Biomarker discovery in heart failure

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Valorization

Heart Failure (HF) is recognized as an escalating public health problem in Western societies with ageing populations [51, 83]. In addition, HF is the most common reason for hospitalization in patients aged 65 years and over which imposes enormous health care costs related to relatively long hospital stays [81, 127]. Thus, HF accounts for almost 2% of health care budget in western countries and its total economic burden is increasing, the greatest portions attributable to HF related hospitalizations. These health care costs can be decreased by having a more precise diagnosis of disease in HF patients and implementing more effective therapy. Diagnosing HF and treating patients on clinical signs and symptoms can be challenging, as signs and symptoms of HF are not specific. Therefore, biomarkers might be helpful in this regard. The obtained results in this thesis improve implementation of biomarkers in diagnosis of HF and guiding individualized medical HF therapy. In addition, we developed new methods with the aim to facilitate investigation of biomarkers. In this thesis the analysis were based on the Trial of Intensified versus standard Medical therapy in Elderly patients with Congestive Heart Failure (TIME-CHF) study [19, 102]. In this chapter we provide valorization opportunities result from this thesis, which may be of interest for medical researchers, patients, clinicians and pharmaceutical companies.

Although HF patients are known to experience repeated hospitalizations, most studies only evaluated the time-to-first event and do not consider the impact of therapy after the initial event. The results in this thesis demonstrated that guiding the therapy based on N-terminal pro-B-type Natriuretic Peptide (NT-proBNP) versus standard symptoms reduces the risk of recurrent hospitalization in HF patients (Chapter 3). This leads to the decrease in hospitalization costs for the health system. Even more importantly, medical intervention studies usually use time-to-first event methods only. Our result show that these methods may result in the wrong conclusions.

The results in Chapter 6 suggest that repeated measurements of biomarkers might be helpful to individually tailor HF treatment to optimize the balance between beneficial and adverse effects of HF drugs in a particular patient. This might also be economically beneficial, since patients would have better outcome (less hospitalizations, less side effects) with less medication, thereby reducing costs. However, this novel predictive, preventive and personalized medicine approach clearly needs confirmation in other studies.

Dichotomizing continuous covariates is widespread in medical prognostic variable studies. In Chapter 4, we proposed a Bayesian approach to dichotomize continuous covariates. This might help clinicians to have a more precise interpretation of the covariate's

effect on the outcome variable and guides them in their choice of therapy. In addition, it can establish eligibility criteria for prospective studies. Moreover, some researchers prefer using dichotomized covariates since they are more straightforward to analyze and the interpretation of the results may be easier.

In Chapter 5, we proposed Generalized Ranking Accuracy (GRA) as a measure for assessing the goodness-of-fit as well as the predictive performance of the models trained on clustered data. Clustered data are very common in biomedical and clinical researches when the observations for each subject are repeated over time. Using GRA for models trained on the clinical cluster data may help the researchers in their result interpretations and help clinicians in making an appropriate treatment decision.