TÜBİTAK

Turkish Journal of Medical Sciences

http://journals.tubitak.gov.tr/medical/

Research Article

Turk J Med Sci
(2013) 43: 46-51
© TÜBİTAK
doi:10.3906/sag-1205-127

Right ventricular function and its relation with TIMI frame count in the coronary slow flow phenomenon

Mustafa YILMAZ[1,*], Fatma Özlem ARICAN ÖZLÜK[1], Tezcan PEKER[1], Adem BEKLER[2], Kemal KARAAĞAÇ[1]

[1]Department of Cardiology, Bursa İhtisas Training and Research Hospital, Bursa, Turkey

[2]Department of Cardiology, Medicalpark Hospital, Bursa, Turkey

Received: 31.05.2012 • **Accepted:** 06.07.2012 • **Published Online:** 18.01.2013 • **Printed:** 18.02.2013

Aim: To investigate right ventricular function using conventional and tissue Doppler echocardiography in patients with coronary slow flow.

Materials and methods: Twenty-two patients with slow coronary flow and 22 healthy subjects were included in the study. Right ventricular function was evaluated by conventional and tissue Doppler echocardiography. Additionally, right ventricular global function was assessed by myocardial performance index.

Results: The tricuspid annulus peak early diastolic velocity (11.4 ± 2.2 cm/s, 13.9 ± 3 cm/s) and ratio of early to late diastolic velocity (0.70 ± 0.17 cm/s, 1.2 ± 0.38 cm/s) were lower in the patient group than in the controls (P = 0.05, P = 0.002, respectively). Late diastolic velocity (16.4 ± 3 cm/s, 14.4 ± 3 cm/s) and isovolumetric relaxation time (80 ± 9 ms, 66 ± 4 ms) were significantly higher in the patient group than in the controls (P = 0.024, P < 0.001, respectively). Right ventricular myocardial performance index was significantly prolonged in the coronary slow flow group (0.51 ± 0.03, 0.40 ± 0.02, P < 0.001). TIMI frame count was negatively correlated with the tricuspid lateral annulus early diastolic velocity and the ratio of tricuspid lateral annulus early to late diastolic velocity, whereas it was positively correlated with tricuspid isovolumetric relaxation time and right ventricular myocardial performance index.

Conclusion: Right ventricular diastolic dysfunction exists in patients with the coronary slow flow phenomenon and it is correlated with TIMI frame count.

Key words: Right ventricle, coronary slow flow

1. Introduction

Coronary slow flow (CSF) is identified by delayed contrast dye opacification of coronary arteries without occlusive disease (1). Its pathophysiology and clinical implications are not clearly understood (2). Previous studies have shown an association between endothelial inflammation and coronary microvascular dysfunction (3–9). Left ventricular systolic and diastolic dysfunctions have been reported in the CSF phenomenon but no study in the literature has evaluated right ventricular function in patients with CSF (10–13). Assessment of right ventricular function is complicated because of the complex geometry. Myocardial velocity determined by tissue Doppler imaging is a new technique that has been used recently to analyze left ventricular function. The development of tissue Doppler imaging opens up the possibility of also assessing right ventricular function (14–16). Accordingly, the aim of the present study was to investigate right ventricular function using conventional and tissue Doppler echocardiography in patients with CSF.

2. Materials and methods

Twenty-two patients with angiographically evaluated CSF but otherwise normal epicardial coronary arteries were enrolled; 22 subjects with angiographically normal coronary arteries were selected as a control group. All patients underwent a coronary angiography because of suspected coronary artery disease. The exclusion criteria were as follows: previous coronary artery disease, congestive heart failure, coronary ectasia, signs of valvular heart disease, pulmonary disease, pulmonary hypertension, diabetes mellitus, hypertension, left bundle branch block, a rhythm other than sinus, and pericarditis. All medications were stopped 48 h before the time of echocardiography. Fasting venous blood samples were taken to determine levels of blood glucose, electrolytes,

* Correspondence: mustafayih@yahoo.com.tr

total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglycerides.

The study was approved by the ethics committee of our hospital and informed consent was obtained from all patients.

2.1. Coronary angiography

All patients underwent coronary angiography by the femoral approach using the standard Judkins technique. Iopromide contrast and a 6F diagnostic catheter were used in all subjects. All the cineangiograms were evaluated by an experienced cardiologist. CSF was identified using the thrombolysis in myocardial infarction (TIMI) frame count (TFC) method (17). In brief, the first frame was accepted when there was more than 70% lumen opacification with antegrade filling. When contrast dye reached distal landmarks, the final frame was determined. The distal landmarks were the distal bifurcation of the left anterior descending artery, the distal bifurcation of the segment with the longest total distance in the left circumflex artery and in the right coronary artery, and the first branch of the posterolateral artery. The left anterior descending (LAD) is the longest artery among the major coronary arteries. In order to obtain corrected TFC, LAD frame counts were divided by 1.7 as previously reported (13). LAD and left circumflex (Cx) arteries' TIMI frame counts were evaluated in the right anterior oblique projection with caudal angulation. For the right coronary artery, left anterior oblique projection with cranial angulation was used.

The mean TFC was calculated for the LAD, Cx, and RCA. Gibson et al. reported cutoff values for TFC (for LAD: 36.2 ± 2.6; for Cx: 22.2 ± 4.1; for RCA: 20.4 ± 3.0) (13). Any TFC values above these levels were considered CSF.

2.2. Echocardiography

All patients underwent complete transthoracic echocardiography and tissue Doppler study using multiple views in the left lateral decubitus position. This study was performed using a 3.5-Mhz transducer on a Vivid 7, GE ultrasonographic system. Echocardiographic measurements were made in accordance with the criteria recommended by the American Society of Echocardiography. All subjects were in sinus rhythm. The measurements were done on 3 consecutive heartbeats, and the average of these measurements was calculated.

In the apical 4-chamber view, the sample volume (size 2 mm) of the pulsed wave Doppler was placed between the tips of the tricuspid leaflets. The tricuspid inflow velocity was traced and the following variables were measured: peak velocity of early (E) and late (A) filling and deceleration time (DT) of the E wave velocity. In the parasternal long-axis view, the RV diameter was measured using the M-mode from the RV anterior wall to the right side of the interventricular septum on the R-wave of the electrocardiogram. RV longitudinal function was assessed by pulsed TDI. Pulsed Doppler sample volume (size 5 mm) was placed on the basal portion of the RV at the level of the lateral tricuspid annulus from the apical 4-chamber view. The Nyquist limit was set at 15 to 20 cm/s. For optimizing the spectral display of myocardial velocities, the monitor sweep speed was adjusted to 50 to 100 mm/s. The pulsed TDI pattern has positive myocardial systolic velocity (Sa) and 2 negative diastolic velocities: early (Ea) and late (Aa).

The diastolic indices of myocardial early (Ea) and atrial contraction (Aa) peak velocities and myocardial systolic wave (Sa) velocity were measured and the ratio of Em/Am was calculated.

The TDI-derived myocardial performance index (MPI) of the right ventricle was measured by dividing the difference between the time interval from the end to the onset of the tricuspid annular velocity pattern during diastole (a) and the duration of tricuspid Sa (b) by the tricuspid Sa duration (b) (RV MPI = $(a - b)/b$).

2.3. Statistical analysis

SPSS version 10.0 was used for the statistical analysis. All the data were expressed as mean ± standard deviation. Categorical variables were compared via chi-square test. Normally distributed variables were compared across groups by means of Student's t test, whereas variables that were not normally distributed were compared by Mann–Whitney U test.

Pearson's correlation analysis was used to evaluate relations between the variables. A P value of <0.05 was considered significant.

3. Results

The clinical characteristics of 22 coronary slow patients and 22 normal coronary angiography subjects are presented in Table 1.

Age, sex, body mass index, diabetes mellitus, dyslipidemia, family history, and smoking status did not differ between the CSF patients and control subjects. Additionally, there were no significant differences in terms of laboratory data (Table 1).

When compared in terms of echocardiographic features, the groups had similar chamber diameters and standard Doppler parameters (Table 2). The tricuspid annular peak systolic velocity (15.1 ± 2.8 cm/s, 14.2 ± 2.1 cm/s) determined by TDI and deceleration time (182 ± 34 ms, 174 ± 15 ms) were higher in the patient group but not significantly so ($P > 0.05$). The tricuspid annulus peak early diastolic velocity (11.4 ± 2.2 cm/s, 13.9 ± 3 cm/s) and ratio of early to late diastolic velocity (0.70 ± 0.17 cm/s, 1.2 ± 0.38 cm/s) were lower in the patient group ($P = 0.05$, $P = 0.002$, respectively). Late diastolic velocity (16.4 ± 3 cm/s, 14.4 ± 3 cm/s) and isovolumetric relaxation time (80 ± 9 ms, 66

Table 1. Demographic and clinical characteristics of the groups.

	Patients	Controls	P
Mean age (years)	51 ± 12	52 ± 12	NS
Male/female	13/9	12/10	NS
Body mass index (kg/m²)	28 ± 5	28 ± 3	NS
Family history	4	3	NS
Smoking	7	6	NS
Diabetes mellitus	2	4	NS
Dyslipidemia	4	7	NS
Glucose (mg/dL)	95 ± 18	109 ± 42	NS
Serum creatinine (mg/dL)	0.9 ± 0.2	0.8 ± 0.2	NS
Hemoglobin (g/dL)	14.1 ± 1.5	13.9 ± 1.3	NS
Total cholesterol (mg/dL)	182 ± 56	185 ± 43	NS
Triglyceride (mg/dL)	149 ± 60	160 ± 78	NS
High density lipoprotein (mg/dL)	38 ± 7	40 ± 13	NS
Low density lipoprotein (mg/dL)	120 ± 37	113 ± 37	NS

NS: Nonsignificant

Table 2. Echocardiographic parameters in the patient group and the control group.

	Patients	Controls	P
LVEDD (mm)	48.07 ± 3.82	48.47 ± 3.95	NS
LVESD (mm)	29.8 ± 4.78	30.43 ± 4.22	NS
IVS (mm)	10.08 ± 1.33	9.90 ± 1.19	NS
LVEF (%)	68.01 ± 7.01	66.31 ± 6.59	NS
RVEDD (mm)	28.78 ± 3.15	28.47 ± 3.67	NS
LA diameter (mm)	36.35 ± 3.81	36.94 ± 3.08	NS
RA diameter (mm)	32.99 ± 4.93	31.31 ± 4.72	NS
Tricuspid E (cm/s)	52.3 ± 19.8	53.1 ± 7.7	NS
Tricuspid A (cm/s)	45.7 ± 12.9	40.8 ± 9.5	NS
Tricuspid E/A ratio	1.23 ± 0.39	1.36 ± 0.33	NS
Tricuspid E DT (msn)	199 ± 31	194 ± 19	NS

LVEDD: left ventricle end-diastolic diameter; LVESD: left ventricle end-systolic diameter; IVS: interventricular septum; LVEF: left ventricle ejection fraction; RVEDD: right ventricle end-diastolic diameter; LA: left atrium; RA: right atrium; NS: nonsignificant

± 4 ms) were significantly higher in the patient group (P = 0.024 and P < 0.001, respectively). Right ventricular MPI was significantly prolonged in the CSF group compared to the controls (0.51 ± 0.03, 0.40 ± 0.02, P < 0.001). Tissue Doppler parameters are presented in Table 3.

Patients were detected to have significantly higher TFC for each major epicardial coronary artery (P < 0.001) (Table 4). There was a strong inverse correlation between mean TFC and right ventricle Ea and Ea/Aa ratio (r = –0.393, P = 0.008; r = –0.398, P = 0.007, respectively). Mean TFC was positively correlated with the right ventricle MPI index (r = 0.795, P < 0.001) and tricuspid IVRT (r = 0.599, P < 0.001). The correlation between TFC and echocardiographic parameters is shown in Table 5.

Table 3. Right ventricular tissue Doppler echocardiography parameters.

	Patients	Controls	P
RV S wave peak velocity (cm/s)	15.1 ± 2.8	14.2 ± 2.1	NS
RV E wave peak velocity (cm/s)	11.4 ± 2.2	13.9 ± 3	0.05
RV A wave peak velocity (cm/s)	16.4 ± 3	14.4 ± 3	0.024
RV Ea/Aa ratio	0.70 ± 0.17	1.02 ± 0.38	0.002
Ea DT (ms)	182 ± 34	174 ± 15	NS
IVRT (ms)	80 ± 9	66 ± 4	<0.001
Tei index RV	0.51 ± 0.03	0.40 ± 0.02	<0.001

RV: right ventricle; Ea: tricuspid lateral annulus early diastolic wave; Aa: tricuspid lateral annulus late diastolic wave; DT: tricuspid lateral annulus E wave deceleration time; IVRT: isovolumetric relaxation time; NS: nonsignificant

Table 4. Comparison of TIMI frame counts between the patient group and the control group.

	Patients	**Controls**	**P**
cLAD	38.87 ± 13.05	18.38 ± 2.54	< 0.001
Cx	40.09 ± 11.64	16.20 ± 2.29	< 0.001
RCA	39.10 ± 16.97	14.48 ± 2.32	< 0.001
Mean	39.32 ± 10.7	16.27 ± 2.05	< 0.001

cLAD: corrected frame count for left anterior descending artery; Cx: circumflex artery; RCA: right coronary artery; Mean TFC: (LAD + Cx + RCA)/3

Table 5. Correlations between TIMI frame count and echocardiographic parameters.

	cLAD		Cx		RCA		Mean	
	r	P	R	P	r	P	r	P
Ea	–0.349	0.02	–0.394	0.008	–0.313	0.039	–0.393	0.008
Ea/Aa ratio	–0.347	0.021	–0.417	0.005	–0.307	0.043	–0.398	0.007
IVRT	0.573	<0.001	0.843	<0.001	0.731	<0.001	0.599	<0.001
MPI	0.618	<0.001	0.810	<0.001	0.697	<0.001	0.795	<0.001

cLAD: corrected frame count for left anterior descending artery; Cx: Circumflex artery; RCA: right coronary artery; IVRT: isovolumetric relaxation time; MPI: right ventricle myocardial performance index

4. Discussion

In this study, it was detected that right ventricular diastolic function is impaired while systolic function is preserved in patients with CSF. In addition, TIMI frame count for coronary arteries was demonstrated to show a negative correlation with tricuspid lateral annulus early diastolic velocity and the rate of tricuspid lateral annulus early and late diastolic velocities and a positive correlation with tricuspid isovolumetric relaxation time and right ventricle myocardial performance index.

A number of studies have been conducted to assess LV function in patients with CSF (10–13). Some authors have reported only impaired diastolic LV function, whereas others have reported both impaired diastolic and systolic LV function in CSF patients. On the other hand, there has been no study to date exploring the involvement of right ventricular systolic and diastolic function in the CSF phenomenon and our study is important since it is the first on this subject. Our study showed significantly impaired RV diastolic function in the CSF phenomenon, as assessed by tissue Doppler.

Several mechanisms for the pathophysiology of CSF were suggested by previous studies, such as increased small vessel resistance, endothelial dysfunction, impairment of platelet function, inflammation, and increased plasma endothelin levels (4–8). Left and right ventricular studies showed small vessel disease in patients with CSF (8,9).

Supporting this, some studies have shown that spontaneous episodes of the CSF phenomenon during angiography are associated with ST elevation in the absence of large vessel spasm (18,19). It is well known that ischemia first impairs ventricular diastolic function (20). In time, systolic function also deteriorates. The primary cause of impaired diastolic function in patients with CSF in our study may have been small vessel disease, which is the primary mechanism of CSF.

Saxena et al. showed in their study that right ventricular tricuspid annular systolic velocity is an indicator of right ventricular systolic function, independent of pulmonary artery pressure (21). Similarly, Meluzin et al. showed that right ventricular tricuspid annular systolic velocity is a rapid and noninvasive marker of right ventricular systolic function (22). We did not detect any significant difference between patients with CSF and the controls in terms of tricuspid lateral annulus systolic velocities. Thus, this supports the notion that right ventricular systolic function is not impaired in patients with CSF.

Myocardial performance index is a marker of systolic and diastolic function used frequently in recent years. This index was first described by Tei et al. (23). It is correlated with invasive measurements as well as being reproducible and easy to perform and it is widely accepted. In coronary artery disease a prolonged Tei index has been shown to be an important precursor of the disease before the development of systolic dysfunction (24).

The markedly prolonged myocardial performance index despite an unchanged tricuspid lateral annulus systolic velocity in patients with CSF compared with the control group is in accord with the hypothesis that prolonged Tei index stems from right ventricular diastolic dysfunction.

In conclusion, it was detected that right ventricular diastolic function deteriorates in the CSF phenomenon and this deterioration is associated with increased TIMI frame count.

References

1. Beltrame JF, Limaye SB, Wuttke RD, Horowitz JD. Coronary hemodynamic and metabolic studies of the coronary slow phenomenon. Am Heart J 2003; 146: 84–90.
2. Hawkins BM, Stavrakis S, Rousan TA, Abu-Fadel M, Schechter E. Coronary slow flow—prevalence and clinical correlations. Circ J 2012; 76: 936–42.
3. Mangieri E, Macchiarelli G, Ciavolella M, Barilla F, Avella A, Martinotti A et al. Slow coronary flow: clinical and histopathological features in patients with otherwise normal epicardial coronary arteries. Cathet Cardiovasc Diagn 1996; 37: 375–81.
4. Cin VG, Pekdemir H, Camsar A, Çiçek D, Akkuş MN, Parmaksız T et al. Diffuse intimal thickening of coronary arteries in slow coronary flow. Jpn Heart J 2003; 44: 907–19.
5. Sezgin AT, Sigirci A, Barutçu I, Topal E, Sezgin N, Özdemir R et al. Vascular endothelial function in patients with slow coronary flow. Coron Artery Dis 2003; 14: 155–61.
6. Kopetz V, Kennedy J, Heresztyn T, Stafford I, Willoughby SR, Beltrame JF. Endothelial function, oxidative stress and inflammatory studies in chronic coronary slow flow phenomenon patients. Cardiology 2012; 121: 197–203.
7. Elsherbiny IA, Shoukry A, El Tahlawi MA. Mean platelet volume and its relation to insulin resistance in non-diabetic patients with slow coronary flow. J Cardiol 2012; 59: 176–81.
8. Fineschi M, Bravi A, Gori T. The "slow coronary flow" phenomenon: evidence of preserved coronary flow reserve despite increased resting microvascular resistances. Int J Cardiol 2008; 127: 358–361.
9. Beltrame JF, Limaye SB, Horowitz JD. The coronary slow flow phenomenon—a new coronary microvascular disorder. Cardiology 2002; 97: 197–202.
10. Sezgin AT, Topal E, Barutcu I, Gullu H, Bardisakaner E, Ermis N et al. Impaired left ventricle filling in slow coronary flow phenomenon: an echo-Doppler study. Angiology 2005; 56: 397–401.

11. Baykan M, Baykan EC, Turan S, Gedikli O, Kaplan S, Kiriş A et al. Assessment of left ventricular function and Tei index by tissue Doppler imaging in patients with slow coronary flow. Echocardiography 2009; 26: 1167–72.

12. Elsherbiny IA. Left ventricular function and exercise capacity in patients with slow coronary flow. Echocardiography 2012; 29: 158–64.

13. Nurkalem Z, Gorgulu S, Uslu N, Orhan AL, Alper AT, Erer B et al. Longitudinal left ventricular systolic function is impaired in patients with coronary slow flow. Int J Catdiovasc Imaging 2009; 25: 25–32.

14. Dell'Italia LJ. Reperfusion for right ventricular infarction. N Engl J Med 1998; 338: 978–980.

15. Ulusoy RE, Yokusoglu M, Baysan O, Kırılmaz A, Kılıçaslan F, Cebeci BS. Ventricular functions, aortic elastic properties, and endothelial functions in patients with hypertensive response to treadmill exercise testing. Turk J Med Sci 2011; 41: 781–787.

16. Çiçekçioğlu H, Ergün İ, Uçar Ö, Yüksel C, Azak A, Abaylı E et al. Cardiac complications of secondary hyperparathyroidism in chronic hemodialysis patients. Turk J Med Sci 2011; 41: 789–794.

17. Gibson CM, Cannon CP, Daley WL, Dodge JT Jr, Alexander B Jr, Marble SJ et al. TIMI frame count: a quantitative method of assessing coronary artery flow. Circulation 1996; 93: 879–88.

18. Kopetz VA, Penno MA, Hoffmann P, Wilson DP, Beltrame JF. Potential mechanisms of the acute coronary syndrome presentation in patients with the coronary slow flow phenomenon—insight from a plasma proteomic approach. Int J Cardiol 2012; 156: 84–91.

19. Acikel S, Bozkaya OA, Akdemir R. The relationship between intermittent left bundle-branch block and slow coronary flow in a patient presenting with acute coronary syndrome. Blood Coagul Fibrinolysis 2010; 21: 595–597.

20. Yalcin F, Thomas J. Diastolic dysfunction: pathogenesis, therapy and the importance of Doppler echocardiography. Turk J Med Sci 1999; 29: 501–506.

21. Saxena N, Rajagopalan N, Edelman K. López-Candales A. Tricuspid annular systolic velocity. A useful measurement in determining right ventricular systolic function regardless of pulmonary artery pressures. Echocardiography 2006; 23: 750–755.

22. Meluzin J, Spinarova L, Bakala J, Toman J, Krejci J, Hude P et al. Pulsed Doppler tissue imaging of the velocity of tricuspid annular systolic motion; a new, rapid and non-invasive method of evaluating right ventricular systolic function. Eur Heart J 2001; 22: 280–82.

23. Tei C. New non-invasive index for combined systolic and diastolic ventricular function. J Cardiol 1995; 26: 135–136.

24. Kang SM, Ha JW, Rim SJ, Chung N. Index of myocardial performance using Doppler-derived parameters in the evaluation of left ventricular function in patients with essential hypertension. Yonsei Med J 1998; 39: 446–52.