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January 2023 at a glance: focus on acute heart failure and medical therapy

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Pathophysiology

Several factors may favour development of heart failure (HF).[1,2] Shi *et al.*[3] assessed the association between clonal haematopoiesis of indeterminate potential (CHIP) and incident HF. A total of 374 participants with incident HF from the Prevention of Renal and Vascular End-stage Disease (PREVEND) cohort were matched 1:1 by age and sex with healthy controls. The frequency of CHIP was overlapping between the two groups and CHIP was not significantly associated with incident HF at multivariable Cox regression models. However, the association was modified by age (p for interaction = 0.002) and CHIP was more frequent in the case cohort compared to controls among those younger than 65 years.

Miranda *et al.*[4] compared exercise haemodynamics between 24 adult patients post-Fontan palliation, 48 patients with HF and preserved ejection fraction (HFpEF) and 48 subjects with non-cardiac dyspnoea (NCD). Resting and exercise pulmonary artery wedge pressure (PAWP) was lower in the Fontan group than HFpEF, but higher than NCD. However, there were no differences in ΔPAWP/ΔQs ratios between post-Fontan and HFpEF patients.

Acute heart failure

Acute heart failure (AHF) has a dramatic burden in terms of symptoms, morbidity and mortality.[5–8] Lee *et al.*[9] investigated the relationship between patient-reported symptoms, evaluated by the Kansas City Cardiomyopathy Questionnaire total symptom score (KCCQ-TSS) (range 0–100; 0 worst), and pulmonary congestion, assessed by lung ultrasound, physical examination and chest X-ray, in patients with AHF. A lower KCCQ-TSS was associated with worse New York Heart Association functional class and peripheral oedema but not with pulmonary congestion.

Intravenous diuretics are the first option for the treatment of congestion in patients with AHF. Data regarding the optimal strategy of their administration are limited.[10,11] Their early administration is often considered as crucial. Among 15 078 patients included in the REPORT-HF registry from seven regions of the world, the median time-to-diuretics was 67 (17–190) min. Time-to-diuretic administration did not have an impact on in-hospital mortality, but was associated with an increase in mortality risk at 30 days, especially in patients at higher risk.[12]

Cotter *et al.*[13] highlighted the importance of the vulnerable period after an episode of acute HF, namely the first 3–6 months post-discharge, that represent an opportunity to intervene and prevent adverse outcome. Therapies shown to be effective if initiated at discharge or in the immediate post-discharge period are available and should be rapidly up-titrated under close monitoring of patient's clinical status and laboratory values.[11,13,14]

A U-shaped relationship between left ventricular ejection fraction (LVEF) and outcome has recently been suggested, with HF patients with supranormal ejection fraction (HFsnEF) presenting a worse prognosis.[15–18] Among 6128 patients enrolled in the RELAX-AHF-2 trial, 55 (2.5%) patients had LVEF >65% and were classified as HFsnEF. Such patients were more likely to be female, with a high prevalence of non-ischaemic HF and presented lower levels of natriuretic peptides. This subgroup presented a higher-risk of non-cardiovascular mortality, compared to other LVEF ranges.[19]

Atrial fibrillation

Atrial fibrillation (AF) often coexists in patients with HFpEF and HF with mildly reduced ejection fraction (HFmrEF). Among 429 464 hospitalized patients with HFmrEF and HFpEF included in the Get With The Guidelines-Heart Failure Registry from 2014 to 2020, a half presented AF, with such proportion slightly increasing over time. The risk of mortality and readmission within 12 months was higher among patients with AF, especially in those with HFpEF. The use of anti-arrhythmic drugs was generally low.[20] Dronedarone has recently been associated with reduced cardiovascular events in patients with paroxysmal or persistent AF and HFpEF or HFmrEF.[21] The ARC-HF and CAMTAF trials randomized patients with persistent AF and HF with reduced ejection fraction (HFrEF) to early routine catheter ablation (CA) versus pharmacological rate control. At 12-month follow-up, patients who underwent early CA showed more symptoms improvement compared to the medical therapy cohort. After the completion of the trial, during a median follow-up of 7.8 (3.9–9.9) years, selected patients from the medical therapy group were referred to delayed CA. No differences in long-term outcome were reported between the early and delayed CA groups.[22]

Medical therapy

A post-hoc analysis of the PARAGON-HF trial, including 4796 patients, showed that patients with HFpEF on higher baseline diuretic doses were at increased risk of HF events. The benefit and safety of sacubitril/valsartan initiation was consistent across the whole spectrum of diuretic regimen.[23] Sacubitril/valsartan modestly reduced new loop diuretic initiations over the course of the trial (hazard ratio 0.83; 95% confidence interval 0.68–1.00, $p = 0.055$).[23] These results are consistent with previous studies showing the independent relationship between treatment with high diuretic doses and mortality.[10,24]

Chronic renal dysfunction or an acute decline in renal function often lead to mineralocorticoid receptor antagonist (MRA) underprescription or discontinuation.[24–26] A retrospective study using data from the Taiwan National Health Insurance Research Database (NHIRD) aimed to assess the effects of MRA in patients with HF and end-stage renal disease starting maintenance dialysis. Patients with an MRA prescription were matched 1:3 with patients without. The risk of both cardiovascular and all-cause mortality was lower among patients in the MRA group.[27] An individual-patient data meta-analysis including 984 patients with HFpEF from three large trials (HOMAGE, Aldo-DHF, and TOPCAT) compared echocardiographic changes in patients on spironolactone versus placebo . The prescription of spironolactone was associated with a reduction in left atrial volume, left ventricular mass and thickness and improved systolic and diastolic function.[28]

Sodium–glucose cotransporter 2 (SGLT2) inhibitors have a central role in the prevention and treatment of HF.[29–33] SGLT2 inhibitors reduced cardiovascular events regardless of several baseline characteristics.[34–36] Anker *et al.*[37] showed consistent benefits of empagliflozin compared to placebo across the whole ranges of body mass index in patients with HFrEF enrolled in the EMPEROR-Reduced trial. Weight loss was associated with higher risk of all-cause mortality, regardless of treatment group.

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