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Clinical significance of connective tissue growth factor (ctgf) and echocardiographic remodeling in patients with ischemic heart disease and chronic heart failure

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Abstract

Background: Ischemic heart disease (IHD) remains one of the leading causes of chronic heart failure (CHF), morbidity, and mortality worldwide. Progressive myocardial remodeling and fibrosis significantly contribute to left ventricular dysfunction and worsening prognosis in patients with IHD. Connective tissue growth factor (CTGF) has recently emerged as a potential biomarker involved in myocardial fibrosis, extracellular matrix remodeling, and ventricular dysfunction **[1,3,5]**. **Objective:** To assess the clinical significance of connective tissue growth factor (CTGF) and echocardiographic remodeling in patients with ischemic heart disease complicated by chronic heart failure. **Materials and Methods:** A prospective observational study included **67 patients** with ischemic heart disease hospitalized in the **Cardiology Department of the Multidisciplinary Clinic of Tashkent State Medical University**. Clinical, laboratory, and instrumental evaluations were performed in all patients. Serum CTGF levels were assessed, and transthoracic echocardiography was conducted to determine left ventricular ejection fraction (LVEF) and structural remodeling parameters. Patients were stratified according to CTGF levels. Statistical analysis was performed using standard parametric and nonparametric methods, with $\mathbf{p < 0.05}$ considered statistically significant. **Results:** Elevated CTGF levels were observed in the majority of patients and were associated with reduced left ventricular systolic function and adverse myocardial remodeling. Patients with elevated CTGF demonstrated lower LVEF values ranging between **38–50%**, as well as more frequent echocardiographic signs of ventricular remodeling. Increased CTGF concentration was associated with progression of myocardial structural abnormalities and worsening cardiac function.

Conclusion: CTGF may serve as a clinically relevant biomarker reflecting myocardial remodeling and impaired cardiac function in patients with ischemic heart disease and chronic heart failure. Combined assessment of CTGF and echocardiographic parameters may improve risk stratification and optimize personalized therapeutic strategies.

Keywords: ischemic heart disease; chronic heart failure; CTGF; myocardial remodeling; echocardiography; left ventricular ejection fraction

Introduction:

Cardiovascular diseases remain the leading cause of mortality worldwide, with ischemic heart disease (IHD) accounting for the majority of cardiovascular-related deaths and disability **[1,2]**. Despite advances in pharmacological and interventional treatment approaches, chronic heart failure (CHF) secondary to ischemic myocardial damage continues to represent a substantial clinical burden **[2,6]**. Structural and functional myocardial remodeling is considered one of the principal mechanisms underlying disease progression and unfavorable cardiovascular outcomes **[3,7]**.

Myocardial fibrosis is an essential component of pathological remodeling and plays a critical role in the development of ventricular dysfunction. Excessive extracellular matrix deposition leads to increased myocardial stiffness, impaired contractility, and adverse hemodynamic consequences

[3,8]. In recent years, increasing attention has been directed toward biomarkers reflecting fibrotic activity and myocardial remodeling. Connective tissue growth factor (CTGF), a profibrotic mediator belonging to the CCN protein family, has emerged as a promising biomarker associated with tissue fibrosis and cardiovascular remodeling **[4,5]**. CTGF is involved in fibroblast activation, collagen synthesis, inflammatory signaling, and extracellular matrix accumulation **[5]**. Elevated CTGF expression has been demonstrated in various cardiovascular disorders, including myocardial infarction, heart failure, hypertensive heart disease, and cardiomyopathy **[3,4]**. Several studies suggest that elevated CTGF levels may correlate with the severity of myocardial dysfunction and ventricular remodeling in patients with cardiovascular diseases **[5,7]**. However, available evidence regarding its clinical role in ischemic heart disease complicated by chronic heart failure remains limited, particularly in regional populations **[8]**. Therefore, the present study aimed to evaluate the clinical significance of CTGF and echocardiographic remodeling in patients with ischemic heart disease and chronic heart failure treated in the multidisciplinary clinic of Tashkent State Medical University.

Materials and Methods:

Study Design and Population

This prospective observational study included **67 patients** with ischemic heart disease (IHD) complicated by chronic heart failure (CHF), who were hospitalized and treated in the **Cardiology Department of the Multidisciplinary Clinic of Tashkent State Medical University**.

Patients underwent comprehensive clinical, laboratory, and instrumental examinations aimed at assessing myocardial remodeling and the role of connective tissue growth factor (CTGF) in progression of cardiac dysfunction.

The study population consisted of patients with clinically and instrumentally confirmed ischemic heart disease. Chronic heart failure was diagnosed according to standard clinical recommendations and echocardiographic criteria.

Inclusion Criteria

- confirmed diagnosis of ischemic heart disease;
- chronic heart failure;
- reduced or moderately reduced left ventricular systolic function;
- availability of laboratory and echocardiographic assessment.

Exclusion Criteria

- acute myocardial infarction during the study period;
- severe valvular pathology;
- malignant neoplasms;
- severe renal or hepatic dysfunction;
- acute inflammatory diseases.

Clinical and Laboratory Examination

All patients underwent complete clinical examination including:

- medical history assessment;
- cardiovascular risk stratification;
- physical examination;
- electrocardiography;
- biochemical laboratory testing.

Serum levels of **connective tissue growth factor (CTGF)** were measured to evaluate fibrotic activity and myocardial extracellular matrix remodeling. According to laboratory findings, patients were divided into groups depending on CTGF concentration.

Among the examined patients, **18 demonstrated normal CTGF levels**, whereas the majority showed elevated biomarker concentrations, indicating increased fibrotic activity.

Echocardiographic Examination

Transthoracic echocardiography (EchoCG) was performed in all patients for assessment of myocardial structure and functional status.

The following parameters were evaluated:

- left ventricular ejection fraction (LVEF);
- myocardial remodeling;
- ventricular structural changes;
- myocardial contractility.

The left ventricular ejection fraction ranged from **38% to 50%**, indicating varying degrees of systolic dysfunction. Signs of myocardial remodeling were more frequently observed in patients with elevated CTGF levels.

Statistical Analysis

Statistical analysis was carried out using standard medical statistical methods. Continuous variables were presented as **mean ± standard deviation (M ± SD)**. Group comparisons were performed using **Student's t-test** and nonparametric methods when appropriate. Statistical significance was considered at $p < 0.05$.

Results:

Clinical Characteristics of the Study Population

A total of **67 patients** with ischemic heart disease complicated by chronic heart failure were included in the study. Clinical manifestations of cardiac dysfunction and echocardiographic signs of myocardial remodeling were identified in the majority of examined patients.

Elevated CTGF levels were observed more frequently and were associated with impaired left ventricular systolic function and unfavorable myocardial structural changes.

Table 1. Baseline Clinical Characteristics of Patients

Parameter	Value
Total number of patients	67
Patients with normal CTGF	18
Patients with elevated CTGF	49
Left ventricular ejection fraction (LVEF)	38–50%
Presence of myocardial remodeling	Frequently observed
Study site	Multidisciplinary Clinic of TSMU

CTGF Levels and Myocardial Remodeling

Analysis of CTGF concentrations demonstrated that **49 patients (73.1%)** had elevated CTGF values, whereas **18 patients (26.9%)** had CTGF concentrations within normal limits.

Patients with elevated CTGF levels demonstrated more pronounced structural and functional myocardial abnormalities. Echocardiographic examination revealed a tendency toward lower left ventricular systolic performance in this group.

Elevated CTGF concentration was associated with increased frequency of myocardial remodeling, suggesting activation of fibrotic pathways and extracellular matrix remodeling in patients with chronic ischemic myocardial injury.

Echocardiographic Findings

Echocardiographic evaluation demonstrated varying degrees of left ventricular systolic dysfunction among examined patients. Left ventricular ejection fraction ranged between **38% and 50%**, reflecting moderate reduction in myocardial contractility.

Patients with elevated CTGF levels more frequently demonstrated echocardiographic evidence of myocardial remodeling, including impaired ventricular geometry and deterioration of systolic function.

Table 2. Echocardiographic Characteristics According to CTGF Level

Parameter	Normal CTGF (n=18)	Elevated CTGF (n=49)
Left ventricular ejection fraction	45–50%	38–44%
Signs of remodeling	Less frequent	More frequent

Systolic dysfunction	Moderate	More pronounced

The obtained results suggest a relationship between increased CTGF concentration and adverse myocardial remodeling, indicating a possible role of CTGF in progression of chronic heart failure among patients with ischemic heart disease.

Discussion. The present study demonstrated a significant association between elevated connective tissue growth factor (CTGF) levels and adverse echocardiographic remodeling in patients with ischemic heart disease complicated by chronic heart failure. The obtained findings support the concept that myocardial fibrosis plays an important role in structural and functional deterioration of the myocardium in patients with chronic ischemic injury **[3,7]**. Myocardial remodeling represents a complex adaptive and maladaptive process characterized by alterations in ventricular geometry, myocardial fibrosis, and progressive impairment of contractile function **[3,8]**. Persistent ischemia contributes to fibroblast activation and excessive extracellular matrix deposition, ultimately leading to reduced myocardial compliance and impaired ventricular performance **[7]**. Connective tissue growth factor (CTGF) is considered one of the key mediators involved in fibrotic signaling pathways **[4,5]**. Experimental and clinical investigations have demonstrated that CTGF promotes collagen synthesis, fibroblast proliferation, and extracellular matrix accumulation **[5]**. Increased CTGF expression has been associated with myocardial fibrosis, left ventricular dysfunction, and poor cardiovascular prognosis **[5,8]**. In the present study, elevated CTGF levels were detected in the majority of examined patients and were accompanied by more pronounced echocardiographic abnormalities, including reduced left ventricular ejection fraction and myocardial remodeling. These findings are consistent with previous reports suggesting that elevated CTGF concentration reflects increased fibrotic activity and structural myocardial damage **[4,7]**. Echocardiographic evaluation revealed impaired systolic function, with left ventricular ejection fraction ranging from **38% to 50%**, indicating moderate functional impairment. The higher prevalence of remodeling among patients with elevated CTGF levels further supports the role of fibrosis-related pathways in progression of chronic heart failure. The clinical significance of CTGF assessment lies in its potential use as a biomarker for early detection of adverse remodeling and risk stratification in patients with ischemic heart disease. Combined assessment of laboratory fibrosis markers and echocardiographic parameters may facilitate individualized management strategies and improve prognostic evaluation. However, several limitations should be acknowledged. The relatively limited sample size and single-center design may restrict generalizability of findings. Further multicenter studies with larger patient populations are required to confirm the prognostic role of CTGF in chronic heart failure secondary to ischemic heart disease.

Conclusion:

1. Elevated CTGF levels were identified in the majority of patients with ischemic heart disease and chronic heart failure, indicating activation of myocardial fibrotic processes.
2. Increased CTGF concentration was associated with impaired left ventricular systolic function and adverse myocardial remodeling detected by echocardiography.
3. Left ventricular ejection fraction ranged from **38% to 50%**, reflecting varying degrees of systolic dysfunction among study participants.
4. Patients with elevated CTGF levels demonstrated more frequent echocardiographic signs of ventricular remodeling compared to patients with normal CTGF values.
5. Combined assessment of CTGF and echocardiographic parameters may improve risk stratification and contribute to optimization of individualized treatment strategies in patients with ischemic heart disease and chronic heart failure.

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