Reviewer’s report

Title: Cardiovascular Outcomes among Elderly Patients with Heart Failure and Coronary Artery Disease and without Atrial Fibrillation: a Retrospective Cohort Study

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Reviewer: Susan Stienen

Reviewer's report:

Zhao et al. studied the impact of coronary artery disease in newly diagnosed hospitalized heart failure patients with reduced ejection fraction AND without atrial fibrillation in a large retrospective cohort of Medicare patients. After propensity-score matching CV outcomes between patients with and without coronary artery disease (N=5,792 per group) were compared. They observed that mortality rates were equal between groups but that incidence rates of myocardial infarction and ischemic stroke were higher in the group of patients with coronary artery disease. There is limited real-world data on outcome in this type of HF patients and the research conducted by the authors is therefore relevant. The manuscript is well-written. However, i feel that there are methodological issues that need to be clarified. I have major comments and some suggestions:

Major:

1) Smoking status and heart failure severity are variables associated with prognosis in HF and may differ between CAD and non-CAD patients. Were these variables considered in the matching procedure? If not, it may be possible that CAD patients had more severe HF and therefore were more prone to for example ischemic strokes. Please clarify.

2) There is no information on medication use in this cohort and it seems that there was no matching for baseline medication. Was the assumption made that by matching patients on medical history in the baseline period medication use (most importantly anticoagulants) was balanced as well?

3) How were the endpoints myocardial infarction and ischemic stroke diagnosed? Also by coding? And what was the timing of collection of the information on the endpoints? This should be clarified (also in the methods section). Moreover, it seems from the kaplan - meier curves that there were patients lost to follow-up? Please clarify.
4) What is the rationale for a sensitivity analysis using a mix of both in- and outpatients. It is clear from previous research that prognosis differs between these types of patients. Moreover, there is no baseline table for this specific population and hence not clear for the reader if they were well-balanced after matching. Also it is not clear what the distribution of in- and outpatients is between CAD and no CAD patients. It is therefore very difficult/impossible to compare results with the primary analyses and likely confuses the reader. However, it may be interesting to study the in- and outpatient populations apart from each other in the primary analyses.

5) It was not clear for me from the title and abstract that the authors studied a specific population of HFrEF patients without atrial fibrillation. Also, the exact rationale for excluding these patients should be discussed. From the methods it seems that the presence of atrial fibrillation was based on a ICD code during the baseline period. However, it is known that atrial fibrillation and HF often co-occur (especially during admission). Were patients with AF during the index admission also excluded? And I feel that the limitations section should mention that a ICD-based AF code does not exclude the possibility that AF patients were included. Also it is possible that AF occurred later during follow-up.

6) It is not clear if the CAD diagnosis was based on information solely before the admission or also during the admission. Regular diagnostic work-up in de novo HF patients consists of coronary ischemia detection. Hence, when the period of admission is not considered for this classification it may be that patients were falsely classified as having non-CAD.

7) A large part of the discussion consists of the authors stating the necessity of exploring treatment options for HF patients with CAD without atrial fibrillation. However, they do not discuss the results of one of the latest landmark trials in this field: the COMMANDER-HF (Zannad et al. NEJM 2018). Please update the discussion in light of these results.

8) An interesting finding of this study are the equal mortality rates in CAD and non-CAD patients. Previous studies observed a higher mortality risk in CAD patients; can the authors elaborate on this finding? In my opinion, this should be mentioned in the discussion section.

Minor:

9) The number of patients with CAD is quite high (~70%) compared to other studies (for example Rusinaru et al Eur J HF 2014 which had ~40% of patients with CAD). Are there differences in CAD definition? Were patients with stable angina pectoris included in this study?

10) Patients with evidence for HF in the baseline period were excluded. How was this defined?
11) The CHADS2 score was amongst others used for matching. To my knowledge, the CHADSVASC score is validated in a HF population in sinus rhythm but not the CHADS2 score. What was the reason for determining the CHADS2 score and not the CHADSVASC?

12) Suggestion to clarify in Figure 1 which part is for the sensitivity analyses and which part for the primary analysis. Also, in case of patients lost to follow-up, please depict this in the flow diagram.

13) Reference 9 seems not correct (different article?), and ref 18 is not about HFrEF but HFpEF patients. Moreover, ref 13 refers to previous guidelines (2012), please update.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

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