinical outcomes of right ventricular response to percutaneous correction of secondary mitral regurgitation. *Eur J Heart Fail*. 2021; **23**: 1765–1774.
192. Adamo M, Pagnesi M, Ghizzoni G, Estévez-Loureiro R, Raposeiras-Roubin S, Tomasoni D, et al. Evolution of tricuspid regurgitation after transcatheter edge-to-edge mitral valve repair for secondary mitral regurgitation and its impact on mortality. *Eur J Heart Fail*.
193. Papadopoulos K, Ikonomidis I, Chrissoheris M, Chalapas A, Kourkoveli P, Parissis J, et al. MitraClip and left ventricular reverse remodelling: a strain imaging study. *ESC Heart Fail*. 2020; **7**: 1409–1418.
194. Keller K, Hobohm L, Schmidtmann I, Munzel T, Baldus S, von Bardeleben

RS. Centre procedural volume and adverse in-hospital outcomes in patients undergoing percutaneous transvenous edge-to-edge mitral valve repair using MitraClip® in Germany. *Eur J Heart Fail*. 2021; **23**: 1380–1389.
195. Witte KK, Kaye DM, Lipiecki J, Siminiak T, Goldberg SL, von Bardeleben RS, et al. Treating symptoms and reversing remodelling: clinical and echocardiographic 1-year outcomes with percutaneous mitral annuloplasty for mild to moderate secondary mitral regurgitation. *Eur J Heart Fail*. 2021; **23**: 1971–1978.
196. Patterson T, Gregson J, Erglis A, Joseph J, Rajani R, Wilson K, et al. Two-year outcomes from the MitrAl ValvE RepaIr Clinical (MAVERIC) trial: a novel percutaneous treatment of functional mitral regurgitation. *Eur J Heart Fail*. 2021; **23**: 1775–1783.
197. Russo G, Taramasso M, Pedicino D, Gennari M, Gavazzoni M, Pozzoli A, et al. Challenges and future perspectives of transcatheter tricuspid valve interventions: adopt old strategies or adapt to new opportunities? *Eur J Heart Fail*. 2022; **24**: 442–454.
198. Dreyfus J, Audureau E, Bohbot Y, Coisne A, Lavie-Badie Y, Bouchery M, et al. TRI-SCORE: a new risk score for in-hospital mortality prediction after isolated tricuspid valve surgery. *Eur Heart J*. 2022; **43**: 654–662.
199. Misumida N, Steidley DE, Eleid MF. Edge-to-edge tricuspid valve repair for severe tricuspid regurgitation 20 years after cardiac transplantation. *ESC Heart Fail*. 2020; **7**: 4320–4325.
200. Andreas M, Russo M, Werner P, Schneider M, Wittmann F, Scherzer S, et al. Transcatheter edge-to-edge tricuspid repair for recurrence of valvular regurgitation after left ventricular assist device and tricuspid ring implantation. *ESC Heart Fail*. 2020; **7**: 915–919.
201. Besler C, Unterhuber M, Rommel KP, Unger E, Hartung P, von Roeder M, et al. Nutritional status in tricuspid regurgitation: implications of transcatheter repair. *Eur J Heart Fail*. 2020; **22**: 1826–1836.
202. Unterhuber M, Kresoja KP, Besler C, Rommel KP, Orban M, von Roeder M, et al. Cardiac output states in patients with severe functional tricuspid regurgitation: impact on treatment success and prognosis. *Eur J Heart Fail*. 2021; **23**: 1784–1794.
203. Reddy YNV, Rikhi A, Obokata M, Shah SJ, Lewis GD, AbouEzzedine OF, et al. Quality of life in heart failure with preserved ejection fraction: importance of obesity, functional capacity, and physical inactivity. *Eur J Heart Fail*. 2020; **22**: 1009–1018.
204. Tomasoni D, Adamo M, Anker MS, von Haehling S, Coats AJS, Metra M. Heart failure in the last year: progress and perspective. *ESC Heart Fail*. 2020.
205. Pieske B, Tschope C, de Boer RA, Fraser AG, Anker SD, Donal E, et al. How to diagnose heart failure with preserved ejection fraction: the HFA–PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). *Eur J Heart Fail*. 2020; **22**: 391–412.
206. Uijl A, Savarese G, Vaartjes I, Dahlstrom U, Brugts JJ, Linssen GCM, et al. Identification of distinct phenotypic clusters in heart failure with preserved ejection fraction. *Eur J Heart Fail*. 2021; **23**: 973–982.
207. Iacovoni A, Palmieri V, Abete R, Vecchi AL, Mortara A, Gori M, et al. Right and left ventricular structures and functions in acute HFpEF: comparing the hypertensive pulmonary edema and worsening heart failure phenotypes. *J Cardiovasc Med (Hagerstown)*. 2022; **23**: 663–671.
208. Kammerlander AA, Nitsche C, Dona C, Koschutnik M, Dannenberg V, Mascherbauer K, et al. Heart failure with preserved ejection fraction after left-sided valve surgery: prevalent and relevant. *Eur J Heart Fail*. 2021; **23**: 2008–2016.
209. Packer M. Do most patients with obesity or type 2 diabetes, and atrial fibrillation, also have undiagnosed heart failure? A critical conceptual framework for understanding mechanisms and improving diagnosis and treatment. *Eur J Heart Fail*. 2020; **22**: 214–227.
210. Omar M, Jensen MD, Borlaug BA. Diabesity and heart failure with preserved ejection fraction: the picture is getting clearer. *Eur J Heart Fail*. 2022; **24**: 510–512.
211. Packer M, Lam CSP, Lund LH, Maurer MS, Borlaug BA. Characterization of the inflammatory-metabolic phenotype of heart failure with a preserved ejection fraction: a hypothesis to explain influence of sex on the evolution and potential treatment of the disease. *Eur J Heart Fail*. 2020; **22**: 1551–1567.
212. Kresoja KP, Rommel KP, Wachter R, Henger S, Besler C, Kloting N, et al. Proteomics to improve phenotyping in obese patients with heart failure with preserved ejection fraction. *Eur J Heart Fail*. 2021; **23**: 1633–1644.
213. Jamaly S, Carlsson L, Peltonen M, Andersson-Assarsson JC, Karason K. Heart failure development in obesity: underlying risk factors and mechanistic pathways. *ESC Heart Fail*. 2021; **8**: 356–367.
214. Quarta G, Gori M, Iorio A, D'Elia E, Moon JC, Iacovoni A, et al. Cardiac magnetic resonance in heart failure with preserved ejection fraction: myocyte, interstitium, microvascular, and metabolic abnormalities. *Eur J Heart Fail*. 2020; **22**: 1065–1075.
215. Rao VN, Fudim M, Mentz RJ, Michos ED, Felker GM. Regional adiposity and heart failure with preserved ejection fraction. *Eur J Heart Fail*. 2020; **22**: 1540–1550.
216. Tromp J, Bryant JA, Jin X, van Woerden G, Asali S, Yiying H, et al. Epicardial fat in heart failure with reduced versus preserved ejection fraction. *Eur J Heart Fail*. 2021; **23**: 835–838.
217. van Woerden G, Gorter TM, Westenbrink BD, Willems TP, van Veldhuisen DJ, Rienstra M. Epicardial fat in heart failure patients with mid-range and preserved ejection fraction. *Eur J Heart Fail*. 2018; **20**: 1559–1566.
218. Wu CK, Lee JK, Hsu JC, Su MM, Wu YF, Lin TT, et al. Myocardial adipose deposition and the development of heart failure with preserved ejection fraction. *Eur J Heart Fail*. 2020; **22**: 445–454.
219. Pugliese NR, Paneni F, Mazzola M, De Biase N, Del Punta L, Gargani L, et al. Impact of epicardial adipose tissue on cardiovascular haemodynamics, metabolic profile, and prognosis in heart failure. *Eur J Heart Fail*. 2021; **23**: 1858–1871.
220. Konishi M, Kagiyama N, Kamiya K, Saito H, Saito K, Ogasahara Y, et al. Impact of sarcopenia on prognosis in patients with heart failure with reduced and preserved ejection fraction. *Eur J Prev Cardiol*. 2021; **28**: 1022–1029.
221. Sorimachi H, Burkhoff D, Verbrugge FH, Omote K, Obokata M, Reddy YNV, et al. Obesity, venous capacitance, and venous compliance in heart failure with preserved ejection fraction. *Eur J Heart Fail*. 2021; **23**: 1648–1658.
222. Yang JH, Obokata M, Reddy YNV, Redfield MM, Lerman A, Borlaug BA. Endothelium-dependent and independent coronary microvascular dysfunction in patients with heart failure with preserved ejection fraction. *Eur J Heart Fail*. 2020; **22**: 432–441.
223. Ahmad A, Corban MT, Toya T, Verbrugge FH, Sara JD, Lerman LO, et al. Coronary microvascular dysfunction is associated with exertional haemodynamic abnormalities in patients with heart failure with preserved ejection fraction. *Eur J Heart Fail*. 2021; **23**: 765–772.
224. Pugliese NR, Pellicori P, Filidei F, De Biase N, Maffia P, Guzik TJ, et al. Inflammatory pathways in heart failure with preserved left ventricular ejection fraction: implications for future interventions. *Cardiovasc Res*. 2022.
225. Myhre PL, Vaduganathan M, Greene SJ. Diagnosing heart failure with preserved ejection fraction in 2019: the search for a gold standard. *Eur J Heart Fail*. 2020; **22**: 422–424.
226. Sepehrvand N, Alemayehu W, Dyck GJB, Dyck JRB, Anderson T, Howlett J, et al. External validation of the H_2F-PEF model in diagnosing patients

with heart failure and preserved ejection fraction. *Circulation*. 2019; **139**: 2377–2379.
227. Sanders-van Wijk S, Barandiaran Aizpurua A, Brunner-La Rocca HP, Henkens M, Weerts J, Knackstedt C, et al. The HFA-PEFF and H_2FPEF scores largely disagree in classifying patients with suspected heart failure with preserved ejection fraction. *Eur J Heart Fail*. 2021; **23**: 838–840.
228. Barandiaran Aizpurua A, Sanders-van Wijk S, Brunner-La Rocca HP, Henkens M, Heymans S, Beussink-Nelson L, et al. Validation of the HFA-PEFF score for the diagnosis of heart failure with preserved ejection fraction. *Eur J Heart Fail*. 2020; **22**: 413–421.
229. Reddy YNV, Carter RE, Obokata M, Redfield MM, Borlaug BA. A simple, evidence-based approach to help guide diagnosis of heart failure with preserved ejection fraction. *Circulation*. 2018; **138**: 861–870.
230. Ouwerkerk W, Tromp J, Jin X, Jaufeerally F, Yeo PSD, Leong KTG, et al. Heart failure with preserved ejection fraction diagnostic scores in an Asian population. *Eur J Heart Fail*. 2020; **22**: 1737–1739.
231. Verbrugge FH, Reddy YNV, Sorimachi H, Omote K, Carter RE, Borlaug BA. Diagnostic scores predict morbidity and mortality in patients hospitalized for heart failure with preserved ejection fraction. *Eur J Heart Fail*. 2021; **23**: 954–963.
232. Nikorowitsch J, Bei der Kellen R, Kirchhof P, Magnussen C, Jagodzinski A, Schnabel RB, et al. Applying the ESC 2016, H_2FPEF, and HFA-PEFF diagnostic algorithms for heart failure with preserved ejection fraction to the general population. *ESC Heart Fail*. 2021; **8**: 3603–3612.
233. Parcha V, Malla G, Kalra R, Patel N, Sanders-van Wijk S, Pandey A, et al. Diagnostic and prognostic implications of heart failure with preserved ejection fraction scoring systems. *ESC Heart Fail*. 2021; **8**: 2089–2102.
234. Tomasoni D, Aimo A, Merlo M, Nardi M, Adamo M, Bellicini MG, et al. Value of the HFA-PEFF and H_2FPEF scores in patients with heart failure and preserved ejection fraction caused by cardiac amyloidosis. *Eur J Heart Fail*. 2022.
235. Guazzi M, Wilhelm M, Halle M, Van Craenenbroeck E, Kemps H, de Boer RA, et al. Exercise testing in heart failure with preserved ejection fraction: an appraisal through diagnosis, pathophysiology and therapy—a clinical consensus statement of the Heart Failure Association and European Association of Preventive Cardiology of the European Society of Cardiology. *Eur J Heart Fail*. 2022; **24**: 1327–1345.
236. Pugliese NR, Mazzola M, Fabiani I, Gargani L, De Biase N, Pedrinelli R, et al. Haemodynamic and metabolic phenotyping of hypertensive patients with and without heart failure by combining cardiopulmonary and echocardiographic stress test. *Eur J Heart Fail*. 2020; **22**: 458–468.
237. Shah AM, Claggett B, Sweitzer NK, Shah SJ, Anand IS, O'Meara E, et al. Cardiac structure and function and prognosis in heart failure with preserved ejection fraction: findings from the echocardiographic study of the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) Trial. *Circ Heart Fail*. 2014; **7**: 740–751.
238. Raisi-Estabragh Z, McCracken C, Condurache D, Aung N, Vargas JD, Naderi H, et al. Left atrial structure and function are associated with cardiovascular outcomes independent of left ventricular measures: a UK Biobank CMR study. *Eur Heart J Cardiovasc Imaging*. 2022; **23**: 1191–1200.
239. Venkateshvaran A, Tureli HO, Faxen UL, Lund LH, Tossavainen E, Lindqvist P. Left atrial reservoir strain improves diagnostic accuracy of the 2016 ASE/EACVI diastolic algorithm in patients with preserved left ventricular ejection fraction: insights from the KARUM haemodynamic database. *Eur Heart J Cardiovasc Imaging*. 2022; **23**: 1157–1168.
240. Anker SD, Butler J, Filippatos G, Ferreira JP, Bocchi E, Bohm M, et al. Empagliflozin in heart failure with a preserved ejection fraction. *N Engl J Med*. 2021; **385**: 1451–1461.
241. Anker SD, Butler J, Filippatos G, Shahzeb Khan M, Ferreira JP, Bocchi E, et al. Baseline characteristics of patients with heart failure with preserved ejection fraction in the EMPEROR-Preserved trial. *Eur J Heart Fail*. 2020; **22**: 2383–2392.
242. Nassif ME, Windsor SL, Borlaug BA, Kitzman DW, Shah SJ, Tang F, et al. The SGLT2 inhibitor dapagliflozin in heart failure with preserved ejection fraction: a multicenter randomized trial. *Nat Med*. 2021; **27**: 1954–1960.
243. Solomon SD, de Boer RA, DeMets D, Hernandez AF, Inzucchi SE, Kosiborod MN, et al. Dapagliflozin in heart failure with preserved and mildly reduced ejection fraction: rationale and design of the DELIVER trial. *Eur J Heart Fail*. 2021; **23**: 1217–1225.
244. Solomon SD, McMurray JJV, Claggett B, de Boer RA, DeMets D, Hernandez AF, et al. Dapagliflozin in heart failure with mildly reduced or preserved ejection fraction. *N Engl J Med*. 2022; **387**: 1089–1098.
245. Reddy YNV, Stewart GM, Obokata M, Koepp KE, Borlaug BA. Peripheral and pulmonary effects of inorganic nitrite during exercise in heart failure with preserved ejection fraction. *Eur J Heart Fail*. 2021; **23**: 814–823.
246. Vaduganathan M, Piccini JP, Camm AJ, Crijns H, Anker SD, Butler J, et al. Dronedarone for the treatment of atrial fibrillation with concomitant heart failure with preserved and mildly reduced ejection fraction: a post-hoc analysis of the ATHENA trial. *Eur J Heart Fail*. 2022; **24**: 1094–1101.
247. Sugumar H, Nanayakkara S, Vizi D, Wright L, Chieng D, Leet A, et al. A prospective STudy using invAsive haemodynamic measurements foLLowing catheter ablation for AF and early HFpEF: STALL AF-HFpEF. *Eur J Heart Fail*. 2021; **23**: 785–796.
248. Lauder L, Pereira TV, Degenhardt MC, Ewen S, Kulenthiran S, Coats AJS, et al. Feasibility and efficacy of transcatheter interatrial shunt devices for chronic heart failure: a systematic review and meta-analysis. *Eur J Heart Fail*. 2021; **23**: 1960–1970.
249. Paitazoglou C, Bergmann MW, Ozdemir R, Pfister R, Bartunek J, Kilic T, et al. One-year results of the first-in-man study investigating the Atrial Flow Regulator for left atrial shunting in symptomatic heart failure patients: the PRELIEVE study. *Eur J Heart Fail*. 2021; **23**: 800–810.
250. Abraham WT. Interatrial shunting for the treatment of heart failure: an on-demand, self-regulating left atrial pressure lowering system. *Eur J Heart Fail*. 2021; **23**: 811–813.
251. Shah SJ, Borlaug BA, Chung ES, Cutlip DE, Debonnaire P, Fail PS, et al. Atrial shunt device for heart failure with preserved and mildly reduced ejection fraction (REDUCE LAP-HF II): a randomised, multicentre, blinded, sham-controlled trial. *Lancet*. 2022; **399**: 1130–1140.
252. Fudim M, Ganesh A, Green C, Jones WS, Blazing MA, DeVore AD, et al. Splanchnic nerve block for decompensated chronic heart failure: splanchnic-HF. *Eur Heart J*. 2018; **39**: 4255–4256.
253. Fudim M, Jones WS, Boortz-Marx RL, Ganesh A, Green CL, Hernandez AF, et al. Splanchnic nerve block for acute heart failure. *Circulation*. 2018; **138**: 951–953.
254. Fudim M, Ponikowski PP, Burkhoff D, Dunlap ME, Sobotka PA, Molinger J, et al. Splanchnic nerve modulation in heart failure: mechanistic overview, initial clinical experience, and safety considerations. *Eur J Heart Fail*. 2021; **23**: 1076–1084.
255. Malek F, Gajewski P, Zymlinski R, Janczak D, Chabowski M, Fudim M, et al. Surgical ablation of the right greater splanchnic nerve for the treatment of heart failure with preserved ejection fraction: first-in-human clinical trial. *Eur J Heart Fail*. 2021; **23**: 1134–1143.
256. Fudim M, Fail PS, Litwin SE, Shaburishvili T, Goyal P, Hummel SL,

et al. Endovascular ablation of the right greater splanchnic nerve in heart failure with preserved ejection fraction: early results of the REBALANCE-HF trial roll-in cohort. *Eur J Heart Fail*. 2022; **24**: 1410–1414.
257. Wehner GJ, Jing L, Haggerty CM, Suever JD, Leader JB, Hartzel DN, et al. Routinely reported ejection fraction and mortality in clinical practice: where does the nadir of risk lie? *Eur Heart J*. 2020; **41**: 1249–1257.
258. van Essen BJ, Tromp J, Ter Maaten JM, Greenberg BH, Gimpelewicz C, Felker GM, et al. Characteristics and clinical outcomes of patients with acute heart failure with a supranormal left ventricular ejection fraction. *Eur J Heart Fail*. 2022.
259. Forrest IS, Rocheleau G, Bafna S, Argulian E, Narula J, Natarajan P, et al. Genetic and phenotypic profiling of supranormal ejection fraction reveals decreased survival and underdiagnosed heart failure. *Eur J Heart Fail*. 2022.
260. Shah S, Segar MW, Kondamudi N, Ayers C, Chandra A, Matulevicius S, et al. Supranormal left ventricular ejection fraction, stroke volume, and cardiovascular risk: findings from population-based cohort studies. *JACC Heart Fail*. 2022; **10**: 583–594.
261. Khan MS, Samman Tahhan A, Vaduganathan M, Greene SJ, Alrohaibani A, Anker SD, et al. Trends in prevalence of comorbidities in heart failure clinical trials. *Eur J Heart Fail*. 2020; **22**: 1032–1042.
262. Vaduganathan M, Pareek M, Kristensen AMD, Biering-Sorensen T, Byrne C, Almarzooq Z, et al. Prevention of heart failure events with intensive versus standard blood pressure lowering across the spectrum of kidney function and albuminuria: a SPRINT substudy. *Eur J Heart Fail*. 2021; **23**: 384–392.
263. Polovina M, Lund LH, Dikic D, Petrovic-Dordevic I, Krljanac G, Milinkovic I, et al. Type 2 diabetes increases the long-term risk of heart failure and mortality in patients with atrial fibrillation. *Eur J Heart Fail*. 2020; **22**: 113–125.
264. Bohm M, Slawik J, Brueckmann M, Mattheus M, George JT, Ofstad AP, et al. Efficacy of empagliflozin on heart failure and renal outcomes in patients with atrial fibrillation: data from the EMPA-REG OUTCOME trial. *Eur J Heart Fail*. 2020; **22**: 126–135.
265. Kloosterman M, Santema BT, Roselli C, Nelson CP, Koekemoer A, Romaine SPR, et al. Genetic risk and atrial fibrillation in patients with heart failure. *Eur J Heart Fail*. 2020; **22**: 519–527.
266. Shin SH, Claggett B, Pfeffer MA, Skali H, Liu J, Aguilar D, et al. Hyperglycaemia, ejection fraction and the risk of heart failure or cardiovascular death in patients with type 2 diabetes and a recent acute coronary syndrome. *Eur J Heart Fail*. 2020; **22**: 1133–1143.
267. Bhatt AS, Ambrosy AP, Dunning A, DeVore AD, Butler J, Reed S, et al. The burden of non-cardiac comorbidities and association with clinical outcomes in an acute heart failure trial—insights from ASCEND-HF. *Eur J Heart Fail*. 2020; **22**: 1022–1031.
268. Dewan P, Jackson A, Jhund PS, Shen L, Ferreira JP, Petrie MC, et al. The prevalence and importance of frailty in heart failure with reduced ejection fraction—an analysis of PARADIGM-HF and ATMOSPHERE. *Eur J Heart Fail*. 2020; **22**: 2123–2133.
269. Huynh QL, Whitmore K, Negishi K, DePasquale CG, Hare JL, Leung D, et al. Cognitive impairment as a determinant of response to management plans after heart failure admission. *Eur J Heart Fail*. 2021; **23**: 1205–1214.
270. Matsue Y, Kamiya K, Saito H, Saito K, Ogasahara Y, Maekawa E, et al. Prevalence and prognostic impact of the coexistence of multiple frailty domains in elderly patients with heart failure: the FRAGILE-HF cohort study. *Eur J Heart Fail*. 2020; **22**: 2112–2119.
271. Sbolli M, Fiuzat M, Cani D, O'Connor CM. Depression and heart failure: the lonely comorbidity. *Eur J Heart Fail*. 2020; **22**: 2007–2017.
272. Tkaczyszyn M, Comin-Colet J, Voors AA, van Veldhuisen DJ, Enjuanes C, Moliner P, et al. Iron deficiency contributes to resistance to endogenous erythropoietin in anaemic heart failure patients. *Eur J Heart Fail*. 2021; **23**: 1677–1686.
273. Graham FJ, Masini G, Pellicori P, Cleland JGF, Greenlaw N, Friday J, et al. Natural history and prognostic significance of iron deficiency and anaemia in ambulatory patients with chronic heart failure. *Eur J Heart Fail*. 2022; **24**: 807–817.
274. Chopra VK, Anker SD. Anaemia, iron deficiency and heart failure in 2020: facts and numbers. *ESC Heart Fail*. 2020; **7**: 2007–2011.
275. Barandiaran Aizpurua A, Sanders-van Wijk S, Brunner-La Rocca HP, Henkens M, Weerts J, Spanjers MHA, et al. Iron deficiency impacts prognosis but less exercise capacity in heart failure with preserved ejection fraction. *ESC Heart Fail*. 2021; **8**: 1304–1313.
276. Ponikowski P, Kirwan BA, Anker SD, McDonagh T, Dorobantu M, Drozdz J, et al. Ferric carboxymaltose for iron deficiency at discharge after acute heart failure: a multicentre, double-blind, randomised, controlled trial. *Lancet*. 2020; **396**: 1895–1904.
277. Metra M, Jankowska EA, Pagnesi M, Anker SD, Butler J, Dorigotti F, et al. Impact of ischaemic aetiology on the efficacy of intravenous ferric carboxymaltose in patients with iron deficiency and acute heart failure: insights from the AFFIRM-AHF trial. *Eur J Heart Fail*. 2022; **24**: 1928–1939.
278. Becher PM, Schrage B, Benson L, Fudim M, Corovic Cabrera C, Dahlstrom U, et al. Phenotyping heart failure patients for iron deficiency and use of intravenous iron therapy: data from the Swedish Heart Failure Registry. *Eur J Heart Fail*. 2021; **23**: 1844–1854.
279. Savarese G, von Haehling S, Butler J, Cleland JG, Ponikowski P, Anker SD. Iron deficiency and cardiovascular disease. *Eur Heart J*. 2022.
280. Sierpinski R, Josiak K, Suchocki T, Wojtas-Polc K, Mazur G, Butrym A, et al. High soluble transferrin receptor in patients with heart failure: a measure of iron deficiency and a strong predictor of mortality. *Eur J Heart Fail*. 2021; **23**: 919–932.
281. Docherty KF, Curtain JP, Anand IS, Bengtsson O, Inzucchi SE, Kober L, et al. Effect of dapagliflozin on anaemia in DAPA-HF. *Eur J Heart Fail*. 2021; **23**: 617–628.
282. Ferreira JP, Anker SD, Butler J, Filippatos G, Iwata T, Salsali A, et al. Impact of anaemia and the effect of empagliflozin in heart failure with reduced ejection fraction: findings from EMPEROR-Reduced. *Eur J Heart Fail*. 2022; **24**: 708–715.
283. Mazer CD, Hare GMT, Connelly PW, Gilbert RE, Shehata N, Quan A, et al. Effect of empagliflozin on erythropoietin levels, iron stores, and red blood cell morphology in patients with type 2 diabetes mellitus and coronary artery disease. *Circulation*. 2020; **141**: 704–707.
284. Kalra PR, Cleland JGF, Petrie MC, Thomson EA, Kalra PA, Squire IB, et al. Intravenous ferric derisomaltose in patients with heart failure and iron deficiency in the UK (IRONMAN): an investigator-initiated, prospective, randomised, open-label, blinded-endpoint trial. *Lancet*. 2022.
285. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, et al. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension: developed by the Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS). Endorsed by the International Society for Heart and Lung Transplantation (ISHLT) and the European Reference Network on rare respiratory diseases (ERN-LUNG). *Eur Heart J*. 2022; **43**: 3618–3731.
286. Riccardi M, Pagnesi M, Sciatti E, Lombardi CM, Inciardi RM, Metra M, et al. Combined pre- and post-capillary pulmonary hypertension in left heart disease. *Heart Fail Rev*. 2022.
287. Nakagawa A, Yasumura Y, Yoshida C, Okumura T, Tateishi J, Yoshida J,

et al. Prognostic importance of right ventricular-vascular uncoupling in acute decompensated heart failure with preserved ejection fraction. *Circ Cardiovasc Imaging*. 2020; **13**: e011430.
288. Obokata M, Reddy YNV, Melenovsky V, Pislaru S, Borlaug BA. Deterioration in right ventricular structure and function over time in patients with heart failure and preserved ejection fraction. *Eur Heart J*. 2019; **40**: 689–697.
289. van Wezenbeek J, Kianzad A, van de Bovenkamp A, Wessels J, Mouratoglou SA, Braams NJ, et al. Right ventricular and right atrial function are less compromised in pulmonary hypertension secondary to heart failure with preserved ejection fraction: a comparison with pulmonary arterial hypertension with similar pressure overload. *Circ Heart Fail*. 2022; **15**: e008726.
290. Lim HS, Gustafsson F. Pulmonary artery pulsatility index: physiological basis and clinical application. *Eur J Heart Fail*. 2020; **22**: 32–38.
291. Santiago-Vacas E, Lupon J, Gavidia-Bovadilla G, Gual-Capllonch F, de Antonio M, Domingo M, et al. Pulmonary hypertension and right ventricular dysfunction in heart failure: prognosis and 15-year prospective longitudinal trajectories in survivors. *Eur J Heart Fail*. 2020; **22**: 1214–1225.
292. Patel RB, Li E, Benefield BC, Swat SA, Polsinelli VB, Carr JC, et al. Diffuse right ventricular fibrosis in heart failure with preserved ejection fraction and pulmonary hypertension. *ESC Heart Fail*. 2020; **7**: 253–263.
293. Task Force for the Management of COVID-19 of the European Society of Cardiology, Baigent C, Windecker S, Andreini D, Arbelo E, Barbato E, et al. European Society of Cardiology guidance for the diagnosis and management of cardiovascular disease during the COVID-19 pandemic: part 1—epidemiology, pathophysiology, and diagnosis. *Cardiovasc Res*. 2022; **118**: 1385–1412.
294. Italia L, Tomasoni D, Bisegna S, Pancaldi E, Stretti L, Adamo M, et al. COVID-19 and heart failure: from epidemiology during the pandemic to myocardial injury, myocarditis, and heart failure sequelae. *Front Cardiovasc Med*. 2021; **8**: 713560.
295. Tomasoni D, Adamo M, Italia L, Branca L, Chizzola G, Fiorina C, et al. Impact of COVID-2019 outbreak on prevalence, clinical presentation and outcomes of ST-elevation myocardial infarction. *J Cardiovasc Med (Hagerstown)*. 2020; **21**: 874–881.
296. Konig S, Hohenstein S, Meier-Hellmann A, Kuhlen R, Hindricks G, Bollmann A, et al. In-hospital care in acute heart failure during the COVID-19 pandemic: insights from the German-wide Helios hospital network. *Eur J Heart Fail*. 2020; **22**: 2190–2201.
297. Cannata A, Bromage DI, Rind IA, Gregorio C, Bannister C, Albarjas M, et al. Temporal trends in decompensated heart failure and outcomes during COVID-19: a multisite report from heart failure referral centres in London. *Eur J Heart Fail*. 2020; **22**: 2219–2224.
298. Nadarajah R, Wu J, Hurdus B, Asma S, Bhatt DL, Biondi-Zoccai G, et al. The collateral damage of COVID-19 to cardiovascular services: a meta-analysis. *Eur Heart J*. 2022; **43**: 3164–3178.
299. Bromage DI, Cannata A, Rind IA, Gregorio C, Piper S, Shah AM, et al. The impact of COVID-19 on heart failure hospitalization and management: report from a Heart Failure Unit in London during the peak of the pandemic. *Eur J Heart Fail*. 2020; **22**: 978–984.
300. Tomasoni D, Inciardi RM, Lombardi CM, Tedino C, Agostoni P, Ameri P, et al. Impact of heart failure on the clinical course and outcomes of patients hospitalized for COVID-19. Results of the Cardio-COVID-Italy multicentre study. *Eur J Heart Fail*. 2020; **22**: 2238–2247.
301. Tomasoni D, Italia L, Adamo M, Inciardi RM, Lombardi CM, Solomon SD, et al. COVID-19 and heart failure: from infection to inflammation and angiotensin II stimulation. Searching for evidence from a new disease. *Eur J Heart Fail*. 2020; **22**: 957–966.
302. Rey JR, Caro-Codon J, Rosillo SO, Iniesta AM, Castrejon-Castrejon S, Marco-Clement I, et al. Heart failure in COVID-19 patients: prevalence, incidence and prognostic implications. *Eur J Heart Fail*. 2020; **22**: 2205–2215.
303. Lebek S, Tafelmeier M, Messmann R, Provaznik Z, Schmid C, Maier LS, et al. Angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker treatment and haemodynamic factors are associated with increased cardiac mRNA expression of angiotensin-converting enzyme 2 in patients with cardiovascular disease. *Eur J Heart Fail*. 2020; **22**: 2248–2257.
304. Bean DM, Kraljevic Z, Searle T, Bendayan R, Kevin O, Pickles A, et al. Angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers are not associated with severe COVID-19 infection in a multi-site UK acute hospital trust. *Eur J Heart Fail*. 2020; **22**: 967–974.
305. Savarese G, Benson L, Sundstrom J, Lund LH. Association between renin–angiotensin–aldosterone system inhibitor use and COVID-19 hospitalization and death: a 1.4 million patient nationwide registry analysis. *Eur J Heart Fail*. 2021; **23**: 476–485.
306. Ameri P, Inciardi RM, Di Pasquale M, Agostoni P, Bellasi A, Camporotondo R, et al. Pulmonary embolism in patients with COVID-19: characteristics and outcomes in the Cardio-COVID Italy multicenter study. *Clin Res Cardiol*. 2021; **110**: 1020–1028.
307. Paris S, Inciardi RM, Lombardi CM, Tomasoni D, Ameri P, Carubelli V, et al. Implications of atrial fibrillation on the clinical course and outcomes of hospitalized COVID-19 patients: results of the Cardio-COVID-Italy multicentre study. *Europace*. 2021; **23**: 1603–1611.
308. Caro-Codon J, Rey JR, Buno A, Iniesta AM, Rosillo SO, Castrejon-Castrejon S, et al. Characterization of NT-proBNP in a large cohort of COVID-19 patients. *Eur J Heart Fail*. 2021; **23**: 456–464.
309. Iorio A, Lombardi CM, Specchia C, Merlo M, Nuzzi V, Ferraro I, et al. Combined role of troponin and natriuretic peptides measurements in patients with Covid-19 (from the Cardio-COVID-Italy multicenter study). *Am J Cardiol*. 2022; **167**: 125–132.
310. Yoo J, Grewal P, Hotelling J, Papamanoli A, Cao K, Dhaliwal S, et al. Admission NT-proBNP and outcomes in patients without history of heart failure hospitalized with COVID-19. *ESC Heart Fail*. 2021; **8**: 4278–4287.
311. Lassen MCH, Skaarup KG, Lind JN, Alhakak AS, Sengelov M, Nielsen AB, et al. Recovery of cardiac function following COVID-19—ECHOVID-19: a prospective longitudinal cohort study. *Eur J Heart Fail*. 2021; **23**: 1903–1912.
312. Zaccone G, Tomasoni D, Italia L, Lombardi CM, Metra M. Myocardial involvement in COVID-19: an interaction between comorbidities and heart failure with preserved ejection fraction. A further indication of the role of inflammation. *Curr Heart Fail Rep*. 2021; **18**: 99–106.
313. Hadzibegovic S, Lena A, Churchill TW, Ho JE, Potthoff S, Denecke C, et al. Heart failure with preserved ejection fraction according to the HFA-PEFF score in COVID-19 patients: clinical correlates and echocardiographic findings. *Eur J Heart Fail*. 2021; **23**: 1891–1902.
314. Lambadiari V, Mitrakou A, Kountouri A, Thymis J, Katogiannis K, Korakas E, et al. Association of COVID-19 with impaired endothelial glycocalyx, vascular function and myocardial deformation 4 months after infection. *Eur J Heart Fail*. 2021; **23**: 1916–1926.
315. Latif F, Farr MA, Clerkin KJ, Habal MV, Takeda K, Naka Y, et al. Characteristics and outcomes of recipients of heart transplant with coronavirus disease 2019. *JAMA Cardiol*. 2020; **5**: 1165–1169.
316. Itzhaki Ben Zadok O, Shaul AA, Ben-Avraham B, Yaari V, Ben Zvi H, Shostak Y, et al. Immunogenicity of the BNT162b2 mRNA vaccine in heart transplant recipients—a prospective cohort study. *Eur J Heart Fail*. 2021; **23**: 1555–1559.

317. Zhang Y, Coats AJS, Zheng Z, Adamo M, Ambrosio G, Anker SD, et al. Management of heart failure patients with COVID-19: a joint position paper of the Chinese Heart Failure Association & National Heart Failure Committee and the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2020; **22**: 941–956.
318. Task Force for the Management of COVID-19 of the European Society of Cardiology. ESC guidance for the diagnosis and management of cardiovascular disease during the COVID-19 pandemic: part 2—care pathways, treatment, and follow-up. *Eur Heart J*. 2022; **43**: 1059–1103.
319. Task Force for the Management of COVID-19 of the European Society of Cardiology. European Society of Cardiology guidance for the diagnosis and management of cardiovascular disease during the COVID-19 pandemic: part 1—epidemiology, pathophysiology, and diagnosis. *Eur Heart J*. 2022; **43**: 1033–1058.
320. Lombardi CM, Cimino G, Pellicori P, Bonelli A, Inciardi RM, Pagnesi M, et al. Congestion in patients with advanced heart failure: assessment and treatment. *Heart Fail Clin*. 2021; **17**: 575–586.
321. Pagnesi M, Lombardi CM, Chiarito M, Stolfo D, Baldetti L, Loiacono F, et al. Prognostic impact of the updated 2018 HFA-ESC definition of advanced heart failure: results from the HELP-HF registry. *Eur J Heart Fail*. 2022; **24**: 1493–1503.
322. Vishram-Nielsen JKK, Tomasoni D, Gustafsson F, Metra M. Contemporary drug treatment of advanced heart failure with reduced ejection fraction. *Drugs*. 2022; **82**: 375–405.
323. Mann DL, Givertz MM, Vader JM, Starling RC, Shah P, McNulty SE, et al. Effect of treatment with sacubitril/valsartan in patients with advanced heart failure and reduced ejection fraction: a randomized clinical trial. *JAMA Cardiol*. 2022; **7**: 17–25.
324. Crespo-Leiro MG, Costanzo MR, Gustafsson F, Khush KK, Macdonald PS, Potena L, et al. Heart transplantation: focus on donor recovery strategies, left ventricular assist devices, and novel therapies. *Eur Heart J*. 2022; **43**: 2237–2246.
325. Padkins M, Breen T, Anavekar N, van Diepen S, Henry TD, Baran DA, et al. Age and shock severity predict mortality in cardiac intensive care unit patients with and without heart failure. *ESC Heart Fail*. 2020; **7**: 3971–3982.
326. Griffith BP, Goerlich CE, Singh AK, Rothblatt M, Lau CL, Shah A, et al. Genetically modified porcine-to-human cardiac xenotransplantation. *N Engl J Med*. 2022; **387**: 35–44.
327. Ben Gal T, Ben Avraham B, Milicic D, Crespo-Leiro MG, Coats AJS, Rosano G, et al. Guidance on the management of left ventricular assist device (LVAD) supported patients for the non-LVAD specialist healthcare provider: executive summary. *Eur J Heart Fail*. 2021; **23**: 1597–1609.
328. Karason K, Lund LH, Dalen M, Bjorklund E, Grinnemo K, Braun O, et al. Randomized trial of a left ventricular assist device as destination therapy versus guideline-directed medical therapy in patients with advanced heart failure. Rationale and design of the SWEdish evaluation of left Ventricular Assist Device (SweVAD) trial. *Eur J Heart Fail*. 2020; **22**: 739–750.
329. Mehra MR, Naka Y, Uriel N, Goldstein DJ, Cleveland JC Jr, Colombo PC, et al. A fully magnetically levitated circulatory pump for advanced heart failure. *N Engl J Med*. 2017; **376**: 440–450.
330. Mehra MR, Cleveland JC Jr, Uriel N, Cowger JA, Hall S, Horstmanshof D, et al. Primary results of long-term outcomes in the MOMENTUM 3 pivotal trial and continued access protocol study phase: a study of 2200 HeartMate 3 left ventricular assist device implants. *Eur J Heart Fail*. 2021; **23**: 1392–1400.
331. Kato TS, Chokshi A, Singh P, Khawaja T, Cheema F, Akashi H, et al. Effects of continuous-flow versus pulsatile-flow left ventricular assist devices on myocardial unloading and remodeling. *Circ Heart Fail*. 2011; **4**: 546–553.
332. Kassner A, Oezpeker C, Gummert J, Zittermann A, Gartner A, Tiesmeier J, et al. Mechanical circulatory support does not reduce advanced myocardial fibrosis in patients with end-stage heart failure. *Eur J Heart Fail*. 2021; **23**: 324–334.
333. Randhawa VK, West L, Luthman J, Estep JD, Soltesz EG, Starling RC. Sacubitril/valsartan in patients post-left ventricular assist device implant: a single-centre case series. *Eur J Heart Fail*. 2020; **22**: 1490–1492.
334. Yuzefpolskaya M, Lumish HS, Javaid A, Cagliostro B, Mondellini GM, Bohn B, et al. Association of preoperative infections, nasal *Staphylococcus aureus* colonization and gut microbiota with left ventricular assist device outcomes. *Eur J Heart Fail*. 2021; **23**: 1404–1415.
335. Mehra MR, Crandall DL, Gustafsson F, Jorde UP, Katz JN, Netuka I, et al. Aspirin and left ventricular assist devices: rationale and design for the international randomized, placebo-controlled, non-inferiority ARIES HM3 trial. *Eur J Heart Fail*. 2021; **23**: 1226–1237.
336. Butler J, Khan MS, Mori C, Filippatos GS, Ponikowski P, Comin-Colet J, et al. Minimal clinically important difference in quality of life scores for patients with heart failure and reduced ejection fraction. *Eur J Heart Fail*. 2020; **22**: 999–1005.
337. Ravera A, Santema BT, Sama IE, Meyer S, Lombardi CM, Carubelli V, et al. Quality of life in men and women with heart failure: association with outcome, and comparison between the Kansas City Cardiomyopathy Questionnaire and the EuroQol 5 dimensions questionnaire. *Eur J Heart Fail*. 2021; **23**: 567–577.
338. Turgeon RD, Barry AR, Hawkins NM, Ellis UM. Pharmacotherapy for heart failure with reduced ejection fraction and health-related quality of life: a systematic review and meta-analysis. *Eur J Heart Fail*. 2021; **23**: 578–589.
339. Shah SJ, Cowie MR, Wachter R, Szecsody P, Shi V, Ibram G, et al. Baseline characteristics of patients in the PARALLAX trial: insights into quality of life and exercise capacity in heart failure with preserved ejection fraction. *Eur J Heart Fail*. 2021; **23**: 1541–1551.
340. Hill L, Prager Geller T, Baruah R, Beattie JM, Boyne J, de Stoutz N, et al. Integration of a palliative approach into heart failure care: a European Society of Cardiology Heart Failure Association position paper. *Eur J Heart Fail*. 2020; **22**: 2327–2339.
341. Sahlollbey N, Lee CKS, Shirin A, Joseph P. The impact of palliative care on clinical and patient-centred outcomes in patients with advanced heart failure: a systematic review of randomized controlled trials. *Eur J Heart Fail*. 2020; **22**: 2340–2346.
342. Tomasoni D, Lombardi CM, Sbolli M, Cotter G, Metra M. Acute heart failure: more questions than answers. *Prog Cardiovasc Dis*. 2020; **63**: 599–606.
343. Gupta AK, Tomasoni D, Sidhu K, Metra M, Ezekowitz JA. Evidence-based management of acute heart failure. *Can J Cardiol*. 2021; **37**: 621–631.
344. Lombardi C, Peveri G, Cani D, Latta F, Bonelli A, Tomasoni D, et al. In-hospital and long-term mortality for acute heart failure: analysis at the time of admission to the emergency department. *ESC Heart Fail*. 2020; **7**: 2650–2661.
345. Harjola VP, Parissis J, Bauersachs J, Brunner-La Rocca HP, Bueno H, Celutkiene J, et al. Acute coronary syndromes and acute heart failure: a diagnostic dilemma and high-risk combination. A statement from the Acute Heart Failure Committee of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2020; **22**: 1298–1314.
346. Labrosciano C, Horton D, Air T, Tavella R, Beltrame JF, Zeitz CJ, et al. Frequency, trends and institutional variation in 30-day all-cause mortality and unplanned readmissions following hospitalisation for heart failure in Australia and New Zealand. *Eur J Heart Fail*. 2021; **23**: 31–40.
347. Davison BA, Senger S, Sama IE, Koch GG, Mebazaa A, Dickstein K, et al. Is acute heart failure a distinctive disorder? An analysis from BIOSTAT-CHF. *Eur J Heart Fail*. 2021; **23**: 43–57.

348. Goetze JP, Balling L, Deis T, Struck J, Bergmann A, Gustafsson F. Bioactive adrenomedullin in plasma is associated with biventricular filling pressures in patients with advanced heart failure. *Eur J Heart Fail*. 2021; **23**: 489–491.
349. Feng S, Janwanishstaporn S, Teerlink JR, Metra M, Cotter G, Davison B, et al. Association of left ventricular ejection fraction with worsening renal function in patients with acute heart failure: insights from the RELAX-AHF-2 study. *Eur J Heart Fail*. 2021; **23**: 58–67.
350. Biegus J, Zymlinski R, Testani J, Marciniak D, Zdanowicz A, Jankowska EA, et al. Renal profiling based on estimated glomerular filtration rate and spot urine sodium identifies high-risk acute heart failure patients. *Eur J Heart Fail*. 2021; **23**: 729–739.
351. Ter Maaten JM, Beldhuis IE, van der Meer P, Krikken JA, Coster JE, Nieuwland W, et al. Natriuresis-guided therapy in acute heart failure: rationale and design of the Pragmatic Urinary Sodium-based treatment algoritHm in Acute Heart Failure (PUSH-AHF) trial. *Eur J Heart Fail*. 2022; **24**: 385–392.
352. McCambridge J, Keane C, Walshe M, Campbell P, Heyes J, Kalra PR, et al. The prehospital patient pathway and experience of care with acute heart failure: a comparison of two health care systems. *ESC Heart Fail*. 2021; **8**: 1076–1084.
353. Mullens W, Dauw J, Martens P, Verbrugge FH, Nijst P, Meekers E, et al. Acetazolamide in acute decompensated heart failure with volume overload. *N Engl J Med*. 2022; **387**: 1185–1195.
354. Trullas JC, Morales-Rull JL, Casado J, Freitas Ramirez A, Manzano L, Formiga F, et al. Rationale and design of the "Safety and Efficacy of the Combination of Loop with Thiazide-type Diuretics in Patients with Decompensated Heart Failure (CLOROTIC) trial:" a double-blind, randomized, placebo-controlled study to determine the effect of combined diuretic therapy (loop diuretics with thiazide-type diuretics) among patients with decompensated heart failure. *J Card Fail*. 2016; **22**: 529–536.
355. Greene SJ, Velazquez EJ, Anstrom KJ, Eisenstein EL, Sapp S, Morgan S, et al. Pragmatic design of randomized clinical trials for heart failure: rationale and design of the TRANSFORM-HF trial. *JACC Heart Fail*. 2021; **9**: 325–335.
356. Mentz RJ. Torsemide comparison with furosemide for management of heart failure—TRANSFORM-HF. 2022. https://www.acc.org/Latest-in-Cardiology/Clinical-Trials/2022/11/04/13/43/transform-hf. Accessed 18 Nov 2022.
357. Voors AA, Angermann CE, Teerlink JR, Collins SP, Kosiborod M, Biegus J, et al. The SGLT2 inhibitor empagliflozin in patients hospitalized for acute heart failure: a multinational randomized trial. *Nat Med*. 2022; **28**: 568–574.
358. Boorsma EM, Beusekamp JC, Ter Maaten JM, Figarska SM, Danser AHJ, van Veldhuisen DJ, et al. Effects of empagliflozin on renal sodium and glucose handling in patients with acute heart failure. *Eur J Heart Fail*. 2021; **23**: 68–78.
359. Schulze PC, Bogoviku J, Westphal J, Aftanski P, Haertel F, Grund S, et al. Effects of early empagliflozin initiation on diuresis and kidney function in patients with acute decompensated heart failure (EMPAG-HF). *Circulation*. 2022; **146**: 289–298.
360. Rosano GMC, Vitale C, Adamo M, Metra M. Roadmap for the management of heart failure patients during the vulnerable phase after heart failure hospitalizations: how to implement excellence in clinical practice. *J Cardiovasc Med (Hagerstown)*. 2022; **23**: 149–156.
361. Mebazaa ADB, Chioncel O, Cohen-Solal A, Diaz R, Filippatos G, Metra M, Ponikowski P, Sliwa K, Voors AA, Edwards C, Novosadova M, Takagi K, Damasceno A, Saidu H, Gayat E, Pang PS, Celutkiene J, Cotter G. Safety, tolerability and efficacy of up-titration of guideline-directed medical therapies for acute heart failure (STRONG-HF): a multinational, open-label, randomised, trial. *Lancet*. 2022; **S0140-6736**: 02076-1.
362. Teerlink JR, Davison BA, Cotter G, Maggioni AP, Sato N, Chioncel O, et al. Effects of serelaxin in patients admitted for acute heart failure: a meta-analysis. *Eur J Heart Fail*. 2020; **22**: 315–329.
363. Carubelli V, Zhang Y, Metra M, Lombardi C, Felker GM, Filippatos G, et al. Treatment with 24 hour istaroxime infusion in patients hospitalised for acute heart failure: a randomised, placebo-controlled trial. *Eur J Heart Fail*. 2020; **22**: 1684–1693.
364. Metra M, Chioncel O, Cotter G, Davison B, Filippatos G, Mebazaa A, et al. Safety and efficacy of istaroxime in patients with acute heart failure-related pre-cardiogenic shock—a multicentre, randomized, double-blind, placebo-controlled, parallel group study (SEISMiC). *Eur J Heart Fail*. 2022; **24**: 1967–1977.
365. Mockel M, de Boer RA, Slagman AC, von Haehling S, Schou M, Vollert JO, et al. Improve Management of acute heart failure with ProcAlCiTonin in EUrope: results of the randomized clinical trial IMPACT EU Biomarkers in Cardiology (BIC) 18. *Eur J Heart Fail*. 2020; **22**: 267–275.
366. Chioncel O, Parissis J, Mebazaa A, Thiele H, Desch S, Bauersachs J, et al. Epidemiology, pathophysiology and contemporary management of cardiogenic shock—a position statement from the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2020; **22**: 1315–1341.
367. Aissaoui N, Puymirat E, Delmas C, Ortuno S, Durand E, Bataille V, et al. Trends in cardiogenic shock complicating acute myocardial infarction. *Eur J Heart Fail*. 2020; **22**: 664–672.
368. Lu DY, Adelsheimer A, Chan K, Yeo I, Krishnan U, Karas MG, et al. Impact of hospital transfer to hubs on outcomes of cardiogenic shock in the real world. *Eur J Heart Fail*. 2021; **23**: 1927–1937.
369. Schrage B, Beer BN, Savarese G, Dabboura S, Yan I, Sundermeyer J, et al. Eligibility for mechanical circulatory support devices based on current and past randomised cardiogenic shock trials. *Eur J Heart Fail*. 2021; **23**: 1942–1951.
370. Task Force for the Management of COVID-19 of the European Society of Cardiology. ESC guidance for the diagnosis and management of cardiovascular disease during the COVID-19 pandemic: part 2—care pathways, treatment, and follow-up. *Cardiovasc Res*. 2022; **118**: 1618–1666.
371. Galinier M, Roubille F, Berdague P, Brierre G, Cantie P, Dary P, et al. Telemonitoring versus standard care in heart failure: a randomised multicentre trial. *Eur J Heart Fail*. 2020; **22**: 985–994.
372. Koehler J, Stengel A, Hofmann T, Wegscheider K, Koehler K, Sehner S, et al. Telemonitoring in patients with chronic heart failure and moderate depressed symptoms: results of the Telemedical Interventional Monitoring in Heart Failure (TIM-HF) study. *Eur J Heart Fail*. 2021; **23**: 186–194.
373. Bekfani T, Fudim M, Cleland JGF, Jorbenadze A, von Haehling S, Lorber A, et al. A current and future outlook on upcoming technologies in remote monitoring of patients with heart failure. *Eur J Heart Fail*. 2021; **23**: 175–185.
374. Zakeri R, Morgan JM, Phillips P, Kitt S, Ng GA, McComb JM, et al. Impact of remote monitoring on clinical outcomes for patients with heart failure and atrial fibrillation: results from the REM-HF trial. *Eur J Heart Fail*. 2020; **22**: 543–553.
375. van Veldhuisen DJ, van Woerden G, Gorter TM, van Empel VPM, Manintveld OC, Tieleman RG, et al. Ventricular tachyarrhythmia detection by implantable loop recording in patients with heart failure and preserved ejection fraction: the VIP-HF study. *Eur J Heart Fail*. 2020; **22**: 1923–1929.
376. Angermann CE, Assmus B, Anker SD, Asselbergs FW, Brachmann J, Brett ME, et al. Pulmonary artery pressure-guided therapy in ambulatory

patients with symptomatic heart failure: the CardioMEMS European Monitoring Study for Heart Failure (MEMS-HF). *Eur J Heart Fail*. 2020; **22**: 1891–1901.
377. Almufleh A, Desai AS, Fay R, Ferreira JP, Buckley LF, Mehra MR, et al. Correlation of laboratory haemoconcentration measures with filling pressures obtained via pulmonary arterial pressure sensors in ambulatory heart failure patients. *Eur J Heart Fail*. 2020; **22**: 1907–1911.
378. Mullens W, Sharif F, Dupont M, Rothman AMK, Wijns W. Digital health care solution for proactive heart failure management with the Cordella Heart Failure System: results of the SIRONA first-in-human study. *Eur J Heart Fail*. 2020; **22**: 1912–1919.
379. Bozkurt B, Fonarow GC, Goldberg LR, Guglin M, Josephson RA, Forman DE, et al. Cardiac rehabilitation for patients with heart failure: *JACC* Expert Panel. *J Am Coll Cardiol*. 2021; **77**: 1454–1469.
380. Kitzman DW, Whellan DJ, Duncan P, Pastva AM, Mentz RJ, Reeves GR, et al. Physical rehabilitation for older patients hospitalized for heart failure. *N Engl J Med*. 2021; **385**: 203–216.
381. Klompstra L, Kyriakou M, Lambrinou E, Piepoli MF, Coats AJS, Cohen-Solal A, et al. Measuring physical activity with activity monitors in patients with heart failure: from literature to practice. A position paper from the Committee on Exercise Physiology and Training of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2021; **23**: 83–91.
382. de Boer RA, Hulot JS, Tocchetti CG, Aboumsallem JP, Ameri P, Anker SD, et al. Common mechanistic pathways in cancer and heart failure. A scientific roadmap on behalf of the Translational Research Committee of the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). *Eur J Heart Fail*. 2020; **22**: 2272–2289.
383. Tromp J, Boerman LM, Sama IE, Maass S, Maduro JH, Hummel YM, et al. Long-term survivors of early breast cancer treated with chemotherapy are characterized by a pro-inflammatory biomarker profile compared to matched controls. *Eur J Heart Fail*. 2020; **22**: 1239–1246.
384. Anker MS, Sanz AP, Zamorano JL, Mehra MR, Butler J, Riess H, et al. Advanced cancer is also a heart failure syndrome: a hypothesis. *Eur J Heart Fail*. 2021; **23**: 140–144.
385. Anker MS, von Haehling S, Coats AJS, Riess H, Eucker J, Porthun J, et al. Ventricular tachycardia, premature ventricular contractions, and mortality in unselected patients with lung, colon, or pancreatic cancer: a prospective study. *Eur J Heart Fail*. 2021; **23**: 145–153.
386. Dobbin SJH, Mangion K, Berry C, Roditi G, Basak S, Sourbron S, et al. Cardiotoxicity and myocardial hypoperfusion associated with anti-vascular endothelial growth factor therapies: prospective cardiac magnetic resonance imaging in patients with cancer. *Eur J Heart Fail*. 2020; **22**: 1276–1277.
387. Jacobse JN, Steggink LC, Sonke GS, Schaapveld M, Hummel YM, Steenbruggen TG, et al. Myocardial dysfunction in long-term breast cancer survivors treated at ages 40–50 years. *Eur J Heart Fail*. 2020; **22**: 338–346.
388. Boekel NB, Duane FK, Jacobse JN, Hauptmann M, Schaapveld M, Sonke GS, et al. Heart failure after treatment for breast cancer. *Eur J Heart Fail*. 2020; **22**: 366–374.
389. Rubio-Infante N, Ramirez-Flores YA, Castillo EC, Lozano O, Garcia-Rivas G, Torre-Amione G. Cardiotoxicity associated with immune checkpoint inhibitor therapy: a meta-analysis. *Eur J Heart Fail*. 2021; **23**: 1739–1747.
390. Rizzo S, De Gaspari M, Basso C. Immune checkpoint inhibitor myocarditis: a call for standardized histopathologic criteria. *Eur J Heart Fail*. 2021; **23**: 1736–1738.
391. Palaskas NL, Segura A, Lelenwa L, Siddiqui BA, Subudhi SK, Lopez-Mattei J, et al. Immune checkpoint inhibitor myocarditis: elucidating the spectrum of disease through endomyocardial biopsy. *Eur J Heart Fail*. 2021; **23**: 1725–1735.
392. Lyon AR, Lopez-Fernandez T, Couch LS, Asteggiano R, Aznar MC, Bergler-Klein J, et al. 2022 ESC guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS). *Eur Heart J*. 2022; **43**: 4229–4361.
393. Restrepo-Cordoba MA, Wahbi K, Florian AR, Jimenez-Jaimez J, Politano L, Arad M, et al. Prevalence and clinical outcomes of dystrophin-associated dilated cardiomyopathy without severe skeletal myopathy. *Eur J Heart Fail*. 2021; **23**: 1276–1286.
394. Linhart A, Germain DP, Olivotto I, Akhtar MM, Anastasakis A, Hughes D, et al. An expert consensus document on the management of cardiovascular manifestations of Fabry disease. *Eur J Heart Fail*. 2020; **22**: 1076–1096.
395. Jackson AM, Petrie MC, Frogoudaki A, Laroche C, Gustafsson F, Ibrahim B, et al. Hypertensive disorders in women with peripartum cardiomyopathy: insights from the ESC EORP PPCM Registry. *Eur J Heart Fail*. 2021; **23**: 2058–2069.
396. Finocchiaro G, Merlo M, Sheikh N, De Angelis G, Papadakis M, Olivotto I, et al. The electrocardiogram in the diagnosis and management of patients with dilated cardiomyopathy. *Eur J Heart Fail*. 2020; **22**: 1097–1107.
397. Sanna GD, De Bellis A, Zecchin M, Beccu E, Carta P, Moccia E, et al. Prevalence, clinical and instrumental features of left bundle branch block-induced cardiomyopathy: the CLIMB registry. *ESC Heart Fail*. 2021; **8**: 5589–5593.
398. Merlo M, Cannata A, Pio Loco C, Stolfo D, Barbati G, Artico J, et al. Contemporary survival trends and aetiological characterization in non-ischaemic dilated cardiomyopathy. *Eur J Heart Fail*. 2020; **22**: 1111–1121.
399. Halliday BP, Wassall R, Lota AS, Khalique Z, Gregson J, Newsome S, et al. Withdrawal of pharmacological treatment for heart failure in patients with recovered dilated cardiomyopathy (TRED-HF): an open-label, pilot, randomised trial. *Lancet*. 2019; **393**: 61–73.
400. Halliday BP, Owen R, Gregson J, Vassiliou SV, Chen X, Wage R, et al. Myocardial remodelling after withdrawing therapy for heart failure in patients with recovered dilated cardiomyopathy: insights from TRED-HF. *Eur J Heart Fail*. 2021; **23**: 293–301.
401. Masri A, Olivotto I. Cardiac myosin inhibitors as a novel treatment option for obstructive hypertrophic cardiomyopathy: addressing the core of the matter. *J Am Heart Assoc*. 2022; **11**: e024656.
402. Merlo M, Pagura L, Porcari A, Cameli M, Vergaro G, Musumeci B, et al. Unmasking the prevalence of amyloid cardiomyopathy in the real world: results from Phase 2 of the AC-TIVE study, an Italian nationwide survey. *Eur J Heart Fail*. 2022.
403. Nitsche C, Aschauer S, Kammerlander AA, Schneider M, Poschner T, Duca F, et al. Light-chain and transthyretin cardiac amyloidosis in severe aortic stenosis: prevalence, screening possibilities, and outcome. *Eur J Heart Fail*. 2020; **22**: 1852–1862.
404. Rosenblum H, Masri A, Narotsky DL, Goldsmith J, Hamid N, Hahn RT, et al. Unveiling outcomes in coexisting severe aortic stenosis and transthyretin cardiac amyloidosis. *Eur J Heart Fail*. 2021; **23**: 250–258.
405. Ternacle J, Krapf L, Mohty D, Magne J, Nguyen A, Galat A, et al. Aortic stenosis and cardiac amyloidosis: *JACC* review topic of the week. *J Am Coll Cardiol*. 2019; **74**: 2638–2651.
406. Jaiswal V, Ang SP, Chia JE, Abdelazem EM, Jaiswal A, Biswas M, et al. Echocardiographic predictors of presence of cardiac amyloidosis in aortic stenosis. *Eur Heart J Cardiovasc Imaging*. 2022; **23**: 1290–1301.
407. Randhawa VK, Vakamudi S, Phelan DM, Samaras CJ, McKenney JK, Hanna M, et al. Mitral and tricuspid stenosis caused by light chain cardiac amyloid deposition. *ESC Heart Fail*. 2020; **7**: 1130–1135.
408. Garcia-Pavia P, Bengel F, Brito D, Damy T, Duca F, Dorbala S, et al. Expert

consensus on the monitoring of transthyretin amyloid cardiomyopathy. *Eur J Heart Fail*. 2021; **23**: 895–905.
409. Fagot J, Lavie-Badie Y, Blanchard V, Fournier P, Galinier M, Carrie D, et al. Impact of tricuspid regurgitation on survival in patients with cardiac amyloidosis. *ESC Heart Fail*. 2021; **8**: 438–446.
410. Nicol M, Deney A, Lairez O, Vergaro G, Emdin M, Carecci A, et al. Prognostic value of cardiopulmonary exercise testing in cardiac amyloidosis. *Eur J Heart Fail*. 2021; **23**: 231–239.
411. Muller ML, Butler J, Heidecker B. Emerging therapies in transthyretin amyloidosis—a new wave of hope after years of stagnancy? *Eur J Heart Fail*. 2020; **22**: 39–53.
412. Adam RD, Coriu D, Jercan A, Badelita S, Popescu BA, Damy T, et al. Progress and challenges in the treatment of cardiac amyloidosis: a review of the literature. *ESC Heart Fail*. 2021; **8**: 2380–2396.
413. Bezard M, Kharoubi M, Galat A, Poullot E, Guendouz S, Fanen P, et al. Natural history and impact of treatment with tafamidis on major cardiovascular outcome-free survival time in a cohort of patients with transthyretin amyloidosis. *Eur J Heart Fail*. 2021; **23**: 264–274.
414. Damy T, Garcia-Pavia P, Hanna M, Judge DP, Merlini G, Gundapaneni B, et al. Efficacy and safety of tafamidis doses in the Tafamidis in Transthyretin Cardiomyopathy Clinical Trial (ATTR-ACT) and long-term extension study. *Eur J Heart Fail*. 2021; **23**: 277–285.
415. Aimo A, Castiglione V, Rapezzi C, Franzini M, Panichella G, Vergaro G, et al. RNA-targeting and gene editing therapies for transthyretin amyloidosis. *Nat Rev Cardiol*. 2022; **19**: 655–667.
416. Gentile P, Merlo M, Peretto G, Ammirati E, Sala S, Della Bella P, et al. Post-discharge arrhythmic risk stratification of patients with acute myocarditis and life-threatening ventricular tachyarrhythmias. *Eur J Heart Fail*. 2021; **23**: 2045–2054.
417. Ammirati E, Varrenti M, Veronese G, Fanti D, Nava A, Cipriani M, et al. Prevalence and outcome of patients with acute myocarditis and positive viral search on nasopharyngeal swab. *Eur J Heart Fail*. 2021; **23**: 1242–1245.
418. Heidecker B, Dagan N, Balicer R, Eriksson U, Rosano G, Coats A, et al. Myocarditis following COVID-19 vaccine: incidence, presentation, diagnosis, pathophysiology, therapy, and outcomes put into perspective. A clinical consensus document supported by the Heart Failure Association of the European Society of Cardiology (ESC) and the ESC Working Group on Myocardial and Pericardial Diseases. *Eur J Heart Fail*. 2022.
419. Sinagra G, Porcari A, Gentile P, Artico J, Fabris E, Bussani R, et al. Viral presence-guided immunomodulation in lymphocytic myocarditis: an update. *Eur J Heart Fail*. 2021; **23**: 211–216.
420. Hazebroek MR, Henkens M, Raafs AG, Verdonschot JAJ, Merken JJ, Dennert RM, et al. Intravenous immunoglobulin therapy in adult patients with idiopathic chronic cardiomyopathy and cardiac parvovirus B19 persistence: a prospective, double-blind, randomized, placebo-controlled clinical trial. *Eur J Heart Fail*. 2021; **23**: 302–309.
421. Tschope C, Van Linthout S, Jager S, Arndt R, Trippel T, Muller I, et al. Modulation of the acute defence reaction by eplerenone prevents cardiac disease progression in viral myocarditis. *ESC Heart Fail*. 2020; **7**: 2838–2852.