Prediction of outcomes in patients with heart failure

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Summary

The main aim of this thesis is to explore risk factors associated to an increased risk of adverse outcomes for heart failure (HF) patients and improve the early re-admission or mortality prediction in HF.

The first part of the thesis includes the general introduction. HF is a progressive disease and a major cause of morbidity and mortality worldwide. HF disease management can be difficult because besides medical treatment it requires significant lifestyle changes such as exercise, restricted fluid and salt intake and medication adherence. Therefore, despite the improvements in disease management, HF is often associated with poor quality of life and multiple hospital admissions. A portion of re-admissions can be prevented by predicting if they will occur and tailoring disease management interventions accordingly. Hence, identifying risk factors affecting adverse events in HF patients is important for patients and healthcare providers, because they may lead to new methods to manage patients and optimize services.

We designed the OPERA-HF study in the UK, to explore a wide range of variables as potential risk factors. In addition to demographic, clinical, imaging and laboratory variables, we explored non-disease specific and non-clinical variables that could act as predictors for re-admission or mortality in patients with HF following an admission for HF. We aimed to identify variables that could improve the discrimination for re-admission or mortality prediction. In order to validate our findings and their generalizability beyond the development cohort we utilized the SAPHIRE study, a patient cohort from the US.

In the second part of the thesis, we study the impact of depression and other psychosocial factors on adverse outcomes. We conducted a systematic review and meta-analysis where we found that the prevalence of both depression and anxiety in the identified studies was on average 29%. We found that depression is a significant and

independent predictor of all-cause mortality among HF patients but with very hetero-geneous effects reported across the different studies. The heterogeneity was associated with the total study population size and the prevalence of depression in the study. On the other hand, there was no significant effect of anxiety on mortality identified.

Subsequently we confirmed the strong association of depression with increased risk of mortality, in the OPERA-HF study. Moderate-to-severe depression was independently associated to all-cause mortality in the year following discharge after an admission to hospital for HF when controlling for age, Charlson comorbidity index, NYHA class IV, NT-proBNP and treatment with mineralocorticoid receptor antagonist, beta-blocker and diuretics. In the OPERA-HF study, moderate-to-severe depression was also significantly associated with recurrent events: unplanned readmission or mortality. Other psychosocial or non-clinical variables independently associated with increasing risk of recurrent events in the year following discharge after a HF hospital admission were: presence of frailty, moderate-to-severe anxiety, living alone and the presence of cognitive impairment.

In the third part of the thesis, we used data from the OPERA-HF study to develop a 30-day composite outcome model and we explored the added predictive value of non-clinical predictors to early outcomes: 30-day unplanned readmission or mortality within 30 days. A model containing clinical variables alone had an area under the receiver-operating characteristic curve (AUC) of 0.68. By including physical frailty and social support in the model the AUC increased to 0.70. The discrimination of the model remained modest reflecting the difficulty in early readmission or mortality prediction due to the diversity in the readmission root causes.

We then used data from the SAPHIRE study to externally validate the model. Our results showed a good calibration and discrimination similar to the original. This means that the model can overcome any difference between the populations of two locations. Early event prediction remains challenging, however, our findings suggest that non-clinical factors may improve the predictions and they should not be neglected when assessing a patient's status and needs.

In the last part of the thesis, the general discussion, we summarize the findings, we provide answers to the main research questions addressed in this thesis and present recommendations for future research.