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# March 2023 at a glance: pathophysiology, medical therapy and devices

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## Pathophysiology and diagnosis

### Pulmonary circulation

Interatrial shunt (IAS) devices are emerging as a novel treatment option for patients with heart failure (HF) and mildly reduced or preserved ejection fraction (HFpEF).[1–3] Latent pulmonary vascular disease might affect the benefits of IAS devices.[1] Schuster *et al.*[4] hypothesized that non-invasive characterization of cardiac and pulmonary physiology by cardiac magnetic resonance (CMR) during exercise may help in patient selection for IAS. Overall, 75 patients with HFpEF who underwent rest and exercise stress right heart catheterization, echocardiography and CMR were included. Latent pulmonary vascular disease, defined as pulmonary vascular resistance during exercise stress ≥1.74 Wood units, was associated with impaired right ventricular (RV) functional reserve and diastolic filling with a consequent reduction in left ventricular cardiac index.

### Cardiac amyloidosis

Cardiac amyloidosis (CA) is associated with disproportionally elevated natriuretic peptide and troponin levels.[5,6] Vergaro *et al.*[7] investigated the diagnostic role of these biomarkers in 1149 patients with suspected CA who underwent a diagnostic work-up in three European centres ($n = 343$, derivation cohort; $n = 806$, validation cohort). N-terminal pro-B-type natriuretic peptide <180 ng/L and high-sensitivity troponin T (hs-TnT) <14 ng/L ruled out the diagnosis of CA, whereas hs-TnT ≥86 ng/L was found as a rule-in cut-off for CA.

## Acute heart failure

Several precipitating factors may lead to acute HF.[8,9] Among them non-cardiac surgery may have a role. Gualandro *et al.*[10] assessed the rate of acute HF in a large series of 9164 consecutive high-risk patients undergoing 11 262 non-cardiac inpatient surgeries. The incidence of acute HF after non-cardiac surgery was 2.5% in the general population and 10% in patients with a history of HF. Post-operative acute HF was an independent predictor of all-cause mortality (hazard ratio [HR] 1.7, 95% confidence interval [CI] 1.3–2.2]; $p < 0.001$) and HF readmission (HR 2.3, 95% CI 1.5–3.7; $p < 0.001$).[10]

## Medical therapy

Personalized care is an essential component of HF management.[11–14] The REWOLUTION HF (REal WOrLd EdUcaTION in HF) programme included two international surveys focused on the management of HF, directed to healthcare professionals, mostly cardiologists, and patients. Items related with quality of life had a similar importance as prolonging the duration of life for most of the patients. Healthcare professionals highlighted the need for a rapid initiation of all guideline-directed medical therapies (GDMT) instead of up-titration of some medications. The most common reasons behind GDMT withdrawal were side effects and intolerance (e.g. low blood pressure and renal dysfunction). The majority of patients reported no difficulties in following the medical prescriptions, although 21.4% considered the prescribed pills too numerous.[15]

Pulmonary hypertension in patients with left heart disease usually reflects increases in left atrial pressure. Isolated post-capillary pulmonary hypertension can progress to combined pre- and post-capillary pulmonary hypertension (CpcPH) when pulmonary vasoconstriction and arteriolar hypertrophy lead to an increase in pulmonary vascular resistance and pressure.[16] The β3 Adrenergic Agonist Treatment in Chronic Pulmonary Hypertension Secondary to Heart Failure (SPHERE-HF) is a multicentre, randomized trial with the aim to assess the efficacy of the selective β3 adrenoreceptor agonist mirabegron in the treatment of CpcPH. Overall, 80 patients were randomized to either mirabegron (50 mg daily, titrated till 200 mg daily) or placebo for 16 weeks. The primary endpoint was the change in pulmonary vascular resistance at right heart catheterization. Mirabegron did not affect the primary endpoint; however, it improved RV ejection fraction, a pre-specified secondary endpoint.[17]

Iron deficiency is a common comorbidity in HF.[18,19] Intravenous ferric carboxymaltose (FCM) reduced the risk of HF hospitalization, improved quality of life and RV function compared to placebo in patients with iron deficiency and HF.[20–23] However, FCM is still underused in clinical practice.[24] McEwan *et al.*[25] conducted a cost-effective analysis using data from five countries. The authors

showed that fewer hospitalizations and a shorter length of stay with FCM have a positive economic impact on healthcare systems.

## Devices

Mitral valve transcatheter edge-to-edge repair (TEER) is an important option for the treatment of secondary mitral regurgitation (SMR).[26–32] Contemporary real-world outcomes in SMR patients treated with third-generation MitraClip systems were evaluated in the prospective, multicentre, international, single-arm EXPAND study. Mitral regurgitation (MR) reduction to MR ≤1+ and MR ≤2+ was achieved in 93.0% and 98.5% of patients, respectively. All-cause mortality at 1 year was 17.7%, while the combined endpoint of all-cause mortality or first HF hospitalization occurred in 34% of patients.[33] In line with previous data,[34,35] an optimal procedural result, i.e. residual MR 1+ or less, was associated with a lower risk of clinical events after TEER.[33] Transcatheter mitral valve replacement (TMVR) may be performed in patients with SMR and high or prohibitive surgical risk.[36,37] Ludwig *et al.*[38] performed a propensity matched analysis comparing TEER and TMVR in patients with SMR. TMVR was associated with a greater reduction in MR severity and symptom improvement without differences in mortality beyond 30 days.

Mechanical circulatory support devices are useful options for the treatment of cardiogenic shock.[39] Varshney *et al.*[40] evaluated outcome in patients with cardiogenic shock bridged to durable left ventricular assist device (LVAD) or heart transplantation. Patients bridged with veno-arterial extracorporeal membrane oxygenation had the highest mortality (22%), followed by catheter-based temporary mechanical circulatory support (10%), intra-aortic balloon pump (9%), and medical therapy (7%). Compared with patients who underwent cardiac transplant, those who received LVAD had higher rates of post-operative complications.[40–42]

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