

Assessment of coronary blood flow in non-ischemic dilated cardiomyopathy with the TIMI frame count method

İskemik olmayan dilate kardiyomiopati hastalarda koroner kan akımının TIMI kare sayısı yöntemi ile değerlendirilmesi

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ABSTRACT

Objective: We aimed to evaluate coronary blood flow by means of the TIMI (Thrombolysis in Myocardial Infarction) frame count in patients with idiopathic dilated cardiomyopathy who had angiographically proven normal coronary arteries and compare the results with those of healthy subjects.

Methods: This retrospective study included 62 patients with idiopathic dilated cardiomyopathy (34 men, 28 women; mean age 59.7±10.6 years) and 62 control subjects without dilated cardiomyopathy (28 men, 34 women; mean age 56.6±9.8 years). All patients and control subjects had angiographically proven normal coronary arteries. Dilated cardiomyopathy patients had a left ventricular ejection fraction <45%. The TIMI frame count was determined for each major coronary artery in each patient. Statistical analysis was performed using Student's t test, Chi-square test and Pearson correlation analysis.

Results: The TIMI frame counts for each major epicardial coronary artery were found to be significantly higher in patients with idiopathic dilated cardiomyopathy compared to control subjects (corrected TIMI frame count for left anterior descending coronary artery: 37.0±12.5 vs 28.7±11.6, respectively, p<0.001; left circumflex coronary artery: 37.7±12.1 vs 31.0±12.5, respectively, p=0.003; right coronary artery: 37.4±12.6 vs 30.7±11.6, respectively, p=0.003). Mean TIMI frame count had significant although weak positive correlation with left ventricular end-diastolic diameter (r=0.350, p<0.001) and left ventricular end-systolic diameter (r=0.358, p<0.001).

Conclusion: We have shown that patients with idiopathic dilated cardiomyopathy and angiographically normal coronary arteries have higher TIMI frame counts for all three coronary vessels, indicating impaired coronary blood flow, compared to control subjects without dilated cardiomyopathy. (*Anadolu Kardiyol Derg 2010 December 1; 10(6): 514-8*)

Key words: Idiopathic dilated cardiomyopathy, TIMI frame count, coronary flow

ÖZET

Amaç: Anjiyografik olarak normal koroner arterleri olan idiyopatik dilate kardiyomiopati hastalarının koroner kan akımlarını TIMI kare sayısı ile değerlendirmeyi ve sağlıklı bireylerin sonuçlarıyla karşılaştırmayı amaçladık.

Yöntemler: Bu retrospektif çalışmaya idiyopatik dilate kardiyomiopati olan 62 hasta (34 erkek, 28 kadın; ortalama yaş 59.7±10.6 yıl) ve dilate kardiyomiopati olmayan 62 kontrol hasta (28 erkek, 34 kadın; ortalama yaş 56.6±9.8 yıl) dahil edildi. Tüm hastalar ve kontrol bireyleri anjiyografik olarak normal koroner arterlere sahipti. Dilate kardiyomiopati hastalarının sol ventrikül ejeksiyon fraksiyonları <45% idi. Her hastada her bir majör koroner arter için TIMI kare sayısı belirlendi. İstatistiksel analizde Student t testi, Ki-kare testi ve Pearson korelasyon analizi kullanıldı.

Bulgular: İdiyopatik dilate kardiyomiopati hastalar kontrol bireyleri ile karşılaştırıldıkları zaman her bir majör epikardiyal koroner arter için TIMI kare sayısı önemli olarak yüksek bulundu (Sol ön inen koroner arter için düzeltilmiş TIMI kare sayısı: 37.0±12.5 ve 28.7±11.6, sırasıyla, p<0.001; sol sirkumfleks koroner arter: 37.7±12.1 ve 31.0±12.5, sırasıyla, p=0.003; sağ koroner arter: 37.4±12.6 ve 30.7±11.6, sırasıyla, p=0.003). Ortalama TIMI kare sayısı sol ventrikül diastol sonu çapı (r=0.350, p<0.001) ve sol ventrikül sistol sonu çapı (r=0.358, p<0.001) ile önemli ancak zayıf pozitif korelasyon gösterdi.

Sonuç: Anjiyografik olarak normal koroner arterlere sahip idiyopatik dilate kardiyomiopati hastalarının, dilate kardiyomiopati olmayan kontrol bireylerle karşılaştırıldığı zaman, her üç koroner damar için daha yüksek TIMI kare sayısına sahip olduklarını gösterdik. Bu bulgu kontrol bireyleri ile karşılaştırıldığında idiyopatik dilate kardiyomiopati hastalarda bozulmuş koroner kan akımını gösterebilir. (*Anadolu Kardiyol Derg 2010 Aralık 1; 10(6): 514-8*)

Anahtar kelimeler: İdiyopatik dilate kardiyomiopati, TIMI kare sayısı, koroner akım

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Introduction

Impairment of coronary flow reserve has been shown in patients with dilated cardiomyopathy (DCM) despite normal epicardial coronary arteries (1-5). Various methods have been used to measure coronary flow in these patients, including coronary sinus thermodilution (3, 6), intracoronary Doppler flow wire (7-9), position emission tomography (PET) (10, 11), and transesophageal echocardiography (12). In all these studies, it has been demonstrated that coronary flow reserve is reduced in DCM patients. Besides, it has been reported that reduced coronary blood flow reserve is associated with unfavorable outcome in patients with DCM (10).

The Thrombolysis in Myocardial Infarction (TIMI) frame count is a simple clinical tool for assessing quantitative indexes of coronary blood flow (13). This technique counts the number of cineangiographic frames from initial contrast opacification of the proximal coronary artery to opacification of distal arterial landmarks. Recently, Brunetti et al. (14) has demonstrated a significant correlation between TIMI frame count and peak oxygen uptake in patients with DCM. However, there is no available data about the difference in TIMI frame counts between patients with DCM and healthy subjects. In the present study, we aimed to evaluate coronary blood flow by means of TIMI frame count in patients with idiopathic DCM who had angiographically proven normal coronary arteries and compare the results with those of healthy subjects.

Methods

Study population

This retrospective study included 62 consecutive patients with idiopathic DCM who were found to have normal coronary angiograms performed between May 2005 and June 2009. A control group consisted of 62 consecutive otherwise healthy patients with atypical chest pain admitted to the hospital for elective coronary angiography and subsequently found to have normal coronary arteries. Patients with idiopathic DCM met the following criteria: normal sinus rhythm, normal coronary arteries, a global left ventricular systolic dysfunction (ejection fraction <45%). Patients with coronary artery disease, history of myocardial infarction, left ventricular hypertrophy, primary valvular heart disease, atrial fibrillation, a history of heavy alcohol abuse, uncontrolled hypertension or any known cause of DCM were excluded from the study. Clinical, echocardiographic and laboratory data were collected from hospital records. Hypertension was considered to be present if the patient was taking antihypertensive drugs at the time of hospital admission or if evidence of ≥ 140 mm Hg systolic, ≥ 90 mm Hg diastolic, or both was found on examination. The diagnosis of diabetes mellitus was based on American Diabetes Association criteria (15). Hyperlipidemia was defined as total cholesterol >220 mg/dl. The local Ethics committee approved the study.

Echocardiography

All patients and control subjects underwent transthoracic echocardiographic examination. Left ventricular end-diastolic and end-systolic diameters were measured from the M-mode trace obtained from the parasternal long-axis view. Left ventricular ejection fraction was measured by the modified Simpson method, as recommended by the American Society of Echocardiography (16).

Evaluation of coronary blood flow

Coronary angiography was performed in multiple orthogonal views by means of the Judkin's technique (Shimadzu Digitex Premier, Kyoto, Japan; 25 frames/sec). Coronary flow was quantified objectively by two interventional cardiologists who were blinded to the clinical characteristics of the patients, using the TIMI frame count method that was first described by Gibson et al. (13). We measured the number of cineframes required for contrast material to opacify standardized distal coronary landmarks. The first frame was defined as the frame in which contrast material extended across the entire width of the origin of the artery with antegrade motion. The last frame was defined as the frame in which contrast material first entered the distal landmark branch. These distal landmarks used for analysis were as follows: the distal bifurcation of the left anterior descending coronary artery (LAD) (the mustache, pitchfork, or whale's tail); the distal bifurcation of the segment with the longest total distance in the left circumflex artery (LCx); and the first branch of the posterolateral artery in the right coronary artery (RCA). The TIMI frame counts in the LAD and LCx were assessed in a right anterior oblique view with caudal angulation, and the RCA was assessed in a left anterior oblique projection with cranial angulation. The TIMI frame count of the LAD artery was corrected by dividing by 1.7 to obtain the corrected TIMI frame count as described earlier (13). The sum of the TIMI frame counts for the LAD, LCx, and RCA was divided by 3 to obtain the mean TIMI frame count for each subject. Data presented here have been converted to and are reported using the most common cine-filming speed in the United States: 30 frames/sec (17).

Statistical analysis

Statistical analysis was performed with SPSS software program, version 16.0 (Chicago, IL, USA). Continuous data are presented as means \pm SD and categorical variables are presented as percentages. Comparison of categorical and continuous variables between the two groups was performed using the chi-square test and Student's t-test, respectively. The correlation between clinical and echocardiographic characteristics and mean TIMI frame count was assessed by the Pearson correlation test. A p value <0.05 was considered statistically significant.

Results

Baseline clinical and echocardiographic characteristics of patients with idiopathic DCM and control subjects are present-

ed in Table 1. There were no significant difference between patients with idiopathic DCM and control subjects regarding age, gender, body mass index, hypertension, hyperlipidemia, diabetes mellitus or smoking status ($p>0.05$) (Table 1). Resting heart rate was significantly higher ($p<0.001$) in patients with idiopathic DCM compared to control subjects. As expected, left atrial diameter, left ventricular end diastolic and end-systolic diameters were significantly higher ($p<0.001$) in patients with idiopathic DCM compared to control subjects (Table 1). Left ventricular ejection fraction was found to be significantly lower ($p<0.001$) in patients with idiopathic DCM compared to control subjects (Table 1).

The TIMI frame counts for each major epicardial coronary artery ($p<0.001$ for LAD, $p=0.003$ for LCx and $p=0.003$ for RCA) and mean TIMI frame count were found to be significantly higher ($p=0.001$) in patients with idiopathic DCM compared to control subjects (Table 2).

The TIMI frame counts for all 3 coronary vessels were found to be significantly correlated with each other. In addition, mean TIMI frame count had significant although weak positive correlation with left ventricular end-diastolic ($r=0.350$, $p<0.001$) (Fig. 1) and left ventricular end-systolic diameter ($r=0.358$, $p<0.001$) (Fig. 2). However, mean TIMI frame count was not correlated with both left ventricular ejection fraction and New York Heart Association (NYHA) functional class.

Discussion

The main finding of our study was that patients with idiopathic DCM and normal epicardial coronary arteries have significantly higher TIMI frame count compared to control subjects without DCM. The accuracy of coronary flow reserve determination using the TIMI frame count method was evaluated in previous studies. It has been reported that TIMI frame count was correlated with flow velocity measured with Doppler guidewire during baseline conditions or hyperemia (18, 19) and this measurement could be used as a surrogate marker for coronary blood velocity and microvascular status (20).

The impairment of coronary blood flow reserve is an early event in the natural history of non-ischemic DCM (6). Measurement of coronary flow reserve using TIMI frame count method is a simple, inexpensive and readily available method during coronary angiography. Our finding of an increased TIMI frame count in idiopathic DCM patients is consistent with previous studies showing reduced coronary flow reserve in these patients. Although the exact mechanism is unclear, endothelial dysfunction, myocardial hypertrophy and increased left ventricular wall stress can be responsible for this impairment (21-24). Brunetti et al. (14) has investigated the relation between coronary flow measured with TIMI frame count method in patients with DCM and oxygen consumption assessed with cardiopulmonary test. They have reported that coronary flow is related to peak oxygen uptake and anaerobic threshold in patients with DCM, suggesting that an increase in baseline coronary flow tries to compensate impaired oxygen needs and consumption.

Table 1. Baseline clinical and echocardiographic characteristics of patients with dilated cardiomyopathy and control subjects

Variables	Dilated cardiomyopathy group (n=62)	Control group (n=62)	p*
Age, years	59.7±10.6	56.6±9.8	0.095
Gender, male/female, n (%)	34 (54.8)/ 28 (45.2)	28 (45.2)/ 34 (54.8)	0.281
Body mass index, kg/m ²	27.1±5.1	29.6±4.9	0.126
Resting heart rate, beats/min	78.2±12.0	69.3±6.7	<0.001
Systolic blood pressure, mmHg	116.5±19.5	113.8±12.1	0.376
Diastolic blood pressure, mm Hg	73.7±12.2	71.2±9.1	0.216
Cigarette smoking, n (%)	18 (29.0)	13 (20.9)	0.30
Diabetes mellitus, n (%)	8 (12.9)	12 (19.3)	0.329
Hypertension, n (%)	39 (62.9)	29 (46.7)	0.07
Hyperlipidemia, n (%)	20 (32.2)	19 (30.6)	0.847
NYHA class	2.1±0.8	-	
LVEDD, cm	6.0±0.8	4.6±0.3	<0.001
LVESD, cm	4.6±0.8	2.8±0.4	<0.001
LVEF, %	29.2±10.3	61.8±5.7	<0.001
Left atrial diameter, cm	4.3±0.6	3.8±0.4	0.001

Data are presented as means±standard deviation or numbers/percentages
*Student's t test and Chi-square test
LVEDD - left ventricular end-diastolic diameter, LVEF - left ventricular ejection fraction, LVESD - left ventricular end-systolic diameter, NYHA - New York Heart Association

Table 2. Comparison of TIMI frame counts between studied groups

Variables	Dilated cardiomyopathy group (n=62)	Control group (n=62)	p*
Left anterior descending artery**	37.0±12.5	28.7±11.6	<0.001
Left circumflex artery	37.7±12.1	31.0±12.5	0.003
Right coronary artery	37.4±12.6	30.7±11.6	0.003
Mean TIMI frame count	37.4±11.5	30.1±10.9	0.001

Data are presented as means±standard deviation
*Student's t test
**Corrected TIMI frame count is given for left anterior descending artery
TIMI - Thrombolysis in Myocardial Infarction

Coronary flow reserve has a prognostic value when it is abnormally reduced in patients with DCM. Reduced myocardial flow reserve may lead to myocardial ischemia, progression of congestive heart failure, and increased mortality (25, 26). Neglia et al. (10) has demonstrated that severely depressed myocardial blood flow assessed by PET imaging is a predictor of poor prognosis in patients with idiopathic left ventricular dysfunction. Rigo et al. (27) also has reported higher incidence rate of spontaneous events including death and worsening of clinical status with lower coronary flow reserve assessed by Doppler echocardiography in patients with non-ischemic dilated cardiomyopathy.

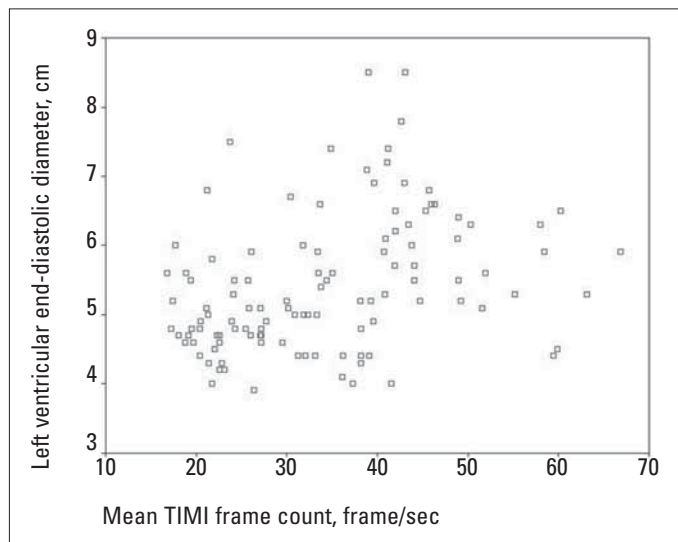


Figure 1. Correlation between mean TIMI frame count and left ventricular end-diastolic diameter (Pearson correlation analysis - $r=0.350$, $p<0.001$)

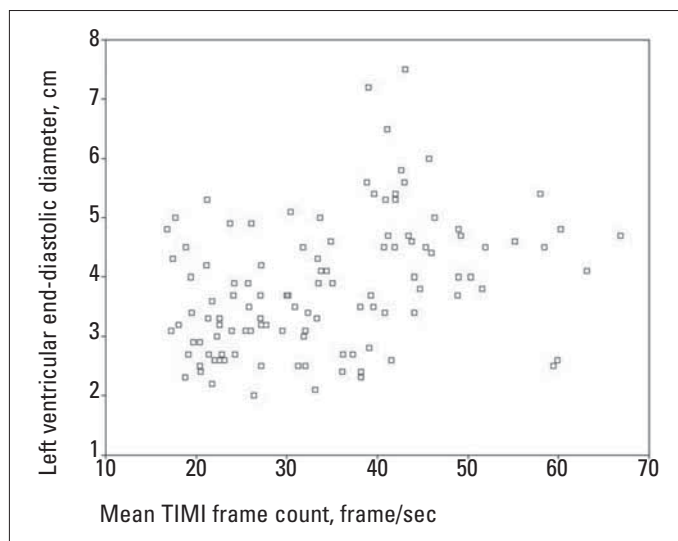


Figure 2. Correlation between mean TIMI frame count and left ventricular end-systolic diameter (Pearson correlation analysis - $r=0.358$, $p<0.001$)

In our study, mean TIMI frame count correlated significantly although weakly with left ventricular diameters but no correlation was found between mean TIMI frame count and both left ventricular ejection fraction and NYHA functional class. In contrast, Brunetti et al. showed a correlation between TIMI frame count of LAD and left ventricular ejection fraction (14). Santagata et al. (28) has reported an association between reduced coronary flow reserve and lower ejection fraction and higher left ventricular volumes. However, in their study NYHA functional class was superior to every other hemodynamic or morphological parameter in its capacity to predict coronary flow reserve reduction.

Study limitations

The TIMI frame count method allows assessing the abnormalities of coronary blood flow under resting conditions, whereas coronary flow velocity reserve reflects both resting and

hyperemic flow. Therefore, the results of this study should be interpreted with caution. A larger prospective study is needed to show the practical use of TIMI frame count method for the prediction of prognosis of patients with idiopathic DCM.

Conclusion

We have shown that patients with idiopathic DCM and angiographically normal coronary arteries have higher TIMI frame counts for all 3 coronary vessels, indicating impaired coronary blood flow, compared to control subjects without DCM.

Conflict of interest: None declared.

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