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Evaluation on the impact of spontaneous reperfusion on cardiac muscle of acute myocardial infarction by three-dimensional speckle tracking imaging

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Abstract. – **OBJECTIVE:** To explore the effect of spontaneous reperfusion (SR) on three-dimensional myocardial strain in patients with acute anterior myocardial infarction by three-dimensional speckle tracking imaging (3D-STI) technology.

PATIENTS AND METHODS: Patients diagnosed with acute anterior myocardial infarction during 2013 to 2016 were consecutively selected and divided into SR group and non-spontaneous reperfusion (Non-SR) group based on whether there was SR. Patients in both groups received direct percutaneous coronary intervention (PCI) in time window. Baseline information, patency rates of culprit vessel, durations of operation, intraoperative non-reflow phenomenon ratios, and thrombolysis in myocardial infarction (TIMI) blood flows after reperfusion of patients in each group were recorded. Hospital stays of patients were compared between the two groups. Before discharge, left ventricular ejection fraction (LVEF) and left ventricular end-diastolic diameter (LVEDd) were measured. Global longitudinal strain (GLS), global radial strain (GRS), and global circumferential strain (GCS) of left ventricular (LV) were also detected by 3D-STI, so as to assess movement situations of ventricular wall and cardiac muscle in occlusive blood vessel distribution area. LVEF, LVEDd and various 3D-STI parameters were reexamined and compared one year after discharge.

RESULTS: There were no significant differences between the Non-SR group and the SR group regarding the patency rate of culprit vessel, duration of operation, intraoperative non-reflow phenomenon ratio, TIMI blood flow after reperfusion, and LVEDd (p>0.05). Both LVEF before discharge and LV three-dimensional strain indexes of the SR group, were clearly higher than those of the Non-SR group (p<0.05). After one-year follow-up, the SR group had a remarkably lower LVEDd than the Non-SR group (p<0.05). LVEF of the SR group was overtly higher than that of the Non-SR group (p<0.05). LV three-dimensional strain indexes were also distinctly higher in the SR group than in the Non-SR group (p<0.05). There were good correlations between GLS, GRS, GCS and LVEF (r values were -0.620, -0.674 and 0.723, respectively).

CONCLUSIONS: SR can improve nosocomial and long-term LV remodeling in patients with acute anterior myocardial infarction, and 3D-STI is able to assess ventricular remodeling after myocardial infarction.

Key Words
Myocardial infarction, Spontaneous reperfusion, Ventricular remodeling, 3D-STI.

Introduction

After acute myocardial infarction treatment enters into the direct percutaneous coronary intervention (PCI) era, obtaining myocardial reperfusion as soon as possible is still an important goal. Myocardial reperfusion methods are divided into spontaneous reperfusion (SR) and non-spontaneous reperfusion (Non-SR) (i.e., reperfused via direct PCI) according to different clinical realities. Among them, SR can make myocardium earlier to be reperfused because SR of occlusive blood vessels is achieved prior to PCI, getting a slim chance of survival[1]. Compared with that of patients needing PCI for reperfusion, there is still no final conclusion on whether SR can improve

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the ventricular remodeling[2,3]. In this study, clinical data of patients, who were diagnosed with acute anterior ST-segment elevation myocardial infarction in Nanjing Hospital and Sir Run Run Hospital of Nanjing Medical University from 2013 to 2016, were retrospectively analyzed. Three-dimensional speckle tracking imaging (3D-STI) technique was used as the evaluation mean to investigate the influence of SR on left ventricular (LV) myocardial remodeling.

Patients and Methods

Participants and grouping

Patients admitted to hospitals from January 2013 to April 2016 due to acute anterior ST-segment elevation myocardial infarction were continuously selected. The diagnostic criteria complied with the definition of myocardial infarction in 2012 European Society of Cardiology (ESC) Guidelines for diagnosis and treatment of acute myocardial infarction[4]. This study was approved by the Ethics Committee of Sir Run Run Hospital and Nanjing Hospital. Signed written informed consents were obtained from all participants before the study. SR diagnosis was in line with Fefer et al[5]: emergency radiographies showed that infarction-related arteries were in open state[5], and reached grade 2 to 3 of thrombolysis in myocardial infarction (TIMI) clinical trial blood flow[6]. This phenomenon was called SR of infarction-related arteries. A total of 128 patients with acute anterior ST-segment elevation myocardial infarction was included and divided into SR group and Non-SR group based on whether there was spontaneous recanalization.

Study methods

Demographic information and clinical baseline data of patients in each group since admission were recorded. Specific variables included age, gender constituent ratio, duration of chest pain, presence of chest pain, Killip classification, history of sublingual nitroglycerin taking, history of smoking, history of aspirin taking and history of hyperlipidemia.

Observation indicators

The following observation indicators were recorded for analysis: patency rate of culprit vessel, duration of operation (the study group defined the duration of operation as the period from the entering of heparin to the end of the last imaging), intraoperative non-reflow phenomenon ratio, TIMI blood flow after reperfusion of the two groups during the hospitalization, recorded hospital stay, as well as left ventricular ejection fraction (LVEF) and left ventricular end diastolic diameter (LVEDd) before discharge. Color Doppler ultrasound diagnostic apparatus (Toshiba Artida SSH-880CV, Tokyo, Japan) was applied, equipped with three-dimensional online analysis software. Subjects took left lateral position, with eupnea, to simultaneously record electrocardiograms. Probe was selected and used to conduct two-dimensional echocardiogram examination and file LVEF and LVEDd. The probe was switched for three-dimensional data acquisition: electrocardiogram gain was adjusted to display distinct electrocardiogram, apical four-chamber view was taken, left ventricular (LV) contour was displayed clearly, and "Pre-4D" button was pressed to synchronously display apical four-chamber view and apical two-chamber view with double-image. After the endocardium was displayed vividly, "Full-4D" button was pressed to start the three-dimensional data acquisition program that acquired three-dimensional image data through electrocardiogram trigger, with an acquisition speed of about 20 frames per second. The following three-dimensional parameters were analyzed: LV global longitudinal strain (GLS), global radial strain (GRS) and global circumferential strain (GCS) (Figure 1-2). For outpatient return visit one year after discharge, Color Doppler Ultrasound diagnostic apparatus (Toshiba Artida SSH-880CV, Tokyo, Japan) was utilized to detect LVEFs and LVEDds of patients in the two groups. The methods described above were applied to re-measure all 3D-STI parameters. Analyses regarding correlations of LVEF with GLS, GRS and GCS data were also performed, respectively.

Statistical Analysis

All data were statistically analyzed via Stata SE12.0 statistical software. Categorical variables were expressed as frequency plus composition ratio. The x^2-test and Fisher exact test were used to compare categorical variables between the two groups. Continuous variables were presented as mean ± standard deviation. The proportion was shown as %. Paired-samples t-test was employed for continuous variables between the two groups. $p<0.05$ suggested that the difference was statistically significant.

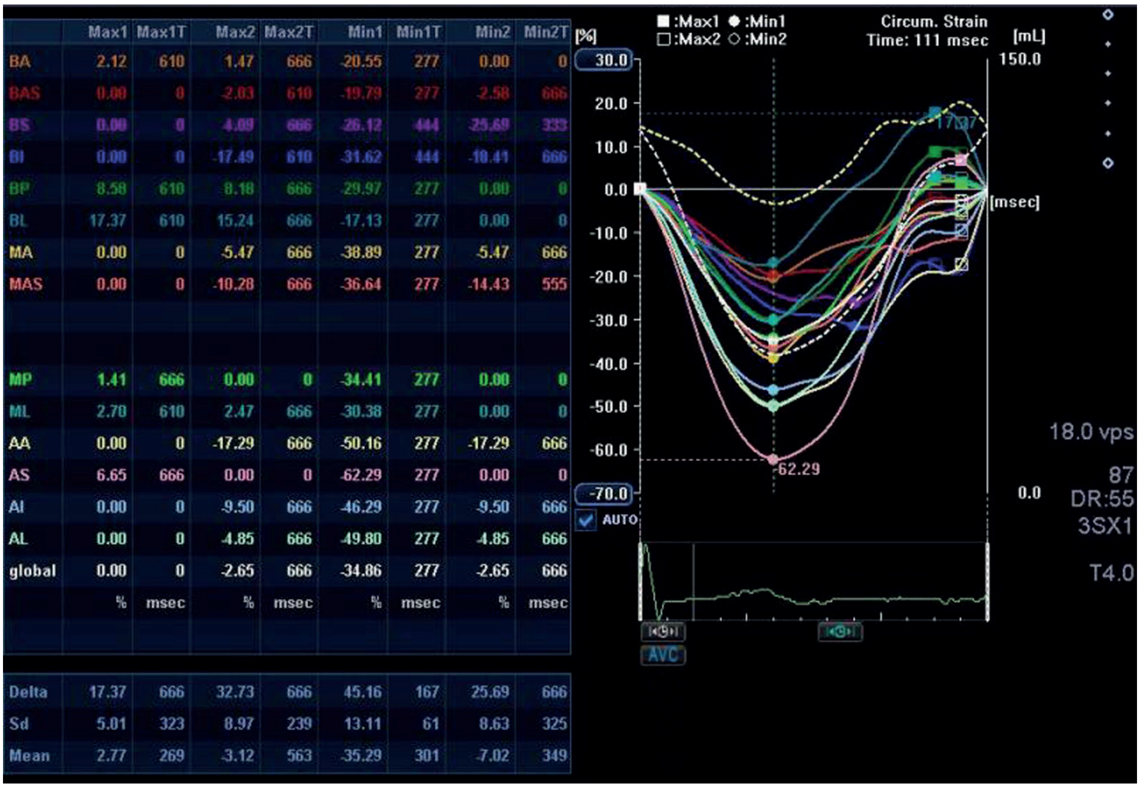

Figure 1. LV GCS of the SR group.

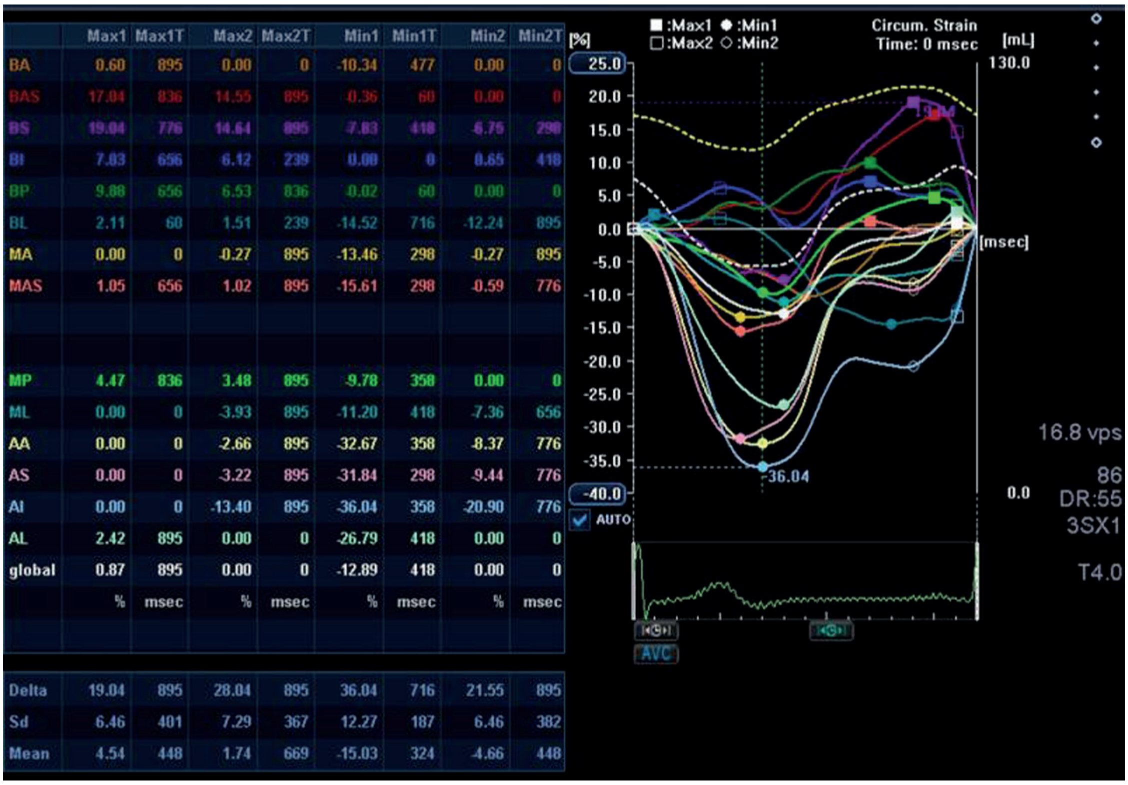

Figure 2. LV GCS of the Non-SR group.

Table I. Comparisons of baseline data between the SR and Non-SR groups.

	SR (n=27)	Non-SR (n=101)	*p*-value
Male ratio (n, %)	22 (81.5%)	83(82.9%)	>0.05
Duration of chest pain (h)	6.9±0.9	7.2±1.8	>0.05
Presence of chest pain (n, %)	27 (100%)	98 (92.7%)	>0.05
History of sublingual nitroglycerin taking (n, %)	5 (18.5%)	17 (17.1%)	>0.05
History of smoking (n, %)	9 (33.3%)	44 (43.9%)	>0.05
History of aspirin taking (n, %)	4 (14.8%)	17 (17.1%)	>0.05
History of diabetes mellitus (n, %)	6 (22.2%)	22 (21.9%)	>0.05
History of hypertension (n, %)	13 (48.2%)	54 (53.7%)	>0.05
History of hyperlipidemia (n, %)	6 (22.2%)	25 (24.7%)	>0.05

Results

Clinical baseline data of patients in the two groups

There were no significant differences in baseline data between the two groups ($p>0.05$) (Table I).

Comparisons of nosocomial information between the SR group and the Non-SR group

Comparisons of data, such as the patency rate of culprit vessel, duration of operation, intraoperative non-reflow phenomenon ratio, TIMI blood flow after reperfusion of the two groups during the hospitalization, recorded hospital stay, LVEF and LVEDd before discharge, were performed; all 3D-STI parameters were measured via 3D-STI (Figures 1-2). The results showed that there was no significant difference between the two groups in LVEDd before discharge. LVEF of the SR group was remarkably higher than that of the Non-SR group ($p<0.05$), while LVEDd of the SR group was significantly lower than that of the Non-SR group ($p<0.05$). GLS, GRS and GCS were higher in the SR group than those in the Non-SR group. Other indexes between the two groups showed no significant differences ($p>0.05$) (Table II).

Comparisons of three-dimensional strain rates and echocardiography indicators in the reexamination after one year

Patients in the two groups received reexaminations one year after discharge, of which one patient in the SR group refused the reexamination, and 5 patients in the Non-SR group got lost during the follow-up period. Comparisons of LVEF and LVEDd discovered that the SR group had significantly higher LVEF ($p<0.05$) and clearly lower LVEDd ($p<0.05$) compared with the Non-SR group. GLS, GRS and GCS were overtly higher in the SR group than those in the Non-SR group. LVEF had good correlations with GLS, GRS, and GCS, and *p*-values were -0.620, -0.674 and 0.723, respectively (Table III).

Discussion

After the occurrence of acute myocardial infarction, sudden ischemia leads to loss of myocardial perfusion. The process of myocardial remodeling starts at this moment, and the remodeling has continuous extension due to the stimulation from cytokine and neurohumour, which will affect the

Table II. Comparisons of nosocomial information between the SR group and the Non-SR group.

	SR (n=27)	Non-SR (n=101)	*p*-value
Patency rate of culprit vessel (n, %)	27 (100%)	101 (100%)	>0.05
Duration of operation (min)	59.2±0.8	63.4±0.9	>0.05
Intraoperative non-reflow phenomenon ratio (n, %)	7 (25.9%)	28 (27.7%)	>0.05
TIMI blood flow after reperfusion (n)	2.5±0.72	2.6±0.86	>0.05
Hospital stay (d)	6.4±0.9	6.9±0.6	>0.05
LVEF before discharge (%)	52.1±2.3	42.6±1.6	<0.05
LVEDd (mm)	44.2±2.7	46.4±5.1	>0.05
GLS (%)	-19.42±4.3	-12.44±3.2	<0.05
GCS (%)	-23.54±3.9	-15.26±3.6	<0.05
GRS (%)	30.82±3.8	22.23±4.2	<0.05

Table III. Comparisons of patients' three-dimensional strain rates and echocardiography indicators between the two groups in the reexamination after one year ($\overline{\chi}$±s, %).

Group	GLS (%)	GCS (%)	GRS (%)	EF (%)	LVEDd (mm)
SR (n=26)	-24.6±4.5*	-26.54±5.2*	34.81±7.1*	54.4±2.5**	43.2±4.1**
Non-SR (n=96)	-13.14±3.8	-16.06±3.9	21.93±6.3	46.4±1.2	54.1±5.2

Note: * Compared with that in the Non-SR group, $p<0.05$; ** Compared with that in the Non-SR group, $p<0.05$

movement of the ventricular wall and result in changes in ventricular cavity diameter and other anatomic forms[7-9]. How to relieve the remodeling after myocardial infarction has been a clinically tough problem. SR achieves autologous revascularization in the most severe ischemic period. Although there is still residual stenosis, the residual blood stream plays critical parts in improving myocardial ischemia and restoring myocardial metabolism. Factors related to SR are unclear, and it has been recently suggested that O-type blood may be more likely to have SR[10]. However, there is still no definite conclusion about whether SR is helpful for the myocardial remodeling after infarction[11-13]. This study divided patients with acute myocardial infarction received PCI in the time window into two groups according to whether there was SR. We aimed to compare whether patients with myocardial infarction gained benefits from SR in addition to timely PCI perfused culprit vessels and to further observe the effect of SR on myocardial remodeling and clinical prognosis. The comparison showed that SR had a positive effect on myocardial remodeling. LVEFs and LVEDd before discharge and after one year were significantly improved. Meanwhile, GLS, GRS and GCS reflecting myocardial strain capacity, were overtly higher in the SR group than those in the Non-SR group, and there were good correlations between GLS, GRS, GCS and LVEF. It was suggested that 3D-STI could effectively evaluate movements of the ventricular wall and myocardium in patients with myocardial infarction. Compared with conventional two-dimensional ultrasound, 3D-STI technique is effective for evaluating LV regional systolic function after acute myocardial infarction[14,15]. The technique tracks the motion and relative motion of ultrasound speckles in the cardiac muscle tissue frame by frame, to accurately evaluate the motion state of the myocardium. After acute myocardial infarction, infarction location has weakened myocardial segmental motion, and the myocardium in this location will have deformation, with low, disappeared or reverse speed[16,17]. Conventional two-dimensional color ultrasound short-axis contractive movement receives limited information in the stage of image collection and analysis. An advantage of the three-dimensional strain is that it tracks two-dimensional objects along the direction of the motion of the chamber wall, rather than along the ultrasonic beam. Another advantage is that three-dimensional strain technique can collect more comprehensive information. Therefore, three-dimensional strain echocardiography can more accurately reflect myocardial contraction and diastolic functions.

Conclusions

3D-STI could effectively evaluate the effect of SR on myocardium of acute myocardial infarction. The technology is simple and noninvasive, and has limited requirements to patients, with short sampling and treatment time, and thus it may be an auxiliary diagnostic tool effectively evaluating the effects of drugs and operations for patients with myocardial infarction, having a broad prospect of application.

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Conflict of Interest

The authors declared no conflict of interest.

References

1) Brener SJ, Mehran R, Brodie BR, Guagliumi G, Witzenbichler B, Cristea E, Xu K, Lansky AJ, Stone GW. Predictors and implications of coronary infarct artery patency at initial angiography in patients with acute myocardial infarction (from the CADILLAC and HORIZONS-AMI Trials). Am J Cardiol 2011; 108: 918-923.

2) Veselova TN, Merkulova IN, Iarovaia EB, Ternovoi SK, Ruda M. The role of multispiral computed tomography in assessment of viability of the myocardium and prognostication of left ventricular remodeling in patients with ST-elevation myocardial infarction. Kardiologiia 2013; 53: 10-18.
3) Szymanski MK, Hillege HL, Danser AH, Garrelds IM, Schoemaker RG. Elevated sensitivity to cardiac ischemia in proteinuric rats is independent of adverse cardiac remodeling. J Hypertens 2013; 31: 966-974.
4) Steg PG, James SK, Atar D, Badano LP, Blomstrom-Lundqvist C, Borger MA, Di Mario C, Dickstein K, Ducrocq G, Fernandez-Aviles F, Gershlick AH, Giannuzzi P, Halvorsen S, Huber K, Juni P, Kastrati A, Knuuti J, Lenzen MJ, Mahaffey KW, Valgimigli M, van T HA, Widimsky P, Zahger D. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J 2012; 33: 2569-2619.
5) Fefer P, Hod H, Hammerman H, Boyko V, Behar S, Matetzky S. Relation of clinically defined spontaneous reperfusion to outcome in ST-elevation myocardial infarction. Am J Cardiol 2009; 103: 149-153.
6) Desmet W, Bogaert J, Dubois C, Sinnaeve P, Adriaenssens T, Pappas C, Ganame J, Dymarkowski S, Janssens S, Belmans A, Van de Werf F. High-dose intracoronary adenosine for myocardial salvage in patients with acute ST-segment elevation myocardial infarction. Eur Heart J 2011; 32: 867-877.
7) Deng J, Liu W, Wang Y, Dong M, Zheng M, Liu J. Polydatin modulates Ca(2+) handling, excitation-contraction coupling and beta-adrenergic signaling in rat ventricular myocytes. J Mol Cell Cardiol 2012; 53: 646-656.
8) Salcido DD, Kim YM, Sherman LD, Housler G, Teng X, Logue ES, Menegazzi JJ. Quantitative waveform measures of the electrocardiogram as continuous physiologic feedback during resuscitation with cardiopulmonary bypass. Resuscitation 2012; 83: 505-510.
9) Sezer M, Cimen AO, Aslanger EK, Yormaz E, Turkmen C, Umman B, Bugra Z, Adalet I, Nisanci Y, Adalet K, Umman S. Infarct remodeling process during long-term follow-up after reperfused acute myocardial infarction. Am J Med Sci 2009; 338: 465-469.
10) Lin XL, Zhou BY, Li S, Li XL, Luo ZR, Li JJ. Correlation of ABO blood groups with spontaneous recanalization in acute myocardial infarction. Scand Cardiovasc J 2017; 51: 217-220.
11) Hennan JK, Elokdah H, Leal M, Ji A, Friedrichs GS, Morgan GA, Swillo RE, Antrilli TM, Hreha A, Crandall DL. Evaluation of PAI-039 [{1-benzyl-5-[4-(trifluoromethoxy)phenyl]-1H-indol-3-yl}(oxo)acetic acid], a novel plasminogen activator inhibitor-1 inhibitor, in a canine model of coronary artery thrombosis. J Pharmacol Exp Ther 2005; 314: 710-716.
12) Aisa Z, Liao GC, Shen XL, Chen J, Li L, Jiang SB. Effect of autophagy on myocardial infarction and its mechanism. Eur Rev Med Pharmacol Sci 2017; 21: 3705-3713.
13) Kusama I, Hibi K, Kosuge M, Nozawa N, Ozaki H, Yano H, Sumita S, Tsukahara K, Okuda J, Ebina T, Umemura S, Kimura K. Impact of plaque rupture on infarct size in ST-segment elevation anterior acute myocardial infarction. J Am Coll Cardiol 2007; 50: 1230-1237.
14) Yousef ZR, Redwood SR, Bucknall CA, Sulke AN, Marber MS. Late intervention after anterior myocardial infarction: effects on left ventricular size, function, quality of life, and exercise tolerance: results of the Open Artery Trial (TOAT Study). J Am Coll Cardiol 2002; 40: 869-876.
15) Lai T, Fallon JT, Liu J, Mangion J, Gillam L, Waters D, Chen C. Reversibility and pathohistological basis of left ventricular remodeling in hibernating myocardium. Cardiovasc Pathol 2000; 9: 323-335.
16) Kanamasa K, Ishikawa K, Ogawa I, Nakabayashi T. Prevention of left ventricular remodeling by percutaneous transluminal coronary angioplasty performed 24 hours after the onset of acute myocardial infarction. J Thromb Thrombolysis 2000; 9: 47-51.
17) Marcassa C, Galli M, Bolli R, Temporelli PL, Campini R, Giannuzzi P. Heterogeneous fate of perfusion and contraction after anterior wall acute myocardial infarction and effects on left ventricular remodeling. Am J Cardiol 1998; 82: 1457-1462.