The International Journal of Cardiovascular Imaging (2019) 35:2197–2203
https://doi.org/10.1007/s10554-019-01676-9

ORIGINAL PAPER

Evaluation of left atrial volume and function in patients with coronary slow flow phenomenon using real-time three-dimensional echocardiography

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Received: 11 April 2019 / Accepted: 22 July 2019 / Published online: 25 July 2019

Abstract
This study aimed to evaluate the left atrial (LA) volume and phasic functions using real-time three-dimensional echocardiography (RT3DE) in coronary slow flow phenomenon (CSFP) patients with preserved left ventricular ejection fraction (LVEF). 56 patients with CSFP (36 males, 20 females) and 48 controls with normal coronary flow (27 males, 21 females) were prospectively enrolled. Comprehensive transthoracic echocardiographic examination and RT3DE for the assessment of LA dynamics were performed in all participants. LA maximum, minimum, and pre-atrial contraction volumes (LAV-max, LAV-min, and LAV-preA) were obtained for every subject. Conventional echocardiographic parameters, except for isovolumetric relaxation time and transmitral deceleration time, did not differ in two groups. RT3DE demonstrated higher LAV-max, LAV-min, LAV-preA, indexed LAV-max (LAVi-max), LA total emptying volume, and LA active emptying volume and fraction for CSFP patients compared with controls (all $P < 0.05$). In addition, LA total emptying fraction and LA passive emptying fraction were found to be lower in CSFP patients than in controls (all $P < 0.05$). Moreover, there were positive correlations between mean thrombolysis in myocardial infarction frame count values and LAV-max, LAV-min, LAV-preA, LAVi-max, and LA total and active emptying volumes. CSFP was associated with enlarged LA volumes, impaired LA reservoir and conduit function and enhanced contractile function. Evaluation of LA dynamics using RT3DE could facilitate recognition of subtle myocardial alterations related with CSFP.

Keywords Coronary slow flow phenomenon · Real-time three-dimensional echocardiography · Left atrium

Introduction

Coronary slow flow phenomenon (CSFP) is an angiographic finding, characterized by delayed distal vessel opacification in the absence of obstructive coronary artery disease [1]. The exact underlying pathophysiological mechanisms have not been fully understood thus far. Many pathologic factors, including microvascular and endothelial dysfunction, inflammation, diffuse atherosclerosis, small vessel defects, lipid metabolism disorder, and platelet dysfunction, may play a role in forming CSFP [2–5].

The left atrium (LA) plays a pivotal role in modulating left ventricular (LV) filling with its three phasic functions: acting as a reservoir during systole, as a conduit during early diastole and diastasis, and as an active pump during late diastole [6, 7]. Left atrial structural and functional remodeling has been recognized as a reliable marker of diastolic pressure burden, and its size has been shown to be a prognostic marker for many cardiovascular conditions [8]. However, there is limited information in the literature about the effect of CSFP on left atrial functions.

Two-dimensional (2D) echocardiography plays a crucial role in evaluating left atrial function in clinical practice, but it may be technically challenging due to geometric assumptions of biplane volume calculations and the timing of various atrial events [9]. Compared with the former, real-time

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three-dimensional echocardiography (RT3DE) has recently been introduced as a novel and reproducible method for the assessment of LA volume and phasic functions [10–13]. Nowadays, the development of RT3DE enabled us to identify left atrial preclinical damage at earlier stages.

Therefore, the primary goal of our study was to evaluate the LA volume and phasic functions in CSFP patients with preserved left ventricular ejection fraction (LVEF). Second, we aimed to clarify the correlation between atrial functional alterations and clinical parameters in these patients.

Methods

Study population

Among patients who underwent coronary angiography (CAG) for angina pectoris in our hospital between April 2016 and July 2018, a total of 57 patients with a diagnosis of CSFP were enrolled in our study [14]. 51 age- and sex-matched volunteers with normal coronary flow were selected as the control group. All subjects were in normal sinus rhythm. Exclusion criteria included the presence of: coronary artery disease, congenital heart disease, proximal lumen diameter of < 3 mm, left ventricular systolic dysfunction (LVEF $< 55\%$), coronary artery ectasia, LV wall abnormality and LV hypertrophy on echocardiography, valvular disease, atrial fibrillation, cardiomyopathy, malignancy, hepatic and renal insufficiency, hematological or inflammatory disorders, hyperthyroidism, hypothyroidism, uncontrolled hypertension, diabetes mellitus and suboptimal echocardiographic images. A written consent was obtained from all subjects, and the study was approved by the ethics committee of Zhongshan Hospital, Fudan University.

Coronary angiography

CAG was performed on all subjects through the femoral approach using the standard Judkins technique. As a contrast agent, iohexol (350/100 ml) was manually delivered (5–6 ml at each injection) in all subjects. Coronary blood flow velocity was documented using the thrombolysis in myocardial infarction frame count (TFC) method first proposed by Gibson et al. [15]. All images were collected at 30 frames/s. To obtain the corrected TFC (cTFC), the counts of left anterior descending coronary artery (LAD) were divided by 1.7 because of its longer length. The TFC values in LAD and left circumflex artery (LCx) were assessed in the right anterior oblique projection, while the assessment of right coronary artery (RCA) was performed in the left anterior oblique projection. The mean TFC for each subject was obtained by dividing the sum of TFC values for LAD, LCx and RCA by three. CAG examinations and TFC calculations were performed by an experienced investigator who was blinded to any clinical data.

Conventional transthoracic echocardiography

Transthoracic echocardiography and measurements were performed by a single experienced cardiologist who was blinded to clinical data of the study population using the iE33 ultrasound system (Philips Medical System, Andover, MA, USA) with an S5-1 transducer. Patients were positioned in the left lateral decubitus position. The LV end-diastolic (LVEDD) and end-systolic (LVESD) diameter, interventricular septal diameter (IVSD), posterior wall diameter (PWD), LA diameter and LV mass were measured according to recommendations of the most recent guideline [16]. The LVEF was calculated using the biplane Simpson's method. Early (E) and late (A) diastolic flow velocities through mitral valves, mitral E-wave deceleration time (DT) and isovolumetric relaxation time (IVRT) were obtained by pulsed-wave Doppler echocardiography. Myocardial systolic (S′) and peak early diastolic (E′) velocities of mitral annulus were obtained by tissue Doppler imaging. The E/E′ and E/A ratios were subsequently calculated. All echocardiographic images of three consecutive cycles were stored in cineloop format.

Real-time 3D echocardiography

RT3DE was performed using the same ultrasound system (Philips Medical Systems) with an X5-1 matrix-array transducer (1–3 MHz). All RT3DE images were acquired in a "full-volume" set in the apical four chamber view and at least four consecutive cardiac cycles were recorded. The RT3DE data were digitally stored and analyzed offline later using software system (Philips QLAB10.4 software). LA models were created by marking 5-point on the atrial surface of the mitral annulus (anterior, inferior, lateral, and septal) and the fifth point at the apex of the LA. Points assumed to be within the pulmonary vein ostia or LA appendage were excluded from the measurement. The LA internal endocardial border of each frame was detected automatically by software. From these data, a 3D model of the LA volume was generated (Figs. 1, 2). The following volumetric measurements were then taken: LA maximum volume at end systole (LAV-max), minimum volume at end diastole (LAV-min), and LA volume before atrial contraction (LAV-preA). From the three volumes, the following parameters were calculated according to previous studies as indices of LA function [14, 17]: (i) LA reservoir function: LA total emptying volume = LAV-max − LAV-min, LA total emptying fraction = (LAV-max − LAV-min)/LAV-max × 100; (ii) LA conduit function: LA passive emptying volume = LAV-max − LAV-preA, LA passive emptying fraction = (LAV-max − LAV-preA)/LAV-max × 100; (iii) LA booster pump

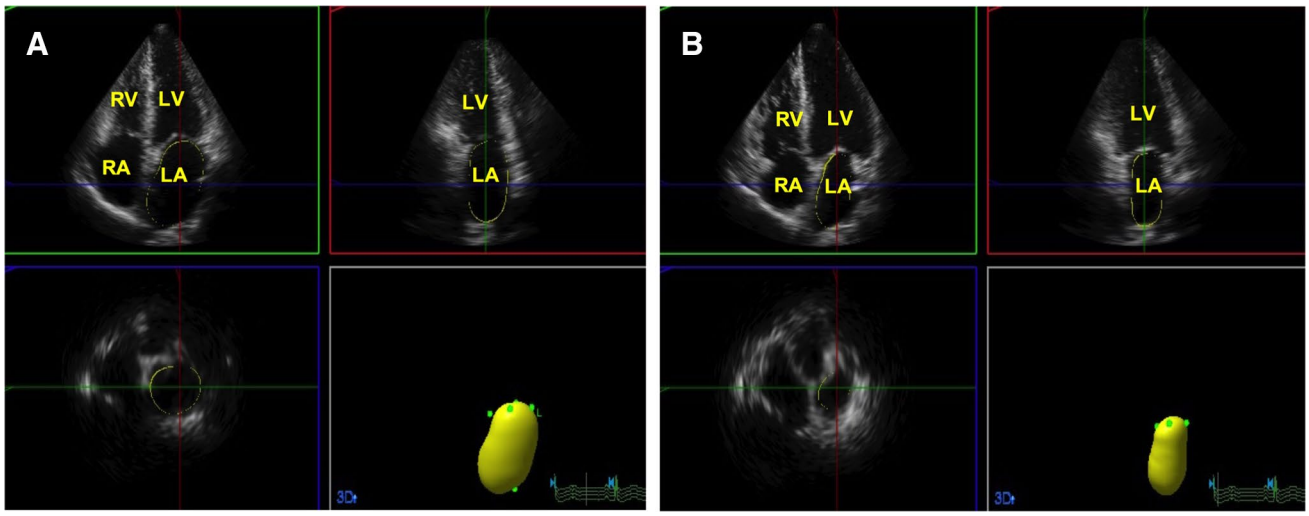

Fig. 1 Real-time three-dimensional echocardiography recordings of maximal left atrial volume (**a**) and minimal left atrial volume (**b**). *LA* left atrium, *LV* left ventricle, *RA* right atrium, *RV* right ventricle

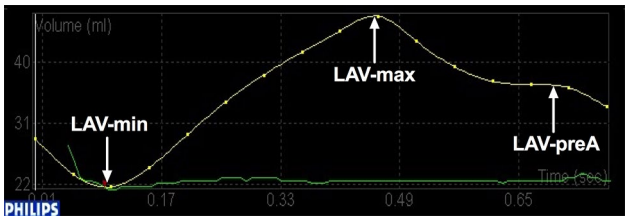

Fig. 2 Time–volume curve with indicating maximum (LAV-max) and minimum (LAV-min) left atrial volumes and before left atrial contraction volume(LAV-preA)

function: LA active emptying volume = LAV-preA − LAV-min, LA active emptying fraction = (LAV-preA − LAV-min)/LAV-preA × 100. All stored digital data were analyzed by two experienced observers blinded to both CSFP and controls.

Reproducibility

Twenty patients were randomly selected to determine intra- and interobserver variability. Intraobserver variability was calculated by one observer measuring RT3DE data twice with a time interval of 2 weeks. A second independent observer blinded to previous results repeated the measurements to determine the interobserver variability.

Statistical analysis

All statistical analyses were performed using SPSS 21.0 software (SPSS Inc., Chicago, IL, USA). Distribution of variables were tested using Kolmogorov–Smirnov test. Continuous variables were presented as the mean ± standard deviation (SD) or median (interquartile range) and categorical variables as percentages. Continuous variables were compared using the independent sample t-test or Mann–Whitney *U* test, where appropriate. Chi-square test was used for the comparison of categorical variables. Correlations between LA phasic functions and clinical parameters were determined by Pearson or Spearman correlation tests where appropriate. Intra-class correlation coefficient (ICC) analysis was used to test the inter- and intraobserver reproducibility of RT3DE data. A P value < 0.05 was considered statistically significant.

Results

Study population

From the initially enrolled 108 subjects (57 CSFP patients, 51 controls), 1 CSFP patient and 3 controls were excluded due to insufficient RT3DE imaging quality. 56 six CSFP patients (20 women and 36 men; mean age, 55.60 ± 7.86 years), and 48 controls (21 women and 27 men; mean age, 53.80 ± 7.82 years) were included in the final analysis.

Clinical characteristics and angiographic findings

Clinical characteristics and angiographic findings of 56 CSFP patients and 48 controls are presented in Table 1. No significant difference was found between the groups in terms of clinical characteristics including age, sex, smoking status, hypertension, heart rate, body mass index (BMI), blood pressure, total cholesterol (TC), low-density lipoprotein

Table 1 Clinical and angiographic characteristics in patients with CSFP and controls

Variables	CSFP (n = 56)	Control (n = 48)	*P*-value
Age (years)	55.60 ± 7.86	53.80 ± 7.82	0.290
Male [n (%)]	36 (64.3)	27 (56.3)	0.409
Smoking [n (%)]	15 (26.8)	11 (22.9)	0.652
Hypertension [n (%)]	13 (23.2)	8 (16.7)	0.407
Heart rate (bpm)	68.38 ± 9.36	71.95 ± 9.52	0.083
BMI (kg/m^2)	24.37 ± 2.46	23.28 ± 2.79	0.059
SBP (mmHg)	121.60 ± 9.42	120.18 ± 9.14	0.478
DBP (mmHg)	75.60 ± 8.77	76.43 ± 5.62	0.608
TC (mmol/L)	4.15 ± 1.12	4.02 ± 1.18	0.606
LDL-C (mmol/L)	2.34 (1.30)	2.09 (1.03)	0.413
HDL-C (mmol/L)	1.09 ± 0.27	1.22 ± 0.21	0.017
TG (mmol/L)	1.94 ± 1.17	1.52 ± 0.77	0.056
FBG (mmol/L)	5.40 (0.60)	5.40 (0.50)	0.212
Medications			
β-blockers [n (%)]	25 (44.6)	16 (33.3)	0.242
Aspirin [n (%)]	42 (71.4)	28 (58.3)	0.072
Statin [n (%)]	34 (66.1)	22 (54.2)	0.132
Calcium channel blocker [n (%)]	6 (16.1)	8 (14.6)	0.387
Nitrates [n (%)]	40 (67.9)	29 (60.4)	0.243
TFC			
cLAD	43.35 ± 11.51	19.75 ± 1.63	< 0.001
LCX	36.98 ± 9.23	19.35 ± 2.02	< 0.001
RCA	37.17 ± 11.94	20.20 ± 1.77	< 0.001
Mean TFC	39.17 ± 7.14	19.77 ± 1.02	< 0.001

BMI body mass index, *DBP* diastolic blood pressure, *SBP* systolic blood pressure, *TC* total cholesterol, *LDL-C* low-density lipoprotein cholesterol, *HDL-C* high-density lipoprotein cholesterol, *TG* triglycerides, *FBG* fasting blood glucose, *TFC* thrombolysis in myocardial infarction frame count, *cLAD* corrected left anterior descending coronary artery, *LCX* left circumflex coronary artery, *RCA* right coronary artery

cholesterol (LDL-C), triglycerides (TG), and fasting blood glucose (FBG) levels and history of medications (all $P > 0.05$). In contrast, the level of high-density lipoprotein cholesterol (HDL-C) was significantly lower in CSFP group as compared to control group ($P < 0.05$). For angiographic data, the TFC values for LAD, LCX, and RCA and the mean TFC were markedly higher in CSFP patients when compared with controls (43.35 ± 11.51 vs. 19.75 ± 1.63, $P < 0.001$; 36.98 ± 9.23 vs. 19.35 ± 2.02, $P < 0.001$; 37.17 ± 11.94 vs. 20.20 ± 1.77, $P < 0.001$; 39.17 ± 7.14 vs. 19.77 ± 1.02, $P < 0.001$, respectively).

Conventional echocardiographic data

As shown in Table 2, there was no significant difference between two groups regarding IVSD, PWD, LVEDD, LVESD, left ventricular mass index (LVMI), LA diameter, LVEF, S′, E/A and E/E′ values (all $P > 0.05$), except for IVRT and DT, which were significantly higher in the CSFP group compared with the control group (94.28 ± 14.12 ms vs. 86.33 ± 12.91 ms, $P = 0.007$; 203.19 ± 36.05 ms vs. 185.90 ± 29.82 ms, $P = 0.016$, respectively).

Table 2 Conventional echocardiographic data in CSFP patients and controls

Parameters	CSFP (n = 56)	Control (n = 48)	*P* value
IVSD (mm)	9.55 ± 0.97	9.18 ± 0.96	0.072
PWD (mm)	9.66 ± 1.01	9.25 ± 1.03	0.065
LVEDD (mm)	47.98 ± 4.67	46.53 ± 4.64	0.150
LVESD (mm)	30.70 ± 4.42	29.40 ± 3.07	0.111
LVMI (g/m^2)	92.03 (36.78)	84.85 (22.42)	0.125
LA diameter (mm)	37.66 ± 4.10	36.68 ± 2.34	0.166
LVEF (%)	64.78 ± 4.76	65.93 ± 5.08	0.278
DT (ms)	203.19 ± 36.05	185.90 ± 29.82	0.016
IVRT (ms)	94.28 ± 14.12	86.33 ± 12.91	0.007
S′ (cm/s)	9.48 ± 1.67	10.10 ± 1.77	0.096
E/A	1.10 (0.44)	1.03 (0.38)	0.756
E/E′	8.28 ± 2.16	7.86 ± 2.55	0.409

IVSD interventricular septal diameter, *PWD* posterior wall diameter, *LVEDD* left ventricular end-diastolic diameter, *LVESD* left ventricular end-systolic diameter, *LVMI* left ventricular mass index, *LVEF* left ventricular ejection fraction, *DT* deceleration time, *IVRT* isovolumetric relaxation time, S′ peak systolic annular myocardial velocity, *E/A* myocardial peak early diastolic velocity/myocardial peak late diastolic velocity, *E/E′* peak velocity of early diastolic flow across mitral valve/myocardial peak velocity of early diastole

RT3DE data

Table 3 summarizes the RT3DE findings of the two groups. Compared with controls, CSFP patients presented with higher LAV-max, LAV-min, LAV-preA, indexed LAV-max (LAVi-max), LA total emptying volume, LA active emptying volume and fraction (all $P < 0.05$) but significantly lower LA total emptying fraction and passive emptying fraction (both $P < 0.05$). There were no significant differences between groups regarding LA passive emptying volume.

Relationship between LA phasic functions and clinical parameters

In the correlation analysis (Table 4), positive correlations were revealed between mean TFC values and LAV-max, LAV-min, LAV-preA, LAVi-max, LA total and active emptying volumes.

Reproducibility

Twenty CSFP patients were randomly selected for the assessment of reproducibility of RT3DE data. For intraobserver

Table 3 RT3DE data in CSFP patients and controls

Parameters	CSFP (n = 56)	Control (n = 48)	*P*-value
LAV-max (ml)	41.53 ± 5.83	36.06 ± 6.34	< 0.001
LAV-min (ml)	16.91 ± 2.82	13.66 ± 2.41	< 0.001
LAV-preA (ml)	28.03 ± 4.50	21.34 ± 4.04	< 0.001
LAVi-max (ml/m^2)	23.79 ± 3.59	21.54 ± 4.88	0.018
LA total emptying volume (ml)	24.62 ± 3.92	22.40 ± 4.64	0.019
LA total emptying fraction (%)	59.25 ± 4.04	61.89 ± 4.24	0.004
LA active emptying volume (ml)	11.12 ± 2.51	7.69 ± 2.49	< 0.001
LA active emptying fraction (%)	39.52 ± 5.19	35.45 ± 7.18	0.004
LA passive emptying volume (ml)	13.50 ± 3.19	14.71 ± 3.54	0.100
LA passive emptying fraction (%)	32.47 ± 5.71	40.69 ± 5.70	< 0.001

LAV-max left atrial maximum volume, *LAV* left atrial minimum volume, *LAV-preA* left atrial volume before atrial contraction, *LAVi-max* indexed left atrial maximum volume

Table 4 The correlations between mean TFC and RT3DE data in the CSFP group

	Mean TFC	
	r	*P*
LAV-max	0.580	< 0.001
LAV-min	0.351	0.015
LAV-preA	0.468	0.001
LAVi-max	0.430	0.003
LA total emptying volume	0.609	< 0.001
LA total emptying fraction	0.204	0.169
LA active emptying volume	0.445	0.002
LA active emptying fraction	0.188	0.205
LA passive emptying fraction	0.057	0.705

Mean TFC mean thrombolysis in myocardial infarction frame count, *LAV-max* left atrial maximum volume, *LAV-min* left atrial minimum volume, *LAV-preA* left atrial volume before atrial contraction, *LAVi-max* indexed left atrial maximum volume

variability, the ICCs of LAV-max, LAV-min, and LAV-preA were 0.952 ($P < 0.001$, 95% CI 0.878–0.981), 0.939 ($P < 0.001$, 95% CI 0.847–0.976) and 0.924 ($P < 0.001$, 95% CI 0.807–0.970) respectively. For interobserver variability, the ICCs of LAV-max, LAV-min, and LAV-preA were 0.935 ($P < 0.001$, 95% CI 0.836–0.974), 0.920 ($P < 0.001$, 95% CI 0.798–0.968) and 0.901 ($P < 0.001$, 95% CI 0.751–0.961), respectively. Taken together, these results indicated satisfactory reproducibility of RT3DE measurements.

Discussion

To the best of our knowledge, this is the first study to quantitatively evaluate LA volumes and phasic functions using RT3DE in CSFP patients with preserved LVEF. The main finding of this study is that CSFP was associated with enlarged LA volumes, impaired LA reservoir and conduit function and enhanced contractile function. In addition, LA volumes were found to be positively correlated with the coronary artery mean TFC.

CSFP, characterized by delayed distal vessel opacification during CAG, occurs in approximately 1% to 7% patients undergoing CAG for stable angina pectoris. Among these patients, more than 80% experienced recurrent chest pain, and almost 20% reported severe clinical symptoms that required readmission [18, 19]. It was first reported by Tambe et al. [1] in 1972 and represents a significant clinical entity for being a potential cause of recurrent angina pectoris, acute myocardial infarction, ventricular arrhythmias, and even cardiac death [20, 21].

Several researchers have comprehensively assessed the ventricular function in CSFP patients [22–25], while scarce was study focusing on LA function. The LA plays an important role in regulating LV filling and optimizing overall cardiac function. It has three important functions in the presence of sinus rhythm: (1) as a reservoir for collecting pulmonary venous blood during the ventricular systole phase; (2) as a conduit for passing this blood from the LA to LV during the early diastole phase; (3) as a contractile pump (booster) for completing the process of LV filling. LA reservoir function represents LA compliance and it is influenced by LV systolic function through descent of the LV base [26, 27]. LA conduit function is closely related to LV relaxation and chamber stiffness, whereas LA booster pump function is dependent on intrinsic LA contractility and LV end-diastolic pressure and compliance [28, 29]. Hence, accurate assessment of LA phasic alternations may be helpful in delineating specific mechanisms behind different stages of disease progression and improve prognosis.

Several imaging methods have been used to evaluate LA dynamics such as 2D, Doppler and speckle tracking echocardiography, magnetic resonance imaging (MRI), cardiac computerized tomography, and angiography [30]. However,

the above techniques have known limitations including low temporal resolution, higher costs, invasive nature, administration of contrast medium, and radiation exposure. In addition, the LA calculations of 2D echocardiography may bear inherent errors due to the oblique position of interatrial septum, shape of the LA appendage, and asymmetric LA enlargement. As measurements are derived from different phases of the cardiac cycle, RT3DE has recently been introduced as a novel and reproducible method for the assessment of LA volume and phasic functions. It is superior to current 2D echocardiography and was found to be comparable to MRI in assessing LA volumes [10, 11].

In our study, in terms of all conventional echocardiographic LV diastolic parameters, except for DT and IVRT, did not differ in two groups. Interestingly, all RT3DE parameters were abnormal in CSFP group. LA active emptying volume and fraction were increased in CSFP patients reflecting enhanced booster pump function. In addition, LA total emptying volume increased while LA total emptying fraction decreased in CSFP, implying compromised reservoir function. Furthermore, LA passive emptying fraction, was found to be decreased in CSFP patents, which indicates impaired LA conduit function. Therefore, identification of LA volume and function abnormalities before obvious LV diastolic dysfunction suggests that, at least in CSFP patients, early LA dynamic alterations may be observed prior to obvious LV diastolic dysfunction.

A possible explanation for the cause of LA dilatation and compromised LA reservoir function is LV dysfunction. As have been suggested, diffuse coronary calcification, intimal thickening and impaired coronary flow reserve [31] were the possible cause of CSFP and its corresponding myocardial dysfunction. When LV diastolic dysfunction begins to develop, the LA may preserve adequate cardiac output by adjusting booster pump and reservoir functions. As LV diastolic compliance deteriorates, LA pressure increases to overwhelm the LV diastolic pressure and provide adequate LV filling but leads to attendant impedance to pulmonary vein flow and thus impaired LA reservoir function. Meanwhile, increased LV stiffness and deteriorated diastolic relaxation, together with increased intra-ventricular pressure, impede LA passive emptying into LV, leading to impaired conduit function and partially to the larger residual volume before LA active contraction. Consequently, the enhanced LA pump function may be explained by the Frank-Starling mechanism (an increased presystolic LA volume and fiber length occurs with increased LA contraction forces [32]).

Our findings are in line with the results of Wang et al. [33] to a degree. They have recently reported that LA conduit function was impaired and contractile function was augmented, but reservoir function and LA volumes were similar between CSFP patients and controls by conventional 2D echocardiography and speckle tracking echocardiography (STE). The differences in echocardiographic techniques applied in two studies could partly account for the discrepancies. Also, the differences in demographics and cardiovascular risk factors of the study patients may also contribute to the minor inconsistencies.

Notably, in our study, there were positive correlations between mean TFC values and LAV-max, LAV-min, LAV-preA, LAVi-max, LA total and active emptying volumes. A greater mean TFC (indicated slower coronary flow) represents more serious coronary artery impairment in CSFP patients. Furthermore, a greater mean TFC may affect the timely compensation of collateral circulation, which in turn may lead to myocardial ischemia and dysfunction. These findings complement our previous explanation of LA dynamics changes. Furthermore, the long-term follow-up of CSFP patients is supported, especially those with greater mean TFC.

This study had serval limitations. First, this study had a relatively small sample size. Further large-scale studies with long-term follow-up needs to be performed to determine the predictive value of LA volumes and mechanical functions in patients with CSFP. Second, LA appendage has an important role in LA reservoir function, but was excluded for the calculation of LA volume and function. Third, LA volume parameters obtained by RT3DE were not evaluated by another imaging techniques such as MRI or computerized tomography. Moreover, the assessment of LA strain alternations by 3D-STE was not performed and needs further confirmation in the future.

Conclusion

In the present study, we demonstrated a deterioration of LA volume and mechanical functions in CSFP patients with preserved LVEF. Evaluation of atrial volume and function using RT3DE may facilitate recognition of subclinical myocardial alternations related with CSFP. Further large-scale prospective studies are needed to determine the prognostic significance of these findings.

Acknowledgements This study was supported by Grant No. 18ZR1436100 from Shanghai Science and Technology Committee, Grant No. 20164Y0240 from Shanghai Municipal Health and Family Planning Commission Fund and Grant No. 81601496 from National Natural Science Foundation of China.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflicts of interest.

References

1. Tambe AA, Demany MA, Zimmerman HA et al (1972) Angina pectoris and slow flow velocity of dye in coronary arteries—a new angiographic finding. Am Heart J 84:66–71
2. Beltrame JF, Limaye SB, Wuttke RD et al (2003) Coronary hemodynamic and metabolic studies of the coronary slow flow phenomenon. Am Heart J 146:84–90
3. Kopetz V, Kennedy J, Heresztyn T et al (2012) Endothelial function, oxidative stress and inflammatory studies in chronic coronary slow flow phenomenon patients. Cardiology 121:197–203
4. Wang X, Nie SP (2011) The coronary slow flow phenomenon: characteristics, mechanisms and implications. Cardiovasc Diagn Ther 1:37–43
5. Ekmekci A, Gungor B, Ozcan KS et al (2013) Evaluation of coronary microvascular function and nitric oxide synthase intron 4a/b polymorphism in patients with coronary slow flow. Coron Artery Dis 24:461–467
6. Blume GG, Mcleod CJ, Barnes ME et al (2011) Left atrial function: physiology, assessment, and clinical implications. Eur J Echocardiogr 12:421–430
7. Bilen E, Kurt M, Tanboga IH et al (2012) Assessment of left atrial phasic functions in heart failure patients with preserved or low ejection fractions. Turk Kardiyol Dern Ars 40:122–128
8. Akdemir B, Altekin RE, Kucuk M et al (2013) The significance of the left atrial volume index in cardioversion success and its relationship with recurrence in patients with non-valvular atrial fibrillation subjected to electrical cardioversion: a study on diagnostic accuracy. Anadolu Kardiyol Derg 13:18–25
9. To AC, Flamm SD, Marwick TH et al (2011) Clinical utility of multimodality LA imaging: assessment of size, function, and structure. JACC Cardiovasc Imaging 4:788–798
10. Buechel RR, Stephan FP, Sommer G et al (2013) Head-to-head comparison of two-dimensional and three-dimensional echocardiographic methods for left atrial chamber quantification with magnetic resonance imaging. J Am Soc Echocardiogr 26:428–435
11. Boyd AC, Thomas L (2014) Left atrial volumes: two-dimensional, three-dimensional, cardiac magnetic resonance and computed tomography measurements. Curr Opin Cardiol 29:408–416
12. Iwataki M, Takeuchi M, Otani K et al (2012) Measurement of left atrial volume from transthoracic three dimensional echocardiographic datasets using the biplane Simpson's technique. J Am Soc Echocardiogr 25:1319–1326
13. Anwar AM, Geleijnse ML, Soliman OI et al (2007) Left atrial Frank-Starling law assessed by real-time, three-dimensional echocardiographic left atrial volume changes. Heart 93:1393–1397
14. Anwar AM, Soliman OI, Geleijnse ML et al (2008) Assessment of left atrial volume and function by real-time three-dimensional echocardiography. Int J Cardiol 123:155–161
15. Gibson CM, Cannon CP, Daley WL et al (1996) TIMI frame count: a quantitative method of assessing coronary artery flow. Circulation 93:879–888
16. Lang RM, Badano LP, Mor-Avi V et al (2015) Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging 16:233–270
17. Lupu S, Mitre A, Dobreanu D (2014) Left atrium function assessment by echocardiography-physiological and clinical implications. Med Ultrason 16:152–159
18. Beltrame JF, Limaye SB, Horowitz JD (2002) The coronary slow flow phenomenon—a new coronary microvascular disorder. Cardiology 97:197–202
19. Hawkins BM, Stavrakis S, Rousan TA et al (2012) Coronary slow flow—prevalence and clinical correlations. Circ J 76:936–942
20. Saya S, Hennebry TA, Lozano P et al (2008) Coronary slow flow phenomenon and risk for sudden cardiac death due to ventricular arrhythmias: a case report and review of literature. Clin Cardiol 31:352–355
21. Sen T (2013) Coronary slow flow phenomenon leads to ST elevation myocardial infarction. Korean Circ J 43:196–198
22. Xing Y, Shi J, Yan Y et al (2019) Subclinical myocardial dysfunction in coronary slow flow phenomenon: identification by speckle tracking echocardiography. Microcirculation 26:e12509
23. Kemaloglu OT, Eren M, Atasoy I et al (2017) Are biventricular systolic functions impaired in patient with coronary slow flow? A prospective study with three dimensional speckle tracking. Int J Cardiovasc Imaging 33:675–681
24. Altunkas F, Koc F, Ceyhan K et al (2014) The effect of slow coronary flow on right and left ventricular performance. Med Princ Pract 23:34–39
25. Zencir C, Cetin M, Gungor H et al (2013) Evaluation of left ventricular systolic and diastolic functions in patients with coronary slow flow phenomenon. Turk Kardiyol Dern Ars 41:691–696
26. Barbier P, Solomon SB, Schiller NB et al (1999) Left atrial relaxation and left ventricular systolic function determine left atrial reservoir function. Circulation 100:427–436
27. Hoit BD, Shao Y, Gabel M et al (1994) In vivo assessment of left atrial contractile performance in normal and pathological conditions using a time-varying elastance model. Circulation 89:1829–1838
28. Toma Y, Matsuda Y, Moritani K et al (1987) Left atrial filling in normal human subjects: relation between left atrial contraction and left atrial early filling. Car diovasc Res 21:255–259
29. Manning WJ, Silverman DI, Katz SE et al (1993) Atrial ejection force: a noninvasive assessment of atrial systolic function. J Am Coll Cardiol 22:221–225
30. Flachskampf FA, Biering-Sørensen T, Solomon SD et al (2015) Cardiac imaging to evaluate left ventricular diastolic function. JACC Cardiovasc Imaging 8:1071–1093
31. Pekdemir H, Cin VG, Cicek D et al (2004) Slow coronary flow may be a sign of diffuse atherosclerosis. Contribution of FFR and IVUS. Acta Cardiol 59:127–133
32. Akturk E, Ermis N, Yagmur J et al (2012) Early left atrial mechanics and volume abnormalities in subjects with prehypertension: a real time three-dimensional echocardiography study. Echocardiography 29:1211–1217
33. Wang Y, Zhang Y, Ma C et al (2016) Evaluation of left and right atrial function in patients with coronary slow-flow phenomenon using two-dimensional speckle tracking echocardiography. Echocardiography 33:871–880