

Prior Angina Reduces Ischemic Mitral Regurgitation in Patients with ST-Elevation Myocardial Infarction, Role of Ischemic Preconditioning

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Abstract

Background

Mitral regurgitation may develop due to left ventricular (LV) remodeling within 3 months following acute myocardial infarction (AMI) and is called ischemic mitral regurgitation (IMR). Ischemic preconditioning (IPC) has been reported as the most important mechanism of the association between prior angina and the favorable outcome. The aim of this study was to investigate the effect of prior angina on the development and severity of IMR at 3rd month in patients with ST elevation MI (STEMI).

Methods

Fourty five (45) patients admitted with STEMI and at least mild IMR, revascularized by PCI were enrolled. According to presence of prior angina within 72 hours before STEMI, patients were then divided into two groups as angina (+) (n:26; 58%) and angina (-) (n:19; 42%). All patients underwent 2D transthoracic echocardiography at 1st, 3rd days and 3rd month. IMR was evaluated by proximal isovelocity surface area (PISA) method: PISA radius (PISA-r), effective regurgitant orifice area (EROA), regurgitant volume (Rvol). LV ejection fraction (EF %) was calculated by Simpson's method. High sensitive troponin T (hs-TnT), creatine phosphokinase myocardial band (CK-MB) and N-terminal pro-brain natriuretic peptid (NTpro-BNP) levels were compared between two groups.

Results

Although PISA-r, EROA and Rvol were similar in both groups at 1st and 3rd days, all were significantly decreased ($p=0.012$, $p=0.007$, $p=0.011$, respectively) and EF was significantly increased ($p< 0.001$) in angina (+) group at 3rd month. NTpro-BNP and hs-TnT levels at 1st day and 3rd month were similar, however CK-MB level at 3rd month was found to be significantly lower in the angina (+) group ($p=0.034$).

Conclusion

At the end of the 3rd month, it was observed that the severity of IMR evaluated by PISA method was decreased and EF increased significantly in patients who defined angina within 72 hours prior to STEMI, suggesting a relation with IPC.

Introduction

Mitral regurgitation (MR) is the most common valve disease in clinical practice [1]. Following acute myocardial infarction (AMI), ischemic mitral regurgitation (IMR) develops in 20% of patients within 3 months [2]. IMR develops as a result of mitral valve annular dilatation or stretching of mitral leaflet chordae due to remodeling of the left ventricle (LV), without structural defects in the mitral apparatus [1, 3]. Regardless of the degree of IMR, it increases morbidity and mortality and is an indicator of poor prognosis [3, 4].

Prior angina pectoris occurring shortly before the onset of MI has shown to be associated with a favorable outcome after infarction [5]. Previous clinical studies suggest that; prior angina may limit infarct size through various mechanisms, including collateral network, reperfusion facilitation, and ischemic preconditioning (IPC) [6, 7, 8]. IPC has been postulated as the most important potential mechanism of the association between prior angina and the favorable outcomes [8].

Ischemic preconditioning (IPC) is a factor that leads to limitation of the infarct size due to recurrent ischemic attacks in the myocardium in the period preceding MI and is defined as the preparation of the myocardium for ischemia [9]. IPC has been shown to be associated with both an early phase of protection lasting approximately 1–2 hours, as well as a delayed phase seen at least 24 hours following the initial sublethal ischemic insult, and lasting up to 72 hours [10]. In the literature it has been stated that, the optimal interval of IPC stimulus occurs between 24 and 72 hours [11, 12]. During this period, stable angina pectoris attacks are observed in most of the patients and unstable angina pectoris only in some [13, 14]. Clinical studies suggest that single or repeated short-term ischemia-reperfusion periods prior to MI may have beneficial effects, such as limiting infarct size [13, 15], improving LV function [16, 17, 19], reducing in-hospital mortality [6, 18] and ensuring better long-term prognosis [15, 18, 19].

Since IMR occurs as a result of remodeling of the LV following MI, it may be thought that IPC, in other words the presence or absence of prior angina pectoris may have an impact on the development of IMR. The aim of this study was to investigate the effect of prior angina on the development and severity of IMR 3 months later in patients with STEMI who were revascularized by PCI.

Methods

Population and Study Design

This prospective study enrolled 45 patients admitted with STEMI and at least mild IMR, regardless of MI location, and all patients were treated with successful primary percutaneous coronary intervention according to the guidelines [20]. Patients with suboptimal imaging, eccentric and multiple mitral regurgitation jets (≥ 2 large jets), primary mitral valve disease, concomitant valve disease other than mitral valve, atrial fibrillation, chronic renal, hepatic disease, active malignancy, active infection, morbid obesity, anemia, hyperthyroidism, previous AMI, myocarditis and history of congestive heart failure were excluded.

A detailed history of prior angina within 72 hours before STEMI was obtained by the attending physicians. The prior angina pectoris was defined as typical chest pain that occurred within 72 hours before STEMI, lasted less than 30 minutes, and occurred at least once [9, 21, 22]. According to this definition, the study group was then divided into two subgroups as angina (+) and angina (-).

The demographic, clinical characteristics and comorbidities of the patients, blood pressure and heart rate at hospital admission, medical treatment at discharge, localization of STEMI, and presence or absence of collaterals at coronary angiography were recorded.

During the clinical follow-up of patients detailed biochemical examinations were performed, out of which only haemoglobin, creatinine, N-terminal pro-brain natriuretic peptide (NT-proBNP), high sensitive troponin T (hs-TnT) and creatine kinase myocardial band (CK-MB) were repeated in the third month. Haemoglobin and creatinine were repeated as patients with secondary mitral regurgitation may demonstrate significant variations in severity from one occasion to the next, depending on volume status and other hemodynamic variables [23]. Hs-TnT, CK-MB were followed to rule out a new acute coronary syndrome that may have been developed, and NT-proBNP for the possibility of heart failure within three months, all of which can affect the evaluation of mitral regurgitation.

Echocardiography

A standard 2D transthoracic echocardiography was performed within the first 24 hours of STEMI, 3rd day and 3rd month in all patients with iE33 xMatrix-DS Ultrasound System (Philips Medical Systems, Bothell, WA), X5-1 (1–5 MHz) transthoracic transducer, as recommended in the guidelines [24] by a single cardiologist (R.O.). IMR was evaluated by the proximal isovelocity surface area (PISA) method. The proximal isovelocity surface of the mitral regurgitant jet was visualized in an image from the apical four-chamber view using zoom mode. The PISA was optimized by shifting the color Doppler aliasing (Nyquist) velocity from 23 to 48 cm/sec (mean 32.60 ± 6.76 cm/sec). The frame with the largest flow convergence region was obtained as coinciding with maximal regurgitant flow for each cardiac cycle. To define the base of the PISA, the leading edge on the atrial side of the mitral valve was chosen. The radius (r) of each PISA were measured and the highest ' r ' value was obtained by measuring the distance of the current convergence ring formed at low aliasing velocity from the orifice. The peak velocity of the regurgitant jet (V_{max}) and time velocity integral (TVI) was determined with continuous-wave Doppler. EROA was calculated by PISA method as $(2 \times \pi \times r^2 \times V_r / V_{max})$, where " r " is the isovelocity radius, V_r is the aliasing velocity, and V_{max} is the maximal velocity of the regurgitant jet. Then IMR regurgitant volume (Rvol) by PISA was calculated as PISA-derived EROA multiplied by the IMR time velocity integral (TVI) [25, 26] (Fig. 1). All data digitally recorded and analyzed by two researchers in at least 5 cardiac cycles for each echocardiographic imaging.

The LV ejection fraction (EF %) was calculated by the method used for volumes and biplane method of discs summation, so called modified Simpson's rule [24].

All patients gave written informed consent before inclusion, which complies with the Declaration of Helsinki. The study protocol was approved by the Istanbul University Local Ethics Committee (Clinical trial registration number: 2015/2001, approval number: 2072).

Statistical Analysis

Statistical analyses were performed using IBM SPSS software version 19.0 for Windows (SPSS Inc, Chicago, IL). Continuous variables were presented as mean \pm standard deviation (SD), and categorical variables were presented as frequencies and percentages. Kolmogorov–Smirnov test was used to assess the normality of data distribution, and variables distributed nonnormally were logarithmically

transformed. Student's independent t or Mann-Whitney tests were used, as appropriate, to compare continuous variable differences. Statistical significance was defined as p value < 0.05.

Results

This prospective study consisted of 45 patients who presented with STEMI and at least mild IMR, revascularized with successful PCI of the infarct related artery within 1 hour from the onset of chest pain on admission. Patients' age was $52,7 \pm 17,4$ years, with male dominance (91 %). Thirteen (29 %) patients had hypertension, 7 (16 %) had type II diabetes and 23 (51 %) were current smokers. Medical treatment was standard for statins and antiplatelets, 5 (11 %) patients were receiving angiotensin converting enzyme inhibitors, 18 (40 %) angiotensin receptor blockers, 16 (36 %) beta blockers and 6 (13 %) diuretics. The localization of myocardial involvement during infarction were; 23 (51,1 %) anterior, 17 (37,8 %) inferior, 3 (6,7 %) infero-posterior, 2 (4,4 %) infero-lateral walls, 15 (33,3 %) patients had Rentrop grade ≥ 2 collaterals. Infarct related artery was left anterior descending artery in 23 (51,1 %) patients, right coronary artery in 20 (44,4 %), and circumflex artery in 2 (4,4 %).

26 of 45 patients (58 %) who described stable angina pectoris were included in the angina (+), and 19 patients (42 %) declared that they did not have angina were included in the angina (-) group.

There were no statistical differences between the two groups in terms of age, gender, BMI, comorbidities, hemodynamic parameters at hospital admission and localization of MI.

Evolution of ischemic mitral regurgitation within 3 months in angina (+) and (-) patients

None of the patients met the criteria for severe MR (EROA 0.2 cm^2 , Rvol 30 ml) [23] throughout the follow-up period. Echocardiographic measurements and calculations of PISA-r, EROA and Rvol were of similar values, with statistically insignificant differences between the angina (+) and angina (-) groups at the 1st day (PISA-r : $0,19 \pm 0,14$ cm versus $0,13 \pm 0,14$ cm, p = 0.178; EROA : $0,08 \pm 0,07 \text{ cm}^2$ versus $0,06 \pm 0,07 \text{ cm}^2$, p = 0.247; Rvol : $8,50 \pm 9,54$ ml, versus $6,37 \pm 8,87$ ml, p = 0.284 respectively) and 3rd day (PISA-r : $0,19 \pm 0,15$ cm versus $0,17 \pm 0,15$ cm, p = 0.666, EROA : $0,08 \pm 0,09 \text{ cm}^2$ versus $0,08 \pm 0,08 \text{ cm}^2$, p = 0.816, Rvol : $8,27 \pm 10,76$ ml versus $9,11 \pm 11,20$ ml, p = 0.852 respectively) of STEMI. At the end of the 3rd month compared to 1st day PISA-r ($0,19 \pm 0,14$ cm versus $0,07 \pm 0,08$ cm; p < 0,001), EROA ($0,08 \pm 0,07 \text{ cm}^2$ versus $0,02 \pm 0,03 \text{ cm}^2$; p < 0,001) and Rvol ($8,50 \pm 9,54$ ml vs. $2,35 \pm 4,11$ ml; p < 0,001) were significantly decreased in the angina (+) group. Whereas in the angina (-) group; PISA-r and EROA were slightly and insignificantly increased at 3rd month compared to 1st day, only Rvol was increased significantly ($6,37 \pm 8,87$ ml versus $11,95 \pm 11,85$ ml, p=0.03). When angina (+) and (-) patients were compared at 3rd month, PISA-r ($0,07 \pm 0,08$ cm versus $0,23 \pm 0,23$ cm, p = 0.012), EROA ($0,02 \pm 0,03 \text{ cm}^2$ versus $0,10 \pm 0,09 \text{ cm}^2$, p = 0.007) and Rvol ($2,35 \pm 4,11$ ml versus $11,95 \pm 11,85$ ml, p = 0.011), were significantly higher in angina (-) patients. The evolution of PISA-r, EROA and Rvol from the first day through the 3rd month had a tendency to decrease in angina (+) patients (decrease PISA-r : $0,12 \pm 0,11$ cm, EROA : $0,06 \pm 0,06 \text{ cm}^2$, Rvol : $6,15 \pm 7,35$ ml) and increase in angina (-) patients (increase PISA-r :

0.09 ± 0.021 cm, EROA : 0.04 ± 0.08 cm 2 , Rvol : 5.58 ± 10.48 ml), and p < 0.001 for each. (Figure 2, Table 2, 3)

Change in left ventricular ejection fraction (EF %) within 3 months

Ejection fraction at 1st ($55,3 \pm 8,3$ % versus $48,9 \pm 9,1$ %, p=0.024) and 3rd day ($56,1 \pm 9,4$ % vs. $49,5 \pm 9,5$ %, p=0.009) of the study were significantly higher in angina (-) group of patients. Throughout the 3rd month, EF of angina (-) group was preserved with a slight decrease ($-1,8 \pm 6,3$ %), whereas a significant increase ($+7,4 \pm 5,5$ %, p < 0,001) in angina (+) group was detected. Despite all these changes in EF, at the end of the 3rd month, angina (+) and angina (-) groups had similar ($56,2 \pm 7,0$ % versus $53,5 \pm 8,6$ %, p = 0,461) values of EF %. (Figure 2, Table 2, 3)

Biochemical markers within 3 months

In both angina (+) and angina (-) groups, 1st day and 3rd month of haemoglobin and creatinine were within normal range and statistically insignificant (haemoglobin 1st day : p = 0,8; 3rd month : p = 0,4; creatinine 1st day p = 0,08; 3rd month p = 0,7). Hs-TnT was insignificantly increased on 1st day as expected in both groups (p = 0,9), and within normal range at 3rd month (p = 0,8). CK-MB levels at 1st day was not statistically significant between the groups (p = 0,918), however CK-MB levels at 3rd month were found to be significantly lower in the angina (+) group compared to the angina (-) although within normal range (p=0,034). NT-proBNP values were found to be increased in both groups with statistically insignificant (p = 0,352) levels at 1st day, decreased at 3rd month nevertheless still slightly high and statistically insignificant (p = 0,662) (Table 4).

Discussion

The result of the current study demonstrated that; in patients presenting with STEMI and undergoing revascularization with standard percutaneous coronary interventions with at least mild ischemic mitral regurgitation, IMR assessed by PISA method was significantly decreased and EF significantly increased within three months of follow-up in patients with angina pectoris 72 hours before MI compared to those without angina.

Appropriate systolic coaptation of the mitral leaflets depends on normal anatomy and function of the different components of the mitral valve apparatus: annulus, leaflets, chordae, papillary muscles and the LV wall [1]. Primary MR is an organic valve disease and secondary MR represents the valvular consequences of a LV disease, with progressive LV global or regional pathological remodeling due to LV remodeling by idiopathic cardiomyopathy or coronary artery disease, the latter is called IMR [1].

The original description of myocardial preconditioning, a phenomenon whereby brief episodes of ischemia and reperfusion protect the myocardium from prolonged ischemic damage, is reported by Murray et al. [9]. There is a general consensus that recent prior angina is the best clinical marker of

possible preconditioning stimulus [8]. The majority of the studies in the literature related to angina-initiated IPC have focused on beneficial effects such as; improvement of LV functions [16, 17], limitation of MI size [13, 15, 19], reducing in-hospital mortality [6, 18] and better prognosis [15, 18, 19]. However, it has been reported that several conditions including aging [27], diabetes mellitus [28], or prior MI [29] may abolish the beneficial effects of prior angina.

The results of these clinical studies on positive effects of IPC were also supported by controlled experimental studies in laboratory animals. A single episode of preconditioning ischemia/reperfusion reduced infarct size in the anesthetized swine *in situ*, the incidence of ventricular tachycardia was significantly decreased and the infarct size was smaller in preconditioned rats, and decreased by up to 70 % in preconditioned *in situ* rabbit hearts [30, 31, 32].

Based on the data provided by these studies, we decided to investigate this issue prospectively in a limited number of patients, with the hypothesis that IMR developing after myocardial infarction may also be affected with prior angina.

In a previous study, Solomon et al. have provided a better understanding of the relationship between presence of prior angina and IPC and LV remodeling, and possible interactions between these mechanisms [14, 17]. Solomon et al. have examined the effects of prodromal angina within 3 months prior to MI on LV functions in 283 patients, in the subgroup of the "Healing and Early Afterload Reducing Therapy (HEART)" study [14]. In the study, 2D TTE was performed at 1st day and 3rd month after acute anterior MI and LV dilatation from 1st day to 3rd month was used as a measure of LV remodeling, LV end-diastolic and end-systolic diameters were found to be significantly decreased in patients with prior angina compared to patients without, however, the change in EF through the 3rd month did not differ between the groups. Other important results of the study were; in patients with prior angina, peak CK levels and infarct segment length were found to be significantly lower and LV dilatation was significantly more limited at 3rd month [14]. It was observed that LV dilatation was significantly more limited in patients with unstable angina prior to acute MI compared to patients with stable angina and patients without angina, and also a well developed collateral network in 21 % of the prior angina and 11 % in the non-angina group [14]. Their comments on these results were; prior angina up to 3 months before acute MI had cardio-protective effects, LV remodeling and more limited LV dilatation detected in patients with prior angina might be related to the presence of collateral network, as well as IPC which is supported by two more studies performed by Kloner et al and Yellon et al [14, 21, 33].

The Intravenous Alteplase for Treatment of Infarcting Myocardial Entry (InTIME-II) Prodromal Symptoms Substudy (InTIME-II PSS) performed by Christenson et al. has examined prodromal unstable angina in 425 patients [15]. The aim of the InTIME-II PSS study was to prospectively test if prodromal unstable angina before major onset of chest pain independently predicts smaller infarct size and better survival in patients with AMI. The presenting symptoms of the patients in this study were classified as either abrupt onset with no previous symptoms, or prodromal unstable angina. Patient follow-up occurred at 30 days, 6 months and 5 years to determine mortality - survival status. To assess infarct size, pre and post treatment

total creatine kinase (CK total) and CK-MB measurements were used. Patients presenting with prodromal unstable angina showed a strong association with smaller CK-MB and CK total measures of infarct size, and lower 30 day, 6 month and 5 years mortality. As a result they reported that, prodromal unstable angina was a significant predictor of smaller infarct size and an important physiological marker that should be routinely collected in clinical trials for risk stratification [15]. In the present study, Hs-TnT, CK-MB and NT-proBNP levels at 1st day were similar and insignificant in both groups, pro-BNP and CK-MB levels at 3rd month were lower in the angina (+) group compared to the angina (-) group, and at 3rd month, the remarkable change was the decrease in CK-MB significantly ($p=0.34$) in angina (+) group, though the values were within normal range. These results can be interpreted as; in both groups Hs-TnT values were similar during acute coronary syndrome, but NT-proBNP decreased further in the angina (+) group, maybe due to the decrease in IMR, and the lower CK-MB at 3rd month can be attributed to the rather smaller infarct area in the angina (+) group.

We would like to explain some of the limitations of the study. In our study, prior angina within 72 hours, induced by exertion or at rest were determined only by detailed questioning of the patients, for they were all on the first day of an AMI. In fact, there is not a consensus on the questioning, grading and time interval of angina, each study has used a different definition and time interval, previous studies have demonstrated that angina up to 1 - 3 days or 3 months prior to AMI had cardio-protective effects [14, 21, 33]. Since the aim of this study was to determine the evolution of IMR as a result of IPC, the focused measurements were mainly PISA-r, EROA and Rvol. LV systolic and diastolic volumes measured during the follow-up of IMR were not specified in the tables and text, instead we based on EF which is calculated with these volumes by Simpson's method. Although the concomitant diseases, localizations of MI, serum enzymes, medications, coronary collateral network were recorded, the study group was too small to provide detailed statistics for subgroup analysis.

Conclusion

We conclude that, in patients with prior angina 72 hours before the onset of an AMI and at least mild IMR treated with conventional PCI, IMR decreases and EF increases significantly suggesting a relation to **IPC** within 3 months. In our opinion, enlarging patient group and keeping the follow-up period longer will allow the data to be interpreted more accurately, subgroup analysis feasible, and a benefit for monitoring morbidity, mortality and prognosis.

Declarations

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Declarations

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Conflicts of interest: The Author(s) declare(s) that there is no conflict of interest.

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Tables

Table 1: Demographic and clinical characteristics of angina (+) and angina (-) patients

	Angina (+) (n=26)	Angina (-) (n=19)	P value
Age, years	51,68 ± 14,32	53,68 ± 27,32	0,91
Male, n (%)	24 (92)	17 (89)	0,73
BMI, (kg/m2)	27,6 ± 7,4	27,2 ± 10,9	0,49
SBP, (mmHg) – at hospital admission	123,8 ± 9,9	124,5 ± 11,6	0,35
DBP, (mmHg) – at hospital admission	70,6 ± 10,2	69,4 ± 10,8	0,78
Heart rate, bpm – at hospital admission	68,9±8,6	71,3±7,2	0,16
Hypertension, n (%)	7 (27)	6 (32)	0,38
Diabetes mellitus, n(%)	5 (19)	2 (11)	0,12
Current smoker, n (%)	13 (50)	10 (53)	0,32
Medical treatment – at discharge			
ACEI, n (%)	3 (12)	2 (12)	0,82
ARB, n (%)	11 (42)	7 (39)	0,66
Beta blockers, n (%)	9 (35)	7 (37)	0,49
Statin, n (%)	26 (100)	19 (100)	1
Spironolactone, n (%)	4 (15)	2 (11)	0,36

Localization of MI			
<i>Anterior, n (%)</i>	15 (58)	8 (42)	0,31
<i>Inferior, n (%)</i>	8 (31)	9 (47)	0,13
<i>Inferoposterior, n (%)</i>	2 (8)	1 (5)	0,47
<i>Inferolateral, n (%)</i>	1 (4)	1 (5)	0,33
Presence of			
collaterals, n(%)	9 (35)	6 (32)	0,24
(Rentrop grade ≥2)			

Abbreviations: BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, ACEI: angiotensin converting enzyme inhibitor, ARB: angiotensin reseptor blocker, MI: myocardial infarction

Table 2: Echocardiographic data of mitral regurgitation and EF at 1st day, 3rd day, and 3rd month in angina (+) and angina (-) patients

	Parameters	Angina (+) (n=26)	Angina (-) (n=19)	p value
1 st day	PISA-r (cm)	0,19±0,14 (0,01-0,40)	0,13±0,14 (0,01-0,40)	0,178
	EROA (cm ²)	0,08±0,07 (0,01-0,24)	0,06±0,07 (0,01-0,21)	0,247
	Rvol (ml)	8,50±9,54 (0,02-38)	6,37±8,87 (0,02-35)	0,284
	EF (%)	48,9±9,1 (29-65)	55,2±8,2 (38-67)	0,024
3 rd day	PISA-r (cm)	0,19±0,15 (0,01-0,50)	0,17±0,15 (0,01-0,40)	0,664
	EROA (cm ²)	0,08±0,09 (0,01-0,35)	0,08±0,08 (0,01-0,26)	0,816
	Rvol (ml)	8,27±10,76 (0,02-43)	9,11±11,20 (0,02-35)	0,852
	EF (%)	49,5±9,5 (30-65)	56,1±9,4 (31-67)	0,009
3 rd month	PISA-r (cm)	0,07±0,08 (0,01-0,30)	0,23±0,23 (0,01-0,80)	0,012
	EROA (cm ²)	0,02±0,03 (0,01-0,12)	0,10±0,09 (0,01-0,25)	0,007
	Rvol (ml)	2,35±4,11 (0,02-15)	11,95±11,85 (0,02-36)	0,011
	EF (%)	56,2±7,0 (42-70)	53,5±8,6 (30-64)	0,461

Abbreviations: PISA-r: radius, EROA: effective regurgitant orifice area, Rvol: regurgitant volume, EF: ejection fraction.

Table 3: Changes in PISA-r, EROA, Rvol and EF between 1st day and 3rd month in angina (+) and angina (-) patients

Parameters	Angina (+) (n=26)	Angina (-) (n=19)	p value
PISA-r (cm) day 1 to 90	-0,12 ± 0,11	+0,09 ± 0,021	<0,001
EROA (cm ²) day 1 to 90	-0,06 ± 0,06	+0,04 ± 0,08	<0,001
Rvol (ml) day 1 to 90	-6,15 ± 7,35	+5,58 ± 10,48	<0,001
LV EF (%) day 1 to 90	+7,4 ± 5,5	-1,8 ± 6,3	<0,001

Abbreviations: PISA-r: radius, EROA: effective regurgitant orifice area, Rvol: regurgitant volume, EF: ejection fraction.

Figures

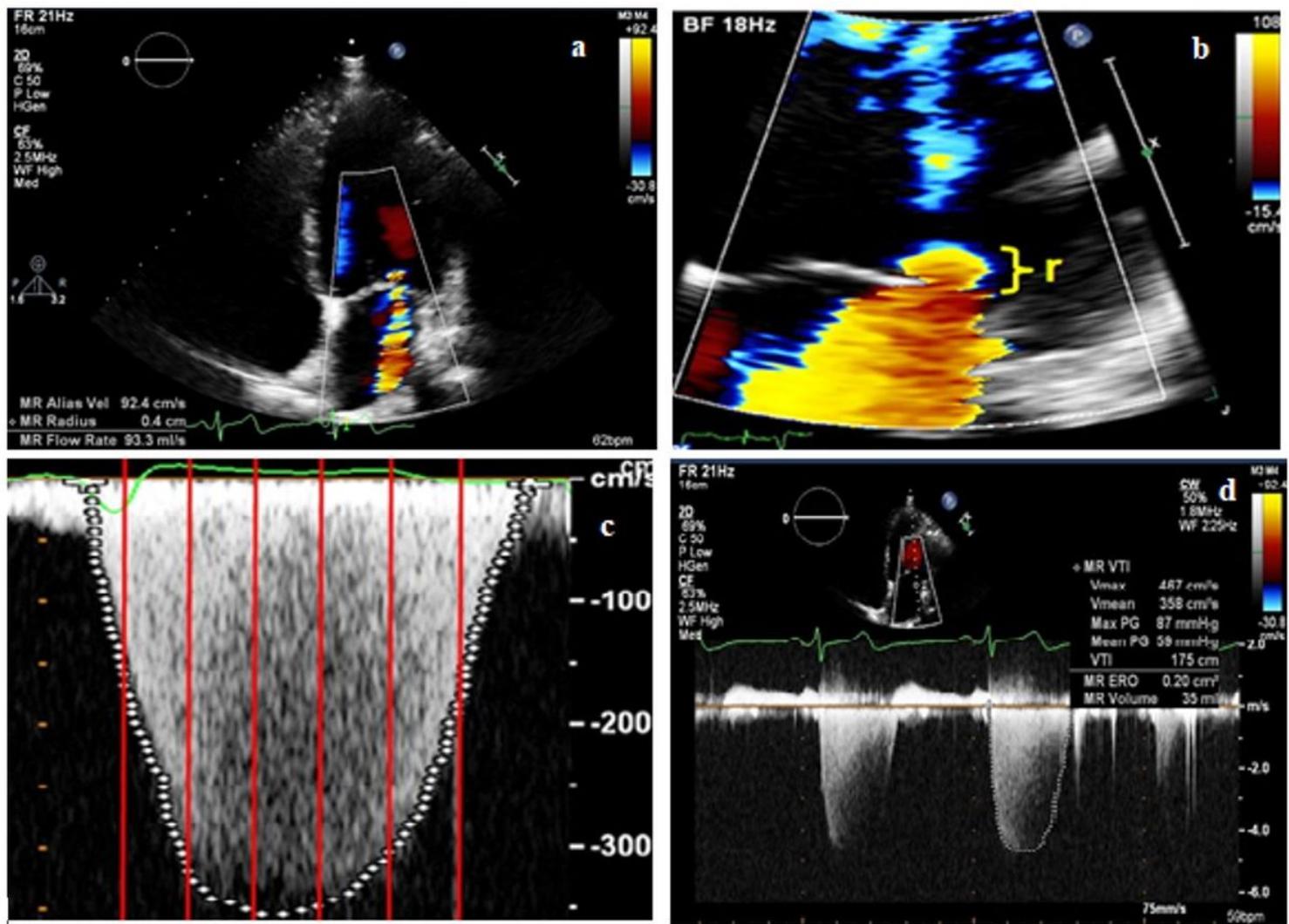


Figure 1

Evaluation of mitral regurgitation (MR) by the proximal isovelocity surface area (PISA) method. a) The proximal isovelocity surface of the MR jet was visualized in an image from the apical four-chamber view by shifting the color Doppler aliasing (Nyquist) velocity (V_r) from 23 to 48 cm/sec (mean 32.60 ± 6.76 cm/sec). b) The radius (r) of each PISA were measured using zoom mode and the highest ' r ' value was obtained by measuring the distance of the current convergence ring formed at low aliasing velocity from the orifice. c) The peak velocity of the regurgitant jet (V_{max}) and time velocity integral (TVI) was determined with CW-Doppler. d) EROA was calculated by PISA method as $(2 \times \pi \times r^2 \times V_r / V_{max})$ Then regurgitant volume (Rvol) of MR by PISA was calculated as PISA-derived EROA multiplied by the TVI.

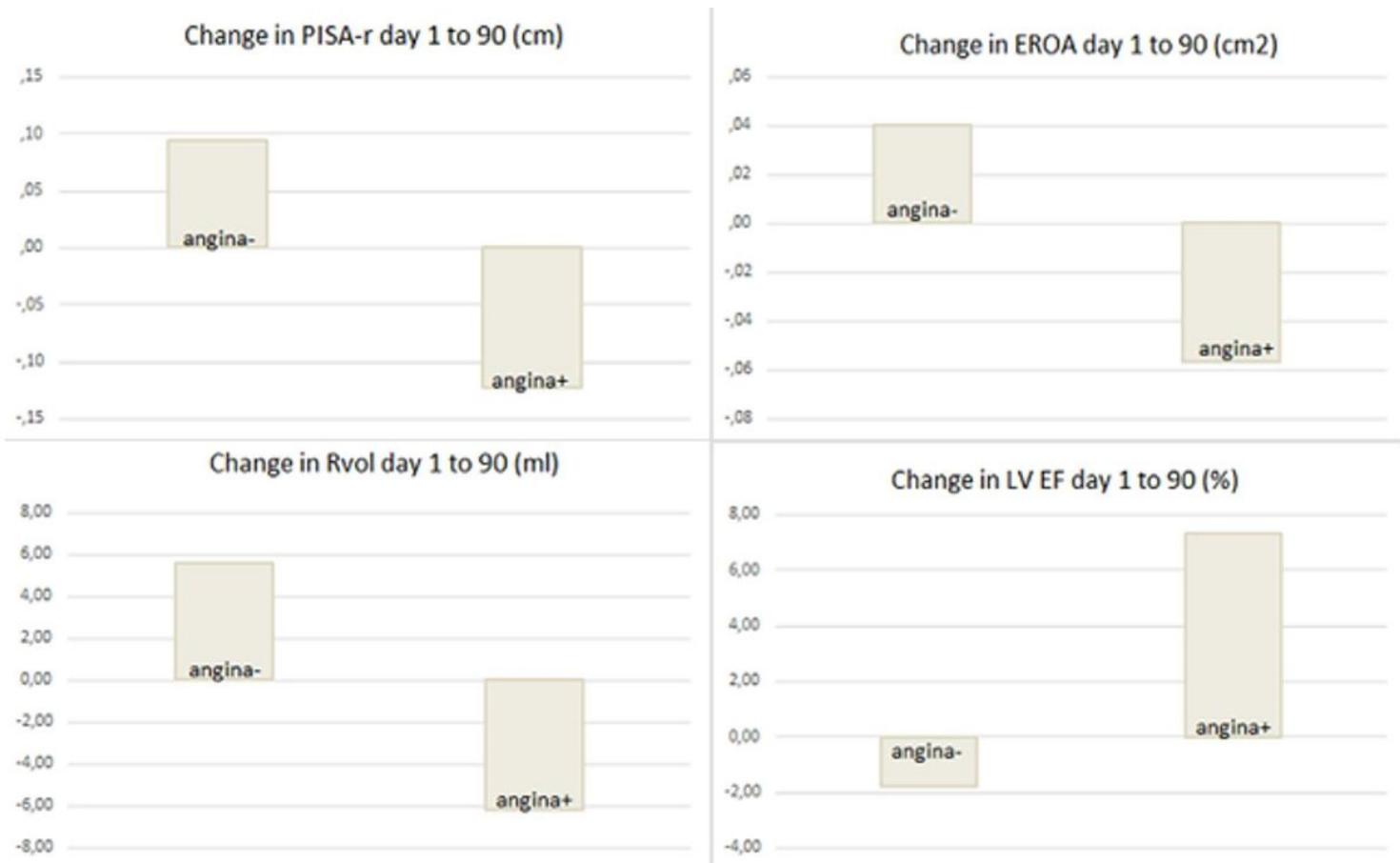


Figure 2

Changes in PISA-r, EROA, Rvol and LV EF between 1st day and 3rd month in angina (+) and angina (-) patients.