Discussion forum response to Canepa et al.

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This commentary refers to ‘Heart failure with preserved ejection fraction: from mechanisms to therapies’, by C.S.P. Lam et al., 2018;39:2780–2792.

We agree with Canepa et al. that hypertrophic cardiomyopathy (HCM) and amyloid cardiomyopathy are important specific diagnoses not to be missed, since they are treatable with specific therapies. By ‘Several specific diseases (e.g. infiltrative cardiomyopathies, amyloid, hypertrophic cardiomyopathy, high output failure, valvular heart disease, and pericardial disease) may present with HF but are not considered as the “common garden” heart failure with preserved ejection fraction (HFrEF) and shall not be discussed further’ we by no means meant to diminish the importance of these alternative diagnoses. Instead, we distinguished these specific diagnoses from the typical HFpEF described in large epidemiologic series and associated with multi-morbidity, because in contrast to the specific proven therapies for HCM and amyloid cardiomyopathy, no therapy has improved survival in typical HFpEF—the focus of our review.1,2 Such a focus was needed given the space constraints of a review article.

Nonetheless, Canepa et al. bring up the interesting discussion of whether specific cardiomyopathies should be included in the spectrum of HFrEF. We acknowledge the lack of consensus on this point: many investigators in this field would not consider infiltrative cardiomyopathies, amyloid, HCM, valvular heart disease, or pericardial disease as HFrEF but rather as differential diagnoses. As such, these specific underlying diagnoses have been largely excluded from the HFpEF outcome trials (e.g. I-PRESERVE, TOPCAT, PARAGON). On the other hand, others argue that such patients should be considered as HFpEF if they present with the clinical syndrome of typical symptoms and signs of HF, normal left ventricular ejection fraction (EF), and raised filling pressures. In fact, wild-type transthyretin amyloidosis has been shown to be present in 13% of such elderly patients with symptoms, EF ≥ 50% and left ventricular end-diastolic wall thickness ≥ 12 mm—a finding all the more note-worthy given the recent evidence of benefit with tafamidis for the treatment of transthyretin amyloid cardiomyopathy.4 To take the controversy even further, should a patient with severe coronary artery disease, normal EF and ischaemia-related elevated filling pressures be considered ‘HFrEF’ (no proven therapy) or ‘symptomatic coronary artery disease’ requiring coronary revascularization? Regardless of the ongoing debate on terminology, there is uniform agreement in the field that specific diagnoses of HCM or amyloid are important considerations, and patients should receive the most appropriate therapy for his/her condition including specific therapy where available.

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