

## References

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## Optimisation of strategies for management of heart failure with preserved ejection fraction

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Editor – The review of empagliflozin for patients with heart failure and preserved ejection fraction (HFpEF) signals an important recognition that the management of HFpEF required a fundamentally different approach from the management of heart failure with reduced ejection fraction (HFrEF).<sup>1</sup> The key feature of HFpEF is that it responds best to preventive strategies that mitigate the risk of incident acute decompensated heart failure (ADHF), thereby significantly reducing rates of subsequent hospitalisation for ADHF rather than modifying the subsequent evolution of the natural history (including mortality risk) of that syndrome.

This effect was seen most strikingly in SPRINT, where intensive systolic blood pressure reduction (target systolic blood pressure <120 mmHg) resulted in a significant ( $p=0.003$ ) reduction in incident ADHF to the same extent in subjects with HFpEF and counterparts with HFrEF.<sup>2</sup> By analogy, in Zinman *et al*, among subjects at high risk of cardiovascular events, empagliflozin generated a significant ( $p=0.002$ ) reduction in risk of hospitalisations for incident ADHF, although, in the latter context, no documentation was made of the left ventricular ejection fraction subtypes.<sup>3</sup>

In the context of hypertension-related HFpEF, the operative factor for the efficacy of intensive systolic blood pressure control might be a mitigation of the risk of myocardial fibrosis, given the fact that in the animal model of hypertension, myocardial stiffness is determined by ventricular fibrosis.<sup>4</sup> In the context of use of sodium-glucose cotransporter-2 inhibitor therapy, mitigation of myocardial inflammation and, hence, myocardial fibrosis might be the operative factor for drug efficacy, given emerging evidence of the anti-inflammatory actions of this drug class.<sup>5–7</sup> Intensive blood pressure control also mitigates the risk of incident atrial fibrillation (AF), arguably by mitigating the risk of myocardial (including atrial) fibrosis.<sup>8</sup> Diabetes, in turn, is also a risk factor for incident AF, arguably as a consequence of the fact that it is a proinflammatory disorder.<sup>9,10</sup> Among patients with AF, modifiable risk factors for subsequent incident ADHF include both hypertension and diabetes.<sup>11</sup>

Accordingly, future management of HFpEF should optimise mitigation of risk of incident ADHF and risk of incident AF. ■

OSCAR JOLOBE

Retired geriatrician, Manchester, UK

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## The significance of the gut microbiome in post-COVID-19 gastrointestinal symptoms

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Editor – I read with interest the article by Cooney and colleagues in which 43.8% of the patients studied reported new-onset gastrointestinal (GI) symptoms in the 6 months after their acute COVID-19 illness and the authors suggest the possible existence of a post-COVID-19 irritable bowel syndrome (IBS).<sup>1</sup> The authors discuss the presence of the angiotensin converting enzyme 2 (ACE-2) receptor throughout the GI tract, which serves as the SARS-CoV-2 receptor, as an important potential factor. However, the potential relevance of gut microbiome disturbance in patients with COVID-19 was not discussed.