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REVIEW

The Biomarker Utility in Risk Stratification in an Ambulatory Heart Failure: ST2 or Galectin-3?

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ABSTRACT

Heart failure (HF) is multi factorial syndrome with high cardiovascular (CV) morbidity and mortality rates associated with an increasingly prevalence worldwide. Measuring plasma levels of cardiac biomarkers may assist in prognostication of HF. However, the role of biomarker models in prediction of death and re-admission in ambulatory HF patients is not still understood. This editorial comment explores the knowledge regarding head-to-head comparison of galectin-3 and ST2 in risk stratification among ambulatory HF individuals. The comment is indicated sST2 and galectin-3 are recommended as alternate biomarkers with defined predictive value in HF and in generally patient population at high risk of HF manifestation. Recent clinical studies do not allow solving whether sST2 is superior then galectin-3 in ambulatory patient with stable HF because the received results are not obvious, although sST2 appears to be more attractive. Probably, more investigations are required to explain the role of each alternate biomarker in HF prognostication.

Key words: Heart Failure; Biomarkers; Galectin-3; ST2; Prognostication; Risk Stratification

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Abbreviations
BNP: brain natriuretic peptide;
CAD: coronary artery disease;
CV: cardiovascular;
HF: heart failure;
HFpEF: heart failure with preserved ejection fraction;
HFrEF: heart failure with reduced ejection fraction;
LV: left ventricle.

INTRODUCTION

Heart failure (HF) remains an important clinical cause that leads to an increased CV mortality and morbidity worldwide[1]. The prevalence of HF gradually increases in developed countries due to improved survival after HF diagnosis[2]. Cardiac biomarkers are considered indispensable tools for diagnosis, risk stratification, and prognostication in acute, acutely decompensated and chronic HF[3-5], while the use of several biomarkers may now present different information in HF with preserved and reduced left ventricular (LV) ejection fraction (EF) especially in persons with various ages, sex and several co-morbidity including renal disease, diabetes, chronic obstructive pulmonary disease, and coronary artery disease[6-9]. The current clinical guidelines underline that serum natriuretic peptides (NPs) and cardiac troponins may demonstrate a limited predictive value for stable HF patients at discharge or at ambulatory and now recommend measurement of galectin-3 and ST2 for additive risk stratification in these settings[10-13]. Moreover, it has been suggested that galectin-3 and ST2 as alternative biomarkers might give insight into the different pathways of HF pathophysiology, and they probably could help to identify generally population individuals at higher risk of HF developing and HF patients with poor outcomes

beyond traditional limitations that are suitable for NPs and cardiac troponins[14-18]. The aim of the editorial comment is head-to-head comparison of galectin-3 and ST2 in risk stratification among ambulatory HF individuals.

GALECTIN-3

Galectin-3 is a soluble beta galactoside-binding lectin produced by activated macrophages which binds and activates the fibroblasts[19]. Results of recent studies have reported that galectin-3 is a biomarker that mediates an important link between inflammation and fibrosis, which play a pivotal role in CV remodeling[20]. The pathogenetic role of galectin-3 in the several setting of pressure overload, neuro-endocrine activation, hypertension, coronary artery disease/myocardial infarction, atrial fibrillation, and HF has strongly established[21-23].

Galectin-3 has emerged a predictive value for the onset of HF in apparently healthy patients and has been found being surrogate marker of a worse prognosis, mortality and re-admission in HF[24]. The results of the sub-study of COACH (The Coordinating Study Evaluating Outcomes of Advising and Counselling in Heart Failure) trial have shown that only galectin-3 was significantly associated with the absence of CV events at 180 days in patients with HF at low risk for death or HF re-hospitalization[25]. Therefore, authors indicated that this biomarker demonstrated an incremental value when added to the clinical risk model without NT-proBNP[25]. In fact, there are not irresistible evidences regarding being of clinically significant advantages of galectin-3 in prediction in HFpEF compared with HFrEF[26]. Interestingly, changes of galectin-3 levels within post discharge 6 months did not add prognostic information to the base-line value in stable HF subjects[27]. In this context, serial measurements of galectin-3 level in ambulatory HF patients might not be of benefit. Overall, galectin-3 is obviously powerful prognosticator of death and re-hospitalization in HF patients at discharge from the hospital and in generally population individuals at higher risk of HF development.

ST2

Soluble suppression of tumorigenicity 2 (sST2), a peptide belonging to the interleukin-1 receptor family, is secreted cardiomyocytes and cardiac fibroblasts under mechanical strain and thus it is concerned a biomarker of myocardial fibrosis, cardiac stretch and CV remodeling[28, 29]. Measurement of sST2 is useful for death risk stratification and prognosis prediction in HF patients beyond other CV risk factors, NYHA functional class, LFEF, and renal function[30,31]. Importantly that the addition of ST2 to a model that includes established mortality risk factors, including NPs, substantially improves the risk stratification for death and HF admission in HF patients[32]. Thus, sST2 appears to be a reliable prognosticator of advice outcomes in HF subjects irrespective of co-morbidity, fluid retention state, and CV risk factors.

HEAD-TO-HEAD COMPARISON OF GALECTIN-3 AND ST2

Although galectin-3 and sST2 represent equal physiopathological pathways in failing heart, recent studies have shown that sST2 may have a special superiority as a risk predictor in HFpEF and HFrEF compared with NPs and galectin-3 among stable patients at discharge from a hospital admission for acute HF[33-35]. Zhang et al[36] reported that sST2 improved prediction for death beyond risk factors without being influenced by renal function, whereas the prognostic value of galectin-3 is less clear below an eGFR of 60 ml/min/1.73 m^2. Miller et al[37] have assessed the value of serial measurements of sST2 and galectin-3 to identify risk for adverse pathophysiologic processes among highest-risk HF outpatients. The results of the study have clarified that both biomarkers might be valuable to guide ambulatory HF patient tailored therapy during follow-up evaluations, whereas sST2 was superior then galectin-3 in this setting. Zhou et al[38] believed that sST2 may possess special superiority as a risk predictor in HF patients when compared with other biomarkers. In generally, it may agree with issue mentioned above, while direct head-to-head comparisons of both biomarkers are limited and statistical power of these studies is not so much high as it is required to keeping in mind possible differences between predictive value of sST2 and galectin-3 in stable HF.

In conclusion, sST2 and galectin-3 are recommended as alternate biomarkers with defined predictive value in HF and in generally patient population at high risk of HF manifestation. Recent clinical studies do not allow solving whether sST2 is superior then galectin-3 in ambulatory patient with stable HF because the received results are not obvious, although sST2 appears to be more attractive. However, more investigations are required to explain the role of each alternate biomarker in HF prognostication.

CONFLICT OF INTERESTS

There are no conflicts of interest with regard to the present study.

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