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RESEARCH ARTICLE

CONSENSUS STATEMENT ON THE USE OF HIGH-SENSITIVITY TROPONIN I ASSAY FOR RISK STRATIFICATION OF APPARENTLY HEALTHY INDIVIDUALS – AN INDIAN DIMENSION

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ABSTRACT

The burden of cardiovascular (CV) diseases in India highlights the need for early prevention and limitations of current practices. Evidences support the use of high-sensitivity troponin I (hsTnI) as a potential stratification tool for identifying at-risk individuals. The currently available hsTnI assay sallow the detection of low circulating cardiac troponin concentrations, thus making ita potential predictor of risk in even asymptomatic individuals. Based on these reports and the availability of a CE-approved, cardiac-specific, ARCHITECT hsTnI, for CV risk stratification in apparently healthy individuals, an expert panel of cardiologists across India was convened. The panel discussed and arrived at a consensus on the feasibility of hsTnI assay in CV risk stratification of apparently healthy individuals in Indian settings and also proposed an algorithm. This consensus statement acts as a pragmatic guide for clinicians on the use of hsTnI assay as a prognostic marker and a guide for planning prevention strategies.

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INTRODUCTION

Cardiovascular diseases (CVDs) are the leading cause of death globally and are estimated to account for more than 23 million deaths per year by 2030.[1]

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In India, CVD-associated deaths increased by ~13% from 1990 to 2016.[2] Therefore, reducing the burden of CVDs by primary prevention is of paramount importance. Effective primary prevention necessitates identification of individuals requiring maximum attention. However, the currently available risk assessment tools, which heavily rely on conventional cardiovascular (CV) risk factors, certainly have limitations that consequently result in inaccurate cardiac risk

estimation. Consequently, patients classified as low risk as per the existing risk-scoring tools continue to experience CV events. To overcome these, several newer biochemical and imaging markers have been developed, which can enable relatively earlier and accurate prediction of the risk of major adverse cardiovascular events (MACE).This in turn allows early intervention, thereby preventing future CV events. Of note, compared with the imaging markers, biochemical markers are advantageous, with wider availability and ease of application. Research has led to the discovery of an array of novel biomarkers associated with CV risk, such as C-reactive protein (CRP), B-type natriuretic peptide (BNP), N-terminal prohormone BNP (NT-proBNP), troponin, lipoprotein-associated phospholipase A2, and fibrinogen. [3]Cardiac troponin I is the most preferred biomarker for the diagnosis of acute myocardial infarction(AMI) owing to its cardiac specificity.[4]Interestingly, the currently available high-sensitivity troponin I (hsTnI) assays have the ability to detect very low concentrations of circulating cardiac troponin even in apparently normal and healthy individuals.[5]Such individuals who present with hsTnI values greater than the limit of detection and lower than the 99th percentile reference limit have been reported to demonstrate an increased risk of CV events .[6]This has led to considerable interest in using hsTnI for CV risk stratification in asymptomatic individuals.

With the aim of understanding and, thereby, promoting the justified use of hsTnI as a biomarker for CV risk stratification in apparently healthy Indian adults, an Indian expert risk stratification advisory board was convened in New Delhi and Mumbai. The expert panel was selected from a pool of eminent practicing cardiologists across India. The panel put together recommendations for the appropriate use of hsTnI in risk stratification based on their understanding of the literature and individual clinical experience. The current document summarizes the key consensus statements derived in this discussion.

Statement 1: Current CVD risk stratification tools have room for improvement: Several risk assessment tools are available for CV risk assessment. Tools, such as Framingham risk score ,[7]American College of Cardiology/American Heart Association (ACC/AHA) risk calculator ,[8]SCORE (Systematic Coronary Risk Evaluation) risk charts ,[9]QRISK2 ,[10] and the Joint British Societies' recommendations (JBS3)[11]are being currently used. These tools are used to estimate 10-year risk of a CVD event and/or CVD-associated death of an individual, based on the presence of traditional risk factors for CVD, such as age, blood pressure, smoking status, lipid profile, obesity, and diabetes mellitus. However, these tools, although well established, present with several limitations; first, these risk factors are not cardiac specific; second, the tools provide only an approximation of the associated CVD risk. In fact, these risk assessment tools are strongly dependent on age as a determinant of CV risk, which, in turn, results in the underestimation of CV risk in young individuals. This is particularly relevant in the Indian population owing to the higher risk of coronary artery disease (CAD) in the younger population compared to other populations.[12]Besides, data from a recent registry showed high prevalence of heart failure (HF) in India; notably, Indian patients presented with HF at a much younger age compared to the Western population. [13]In addition, each of the above mentioned tools has been derived from population-specific epidemiologic data, mostly involving the western population, and hence, there is no single tool that is applicable across all populations. The most widely used Framingham risk score has been reported to overestimate the CV risk in a few low-risk populations ,[14] with potential overestimation of risk of coronary heart disease (CHD)-associated deaths in European populations .[15] An Indian study suggested that in comparison with the Framingham score and ACC/AHA risk calculator, the JBS3 risk assessment tool identified a large proportion of the Indian patients at "highrisk".[16] The QRISK2 score was found to better predict the risk in the UK population.[10]Besides, an overall improvement in the traditional risk factors did not lead to an improvement in CV outcomes at the population level.[17] Finally, these CVD risk calculators do not incorporate any variable(s), indicating the present status of the cardiac myocyte injury. Therefore, there is a scope for improvement in the current methods of risk stratification for CVDs.

Statement 2: Existing biomarker hsCRP lacks cardiac specificity and inaccurately stratifies cardiovascular risk in apparently healthy individuals: High-sensitivity CRP has been used for CV risk assessment.[18]Based on multiple epidemiologic and interventional studies, minor hsCRP elevation has been shown to be associated with future CV risk (hs CRP:<1 mg/L=low risk; 1–3mg/L=intermediate risk; 3–10mg/L=high risk; >10mg/L=unspecific elevation). [19]However, in the Indian population, owing to elevated basal levels of hs CRP associated with the high rates of subclinical infections, the role of hs CR Premains unclear.[20] Hence, the use of hs CR Passay can lead to an inaccurate risk stratification of the majority of population. Also, hs CR Pdoes not significantly aid in differentiating between healthy and at-risk population. In essence, although CRP is highly sensitive to general inflammatory responses, it does not fulfil the existing gaps in risk stratification in terms of cardiac specificity and cardiac myocyte injury detection. This further necessitates deciphering a marker that would facilitate accurate risk assessment and also suggest the impact of CV outcomes across populations.

Statement 3: High-sensitivity troponin I can aid in accurate cardiovascular risk assessment in apparently healthy individuals: Cardiac troponin I is the preferred cardiac-specific marker of myocardial injury and is used preferably for the evaluation of AMI.[21] The hsTnI assay offers high analytic sensitivity and cardiac specificity, which makes it an ideal candidate marker for use in the risk stratification of healthy individuals. In a population-based cohort study named the Nord-Trøndelag Health (HUNT) Study, hsTnI was strongly associated with an increased risk of CV death (adjusted hazard ratio [HR] 1.23 [95% CI 1.15–1.31]). Similarly, a recently published ARIC study demonstrated a strong association between elevated hsTnI levels and an increased global CVD incidence, independent of the conventional risk factors. [22,23]The Biomar CaRE study that involved ~75,000 subjects reported the potential of hsTnI assay in risk stratification. Cardiovascular risk increased significantly with increasing hsTnI concentrations, with the highest hsTnI quintile conferring 63% increase in total mortality compared to the lowest hsTnI quintile.[24] In line with these reports, the JUPITER trial demonstrated that the incidence of CV mortality and nonfatal myocardial infarction (MI) was elevated among individuals in the high-risk category of hsTnI compared to the low-risk category

(HR 2.61 [95%CI, 1.81–3.78]).[25] In fact, the PROMISE trial showed that elevated hsTnI levels were associated with an increased incidence of obstructive coronary disease.[26]The hsTnI cut-off values showed a strong association with CV risk assessment and also yielded better outcomes in various studies across all age groups ranging from 20 to 98 years, as summarized in Table 1. Overall, based on these studies, hsTnI >3.9ng/L has shown strong association with the incidence of CVDs, and it is evident that a gender-specific approach is required for risk stratification using hsTnI.

Statement4: ARCHITECT hsTnI assay is approved for use in risk stratification of apparently healthy individuals for future cardiovascular events: In order to universally define the term, "highly sensitive", the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Task Force recommended the following analytic attributes:(i) Total imprecision at the 99th percentile value should be ≤10%;(ii) the assay should be able to detect at least 50% of normal healthy individuals with quantifiable values above the limit of detection. In line with the above criteria, the Abbott ARCHITECT hsTnI assay is the first hs TnIassay to be commercially available, with an ability to detect circulating hsTnI values in 96% of apparently healthy subjects.In a meta-analysis of 28 trials of 154,052 subjects, hsTnI assay detected cardiac troponin concentrations in 82.6 % of subjects. [27,28]This significant and improved detectability in normal healthy individuals and the strong association of low levels of circulating hsTnI with CVD incidence suggested the application of hsTnI assay in risk stratification. Circulating cardiac troponin levels are considered as indices of subclinical myocardial injury. Studies demonstrate the prognostic value of troponins and their positive correlation with CV risk factors such as body mass index and systolic blood pressure.[29]Unlike other hs Tnassays currently in use for diagnosing AMI, ARCHITECT hsTnI assay is the first and, currently, the only CE-marked hsTnI assay that aids in the prediction of future cardiac events in the general population as well as risk stratification of asymptomatic individuals into three categories, i.e., low, moderate, and high risk. This has also been discussed in the HUNT and ARIC study.[23,30] Table 2 summarizes the gender-specific hsTnI cut-off values for risk stratification of apparently healthy individuals based on the existing literature, along with validation results from the ARCHITECT hsTnI package insert and HUNT study.[23,29,31]

Statement5: Addition of hsTnI to current risk stratification tools and biomarkers may improve the prognostic accuracy: The evaluation of hsTnI in comparison with the existing risk stratification algorithms and biomarkers shows promising results, particularly, improved prognostic accuracy. Elevated hsTnI levels are strongly associated with an increased global CVD incidence in the general population, independent of the conventional risk factors; of note, hsTnI levels/values provide complementary information, thereby allowing improved risk prediction. The evaluation of risk factors, including BNP, CRP, and hsTnI, in a community-based cohort demonstrated that —only hsTnI levels were associated with incident atrial fibrillation (AF).[34]High-sensitivity troponin I is also reported to be better suited for CV risk assessment of the general population vs. hsCRP.[28] Moreover, the addition of hsTnI to the pooled cohort equation model improved risk assessment for HF, atherosclerotic CVD, and global CVD.[30]High-sensitivity troponin I assay has been reported to detect more at-risk patients and improve current risk stratification algorithms.[35]Among patients with diabetes, increased levels of hsTnI have been reported to be strongly associated with an increased risk of MACE, HF, and CV mortality; this, in turn, suggests that hsTnI assay is a robust predictor of CV risk in patients with diabetes.[36]In addition, hsTnI assay is also reported toaid in differentiating between no plaques vs. noncalcified and calcified coronary plaques and distinguishing different Agatston scores.[37]Moreover, the application of hsTnI assay along with the existing CV risk-scoring algorithms could provide a solution to the age limitations associated with the existing algorithms that primarily focus on individuals >40 years and elderly population. Interestingly, hsTnI assay has been well recognized in the risk stratification of younger populations as early as 20 years.[23,24] In conclusion, the addition of hsTnI to the traditional risk factors would provide clinicians with more cardiac-specific information and an improved diagnostic accuracy. Thus, hsTnI, along with the existing risk factors and/or CV risk scoring systems, would aid in improved risk assessment.

Statement 6: The use of hsTnI in asymptomatic healthy individuals would aid in better management of at-risk individuals: The circulating levels of troponinI (<4 and <6 ng/L for F/M), measured using high-sensitivity immunoassays, may be considered as a reliable estimate of the physiologic turnover of human myocardial tissues in healthy individuals at low risk of CVDs.[38]As hsTnI is the only cardiac-specific indicator of myocardial injury, high levels of hsTnI (greater than the above-mentioned values)are predictive of more severe CAD and its accelerated angiographic progression. This may guide clinicians to assess the need for intervention in identified high-risk individuals.[39] In a prospective cohort study (Dallas Heart Study) with a median follow-up of 6.4 years, elevated levels of hsTnI were associated with a high incidence of structural heart diseases, including left ventricular hypertrophy and systolic dysfunction and all-cause mortality.[40]In addition, the hs Tnlassay may identify at-risk individuals who require more intensive primary prevention and thus allow early disease-modifying treatment.[41]In comparison to cardiac evaluation modalities such as echocardiography, computed tomography (CT), and angiography, hsTnI assay would not only be more cost-effective at the hospital level but also provide benefits of lower exposure to radiation.

Several studies suggest that hsTnI assay would aid in better identification of patients for further evaluation as compared to the current risk stratification practices. The HUNT study reported hsTnI assay to have better prognostic accuracy in risk stratification vs. hsCRP as demonstrated by greater C-statistics compared to hs-CRP, and additionally, it provided a better net reclassification index than hs-CRP when added to the Framingham score (35% vs. 21%).[23] The COMPASS trial demonstrated that hsTnI assay improves patient identification for further investigation and treatment.[42]The addition of coronary artery calcium score to hsTnI values also improves the identification of low-risk subjects in whom CT angiography might be avoided.[43]

Statement 7: Statin therapy may benefit moderate and high-risk individuals: Baseline troponin is an independent predictor of MI or death due to CHD: HR, 2.3 (95% CI, 1.4–

3.7) for the highest (≥5.2 ng/L) vs. lowest (≤3.1 ng/L) quarter of troponin (p<0.001). Statins are the most widely prescribed agents for treating CVD and are known for their pleiotropic (lipid-lowering independent) effects. The West of Scotland Coronary Prevention Study (WOSCOPS) found that stat in therapy led to troponin reduction and benefited individuals with hsTnI >5.2ng/L. The reduction in troponin levels was associated with better outcomes, independent of lowering levels of low-density lipoprotein cholesterol. Individuals with the greatest decrease in hsTnI values had a 5-fold reduction in CVD events compared to those with increased hsTnI values.[41]In line with various reports on the association of reduction in hsTnI levels by statins with better CV outcomes, statins may be beneficial in individuals with elevated hsTnI levels and with no conventional risk factors (JUPITER, BiomarCaRE). A significant reduction (8%) of hsTnI levels was seen as early as six weeks of treatment with a low dose of statins.[44] These findings also suggest the use of hsTnI assay to assess the response to intervention for CAD prevention. High-sensitivity troponin I levels have been reported to be responsive to interventions that modify CV risk factors, such as statin therapy, physical activity, and obesity control, and thus these may be used to support and guide these interventions.[29,45,46]

Statement 8: Creatinine clearance, skeletal muscle, and other interferences should be considered before evaluation of hsTnI risk stratification scores: Nonspecific causes for altered troponin levels, such as renal impairment, skeletal muscle-induced elevation, and biotin interference, were also points for discussion among the panelists. There have been reports on elevated troponin levels inchronic kidney disease patients, especially in case of hsTnT,in comparison to hsTnI.[47,48] It is imperative that physicians using hsTnI also measure creatinine to prevent mismanagement based on troponin elevation due to renal dysfunction (decreased glomerular filtration rate). Based on reports on how to clinically evaluate troponins in patients with impaired renal function, the panel recommended that creatinine clearance should be considered while interpreting the results of hsTnI, particularly in nonacute conditions.

Reports demonstrate elevated levels of cardiac troponin emanating from skeletal muscle injury. Also, 68.9% of patients with skeletal myopathies and no known cardiac disease showed elevated cardiac troponin T levels (cTnT), with mild elevation (4.1%) of hsTnI levels. This indicates that patients with skeletal muscle disease may have elevated levels of cTnT, regardless of the presence or absence of any cardiac diseases.[48,49]In fact, another study showed that a significant and prolonged (>24 hours) troponin elevation after endurance exercise is associated with obstructive CAD on coronary CT angiography, while assessment of troponin levels immediately after exercise showed no such association.[50] The recent Food and Drug Administration (FDA) alert on biotin interference in troponin assays also led to the discussion among the panelists. Biotin consumption is on the rise due to its health and cosmetic benefits, and there have been a series of reports on biotin interference in cardiac troponin assays.[51]Hence, biotin interference-free hsTnI assays should be used to avoid false results and incorrect risk assessment.[52,53] In conclusion, hsTnI would be a better marker for CVD risk stratification in asymptomatic individuals as compared to cTnT.

However, hsTnI levels should always be interpreted within the context of other clinical findings, interferences as well as patient history for improved and accurate prognosis, thus offering cardiac-specific and personalized risk modification advice.

Statement9: Serial hsTnI measurements have major potential to monitor cardiovascular risk and the impact of therapeutic interventions: Serial troponin measurements have major potential to assess CV risk and monitor the impact of therapeutic interventions.[41]Periodic evaluation of hsTnI may have a role in prevention strategies either by intensifying therapy in patients at high risk of CV events or developing novel therapeutic strategies. High-sensitivity troponin I measurements may identify patients requiring further evaluation for preventing worse outcomes and also reduce unwanted evaluation of low-risk individuals.[42]Recently, it was shown that the relative and absolute increases in hsTnI levels are independent predictors of CVrisk.[52]Additionally, hsTnIassay may help identify at-risk individual candidates for more intensive primary prevention long before the development of overt events.[41]The addition of hsTnI to traditional risk factor assessment may aid in developing personalized therapeutic strategies. For instance, a patient with diabetes with low hsTnI levels and one with elevated levels of hsTnI would be managed differently depending on the extent of myocardial injury, independent of metabolic derangement.

Serial measurements of cardiac troponins using hsTnI assay for monitoring the effect of lifestyle intervention appears promising as compared to a single hsTnI measurement. Physical activity has been reported to attenuate resting troponin concentrations.[46] The panel was of the view that serial hsTnI evaluations would provide hsTnI baseline value, which could be monitored to identify the cardiac status.As mentioned earlier, a significant and prolonged (>24 hours) troponin elevation after endurance exercise was found to be associated with obstructive CAD.[50]This rise and fall pattern of hsTnIlevels could be regulated by evaluating the decline in hsTnI levels post 72h of exercise-induced stress test. This may add to the prognostic utility of stress testing in high-risk individuals. Thus, the panel put forth a prospective algorithm for use of hsTnI as a biomarker in general population, as shown in Figure 1. Timely follow-up along with monitored lifestyle modification measures seems to be a reasonable approach considering the benefits of weight control and exercise training on hsTnconcentrations for low-risk and moderate-risk individuals without comorbidities. However, a personalized guided approach would be beneficial for individuals with elevated hsTnI levels along with the presence of traditional risk factors. In conclusion, the cardiac specificity and cost-effectiveness of this noninvasive blood-based biomarker make it more suitable for risk prediction in apparently healthy individuals vs.the existing tests,such as CT coronary calcium/CT angiography. High-sensitivity troponin I sampling at multiple time points may have the potential to refine biomarker-based risk estimation.[54,55]Hence,the serial measurement of hsTnI appears to be a useful tool for monitoring CV health, with a progressive rise in troponin I, suggestive of increasing risk.

Statement10: High-sensitivity troponin I holds potential in post-operative monitoring: Evidence supports the use of hsTnI in post-operative conditions. Decrease in hsTnI

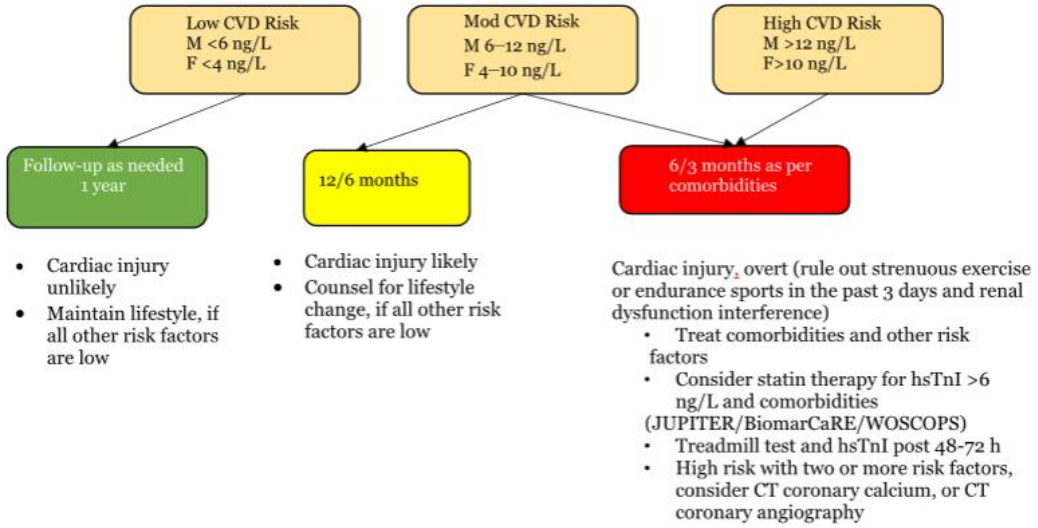

Figure 1: Consensus-based algorithm for risk stratification of apparently healthy population: Use of hsTnI in conjunction with other clinical findings. Serial hsTnI evaluations at recommended timings would provide additional information about individuals' cardiac status and these would aid in guiding and monitoring therapeutic strategies.Low-risk individuals (hsTnI <4 ng/L for females [F] and <6 ng/L for males [M]) without any classic risk factors need to be assessed annually, as cardiac injury is unlikely. Moderate-risk individuals (hsTnI 4–10 ng/L for females [F]; 6–12 ng/L for males [M]) without any risk factors or comorbidities are recommended to be assessed annually, although with counseling for lifestyle modification. However, moderate-risk individuals (hsTnI 4–10 ng/L for females [F] and 6–12 ng/L for males [M]) with comorbidities and high-risk individuals (hsTnI >10 ng/L-F/>12 ng/L-M) with and without comorbidities need to be assessed within 6/3 months depending on the individuals' status and other clinical findings, as elevated hsTnI levels are strongly associated with an increased CVD incidence. Care should be taken to rule out strenuous exercise in past 3 days and/or renal dysfunction interference. Meanwhile, the underlying cause is to be treated depending on the individuals' clinical conditions. Statin has been reported to benefit individuals with elevated hsTnI levels. The line of treatment lies with the clinician. Further investigations like treadmill test and hsTnI post 48–72h of TMT are recommended. For individuals with elevated hsTnI levels along with two or more risk factors, coronary calcium scoring and if required, CT coronary angiography, may be recommended.

Table 1. Studies using hsTnI for risk stratification in different populations with cut-off values used, age of subjects tested, follow-up years, and outcomes

	Population	No. of subjects	Age group in years	Follow-up years	Cut-off values	Outcome
ARIC study (2019) (Jia *et al*., 2019)	4 US communities	8121	54–74	15	Low: <4.0 ng/L Moderate: 4–10 ng/L High: >10 ng/L (♀) Low: <6.0 ng/L Moderate: 6–12 ng/L High: >12 ng/L (♂)	Atherosclerotic CVD, heart failure, and global CVD
HUNT study (2018) (Sigurdardottir *et al*., 2018)	Norway	9005	>20 years	13.9	>10 ng/L (♀) >12 ng/L (♂	Composite of hospitalization for AMI or HF, or CV death
Busselton Health Study (2017) (Zhu *et al*., 2018)	Australia	3939	25–84 years	20	≥4.0 ng/L (♀) ≥6.0 ng/L (♂)	CVD event
AGES study (2016) (Thorsteinsdottir *et al*., 2016)	Iceland	5764	66–98 years	10	>10.6 ng/L	All-cause death, CV events, and coronary heart events
BiomarCaRE project (2016) (Blankenberg *et al*., 2016)	Europe	74,738	20–79 years	13.8	≥6.0 ng/L	CVD and overall mortality
JUPITER study (2015) (Everett *et al*., 2015)	26 countries	12,956	>50 years	2.0	>3.9 ng/L (♀) >4.6 ng/L (♂)	Major CV events and all-cause Mortality

hsTnI: High-sensitivity troponin I; ARIC: Atherosclerosis Risk in Communities; HUNT: Nord-Trøndelag Health Study; CVD: Cardiovascular disease; AMI: Acute myocardial infarction; HF: Heart failure; CV: Cardiovascular; MI: Myocardial infarction

Table 2*. Recommended hsTnI risk stratification cut-off values for asymptomatic individuals using ARCHITECT hsTnI assay

Gender	Risk category		HR	95% CI	p-value	Outcomes
Female	Moderate risk: 4–10 ng/L	6386	2.37	2.00–2.78	<0.0001	Global CVD, MI, stroke, CHF, and cardiac death
	High risk:>10 ng/L		1.67	1.35–2.04	<0.0001	
Male	Moderate risk: 6–12 ng/L	4649	1.68	1.40–2.01	<0.0001	
	High risk:>12 ng/L		1.43	1.18–1.72	10.0002	

hsTnI: High-sensitivity troponin; CVD: Cardiovascular disease; MI: Myocardial infarction; CHF: Chronic heart failure.

concentration post percutaneous coronary intervention in patients with stable CAD showed a strong association with reduced MACE incidence.[55]Routine post-operative hsTnI evaluation in patients who have undergone vascular surgery showed association with an increased risk for perioperative MI and six-month mortality.[56]Considering the results of the SCOT-HEART trial and the growing evidence of prognostic value of hsTnI, Mills and Omland proposed that targeted imaging in patients with possible stable angina and persistent increase in hsTnI values below the 99th percentile would improve long-term outcomes.[57]As a marker of myocyte injury, post-operative troponin I concentrations may be helpful in identifying patients with a high risk of mortality and morbidity after major vascular surgery. Overall, evidence supports an improved cardiac risk assessment by addition of hsTnI to the current standard of care.

Conclusion

The burden of CV diseases continues to rise in developing countries, such as India. The contribution of CVDs, particularly ischemic heart disease, to disease burden and mortality in India has almost doubled since 1990.Immediate action should be taken to prevent and control the rising disease burden through appropriate measures such as early and periodic screening for CV risk factors. The current tools for risk assessment, e.g., SCORES/ Framingham/ Reynolds/JBS3, have limitations to their use, viz. inaccurate categorization of moderate- and low-risk young individuals, and are not cardiac specific. High-sensitivity troponin I is the only CE-approved cardiac-specific marker for risk stratification that accurately predicts the risk of future cardiac events, which may eventually help in the reduction of the existing CVD burden. Application of these insights into practice may be advantageous, while the use of cardiac troponin for noninvasive testing may fine-tune risk stratification strategies. More prospective and randomized controlled studies are needed to further strengthen the management protocols for elevated hsTnI values and their association with CV incidence.

Statement of Authorship: All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Conflict of Interest

Author Abraham Oomman has been Speaker and received honoraria / Consultancy from Serdia, Novartis, Astra – Zeneca, Boehringer Ingelheim, Pfizer, Bayer, Dr Reddys , Torrent, Lupin, Abbott, Cipla, Zydus, Glenmark, Emcure, GE healthcare. Has received research grant /contract from USV, Sunpharma, Lupin, Bayer and received honorarium supported by Abbott Diagnostics, India. Author Sanjeev Gera has been part of advisory boards of AstraZenecea, Servier and Cipla and received honorarium supported by Abbott Diagnostics, India. Authors Jamshed Dalal, C.K. Ponde, Manish Bansal, J.P. Sawhney, Brian Pinto, Neeraj Bhalla, Peeyush Jain, Rishi Gupta, Akshay Mehta, Bharat Shivdasani, Kiron Varghese, Sadanand Raghunath Shetty, Subhash Chand Manchanda, Nikhil Parchure, M. Kathiresan, B.B. Chanana, Kuldeep Arora, Saket Bharadwaj, VT Shah, have received honorarium supported by Abbott Diagnostics, India and do not report any other conflicts.

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