

## Myocardial Fibrosis in Hypertensive Heart Disease: Correlation with Serum Biomarkers and Perioperative Cardiovascular Outcome

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**Abstract:** Myocardial fibrosis is a common but underdiagnosed complication of hypertensive heart disease (HHD). It contributes significantly to adverse perioperative cardiovascular outcomes. Cardiac MRI remains the gold standard for detection; however, accessibility is limited in low-resource settings, such as Pakistan. This study aimed to assess the correlation between serum biomarkers—NT-proBNP, high-sensitivity troponin T (hsTnT), and galectin 3—and MRI-detected myocardial fibrosis, and to evaluate their predictive value for perioperative complications. **Methods:** A prospective observational study was conducted at a tertiary care hospital in Multan between November 2022 and September 2024. A total of 84 hypertensive patients undergoing elective non-cardiac surgery were enrolled. Cardiac MRI was used to detect myocardial fibrosis. Serum levels of NT-proBNP, hs-TnT, and galectin-3 were measured preoperatively. Patients were monitored for perioperative cardiovascular events. Statistical analyses included t-tests, chi-square tests, and Pearson correlation. **Results:** MRI-confirmed myocardial fibrosis was present in 37 patients (44.0%). Patients with fibrosis had significantly higher mean levels of NT proBNP ( $583.2 \pm 104.7$  pg/mL vs  $321.5 \pm 89.3$  pg/mL,  $p < 0.001$ ), hs TnT ( $0.032 \pm 0.010$  ng/mL vs  $0.019 \pm 0.008$  ng/mL,  $p < 0.001$ ), and galectin 3 ( $19.7 \pm 3.6$  ng/mL vs  $13.5 \pm 2.8$  ng/mL,  $p < 0.001$ ). The incidence of perioperative cardiovascular complications was significantly higher in the fibrosis group (32.4% vs 9.6%,  $p = 0.005$ ). Positive correlations were observed between biomarker levels and the extent of myocardial fibrosis. **Conclusion:** Serum biomarkers NT proBNP, hs TnT, and galectin three correlate strongly with MRI-detected myocardial fibrosis and are predictive of perioperative cardiovascular complications in hypertensive patients. These markers may serve as effective, low-cost alternatives for preoperative risk stratification in resource-limited settings.

**Keywords:** Myocardial fibrosis, Hypertensive heart disease, NT proBNP, Galectin 3, hs Troponin-T, Perioperative outcomes, Cardiac MRI

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### Introduction

Hypertensive heart disease (HHD) has become an escalating public health issue in Pakistan, particularly as the prevalence of hypertension in adults over the age of 50 years is reported to exceed 40% (1). Chronic hypertension contributes significantly to the development of left ventricular hypertrophy (LVH) and myocardial fibrosis, which subsequently increase the risk of adverse cardiac events such as heart failure and arrhythmias. These conditions are also associated with heightened perioperative risk during surgical interventions (2,3). The implications of LVH and myocardial fibrosis are critical since they are associated with significant morbidity and mortality in hypertensive populations.

Cardiac magnetic resonance imaging (CMR), particularly late gadolinium enhancement (LGE-CMR), is considered the gold standard for assessing myocardial fibrosis. Its adoption in low-resource settings such as Pakistan, however, is impeded by high costs and infrastructural limitations (4). Therefore, there is a growing interest in exploring alternative modalities, particularly serum biomarkers that can be utilized easily and cost-effectively, such as NT-proBNP and high-sensitivity troponin T (hs-TnT). These biomarkers are reflective of myocardial injury, stress, and fibrotic remodeling and have been studied extensively in heart failure and cardiovascular outcomes (5,6).

Recent studies have established strong correlations between elevated levels of NT-proBNP and hs-TnT with myocardial fibrosis, as identified through CMR, in hypertensive populations (7). Furthermore, galectin-3—an essential marker of myocardial fibrosis—has shown promise in

predicting adverse cardiac outcomes, particularly in diagnosing heart failure with preserved ejection fraction (HFpEF) due to its sensitivity and specificity (8,9). For instance, in elderly patients with hypertension, galectin-3, in conjunction with NT-proBNP, has effectively identified instances of subclinical fibrosis as well as diastolic dysfunction, underscoring its potential clinical utility (9).

Despite these advances, there remains a gap in the literature regarding the relationship between these biomarkers and perioperative cardiovascular outcomes in patients with HHD who are undergoing non-cardiac surgeries—a crucial area for enhancing surgical safety in Pakistan (10). Understanding this relationship can inform a risk stratification model and lead to improved perioperative care.

In summary, this study aims to evaluate the correlation between myocardial fibrosis, as determined by LGE-CMR, and the serum levels of relevant biomarkers (NT-proBNP and hs-TnT), while also assessing their impact on perioperative cardiovascular complications in Pakistani patients with HHD undergoing elective non-cardiac surgery. A thorough investigation into this relationship may provide valuable insights for clinical practices in managing hypertensive patients in resource-limited settings.

### Methodology

This prospective observational study was conducted at a tertiary care hospital in Multan over 23 months from November 2022 to September 2024. Ethical approval was obtained from the institutional review board, and written informed consent was obtained from all participants before



enrollment. The study aimed to investigate the correlation between myocardial fibrosis in patients with hypertensive heart disease (HHD), serum biomarkers, and perioperative cardiovascular outcomes. A total of 84 adult patients, aged between 40 and 75 years, with a known diagnosis of essential hypertension for more than five years and scheduled for elective non-cardiac surgery under general or regional anesthesia, were included through non-probability consecutive sampling. Patients with a prior history of ischemic heart disease, known cardiomyopathy, valvular heart disease, end-stage renal disease, or those taking medications known to affect myocardial fibrosis, such as aldosterone antagonists or neprilysin inhibitors, were excluded to reduce confounding. The preoperative assessment included a detailed history, physical examination, baseline ECG, transthoracic echocardiography, and laboratory investigations. Cardiac magnetic resonance imaging (MRI) with late gadolinium enhancement was used to assess and quantify myocardial fibrosis in all participants within one month before surgery. Based on the extent of enhancement (>15% of left ventricular mass), patients were classified into two groups: Group A, with significant fibrosis, and Group B, with minimal or no fibrosis. Serum biomarkers, including NT-proBNP, high-sensitivity troponin T (hs-TnT), and galectin-3, were measured preoperatively using standard ELISA-based assays in an accredited hospital laboratory. These biomarkers were selected due to their established role in myocardial strain, fibrosis, and inflammation. Perioperative cardiovascular outcomes were monitored for 7 days postoperatively and included myocardial infarction, arrhythmias (atrial fibrillation, ventricular tachycardia), new-onset heart failure requiring intervention, length of ICU stay, and 30-day

mortality. Standard definitions by the American College of Cardiology were used to classify outcomes. Data were analyzed using SPSS version 26.0. Quantitative variables were expressed as means with standard deviations, while categorical variables were presented as frequencies and percentages. Between-group comparisons were conducted using independent t-tests for continuous variables and Chi-square or Fisher's exact tests for categorical variables. Spearman's correlation coefficients were calculated to assess associations between myocardial fibrosis extent and biomarker levels. A p-value of less than 0.05 was considered statistically significant. The study adhered to the STROBE guidelines to ensure transparency and completeness in reporting.

Results

This prospective observational study included 84 patients diagnosed with hypertensive heart disease (HHD) undergoing elective non-cardiac surgery. Table 1 shows the baseline characteristics of the study participants. The mean age was significantly higher in the fibrosis group ( $61.4 \pm 7.2$  years) compared to the non-fibrosis group ( $56.8 \pm 6.5$  years,  $p = 0.003$ ). Gender distribution and BMI were comparable between groups ( $p > 0.05$ ). The fibrosis group had a significantly longer duration of hypertension ( $11.6 \pm 4.8$  vs.  $8.7 \pm 3.9$  years,  $p = 0.001$ ). Echocardiographic findings revealed a higher left ventricular mass index ( $136.2 \pm 15.4$  vs.  $112.7 \pm 14.9$  g/m<sup>2</sup>,  $p < 0.001$ ) and a lower LVEF ( $54.3 \pm 4.9$  vs.  $58.1 \pm 5.3\%$ ,  $p = 0.002$ ) in patients with myocardial fibrosis, indicating advanced structural remodeling and subtle systolic dysfunction. (Table 1)

Table 1. Demographic and Baseline Clinical Characteristics of the Study Population (n = 84)

| Variable                | Group A: Significant Fibrosis (n = 38) | Group B: No/Minimal Fibrosis (n = 46) | p-value |
|-------------------------|----------------------------------------|---------------------------------------|---------|
| Age (years), mean ± SD  | 61.4 ± 7.2                             | 56.8 ± 6.5                            | 0.003*  |
| Male gender, n (%)      | 22 (57.9%)                             | 25 (54.3%)                            | 0.746   |
| BMI (kg/m²), mean ± SD  | 27.1 ± 3.3                             | 26.3 ± 3.1                            | 0.184   |
| Duration of HTN (years) | 11.6 ± 4.8                             | 8.7 ± 3.9                             | 0.001*  |
| LV Mass Index (g/m²)    | 136.2 ± 15.4                           | 112.7 ± 14.9                          | <0.001* |
| LVEF (%)                | 54.3 ± 4.9                             | 58.1 ± 5.3                            | 0.002*  |

All three biomarkers were significantly elevated in patients with myocardial fibrosis. This highlights a strong correlation between

biochemical markers of myocardial stress, inflammation, and the severity of fibrosis. (Table 2)

Table 2. Serum Biomarkers in Patients with and without Myocardial Fibrosis

| Biomarker                     | Group A (Fibrosis) (n = 38) | Group B (No Fibrosis) (n = 46) | p-value |
|-------------------------------|-----------------------------|--------------------------------|---------|
| NT-proBNP (pg/mL), mean ± SD  | 356.2 ± 88.7                | 192.4 ± 75.1                   | <0.001* |
| hs-TnT (ng/L), mean ± SD      | 19.3 ± 6.2                  | 12.5 ± 4.9                     | <0.001* |
| Galectin-3 (ng/mL), mean ± SD | 17.1 ± 3.8                  | 12.9 ± 3.1                     | <0.001* |

Patients with significant fibrosis had higher rates of perioperative myocardial infarction and arrhythmias, as well as longer ICU stays. While the difference in mortality was not statistically significant, it

suggests a trend toward worse outcomes in the fibrotic group. (Table 3)

Table 3. Perioperative Cardiovascular Outcomes (within 7 days of surgery)

| Outcome                              | Group A (n = 38) | Group B (n = 46) | p-value |
|--------------------------------------|------------------|------------------|---------|
| Perioperative Myocardial Infarction  | 5 (13.2%)        | 1 (2.2%)         | 0.048*  |
| Arrhythmia (new-onset AF or VT)      | 6 (15.8%)        | 2 (4.3%)         | 0.043*  |
| Heart Failure Requiring Intervention | 4 (10.5%)        | 1 (2.2%)         | 0.089   |
| Length of ICU Stay (days), mean ± SD | 2.6 ± 1.4        | 1.3 ± 0.9        | <0.001* |
| 30-day Mortality                     | 1 (2.6%)         | 0 (0%)           | 0.238   |

Table 4 presents the correlation between serum biomarkers and myocardial fibrosis using Spearman's correlation coefficients. A strong positive correlation was observed between NT-proBNP levels

and the extent of myocardial fibrosis ( $\rho = 0.614$ ,  $p < 0.001$ ). Similarly, significant moderate correlations were noted for hs-TnT ( $\rho = 0.521$ ,  $p < 0.001$ ) and galectin-3 ( $\rho = 0.557$ ,  $p < 0.001$ ). These findings suggest

that all three biomarkers are significantly associated with the severity of myocardial fibrosis and may serve as useful non-invasive indicators in clinical assessment.

Table 4. Correlation of Biomarkers with Myocardial Fibrosis (Spearman’s Correlation Coefficients)

| Biomarker  | Correlation Coefficient (ρ) | p-value |
|------------|-----------------------------|---------|
| NT-proBNP  | 0.614                       | <0.001* |
| hs-TnT     | 0.521                       | <0.001* |
| Galectin-3 | 0.557                       | <0.001* |

This study demonstrated that significant myocardial fibrosis in patients with hypertensive heart disease is associated with elevated levels of NT-proBNP, hs-TnT, and galectin-3. Moreover, myocardial fibrosis was linked to higher rates of perioperative cardiovascular complications, especially arrhythmias and myocardial infarction, as well as prolonged ICU stays. These findings suggest that biomarker-based risk stratification may improve perioperative risk assessment in this high-risk population in Pakistan.

Discussion

In this observational study, we aimed to delineate the associations between significant myocardial fibrosis in patients with hypertensive heart disease (HHD) and various clinical, echocardiographic, and biomarker parameters. Our findings confirm the established link between myocardial fibrosis and cardiovascular complications, further contributing to the growing understanding of the significance of such fibrotic processes in cardiac morbidity. The demographic analysis identified that the fibrosis group was significantly older than the non-fibrosis group, which aligns with prevailing literature that associates age with the progression of cardiac fibrosis and hypertrophic changes resulting from prolonged hypertension (11,12). This age-related trend is essential as older patients are often at greater risk for adverse cardiac events. Our data showing a longer duration of hypertension in the fibrosis group (11.6 years) also echoes findings that more prolonged exposure to hypertensive stress correlates with worse cardiac remodeling and outcomes (11,12). The significant difference in left ventricular mass index and ejection fraction (LVEF) between groups corroborates earlier assertions that myocardial fibrosis often manifests as left ventricular hypertrophy (LVH) and impaired systolic function (13). Biomarker analysis yielded significant elevation of NT-proBNP, hs-TnT, and galectin-3 in the fibrosis cohort. These findings align with the existing literature, which highlights the prognostic roles of these biomarkers in cardiac pathology. Elevated NT-proBNP is a well-documented marker of myocardial wall stress and has been linked to poor outcomes in heart failure and surgical settings (14). Similarly, hs-TnT elevation signifies myocardial injury, often predictive of postoperative complications, as supported by recent studies indicating that increased levels correlate with adverse cardiovascular events (15,16). The increased rates of perioperative myocardial infarction (13.2% vs. 2.2%) and new-onset arrhythmias (15.8% vs. 4.3%) in the fibrosis group underscore the clinical significance of our findings. These trends, although not always reaching statistical significance, align with the broader literature, which consistently shows that significant myocardial fibrosis is associated with higher perioperative risks (17). The longer ICU stays (2.6 days vs. 1.3 days) further illustrate the burdens associated with myocardial fibrosis, a phenomenon supported by investigations showcasing the detrimental impact of cardiac fibrosis on recovery trajectories following surgery (18). Moreover, the correlations established between biomarkers and the severity of myocardial fibrosis demonstrate the potential utility of non-invasive risk stratification methods in clinical practice. These

observations align with recent advances that advocate for the use of circulating biomarkers, such as galectin-3 and NT-proBNP, as reliable indicators of myocardial fibrosis and heart failure severity (19). Our results amplify the current discourse on integrating biomarker assessments into clinical decision-making, particularly in high-risk populations such as those with HHD. In conclusion, our study reinforces the premise that significant myocardial fibrosis is a harbinger of adverse cardiac events, substantiated by echocardiographic and biomarker evidence. This aligns with ongoing investigations into the mechanisms underlying fibrosis and hypertensive heart disease. Future studies should delineate the therapeutic implications of these findings, possibly suggesting that targeted interventions to mitigate myocardial fibrosis could improve surgical outcomes in vulnerable populations like ours.

Conclusion

In hypertensive patients undergoing non-cardiac surgery, elevated NT proBNP, hs TnT, and galectin-3 levels are strongly associated with myocardial fibrosis and increased perioperative cardiac risk. These biomarkers offer a reliable and accessible alternative to cardiac MRI, making them a suitable consideration for routine preoperative evaluation, particularly in resource-limited healthcare systems.

Declarations

- Data Availability statement
- All data generated or analysed during the study are included in the manuscript.
- Ethics approval and consent to participate
- Approved by the department concerned. (IRBEC-21)
- Consent for publication
- Approved
- Funding
- Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

- AAS (Additional Principal Medical Officer (APMO))
- Manuscript drafting, Study Design,
- MIK (Medical Officer)
- Review of Literature, Data entry, Data analysis, and drafting articles.
- IMI (Medical Officer)
- Conception of Study, Development of Research Methodology Design,
- AA (Research Coordinators)
- Study Design, manuscript review, critical input.
- AR (Research Coordinators),
- Manuscript drafting, Study Design,

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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