March 2021 at a glance: focus on epidemiology, prevention and COVID-19

Matteo Pagnesi, Marianna Adamo, and Marco Metra

Cardiology and Cardiac Catheterization Laboratory, ASST Spedali Civili and Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Brescia, Italy

The universal definition of heart failure

This issue hosts a landmark paper with the universal definition of heart failure (HF) developed by the HF Association (HFA), the HF Society of America and the Japanese HF Society and endorsed by four other HF societies.[1] HF is defined as 'a clinical syndrome with symptoms and/or signs caused by a structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide levels and/or objective evidence of pulmonary or systemic congestion.' Four stages are described: Stage A, for patients at risk for HF but without evidence of heart disease; Stage B, pre-HF, for patients without current or prior symptoms or signs of HF but with evidence of structural heart disease or abnormal cardiac function, or elevated natriuretic peptide levels; Stage C, HF, for patients with current or prior symptoms and/or signs of HF caused by a structural and/or functional cardiac abnormality; Stage D, advanced HF, for patients with severe symptoms and/or signs of HF at rest, recurrent hospitalizations despite guideline-directed medical therapy (GDMT), refractory or intolerant to GDMT, and requiring advanced therapies such as transplant, mechanical circulatory support, or palliative care.[1] Stage D overlaps with advanced HF, as previously defined by a HFA position statement.[2] A classification of HF according to left ventricular ejection fraction (EF) is also adopted with patients classified into those with reduced EF (HFrEF, EF ≤40%), mildly reduced EF (HFmrEF, EF 41-49%), preserved EF (HFpEF, EF ≥50%) and improved EF (HFimpEF, baseline EF ≤40%, a ≥10 point increase in EF and a second EF >40%).[1] Attended by an outstanding editorial comments by Dr. Braunwald,[3] and in line with recent consensus recommendations on definitions for the assessment of HF therapies,[4] the universal definition of HF represents a fundamental framework to standardize the identification and classification of patients with HF both for daily practice and clinical studies.

Prevention

A substudy of SPRINT confirmed the role of kidney function and albuminuria for the prediction of HF events in hypertensive subjects. In addition, these variables did not influence the effects of intensive blood pressure control (target systolic blood pressure <120 mmHg), compared to standard treatment, for the reduction of HF risk.[5] In PREVEND, enrolling 8202 individuals with a mean follow-up of 11.3 ± 3.1 years, N-terminal pro-B-type natriuretic peptide (NT-proBNP), mid-regional pro-A-type natriuretic peptide (MR-proANP) and cardiac troponin T (cTnT) were associated with incident HF, and combined NT-proBNP and cTnT measurements improved HF risk prediction in overweight and obese subjects (both $P < 0.001$).[6] These findings reinforce available evidence on the role of NT-proBNP, and/or the NT-proBNP and troponin combination, for the prediction of incident HF.[7–9]

Epidemiology

Changes in the epidemiology and characteristics of cardiogenic shock and acute HF have occurred in the last years.[10–13] Consistently, a systematic review and meta-regression of 285 studies, representing 15 million acute HF events, found a decline in 30-day mortality [odds ratio (OR) for a 10-year increment, 0.74, 95% confidence interval (CI) 0.61–0.91, $P = 0.004$] and 1-year mortality (OR 0.86, 95% CI 0.77–0.96, $P = 0.007$) after acute HF, in the last four decades. However, 30-day and 1-year readmission rates were unchanged.[14]

Prognosis

Left ventricular EF remains the most important measurement to classify patients with HF.[1] In a cohort study on 499 153 patients in Australia, Stewart et al.[14] identified sex-based differences in the risk of mortality associated with a left ventricular EF <65.0–69.9%, nadir of mortality in both sexes, with a greater risk at higher left ventricular EF values in women, compared with men.

Advanced age is associated with a decline in GDMT use and higher mortality in patients with HF.[15] In an analysis of BIOSTAT-CHF, Mordi et al.[16] demonstrated that achieving higher doses of angiotensin-converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARBs) was associated with lower mortality or HF hospitalizations regardless of age, whereas achieving higher doses of β-blockers was associated with improved outcome only in younger patients (interaction $P = 0.034$). These findings could be helpful to refine ACEi/ARB and β-blocker up-titration in patients with HF.[17]

COVID-19

In line with available evidence showing worse clinical outcomes in COVID-19 patients with concomitant HF,[18–22] an analysis of a Spanish cohort showed that NT-proBNP is frequently elevated in COVID-19 and independently associated with mortality (adjusted hazard ratio per logarithmic unit 1.28, 95% CI 1.13–1.44, $P < 0.001$).[23] Cardiopulmonary and haemodynamic abnormalities characterize critically ill COVID-19 patients.[18,24] Of note, these patients showed a typical and rather specific inflammatory and cardiac myocyte-related microRNA up-regulation.[25]

Consistent with published data showing the lack of increased COVID-19 severity in patients treated with ACEi or ARBs despite increased ACE2 expression,[19,26,27] an analysis on 1.4 million patients from the Swedish National Patient Registry did not find an association between the use of ACEi/ARBs or mineralocorticoid receptor antagonists and an increased risk of hospitalization for or death from COVID-19.[28]

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