

## Severity of heart failure and risk of incident diabetes: a reverse causation?

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*To the Editor:* We read with interest the article by Demant et al [1], which reported that severity of heart failure was associated with a graduated risk of new-onset diabetes. Demant et al underscored the importance of focusing on the underlying concomitant disease and its effect on future outcomes in patients with heart failure.

However, we think that it is premature to draw a conclusion on the cause-and-effect relationship between severity of heart failure and incident diabetes. In fact, the observation in the study can be explained by reverse causality: pre-existing metabolic disturbance resulting in a higher dosage of loop diuretics. Most of the risk factors for diabetes, e.g. race, weight, physical activity, dietary quality, smoking [2], were not presented in the article. As the renin–angiotensin system and sympathetic system activation are involved in obesity [3, 4], impaired glucose tolerance and prehypertension [5], contraction of renal artery smooth muscle could contribute to diuretic resistance, which can be reflected by a higher loop-diuretic dosage. Thus, the dosage of loop diuretic might be a proxy for metabolic disorder severity rather than heart failure severity. The higher proportion of patients with atrial flutter/fibrillation, chronic obstructive pulmonary disease and renal disease in the higher diuretic dosage groups shown in Table 1 of the paper by Demant et al [1] not only frequently coexists with more severe heart failure, but also closely associates with more serious metabolic syndrome [6, 7]. Thus, it is not clear whether more severe heart failure or more severe metabolic syndrome underlies the increased risk of diabetes in the patients receiving the higher diuretic dosage. In conclusion,

further investigations are urgently needed to assess the independent effect of heart failure on the risk of diabetes development.

**Duality of interest** The authors declare that there is no duality of interest associated with this manuscript.

**Contribution statement** Both HBT and CM contributed to the conception, drafting and final approval of the version to be published.

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