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Serial high-sensitivity troponin I monitoring as a prognostic marker in acute ischemic stroke

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ABSTRACT

Introduction and aim. Acute ischemic stroke (AIS) is a complex disease with multifactorial etiologies, often masking underlying cardiovascular morbidities that contribute to clinical outcomes. This study explored the role of serial high-sensitivity troponin I (hs-TnI) monitoring in AIS patients as a prognostic marker of cardiovascular morbidity and mortality. The results offer substantial information on the relationship between hs-TnI elevations and clinical, electrocardiographic (ECG), echocardiographic (ECHO), and angiographic parameters in patients with AIS.

Material and methods. A prospective observational study was conducted on 60 patients with AIS in a tertiary care center, Tamil Nadu. Hs-TnI levels were measured at the time of admission and after 48 h together with ECG, ECHO. Angiographic evaluations were done in patients with elevated hs-TnI at 48 h after admission.

Results. Among the study population, hs-TnI levels increased significantly from 11.7% at admission to 20% after 48 h (p=0.02).Logistic regression showed hs-TnI at 48 h predicted mortality (odds ratio [OR]=28.5, 95% confidence interval [CI]: 5.9–137.1, p<0.001) and coronary artery disease (CAD) (OR=48.2, 95% CI: 9.8–236.5, p<0.001).

Conclusion. Serial monitoring of hs-TnI in AIS patients revealed its potential role in the identification of culprit lesions on coronary angiogram, which is correlated with the presence of CAD and mortality.

Keywords. acute ischemic stroke, cardiac mortality, high-sensitivity troponin I

Introduction

Acute ischemic stroke (AIS) is among the leading causes of mortality and disability contributing to the economic burden of the disease worldwide. AIS is often accompanied by cardiovascular complications that may remain undiagnosed, exacerbating patient outcomes.[1] Key predictors of outcomes in AIS include the following clinical determinants, such as age, location of the injury, stroke severity, and presence of comorbidities. Cardiac manifestations such as myocardial infarction, arrhythmias, and left ventricular dysfunction are frequently observed in AIS patients.[2] The prognostic relevance of such abnormalities remains underexplored. Identifying patients at risk for underlying cardiovascular disease (CVD) early in the course of stroke management is crucial for optimizing clinical interventions thereby reducing morbidity and mortality.[3]

Troponin and CK-MB are cardiac biomarkers that identify and quantify myocardial injury and prognosis in stroke patients, but the outcomes have been conflicting and uncertain.[4] High-sensitivity troponin I (hs-TnI) is one such established biomarker that is also identified in conditions such as sepsis, heart failure, chronic kidney disease, cardiomyopathy etc.[5] Increasing evidence suggests that the cardiac dysfunction, arrhythmia, results from stroke induced disruption of the central autonomic pathways leading to neural-cardiac dysregulation. This is referred to as Stroke-Heart syndrome that typically occurs between 72 h and 30 days of AIS.[6,7] The Fourth Universal definition of myocardial infarction, states that myocardial injury is indicated by the elevation of cardiac troponin above the 99th percentile upper reference limit (URL).[8] Troponin peaks after 12–48 h and remains elevated for 4–10 days.[9]

The recent systematic review and meta-analysis by Gulia A et al. concluded that elevated cTn levels were associated with mortality during hospital stay and follow-up periods in patients with AIS underscoring its clinical importance.[10] Current guidelines recommend routine baseline assessment of cardiac troponin in patients with AIS yet its association with the need of invasive diagnostic and therapeutic modalities, long

term consequences of troponin elevation and the timeframe for serial testing remain poorly elucidated.[11] We hypothesize that dynamic changes in hs-TnI levels over the first 48 h post-admission may provide valuable insights into the presence of undiagnosed cardiac pathology.[12,13] Furthermore, by identifying patients with an increased cardiovascular risk profile, serial hs-TnI monitoring may facilitate early therapeutic interventions, improving overall patient outcomes.[14]

Justification of the study

Contemporary studies involving patients with AIS have shown that hs-TnI is elevated in 30–60% of the patients.[15] While guidelines do not mandate a specific 48 h troponin check, this timeframe window was chosen for detection of delayed or evolving cardiac injury as evidenced by stroke heart syndrome. Persistently elevated levels may also be linked to ongoing cardiac strain and measuring at 48 h may allow for clinical stabilization, risk benefit assessment and mitigate confounders from non-coronary causes of troponin elevation.

Aim

The aim of this study was to evaluate the clinical utility of serial hs-TnI monitoring in AIS patients over the first 48 h of admission through its correlation with electrocardiographic (ECG) echocardiographic (ECHO) and angiographic abnormalities in terms of the presence of significant coronary artery occlusion and to determine its prognostic value in predicting cardiovascular mortality and morbidity.

Material and methods

Study design and setting

A prospective observational study was undertaken at a tertiary care academic medical center in South India between September 2023 and April 2024. The study was carried out at the Department of General Medicine at a tertiary care academic center equipped with facilities for neuroimaging, cardiac investigations and coronary angiography (CAG). The study sought to evaluate elevation of hs-TnI at baseline and at 48 h in AIS patients, correlate the same with ECG ECHO and angiographic observations and to investigate the prognostic significance of serial hs-TnI measurements in AIS patients while adjusting for potential confounding variables.

Sample size

Assuming an odds ratio of 3.0, α=0.05, and 80% power, the required sample size was calculated to be 52, using G power. A sample size of 60 was chosen to adjust for potential dropouts and missing data.

Inclusion and exclusion criteria

A total of 60 patients diagnosed with new-onset AIS based on Magnetic Resonance Imaging (MRI) findings, and aged more than 18 years were enrolled. Patients with hemorrhagic stroke, recurrent CVA, CKD, COPD and known coronary artery disease (CAD) were excluded to limit non-coronary causes for hs-TnI elevation. Patients who died within 48 h of admission or left against medical advice or those who developed stroke in-hospital admission were also excluded.

Data collection

Each patient underwent a comprehensive clinical evaluation that included a detailed medical history, vital signs, and relevant laboratory investigations. Demographic details such as age, gender, smoking status, and alcohol consumption were recorded. The presence of comorbidities, including systemic hypertension type 2 diabetes mellitus (T2DM) and dyslipidemia, preexisting coronary artery disease (CAD) along with their treatments was documented. Key variables included hs-TnI levels at baseline and at 48 h, Electrocardiogram, transthoracic echocardiography, coronary angiography (CAG) and in-hospital cardiovascular morbidity and mortality. Potential confounders such as prior cardiac disease, age, medication use and renal function were documented and adjusted for in the analysis.

Stroke classification

Stroke types were categorized based on MRI findings into anterior cerebral artery (ACA) middle cerebral artery (MCA) infarct, lacunar stroke, multi-infarct stroke, posterior cerebral artery (PCA) infarct, pontine infarct, and thalamic stroke.

Hospital stay and outcome measures

The duration of hospitalization was recorded for each patient, with categories ranging from 2–8 days to more than 14 days. Clinical outcomes including mortality, presence of coronary artery occlusions, were also assessed.

Laboratory investigations

Routine laboratory tests, including fasting lipid profile, fasting blood sugar (FBS), postprandial blood sugar (PPBS), glycated haemoglobin (HbA1C), urea, and creatinine, were performed. These biomarkers were analysed in relation to troponin I levels and cardiovascular risk stratification.

Cardiac assessment

Serial hs-TnI levels were measured at two time points: upon admission and 48 h post-admission. Patients were classified based on reference values from an Asian study where the 99th percentile upper reference

limit (URL) for hs-TnI was established at 33.9 ng/L, with gender-specific values of 38.41 ng/L for males and 15.73 ng/L for females.[16] The myocardial injury was considered acute if there was dynamic rising and/or falling (20%) pattern of cTn values.[15] All participants in this study underwent a standard 12 lead ECG at the time of admission and repeated if indicated clinically. ECGs were obtained at a paper speed of 25 mm/s with an amplitude calibration of 10 mm/mV and were interpreted by qualified physicians. ECG changes such as sinus tachycardia T-wave inversions, ST-segment abnormalities (elevation and depression), left bundle branch block (LBBB), right bundle branch block (RBBB) were recorded. ECHO parameters, including regional wall motion abnormalities (RWMAs), left ventricular ejection fraction (LVEF), left ventricular hypertrophy (LVH), were recorded. Left ventricular ejection fraction (LVEF) is classified according to the American College of Cardiology (ACC).[17] The regional wall motion abnormalities (RWMA) were assessed by the Wall Motion Score Index (WMSI).[18] All the cardiac interpretations were reviewed and confirmed by a cardiologist blinded to the patient's troponin values.

Angiographic findings

CAG was performed in patients of AIS with elevated hs-TnI at 48 h, to identify the presence of CAD, its location and severity. CAD is defined as obstructive if the diameter stenosis >50% and non-obstructive will be used to indicate CAD <50% stenosis. Culprit lesion is defined as the coronary artery lesion that demonstrates plaque rupture, erosion or intraluminal thrombi.[19] Angiographic findings were interpreted by cardiologists blinded to the troponin levels. The outcomes measured were changes in hs-TnI levels at 48 h, presence of coronary lesions in angiography. Number of patients who died during the in hospital follow up was recorded.

Statistical analysis

The participants baseline characteristics were summarized using descriptive statistical methods. Chi-square and Fisher's exact tests were applied to compare categorical variables, while continuous variables were assessed using independent t-tests or Mann-Whitney U tests based on normality. Spearman's correlation was used for exploratory analysis of associations involving ordinal or non-normally distributed data, including CAD and mortality. Logistic regression was employed for binary outcome modeling (e.g., presence of CAD, mortality) to estimate adjusted odds ratios. The predictors of mortality were identified by univariate and multivariate logistic regression models. Variables included in the multivariate logistic regression were age, gender, T2DM Systemic hypertension , dyslipidemia, stroke type, and hs-TnI at 48 h. Multicollinearity was assessed using the Variance Inflation Factor (VIF), and all included variables had VIF values below 2.0, indicating no significant collinearity. The odds ratios (ORs) with 95% confidence intervals (CIs) were calculated and statistical significance was set at $p<0.05$. Analyses were performed using SPSS (IBM, Armonk, NY, USA).

Ethical considerations

The study was approved by the Institutional Ethics Committee (IEC) of Chettinad Hospital and Research Centre, Tamil Nadu, India (074/IHEC/2020). Written informed consent was obtained from all the patients. The Institutional Human Ethics Committee approved our proposal (Proposal Number 074/IHEC/July2020). This prospective observational study was conducted in India where registration with Clinical Trials Registry India is not mandatory for such studies. Retrospective registration is considered and future studies will comply with the same.

Results

Demographic and clinical characteristics

The study included 60 patients diagnosed with AIS, with a male predominance (60%) and a majority aged above 60 years (56.7%). Patients aged between 40 and 60 years constituted 40%, whereas only 3.3% were between 20 and 40 years. Comorbid conditions were highly prevalent, with T2DM in 53.3%, Systemic hypertension in 46.7%, and dyslipidemia in 26.7%. Lifestyle risk factors included smoking (63.3%) and alcohol consumption (46.7%) (Table 1).

The clinical parameters of the study population were monitored from admission to 48 h thereafter, revealing significant changes to emphasize the need for serial prognostic monitoring.

Laboratory findings and correlations

Various biochemical parameters have been assessed (Table 1). Biochemical analysis showed a mean FBS of 170±80 mg/dL and postprandial blood sugar (PPBS) of 253±96 mg/dL. HbA1C had a mean of 7.2±1.6%, indicating poor glycaemic control. Total cholesterol (TC) levels averaged 232±7.6 mg/dL, indicating hypercholesterolemia in the cohort. Triglycerides (TG) levels were at a mean of 145±7 mg/dL. High-density lipoprotein (HDL) cholesterol averaged 39.5±6.1 mg/dL, which is below the recommended level, suggesting a risk factor for CVD. Low-density lipoprotein (LDL) levels were elevated (mean 182±33 mg/dL), indicating a high risk for atherosclerosis contributing to cardiovascular risk.

Pearson correlation analysis revealed strong positive associations between hs-TnI (admission vs. 48 h) (r=0.86), FBS and PPBS (r=0.83), and HbA1C and PPBS (r=0.81). Moderate correlations were found between hs-TnI (48 h) and HbA1C (r=0.29)

Table 1. Patient demographics, clinical characteristics, and laboratory findings (n=60)*

Category	Details	Frequency n (%) or mean±SD
Demographics		
Age (years)	20–40	2 (3.3)

	40–60	24 (40.0)
	>60	34 (56.7)
Gender	Male	36 (60.0)
	Female	24 (40.0)
Comorbidities		
	T2DM	32 (53.3)
	Systemic hypertension	28 (46.7)
	Dyslipidemia	16 (26.7)
Lifestyle	Smoker	38 (63.3)
	Alcohol consumer	28 (46.7)
Clinical data		
Stroke subtype (MRI)	MCA	22 (36.7)
	Multi-infarct	9 (15.0)
	Lacunar stroke	8 (13.3)
	PCA	5 (8.3)
	Cerebellar/pontine infarct	7 (11.7)
	Other	9 (15.0)
Hospital stay (days)	2–8	41 (68.3)
	9–14	16 (26.7)
	>14	3 (5.0)
Laboratory findings		
	FBS	170±80 mg/dL
	PPBS	253±96 mg/dL
	HbA1c	7.2±1.6 %
	TC	232±7.6 mg/dL
	LDL	182±33 mg/dL
	HDL	39.5±6.1 mg/dL
	TG)	145±7 mg/dL

* percentages are calculated based on the total study population (n=60), stroke subtypes were categorized based on MRI findings, comorbidities were documented based on clinical history and prior diagnosis, MCA – middle cerebral artery, MRI – magnetic resonance imaging, PCA – posterior cerebral artery, laboratory values are presented as mean±standard deviation (SD), reference ranges (for general adult population): TC<200 mg/dL, TG<150 mg/dL, HDL>40 mg/dL (men)/>50 mg/dL (women), LDL<100 mg/dL, FBS 70–

99 mg/dL, PPBS<140 mg/dL, HbA1c 4.0–5.6%, urea 8–20 mg/dL, creatinine Female: 0.50–1.10 mg/dL; male: 0.70–1.30 mg/dL[20]

hs-TnI trends and significance

hs-TnI levels exhibited dynamic changes over 48 h (Table 2). At admission, 61.6% of patients had normal hs-TnI levels, which declined to 55.0% at 48 h (p=0.042). Conversely, the proportion of patients with high levels increased from 38.3% to 45.0% over the same period (p=0.038), indicating a statistically significant upward trend.

ECG and ECHO findings

ECG and ECHO findings have been listed in Table 2. ECG abnormalities were observed in 55% of patients at admission and increased to 60% at 48 h. Notable changes included an increase in T-wave inversions in inferior leads from 25% to 36.7% (p=0.03). ST depression in the anterior (ANT) leads was consistent at 18.3%, and in the lateral leads at 5%. T-wave inversions in the anterior leads were initially observed in 1.7% but were not noted at 48 h. Severe LVEF impairment rose significantly from 5% to 13.3% (p=0.02), severe hypokinesia increased from 8.3% to 10% (p=0.01). RWMAs slightly decreased from 36.7% to 33.3% (p=0.01).

Table 2. Temporal trends in cardiac parameters (n=60)*

Parameter	**Admission, n (%)**	**At 48 hours, n (%)**	**Change**	**p**	**95% CI for change**
hs-Troponin I Level					
Normal	37 (61.6)	33 (55.0)	↓	0.042*	
High	23 (38.3)	27 (45.0)	↑	0.038*	(0.51-1.00)
ECG findings					
T-wave inversions (inferior)	15 (25.0)	22 (36.7)	↑	0.03*	(0.65-1.00)
ST depression (anterior)	11 (18.3)	11 (18.3)	No change	-	
Left bundle branch block (LBBB)	9 (15.0)	7 (11.7)	↓	0.42	
Echocardiographic findings					

Mild LVEF impairment	11 (18.3)	7 (11.7)	↓		
Moderate LVEF impairment	5 (8.3)	6 (10)	↑		
Severe LVEF impairment	3 (5.0)	8 (13.3)	↑	(0.57 – 1.00)	0.02*
Regional wall motion abnormalities	22 (36.7)	20 (33.3)	↓	(0.00– 0.66)	0.01*
Mild hypokinesia	18 (30)	16 (26.7)	↓		
Moderate hypokinesia	1 (1.7)	0 (0)	↓		
Severe hypokinesia	5 (8.3)	6 (10)	↑	(0.21– 1.00)	0.01*
LVH (left ventricular hypertrophy)	28 (46.7)	20 (33.3)	↓	(0.00– 0.32)	0.01*

* a significant proportion of patients showed dynamic changes in hs-TnI levels between admission and 48 h, CI – confidence interval, hs-TnI – high-sensitivity troponin I, ECG – electrocardiogram, ECHO – echocardiography, LVEF – left ventricular ejection fraction, LVH – left ventricular hypertrophy

Correlation analysis

Chi-square tests revealed that hypertension, T2DM, dyslipidemia, and stroke type significantly influenced patient outcomes ($p<0.0001$). Pearson's correlation analysis demonstrated a strong positive correlation between troponin I levels at admission and 48 h ($r=0.86$), as well as between FBS and PPBS ($r=0.83$) .

Multiple regression analysis demonstrated that the predictive model for troponin I ($R^2=0.158$, adjusted $R^2=0.062$) had weak explanatory power. These findings suggest that additional clinical variables, such as stroke severity and inflammatory markers, should be integrated into future predictive models for better prognostic accuracy.

Mortality and length of hospital stay

The spearman's correlation analysis further confirmed that troponin I is a key biomarker for both CAD and mortality risk. Two weeks post-stroke, 11 patients with high hs-TnI levels succumbed ($p<0.001$) indicating a significant positive relationship with mortality ($\rho=0.75$), reinforcing its role as an indicator of mortality Additionally there was a positive correlation between hs-TnI and presence of CAD ($\rho=0.87$) (Table 3). A

moderate correlation between CAD and death (ρ=0.60) indicates that individuals diagnosed with CAD in AIS patients face a higher risk of dying in the present study population. With all correlations showing high statistical significance (p<0.001), these findings emphasize the importance of serial monitoring of hs-TnI levels in clinical practice to predict both CAD and death risk. While hs-TnI elevation showed a minor trend toward prolonged hospitalization, no statistically significant association was found between troponin I and hospital stay duration.

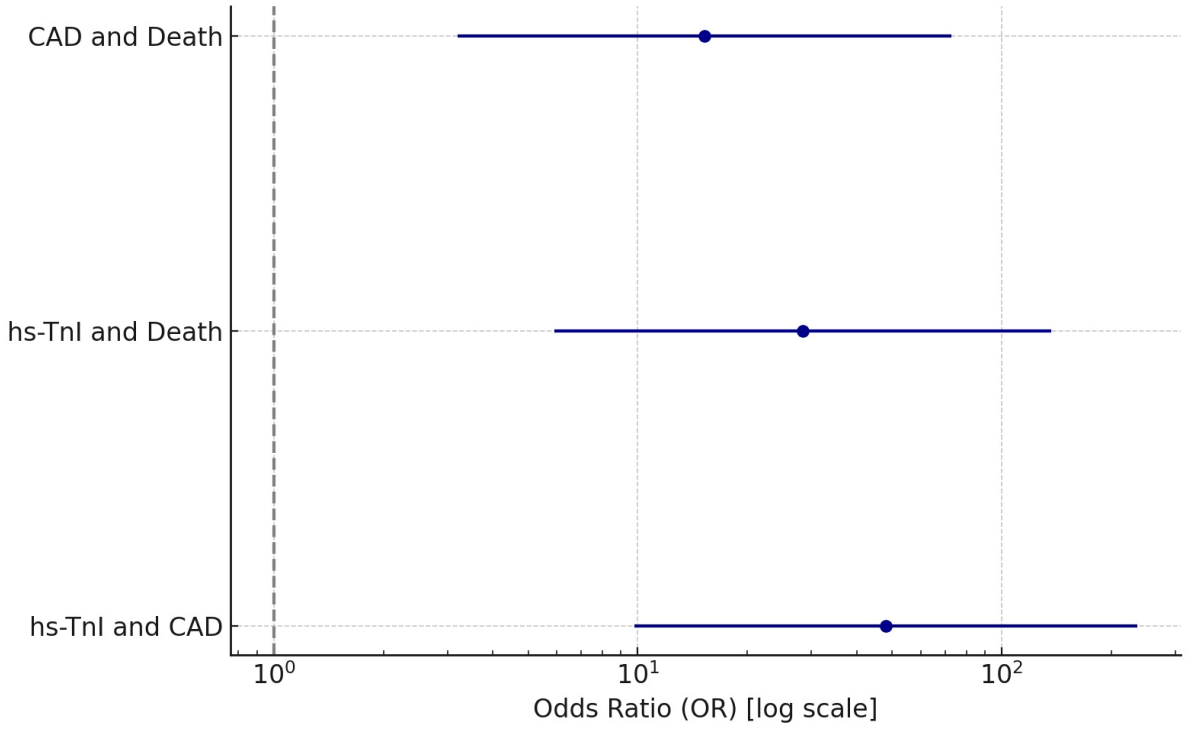

Fig. 1. Forest plot depicting associations of hs-TnI with mortality and CAD

Forest plot showing odds ratios (OR) with 95% CI for associations between hs-TnI, coronary artery disease (CAD), and mortality in AIS patients. Elevated hs-TnI was significantly associated with both CAD (OR =48.2, 95%CI: 9.8–236.5) and mortality (OR=28.5, 95%CI: 5.9–137.1). Presence of CAD also increased the odds of death (OR=15.3, 95% CI: 3.2–72.8). None of the CIs cross the null value (OR=1), indicating statistically significant associations across all pairs.

Angiographic findings

A total of 25 patients with AIS underwent CAG as part of the study. The CAG findings summarized in Table 3 revealed that 8 patients (32%) had obstructive CAD, while 7 patients (28%) had non-obstructive CAD. Notably, 10 patients (40%) demonstrated normal coronary arteries on angiography.

Analysis of vessel involvement showed that the left anterior descending artery (LAD) was the most frequently affected vessel, involved in 10 cases (40%), followed closely by the right coronary artery (RCA) in 9 cases (36%). The left circumflex artery (LCX) was involved in 5 cases (20%).

Assessment of the extent of coronary artery involvement revealed that single-vessel disease (SVD) was present in 9 patients (36%), while double-vessel disease (DVD) and triple-vessel disease (TVD) were each found in 3 patients (12%), respectively .

Regarding the nature of coronary lesions, calcified plaques were identified in 10 patients (40%), while non-calcified lesions were present in 8 patients (32%). Additionally, culprit lesions – those potentially responsible for significant ischemic events – were observed in 6 patients (24%).

Table 3. Correlations and angiographic findings

Category	**Details**	**Results**
Correlation analysis		
Correlation pair	Spearman's ρ (p)	OR and (95% CI)
hs-TnI and CAD	0.87 (<0.001)	48.2 (9.8–236.5)
hs-TnI and Death	0.75 (<0.001)	28.5 (5.9–137.1)
CAD and Death	0.60 (<0.001)	15.3 (3.2–72.8)
Coronary angiography (n=25)	Finding	Number of cases (%)
Overall result	Obstructive CAD	8 (32.0)
	Non-obstructive CAD	7 (28.0)
	Normal coronaries	10 (40.0)
Vessel involvement	Left anterior descending (LAD)	10 (40.0)
	Right coronary artery (RCA)	9 (36.0)
	Left circumflex (LCX)	5 (20.0)
Extent of disease	Single-vessel disease	9 (36.0)
	Double-/Triple-vessel disease	6 (24.0)
Lesion type	Calcified lesion	10 (40.0)
	Non-calcified lesion	8 (32.0)
	Culprit lesion	6 (24.0)

* percentages are calculated based on the total number of patients (n=25), the data on extent of disease were available for 15 patients, remaining 10 patients had normal coronaries, lesion types are not mutually exclusive, some patients had multiple lesion types

Discussion

AIS is a multifaceted condition with various underlying causes, frequently revealing cardiovascular comorbidities that influence patient outcomes. This study investigated the potential of serial hs-TnI measurements in AIS patients as a prognostic marker for cardiovascular morbidity and mortality. The recognition of cardiac involvement in acute stroke dates back to the late 1970s, when Norris et al. studied the rise of cardiac biomarkers in AIS patients, identifying myocardial dysfunction as a consequence rather than a cause of the stroke.[21] Serial measurements allow differentiation between acute and chronic myocardial injury. Studies have demonstrated that dynamic troponin patterns (defined by fluctuations of more than 20%) are associated with evolving myocardial injury whereas stable levels suggest chronic cardiac pathology.[22] In parallel, findings from our study revealed a significant increase in the proportion of AIS patients with elevated hs-TnI at 48 h (from 38.3% to 45%; p=0.038). while the number of patients with normal hs-TnI levels showed a decline (from 61.6% to 55%), thus revealing dynamic changes. The consistency between the above observed changes and Rosso et al. paradigm further highlights the importance of serial troponin measurements as opposed to single point values.[22] Serial hs-TnI assay revealed dynamic elevation at 48 h signifying evolving myocardial injury that might otherwise remain undetected and can unmask hidden or subclinical cardiac dysfunction.

The evolving nature of the cardiac biomarker demonstrates the interplay between neurological insult and cardiac dysfunction-central to the concept of Stroke-Heart Syndrome. It encompasses the clinical spectrum that includes acute myocardial injury, type 1 and 2 myocardial infarction–ischemic and non-ischemic manifestations like left ventricular dysfunction, cardiac arrhythmias, ECG changes, Takotsubo syndrome and contraction band necrosis.[6,7] Prediction of acute coronary syndrome in AIS by Nolte et al. concluded type 1 MI was common mechanism of myocardial injury in stroke and a higher baseline hs-cTn values, whereas our study aligned with the concept of evolving myocardial stress in AIS supporting the need for comprehensive cardiac evaluation in management of AIS patients.[23]

In this study ECG abnormalities were observed in 55% of patients at admission an increased to 60% at 48 h, with significant increase in T-wave inversions in the inferior leads (p=0.03) with no significant changes in ST depression or bundle branch blocks. The study by Fure et al. on ECG abnormalities in the early stage of ischemic stroke identified the following: prolonged QTc, ST-segment depression, atrial fibrillation, and T wave inversion. ST depression and Q waves were associated with an increase in TnT levels.[24] Severe LVEF impairment increased from 5% to 13.3% (p=0.02), in those patients with hs-TnI elevations after 48 h however mild LVEF impairment got resolved after 48 h. ECHO abnormalities like RWMA s in the septum and inferior wall with variable grades of severity was observed in patients with acute stroke with elevated troponin levels and was consistent after the 48 h interval with a statistical significance. These findings are in accordance with the results by a study done by Amir Darke et al., in which 67% of patients with elevated troponin had new RWMA.[19] These findings highlight the evolving nature of cardiac dysfunction in AIS

patients, underscoring the importance of serial cardiac monitoring. Given the significant correlations between Troponin I and ECG/ECHO abnormalities, angiographic screening may be warranted in AIS patients with unexplained dynamic hs-TnI elevations to identify underlying CAD.

This study highlights a significant prevalence of CAD among patients with AIS. Of the 25 patients who underwent CAG, obstructive CAD was found in 32%, non-obstructive CAD in 28%, and normal coronaries in 40%. These findings suggest that a substantial proportion of stroke patients have coexisting but variable degrees of coronary involvement. The LAD was the most commonly involved vessel, followed by the RCA and LCX. SVD was more frequent than multi-vessel involvement, suggesting a different pathophysiological mechanism compared to patients with acute coronary syndrome. Lesion analysis revealed calcified plaques in 40%, non-calcified plaques in 32%, and culprit lesions in 24% of patients. This suggests both chronic and potentially unstable coronary pathology among stroke patients. These findings are in accordance with TRELAS study which concluded prevalence of SVD was higher than multivessel involvement and significantly lesser prevalence of culprit lesion compared with NSTE-ACS patients (7 out of 29 vs. 23 of 29).[25] As discussed earlier both ischemic and non-ischemic causes leads to the elevation of hs-TnI in patients with AIS. The differentiation between true CAD versus neurogenic myocardial injury lies in the fact that the former would typically present with dynamic change of cTn>20%, new ischemic ECG changes, imaging evidence of RWMAs whereas the latter has predominantly insular involvement, QT prolongation, global LV dysfunction.[26] Coronary Angiography is considered gold standard in aiding the differentiation between the two.[8] The presence of culprit lesion indicated significant CAD, which aligns with 24% occurrence of culprit lesions in our study.[25] Mortality are also observed even after exclusion of patients with known CAD. 40% of patients with elevated hs-TnI had normal coronaries. Thus it is concluded that not all troponin elevation in stroke indicates true CAD and integration of cardiac and neurological diagnostic modalities would be vital.

MRI findings revealed that MCA infarcts were the most prevalent stroke type (36.7%), followed by multi-infarct strokes (15%) and lacunar strokes (13.3%). Stroke type significantly influenced outcomes (p=0.001), with larger infarcts associated with higher troponin I elevations and increased cardiovascular complications. Von Rennenberg et al. concluded that a strong correlation between elevated cardiac biomarkers in patients with acute stroke were significantly linked to abnormal cardiac MRI findings such as focal fibrosis, LVH, decreased LVEF and left atrial dilatation.[27] These findings emphasize the need for thorough cardiac assessment and timely integration of cardiology in stroke care. Stroke was significantly more common in the right cerebral hemisphere in patients with increased troponin I without any ischemic changes on the ECG. In patients with elevated troponin, the functional status based on Modified Rankin Scale showed a significant worsening in 30 days post-stroke.[28] The major risk factors for cardiovascular morbidity includes diabetes mellitus, hypertension, dyslipidemia. In this study the mean FBS of 170±80 mg/dL and PPBS of 253±96 mg/dL with a mean HbA1C of 7.2±1.6%, indicated poorer glycemic control in patients with

elevated troponin levels. A lower recommended level of HDL cholesterol of 39.5±6.1 mg/dL along with raised LDL levels with a mean of 182±33 mg/dL, suggests a high risk for atherosclerosis thus contributing to cardiovascular risk. The meta-analysis by YuFan et al. demonstrated an association between cardiac troponin elevation and all-cause mortality (RR: 2.53) in patients with AIS.[29] The analysis of PROCIS-B cohort by Scheitz et al., highlighted that elevated hs cTnT Was linked to increased risk of recurrent vascular events and mortality in individuals experiencing their first ever mild to moderate ischemic stroke.[30]

Baseline levels of cTnI were associated with a higher risk of mortality both in hospital and at 6 months follow-up with an increased likelihood of non-fatal cardiac events.[31] In this study 11 patients with high levels succumbed during the hospital stay thereby revealing the nexus between troponin and cardiovascular mortality in the study cohort. The cause of death during the first week of ischemic stroke includes cerebral edema and hemorrhagic transformation whereas heart failure, acute myocardial infarction, ventricular fibrillation, ventricular tachycardia, are the predominant causes of death within first 3 months of stroke attributed to autonomic dysfunction in lesions of insular cortex.[32] Overall, patients with dynamic changes were more likely to show ischemic changes in ECG, reduced LVEF, RWMAs and higher prevalence of angiographically confirmed CAD suggesting serial hs Troponin measurements more effectively indicate the likelihood of in-hospital mortality and cardiovascular outcomes as evidenced by strong positive correlations between Troponin I levels and both CAD (ρ=0.87, p<0.001) and mortality (ρ=0.75, p<0.001). Evidence of damaged myocardial fibers were present in patients with intracranial lesions.

Myocardial alterations following stroke resembles those that of Takotsubo Cardiomyopathy characterized by autonomic imbalance with increased catecholamine release.[33] Evidence from recent research suggested that cardiac biomarkers were associated with vascular cognitive impairment and dementia.[34]

Damage to the right dorsal anterior insular cortex in stroke disrupts autonomic regulation, leading to heightened sympathetic activity and increased risk of myocardial injury.[35] The concentration of troponin rises over several days which can be detected by serial measurements after stroke onset. Several studies showed elevated troponin at admission is a prognostic marker and an individual predictor of mortality at 30 days, 6 months and a mean follow-up at 19 months of ischemic stroke.[36] The underlying cause of elevated troponin levels is associated with both increased case fatality and higher degree of disability. In summary, guidelines support baseline hs-TnI testing in all ischemic stroke patients for early cardiac risk detection.

Clinical and research implications

The findings of this study emphasize the need for routine serial hs-TnI monitoring in AIS patients, as dynamic changes in the levels may provide early indicators of cardiac stress. Given the significant correlations between hs-TnI and ECG/ECHO abnormalities, and coronary angiogram findings, stroke management protocols should integrate cardiac assessments to optimize risk stratification. Furthermore,

angiographic screening may be warranted in AIS patients with unexplained hs-TnI elevations to identify underlying CAD.

Study limitations

The present study had a small sample size from a single centre and most of the patients were from critical care. Further studies involving larger sample size would provide more insights. Excluding patients who died or were discharged early may have led to selection bias, which could possibly restrict the generalizability of the results. Exploring the role of inflammation, autonomic dysfunction, and neuro-cardiac interactions in AIS patients with elevated hs-TnI would provide a better understanding of the correlation. Another limitation of the study was lack of long term follow-up of patients and no stroke severity score like NIHSS were adjusted in analysis. Additionally, larger multicenter studies with longer follow-up periods could help establish the prognostic utility of troponin I in predicting long-term cardiovascular outcomes in stroke patients.

Conclusion

In conclusion, serial hs-TnI elevations in acute ischaemic stroke patients are associated with evolving cardiovascular complications, particularly in those with preexisting metabolic disorders and silent coronary artery disease. The dynamic changes of hs-TnI correlate with abnormalities in ECG, ECHO, and angiographic findings, emphasizing its role in cardiovascular risk assessment. The integration of serial troponin I monitoring in AIS protocols may enhance early detection of cardiac complications, ultimately improving clinical outcomes in stroke patients. Hs-TnI is an independent predictor of cardiovascular mortality. Hence it serves as a marker with prognostic significance .Further studies are needed to refine predictive models and explore targeted interventions for AIS patients with elevated troponin I levels.

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Declarations

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Author contributions

Conceptualization, N.D.C. and P.V.A.; Methodology, N.D.C. and P.V.A.; Software, N.D.C., M.S.T.; Validation, N.D.C. and P.V.A.; Formal Analysis, D.S.V., P.V.A. and D.R.; Investigation, P.V.A., P.K. and D.S.V.; Resources, N.D.C. and P.V.A.; Data Curation, N.D.C.; Writing – Original Draft Preparation, N.D.C. and P.V.A.; Writing – Review & Editing, N.D.C., P.V.A., and D.S.V.; Visualization, N.D.C. and P.V.A.; Supervision, N.D.C. and P.V.A., V.M.R.; Project Administration, N.D.C.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Data availability

All data generated or analyzed during this study are included in this published article. Additional data are available from the corresponding author upon reasonable request.

Ethics approval

The study adhered to the guidelines set forth in the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the Institutional Ethics Committee of Chettinad Hospital and Research Institute, Tamil Nadu, India (074/IHEC/2020).

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