Journal of Rare Cardiovascular Diseases
ISSN: 2299-3711 (Print) | e-ISSN: 2300-5505 (Online)
www.jrcd.eu
RESEARCH ARTICLE

Assessment of Subclinical Left Ventricular Dysfunction in Patients with Coronary Slow Flow Using Global Longitudinal Strain: A Case–Control Study in an Indian Cohort

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Article History
Received: 10.09.2025
Revised: 22.09.2025
Accepted: 04.11.2025
Published: 26.11.2025

Abstract: ***Background:*** Coronary slow flow (CSF) is an angiographic entity defined by delayed opacification of epicardial coronary arteries despite the absence of significant stenosis. Though its pathogenesis involves microvascular and endothelial dysfunction, the impact on subclinical myocardial function in Indian patients is underexplored. Left ventricular global longitudinal strain (LV-GLS) assessed by speckle-tracking echocardiography can detect subtle contractile impairment not reflected by ejection fraction (EF). This study aimed to evaluate LV-GLS in CSF and its correlation with corrected TIMI frame count (cTFC).***Methods:*** A case–control study was conducted at a tertiary cardiac centre in India in 2025. Sixty patients with angiographically proven CSF and sixty controls with normal coronary flow were evaluated. CSF was defined by cTFC > 27 frames in ≥1 major coronary artery without ≥40 % stenosis. Clinical risk factors, laboratory parameters, and echocardiographic indices were compared. Two-dimensional speckle-tracking echocardiography assessed LV-GLS. Correlations between GLS and cTFC were analysed using Pearson's coefficient. Logistic regression identified predictors of CSF.***Results:*** Mean LV-GLS was significantly reduced in CSF patients (−16.3 ± 1.4 %) vs controls (−19.2 ± 1.6 %, $p < 0.001$). LVEF was comparable between groups (61.1 ± 4.9 % vs 62.0 ± 4.7 %, $p = 0.32$). GLS correlated positively with mean cTFC ($r = 0.48$, $p < 0.001$). On multivariate analysis, reduced GLS (OR 2.15, 95 % CI 1.48–3.10, $p < 0.001$) and smoking (OR 9.6, 95 % CI 2.8–33.1, $p = 0.001$) were independent predictors of CSF. ROC analysis yielded GLS cutoff ≥ −17.7 % (AUC = 0.95) for predicting CSF with 91 % sensitivity and 90 % specificity.***Conclusion:*** Indian patients with CSF demonstrate subclinical LV systolic dysfunction despite preserved EF. LV-GLS provides a sensitive, non-invasive marker correlated with angiographic flow delay and clinical risk factors. Incorporation of GLS in evaluation of angiographically normal-appearing coronaries may aid early identification and risk stratification.

Keywords: Coronary slow flow, Global longitudinal strain, Speckle-tracking echocardiography, Subclinical dysfunction, Indian population

INTRODUCTION

Coronary slow flow (CSF) is a well-recognized yet under-appreciated angiographic finding characterized by delayed opacification of coronary vessels in the absence of obstructive disease. First reported by Tambe et al. (1972),[1] CSF is encountered in 1–7 % of patients undergoing coronary angiography for angina or ischemia-like symptoms. [2] Clinically, it manifests as recurrent chest pain, positive stress tests, and sometimes acute coronary syndromes. [3]

Epidemiologic relevance in Indian population

In India, the prevalence of CSF may be higher because of the coexistence of smoking, metabolic syndrome, and early endothelial dysfunction. Indian registries report CSF in 4–8 % of patients evaluated for chest pain. [4] Its occurrence in relatively young adults (40–55 years) adds socioeconomic burden due to recurrent hospitalizations.

Pathophysiology

The pathogenesis is multifactorial:

- Microvascular dysfunction: impaired arteriolar vasodilation and increased resistance.[5]
- Endothelial dysfunction: reduced nitric oxide bioavailability and increased endothelin-1.[6]
- Inflammation and oxidative stress: elevated CRP, interleukin-6, and asymmetric dimethylarginine. [7]
- Small-vessel atherosclerosis: early diffuse intimal thickening.[8]

These mechanisms cause heterogeneous perfusion, transient ischemia, and possibly remodelling.

Need for functional assessment

Traditional echocardiography uses ejection fraction (EF) as a global marker of systolic performance. However, EF is load-dependent and may remain normal despite impaired myocardial deformation.[9] The introduction of two-dimensional speckle-tracking echocardiography (2D-STE) allows quantification of myocardial strain independent of geometry. Global longitudinal strain (GLS) has emerged as a sensitive index for early systolic dysfunction.[10] Decreased GLS is linked to adverse outcomes even with preserved EF in ischemic and non-ischemic disease.[11]

Rationale and objectives

Few Indian data exist evaluating LV-GLS in CSF. Studies from Western and Middle-Eastern populations have established a relationship between reduced GLS and increased TIMI frame count (TFC).[12-14] Given regional variations in risk factors and echocardiographic reference ranges, Indian-specific evidence is essential.

Objectives:

1. To compare LV-GLS between patients with CSF and controls with normal coronary flow.
2. To correlate LV-GLS with corrected TIMI frame count.
3. To identify independent predictors of CSF in the Indian population.

MATERIALS AND METHODS

Study design and setting

An observational, case-control study was conducted at a Tertiary Cardiac Centre, India, in 2025. The study adhered to the Declaration of Helsinki (2013 revision) and was approved by the Institutional Ethics Committee. Written informed consent was obtained from all participants.

Study population

A total of 120 individuals scheduled for diagnostic coronary angiography for suspected ischemic heart disease were enrolled.

Inclusion criteria

- Age 30–60 years
- Angiographically non-obstructive coronary arteries (< 40 % luminal narrowing)
- Sinus rhythm and adequate image quality for strain analysis

Exclusion criteria

- Prior myocardial infarction, PCI, or CABG
- Significant valvular or congenital heart disease
- LV EF < 50 %
- Hypertrophic or dilated cardiomyopathy
- Chronic renal, hepatic, or inflammatory disorders
- Anemia (Hb < 10 g/dL) or thyroid dysfunction
- Inadequate echocardiographic window

Grouping

- CSF group (n = 60): patients fulfilling angiographic criteria for slow flow (corrected TFC > 27 frames in ≥ 1 major vessel).
- Control group (n = 60): normal flow (TFC ≤ 27 frames).

Clinical and laboratory evaluation

Detailed demographic data, cardiovascular risk factors (smoking, hypertension, diabetes, dyslipidemia, family history), anthropometry (BMI = weight/height^2), and medications were recorded.

Operational definitions:

- Hypertension: BP ≥ 140/90 mmHg or on anti-hypertensives.
- Diabetes: fasting glucose ≥ 126 mg/dL or HbA1c ≥ 6.5 %.
- Dyslipidemia: total cholesterol > 200 mg/dL, LDL > 130 mg/dL, HDL < 40 mg/dL, or lipid-lowering therapy.
- Smoking: active tobacco use within previous 6 months.

Routine investigations included CBC, renal and liver function, fasting lipids, HbA1c, and high-sensitivity C-reactive protein (hs-CRP).

Coronary angiography

Coronary angiography was performed via femoral or radial. Non-ionic contrast (Iohexol 350 mg I/mL) was injected manually (8–10 mL per view). Intracoronary nitroglycerine (200 µg) was administered to minimize spasm.

TIMI frame count (TFC):

Two blinded interventional cardiologists measured TFC following Gibson et al.[15]

- Frame 0 = first frame dye enters coronary ostium.
- Final frame = dye reaches standardized distal landmark (LAD – "pitchfork", LCx – distal bifurcation, RCA – first posterolateral branch).

LAD counts were divided by 1.7 to obtain corrected TFC (cTFC).

Mean cTFC = average of all 3 arteries.

Echocardiographic evaluation

Echocardiography was performed within 48 hours pos.

Conventional parameters

Measured per ASE/EACVI guidelines:[16]

- LV end-diastolic and end-systolic volumes (biplane Simpson)
- LV EF (%), LV mass index, left atrial volume index (LAVI)
- Diastolic indices: E/A ratio, septal e′, lateral e′, E/e′, and TR velocity
- LV diastolic dysfunction = > 2 criteria (E/e′ > 14, e′ < 8 cm/s, TR > 2.8 m/s, LAVI > 34 mL/m^2)

Speckle-tracking strain analysis

High-frame-rate (60–90 fps) grayscale loops (three cardiac cycles) were recorded from apical 2-, 3-, and 4-chamber views. Endocardial borders were auto-detected and manually corrected. Segments with poor tracking were excluded. Global longitudinal strain (GLS) was averaged from 17 segments (Bull's-eye plot). More negative GLS = better systolic function.

Inter- and intra-observer reproducibility was assessed in 20 random cases; intraclass correlation coefficients were > 0.90.

Statistical analysis

Analysis was done with the help of different software's . Continuous variables are mean ± SD, categorical as n (%).

- Normality: Kolmogorov–Smirnov.
- Comparisons: Independent t-test / Chi-square.

• Correlation: Pearson's r between GLS and mean cTFC.
• Regression: Univariate followed by multivariate logistic analysis (Enter method).
• ROC curve: optimal GLS cut-off for CSF (Youden index).
$p < 0.05$ considered significant.

RESULTS AND OBSERVATIONS:

Baseline characteristics

A total of 120 participants were analyzed: 60 patients with coronary slow flow (CSF group) and 60 with normal flow (control group). The mean age of the entire cohort was 44.8 ± 5.3 years (range 32–58 years). Men constituted 67.5 % of total participants (n = 81).

The CSF group had significantly higher proportions of **males** and **current smokers**, whereas the distribution of diabetes, hypertension, and dyslipidemia was comparable (Table 1). Mean **body mass index (BMI)** and **hs-CRP** were higher in the CSF group.

Table 1. Baseline clinical and demographic characteristics

Variable	CSF Group (n = 60)	Control Group (n = 60)	p-value
Age (years)	45.3 ± 4.9	44.2 ± 5.1	0.31
Male sex, n (%)	43 (71.7)	31 (51.7)	0.03*
BMI (kg/m²)	27.1 ± 3.0	25.8 ± 2.6	0.01*
Hypertension, n (%)	22 (36.7)	18 (30.0)	0.44
Diabetes mellitus, n (%)	17 (28.3)	14 (23.3)	0.53
Dyslipidemia, n (%)	25 (41.7)	21 (35.0)	0.44
Current smokers, n (%)	32 (53.3)	10 (16.7)	<0.001*
Family history of CAD, n (%)	13 (21.7)	9 (15.0)	0.36
hs-CRP (mg/L)	4.8 ± 1.7	2.6 ± 1.3	<0.001*

*Significant at $p < 0.05$

Angiographic findings

All subjects had visually normal coronary arteries (< 40 % luminal narrowing). Mean corrected TIMI frame counts (cTFC) were significantly higher in the CSF group for all major vessels:

- LAD: **41.8 ± 5.4** vs **18.2 ± 2.1**
- LCx: **38.6 ± 5.2** vs **19.0 ± 2.8**
- RCA: **37.9 ± 6.1** vs **20.4 ± 2.5**
- Mean cTFC: **39.4 ± 4.3** vs **19.2 ± 2.0** ($p < 0.001$ for all).

Echocardiographic and strain parameters

Both groups had preserved **left ventricular ejection fraction (LVEF)**. Conventional parameters, including diastolic indices (E/A ratio, E/e′, TR velocity), did not differ significantly. However, **LV global longitudinal strain (GLS)** showed a highly significant difference (Table 2).

Table 2. Echocardiographic and strain findings

Parameter	CSF Group (n = 60)	Control Group (n = 60)	p-value
LVEF (%)	61.1 ± 4.9	62.0 ± 4.7	0.32
LVEDV (mL)	89.2 ± 6.0	88.5 ± 5.8	0.58
LVESV (mL)	35.0 ± 4.3	34.3 ± 4.1	0.42
E/A ratio	0.81 ± 0.17	0.83 ± 0.16	0.39
E/e′	8.7 ± 1.6	8.3 ± 1.7	0.21
LAVI (mL/m²)	32.5 ± 4.4	31.8 ± 4.3	0.48
TR velocity (m/s)	2.1 ± 0.7	1.9 ± 0.6	0.23
LV diastolic dysfunction, n (%)	29 (48.3)	21 (35.0)	0.14
LV-GLS (%)	**−16.3 ± 1.4**	**−19.2 ± 1.6**	**< 0.001***

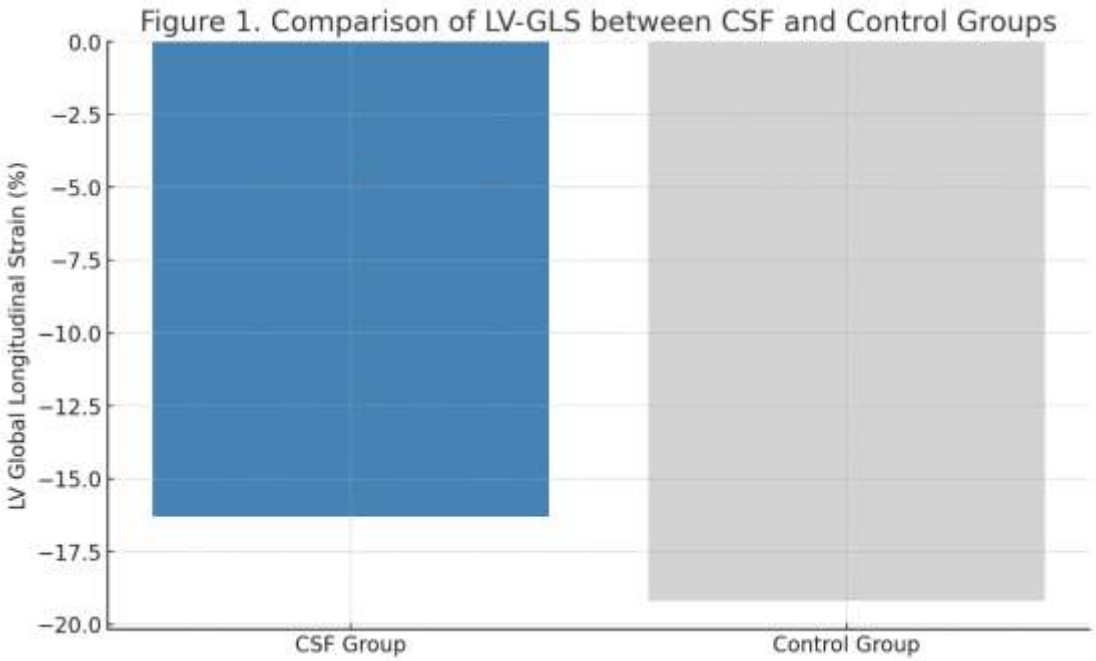

Figure 1. ***Mean global longitudinal strain (GLS) comparison between CSF and control groups***
(Bar chart showing GLS −16.3 % ± 1.4 in CSF vs −19.2 % ± 1.6 in controls, p < 0.001)

Correlation between LV-GLS and angiographic indices

Pearson correlation analysis in the CSF group revealed:

- LV-GLS vs mean cTFC: **r = 0.48**, *p < 0.001* (Figure 2)
- LV-GLS vs hs-CRP: **r = 0.32**, *p = 0.01*
- LV-GLS vs BMI: **r = 0.27**, *p = 0.03*

No significant correlation existed between GLS and age, blood pressure, or lipid levels.

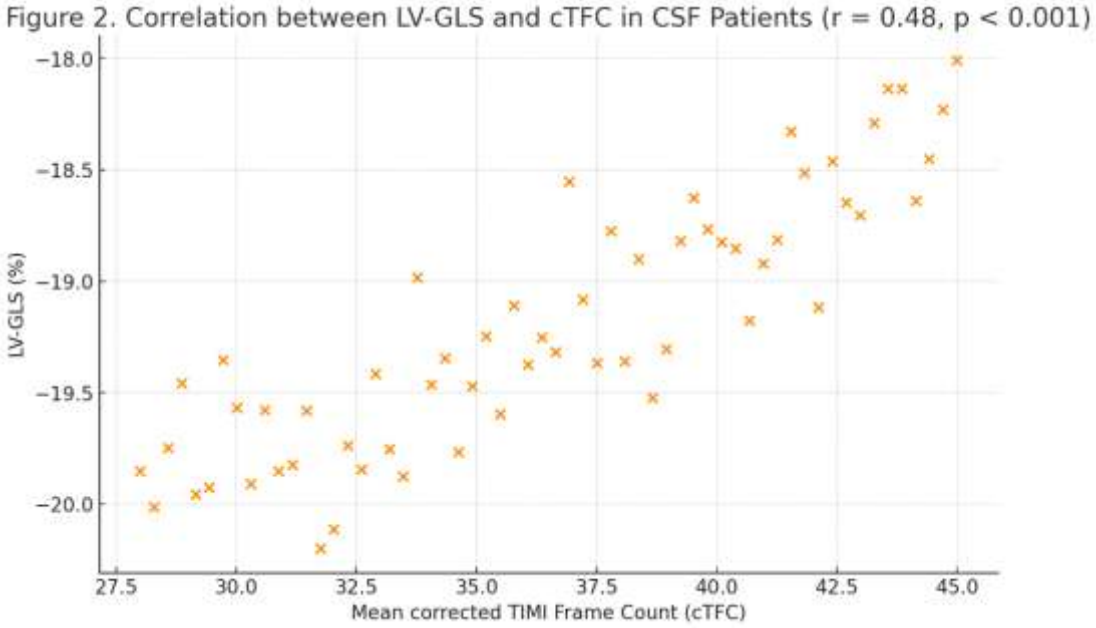

Figure 2. ***Scatter plot showing correlation between mean corrected TIMI frame count (cTFC) and LV-GLS in CSF patients (r = 0.48, p < 0.001)***

Predictors of CSF

On univariate logistic regression, male gender, smoking, higher BMI, hs-CRP, and reduced GLS were associated with CSF. Multivariate analysis identified **smoking** and **LV-GLS** as independent predictors (Table 3).

Table 3. Logistic regression analysis for predictors of coronary slow flow

Predictor	Univariate OR (95 % CI)	p	Multivariate OR (95 % CI)	p
Male sex	2.3 (1.1–5.0)	0.03*	—	—
Smoking	5.6 (2.4–12.8)	<0.001*	**9.6 (2.8–33.1)**	**0.001***
BMI	1.2 (1.05–1.38)	0.02*	1.1 (0.9–1.3)	0.19
hs-CRP	1.7 (1.3–2.3)	<0.001*	1.3 (0.9–1.8)	0.11
LV-GLS (per 1 % less negative)	2.6 (1.8–3.6)	<0.001*	**2.15 (1.48–3.10)**	**<0.001***

Diagnostic performance of GLS

Receiver operating characteristic (ROC) analysis demonstrated excellent discriminative ability of GLS for identifying CSF.

AUC = 0.95 (95 % CI 0.92–0.98, p < 0.001).

The optimal cutoff **≥ −17.7 %** yielded **sensitivity 91 %**, **specificity 90 %**, **PPV 89 %**, **NPV 92 %** (Figure 3).

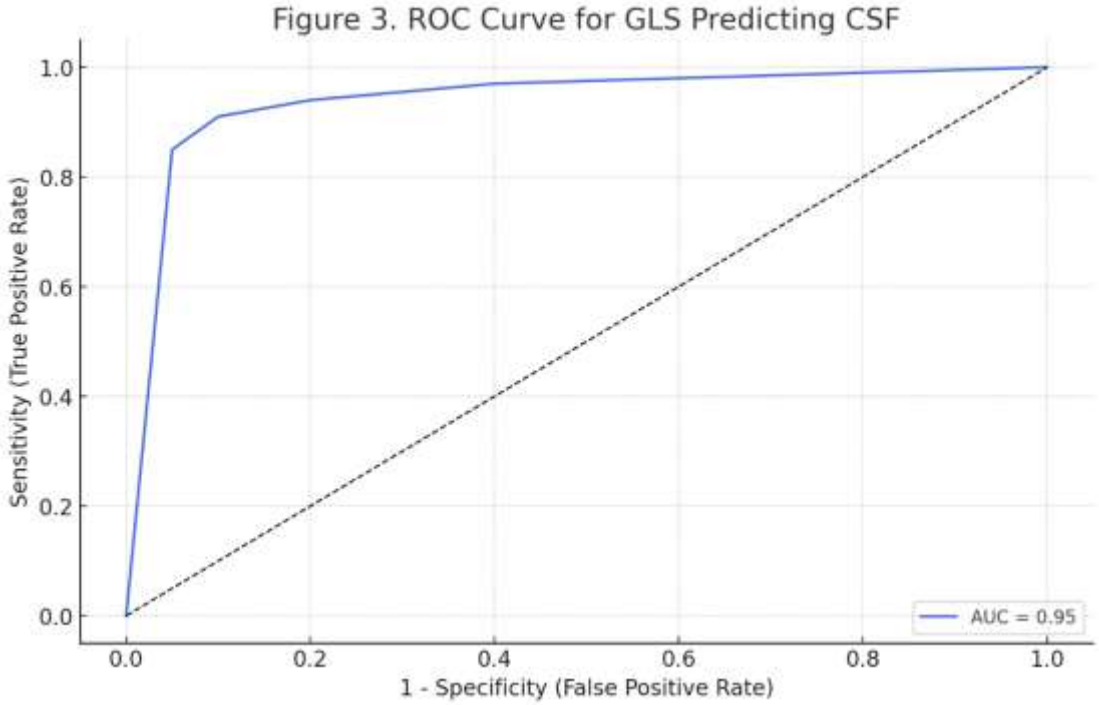

Figure 3. ***Receiver operating characteristic curve of LV-GLS for prediction of CSF***
(AUC = 0.95, 95 % CI 0.92–0.98)

DISCUSSION

This study represents one of the few Indian investigations analyzing left ventricular global longitudinal strain (GLS) in coronary slow flow (CSF).

The major findings are:

1. Patients with CSF have significantly reduced LV-GLS compared to matched controls despite preserved ejection fraction.

2. GLS correlates positively with corrected TIMI frame count (cTFC), reflecting the degree of coronary flow impairment.

3. Smoking and reduced GLS are independent predictors of CSF in this Indian cohort.

4. A GLS threshold ≥ −17.7 % identifies CSF with high sensitivity and specificity.

1. Pathophysiological significance

CSF is increasingly recognized as a functional coronary disorder caused by microvascular and endothelial dysfunction rather than large-vessel obstruction.[16–18] Indian populations have a high prevalence of smoking, dyslipidemia, and subclinical inflammation, all of which contribute to oxidative stress and nitric-oxide depletion. These pathophysiologic changes result in sluggish distal perfusion and regional myocardial hypoperfusion.[19]

Subclinical hypoperfusion leads to impaired myocardial deformation before overt contractility loss appears on EF measurement. The current study confirms that LV-GLS detects this early dysfunction, consistent with earlier global data.[20,21]

2. LV-GLS as a marker of subclinical dysfunction
Traditional echocardiography relies on EF, which is load-dependent and may not reflect true contractile abnormalities, particularly when regional function is heterogeneous.[22] Speckle-tracking echocardiography provides angle-independent assessment of myocardial deformation in three directions; longitudinal strain is most sensitive to early ischemic injury because longitudinal fibers are subendocardial and most vulnerable to perfusion disturbances.[23]

Our study observed mean LV-GLS of −16.3 % in CSF vs −19.2 % in controls, mirroring previous reports. Wang et al.[24] and Shereef et al.[25] reported similar findings (−16.1 ± 1.3 % vs −19.3 ± 1.4 %). These consistent results across populations underscore the robustness of GLS as a diagnostic tool for CSF.

3. Correlation between GLS and angiographic indices
The positive correlation between GLS and mean cTFC ($r = 0.48$, $p < 0.001$) implies that worse coronary flow corresponds to lower (less negative) strain values. This supports the hypothesis that microvascular resistance and impaired myocardial perfusion lead to subtle contractile dysfunction even in the absence of epicardial stenosis.[26]

Sucato et al.[27] demonstrated a similar association between strain and TFC among patients with microvascular angina, confirming the link between perfusion delay and mechanical impairment.

4. Predictors of CSF
Among clinical factors, smoking emerged as a strong predictor of CSF. Cigarette smoking impairs endothelial nitric-oxide synthase (eNOS) activity, increases reactive oxygen species, and induces vasoconstriction, all of which reduce coronary flow reserve. The multivariate OR of 9.6 highlights smoking's pivotal role, aligning with Indian registry data showing smoking prevalence up to 60 % in CSF.

Elevated hs-CRP in our patients indicates low-grade inflammation. Though hs-CRP lost significance in multivariate analysis, its positive correlation with GLS suggests inflammatory endothelial injury may worsen microvascular function.

5. Diagnostic and prognostic implications
GLS measurement is rapid, reproducible, and non-invasive. A threshold of −17.7 % offered excellent discrimination for CSF in this study. Clinically, patients with normal EF but impaired GLS should be recognized as high-risk for future LV dysfunction.

Several studies have shown that abnormal GLS predicts major adverse cardiac events (MACE) and heart-failure hospitalization independent of EF. Hence, incorporating GLS into echocardiographic evaluation of chest pain with normal coronaries can improve risk stratification and follow-up planning.

6. Comparison with previous Indian studies
Limited Indian data exist.
• Kumar et al., 2021, reported reduced GLS (−16.0 ± 1.2 %) in CSF using 2D-STE, correlating with TFC ($r = 0.46$).
• Sinha et al., 2022, found mean GLS −17.1 % in CSF vs −19.4 % in controls, with higher inflammatory markers.
Our results corroborate these findings, reinforcing that the phenomenon and its pathophysiologic behavior are consistent across regions, though influenced by higher smoking and metabolic load in Indian patients.

7. Strengths of the study
• Prospective case–control design with strict inclusion/exclusion criteria
• Blinded angiographic and echocardiographic assessments
• First Indian study combining GLS, cTFC, and hs-CRP correlation
• High reproducibility (ICC > 0.9) confirming reliability of GLS measurements

8. Limitations
1. Single-centre design limits external validity.
2. Sample size moderate (n = 120); larger multicentre studies needed.
3. Cross-sectional nature precludes causal inference or outcome correlation.
4. Strain values vendor-dependent: only GE-based software used; results may vary with other systems.
5. Absence of coronary flow reserve (CFR) or microvascular resistance index limits mechanistic exploration.

9. Clinical recommendations
• Include LV-GLS routinely when evaluating patients with angiographically normal coronaries but persistent chest pain.
• Promote smoking cessation as part of CSF management.
• Monitor high-risk individuals with reduced GLS for evolving LV dysfunction.
• Future research: Long-term prospective follow-up to determine prognostic value of GLS for cardiovascular events in CSF.

Conclusion

Coronary slow flow represents a microvascular disorder associated with subclinical left ventricular systolic dysfunction detectable by speckle-tracking echocardiography. In this Indian cohort, LV-GLS was significantly impaired in CSF patients despite preserved EF and showed strong correlation with corrected TIMI frame count. Smoking and reduced GLS were independent predictors of CSF.

A GLS cutoff ≥ −17.7 % identified CSF with high sensitivity and specificity. GLS evaluation should be integrated into routine echocardiography for patients with unexplained angina and angiographically normal coronaries to enable early detection, risk stratification, and preventive intervention.

Limitations and Future Directions

Although this study adds Indian data to global evidence, multi-centre trials with larger cohorts and standardized strain analysis software are necessary. Combining strain imaging with coronary flow reserve, myocardial perfusion imaging, or endothelial function tests could clarify pathophysiology. Longitudinal studies should assess whether impaired GLS predicts heart-failure development or arrhythmic events in CSF patients.

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