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ORIGINAL ARTICLE

Long-term Follow-up of Patients with Coronary Slow Flow: A Speckle-tracking Echocardiography Study

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ABSTRACT

Background: While earlier studies have indicated that patients with coronary slow flow (CSF) tend to have favorable outcomes, long-term prospective data remain limited.

Aim: This study aimed to assess the long-term clinical significance of CSF and its effect on cardiac function.

Study Design: A 5-year clinical follow-up was conducted to assess cardiac function in patients with CSF using both conventional and speckle-tracking echocardiography.

Methods: Nineteen patients diagnosed with CSF were included. Echocardiographic and strain parameters were recorded at baseline and re-evaluated after five years. Clinical follow-up was maintained throughout the study period.

Results: No significant changes were observed in echocardiographic or longitudinal strain parameters, all of which remained within normal limits. During the follow-up, there were no cases of mortality, cardiac-related hospitalizations, or acute coronary syndromes.

Conclusion: Patients with CSF demonstrated preserved cardiac function and a favorable long-term prognosis. Ongoing medical treatment likely played a role in maintaining these outcomes.

Keywords: Coronary slow flow, speckle-tracking echocardiography, strain imaging, long-term follow-up

INTRODUCTION

Coronary slow flow (CSF) is identified in approximately 2% of coronary angiographic procedures, yet its clinical relevance and long-term outcomes remain uncertain, and no standardized treatment guidelines have been established.[1-3] Several cross-sectional studies have examined the impact of CSF on cardiac function. Comparative analysis using echocardiographic techniques have found that left ventricular (LV) volumes and function in these patients are generally comparable to those of individuals without CSF.[4-7] Some studies have investigated the effects of pharmacologic therapies and treatment response, typically evaluating coronary flow during short-term follow-up; however, long-term data on ventricular function are limited.[8-10] Additionally, no prospective studies have assessed the extended effects of CSF. The exact pathology of CSF remains poorly defined. Although multiple theories have been proposed and explored, the underlying mechanism is not fully understood. Known secondary causes of CSF include coronary ectasia, coronary spasm, ventricular dysfunction, valvular heart disease, and connective tissue disorders.[2,11-15] Nonetheless, CSF is considered a distinct clinical entity, separate from these conditions. Although CSF has occasionally been associated with ventricular arrhythmias and, in rare cases, sudden cardiac death, it most commonly presents as acute coronary syndrome. While it may contribute to morbidity, a direct link to increased mortality has not been established. Although prior studies indicate that patients with CSF generally have a favorable prognosis, there is a lack of long-term prospective data on this condition.[3,12,16] Speckle-tracking echocardiography (STE) is an advanced imaging technique that allows semiautomatic assessment of LV function, offering greater reproducibility and accuracy than conventional echocardiographic methods. It has been shown to be more effective in evaluating cardiac function and predicting cardiovascular outcomes.[17-19] In this study, we aimed to assess the effect of CSF on

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cardiac function and its clinical relevance by conducting a 5-year clinical follow-up using both conventional echocardiography and STE.

METHODS

Study Population

This study was approved by the Çanakkale Onsekiz Mart University Clinical Research Ethics Committee (approval no: 2011-KAEK-27/2018-E.1800184834, decision date: 16.01.2019) and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants. This prospective study excluded patients with secondary causes of CSF, such as coronary ectasia, coronary spasm, ventricular dysfunction, valvular heart disease, and connective tissue disorders. Individuals with structural cardiovascular conditions-including LV dysfunction, LV hypertrophy, cardiomyopathies, or atherosclerotic coronary artery disease-were not included. Additional exclusion criteria were the presence of atrial fibrillation, valvular heart disease, congenital heart defects, pericardial disease, or stage 3-4 hypertension. Patients with bundle branch block on electrocardiography, a history of thoracic surgery, chronic systemic or inflammatory conditions, or malignancy were also excluded. Based on these criteria, 19 patients diagnosed with CSF were enrolled. At baseline, all patients underwent both standard and STE. Clinical follow-up continued for five years, after which echocardiographic assessments were repeated using the same equipment and performed by the same operators to maintain measurement consistency.

TIMI Frame Count and Definition of CSF

The diagnosis of CSF was established using the TIMI frame count method, as described by Gibson et al.[10] A cardiologist blinded to clinical details of the patients performed the frame count analysis. In this method, the initial frame is defined as the point at which contrast dye first enters the ostium of the coronary artery, and the final frame is the one in which the contrast reaches the first bifurcation of the posterior branch of the right coronary artery (RCA) and the distal bifurcations of the circumflex (Cx) and left anterior descending (LAD) arteries. For angiograms recorded at 30 frames per second, normal TIMI frame counts are defined as 20.4±3.0 for the RCA, 22.2±4.1 for the Cx, and 36±2.6 for the LAD. The corrected TIMI frame count for the LAD is obtained by dividing the LAD value by 1.7, with a normal reference value of 21.1±1.5. The average TIMI frame count is calculated from the values of all three major coronary arteries. Patients who showed CSF in at least one of these vessels were classified as having CSF.[20]

Standard Echocardiography

Echocardiographic assessments were performed using a high-resolution imaging system (Vivid 7, GE, USA). Measurements of LV and left atrial (LA) dimensions followed the guidelines of the European Society of Echocardiography.[21] The LA volume index and LV ejection fraction were calculated using the modified biplane Simpson's method. Diastolic function was evaluated by recording early (E) and late (A) diastolic LV filling velocities, along with E-wave deceleration time, using Doppler imaging. Pulsed-wave Doppler of mitral inflow and LV outflow were used to define the timing of mitral and aortic valve opening and closure. Tissue Doppler imaging (TDI) was employed to measure the E' and A' velocities at the lateral wall and septum. The E/E' ratio was calculated manually. Care was taken to optimize image quality by reducing interference from extracardiac structures and ensuring clear visualization of the myocardium.

Speckle-tracking Echocardiography

Speckle-tracking imaging was performed using grayscale B-mode echocardiography at a minimum frame rate of 80 frames per second. The cardiac cycle with the best image quality was selected for analysis, and the LV endocardial borders were traced at end-systole. Speckle-tracking analysis was carried out using an EchoPAC workstation (version 4.2.0, GE Vingmed Ultrasound AS, Horten, Norway). To measure global longitudinal strain (GLS), apical four-chamber, apical long-axis, and two-chamber views were acquired during breath-hold with continuous echocardiography monitoring. The automatic function imaging tool was used to define the regions of interest (ROI) by marking the endocardial surface at the mitral annulus and apex. The software then generated the epicardial surface and constructed the ROI, which was manually adjusted when necessary (Figure 1). Each ROI was segmented into six parts, and the software automatically assessed the tracking quality. A 17-segment LV model was applied to calculate peak systolic strain values, with end-systole identified as the point of aortic valve closure in the apical long-axis view.[22] Final GLS values were presented in a bullseye summary format (Figure 2).

Statistical Analysis

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) software, version 21.0 (SPSS Inc., Chicago, IL, USA). Echocardiographic measurements and calculations were independently assessed by two cardiologists. Descriptive statistics were used to summarize the sociodemographic data of the study population. The Wilcoxon signed-rank test was used to compare baseline and follow-up parameters. A p value of <0.05 was considered statistically significant.

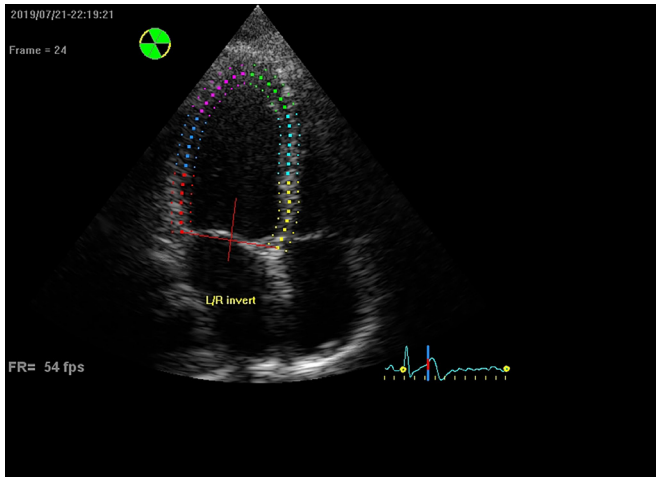

Figure 1. Marking the endocardial borders to define regions of interest

RESULTS

A total of 19 patients were enrolled in the study. Baseline echocardiographic and strain imaging data were collected 5 years earlier, and patients were clinically monitored throughout the follow-up period. At the end of the 5 years, standard echocardiography and strain imaging were repeated using the same echocardiography system. However, repeat imaging could not be performed in the nine patients. For these individuals, clinical status was assessed using national health database records and follow-up phone interviews.

Notably, no deaths occurred during the follow-up period, including among the nine patients who did not undergo repeat imaging. In addition, none of the participants experienced a major acute cardiac event over the 5 years. For the remaining 10 patients who completed follow-up imaging, both standard and STE were conducted. The demographic and clinical profiles of the study population remained consistent, as presented in Table 1.

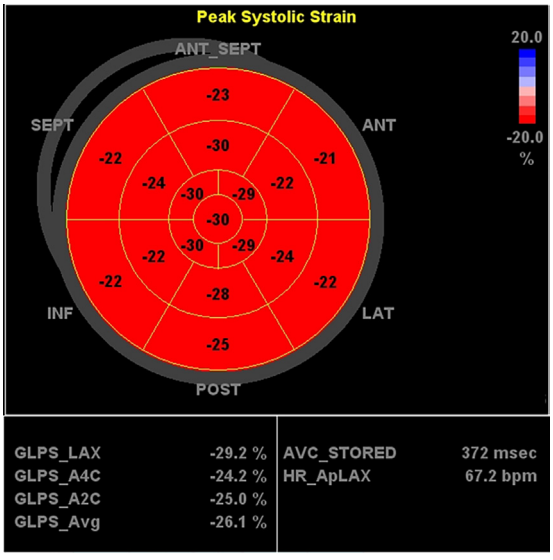

Figure 2. Longitudinal strain bull's-eye plot

Table 1. Demographic characteristics of the study population (n=10)

Variables	
Age (years)	50.60±8.68
Gender/male (%)	8 (80.0%)
BMI (kg/m^2)	29.39±4.81
BSA (m^2)	2.03±0.22
Systolic blood pressure (mmHg)	130.30±11.99
Diastolic blood pressure (mmHg)	79.70±6.62
Heart rate	72.20±7.42
Smoking	60.0% (6)
Alcohol	50.0% (5)
Hypertension	40.0% (4)
Diabetes mellitus	30.0% (3)
Hyperlipidemia	50.0% (5)

BMI: Body mass index, BSA: Body surface area

At 5 years, no statistically significant changes were detected in standard echocardiographic measurements (Table 2). Likewise, longitudinal strain values obtained through STE remained within normal limits and showed no significant differences compared to baseline (Table 3, Figure 3).

DISCUSSION

To our knowledge, this is the first study to provide a 5-year follow-up on patients with CSF. The results show a positive prognosis for all patients, with no reported deaths, cardiac-related hospitalizations, or acute coronary syndromes during the follow-up. Echocardiographic assessments showed no significant decline in LV function or volume over time.

This study used STE, a sensitive imaging technique capable of detecting early myocardial dysfunction even in patients with normal ejection fractions.[17-19] Importantly, strain parameters remained unchanged from baseline to follow-up, reinforcing the idea that CSF does not lead to progressive ventricular dysfunction. Although previous studies have suggested that patients with CSF generally have a good prognosis, long-term data on this condition have been limited.

Previous echocardiographic studies on CSF have mostly been cross-sectional, providing only a snapshot of its effects rather than long-term outcomes. These studies typically found that conventional echocardiographic parameters were similar between CSF patients and controls, but parameters indicating early myocardial dysfunction, such as TDI and strain imaging, were slightly lower in CSF patients.[4-7] However, the lack of longitudinal data leaves uncertainty about the clinical significance of these findings.

Table 2. Echocardiographic parameters of the study population

Parameters	Baseline n=10	Follow-up n=10	p value
Left ventricular diastolic diameter (mm)	48.60±5.44	48.80±4.76	0.959
Left ventricular systolic diameter (mm)	35.70±2.41	35.20±2.39	0.347
Left ventricular ejection fraction (%)	59.09±4.11	58.40±4.45	0.396
Posterior wall thickness (mm)	10.50±1.27	10.50±.0.97	0.943
Interventricular septum thickness (mm)	10.40±1.26	10.60±1.51	0.669
Left atrial diameter (mm)	36.80±5.35	34.70±1.64	0.181
Right ventricular diastolic diameter (mm)	31.10±5.13	31.30±4.19	0.953
Mitral inflow E wave (cm/s)	79.50±19.91	73.13±10.29	0.293
Mitral inflow A wave (cm/s)	74.50±15.69	72.38±18.21	0.674
Medial E' (cm/s)	10.38±2.92	9.88±2.47	0.777
Medial A' (cm/s)	11.13±1.96	11.38±1.30	0.715
Lateral E' (cm/s)	10.63±3.02	10.25±3.20	0.435
Lateral A' (cm/s)	12.14±2.73	10.71±2.69	0.066

E: Early, A: Late

Table 3. Strain parameters of CSF patients at baseline and 5-year follow-up

Variables	Baseline n=12	5-year follow-up n=10	p value
Global longitudinal strain	-20.79±2.24	-21.88±2.75	0.059
4 CH longitudinal strain	-20.48±2.51	-22.34±2.51	0.093
3 CH longitudinal strain	-21.14±2.39	-21.49±1.88	0.507
2 CH longitudinal strain	-20.85±3.08	-22.03±5.18	0.114

CH: Chamber, CSF: Coronary slow flow

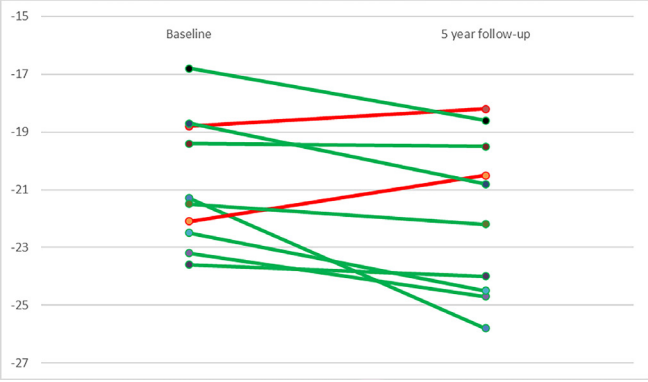

Figure 3. Global longitudinal strain at baseline and 5-year follow-up

Several pharmacological studies have evaluated the short-term effects of various medications on CSF. Some have reported improvements in symptoms and coronary flow following treatment.[8-10] For example, a study on calcium channel blockers showed that anginal symptoms improved in all patients after an average follow-up of 13.6 months.[23] However, long-term evaluations of cardiac function in these patients are missing. A prior study that followed patients with microvascular disease and CSF for an extended period noted persistent symptoms despite a generally favorable prognosis, though cardiac function was not assessed in that study.[24]

Our study offers both long-term clinical follow-up and comprehensive echocardiographic assessment. A recent retrospective observational study examined the link between previous coronary events and long-term outcomes in CSF patients. It found that only those with a history of myocardial infarction had a worse prognosis, while CSF alone was not associated with increased all-cause mortality.[25] In line with these findings, none of the patients in our cohort had a history of myocardial infarction, and all underwent coronary angiography due to anginal symptoms. Our results further support the evidence that patients with CSF, in the absence of prior myocardial infarction, have a favorable long-term prognosis. Additionally, through objective prospective measurements, we showed that their cardiac function remained stable over time.

Although various pharmacological treatments have been explored for tCSF,[8,10,23,26] the clinical trials conducted thus far have been too small to influence clinical guidelines. Currently, there is no standardized treatment protocol for CSF. However, based on expert consensus and previous research, statins and calcium channel blockers are commonly prescribed. In our study, most patients were on these medications. The stability of strain values over the 5-year period suggests that these treatments may have helped preserve cardiac function, although this remains speculative. Previous cross-sectional studies have reported similar medication use among CSF patients, and while not statistically significant, the slight improvements in strain values observed in our study may indicate the potential benefits of long-term medical management.

Study Limitations

This study has several limitations. First, the sample size was relatively small, which may limit the generalizability of the results. A larger cohort would provide more statistical power to detect subtle changes in cardiac function over time. Second, echocardiographic follow-up was not possible for all patients, as nine individuals could not undergo repeat assessments. Although their clinical status was monitored through national health records and phone calls, the lack of follow-up echocardiographic data for these patients may have affected the overall results. Third, while STE is a sensitive tool for assessing myocardial function, its accuracy depends on image quality and operator skill. Despite efforts to ensure high-quality imaging, minor variations in image acquisition and analysis may still exist. Additionally, although most patients were on medical therapy, the study did not systematically assess the impact of different medications on clinical and echocardiographic outcomes. Variations in medication adherence or changes in treatment during follow-up could have influenced the results. Finally, the study did not include a control group of healthy individuals or patients with similar risk factors but without CSF. A comparison with such groups would have provided more insight into whether the observed findings were specific to CSF or influenced by other factors.

Despite these limitations, this study provides valuable long-term data on the prognosis and cardiac function of CSF patients, emphasizing the need for further large-scale prospective studies to validate and expand these findings.

CONCLUSION

Patients with CSF appear to have a favorable long-term prognosis, with cardiac function remaining preserved over time. This suggests that either medical treatment may have a protective effect or CSF does not significantly impair myocardial perfusion to the extent that it affects ventricular function. Large-scale prospective studies are needed to confirm these findings and establish standardized management strategies for CSF.

Ethics Committee Approval: This study was approved by the Çanakkale Onsekiz Mart University Clinical Research Ethics Committee (approval no: 2011-KAEK-27/2018-E.1800184834, decision date: 16.01.2019) and conducted in accordance with the Declaration of Helsinki.

Informed Consent: Written informed consent was obtained from all participants.

Authorship Contributions: Concept: M.A., Ö.Ö.K., Design: M.A., Ö.Ö.K., Data Collection or Processing: M.A., Ö.Ö.K., Analysis or Interpretation: A.B., K.O.T., Literature Search: Ç.A.Ü., C.T., Writing: Ç.A.Ü., C.T.

Conflict of Interest: No conflict of interest was declared by the authors.

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