ESC European Society of Cardiology

European Journal of Heart Failure (2023) **25**, 445–447
doi:10.1002/ejhf.2866

April 2023 at a glance: focus on diagnosis and comorbidities

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Consensus statements

Advanced heart failure

Patients with advanced heart failure (HF) have poor prognosis and severe impairment of quality of life.[1,2] Improving their treatment is a major unmet need.[3] In this issue of the Journal, the Heart Failure Association (HFA) of the European Society of Cardiology (ESC) provides a consensus statement on the pharmacology, indications and unmet needs regarding inotropic agents in patients with advanced HF, focusing also on palliative care and end-of-life aspects.[4]

Pulmonary arterial hypertension

Treatment of primary pulmonary arterial hypertension (PAH) has consistently improved in the last years.[5,6] The ESC developed quality indicators for the assessment of care and outcomes in adults with PAH. Such quality indicators provide a tool to implement patients' adherence to guideline-directed medical therapy (GDMT) and to improve their prognosis.[7]

Epidemiology, diagnosis and assessment

Patient-reported outcomes (PROs) are major endpoints in HF clinical trials though some aspects remain unsettled.[8,9] Zannad *et al.*[10] suggest standardization and implementation of PROs not only for clinical trials but also in clinical practice, involving patients, as well as their families and caregivers.

Hypertension is a major cause of HF.[11,12] Pugliese *et al.*[13] analysed the hypertensive response to exercise (HRE) in 369 patients with HF, 201 subjects at risk of HF and 58 healthy controls using cardiopulmonary exercise testing and echocardiography. After adjusting for age and sex, the systolic blood pressure/workload slope was similar in patients with HF and reduced ejection fraction (HFrEF) vs. control subjects. Hypertensive subjects and patients with HF and preserved ejection fraction (HFpEF) had an increased slope. At 16-month follow-up, HRE was independently associated with adverse outcomes.

Cardiac amyloidosis

Sex differences have been described among patients with transthyretin amyloidosis (ATTR).[14] In a multicentre study involving 330 consecutive patients with transthyretin cardiac amyloidosis (ATTR-CA), Aimo *et al.*[15] showed that interventricular septum and posterior wall thickness were lower in women than men, although most differences were abolished when indexing by body surface area, height, or weight$^{2.7}$. The adoption of different left ventricular thickness cut-off values as a red flag of cardiac amyloidosis could reduce the risk of underdiagnosis.[2,15,16] In elderly patients, ATTR-CA is often assumed to be associated with the wild-type ATTR form.[16,17] However, the prevalence of variant ATTR-CA (ATTRv-CA) was of 20.7% among 2029 patients aged ≥70 years with ATTR-CA from the UK National Amyloidosis Centre. The ATTRv-CA was associated with increased risk of all-cause mortality, especially when related to the V122I mutation.[18]

Comorbidities

Cancer

Cancer and HF may share common pathways.[19,20] Dobbin *et al.*[21] examined the association between cancer history and outcomes in patients with HFrEF or HFpEF enrolled in the PARADIGM-HF, ATMOSPHERE, PARAGON-HF and CHARM-Preserved trials. Overall, 658 (4.3%) and 624 (8.5%) patients had a history of cancer in the HFrEF and HFpEF trials, respectively. HFrEF patients with a history of cancer had a higher risk of HF hospitalization and non-cardiovascular (CV) death than those without. Patients with HFpEF with and without a history of cancer had a similar outcome.

Iron deficiency

Iron deficiency is common among patients with HF and intravenous (IV) iron improves quality of life and outcomes in them.[22–26] A meta-analysis including 10 randomized controlled trials and 3373 patients evaluated the impact of IV iron administration on outcome. IV iron reduced the composite of recurrent HF hospitalization and CV death (rate ratio 0.75, 95% confidence interval [CI] 0.61–0.93; $p < 0.01$) and first hospitalization for HF or CV death (odds ratio 0.72, 95% CI 0.53–0.99; $p = 0.04$).[27]

Mitral regurgitation

Mitral regurgitation (MR) is associated with poor prognosis in patients with both chronic HF and worsening HF.[28,29] Pagnesi *et al.*[30] investigated the impact of MR on outcomes in patients with acute HF enrolled in the Relaxin in Acute Heart Failure 2 (RELAX-AHF-2) trial. Out of 6420 patients with available data regarding MR, 1810 patients (28.2%) had moderate/severe MR. These patients had a worse clinical profile compared to patients with no/mild MR and had a higher unadjusted risk of the composite of CV death or rehospitalization for HF/renal failure. However, the association between moderate/severe MR and poorer outcome was not maintained at multivariable analysis.

Multiple factors may affect the outcome of patients with severe MR undergoing percutaneous treatment.[31–34] Feng *et al.*[35] assessed the role of serum albumin in 559 patients with baseline serum albumin levels available enrolled in the COAPT trial (median albumin level 4.0 g/dl, interquartile range 3.7–4.2 g/dl). Patients with albumin <4.0 g/dl were older, had higher 4-year rates of all-cause death, but a similar risk of HF hospitalizations or all-cause hospitalizations, compared to those with albumin ≥4.0 g/dl. Transcatheter edge-to-edge repair (TEER) of secondary MR was more effective than GDMT alone, irrespective of baseline levels of serum albumin.

Mechanical circulatory support

The mortality of cardiogenic shock remains exceedingly high.[36] Shrage *et al.*[37] compared with propensity matching 267 patients treated with mechanical circulatory support (MCS) with 267 patients treated without in a multicentre, international, cohort of patients with non-ischaemic cardiogenic shock. MCS was associated with a lower 30-day mortality (hazard ratio 0.76, 95% CI 0.59–0.97), even if complications occurred more frequently (e.g. severe bleeding: 16.5% vs. 6.4%, and access site-related ischaemia: 6.7% vs. 0%).

Cell therapy

Mesenchymal stromal cell therapy is emerging as a possible treatment option in HF patients.[38] SCIENCE was a European, multicentre, randomized trial, with the aim to investigate safety and efficacy of direct intramyocardial injections of adipose tissue-derived mesenchymal stromal cells in chronic ischaemic HFrEF patients. Overall, 133 patients were included and randomized 2:1 to either cell therapy or placebo. Treatment was safe, but the pre-defined endpoints were not reached and no improvement in cardiac function and symptoms was observed.[39]

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