Myocardial perfusion SPECT and dobutamine stress tissue Doppler imaging in evaluation of patients with stable angina pectoris

Stabil anjina pektoris'li hastaların değerlendirilmesinde dobutamin stres doku Doppler görüntüleme ve miyokardiyal perfüzyon SPECT

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ABSTRACT

Objective: To evaluate longitudinal function of ischemic and nonischemic myocardial tissue detected by Tc-99m MIBI single photon emission computed tomography (SPECT) prior to coronary revascularization in patients with stable angina pectoris.

Methods: We studied 24 consecutive patients (mean age 62±9 years; 5 women) with stable angina pectoris. All patients underwent myocardial perfusion SPECT. Tissue Doppler imaging (TDI) was performed to detect myocardial systolic velocities of anterior, inferior, septum and lateral walls at rest and peak dobutamine stress.

Results: A total of 96 segments were visualized with SPECT study. Maximum mean septal, lateral, anterior and inferior TDI systolic velocities were similar in ischemic and nonischemic segments (6.73±1.04 cm/sec, 6.93±1.34 cm/sec, respectively) at rest. At peak stress, maximum mean TDI systolic velocities were lower in the 37 ischemic segments (11.00±2.03 cm/sec) than 59 nonischemic segments (13.76±1.97cm/sec, p < 0.001). Because we detected ischemia in whole group using both diagnostic tests, coronary angiography was decided. Critical coronary artery stenosis related to ischemic segments was detected and coronary revascularization decided.

Conclusion: TDI with dobutamine stress can be used in patients with stable angina pectoris. In this study, we observed that quantitative data by TDI associated with SPECT showed an agreement for coronary revascularization. *(Anadolu Kardiyol Derg 2010; 10: 334-39)*

Key words: Coronary artery disease, stable angina pectoris, Tc-99m MIBI SPECT, pulsed Doppler tissue imaging, dobutamine stress echocardiography

ÖZET

Amaç: Koroner revaskülarizasyon öncesi stabil anjina pektorisli hastalarda Tc-99m MIBI SPECT ile saptanan iskemik ve normal miyokardiyal dokunun longitüdinal fonksiyonunu değerlendirmektir.

Yöntemler: Stabil anjina pektoris'li 24 ardışık hasta çalışmaya dahil edildi (ortalama yaş 62±9 yıl; 5 kadın). Tüm hastalara miyokardiyal perfüzyon SPECT sintigrafisi yapıldı. İstirahatta ve zirve dobutamin streste ön, alt, septum ve yan duvarların doku Doppler görüntüleme (DDG) ile miyokardiyal sistolik hızları tespit edildi.

Bulgular: SPECT çalışmasında toplam 96 segment görüntülendi. İstirahatta ortalama en yüksek septal, yan, ön ve aşağı duvar DDG sistolik hızları iskemik olan ve iskemik olmayan segmentlerde benzerdi (sırasıyla 6.73±1.04 cm/sn, 6.93±1.34 cm/sn). Zirve streste, ortalama en yüksek DDG sistolik hızları 37 iskemik segmentte (11.00±2.03 cm/sn), 59 iskemik olmayan segmente (13.76±1.97cm/sn, p < 0.001) göre daha düşüktü. Her iki tanı testi ile tüm hasta grubunda iskemi tespit etmemiz nedeniyle tüm vakalara koroner anjiografi uygulandı ve iskemik segmentlerle ilişkili kritik koroner arter darlıkları saptandı.

Sonuç: Anlamlı koroner arter darlıkların saptanmasında DDG yöntemi SPECT ile uyumlu olarak ek bilgi sağlayabilir. *(Anadolu Kardiyol Derg 2010; 10: 334-39)*

Anahtar kelimeler: Koroner arter hastalığı, stabil anjina pektoris, Tc-99m MIBI SPECT, doku Doppler görüntüleme, dobutamin stres ekokardiyografi

Introduction

Left ventricular (LV) systolic function has classically been evaluated by the detection of echocardiographic LV cavity size and volume. However, evaluation of regional systolic function has been more difficult because of the limited applicability of qualitative wall motion analysis (1). In this study, in addition to single photon emission computed tomography (SPECT) with Tc-99m MIBI (methoxyisobutylisonitrile), we used pulsed tissue Doppler imaging (TDI) with dobutamine stress to assess peak systolic myocardial velocities quantitatively in the ischemic region which is under consideration for reperfusion and those in the other regions of myocardium remote from ischemia at rest and dobutamine stress. Longitudinal myocardial contractility is the earliest affected myocardial functional parameter by CAD and can be evaluated by TDI (2).

Therefore, we planned to evaluate the importance of longitudinal functional evaluation in addition to perfusion in patients with stable angina pectoris.

Methods

The study group consisted of 24 patients (19 men, 5 women), aged 48-82 years, mean age 62±9 years. Their ischemic symptoms were initiated by exercise and relieved by rest and had less than 15 minutes duration. Therefore, all of them were diagnosed with stable angina pectoris with Canadian Heart Association, Class 2 angina pectoris. Patients either with severe valvular regurgitation or stenosis, left bundle branch block and/ or the clinically unstable angina were excluded from the study. Beta-blockers and calcium channel blockers were discontinued 2 days before the diagnostic tests. Tc-99m MIBI myocardial perfusion SPECT was performed at rest and peak exercise stress. TDI combined with dobutamine stress echocardiography was performed three days after myocardial perfusion SPECT at rest and peak stress. After completion of both diagnostic tests, in the case of detection of ischemia coronary angiography was performed. Proven coronary artery disease (CAD) was documented by >70% diameter stenosis of at least one major coronary artery at angiogram. Patients with their permission underwent dobutamine stress echocardiography with same protocol as we previously used (3).

Tc-99m MIBI SPECT

All patients underwent Tc-99m MIBI myocardial perfusion scintigraphy with the same day protocol. Either treadmill exercise or pharmacological stress with dipyridamole was used depending on exercise capability of the patients. Exercise consisted of a treadmill stress test with Bruce protocol. The criteria to terminate the study were achievement of at least 85% age-predicted heart rate, severe chest pain, significant ECG changes (ST depression ≥2 mm), development of significant arrhythmia, or blood pressure changes (hypertension, diastolic blood pres-

sure ≥120 mmHg or systolic blood pressure ≥240 mmHg; hypotension, decrease in systolic blood pressure ≥30 mmHg compared to basal value). At peak exercise, 8-10 mCi Tc-99m MIBI was injected and patients were asked to continue exercise for a period of up to 1.5 min. For dipyridamole stress test, patients were asked to refrain from consuming caffeinated beverages midnight prior to testing and 0.56 mg/kg dipyridamole was infused intravenously over 4 min. Tc-99m MIBI (8-10 mCi) was injected 8 min after the start of dipyridamole infusion in all patients. ECG was monitored continuously and blood pressure and heart rate were obtained at 2-min intervals. All side effects and ECG changes were recorded. Tc-99m MIBI SPECT imaging was begun 45 min after the 8-10 mCi tracer injection at stress and 1 h after the injection of 24-28 mCi Tc-99m MIBI at rest, and there was at least a 4-hour interval between the stress and rest imaging. SPECT studies were acquired on a dual head 90° angles gamma camera (Siemens, e-cam, Germany) equipped with low-energy, high resolution parallel hole collimators. Images were acquired using a step-and-shoot circular orbit over a 180° arc, starting at the 45° right anterior oblique projection and ending at the 45° left posterior oblique projection, for a total of 64 projections at 25 seconds per projection at stress and 20 seconds per projection at rest. All projection images were acquired into 64x64 matrices. SPECT images were reconstructed by filtered backprojection with a two-dimensional Butterworth filter (order 5; cutoff frequency, 0.4 cycles per pixel) combined with a ramp filter.

Echocardiography

Rest echocardiography was performed using Acuson 128XP10 device (Mountain View, California, USA) equipped with a variable-frequency phased-array transducer (2.5-3.5-4.0 MHz). The pattern of LV wall motion was assessed from standard left apical views, with the patient in the left semilateral position. Systolic and diastolic LV dimensions were measured from the M-mode recording of the LV long axis, with the cursor by the tips of mitral valve leaflets. Ejection fraction was calculated using Teichholz formula (4).

Dobutamine stress echocardiography

Twelve-lead electrocardiographic (ECG) electrodes and a blood pressure cuff were applied with the patient in the semilateral resting position. Dobutamine hydrochloride was delivered intravenously at a starting dose of 5 mcg/kg/min by an infusion pump. The infusion rate was increased from 5 mcg/kg/min to 10, 20 and 40 mcg/kg/min for four stages, each lasting 3 min. Before infusion and when maximum heart rate was reached, TDI measurements were performed. LV wall motion was analyzed for the appearance of new regional abnormalities. A 12-lead ECG was routinely obtained at rest and during the last minute of each stage. Blood pressure was measured for each step of the stress. Stress end points were significant shortness of breath or chest pain, an increase in systolic blood pressure >200 mmHg, symptomatic hypotension, significant ventricular arrhythmia or attainment of >85% of the maximal predicted heart rate (220 beats/min minus age).

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Tissue Doppler imaging

Pulsed TDI was performed at transducer frequencies of 3.5-4.0 MHz, adjusting spectral Doppler filters until a Nyquist limit of 15-20 cm/s was reached, and using minimal adequate gain. The sample volume was subsequently placed on basal segment of septal, lateral, anterior and inferior LV walls to determine regional tissue systolic velocities from the apical four-chamber view and two-chamber view To determine regional tissue systolic velocities the sample volume was subsequently placed on basal segments of septal and lateral walls from the apical four-chamber view and basal segments of anterior and inferior LV walls from two-chamber view (5). In addition to measurements at rest, we measured maximum TDI systolic velocities at peak stress on basal segment of septal, lateral from apical four-chamber view and anterior, inferior from apical two-chamber view, respectively.

Statistical analysis

The results were expressed as mean±standard deviation. Data comparison on ischemic and non ischemic segments in rest and stress was made by Student's T-test. The level of p<0.05 is accepted as meaningful statistically.

Results

Total 24 patients who had ischemia on SPECT were evaluated. Demographic data are shown in the Table 1 (Table 1). Both diagnostic tests were completed in 24 patients with stable angina pectoris. All the patients were in sinus rhythm. Mean LV ejection fraction was 57±1.5%. Because we detected ischemia, coronary angiography was performed in all patients. In all patients who had ischemia on SPECT, >70% diameter stenosis of at least one major ischemia-related coronary artery was detected on angiography (Table 1).

SPECT

SPECT with Tc-99m MIBI was completed in all patients without any complication dipyridamole was used for seven patients while exercise was enough to complete the test in rest of the

Table 1. Clinical, demographic and coronary angiography data of patients

Patient Number	Sex*	Age, years	DM	HT	HL	Smoking	Coronary lesion location	Number of coronary arteries with >70% lesion	Coronary lesion percentage, %
1	M	62	+	+	-	-	RCA	1	100
2	M	51	+	-	-	+	LAD,CX	2	80
3	F	52	-	+	+	-	LAD,CX	2	90
4	M	68	+	-	+	+	CX,RCA	2	90
5	M	48	-	-	+	+	RCA	1	80
6	M	65	+	+	-	-	CX,RCA	3	80
7	F	54	+	+	+	-	CX,RCA	2	80
8	F	60	+	+	+	-	LAD,CX	4	90
9	F	74	+	+	+	-	RCA	1	70
10	M	82	-	+	-	-	LAD	1	95
11	F	61	+	+	+	-	LAD	1	70
12	M	69	-	+	+	-	CX,RCA	2	80
13	M	77	-	+	-	-	LAD,CX	3	100
14	M	75	+	+	+	+	LAD,RCA	2	80
15	M	60	-	-	-	+	LAD,CX	4	80
16	M	74	-	+	+	+	LAD,CX,RCA	1	95
17	M	65	-	+	-	+	CX,RCA	2	80
18	M	51	-	+	+	+	LAD,CX,RCA	1	100
19	M	59	-	+	-	-	LAD,RCA	2	95
20	M	65	-	+	+	-	CX	1	100
21	M	62	-	-	+	+	RCA	4	80
22	M	50	-	-	+	+	LAD,CX,RCA	1	95
23	M	56	-	+	-	-	CX	1	70
24	M	53	+	-	+	-	LAD,CX	2	90

CX - circumflex artery, F - female, LAD - left anterior descending artery, M - male, RCA - right coronary artery

patients. We evaluated normal (nonischemic) and ischemic LV walls which were shown by SPECT (Fig. 1). On myocardial scintigraphy the anterior wall, septum and apex were assumed to represent the territory of the left anterior descending artery, the lateral wall to represent the left circumflex artery and the inferior wall the right coronary artery. A total of 96 LV segments (37 ischemic and 59 nonischemic) of 24 patients with stable angina pectoris were visualized by myocardial SPECT study. There were no patients with scar finding, which reflects previous myocardial infarction (MI) in myocardial SPECT study.

TDI

Dobutamine stress test that combined with TDI prior to coronary angiography was performed for each patient. No patient had symptomatic hypotension or significant ventricular arrhythmia during the dobutamine stress test. The heart rate was 75±6 bpm at rest and 139±9 bpm at peak dose dobutamine. Maximum mean TDI systolic velocities on basal segment of LV septal, lateral, anterior and inferior walls were similar in ischemic and nonischemic segments (6.73±1.04 cm/sec, 6.93±1.34 cm/sec, respectively) at rest (Table 2, Fig. 2). At peak stress, maximum mean TDI systolic velocities were lower in the 37 ischemic segments (11.00±2.03 cm/sec) than 59 nonischemic segments (13.76±1.97 cm/sec, p < 0.001, Table 2, Fig. 2). TDI systolic velocities were measured at rest and at peak stress (Fig. 3).

Discussion

In our study, at rest peak systolic TDI velocities were similar between basal segments of ischemic and nonischemic LV walls on myocardial SPECT in patients with stable angina pectoris. Blomstrand et al. (5) have shown the effect of ischemia on TDI velocities in patients with unstable angina pectoris. On the other hand, stable angina pectoris patients have lower sympathetic activity than unstable patients (6). Therefore, our results reflect a documentation of the specific group of patients with CAD.

However, at peak stress compared to nonischemic segments systolic velocities were significantly lower in ischemic segments. Our finding of blunted myocardial tissue mean systolic velocity related to ischemia was consistent with the results in previous reports of unselected population of CAD, patients with unstable angina pectoris, acute MI, patients with stunned, hibernating, scarred myocardium and dilated cardiomyopathy (7-11). TDI records quantitative LV wall motion velocities (12). TDI provides accurate myocardial wall velocity data at rest and quantitatively detects decreased systolic and diastolic myocardial velocities in the ischemic myocardial regions with perfusion defects in the Tc-99m MIBI SPECT study (13-15).

We used apical views to quantify longitudinal motion of LV walls in the current study. While qualitative myocardial motion is evaluated by radial direction, TDI evaluates longitudinal myocardial motion of base to apex (16). There was a difficulty to measure systolic tissue velocity of anterior LV wall because of

Tablo 2. Mean values of TDI velocities (cm/sec) of ischemic and nonischemic segments

Variables	Nonischemic segments (n=59)	Ischemic segments (n=37)	p*
Rest TDI velocities, cm/sec	6.93±1.34	6.73±1.04	0.436
Stress TDI velocities, cm/sec	13.76±1.97	11.00±2.03	0.000

Data are represented as mean±SD
*Student's t test
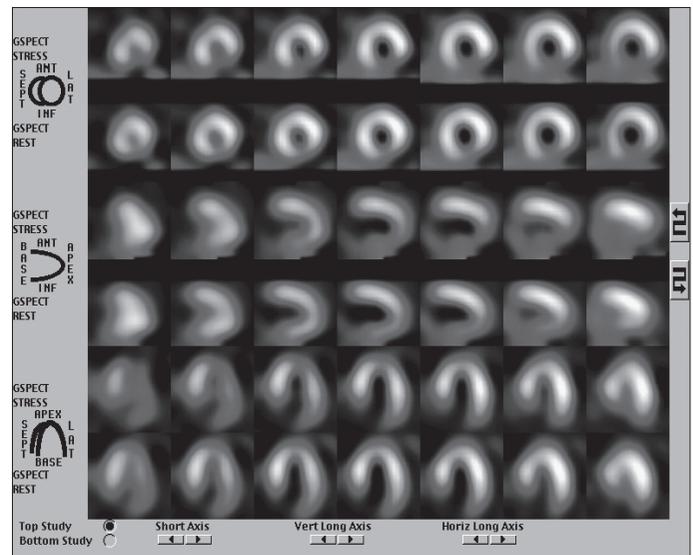TDI - tissue Doppler imaging

Figure 1. Inferolateral perfusion defect on the stress SPECT images in a patient with stable angina pectoris and proven CAD
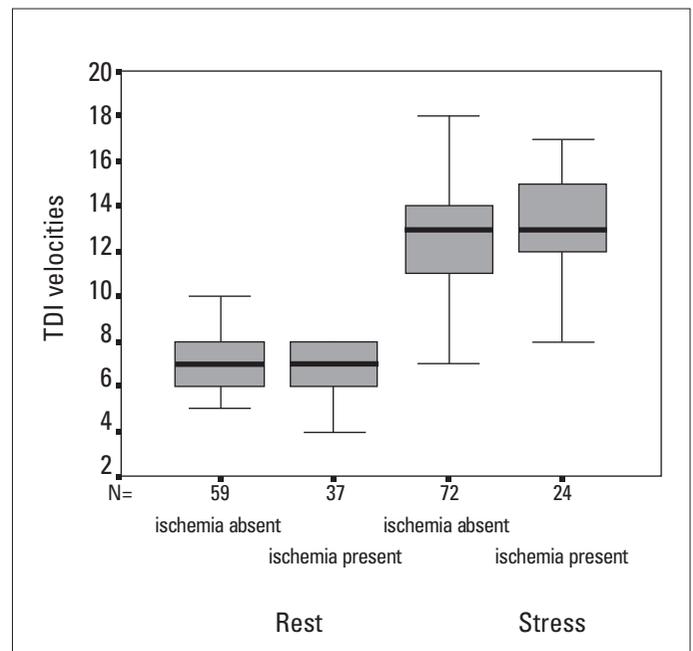
CAD - coronary artery disease

Figure 2. Rest and stress TDI velocities of ischemic and nonischemic segments based on myocardial perfusion scintigraphy

TDI - tissue Doppler imaging

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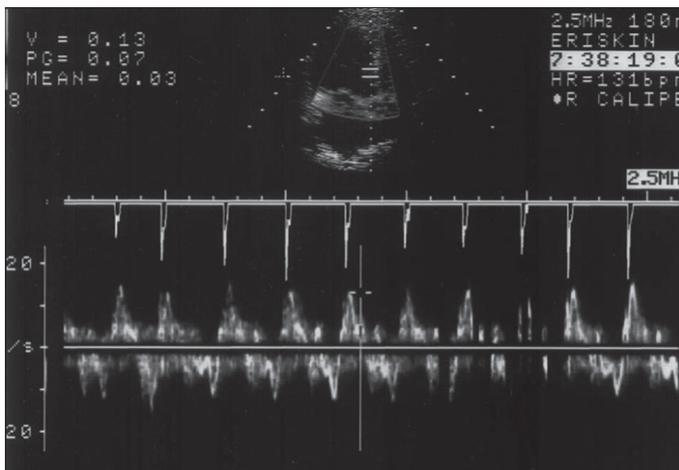
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Figure 3. Maximum pulsed Doppler tissue velocity of basal segment of the septal LV wall in the patient at peak dobutamine stress
LV - left ventricular

respiratory interference and particular shape of the wall as previously described (7). Despite this difficulty, ischemic anterior segments also showed a lower mean systolic tissue velocity at peak stress compared with that in nonischemic LV segments in our study. We used basal segment of LV walls for evaluation of myocardial function by pulsed TDI which detects peak systolic tissue velocity. Basal segment of LV wall from apical four-chamber view can be used to detect myocardial tissue velocities during dobutamine stress according to previous reports including our own experience (5-7, 17). It was reported that peak systolic tissue velocity by pulsed TDI is feasible to quantify LV wall motion during dobutamine stress testing (7).

To our knowledge, combined usage of both Tc-99m MIBI SPECT and myocardial tissue systolic velocities with dobutamine stress prior to revascularization (prior to CAG) was not evaluated in selected group of patients with stable angina pectoris. We previously observed that diastolic TDI velocities is more resistant to preload alterations compared to transmitral diastolic filling velocities in the resting conditions (18). However, tachycardia during stress inhibits the ability to separate diastolic E and A waves and evaluation may become difficult, although diastolic function is affected by CAD (5). In the current study, we concentrated on the systolic function and detected blunted systolic tissue velocities at stress reflecting impaired longitudinal motion of ischemic LV walls. The effect of revascularization on recovery of decreased tissue velocities related to ischemia was previously documented (19).

Study limitations

Myocardial perfusion SPECT with Tc-99m MIBI has approximately 80-90% sensitivity and 70-88% specificity in the diagnosis of CAD, however in this diagnostic test the patients are exposed to radiation and multivessel disease and obstruction under 50% might be missed with perfusion scan (20). Pulsed TDI evaluation of myocardial velocity may not be optimal, if the ultrasound beam is not parallel to the myocardial motion. We used apical

views for pulsed TDI evaluation to avoid this limitation as much as possible in evaluation of longitudinal myocardial motion. Different types of stress during the diagnostic tests was the other limitation of the study. Because of technical difficulty of TDI with treadmill exercise, we prefer to use dobutamine stress in evaluation of longitudinal myocardial motion by pulsed TDI. We did not assess ischemic alteration of diastolic function. However, it was reported that pulsed TDI evaluation of diastolic function has a low feasibility during dobutamine stress (7). It is necessary to complete larger and multicenter studies in patients with stable angina pectoris for documentation of diagnostic value of combined usage of both SPECT and TDI in clinical practice.

Conclusion

TDI with dobutamine stress can be used as an adjunctive to SPECT in patients with stable angina pectoris. Quantitative data by TDI with dobutamine stress in addition to SPECT may be beneficial for evaluation of the selected group of patients with stable angina pectoris and may provide better agreement for coronary revascularization.

Conflict of interest: None declared

References

1. Picano E, Lattanzi F, Orlandini A, Marini C, L'Abbate A. Stress echocardiography and the human factor: the importance of being expert. J Am Coll Cardiol 1991; 17: 666-9.
2. Kostkiewicz M, Plazak W, Podolec P, Olszowska M, Hlawaty M, Tracz W. Influence of left ventricular regional myocardial ischaemia on regional systolic and diastolic function in ischaemic heart disease patients. Acta Cardiol 2002; 57: 52-3.
3. Yalçın F, Müderrisoğlu H, Korkmaz ME, Özin B, Baltalı M, Yiğit F. The effect of dobutamine stress on left ventricular outflow tract gradients in hypertensive patients with basal septal hypertrophy. Angiology 2004; 55: 295-301.
4. Teichholz LE, Kreulen T, Herman MV. Problems in echocardiographic volume determinations: echocardiographic-angiographic correlations in the presence or absence of asynergy. Am J Cardiol 1976; 37: 7-11.
5. Blomstrand P, Maret E, Ohlsson J, Scheike M, Karlsson JE, Säfström K, et al. Pulsed tissue Doppler imaging for the detection of myocardial ischaemia, a comparison with myocardial perfusion SPECT. Clin Physiol Funct Imaging 2004; 24: 289-95.
6. McCance AJ, Forfar JC. Plasma noradrenaline as an index of sympathetic tone in coronary arterial disease: the confounding influence of clearance of noradrenaline. Int J Cardiol 1990; 26: 335-42.
7. Pasquet A, Armstrong G, Rimmerman C, Marwick TH. Correlation of myocardial Doppler velocity response to exercise with independent evidence of myocardial ischemia by dual-isotope single-photon emission computed tomography. Am J Cardiol 2000; 85: 536-42.
8. Fraser AG, Payne N, Mädler CF, Janerot-Sjøberg B, Lind B, Grocott-Mason RM, et al. MYDISE Investigators. Feasibility and reproducibility of offline tissue Doppler measurement of regional myocardial function during dobutamine stress echocardiography. Eur J Echocardiography 2003; 4: 43-53.

9. Nishino M, Tanouchi J, Tanaka K, Ito T, Kato J, Iwai K, et al. Dobutamine stress echocardiography at 7.5 mg/kg/min using color tissue Doppler imaging M-mode safely predicts reversible dysfunction early after reperfusion in patients with acute myocardial infarction. Am J Cardiol 1999; 83: 340-4.

10. Bountioukos M, Schinkel AF, Bax JJ, Rizzello V, Valkema R, Krenning BJ, et al. Pulsed wave tissue Doppler imaging for the quantification of contractile reserve in stunned, hibernating, and scarred myocardium. Heart 2004; 90: 506-10.

11. Plewka M, Drozdz J, Krzeminska-Pakula M, Ciesielczyk M, Peruga JZ, Kasprzak JD. Tissue Doppler echocardiography during low-dose dobutamine infusion in patients with ischaemic and idiopathic dilated cardiomyopathy. Acta Cardiol 2002; 57: 68-9.

12. Katz WE, Gulati VK, Mahler CM, Gorcsan J 3rd. Quantitative evaluation of the segmental left ventricular response to dobutamine stress by Doppler tissue echocardiography. Am J Cardiol 1997; 79: 1036-42.

13. Kostkiewicz M, Plazak W, Olszowska M, Hlawaty M, Podolec P, Tracz W. Myocardial ischemia assessed by Tc99m-MIBI SPECT and left ventricle regional systolic and diastolic function evaluated by tissue Doppler echocardiography. Int J Cardiovasc Imaging 2003; 19: 315-21.

14. Özer N. The role of Doppler echocardiography in the evaluation of myocardial ischemia and regional function abnormalities in patients with coronary artery disease. Anadolu Kardiyol Derg 2008; 8: suppl 1; 23-8.

15. Yılmaz R, Baykan M, Erdöl C. Pulsed wave doku Doppler ekokardiyografi. Anadolu Kardiyol Derg 2003; 3: 54-9.

16. Jones CJ, Raposo L, Gibson DJ. Functional importance of the long axis dynamic of the human left ventricle. Br Heart J 1990; 63: 215-20.

17. Yalçın F, Yiğit F, Erol T, Baltalı M, Korkmaz ME, Müderrisoğlu H. Effect of dobutamine stress on basal septal tissue dynamics in hypertensive patients with basal septal hypertrophy. J Hum Hypertens 2006; 20: 628-30.

18. Yalçın F, Kaftan A, Müderrisoğlu H, Korkmaz ME, Flachskampf F, Garcia M, et al. Is Doppler tissue velocity during early left ventricular filling preload independent? Heart 2002; 87: 336-9.

19. Bach DS, Armstrong WF, Donovan CL, Muller DW. Quantitative Doppler tissue imaging for assessment of myocardial velocities during transient ischemia and reperfusion. Am Heart J 1996; 132: 721-5.

20. Mahmarian JJ, Boyce TM, Goldberg RK, Cocanougher MK, Roberts R, Verani MS. Quantitative exercise thallium-201 single photon emission computed tomography for the enhanced diagnosis of ischemic heart disease. J Am Coll Cardiol 1990; 15: 318-29.