Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/ihj

Sponsored Article

The Indian Consensus Document on cardiac biomarker

I. Satyamurthy [a,*], Jamshed J. Dalal [b], J.P.S. Sawhney [c], J.C. Mohan [d], Shubha A. Chogle [e], Nagaraj Desai [f], Shireesh P. Sathe [g], Alan S. Maisel [h]

[a] Director, Cardiology, Department of Cardiology at Apollo Hospitals, Chennai, India
[b] Director, Centre for Cardiac Sciences, Kokilaben Dhirubhai Ambani Hospital, Mumbai, India
[c] Chairman, Department of Cardiology and Member, Board of Management at Sir Gangaram Hospital, New Delhi, India
[d] Prof., Chief of Cardiology, Jaipur Golden Hospital, New Delhi, India
[e] Clinical Biochemist Breach Candy Hospital, Mumbai, India
[f] Professor and Advisor of Cardiology, SS Medical College and Hospital, Mysore, India
[g] Consultant Cardiologist, Director – Cardiology, Deenanath Mangeshkar Hospital, Pune, India
[h] Director, Coronary Care Unit and Heart Failure Program, VA San Diego, USA

Keywords:
Biomarkers
Heart failure
Brain natriuretic peptide
NT-proBNP

ABSTRACT

Despite recent advances, the diagnosis and management of heart failure evades the clinicians. The etiology of congestive heart failure (CHF) in the Indian scenario comprises of coronary artery disease, diabetes mellitus and hypertension. With better insights into the pathophysiology of CHF, biomarkers have evolved rapidly and received diagnostic and prognostic value. In CHF biomarkers prove as measures of the extent of pathophysiological derangement; examples include biomarkers of myocyte necrosis, myocardial remodeling, neurohormonal activation, etc. In CHF biomarkers act as indicators for the presence, degree of severity and prognosis of the disease, they may be employed in combination with the present conventional clinical assessments. These make the biomarkers feasible options against the present expensive measurements and may provide clinical benefits.

1. Introduction

A variety of circulating molecules referred to as biomarkers have been introduced in clinical cardiovascular research, including heart failure (HF) research, because of basic science discoveries and technological progress in the last decade. Research papers related to biomarker research in HF have been exponentially circulating over the last decade (Fig. 1). The dissemination of knowledge about biomarkers in HF clinical practice, however, is limited mostly to diagnostic uses of B-type natriuretic peptide (BNP) or its precursor fragment, N-terminal prohormone of brain natriuretic peptide (NT-proBNP). Biomarkers in circulation include a variety of molecules that range from traditional protein-based markers to newer markers and micro RNAs. Protein markers in circulation typically comprise hormones and prohormones with vasoactive properties which include natriuretic peptides

Abbreviations: BNP, B-type natriuretic peptide; HF, heart failure.

* *Corresponding author.* Tel.: +91 (0) 9840061262.
E-mail address: drismurthy@gmail.com (I. Satyamurthy).

0019-4832/$ – see front matter
http://dx.doi.org/10.1016/j.ihj.2013.12.053

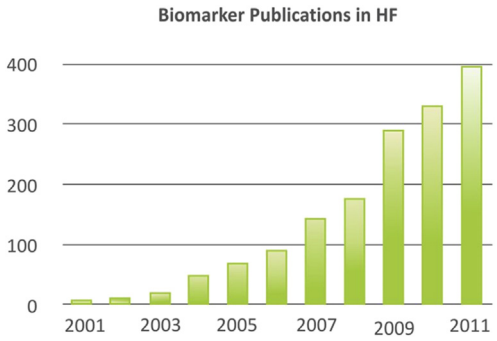

Fig. 1 – "Biomarker" and "Heart failure" articles published from 2001 to 2011.[1]

(NPs), endothelin, mid-regional pro-adrenomedullin, and C-terminal provasopressin (copeptin); structural proteins which include troponins; and various proteins with enzymatic activities which include myeloperoxidase and galectin-3. The current status of biomarker application for diagnosis and management of HF is confusing. A general framework proposed for cardiovascular biomarkers exists and this framework can help to identify the challenges of biomarker adoption for risk prediction, disease management, and treatment selection in HF.[1]

2. Pathogenesis of heart failure

Heart failure is a multi-factorial disease with causes varying in different parts of the world. Minimum 50% of the patients with HF have a reduced ejection fraction (REF) i.e. HF-REF which is the most understood type of HF in terms of the disease pathophysiology and treatment. In approximately two-thirds of cases of systolic HF, coronary artery disease (CAD) is the cause, although hypertension and diabetes are probable contributing factors in many cases. Other factors responsible for HF include a history of viral infections (known or unknown), chemotherapy (e.g., doxorubicin or trastuzumab), alcohol abuse, and 'idiopathic' dilated cardiomyopathy (in some of the cases the cause may be genetic).[2]

The epidemiological profile in HF with preserved ejection fraction (HF-PEF) seems to be different from epidemiological and etiological profile in HF-REF. The patient with HF-PEF is older, and more often female and obese than those with HF-REF. They are less likely to have coronary heart disease and more likely to have hypertension and atrial fibrillation (AF). As compared to patients with HF-REF, the patients with HF-PEF have better prognosis.[2]

When LV systolic function is reduced, the maladaptive changes occur in surviving myocytes and in extracellular matrix after myocardial injury (e.g., myocardial infarction) that lead to pathological 'remodeling' of the ventricle with dilatation and impaired contractility, one measure of which is a reduced EF. In cases of unmanaged systolic dysfunction, there is progressive worsening of these changes over time with an increased enlargement of the left ventricle and declining EF, the patient may be symptomless initially.[2]

This progression occurs due to two mechanisms, of which the first one is occurrence of further events leading to additional myocyte death (e.g., recurrent myocardial infarction). The second mechanism is the systemic responses that are induced by the decline in systolic function, particularly neurohumoral activation. The renin-angiotensin-aldosterone system and sympathetic nervous system are the two key neurohumoral systems activated in HF. These systemic responses cause further myocardial injury; leading to detrimental effects on the blood vessels, kidneys, muscles, lungs, and liver; and form a pathophysiological 'vicious cycle', responsible for various clinical features of the HF syndrome, including myocardial electrical instability.[2]

The basis of much of the effective treatment of HF is interruption of these two key processes. The aforementioned changes are associated with the clinical development of symptoms and worsening of these over time. This results in reduced quality of life, degrading functional capacity, recurring frank decompensation episodes leading to hospitalization and premature death, commonly as a result of arrhythmias or pump failure. These patients have a limited cardiac reserve which also is dependent on atrial contraction, synchronized contraction of atria–ventricles and a normal interaction between the right and left ventricles.[2]

Acute decompensation can result from intercurrent events affecting any of these [e.g., the development of AF or conduction abnormalities, such as left bundle branch block (LBBB)] or imposing an additional hemodynamic load on the failing heart (e.g., anemia). The outcome of HF patients can be improved with effective treatment, with a relative reduction of 30–50% in hospitalization in recent years, and small but significant decrease in mortality.[2]

3. Incidence of heart failure: Indian scenario

Framingham study was a landmark study indicating that the incidence of CHF increases with age and is higher in men than in women. Although data on incidence of HF from India are scarce, a 2013 study from India was conducted to measure the burden of disease. This study was conducted in southern India and it was found that 258 males (82%) and 137 females (73%) had left ventricular HF predominantly, as compared to biventricular HF. In this study, an interesting feature noted was that multi-factorial cause was the commonest etiology for CHF with CAD being the single most common factor contributing to 66% of cases of HF. Out of all cases of CAD in this study, 66% cases of HF were men and 34% were women.[3] Coronary artery disease in the Framingham study, accounted for only 46% of cases of HF in men and 27% of chronic HF cases in women. Following CAD, hypertension was the leading factor accounting for 65.6% of cases in this study, while 45.8% of the population was diabetic. They are, however, not mutually exclusive. In the Indian study, it was also found that myocardial infarction in siblings was a significant risk factor. 69% of the patients in the present study had hypertension; among them 61% were males and 39% were females. There were 310 (62%) males and 190 (38%) females. The highest incidence of HF was observed between 50 and 70 years in both males and females. The researchers from the Indian study