

# February 2021 at a glance: focus on amyloidosis, myocarditis and cardiomyopathy

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## Cardiac amyloidosis

### Prognosis

Cardiac amyloidosis (CA) is emerging as a major cause of heart failure (HF).<sup>1–3</sup> Castiglione *et al.*<sup>4</sup> reviewed the role of circulating biomarkers as tools to guide diagnosis, prognostic stratification, and therapy in CA. The independent prognostic role of cardiopulmonary exercise testing in patients with light chain or transthyretin CA (TTR-CA) was shown by Nicol *et al.*<sup>5</sup> in a multicentre study. Both peak oxygen consumption ( $\text{VO}_2$ )  $\leq 13$  mL/kg/min and N-terminal pro B-type natriuretic peptide (NT-proBNP)  $\geq 1800$  ng/L had independent prognostic value with a hazard ratio (HR) of 2.7 [95% confidence interval (CI) 1.6–4.8] and 2.2 (95% CI 1.1–4.3), respectively. No events occurred in patients with peak  $\text{VO}_2 > 13$  mL/kg/min and NT-proBNP  $< 1800$  ng/L during a median follow-up of 20 months, despite overall 25% mortality and 29% hospitalization rates.

### Association with aortic stenosis

Amyloidosis may be present in patients with severe aortic stenosis.<sup>2,6</sup> TTR-CA was detected in 13% of patients with severe aortic stenosis undergoing transcatheter aortic valve replacement. It had no impact on mortality but was associated with a higher HF hospitalization rate during a 3-year follow-up.<sup>3</sup>

### Therapy

Tafamidis has emerged as an effective treatment option to improve prognosis in patients with TTR-CA.<sup>7,8</sup> A single-centre study in 648 real-world patients with TTR-CA matching the inclusion criteria of the Tafamidis in Transthyretin Cardiomyopathy Clinical Trial (ATTR-ACT) showed a significant benefit of tafamidis on major cardiovascular outcomes (HR after propensity score matching 0.546,  $P = 0.0132$ ).<sup>9</sup> In an analysis of the long-term extension of ATTR-ACT, both tafamidis 80 mg and 20 mg reduced all-cause mortality and cardiovascular hospitalizations at 30 months compared with placebo, with the higher dose associated with better outcomes without safety issues in the long-term extension.<sup>10</sup>

## Myocarditis

Sinagra *et al.*<sup>11</sup> reviewed data about the role of viral detection for immunomodulation in acute lymphocytic myocarditis, highlighting current limitations of this approach and providing a framework for future dedicated studies. The Authors pointed out that the value of viral presence to guide immunosuppressive treatment in lymphocytic myocarditis requires more evidence and remains a subject of debate. As a further support, intravenous immunoglobulin did not improve cardiac systolic function or functional status in patients with chronic inflammatory cardiomyopathy, namely idiopathic dilated cardiomyopathy with parvovirus B19 persistence, in a randomized controlled trial.<sup>12</sup>

## Cardiomyopathy

Over the last years, improvement in survival was observed in patients with dilated cardiomyopathy, with many patients with new-onset cardiomyopathy who may show reverse remodelling.<sup>13,14</sup> In TRED-HF, withdrawal of pharmacological treatment for HF in patients with recovered dilated cardiomyopathy was associated with relapses in 44% of patients.<sup>15</sup> In a further analysis by cardiac magnetic resonance, treatment withdrawal resulted in early ventricular remodelling with an increase in myocardial mass and a reduction in global longitudinal strain. Interestingly, these changes may also occur in patients who do not show clinical deterioration.<sup>16</sup>

## Chronic heart failure

### Prognosis

Shorter left ventricular systolic ejection time has been identified as a marker of worse prognosis among patients with HF with reduced ejection fraction (HFrEF).<sup>17</sup> Alhakak *et al.*<sup>18</sup> confirmed the prognostic impact of left ventricular systolic ejection time on mortality in a large HFrEF population (per 10 ms decrease: adjusted HR 1.06, 95% CI 1.01–1.11,  $P = 0.030$ ), hence supporting its use to stratify patients' risk and to guide therapeutic response. Heightened chemosensitivity has a major role in the excessive ventilatory response to exercise and sleep breathing

abnormalities in patients with HF. Buspirone, a 5HT<sub>1A</sub> receptor agonist that inhibits serotonergic chemoreceptor neuron firing, reduced carbon dioxide chemosensitivity and improved central apnoeas in patients with HF.<sup>19</sup>

## Advanced heart failure

A relatively large number of patients with advanced HF may benefit from long-term mechanical circulatory support.<sup>20</sup> This indication might be further expanded if this device therapy may cause regression of myocardial fibrosis. Unfortunately, such hypothesis was not proven in a recent study in 125 patients.<sup>21</sup>

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