VIA MEDICA

ORIGINAL ARTICLE

Cardiology Journal
2023, Vol. 30, No. 6, 929–937
DOI: 10.5603/CJ.a2023.0046

ISSN 1897–5593
eISSN 1898–018X

Evaluation of left ventricular function in patients with coronary slow flow: A systematic review and meta-analysis

Tianxin Dong[1, 2]*, Qing Zhu[1, 2]*, Shang Wang[3], Shuo Liu[1, 2], Shitong Wang[1, 2], Yonghuai Wang[1, 2], Honghe Li[4, 5], Guangyuan Li[1, 2], Chunyan Ma[1, 2]

[1]Department of Cardiovascular Ultrasound, The First Hospital of China Medical University, Shenyang, Liaoning, China
[2]Clinical Medical Research Center of Imaging in Liaoning Province, Shenyang, Liaoning, China
[3]Dalian Medical University, Dalian, Liaoning, China
[4]School of Computer Science and Engineering, Northeastern University, Shenyang, Liaoning, China
[5]Key Laboratory of Intelligent Computing in Medical Image, Ministry of Education, Northeastern University, Shenyang, Liaoning, China

Abstract

Background: *Coronary slow flow (CSF) is an angiographic finding defined as delayed distal vessel perfusion without severe stenosis of the epicardial coronary arteries. However, definite alterations in left ventricular (LV) function in patients with CSF remains inconsistent. This study aimed to clarify the changes in LV function in patients with CSF and explore the factors that may influence LV function.*

Methods: *PubMed, Embase, and Cochrane Library databases were systematically searched. Standardized mean differences and 95% confidence intervals (CI) for the LV function parameters were calculated. Subgroup analysis, meta-regression analysis, and correlation analysis were performed to explore the factors influencing LV function.*

Results: *Twenty-two studies (1101 patients with CSF) were included after searching three databases. In patients with CSF, LV ejection function in patients with CSF was marginally lower (61.8%; 95% CI: 61.0%, 62.7%), global longitudinal strain was decreased (–18.2%; 95% CI: –16.7%, –19.7%). Furthermore, left atrial diameter, left atrial volume index, and E/e' were significantly increased, while E/A and e' were significantly decreased. The mean thrombolysis in myocardial infarction frame count (TFC) was linearly associated with LV function; the larger the mean TFC, the greater the impairment of LV function.*

Conclusions: *Left ventricular systolic and diastolic functions were impaired in patients with CSF, and this impairment was aggravated with increasing mean TFC.* (Cardiol J 2023; 30, 6: 929–937)

Key words: left ventricular function, global longitudinal strain, echocardiography, coronary slow flow, meta-analysis

Address for correspondence: Chunyan Ma, MD, PhD, Professor, Department of Cardiovascular Ultrasound, The First Hospital of China Medical University, No. 155 Nanjingbei Street, Shenyang, Liaoning 110001, China, tel/fax: +86-24-83282114, e-mail: cmu1h_mcy@126.com

Received: 20.09.2022 Accepted: 15.06.2023 Early publication date: 28.07.2023

**Co-first authors: Tianxin Dong and Qing Zhu*

Introduction

Coronary slow flow (CSF) is an angiographic observation, characterized by delayed perfusion in the distal vessel without significant stenosis of the epicardial coronary arteries, in the absence of other organic heart disorders [1, 2]. It has been reported in 7% of patients undergoing coronary angiography (CAG) for chest pain [3]. The mechanism of CSF is still unclear, but it is thought to be related to endothelial dysfunction, microvascular dysfunction, inflammation, subclinical atherosclerosis, abnormal blood cells, and genetics [4]. Recurrent chest pain is the dominant manifestation of CSF, followed by acute coronary syndrome, fatal cardiac arrhythmias, and sudden cardiac death, all of which require urgent clinical attention [1, 5–8].

In recent years, a growing body of research has focused on the effects of CSF on left ventricular (LV) function. Echocardiography, the method of choice for evaluating heart function, is being widely used to assess LV function in patients with CSF [9]. However, definite alterations in the echocardiographic parameters of LV function in patients with CSF remain inconsistent. Therefore, this systematic review and meta-analysis was performed to identify any alterations in the LV systolic and diastolic function, and explore the factors affecting LV function in patients with CSF.

Methods

The systematic review and meta-analysis were performed adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and the Cochrane Handbook for Systematic Reviews of Interventions recommendations [10, 11]. The study was prospectively registered with the International Prospective Register of Systematic Reviews (https://www.crd.york.ac.uk/PROSPERO/) on February 12, 2022 (No: CRD42022300680).

Literature search

PubMed, Embase, and Cochrane Library databases were systematically searched with the keywords "coronary slow flow," "left ventricular," and "echocardiography" to identify relevant studies from inception until April 1, 2022.

Inclusion and exclusion criteria

The inclusion criteria were as follows: i) studies involving an experimental group (patients with CSF) and a control group (patients with normal coronary flow); ii) echocardiography performed before or after CAG; and iii) in case of articles with an overlap in the study population, the study published most recently or with the greatest number of cases. Exclusion criteria were as follows: i) patients with organic heart disease; ii) data not reported, or inability to obtain the necessary data from the original literature; iii) reviews, case reports, commentaries, conference abstracts, animal model studies, etc.; and iv) studies not published in English.

Study selection

Two authors independently screened the articles according to predefined inclusion and exclusion criteria. Duplicate articles were excluded. Titles and abstracts were then read to eliminate irrelevant articles. Thereafter, rigorous screening of the remaining articles was performed by reading the full text. If the content was controversial, a third person made the final decision.

Data extraction and quality assessment

The following data were independently extracted by two authors: i) study information: first author, year of publication, country, and sample size; ii) clinical characteristics, including age, sex, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), triglyceride (TG), total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), diabetes mellitus (DM), hypertension (HTN), smoking history, and family history of coronary artery disease (CAD); iii) CAG results: mean thrombolysis in myocardial infarction frame count (TFC) and coronary artery involvement; iv) echocardiographic parameters: LV ejection fraction (LVEF), global longitudinal strain (GLS), E-wave to A-wave ratio (E/A), deceleration time (DT), mean velocities of the mitral ring in the early diastole (e'), E/e', left atrial diameter (LAD), left atrial volume index (LAVI), and myocardial performance index (MPI). Echocardiographic parameters were selected according to the American Society of Echocardiography guidelines [12, 13]. Quality assessment of the included studies was performed using the Newcastle–Ottawa Scale (NOS) critical appraisal tool. NOS provides evaluation criteria for observational studies in three aspects: selection (0–4 points), comparability (0–2 points), and exposure (0–3 points); with the highest score being 9 points [14].

Statistical analysis

A meta-analysis of the clinical characteristics and echocardiographic indices was performed. Pooled relative ratios (RR) and 95% confidence

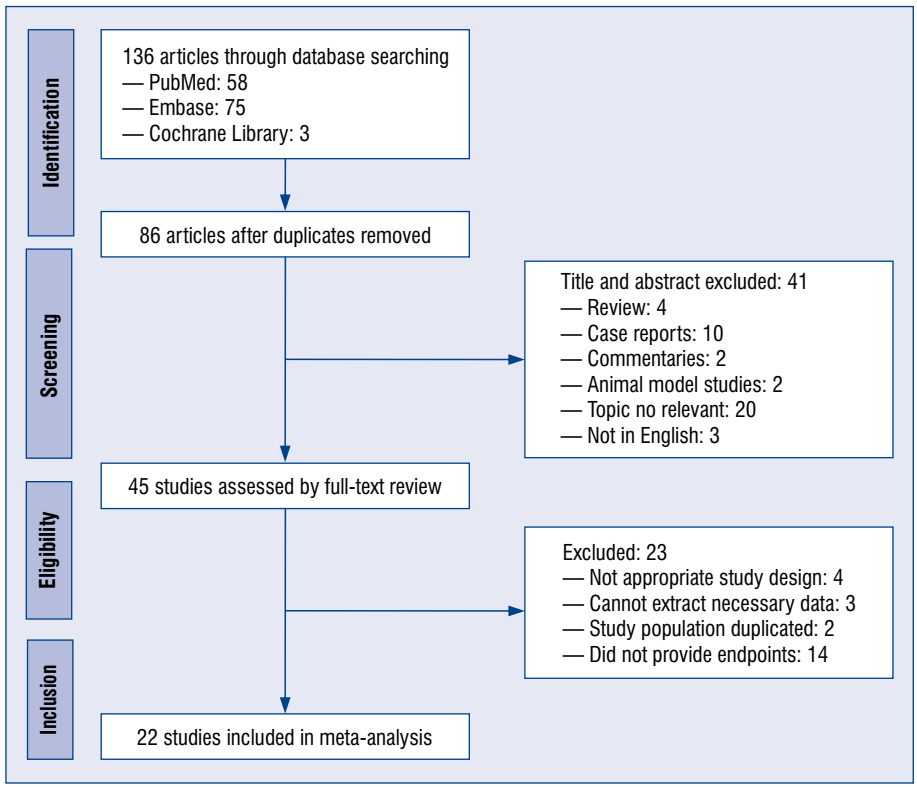

Figure 1. Flowchart of the study selection process.

intervals (CIs) were calculated for dichotomous outcomes; and the pooled standardized mean difference (SMD) and 95% CI were calculated for continuous outcomes. The results are presented as forest plots or summary tables. The Cochrane Q test and inconsistency index (I^2) were used to assess the heterogeneity of the pooled effect sizes. $I^2 < 40\%$ indicated no significant heterogeneity, and a fixed-effects model was used. $I^2 > 40\%$ suggested significant heterogeneity; a random-effects model was applied, and subgroup analysis or meta-regression analysis was performed [11]. To determine the correlations between the mean TFC and LV function, correlation coefficients (r) were converted to Z values for the meta-analysis. Subsequently, the pooled Z values were back-transformed into r. The Begg's test was used to evaluate publication bias; a p-value of > 0.05 suggested there was no significant publication bias [11]. STATA software (version 15) was used for all the analyses.

Results

Studies selection

Based on the pre-formulated search strategy, 136 articles were retrieved from the three databases. First, 50 duplicate articles were removed. And then, in the title and abstract review, 41 publications that were reviews, case reports, commentaries, animal studies, unrelated topics, and publications not published in English were excluded. Following that, a full-text review on 45 studies was performed, out of which 23 more articles were excluded. Eventually, a total of 22 articles that met the inclusion criteria [9, 15–35] were included. The flowchart in Figure 1 shows the detailed process and reasons for exclusion. Table 1 presents the clinical characteristics of the included studies. The included studies were published from 2007 to 2021. There were 13 studies from Turkey, 4 from China, 3 from Iran, and one each from Spain and Egypt. The diagnostic criteria for CSF were consistent: patients with a corrected TFC of > 27 in at least one major coronary vessel [36]. According to the NOS scale, no low-quality studies were found.

Clinical characteristics

The pooled results of the clinical characteristics suggested that the CSF group was older, more likely to be male, and had a greater prevalence of smoking than the control group. Meanwhile, the CSF group had a higher BMI and SBP, with lower

Table 1. The characteristics of the included studies.

Author, year	Country	Blind	Sample size		Male%		Mean age		HTN%		Mean TFC		Vendor	Echocardiographic parameters
			CSF	CG	CSF	CG	CSF	CG	CSF	CG	CSF	CG		
Sevimli, 2007	Spain	Y	22	22	55%	64%	48.0 ± 12.0	47.0 ± 11.0	NR	NR	49.7	17.7	GE	LVEF, E/A, DT, e', E/e'
Merih, 2009	Turkey	Y	50	27	84%	56%	52.0 ± 11.0	51.0 ± 8.0	40%	52%	40.7 ± 7.8	18.4 ± 3.7	HP SONOS 5500	LVEF, E/A, DT, e', LAD, MPI
Nurkaem, 2009	Turkey	Y	35	21	71%	76%	48.0 ± 7.0	50.0 ± 12.0	43%	38%	45.2 ± 14.3	20.8 ± 2.4	NR	LVEF, E/A, LAD
Tanrierdi, 2010	Turkey	N	81	73	62%	52%	56.3 ± 10.0	55.2 ± 9.5	41%	49%	42.6 ± 11.0	22.3 ± 4.0	GE Vivid 7	LVEF, E/A
Guns, 2011	Turkey	N	32	25	63%	56%	56.5 ± 12.2	53.9 ± 9.3	44%	32%	43.1	25.7	GE Vivid 3	LVEF, E/A, DT
Elsherbiny, 2012	Egypt	N	60	20	NR	NR	56.4 ± 7.0	54.8 ± 7.4	33%	35%	52.6 ± 10.3	18.6 ± 3.2	HP SONOS 5500	LVEF, E/A, e', E/e', MPI
Balci, 2013	Turkey	N	86	66	69%	64%	54.0 ± 10.0	55.0 ± 8.0	NR	NR	43.0	26.0	GE Vivid 7	LVEF, E/A, DT, e', LAD, MPI
Altunas, 2014	Turkey	Y	35	35	57%	40%	55.0 ± 11.0	54.0 ± 9.0	54%	40%	32.0 ± 10.0	21.0 ± 2.0	Philips EnVisor C	LVEF, E/A, DT, e', E/e', LAD, MPI
Barutu, 2015	Turkey	N	20	20	75%	80%	47.0 ± 8.0	44.0 ± 10.0	25%	20%	29.3	22.5	GE Vivid 7	LVEF, GLS, E/A, DT, E/e', LAVI
Chen, 2015	China	N	36	20	58%	60%	56.8 ± 5.9	55.7 ± 4.8	36%	35%	NR	NR	GE	E/A
Wang, 2015	China	Y	62	44	58%	43%	56.7 ± 8.6	55.5 ± 8.2	44%	41%	38.6 ± 13.5	21.5 ± 2.3	GE Vivid 7	LVEF, GLS, E/A, DT, e', E/e', LAD
Gulel, 2016	Turkey	N	20	20	40%	55%	59.2 ± 9.6	54.1 ± 9.0	65%	55%	39.1 ± 10.9	20.6 ± 3.0	GE Vivid E9	LVEF, GLS, E/A, E/e', LAD
Narimni, 2016	Iran	Y	36	36	69%	69%	53.9 ± 8.3	54.5 ± 9.4	42%	42%	40.0 ± 10.7	15.2 ± 3.5	GE Vivid S5	LVEF, E/A
Simse, 2016	Turkey	Y	67	38	57%	87%	53.3 ± 9.9	49.9 ± 8.8	13%	21%	51.4	22.5	GE Vivid 3	LVEF, E/A, DT, LAD
Suner, 2016	Turkey	N	40	40	80%	70%	47.2 ± 7.4	46.7 ± 5.3	33%	25%	36.7 ± 7.2	25.5 ± 4.1	GE Vivid S5	LVEF, E/A, DT, e', LAD, MPI
Kemalglu, 2017	Turkey	Y	40	40	65%	55%	53.4 ± 11.7	54.1 ± 10.8	53%	48%	40.6 ± 7.5	22.4 ± 1.3	Philips iE 33	LVEF, GLS, E/A, DT, LAD
Seyis, 2018	Turkey	N	110	109	53%	57%	56.4 ± 7.5	56.7 ± 6.7	NR	NR	36.0 ± 5.3	15.3 ± 0.6	GE Vivid 7	LVEF, LAD
Pan, 2019	China	Y	60	51	72%	53%	56.8 ± 8.0	52.6 ± 9.3	38%	35%	39.8 ± 7.3	19.9 ± 1.3	GE Vivid E9	LVEF, GLS, E/A, E/e', LAVI
Aslan, 2021	Turkey	N	50	40	80%	58%	48.6 ± 12.5	47.8 ± 6.0	20%	35%	28.7 ± 5.6	23.3 ± 1.7	GE Vivid S5	LVEF, E/A, e', E/e', LAD, LAVI
Hamidreza, 2021	Iran	Y	33	11	70%	64%	53.3 ± 12.2	55.9 ± 11.8	36%	36%	NR	NR	GE Vivid S5	LVEF, E/A, DT, e', E/e'
Liu, 2021	China	Y	73	60	62%	37%	56.4 ± 9.1	55.6 ± 8.2	37%	43%	35.6 ± 13.5	19.9 ± 3.7	Philips iE 33	LVEF, GLS, E/A, e', E/e', LAVI
Seyyed, 2021	Iran	Y	53	69	68%	38%	55.1 ± 18.5	51.8 ± 10.4	58%	25%	NR	NR	NR	GLS, E/A, DT

Data are presented as mean ± standard deviation or percentages; NR — not reported; Y — yes; N — no; CSF — coronary slow flow; CG — control group; HTN — hypertension; TFC — thrombolysis in myocardial infarction frame count; LVEF — left ventricular ejection fraction; GLS — global longitudinal strain; E/A — early-to-late velocity ratio; DT — deceleration time of the mitral E-wave; E — early diastolic flow velocity; e' — peak early diastolic mitral annular velocity; LAD — left atrial diameter; LAVI — left atrial volume index; MPI — myocardial performance index

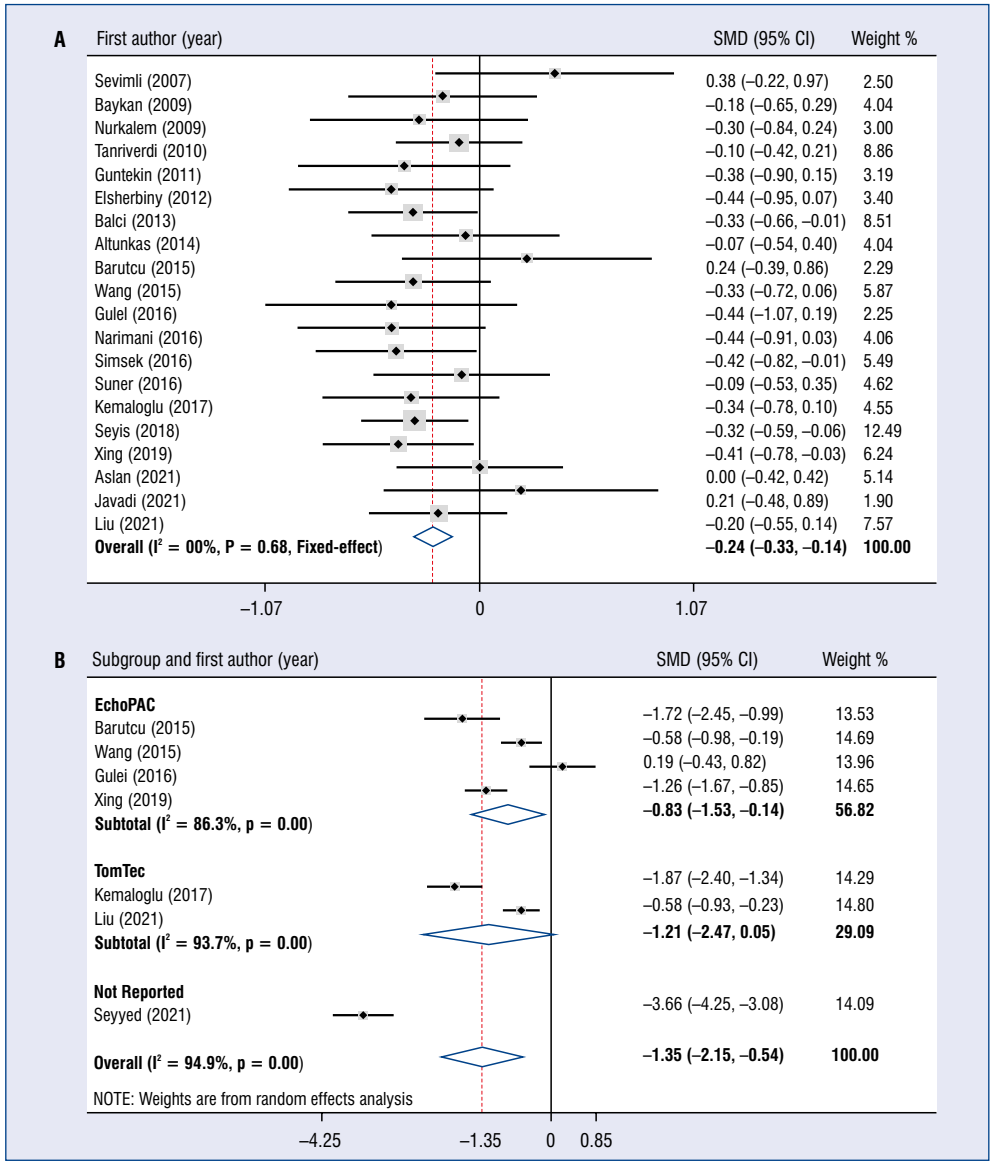

Figure 2. Forest plot for left ventricular ejection fraction (LVEF; **A**) and global longitudinal strain (GLS; **B**); SMD — standardized mean difference; CI — confidence interval.

HDL, while there were no significant differences in the DBP, HTN, DM, family history of CAD, TG, TC, and LDL. The results of the CAG were pooled [9, 17, 20, 22, 25, 26, 30, 33, 34, 37], suggesting that among the three coronary arteries, left anterior descending artery involvement was observed in 73% of patients, left circumflex artery involvement in 63%, and right coronary artery involvement in 54%. In 43% of patients with CSF, all three vessels were affected, while two-vessel and one-vessel diseases were observed in 31% and 26% of cases, respectively.

Echocardiography characteristics

LV systolic function

Of the 22 studies, 2 were excluded from the meta-analysis because they did not report the measurement method of LVEF [24, 34]. Twenty studies assessed LVEF using the modified biplane Simpson method; 1012 in the CSF group and 798 in the control group. The results showed that LVEF was lower in the CSF group than in the control group (SMD: –0.236; 95% CI: –0.33, –0.14; $I^2 = 0\%$) (Fig. 2A). The mean LVEF in the CSF group was 61.8% (95% CI: 61.0%, 62.7%). The Begg's test did

Table 2. The results of meta-analysis of diastolic function.

Parameter	Studies, n	CSF, n	Pooled mean in CSF	I^2 *	Control, n	Pooled mean in control	I^2 **	SMD	95% CI	I^2
E/A	20	971	0.94	87.8	758	1.07	93.6	–0.43	–0.66 to –0.20	80.7
DT	15	761	207.12	96.7	514	198.52	95.3	0.19	–0.00 to 0.38	60.6
e'	10	511	9.25	99.7	365	10.80	99.7	–1.21	–1.98 to –0.44	95.9
E/e'	10	435	7.92	81.4	323	7.27	97.2	0.37	0.02–0.72	80.4
LAD	14	722	34.68	95.0	587	33.89	96.7	0.32	0.04–0.60	83.3
LAVI	3	153	27.87	98.0	131	26.82	98.9	0.26	0.03–0.50	0.00

CSF — coronary slow flow; SMD — standardized mean difference; CI — confidence interval; E/A — early-to-late velocity ratio; DT — deceleration time of the mitral E-wave; e' — peak early diastolic mitral annular velocity; LAD — left atrial diameter; LAVI — left atrial volume index; *I^2 within CSF group; **I^2 within control group

not suggest a significant publication bias (**Suppl. Fig. S1**).

Seven studies reported GLS [23, 25, 27, 30, 32–34]: 328 in the CSF group and 304 in the control group. The GLS of the CSF group was reduced when compared to the control group (SMD: –1.35; 95% CI: –2.15, –0.54; I^2 = 94.9%) (Fig. 2B). The mean GLS value in the CSF group was –18.2% (95% CI: –16.7%, –19.7%). Subgroup analysis for GLS was performed according to the software: four EchoPAC, two TomTec; and one did not report. The EchoPAC group had an I^2 of 86.3% (SMD: 0.83; 95% CI: –1.53, –0.14), whereas the TomTec group had an I^2 of 93.7% (SMD: –1.21; 95% CI: –2.47, 0.05).

LV diastolic function

The combined results of diastolic function are displayed in Table 2. The CSF group had a higher E/e', LAD, and LAVI, and lower E/A and e', whereas DT did not change. Except for LAVI, the heterogeneity of the other diastolic indices was significant ($I^2 > 40$). The results of the meta-regression analysis shown in **Supplementary Table S1A** revealed that the country was the source of the heterogeneity of DT and e', and the year of publication could explain the heterogeneity of e' and E/e'. High heterogeneity was observed in the CSF and control groups. **Supplementary Table S1B–S1C** present the sources of heterogeneity within each group. SBP caused heterogeneity within the CSF and control groups for E/A. Heart rate was the source of heterogeneity of E/e' in the CSF group. Sex and DBP caused heterogeneity in E/e' in the control group. The Begg's test indicated no publication bias for any of the diastolic function indices (**Suppl. Fig. S1**).

Correlation of LV function with the mean TFC

The pooled correlation coefficients are presented in **Supplementary Table S2**. The results suggested a weak positive relationship between the mean TFC and E/e' (r = 0.36; 95% CI: 0.19, 0.50; p < 0.01), a moderate negative correlation between the mean TFC and GLS (r = –0.44; 95% CI: 0.14, 0.67; p = 0.006), and a moderate positive correlation between the mean TFC and MPI (r = = 0.41; 95% CI: 0.20, 0.59; p < 0.01). The correlation between mean TFC and E/A was not statistically different (p = 0.05).

Subgroup analysis according to the mean TFC

The average value of the mean TFC for the CSF group was calculated to explore the cutoff value that would result in an obvious alteration of LV function. Subgroup analysis was performed based on a mean value of 39 (95% CI: 36, 42) (**Suppl. Table S3**). The results suggested that for the mean TFC ≤ 39 group, the E/e' (SMD: 0.11; 95% CI: –0.26, 0.47) and EDT (SMD: 0.05; 95% CI: –0.29, 0.40) of the CSF group did not change, while both E/e' (SMD: 0.93; 95% CI: 0.26, 1.61) and EDT (SMD: 0.34; 95% CI: 0.07, 0.61) significantly increased in the mean TFC > 39 group. In the mean TFC > 39 group, LVEF, GLS, and e' had greater pooled effect sizes than in the mean TFC ≤ 39 group (SMD: –0.285 vs. –0.196; SMD: –1.543 vs. –0.640; SMD: –2.528 vs. –0.520, respectively).

Discussion

The results of the meta-analysis suggested that: i) both LV systolic and diastolic functions were decreased in patients with CSF, and ii) the mean

TFC was linearly associated with LV function, the larger the mean TFC, the more severe the impairment of LV function.

Coronary slow flow was originally described by Tambe et al. in 1972 [37] and it has a negative impact on patients' quality of life. More than 80% of patients with CSF experience recurrent chest pain, and 20% are admitted to the hospital multiple times due to exacerbation [5]. Results herein, suggested that males and the older adults were susceptible to CSF. Moreover, higher SBP, larger BMI, lower HDL, and smoking might be potential risk factors for CSF, which are similar to those for CAD. Among the three major coronary arteries, CSF was more likely to occur in the left anterior descending artery, and a significant proportion of patients had concurrent involvement of all three coronary arteries. Previous studies suggest that the affected blood vessels can affect the myocardial strain of the relevant cardiac segments [30]. Moreover, the more involved the number of coronary arteries, the more serious cardiac dysfunction [33]. Therefore, close monitoring of patients with CSF is necessary.

Left ventricular systolic function is vital to the assessment and prognosis of the condition, and LVEF measurement is the most commonly used evaluation method. Of the 20 studies included in the meta-analysis, 19 reported no change in LVEF in the CSF group, while one suggested a reduced but normal LVEF [21]. The results of the meta-analysis suggested that LVEF in patients with CSF was marginally lower, but still within normal ranges. However, LVEF was not sensitive; therefore, normal LVEF cannot exclude impaired LV systolic function.

Recently, GLS, measured using two-dimensional speckle tracking echocardiography, was used to detect impaired LV systolic function early and sensitively [38]. Eight of the included studies applied GLS, and 6 studies showed reduced GLS in the CSF group [23, 25, 30, 32–34], while 2 studies found no reduction in GLS [26, 27]. The results suggested that GLS was reduced in CSF patients, with a mean value of –18.2%, which was smaller than the normal value [39]. Moreover, 2 studies used three-dimensional speckle tracking echocardiography to describe the decreased LV systolic function in patients with CSF [30, 33]. In summary, LV systolic function was decreased in patients with CSF.

Research has shown that GLS is affected by the analysis software [13]; therefore, a subgroup analysis was performed according to TomTec and EchoPAC. But no significant differences were found in the GLS derived from different software, which may be because they use similar platforms and analysis methods.

Many cardiovascular diseases may present with diastolic dysfunction in the early stages, which is related to prognosis and treatment; therefore, assessing diastolic function has become increasingly important [12]. Of the 22 included studies, 8 studies found reduced LV diastolic function in CSF patients [15, 17, 19, 20, 25, 28, 29, 33], while 4 studies reported no change in LV diastolic function parameters [22, 26, 30, 32]. The results of the meta-analysis indicated impaired LV diastolic function in CSF patients. According to meta-regression analysis, LV diastolic function was affected by SBP, DBP, and heart rate; therefore, clinical characteristics should be considered when evaluating LV diastolic function in patients with CSF.

Mean TFC as a quantitative indicator of coronary blood flow may be a crucial factor affecting LV function in patients with CSF. A larger mean TFC indicates slower coronary blood flow, which may have a greater impact on the LV function. Five studies performed correlation analyses between the mean TFC and LV function [15, 20, 32, 33, 35], suggesting that the mean TFC is linearly associated with LV function. The results of the meta-analysis of correlation coefficients suggested that LV function was more significantly impaired with an increasing mean TFC. This may be because slow coronary blood flow can aggravate ischemia and hypoxia of myocardial cells and further impair LV function. It was expected that to obtain a cut-off value for the mean TFC would lead to significant changes in LV function in patients with CSF. Results revealed that LV function was significantly impaired in patients with CSF when the mean TFC was > 39, which suggests that clinicians should pay more attention to these patients. Further clinical studies are required to confirm this conclusion.

The findings of the meta-analysis provide several LV functional parameters that are altered in patients with CSF, which may serve as an important basis for monitoring and assessing disease severity in these patients. Currently, dipyridamole has been suggested as a potential treatment for improving LV function impairment in patients with CSF [28]; however, further research is necessary to confirm these findings.

Limitations of the study

This meta-analysis had several limitations. Although subgroup and meta-regression analyses were performed, the heterogeneity of GLS,

E/A, e', and E/e' could not be entirely explained. Moreover, the characteristics of patients with CSF were inconsistent across studies, including different severity of CSF, duration, and differences in involved coronary arteries or the number of involved branches, which may have had an impact on the results. The influence on LV function between the involvement of individual arteries or multiple lesions in the case of CSF and cannot be quantified due to limitations of the original research. Moreover, half of the studies did not specify the timing of echocardiography (before or after CAG), which prevented a more in-depth analysis. Therefore, more high-quality, multicenter studies with large sample sizes are required to verify the results of this meta-analysis in the future.

Conclusions

Patients with CSF have impaired LV systolic and diastolic function, and this impairment is aggravated with increasing mean TFC. A comprehensive and precise assessment of LV function of patients with CSF should be performed to determine the condition and guide clinical treatment.

Acknowledgments

National Natural Science Foundation of China (grant numbers U21A20387 and 81871373); The Project from Department of Science and Technology of Liaoning Province (grant numbers 2021JH1/10400051); Liaoning Province "Xingliao Talents Plan" project (grant numbers XLYC1905001); and Shenyang Science and Technology Plan (grant numbers 20-205-4-014).

Conflict of interest: None declared

References

1. Beltrame JF. Defining the coronary slow flow phenomenon. Circ J. 2012; 76(4): 818–820, doi: 10.1253/circj.cj-12-0205, indexed in Pubmed: 22374148.
2. Wang X, Nie SP. The coronary slow flow phenomenon: characteristics, mechanisms and implications. Cardiovasc Diagn Ther. 2011; 1(1): 37–43, doi: 10.3978/j.issn.2223-3652.2011.10.01, indexed in Pubmed: 24282683.
3. Mangieri E, Macchiarelli G, Ciavolella M, et al. Slow coronary flow: clinical and histopathological features in patients with otherwise normal epicardial coronary arteries. Cathet Cardiovasc Diagn. 1996; 37(4): 375–381, doi: 10.1002/(SICI)1097-0304(199604)37:4<375::AID-CCD7>3.0.CO;2-8, indexed in Pubmed: 8721694.
4. Zhu Q, Wang S, Huang X, et al. Understanding the pathogenesis of coronary slow flow: Recent advances. Trends Cardiovasc Med. 2022 [Epub ahead of print], doi: 10.1016/j.tcm.2022.12.001, indexed in Pubmed: 36516963.
5. Beltrame JF, Limaye SB, Horowitz JD. The coronary slow flow phenomenon--a new coronary microvascular disorder. Cardiology. 2002; 97(4): 197–202, doi: 10.1159/000063121, indexed in Pubmed: 12145474.
6. Ayhan E, Uyarel H, Isık T, et al. Slow coronary flow in patients undergoing urgent coronary angiography for ST elevation myocardial infarction. Int J Cardiol. 2012; 156(1): 106–108, doi: 10.1016/j.ijcard.2012.01.001, indexed in Pubmed: 22264870.
7. Cutri N, Zeitz C, Kucia AM, et al. ST/T wave changes during acute coronary syndrome presentation in patients with the coronary slow flow phenomenon. Int J Cardiol. 2011; 146(3): 457–458, doi: 10.1016/j.ijcard.2010.10.120, indexed in Pubmed: 21126779.
8. Saya S, Hennebry TA, Lozano P, et al. Coronary slow flow phenomenon and risk for sudden cardiac death due to ventricular arrhythmias: a case report and review of literature. Clin Cardiol. 2008; 31(8): 352–355, doi: 10.1002/clc.20266, indexed in Pubmed: 17957738.
9. Javadi H, Sotudeh S, Javadi A, et al. Echocardiographic evaluation of left and right ventricular function in patients with coronary slow flow syndrome: a comparative study. Curr Probl Cardiol. 2022; 47(9): 100925, doi: 10.1016/j.cpcardiol.2021.100925, indexed in Pubmed: 34364691.
10. Page MJ, McKenzie JE, Bossuyt PM, et al. Updating guidance for reporting systematic reviews: development of the PRISMA 2020 statement. J Clin Epidemiol. 2021; 134(3): 103–112, doi: 10.1016/j.jclinepi.2021.02.003, indexed in Pubmed: 33577987.
11. Higgins JPT TJ, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.3. www.training.cochrane.org/handbook (Updated February 2022).
12. Nagueh SF, Appleton CP, Gillebert TC, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. J Am Soc Echocardiogr. 2009; 22(2): 107–133, doi: 10.1016/j.echo.2008.11.023, indexed in Pubmed: 19187853.
13. Voigt JU, Pedrizzetti G, Lysyansky P, et al. Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. J Am Soc Echocardiogr. 2015; 28(2): 183–193, doi: 10.1016/j.echo.2014.11.003.
14. Wells GAS B; O'Connell D; Peterson J; Welch V; Losos M. The Newcastle-Ottawa Scale (NOS) for Assessing the Quality if Nonrandomized Studies in Meta-Analyses. 2017. http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm.
15. Sevimli S, Büyükkaya E, Gündoğdu F, et al. Left ventricular function in patients with coronary slow flow: A tissue Doppler study. Turk Kardiyoloji Dernegi Arsivi. 2007; 35(6): 360–365.
16. Nurkalem Z, Gorgulu S, Uslu N, et al. Longitudinal left ventricular systolic function is impaired in patients with coronary slow flow. Int J Cardiovasc Imaging. 2009; 25(1): 25–32, doi: 10.1007/s10554-008-9341-1, indexed in Pubmed: 18626788.
17. Baykan M, Baykan EC, Turan S, et al. Assessment of left ventricular function and Tei index by tissue Doppler imaging in patients with slow coronary flow. Echocardiography. 2009; 26(10): 1167–1172, doi: 10.1111/j.1540-8175.2009.00939.x, indexed in Pubmed: 19725862.
18. Tanriverdi H, Evrengul H, Kilic ID, et al. Aortic pressures, stiffness and left ventricular function in coronary slow flow phenomenon. Cardiology. 2010; 116(4): 261–267, doi: 10.1159/000316652, indexed in Pubmed: 20798537.

19. Guntekin U, Gumrukcuoglu HA, Gunes Y, et al. The effects of perindopril on QT duration and dispersion in patients with coronary slow flow. Heart Vessels. 2011; 26(4): 357–362, doi: 10.1007/s00380-010-0058-4, indexed in Pubmed: 21140270.
20. Elsherbiny IA. Left ventricular function and exercise capacity in patients with slow coronary flow. Echocardiography. 2012; 29(2): 158–164, doi: 10.1111/j.1540-8175.2011.01552.x, indexed in Pubmed: 22044729.
21. Balci MM, Arslan U, Kocaoğlu I, et al. Right ventricular functions in patients with slow coronary flow. Acta Cardiol. 2013; 68(2): 161–166, doi: 10.1080/ac.68.2.2967273, indexed in Pubmed: 23705558.
22. Altunkas F, Koc F, Ceyhan K, et al. The effect of slow coronary flow on right and left ventricular performance. Med Princ Pract. 2014; 23(1): 34–39, doi: 10.1159/000355471, indexed in Pubmed: 24217066.
23. Barutçu A, Bekler A, Temiz A, et al. Left ventricular twist mechanics are impaired in patients with coronary slow flow. Echocardiography. 2015; 32(11): 1647–1654, doi: 10.1111/echo.12918, indexed in Pubmed: 25739451.
24. Chen Z, Chen X, Li S, et al. Nicorandil improves myocardial function by regulating plasma nitric oxide and endothelin-1 in coronary slow flow. Coron Artery Dis. 2015; 26(2): 114–120, doi: 10.1097/MCA.0000000000000179, indexed in Pubmed: 25325437.
25. Wang Y, Ma C, Zhang Y, et al. Assessment of left and right ventricular diastolic and systolic functions using two-dimensional speckle-tracking echocardiography in patients with coronary slow-flow phenomenon. PLoS One. 2015; 10(2): e0117979, doi: 10.1371/journal.pone.0117979, indexed in Pubmed: 25706989.
26. Narimani S, Hosseinsabet A, Pourhosseini H. Effect of coronary slow flow on the longitudinal left ventricular function assessed by 2-dimensional speckle-tracking echocardiography. J Ultrasound Med. 2016; 35(4): 723–729, doi: 10.7863/ultra.15.05075, indexed in Pubmed: 26939598.
27. Gulel O, Akcay M, Soylu K, et al. Left ventricular myocardial deformation parameters are affected by coronary slow flow phenomenon: a study of speckle tracking echocardiography. Echocardiography. 2016; 33(5): 714–723, doi: 10.1111/echo.13146, indexed in Pubmed: 26668075.
28. Suner A, Cetin M. Is dipyridamole useful in improving left ventricular systolic and diastolic function in patients with coronary slow flow? Echocardiography. 2016; 33(10): 1472–1478, doi: 10.1111/echo.13290, indexed in Pubmed: 27343175.
29. Simsek H, Yaman M, Babat N, et al. Decreased risk of ventricular arrhythmias with treatment of nebivolol in patients with coronary slow flow. Kardiol Pol. 2016; 74(10): 1174–1179, doi: 10.5603/KP.a2016.0060, indexed in Pubmed: 27160173.
30. Kemaloğlu Öz T, Eren M, Atasoy I, et al. Are biventricular systolic functions impaired in patient with coronoray slow flow? A prospective study with three dimensional speckle tracking. Int J Cardiovasc Imaging. 2017; 33(5): 675–681, doi: 10.1007/s10554-016-1054-2, indexed in Pubmed: 28063138.
31. Seyis S. Effect of coronary slow flow on intrinsicoid deflection of QRS complex. Cardiol Res Pract. 2018; 2018: 2451581, doi: 10.1155/2018/2451581, indexed in Pubmed: 29484206.
32. Xing Y, Shi J, Yan Y, et al. Subclinical myocardial dysfunction in coronary slow flow phenomenon: Identification by speckle tracking echocardiography. Microcirculation. 2019; 26(1): e12509, doi: 10.1111/micc.12509, indexed in Pubmed: 30365186.
33. Liu S, Wang Y, Li J, et al. Incremental value of three-dimensional speckle-tracking echocardiography for evaluating left ventricular systolic function in patients with coronary slow flow. Curr Probl Cardiol. 2022; 47(9): 100928, doi: 10.1016/j.cpcardiol.2021.100928, indexed in Pubmed: 34353632.
34. Seyyed Mohammadzad MH, Gardeshkhah S, Khademvatani K, et al. Echocardiographic and laboratory findings in coronary slow flow phenomenon: cross-sectional study and review. BMC Cardiovascular Disorders. 2021; 21(1), doi: 10.1101/2020.07.03.20145995.
35. Aslan B, Peker T, Tenekecioğlu E, et al. Assessment of left atrial volumes and functions in patients with coronary slow flow. e-Journal of Cardiovascular Medicine. 2021; 9(2): 113–121, doi: 10.32596/ejcm.galenos.2021-02-014.
36. Gibson CM, Cannon CP, Daley WL, et al. TIMI frame count: a quantitative method of assessing coronary artery flow. Circulation. 1996; 93(5): 879–888, doi: 10.1161/01.cir.93.5.879, indexed in Pubmed: 8598078.
37. Tambe AA, Demany MA, Zimmerman HA, et al. Angina pectoris and slow flow velocity of dye in coronary arteries: a new angiographic finding. Am Heart J. 1972; 84(1): 66–71, doi: 10.1016/0002-8703(72)90307-9, indexed in Pubmed: 5080284.
38. Smiseth OA, Torp H, Opdahl A, et al. Myocardial strain imaging: how useful is it in clinical decision making? Eur Heart J. 2016; 37(15): 1196–1207, doi: 10.1093/eurheartj/ehv529, indexed in Pubmed: 26508168.
39. Yingchoncharoen T, Agarwal S, Popović ZB, et al. Normal ranges of left ventricular strain: a meta-analysis. J Am Soc Echocardiogr. 2013; 26(2): 185–191, doi: 10.1016/j.echo.2012.10.008, indexed in Pubmed: 23218891.