Evaluation of left ventricular function using Tei index in patients with preinfarction angina

İnfarktüs öncesi anjinası olan hastalarda sol ventrikül fonksiyonlarının Tei indeksi kullanımı ile değerlendirilmesi

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ABSTRACT

Objective: The study investigated whether preinfarction angina influences left ventricular functions assessed by using Tei index, which is an independent predictor for left ventricular dysfunction in acute myocardial infarction.

Methods: We studied 96 patients with acute myocardial infarction with ST segment elevation (80 men, 16 women; mean age 57.5±9.9 years) who were assigned into 2 groups: with and without preinfarction angina. All patients were serially evaluated by 2-dimensional and Doppler echocardiography on the days 1, 6, and 30, and were followed up for 30 days for incidence of complications.

Results: We observed that Tei indexes was lower on the days 1, 6 and 30 (0.49±0.20 vs. 0.59±0.20, p=0.003, 0.46±0.20 vs. 0.56±0.20, p=0.001, 0.44±0.20 vs. 0.53±0.10, p=0.01) in patients with preinfarction angina as compared with those without angina. Tei index significantly decreased during follow-up (0.49±0.20, 0.46±0.20, 0.44±0.20; p=0.02) in patients with preinfarction angina, while it did not change significantly in patients without preinfarction angina (p=0.2). Echocardiographically significant improvements were observed in E deceleration time, isovolumic relaxation time and ejection time in all patients, whereas significant improvements in ejection fraction, wall motion score index and isovolumic contraction time were observed only in patients with preinfarction angina during follow-up. Mortality, Killip class ≥2, pericarditis, atrial fibrillation, and left ventricular thrombus were lower in patients with preinfarction angina.

Conclusion: These data indicated that the patients with preinfarction angina had better preserved systolic left ventricular function and Tei index values. Also, it was observed that preinfarction angina may cause earlier and more prominent myocardial functional recovery and confer protection against complications on short-term after first acute myocardial infarction. *(Anadolu Kardiyol Derg 2006; 6: 3-8)*

Key words: Preinfarction angina, Tei index, echocardiography

ÖZET

Amaç: Akut miyokard infarktüslü hastalarda infarktüs öncesi anjinanın ventrikül fonksiyonlarına etkisi, infarktüs sonrası sol ventrikül fonksiyon bozukluğunun bağımsız bir göstergesi olan Tei indeksinin kullanımıyla belirlenmesi amaçlandı.

Yöntemler: ST segment yüksekliği olan akut miyokard infarktüsü tanılı 96 hasta (80 erkek, 16 kadın; ortalama yaş 57.5±9.9 yıl) infarktüs öncesi anjinası olan ve olmayanlar olmak üzere 2 gruba ayrıldılar. Hastaların tümü 1., 6. ve 30. günlerde 2 boyutlu ve Doppler ekokardiyografi yapılarak karşılaştırıldı ve seri olarak değerlendirildiler. Ayrıca hastalar komplikasyon gelişimi bakımından 30 gün takip edildiler.

Bulgular: İnfarktüs öncesi anjinası olan hastalarda 1, 6 ve 30. günlerde elde edilen Tei indeksleri anjinası olmayanlardan daha düşüktü (0.49±0.20'ye 0.59±0.20, p=0.003, 0.46±0.20'ye 0.56±0.20, p=0.001, 0.44±0.20'ye 0.53±0.10, p=0.01) ve takip sırasında anlamlı azalma gösterdi (0.49±0.20, 0.46±0.20, 0.44±0.20; p=0.02). Tei indeksi infarktüs öncesi anjinası olmayan hastalarda anlamlı değişmedi (p=0.2). Hastaların tümünde takip sırasında E deselerasyon, izovolumik gevşeme ve ejeksiyon zamanlarında anlamlı düzelme gözlenirken, ejeksiyon fraksiyonu, duvar hareket skor indeksi ve isovolümik kasılma zamanında sadece infarktüs öncesi anjinası olanlarda anlamlı düzelmeler gözlendi. Ölüm, ≥2 Killip sınıfı, perikardit, atriyal fibrilasyon, sol ventrikül trombüsü gelişim oranları infarktüs öncesi anjinası olanlarda daha düşüktü.

Sonuç: Bu veriler infarktüs öncesi anjinası olan hastaların daha iyi korunmuş sistolik sol ventrikül fonksiyonlarına ve Tei indeksi değerlerine sahip olduğunu gösterdi. Ayrıca, infarktüs öncesi anjina varlığının miyokard fonksiyonlarında daha erken ve belirgin iyileşmeye neden olduğu ve miyokard infarktüsü sonrası erken dönemde komplikasyon gelişimini azalttığı gözlendi. *(Anadolu Kardiyol Derg 2006; 6: 3-8)*

Anahtar kelimeler: İnfarktüs öncesi anjina, Tei indeksi, ekokardiyografi

Introduction

Several clinical studies have demonstrated that anginal attacks shortly before the onset of acute myocardial infarction (AMI) limit infarct size and improve short and long-term outcomes (1-3). Also, it was suggested that patients with preinfarction angina have a better prognosis because of a beneficial effect on left ventricular (LV) function (1,4,5). However, the results of

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other studies have been inconsistent as they found no benefit or even a deleterious effect of antecedent angina (6-8).

Recently, a new noninvasive Doppler-derived myocardial performance index expressed as Tei index was proposed by Tei et al. (9). The Tei index, which combines both systolic and diastolic functions and correlates with invasive measures, may give a better reflection of the global LV function than an isolated evaluation of either ejection or relaxation (9,10). Both LV systolic and diastolic functions are affected in AMI, and the geometry of the LV is distorted during the LV remodelling process, the index could theoretically be an attractive alternative to standard measures of LV function after AMI (11,12). Increased Tei index was shown to be a prognostic index and independent predictor for cardiac complications in various heart diseases including AMI (13-15).

There are no studies that have serially assessed the impact of preinfarction angina on LV function by using Tei index. In the present study, we aimed to examine the effects of preinfarction angina on LV functions and myocardial functional recovery in patients with AMI with ST segment elevation. Therefore, Tei index and conventional echocardiographic LV function parameters and serial changes of these parameters in patients with preinfarction angina during 30 days of follow-up were compared with those patients without preinfarction angina. In addition, the effects of preinfarction angina on cardiac complications and infarct size estimated creatinine kinase (CK)-MB levels were investigated.

Methods

Clinical Characteristics of Patients

Between June 2003 and June 2004, we prospectively studied 96 consecutive patients (80 men, 16 women; mean age 57.5±9.9 years) who were admitted to the coronary care unit with the diagnosis of AMI at Karadeniz Technical University in Turkey. Diagnosis of AMI required ≥2 of these characteristics: typical chest pain persisting for ≥30 minutes; ST segment elevation of at least 0.1 mV in 2 limb leads or 0.2 mV in 2 contiguous chest leads, on the standard electrocardiogram; and a serum peak CK-MB concentration of more than two times the upper limit of normal 6-12 h after the admission Patients with a history of prior MI, bundle brunch block, atrial fibrillation, paced rhythm, atrioventricular block, valvular heart disease, cardiomyopathies, chronic lung disease, chronic renal failure, and inadequate echocardiographic tracing were excluded from the study. Clinical evaluation, electrocardiogram, and blood pressure measurement were performed and routine blood samples were taken every day during hospitalization. Venous blood samples were obtained on admission and every 6 hours thereafter during the first 24 hours and then every 24 h for at least 4 days as previously described (16). The CK-MB levels were measured by a Hitachi 917 autoanalyser using Roche diagnostic kits.

Preinfarction angina was defined as ≥1 episode of typical chest pain at rest or during exercise lasting <30 minutes during one week before the onset of myocardial infarction. Postinfarction angina was diagnosed in the presence of new angina pectoris within two weeks after myocardial infarction.

Echocardiographic Analysis

All examinations were performed with Hewlett-Packard SONOS 5500 machine with a 2.5 MHz transducer. Left ventricular diastolic filling patterns were determined by the mitral inflow pulsed wave Doppler examination. Ratio of peak early (E) and late (A) transmitral filling velocities (E/A) and the deceleration time of the E wave velocity (E DT) were calculated. The isovolumic relaxation time (IVRT) was measured from closure of the aortic valve to opening of the mitral valve. The isovolumic contraction time (IVCT) was measured from closure of the mitral valve to opening of the aortic valve. The both IVRT and IVCT were assessed by simultaneously measuring the flow into the LV outflow tract and mitral inflow by Doppler echocardiography. Ejection time (ET) was measured from the opening to the closure of the aortic valve on the LV outflow velocity profile. Tei index was equal to the sum of the IVRT and IVCT divided by the ET (10). Left ventricular ejection fraction (EF) was computed by using a modified Simpson's biplane method from apical 2-and 4-chamber views. Each representative value was obtained from the average of consecutive three measurements. Standard 2- and 4-chamber apical views were used to assess the LV wall motions. Segmental regional wall-motion analysis was performed with the use of a standard 16-segment model (17). For each segment, wall motion was scored from 1 (normal) to 4 (dyskinetic). Wall motion score index (WMSI) was calculated by summation of individual segment scores divided by the number of interpreted segments.

All patients were evaluated by two-dimensional and pulsed wave Doppler echocardiography within first day after thrombolytic therapy and again on the days 6 and 30 after AMI. All echocardiograms were performed and analyzed by one observer. The two- dimensional and Doppler tracings were recorded on strip charts at a paper speed of 50 mm/s or 100 mm/s and videotaped for later playback and analysis.

The patients were divided into 2 groups according to the presence or absence of preinfarction angina. The patients were followed up for 30 days regarding occurrence of complications such as cardiac death, Killip class ≥2, postinfarction angina, pericarditis, atrial fibrillation, and LV thrombus. We called up the patients by phone and questioned their health condition once a week, after they were discharged from our clinic. During weekly interview, if needed, we called the patient to our clinic. Then all the patients were routinely examined at the 30th day after AMI.

Therapy

Thrombolytic therapy was administered in 57 of 96 (59.4%) patients with AMI. Of these, 67% received streptokinase (1500000 IU intravenously over 1 hour) and 33% - tissue-type plasminogen activator (100 mg intravenously over 90 minutes). Thirty-nine patients did not receive thrombolytic therapy as a result of contraindication for thrombolysis or late admission after the onset of pain. Thrombolysis was administered in 61% of patients with preinfarction angina, 58% of patients without preinfarction angina. All patients received intravenous heparin for 2 days followed by low molecular-weight heparin or low molecular-weight heparin alone during hospitalization. Aspirin as antiplatelet therapy was started on the first day of treatment in all patients. Patients also received the following medications during and after hospitalization; nitrates, angiotensin-converting enzyme inhibitors, beta-blockers, and statins.

Statistical Analysis

All the results are expressed as the mean ± standard deviation. The variables were tested for normal distribution with Kolmogorov-Smirnov test. The Chi-square test was used to determine the differences of the categorical variables between the groups. Unpaired t test and Mann Whitney test were used to compare parameters between the groups. Changes in echocar-

diographic variables over time were assessed by repeated-measures analysis of variance and Friedman test. For calculation of correlations we used Pearson and Spearman correlation coefficients. A p value < 0.05 was considered to be significant.

Results

The patients were divided into 2 groups according to the presence (44 patients, 46%) or absence (52 patients, 54%) of preinfarction angina. The baseline characteristics of the patients are listed in the Table 1. There were no significant differences between the two groups regarding age, gender, presence of diabetes mellitus, hypertension, obesity, smoking status, location of MI, therapies after admission, choice of thrombolytic therapy, and time from onset of chest pain to thrombolysis. Peak CK-MB levels in patients with preinfarction angina were significantly lower than in patients without preinfarction angina (248.5±213 U/l vs. 341.3±237.7 U/l, p=0.02, respectively).

Two-dimensional and Doppler echocardiographic variables of LV systolic, diastolic functions and Tei index were compared between the groups and data are represented in the Table 2. Tei index values on the days 1, 6, and 30 were lower in patients with preinfarction angina than in patients without preinfarction angina (p<0.01, p<0.01, and p<0.05, respectively). Similarly, on the days 1, 6, and 30, EF was higher (p<0.001, p<0.001 and p<0.01, respectively), WMSI was lower (p<0.05, p<0.05 and p<0.05, respectively), ET was longer (p<0.05, p<0.05 and p<0.05, respectively), and IVCT was shorter (p<0.01, p<0.01 and p<0.01, respectively), in patients with preinfarction angina than in those without. There were no significant differences in E DT, E/A, and IVRT on the days 1, 6, and 30 between the patients with and without preinfarction angina.

Serial changes in the left ventricular function parameters in the patients with and without preinfarction angina during follow-up

Table 2 lists serial Doppler echocardiographic changes from days 1 to 30 and statistical comparison of these changes in 96 patients with AMI. The Tei index significantly reduced from day 1 to day 30 (p=0.02) in patients with preinfarction angina, while changes in Tei index during the same period in patients without angina did not reach statistical significance (p>0.05). The E/A did not significantly change in both groups of patients during observation period. However, the IVRT (p<0.001 and p=0.01, respectively), E DT (p<0.001 and p=0.002, respectively) and ET (p=0.001 and p=0.001, respectively) showed significant prolongation from day 1 to day 30 in both groups of patients with and without preinfarction angina. In contrary, the IVCT significantly shortened (p=0.03), EF increased (p=0.002) and WMSI (p=0.009) decreased during follow-up period only in the patients with preinfarction angina. In addition, the differences for each parameter between days (1-6, 1-30) during follow-up period are stated in the Table 2.

Cardiac complications during 30 days are shown in Table 3. The mortality rate was 7% in patients with preinfarction angina and 23% in patients without preinfarction angina (p=0.05). The percentage of ≥2 Killip class (p=0.002), pericarditis (p=0.03), atrial fibrillation (p=0.009), LV thrombus (p=0.03) in patients with preinfarction angina were significantly lower than in patients without preinfarction angina. There was no significant difference between the two groups in the incidence of postinfarction angina.

Although, Tei index values obtained on the 1st, 6th, and 30th days were positively correlated with CK-MB levels in patients with preinfarction angina (r=0.30, p=0.04; r=0.34, p=0.02; r=0.55, p<0.001; respectively), no such correlation was found for patients without preinfarction angina (p>0.05 for all).

Table 1. Clinical characteristics of study population

	The patients with preinfarction angina (n=44)	The patients without preinfarction angina (n=52)	P
Age,years	55.4±10.9	59.2±8.7	0.06
Sex, n (men/women)	38/6	42/10	NS
Anterior MI,%	48	61	NS
Inferior MI, %	25	17	NS
Inferoposterolateral MI, %	21	22	NS
DM, %	16	15	NS
Hypertension, %	34	48	NS
Smoking, %	64	58	NS
Obesity, %	18	15	NS
Beta blocker, %	75	54	0.06
ACE inhibitor, %	77	69	NS
Thrombolytic therapy, %	61	58	NS
t-PA, %	26	40	NS
Streptokinase, %	74	60	NS
Time from onset of chest pain to thrombolysis, hours	3.3±1.2	3.9±1.7	NS
Peak CK-MB, IU/L	248.5±213	341.3±237.7	0.02

According to unpaired t test, Mann-Whitney test and Chi-square test
ACE - angiotensin converting enzyme, CK - creatinine kinase,
DM - diabetes mellitus, MI- myocardial infarction, NS - nonsignificant, t-PA - tissue-plasminogen activator

Discussion

As far as we know, this is the first study to demonstrate positive changes in Tei index obtained with pulsed wave Doppler echocardiography in patients with preinfarction angina during 30 days of follow-up. In the present study, it was observed that Tei index in patients with preinfarction angina was lower than in patients without angina and showed significant gradual decrease during follow-up only in patients with preinfarction angina. In addition, while the significant improvements were observed in E DT, IVRT and ET in both patients groups, the marked improvements through the follow-up period in EF, WMSI and IVCT we-

Table 2. Serial echocardiographic measurements in patients with and without preinfarction angina

	Day 1 (n=52/44)	Day 6 (n=44/43)	Day 30 (n=40/42)	p	Intragroup differences p[1]	
					p1-6	p1-30
E/A ratio						
Preinfarction angina -	1.0±0.6	0.9±0.6	1.0±0.5	NS	NS	NS
Preinfarction angina +	0.9±0.4	0.9±0.4	1.1±0.6	NS	NS	NS
IVRT, ms						
Preinfarction angina -	72±19	79±19	84±15	0.01	0.04	0.01
Preinfarction angina +	77±20	80±17	87±18	<0.001	0.04	<0.001
E DT, ms						
Preinfarction angina -	140±42	161±42	173±39	0.002	0.001	0.001
Preinfarction angina +	153±43	165±42	182±46	<0.001	0.002	<0.001
ET, ms						
Preinfarction angina -	244±42	256±34	272±33	<0.001	NS	0.001
Preinfarction angina +	263±41*	271±31*	287±30*	0.001	NS	0.001
IVCT, ms						
Preinfarction angina -	66±29	61±31	58±33	NS	NS	NS
Preinfarction angina +	46±31†	40±28†	36±26†	0.03	0.01	0.03
EF, %						
Preinfarction angina -	38±14	41±14	43±15	NS	NS	NS
Preinfarction angina +	49±12‡	51±11‡	53±11†	0.002	0.02	<0.001
Tei index						
Preinfarction angina -	0.59±0.2	0.56±0.2	0.53±0.1	NS	NS	NS
Preinfarction angina +	0.49±0.2†	0.46±0.2†	0.44±0.2*	0.02	0.05	0.04
WMSI						
Preinfarction angina -	1.9±0.5	1.7±0.5	1.7±0.5	NS	NS	NS
Preinfarction angina +	1.6±0.5*	1.5±0.5*	1.5±0.4*	0.009	0.02	0.004

*p<0.05, †p<0.01, ‡p<0.001; denotes comparisons between in the patients with and without preinfarction angina according to unpaired t test and Mann Whitney test
p - intragroup statistical comparisons of changes from the 1st to 30th day in the patients with and without preinfarction angina according to ANOVA repeated measures test and Friedman test
p[1] - intragroup differences between days 1 and 6, days 1 and 30 according to paired t and Wilcoxon tests
E/A- ratio of the early to the late peak diastolic transmitral flow velocity, E DT- deceleration time E
EF- ejection fraction, ET- ejection time, IVCT- isovolumic contraction time, IVRT- isovolumic relaxation time, NS- nonsignificant, WMSI- wall motion score index

Table 3. Cardiac complications during follow-up

	The patients with preinfarction angina (n=44)	The patients without preinfarction angina (n=52)	P
Mortality, %	7	23	0.05
Killip Class ≥2, %	7	35	0.002
Postinfarction angina, %	13	15	NS
Pericarditis, %	-	11	0.03
Atrial fibrillation, %	11	36	0.009
Thrombus, %	9	29	0.03

According to Chi-square test,
NS- nonsignificant

re observed in only patients with preinfarction angina. Thus, we observed more prominent positive changes in echocardiographic functional parameters of global systolic and diastolic function, global and regional contractility in patients with preinfarction angina during follow-up.

Echocardiographic studies evaluated the effects of presence of preinfarction angina on AMI were usually performed using conventional systolic function parameters (4, 18). It is clear that both LV systolic and diastolic functions are affected in AMI. In the present study, the patients with preinfarction angina had better systolic left ventricular function parameters because EF, WMSI, ET and IVCT, which are known as systolic function parameters, whereas no significant differences were observed in E/A, E DT and IVRT, namely, the conventional diastolic function parameters between two groups. Many studies have demonstrated that Tei index reflects both systolic and diastolic cardiac function (9-12). In our study, it was found that Tei index was significantly different between the patients with and without preinfarction angina. But, the increased Tei index in patients without preinfarction angina was due to changes in systolic function parameters, such as prolongation of IVCT and shortening of ET. In another study, we evaluated LV functions in the patients with and without preinfarction angina by using Doppler tissue imaging in addition to conventional pulsed wave Doppler echocardiography. Similarly, we found no significant difference in E/A, E DT, and IVRT obtained by two-dimensional Doppler echocardiography between the patients with and without preinfarction angina (19). In mentioned study, we indicated that Doppler tissue imaging was superior to conventional mitral Doppler indices for the assessment of a favorable LV diastolic function in the presence of preinfarction angina. Therefore, we suggest that further studies are needed to investigate association between diastolic LV function and preinfarction angina on AMI by using conventional and/or new echocardiographic methods.

At present, it was observed that patients with angina within 7 days before infarction had a lower 30-day cardiac event rate. Several studies investigated the effect of previous angina on in-hospital outcome. The results were not consistent. Some studies (20,21) showed a higher incidence of in-hospital death in patients with preinfarction angina, and other studies (22,23) failed to show this result. In TIMI 4 trial (2), it was suggested that a history of angina at any time before AMI reduced the incidence of in-hospital cardiac events and the infarct size determined by CK release.

It was observed that patients with preinfarction angina within 7 days before AMI have a trend towards smaller infarcts, estimated by CK-MB levels. The TIMI 9B study (3) as a prospective analysis was suggested that patients with angina had a lower 30-day cardiac event rate and a trend towards smaller infarcts (estimated by CK-MB levels). Measurement of peak CK-MB is a classic method to estimate infarct size. Sasao et al. (24) observed that Tei index had a significant positive correlation not only with peak CK value but also with 99m Tc-tetrofosmin score. Their findings indicated that the Tei index in the acute phase reflected infarct size after AMI. In the present study, Tei index was positively correlated CK-MB levels in only patients with preinfarction angina. Therefore, we suggest that Tei index may be used as a new parameter to estimate infarct size in patients with preinfarction angina. But, this is not a strong correlation. The reason of this incomplete correlation between Tei index and CK-MB levels in the patients without preinfarction angina is unclear. Further studies are needed to clarify this issue.

After AMI, the presence of preinfarction angina has a limitative effect on necrosis extent and LV remodeling (25). The exact mechanism of this protective effect is not known, but it may include ischemic preconditioning, development of collaterals, and a speeding up of clot lysis by the thrombolytic agent (26-28). Some investigators (28) have shown that the smaller infarct size observed in patients with preinfarction angina was a result of more rapid reperfusion after the thrombolytic treatment. However, there was no significant difference in the frequency of thrombolytic therapy administration and thrombolytic agents between two groups, some patients did not receive thrombolytic therapy, in the present study. In addition, we did not have coronary angiography data to demonstrate vessel patency in patients who underwent thrombolytic therapy. This was an important limitation of our study.

There are further limitations in our study. No examination (except at day 30) and ambulatory electrocardiography were routinely performed after discharge. Therefore, some complications as atrial fibrillation and pericarditis may have not been determined in this period. Beta-blocker medication in patients with preinfarction angina was given more frequent than in the patients without preinfarction angina and this difference was close to statistical significance (p=0.06). Therefore, the higher occurrence of atrial fibrillation in patients without angina may be explained by differences in the use of beta-blocker treatment.

Conclusions

It was suggested that the presence of angina, one week before a first AMI, has beneficial effects on LV functions and may cause earlier and more prominent myocardial functional recovery. Preinfarction angina may confer protection against complications on short-term after myocardial infarction.

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