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A Histological Study of Myocardial Fiber Disruption and Serum CK-MB in Ischemic Heart Disease

Ahmad Farzad Qureshi[1], Nadia Ahmad[2], Uzma Hanif[3], Muhammad Shakil Sadiq[4], Muhammad Muneeb Ather[5], Waqas Iqbal[6]

[1] Associate Professor, Anatomy, Sahiwal Medical College, afarzad2001@gmail.com.
[2] Associate Professor, Shalamar Medical and Dental College, diaejaz_74@hotmail.com.
[3] Acting Assistant Professor, Anatomy, Rashid Latif Medical College, Druzmahanif1212@gmail.com.
[4] Associate Professor of Anatomy, Poonch Medical College, Rawalakot, AJK, mshakilsadiq@yahoo.com.
[5]Assistant Professor, Anatomy, Shalamar Medical & Dental College, Lahore, drmuneebathar@gmail.com.
[6] Associate Professor of Anatomy, Sharif Medical and Dental College, Lahore, drwaqasiqbal@gmail.com.

Abstract

Ischemic heart disease (IHD) precipitates disruption of myocardial fiber integrity and elevates serum creatine kinase–MB (CK-MB), yet precise correlation remains underexplored. In this experimental study, myocardial biopsy specimens from 60 adult patients undergoing coronary artery bypass grafting were compared with 30 age-matched controls without IHD. Histological evaluation quantified fiber disruption using a validated scoring system, and preoperative serum CK-MB levels were assayed. Cases demonstrated significantly greater disruption scores (mean ± SD: 3.8 ± 0.6) than controls (1.2 ± 0.4; $p < 0.001$), with a strong positive correlation to CK-MB activity ($r = 0.72$, $p < 0.001$). Multivariate regression confirmed fiber disruption score as an independent predictor of CK-MB ($\beta = 0.54$; $p < 0.01$), adjusting for age, hypertension, and diabetes. This study introduces a novel quantitative histopathological metric and establishes its robust association with biochemical myocardial injury. Histological assessment of fiber disruption may serve as a tissue-based biomarker reflecting CK-MB release in IHD, offering potential utility in diagnostic stratification and prognostic evaluation.

Keywords: myocardial fiber disruption; CK-MB; ischemic heart disease

Introduction

Ischemic heart disease (IHD) remains the leading cause of cardiovascular morbidity and mortality worldwide, reflecting a chronic imbalance between coronary oxygen supply and myocardial

demand. Major advances in diagnostic and therapeutic modalities have shifted focus from clinical symptomatology to deeper pathological mechanisms, particularly at the cellular and architectural levels of myocardium. While serum biomarkers such as CK-MB and troponins have been pivotal in detecting myocyte injury, their capacity to mirror the exact structural disruption at the myofiber level is not fully characterized[1].

Myocardial fiber disruption—characterized by fragmentation of sarcomeric structures, disarray, and loss of parallel alignment—has been qualitatively observed in both experimental and clinical IHD settings. However, the absence of a standardized method to quantify these histological features hinders their integration into diagnostic and prognostic frameworks[2]. Recent histomorphometric approaches, published since 2022, have begun to provide semi-automated quantification of fiber disarray, primarily in animal models and biopsy specimens[3–5]. These studies underscore the potential for correlating structural damage with clinical parameters, yet have not extended to concurrent biochemical markers.

Serum CK-MB, although surpassed in sensitivity by high-sensitivity troponins for acute infarction diagnosis, remains integral to understanding membrane disruption and muscle turnover. CK-MB kinetics have been correlated with infarct size and ventricular remodeling, and elevated levels have prognostic significance in IHD[6–9]. Despite this, no studies have directly linked serum CK-MB levels with histological scoring of fiber pathology, representing a significant knowledge gap in translational pathology.

Bridging this gap, the present study develops a novel histopathological scoring protocol for myocardial fiber disruption and explores its association with serum CK-MB levels. This approach aligns with recent initiatives in multimodal cardiac assessment, integrating morphological and biochemical metrics to enhance disease phenotyping[10–12]. By comparing myocardial tissue from revascularized IHD patients with that from non-IHD controls, this study aims to establish both diagnostic validity and biochemical correlation.

Furthermore, multivariate analyses will test whether fiber disruption score predicts CK-MB independently of classical cardiac risk factors such as age, hypertension, and diabetes. This step addresses calls for histological markers with actionable prognostic value[13–15]. Establishing such links could inform future protocols where histology complements serum assays in post-ischaemic risk assessment and management.

Methodology

A prospective experimental design was implemented at Sahiwal Medical College, enrolling 60 adults (35–75 years) undergoing elective coronary artery bypass surgery with angiographically confirmed multi-vessel IHD, and 30 age- and sex-matched control subjects undergoing valvular surgery without evidence of IHD. Sample size calculation using Epi Info identified that 78 subjects would provide 80% power (α=0.05) to detect a 1.0-point difference in histological fiber disruption (SD 0.8), so 90 were recruited to allow attrition. Subjects with coexisting cardiomyopathies, active infections, prior myocardial infarction within six months, or elevated troponin were excluded. Verbal informed consent was obtained in accordance with institutional ethics guidelines.

During surgery, a standardized endomyocardial biopsy was performed from the left ventricular anterior wall. Tissues were fixed in neutral buffered formalin, paraffin-embedded, and sectioned (4 μm), then stained with hematoxylin-eosin and Masson's trichrome. A novel histological scoring system was employed: (0 = normal parallel fibers, 1 = mild disarray, 2 = moderate fragmentation, 3 = severe disruption, 4 = extensive necrosis/discontinuous fibers). Two independent pathologists blinded to clinical data scored each section; inter-rater reliability (κ = 0.87) confirmed reproducibility.

Preoperative blood samples were collected within 24 hours of biopsy. Serum CK-MB levels were measured using standardized immunoinhibition enzymatic assays. Demographic and clinical variables (age, sex, BMI, hypertension, diabetes) were recorded. Statistical analysis employed SPSS v27. Histological scores and CK-MB values were compared between cohorts using independent t-tests. Correlation analysis utilized Pearson's coefficient. Multivariate linear regression assessed the predictive relationship, adjusting for covariates. Statistical significance was set at $p<0.05$ for all analyses.

Results

Table 1. Demographic and Clinical Characteristics

Variable	IHD (n = 60)	Controls (n = 30)	p-value
Age (years)	62.3 ± 7.8	60.9 ± 8.1	0.42
Male sex, n (%)	44 (73%)	22 (73%)	1.00
Hypertension, n (%)	38 (63%)	16 (53%)	0.34

Variable	IHD (n = 60)	Controls (n = 30)	p-value
Diabetes, n (%)	27 (45%)	11 (37%)	0.48

Table 2. Histological Disruption Score and Serum CK-MB

Parameter	IHD (n = 60)	Controls (n = 30)	p-value*
Fiber disruption score	3.8 ± 0.6	1.2 ± 0.4	<0.001
Serum CK-MB (ng/mL)	28.4 ± 7.2	9.6 ± 2.8	<0.001

Table 3. Correlation and Multivariate Regression

Analysis	Coefficient	p-value
Pearson r (Score vs CK-MB)	0.72	<0.001
Regression β (adjusted score → CK-MB)	0.54	0.004

*Independent t-tests for IHD vs controls.

IHD patients exhibited significantly elevated histological fiber disruption and serum CK-MB. A strong correlation ($r = 0.72$) and independent predictive value of disruption score ($\beta = 0.54$) were demonstrated, underscoring the relevance of structural pathology to enzyme release.

Discussion

The present study establishes a novel histological scoring system for myocardial fiber disruption and demonstrates its statistically significant correlation with serum CK-MB levels in IHD. The high correlation (r=0.72) and independent predictive value following adjustment for comorbidities highlight this metric's potential as a tissue-based biomarker in clinical evaluation[16–17]. This aligns with recent histomorphometric research, though earlier studies have focused primarily on fibrosis and troponin correlations without capturing fiber architecture[6–8].

Fiber disruption reflects acute structural compromise at the sarcomeric level. Its quantification fills a critical gap, offering a histological counterpart to biochemical markers. This extends prior imaging-based assessments and provides direct tissue-level validation[18–20]. The consistency of findings between pathologists ($\kappa = 0.87$) also supports the tool's reproducibility in research and potentially, diagnostic settings.

Serum CK-MB, while superseded by troponins in clinical practice, remains useful for gauging active myocardial membrane disruption. The independent association between histological score and CK-MB reinforces the biological plausibility that disrupted fiber integrity facilitates enzyme leakage[21–23]. These findings suggest histological disruption score could complement serum assays for stratifying ongoing injury, particularly in chronic IHD contexts.

Importantly, this study controlled for major confounders, and the regression model demonstrated the histological metric's independent significance. This addresses concerns from earlier studies where structural and biochemical markers were evaluated in isolation[24–25]. By integrating both, this work contributes to a more holistic understanding of myocardial injury patterns.

In contrast to studies using only infarct size or fibrosis as endpoints, this research emphasizes fiber orientation and degradation—parameters more intimately tied to mechanical and electrical myocardial function[26–28]. These characteristics may have prognostic relevance, particularly in predicting post-revascularization remodeling and arrhythmogenesis.

However, the study has limitations. It evaluated CK-MB rather than high-sensitivity troponin; future investigations should examine whether fiber disruption correlates more robustly with troponin isoforms or novel biomarkers. The biopsy sample, taken from a single ventricular region, may not represent global myocardial architecture; multi-site sampling could enhance validity[29].

Future studies should explore longitudinal outcomes, including remodeling and functional recovery, in relation to histological disruption scores and enzyme kinetics. Integrating automated image analysis could further standardize scoring and facilitate wider application[30].

Conclusion

Quantification of myocardial fiber disruption serves as a reliable structural correlate of serum CK-MB in ischemic heart disease. This novel histological biomarker enhances understanding of tissue-pathological dynamics and addresses a critical gap in translational cardiac pathology. Future research should integrate this metric into prognostic models and explore its association with outcomes and troponin assays.

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