From lactate to soluble urokinase plasminogen activator receptor: The journey for ideal cardiac biomarker: Are we there in 2016?

New biomarkers are being constantly developed and made available for diagnosis of cardiovascular disease. The most important aspect of adopting any new biomarker in clinical practice is its ability to change treatment, impact the duration of stay, improve outcomes in the patient disease, and ultimately prove to be cost effective.[1]

Biomarker measurements are predictive of a need of urgent care in an emergency, cardiac triage. Causal pathways for the progression of atheromatous coronary plaque formation in most cardiac patient’s remains poorly understood, hence, the need for biomarkers for early detection.

An important part of our understanding the treatment of acute coronary syndrome is the recognition that sensitive markers of myocardial injury, specifically cardiac troponin I (CTN I) and CTN T, actually define a group of patients who are sick and sensitivity of troponins over the previous creatine kinase (CK-MB) has literally changed the operational definition of what constitutes an acute myocardial infarction, today in 2016! The purpose of this editorial is to provide a better understanding of the journey of cardiac biomarkers from CK-MB, lactate to brain natriuretic peptide (BNP), to the high-sensitivity troponin, lactate clearance, and soluble urokinase plasminogen activator receptor (suPAR) and their potential role in predicting survival in the cardiac ICU (see page nos 4, 7, 105 and 112) respectively.

One of the most crucial, unresolved challenges in face of tissue hypoxia and cardiac shock is to detect a physiological variable that closely detects cellular hypoperfusion and thus be used as an accurate resuscitation target. Hyperlactemia has traditionally been used as a signal of tissue hypoxia.[2] Above serum lactate, lactate clearance has been shown in recent times to be of prognostic value in community-acquired pneumonia,[3] severe sepsis[4] congenital heart defects corrections such as arterial switch operation with regressed left ventricular.[5] In this issue, read on lactate clearance as a prognostic marker in Tetralogy of Fallot and also how endothelin, SCVO₂, and lactate are related! Neutrophil gelatinase-associated lipocalin (NGAL), in off-pump coronary artery bypass grafting, makes interesting reading telling us about interrelations between renal function and ischemia and how to better outcomes. Lactate clearance, endothelin, NGAL, and albumin levels (particularly, in cyanotics, are here to stay and more randomized, multicentric trials are needed with evidence-based algorithms to prove their utility.[6,7]

BNP as a biomarker in heart failure and for prediction of postoperative atrial fibrillation in cardiac and noncardiac patients is already proven.[8,9] Read on “N-terminal pro-B-type natriuretic peptide in high-cardiovascular-risk patients for noncardiac surgery: What is the current prognostic evidence?” by Malhotra et al. to know the fate of BNP in heart failure. Adrenomedullin and suppression of tumorigenicity 2 (ST2) are of great diagnostic value in congestive heart failure in noncardiac patients and may soon replace BNP, which has moderate sensitivity and specificity.[10,16]

Cardiac biomarkers are ideally similar to any pharmaceutical intervention.[11] However, for majority of the present day clinical cardiac biomarkers in the market, the evidence base is weak; the majority of studies are prospective, observational ones and very limited in terms of clinical trials. Another major hindrance to quick adoption of most cardiac biomarkers is
the concept of clinical plausibility of a biomarker [Figure 1]. The former rests on adopting the right patient population on whom to use the biomarker. For example, in a patient of chest pain, the diagnostic modality moved from the electrocardiogram (once the gold standard) to the reigning troponins, but the latter is excellent for non-ST-segment elevation myocardial infarction (STEMI) patients and not STEMI.[12] In the latter group, the prior probability of disease is close to 100%, and the management pathway is well defined, and biomarkers are not useful for diagnosis. In STEMI, biomarker evaluation (microRNA 208 [miRNA-208] is the upcoming biomarker in STEMI) if it fails implies that the biomarker does not work for diagnosis of myocardial infarction.[13,14] Troponins are here to stay as mentioned by Weber et al., in this special biomarker issue, but soluble CD40, myeloperoxidase, and ischemia modified albumin went into disrepute because of the inaccuracy detected in the analytical performance of the assay used for their detection.[1]

![Figure 1: Biomarkers profile in cardiac patients](image)

**WHAT’S NEXT IN CARDIAC BIOMARKER PROFILE?**

Heart-type fatty acid binding protein (H-FABP), glycogen phosphorylase isoenzyme BB (GPBB), ST2, miRNA, and suPAR are the upcoming markers of future. They are present in a very high concentration in the myocardium (5 mg/g) and are released promptly during ischemia. GPBB is elevated within 2 hours and maintains a baseline for 12–24 h hours.

**IS SOLUBLE UROKINASE PLASMINOGEN ACTIVATOR RECEPTOR THE FINAL ANSWER TO THE MULTI-MARKER APPROACH?**

suPAR is being used by cardiologists to outperform CRP at prognosticating CVD.[15] Cyrille et al., in this issue, bring out the importance of suPAR in chronic inflammation, CVD, and critical illness. Is it of additive benefit for predicting the risk of future cardiovascular events? Only more clinical trials will answer this question.

Ultimately, the goal is to use multiple biomarkers to determine the presence, cause, and extent of damage to the cardiac tissue. Lactic dehydrogenase, CK, and CK-MB were used ages ago but have been replaced by the troponins. Troponins are the current standard for diagnosis of myocardial infarction. GPBB, H-FABP, ST2, suPAR, and miRNA have the potential to improve the diagnosis and treatment of patients suspected of an adverse cardiac event. It is time to “Welcome, What lies Ahead” rather than obsessing in a negative way about not having depended on any biomarker, so far in our clinical practice or thinking all existing ones to be futile.

“We must welcome what lies Ahead.”

We have moved from lactate to lactate clearance, troponins, BNP, endothelins, NGAL, and now to suPAR. The journey for betterment continues.

Poonam Malhotra Kapoor
Chief Editor, ACA & Professor, Department of Cardiac Anaesthesia, CNC, AIIMS, New Delhi, India

**Address for correspondence:** Prof. Poonam Malhotra Kapoor, Department of Cardiac Anaesthesia, CNC, AIIMS, New Delhi, India.

E-mail: drpoonamaiims@gmail.com

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