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Mustafa CEMRİ[1]
Rıdvan YALÇIN[1]
Bülent BOYACI[1]
Özlem KAPUCU[2]
Tamer ATASEVER[2]
Atiye ÇENGEL[1]
Övsev DÖRTLEMEZ[1]
Halis DÖRTLEMEZ[1]

Determination of Viable Myocardium in Patients with Ischaemic Left Ventricular Dysfunction: Comparison of Thallium–201 Single–Photon Emission Computed Tomography with Nitrate and Dobutamine Echocardiography

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Departments of [1]Cardiology, [2]Nuclear Medicine, Faculty of Medicine, Gazi University, Ankara-Turkey

Abstract: The method of Thallium – 201– single – photon emission computed tomography (Tl–201 SPECT) have been commonly used to detect uncontractile but viable myocardium in patients with ischemic left ventricular dysfunction. The aim of this study was to establish the value of nitrate echocardiography (NE) and low dose dobutamine echocardiography (LDDE) to detect viable myocardium when compared to Tl–201 SPECT. Twently patients (16 M, 4F; mean age: 56.4±9.6 years) who had anterior myocardial infarction in the last three months were studied. Within the same week, but on different days NE, LDDE and Tl–201 SPECT procedures were performed to the patients. In NE and LDDE procedures, patients were given 0.4–2 µg/kg/min. nitroglycerin and 5–10 µg/kg/min. dobutamine infusion, respectively. Evaluation of both the SPECT and the echocardiography (NE and LDDE) were done with sixteen–segment model. Regional thallium activity scores ranged from 0 (severe reduction in activity) to 3 (normal activity). At Tl–201 SPECT, on segments which have perfusion defect, identifying at least one degree of perfusion recovery, was evaluated as viability. At NE and LDDE, on segments which have two or more contiguous dysfunctional behaviour, determining at least one degree of wall motion recovery, was evaluated as viability. The wall motion score index (WMSI) was derived by summation of individual segment scores (1: normal; 4: dyskinetic) divided by the number of interpreted segments. Tl–201 SPECT showed a reversible defect in 91 (75%) segments among the 121 baseline echocardiographic dyssynergic segments. İmprovement of both the SPECT and the LDDE were determinated in 70 (57%) segments. At both NE and LDDE, WMSI decreased according to baseline echocardiographic scrore index ($p < 0.05$). At baseline echocardiography, NE and LDDE, WMSI was 1.76±0.32, 1.58±0.33 and 1.56±0.30, respectively. When Tl–201 SPECT was taken as a gold standard, it was observed that at segments level, the sensivity of NE was 75% and specificity of it was 86%; the sensivity of LDDE was 76% and specificity of it was 80%. As a result, in determination of viable myocardium in patients with ischaemic left ventricular dysfunction, it was considered that NE and LDDE are as reliable as Tl–201 SPECT, easily appliable, and they can be preferred because they are much cheaper.

Key Words: Myocardial Viability, Nitrate Echocardiography, Low Dose Dobutamine Echocardiography, Ischaemic Left Ventricular Dysfunction.

Introduction

It was been shown that the myocardial infarction is one of the commonest cause of left ventricular systolic dysfunction (1). The dysfunction may be caused by necrotic, stunned or hibernating myocardium (1–3). It has been thought that myocardium may be viable if there is a reversible functional disorder in the segments of myocardium (2–3).

The detection of reversible myocardial dysfuction may improve the management of patients with ischemic left ventricular dysfunction. Accurate identification of reversible dysfunction may identify patients who are most likely to benefit from revascularization. The presence of myocardial viability in patients with end–stage coronary artery disease may favor revascularization over cardiac transplantation. If the dysfunction is due to myocardial stunning or hibernation, recovery is observed; if it is due to scarring, no recovery occurs. After myocardial infarction, prognosis strongly correlates with myocardial viability.

Up to date, many electrocardiographic, echocardiographic, angiographic, radiologic, and nuclear cardiologic techniques (For example, rest electrocardiography and exercise electrocardiography, rest echocardiography, low dose dobutamine echocardiography, dipyridamole echocardiography, nitrate echocardiography, dobutamine transesophageal echocardiography, dobutamine magnetic resonance imaging, myocardial contrast echocardiography, post–extrasystolic potentiation, thallium–201 imaging, technetium–99 m sestamibi imaging, technetium 99m tetrafosmin imaging, positron emission tomography, collateral circulation, tissue doppler echocardiography) have been used to detect myocardial viability (3–26). Nevertheless, all above techniques cited in the literature are far from being ideal to attain best result in this field. In this study we compared nitrate echocardiography (NE) and low dose dobutamine echocardiography (LDDE) techniques with thallium–201 single photon emission tomography (Tl–201 SPECT) to determine viability of myocardium in patients with ischaemic left ventricular dysfunction.

Methods

We studied 20 consecutive patients with recent (3 months) anterior myocardial infarction (16 men, 4 women; mean age 56.4+9.6 years) admitted to the Cardiology Department of Gazi University Medical Faculty. The diagnosis of a previous myocardial infarction was based on hospital records, serial electrocardiogram recordings, serum enzyme determinations and echocardiographic findings. Functional status was assessed in all as class II or III (New York Heart Association criteria).

Within the same week, but on different days NE, LDDE and Tl–201 SPECT procedures were performed to the patients. During procedures anginal therapy had been withdrawn for 1 week. There was no acute cardiac event during procedures. Patients were excluded if any of the following were present; unstable angina, history of sustained ventricular tachycardia, atrial flutter or fibrilalation, uncontrolled cardiac failure, valvular heart disease, technically inadequate echocardiogram. The study was approved by the Human Research Ethics Committee of our hospital; informed consent was obtained from all patients before the investigations.

Nitrate Echocardiography

General Electric RT6800 apparatus with 2.5 and 3.5 mHZ probes was used for NE. Blood pressure and three–lead electrocardiogram (ECG) monitorization were performed for each patient during the procedure. Before the start of nitroglycerine infusion, a complete baseline two–dimensional transthoracic echocardiographic and Doppler assessment was performed for each patient. Images in the parasternal long –and short– axis and apical four –and two– chamber views were acquired before the start of nitroglycerine infusion and at the end of each dose interval, and were recorded to videotapes.

Nitroglycerine was administered intravenously beginning at a dose of 0.4 µg/kg/min. NE protocol involves the use five 3–minute stages of nitroglycerine infusion, at doses of 0.4, 0.8, 1.2, 1.6, and 2 µg/kg/min. The infusion was terminated when the patient developed more than a 20 mmHg decline in systolic blood pressure from baseline, significant side effects, or arrhythmia. If none of the above end points were achieved, the infusion was discontinued at a maximal dose of 2 µg/kg/min.

Identical left ventricular segments at baseline and during administration of 0.4, 0.8, 1.2, 1.6, and 2 µg/kg per min. of nitroglycerine were analysed for regional wall motion with standard 16 segment model of echocardiography experienced observed independently, who had no knowledge of the clinical details (Fig. 1). A third observer was asked in cases of diageement and a

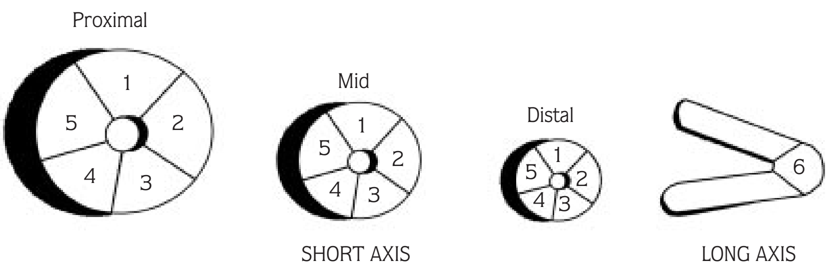

Figure 1. Segmental evaluation pattern for corresponding echocardiography and myocardial scintigraphy. The left ventircular apex (segment 6) was evaluated from vertical long–axis slices. The remaining portions of the left ventricle were analyzed from short–axis slices that were divided into distal, mid and proximal levels, and at each level the myocardium was divided into five regions: anterior(1), lateral(2), inferior(3), inferoseptal(4) and anteroseptal(5).

majority decision was accepted. By visual assessment of endocardial motion and wall thickening, each segment was classified as normal, hypokinetic, akinetic or dyskinetic, each carrying wall motion score of 1, 2, 3 or 4, respectively. The left ventricular wall motion score index was calculated as the ratio between the sum of all available segmental wall motion score of 1, 2, 3 or 4, respectively. The left ventricular wall motion score index was calculated as the ratio between the sum of all available segmental wall motion scores and the number of segments visualised. Myocardial viability in a dysfunctional segment at rest was defined as an improvement in the wall motion score of that segment during either stage of the nitroglycerine infusion by one or more grades in comparison with the baseline score. Interobserver and intraobserver agreement on wall motion score was 90 and 92%, respectively.

Dobutamine Echocardiography

Dobutamine was infused intravenously in a solution of 5% dextrose through a peripheral arm vein, beginning at a dose of 5 µg/kg body weight permin. After 3 min, the infusion rate was increased to 10 µg/kg per min. and continued for 3 additional min. Images in the parasternal long–and short–axis and apikal four–and two–chamber views were acquired before the start of dobutamine infusion and at the end of each dose interval, and were recorded. Video records were evaluated as described in NE. Dobutamine–induced contractile reserve in a dysfunctional segment at rest was defined as an improvement in the wall motion score of that segment during either stage of the dobutamine infusion by one or more grades in comparison with the baseline score. Interobserver and intraobserver agreement on wall motion score was 92% and 94%, respectively.

Thallium–201 SPECT

Stress–redistribution–reinjection imaging was performed on 12 patients who had class II functional capacity. Rest–redistribution imaging was performed on 8 patients with class III functional capacity.

a) Stress–Redistribution–Reinjection Imaging

12 patients performed symptom limited exercise stress test (modified Bruce protocol) in the fasting state in the morning. Three millicuries of thallium 201 were injected at 75% of the age–predicted heart rate, and exercise was continued for 1 minute. Scintigraphic imaging was started within 5 minutes of the injection of thallium. Redistribution imaging was taken 3 hours later. Reinjection imaging was assessed 30 minutes after reinjection of 1 mCi of thallium.

b) Rest–Redistribution Imaging

On fasting, 3 millicuries of thallium 201 was injected intravenously at rest. Rest–redistribution Tl–201 SPECT images was started within 20 minutes after the injection and repeated 3 hours later.

Evaluation of Tl–201 SPECT

The image of Tl–201 SPECT was taken with a dual head gamma camera (General Electric Optima), which is suitable for cardiac research. Thirty two projections were acquired over a 180– degree arc beginning from left posterior oblique. The interpretation of the images reconstructed with 180–degree acquisition was made on the basis of short– axis, vertical, and horizontal long–axis slices. The interpretation of the images were made by two blinded investigators who had no knowledge of the results of nitrate and dobutamine echocardiography. A third observer was asked in cases of disagreement, and a majority decision was accepted. To obtain a matched regional assessment of wall motion and thallium uptake, the same 16–segment model used for interpretation of the echocardiogram was applied to interpret the SPECT images (Fig. 1). Regional thallium activity scores ranged from 0 (severe reduction in activity) to 3 (normal activity). At Tl–201 SPECT, on segments which have perfusion defect, identifying at least one degree of perfusion recovery, was evaluated as viability.

Statistics

In this study, Wilcoxon Matched–Pairs Signed–Ranks Test and Mann Whitney U–Wilcoxon Rank Sum W Test were used for statistical analysis. Continuous data are presented as mean ± SD. A p value < 0.05 was considered significant.

Results

A total of 320 myocardial segments were analyzed on baseline echocardiography of 20 patients with anterior myocardial infarction. On baseline echocardiography, 21 segments were judged dyskinetic, 79 akinetic, 21 hypokinetic, and 199 normal. Each patient had two or more contiguous dyssynergic segments.

Thallium–201 SPECT showed a reversible defect in 91 segments and a fixed defect in 30 segments among the 121 dyssynergic segments detected on baseline echocardiography.

Nitroglycerin infusion was well tolerated in all patients. Regional wall motion improved by one grade or more during nitroglycerin infusion in 72 myocardial segments.

Improvement of both the SPECT and the NE were determined in 68 segments among the 121 baseline echocardiographic dyssynergic segments. Thallium–201 SPECT also showed perfusion recovery in 23 of 49 myocardial segments which were not affected by NET (Table 1). When thallium–201 SPECT was taken as a gold standard, it was observed that at segments level, the sensivity of it was 86%.

Dobutamine echocardiography was also successfully applied to all patients without any serious comlications. Myocardial viability was detected by LDDE in 76 of 121 baseline echocardiographic dyssynergic segments. Improvement of both the SPECT and the LDDE were determinated in 70 segments (Table 2).

When thallium–201 SPECT was taken as a gold standard, it was observed that at segments level the sensivity of LDDE was 76% and specificity of it was 80% (Table 3). During both NE and LDDE, WMSI significantly decreased according to baseline echocardiographic score index ($p<0.05$). At baseline echocardiography, NE and LDDE, WMSI was 1.76±0.32, 1.58±0.33 and 1.56±0.30, respectively (Tablo 4).

Table 1. Concordance between Tl–201 SPECT and nitrate echocardiography results in the 121 baseline dyssynergic segments.

		Thallim–201 SPECT		
		Reversible defect	Fixed defect	Total
Echocardiography of the left ventricle during nitroglycerine	Wall–motion improvement	68	4	72
	No wall–motion improvement	23	26	49
	Total	91	30	121

Table 2. Concordance between Tl–201 SPECT and dobutamine echocardiography results in the 121 baseline dyssynergic segments.

		Thallim–201 SPECT		
		Reversible defect	Fixed defect	Total
Echocardiography of the left ventricle dobutamine infusion	Wall–motion improvement	70	6	76
	No wall–motion improvement	21	24	45
	Total	91	30	121

Table 3. Prediction of recovery of dyssynergic segments per segment by using nitrate echocardiography and dobutamine echocardiography.

	Nitrate Echocardiography	Dobutamine Echocardiography
Sensivity	75	76
Specificity	86	80

Table 4. Values of WMSI on baseline, nitrate echocardiography and dobutamine echocardiography. During both NE and DE, WMSI significantly decreased according to baseline WMSI.

	Wall Motion Score Index (WMSI)	P value (according to baseline echocardiography)
Baseline Echocardiography	1.76±0.32	
Nitrate Echocardiography (NE)	1.58±0.33	< 0.05
Dobutamine Echocardiography (DE)	1.56±0.30	< 0.05

Discussion

The left vetricular dysfunction may be caused by coronary artery disease, hypertension, cardiomyopathy, and valve disease of heart (1). However, coronary artery disease, particularly actue myocardial infarction is a common cause of left ventricular dysfunction (1). The mechanism of left ventricular dysfunction after an acute myocardial infarction are prolonged coronary obstruction, transient coronary obstruction, complete reperfusion, and prolonged hypoperfusion (1–3). Prolonged obstruction results in myocardial necrosis and fixed dysfunction. Transient obstruction and complete reperfusion causes stunned myocardium. Prolonged hypoperfusion produces myocardial dysfunction called as hibernating myocardium.

In our study, all the patients had anterior myocardial infarction. Anterior and apical walls of left venricle are the easiest segments to visualise by echocardiographic analysis. Furthermore, this segments can be analyzed easily by the Tl–201 SPECT. Circumflex artery obstruction–dependent myocardial perfusion defect is more difficult than left anterior desending (LAD) artery obstruction–dependent myocardial perfusion defect for the evaluation of theT1–201 SPECT. Therefore, it is preferred to study patients with LAD artery–dependent anterior myocardial infarction. The same 16– segment left ventricle model was used in both echocardiographic and scintigraphic studies so that interpretation errors could be minimised.

In our study, three different methods were used to evaluate myocardial viability. Up to date, Tl–201 SPECT it the most commonly used method to detect myocardial viability. However, Tl–201 SPECT is more expensive, time–taking and not available in all medical centre. Two different Tl–201 SPECT techniques were used according to the clinical conditions of patients. Tl–201 SPECT with stress–rest–reinjection is more predictive than Tl–201 SPECT with rest–redistribution for the identification of myocardial viability (2, 14, 20). However, Dilsizian et al have shown than both of methods had identical predictive value if regional thallium activity was measured semiquantitatively like our study (13).

LDDE is commonly used for echocardiographic evaluation of myocardial viability after acute myocardial infarction. LDDE is less time consuming than NE. The studies by many investigators have detected that the sensivity of LDDE was 53–86% and specificity of it was 75–95% for identification of myocardial viability (1,4–6, 9, 14, 18, 19). When Tl–201 SPECT was taken as a gold standard, it was observed that at segments level, we found the sensivity of LDDE 76% and specificity 80%. Our results correlate with the literature.

Nitrates have been shown to increase the regional coronary blood flow to ischaemic myocardial regions. Thus, nitrates can stimulate the myocardial contractility. However, NE is rarely used for evaluation of myocardial viability. Pontillo et al have demonstrated that the sensivity of NE was 86% and specificity of it was 83% (23). We found that the sensivity of NE was 75% and specifivity of it was 86% for detection of myocardial viability.

In our study to detect myocardial viability, the WMSI of left ventricle was significantly reduced in both NE and LDDE. This may be an indirect finding of the myocardial viability.

There are several limitations to our study. The most important one is that digital echocardiography equipment was not avaible in our study. Two observers blinded to the patienrs scintigraphic data interpreted both NE and LDDE so that interpretation errors could be minimised. A third observer was asked in cases of disagreement, and a majority decision was reached. In this study, two different Tl–201 SPECT techniques according to the clinical conditions of patients. However, the clinical value for assessment of myocardial viability of rest redistribution Tl–201 imaging seems to be similar to stres–rest–reinjection Tl–201 imaging. Regional thallium activity was also measured semiquantitatively in our study. Another limitation of our study is the lack of data of positron emission tomography (PET) in our patients. Although it is the standart technique for evaluation of myocardial viability, PET is uvavaible in our country for the now being which makes the evaluation of the significance of other techniques more important.

As a result, in determination of viable myocardium in patients with ishemic left ventricular dysfunction, it was considered that NE and LDDE are as reliable as Tl–201 SPECT, easily appliable, and they can be preferred because they are much cheaper.

Correspondence author:
Dr. Mustafa CEMRİ
Işık Sk. 5/10
Tandoğan
06570 Ankara

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