ORIGINAL ARTICLE

Effect of postconditioning on infarction size, adverse left ventricular remodeling, and improvement in left ventricular systolic function in patients with first anterior ST-segment elevation myocardial infarction

Marek Elżbieciak, Krystian Wita, Marek Grabka, Jarosław Chmurawa, Anika Doruchowska, Maciej Turski, Artur Filipecki, Maciej Wybraniec, Katarzyna Mizia-Stec

1st Department of Cardiology, Medical University of Silesia, Katowice, Poland

KEY WORDS

contrast-enhanced magnetic resonance imaging, heart necrosis, postconditioning

ABSTRACT

INTRODUCTION A key method in the treatment of ST-elevation myocardial infarction (STEMI) is recanalization of the infarct-related artery, but this causes heart reperfusion injury. One of the methods to reduce this injury is postconditioning. The available data on the efficacy of this method are contradictory.

OBJECTIVES The aim of the study was to determine the safety of postconditioning as well as its effect on infarction size, improvement in left ventricular ejection fraction (LVEF), and adverse LV remodeling during a 3-month follow-up.

PATIENTS AND METHODS The study involved 39 patients with first anterior STEMI (aged 58 ±10 years) up to 12 hours from the onset of symptoms. They were randomly assigned to a traditional-reperfusion group (n = 21) or to a postconditioning group (n = 18). The area at risk (AAR) was assessed angiographically. LV remodeling and LVEF were evaluated using echocardiography at 6 days and at 3 months. The infarction size was defined on the basis of magnetic resonance imaging (MRI) at 3 months.

RESULTS In a univariate logistic regression analysis, postconditioning did not affect the improvement of LVEF (odds ratio [OR], 1.63; 95% confidence interval [CI], 0.34–7.7; $P = 0.52$) or the development of adverse LV remodeling (OR, 0.62; 95% CI, 0.15–2.53; $P = 0.5$). Moreover, there were no significant differences in infarction size between the groups as measured by MRI after adjustment for the AAR, time to reperfusion, and ST-segment elevation prior to percutaneous coronary intervention.

CONCLUSIONS Postconditioning is a safe method but its application did not affect the volume of the infarction as well as did not improve LVEF or the development of adverse LV remodeling in a 3-month follow-up.

Correspondence to:
Marek Elżbieciak, MD, I Klinika i Katedra Kardiologii, Śląski Uniwersytet Medyczny, ul. Ziołowa 45/47, 40-635 Katowice, Poland, phone: +48-32-359-88-90, fax: +48-32-252-36-58, e-mail: elzbie20@gmail.com
Received: February 18, 2013.
Revision accepted: May 14, 2013.
Published online: May 14, 2013.
Conflict of interest: none declared.
Pol Arch Med Wewn. 2013; 123 (6): 268-276

INTRODUCTION Complete occlusion of the coronary artery causes ST-segment elevation myocardial infarction (STEMI). The primary objective of treatment is to restore blood flow in the culprit coronary artery to diminish the degree of necrosis. The introduction of reperfusion therapy, especially its most effective form – percutaneous coronary intervention (PCI) – has decreased early in-hospital mortality from STEMI from 16% to 4%–6%.[1,2] Nevertheless, long-term mortality from heart failure is still high. Undoubtedly, one of the reasons for this high mortality is myocardial injury after sudden restoration of flow within the infarct-related artery (IRA). It is called reperfusion injury and, as indicated by animal studies, it may be responsible for up to 50% of the final volume of the infarct.[3]

Potential mechanisms responsible for reperfusion injury include embolization of the distal vessels by the contents of ruptured atheromatous

plaque or intracoronary thrombus; platelet activation and aggregation in the ischemic region; contraction of cardiomyocytes as a result of reperfusion; enhanced inflammation; increased neutrophil accumulation in the infarction region; opening of mitochondrial permeability transition pores with progressive cell apoptosis[4]; production of free radicals (reactive oxygen and reactive nitrogen species), which is particularly enahnced in the early reperfusion period[5,6]; and, finally, closure of mitochondrial ATP-dependent potassium channels, which entails an increase in the ATP production.[7]

Vinten-Johansen et al.[8] were the first to describe the concept of postconditioning in an animal model as an easy and effective method to diminish infarction size by inducing triple short-term (30 s) episodes of alternate ischemia and reperfusion that occur immediately after the opening of the left anterior descending artery (LAD), which was closed for 60 minutes. Their observations were confirmed in other animal models.[9]

Recent reports on the clinical significance and usefulness of postconditioning with respect to the treatment of STEMI are contradictory. However, the latest reports on the use of contrast-enhanced magnetic resonance imaging (MRI) suggest that postconditioning is beneficial only for patients with a large extent of the myocardium at risk (area at risk – AAR),[10] while other reports suggest that this method does not result in a satisfactory reduction of the infarction size or in any improvement of the systolic function, and that it may even be harmful.

The aim of the study was to: 1) determine the safety of postconditioning with reference to acute STEMI of the anterior wall; 2) determine the significance of postconditioning with regard to the final infarction size as evaluated using contrast-enhanced MRI; 3) determine the significance of postconditioning with respect to any improvement in the left ventricular ejection fraction (LVEF) evaluated using two-dimensional (2D) echocardiography in a 3-month follow-up; 4) determine the significance of postconditioning with regard to adverse remodeling of the left ventricle (LV) evaluated using 2D echocardiography in a 3-month follow-up; and 5) assess the occurrence of the composite endpoint, which was defined as death, reinfarction not resulting in death or hospitalization due to heart failure in patients who had been treated either with postconditioning or with traditional reperfusion.

PATIENTS AND METHODS

The study included 39 patients (aged 58 ±10 years; 29 men) who had suffered their first anterior wall STEMI and were admitted to the 1st Department of Cardiology, Medical University of Silesia in Katowice, Poland. Written informed consent was obtained from all patients prior to the study. The inclusion criteria were as follows: age of 18–80 years, anterior-wall STEMI with symptoms lasting no longer than 12 hours, occlusion of the LAD artery diagnosed using coronary angiography, and normal flow after the opening of the IRA (TIMI 3). The exclusion criteria were as follows: history of infarction or coronary revascularization, serious valvular disease, hypertrophic cardiomyopathy, obesity (body mass index >40 kg/m^2), or a contraindication to contrast-enhanced MRI examination. Patients were treated according to the standards of the European Society of Cardiology (acetylsalicylic acid, loading dose of 300 mg and 75–150 mg/dl; clopidogrel, loading dose of 600 mg and then 75 mg/d; heparin; and primary PCI). The decision to administer a glycoprotein-IIb/IIIa inhibitor was made by a physician who performed PCI. The characteristics of the study group are presented in TABLE 1.

Primary percutaneous coronary intervention Coronary angiography was performed in all patients immediately after admission. When angiography was finished and recent occlusion of the LAD was confirmed, patients were randomly assigned to the traditional-reperfusion group with stent implantation (group A) or to the postconditioning group (group B). In group B, after restoring the patency of the artery and before stenting, 4 low-pressure balloon inflations (4–6 atm) and 4 alternate deflations at 1-minute intervals were performed within the next 8 minutes. The balloon was placed in the culprit vessel so as not to close any other ramifications. Subsequently, a stent was implanted and a control angiography was performed; however, none of the patients were treated with simultaneous thromboaspiration. Randomization was conducted by means of a coin toss. The AAR was assessed angiographically using the modified APPROACH score.[11] In this method, the site of LAD occlusion (proximal or medial distal) and the size of diagonal branches (small, medium, or large) were considered to estimate the percentage of the LV mass threatened by infarct. Coronary collateral vessels were analyzed according to the Rentrop grading system.[12] This scale is based on visualization of the collateral arteries filled with a contrast agent; grade 0, no collaterals; grade 1, small collateral vessels branching from the recipient artery and not contrasting the main epicardial artery; grade 2, collaterals partially filling the main epicardial recipient artery; and grade 3, collaterals completely filling the main epicardial recipient artery up to the level of occlusion. However, the degree of collateral circulation assessed by the Rentrop score during primary PCI is not a useful long-term prognostic factor in the population with STEMI.[13]

Transthoracic echocardiography A resting 2D transthoracic echocardiography (TTE) in 3 apical projections of the LV was performed using the Vivid system (GE, Vingmed, Norway) on the day of discharge from the hospital (usually day 6 of hospitalization) and at 3 months. Following the guidelines of the American Society

of Echocardiography, 4-, 2-, and 3-chamber examinations were performed. The physician performing echocardiography was blinded to the results of randomization. The LV wall was divided into 16 segments. Each segment was described as normo- (k = 1), hypo- (k = 2), a- (k = 3), or dyskinetic (k = 4), which corresponds to a scale ranging from 1 to 4 points, based on the subjective evaluation of the amplitude of ventricular wall motion and systolic thickening of the myocardium. The wall motion score index was the ratio of the sum of regional contractility evaluation and the number of assessed segments. Evaluation of the mitral regurgitation grade involved a quantitative method that involved the measurement of the vena contracta.

LV end-diastolic volume (LVEDV) and LV end-systolic volume (LVESV) were acquired using the Simpson method with the assumption that the chambers are spherical and constitute the arithmetic mean of the indicated volumes in both the 4- and 2-chamber projections. LVEF constituted the ratio of stroke volume and LVEDV and was calculated as the arithmetic mean of 3 subsequent measurements.

An echocardiographic examination based on the non-Doppler method involving the evaluation of myocardial strain (speckle tracking imaging) was performed immediately after standard echocardiographic examination. Typical apex projections were used with the frame rate between 60 and 90/fps with an automatic measurement of the strain using an EchoPAC PC 6.0.0 GE Medical System (Norway). The analysis of all strain measurements was conducted offline. A longitudinal strain was defined as the difference between the LV end-systolic and end-diastolic lengths, and then divided by the end-systolic length ($\Delta L/L_0$). The mean peak values of the longitudinal strain of all 16 segments of the LV (global longitudinal strain), and, separately, of the strain of 9 matching segments of the anterior wall (anterior global longitudinal strain) were evaluated.

Electrocardiography A 12-lead electrocardiogram (ECG) was performed directly before and 60 minutes after PCI of the IRA. On the first ECG acquisition, the following parameters were analyzed: heart rhythm, maximum single-lead ST-segment elevation, and the sum of ST-segment elevations from all leads (ΣST). During the second ECG acquisition, the sum of ST-segment elevations and the maximum ST-segment elevation from a single lead were evaluated.

Magnetic resonance imaging MRI was performed through the short axis of the heart, in 2- and 4-chamber projections at 3 months after

TABLE 1 Characteristics of the study groups

	Group A (n = 21)	Group B (n = 18)	*P*
age, y	58.4 ±10.90	60.1 ±9.53	0.60
men, %	85.7	66.7	0.30
weight, kg	80.3 ±8.9	75.4 ±10.6	0.13
arterial hypertension, %	90.5	77.7	0.15
hyperlipidemia, %	85.7	61.2	0.52
diabetes, %	23.8	22.2	0.90
smoking, %	52.4	66.6	0.88
stroke in history, %	9.5	0	0.15
time to reperfusion, min	317.6 ±195.8	225.6 ±139.4	0.10
duration of hospitalization, d	6.6 ±1.1	6.5 ±0.9	0.72
door-to-balloon time, min	26.7 ±23.2	24.6 ±23.7	0.77
creatinine, mg%	0.89 ±0.25	0.79 ±0.14	0.13
troponin T on admission, ng/ml	1.38 ±2.2	1.02 ±2.7	0.65
peak troponin T, ng/ml	13.4 ±11.8	9.8 ±6.9	0.26
CK-MB on admission, U/l	63.1 ±71.9	60.0 ±111.4	0.91
peak CK-MB, U/l	188.00 ±240.2	241.6 ±166.8	0.44
multivessel disease, %	57.1	38.9	0.25
LAD proximal occlusion, %	33.33	30.77	0.20
LAD medial occlusion, %	25.64	10.26	0.20
AAR (modified APPROACH score), %	38.57 ±9.2	41.94 ±7.4	0.23
MSI	0.46 ±0.4	0.34 ±0.29	0.32
BMS implantation, %	56.4	35.9	0.36
DES implantation, %	2.56	5.13	0.36
collateral circulation (RENTROP >1), %	10.26	12.82	0.26

Abbreviations: AAR – area at risk, BMS – bare-metal stent, CK-MB – creatine kinase MB, DES – drug-eluting stent, LAD – left anterior descending artery, MSI – myocardial salvage index

TABLE 2 Magnetic resonance imaging data at 3 months

	Group A (n = 21)	Group B (n = 18)	*P*
LVEF, %	47.95 ±12.6	49.52 ±13.03	0.70
percentage of the LV mass affected by infarct, %	26.18 ±23.0	25.26 ±12.88	0.88
infarct mass, g	34.52 ±31.19	39.28 ±23.41	0.60
infarct mass / AAR, g/%	0.84 ±0.68	1.04 ±0.56	0.33
damage >30 g of the LV muscle, %	45	66.67	0.18
damage >20% of the LV mass, %	55.0	61.11	0.70

Abbreviations: LV – left ventricular, LVEF – left ventricular ejection fraction, others – see **TABLE 1**

TABLE 3 Electrocardiographic and echocardiographic data of the study groups

	Group A (n = 21)	Group B (n = 18)	*P*
sinus rhythm, %	100	100	1.0
ΣST prior to PCI, mm	10.61 ±5.16	17.25 ±9.5	0.0089
max ST prior to PCI, mm	3.42 ±1.3	4.77 ±2.29	0.027
ΣST 60 min after PCI, mm	5.47 ±4.3	8.5 ±6.7	0.01
max ST 60 min after PCI, mm	1.83 ±1.12	2.75 ±2.1	0.09
LVEDV at discharge, ml	104.21 ±32.1	106.44 ±23.2	0.8
LVEDV at 3 months, ml	114.45 ±29.12	109.07 ±24.28	0.53
LVESV at discharge, ml	58.52 ±22.19	53.30 ±14.65	0.4
LVESV at 3 months, ml	60.13 ±24.24	54.29 ±24.03	0.45
LVEF at discharge, %	46.06 ±8.8	49.56 ±7.8	0.07
LVEF at 3 months, %	48.28 ±11.53	51.77 ±14.17	0.40
GLS at discharge, %	–12.05 ±4.94	–13.4 ±4.41	0.38
AGLS at discharge, %	–9.81 ±6.89	–9.83 ±5.89	0.99
mitral valve regurgitation, %	33.3	27.8	0.27
improvement of LVEF, %	80.95	72.22	0.79
remodeling, %	38.1	27.78	0.49

Data are presented as mean ± standard deviation or percentage.

Abbreviations: AGLS – anterior wall global longitudinal strain, GLS – global longitudinal strain, LVEDV – left ventricular end-diastolic volume, LVESV – left ventricular end-systolic volume, PCI – percutaneous coronary intervention, max ST – maximum ST-elevation, ΣST – ST-elevation sum in all leads

the infarction: without contrast in the FIESTA cine sequences and after intravenous administration of the MultiHance® contrast agent, which comprises gadolinium in the FGR sequences. After a 12-minute delay, LVEDV, LVESV, LVEF, and myocardial mass were evaluated. After the contrast agent was added, the thickness of late enhancement regions in relation to each of the 16 segments were evaluated. The total myocardial mass with pathological accumulation of contrast was used as a postinfarction myocardial scarring measure. The accumulation and subsequent prolonged clearance of the contrast agent from the myocardium was regarded as a pathology. A major infarction was defined when the mass of the myocardium with pathological accumulation of the contrast agent was equal to or more than 20% of the LV mass.

After MRI, the myocardial salvage index was calculated as the difference between the AAR according to the modified APPROACH score and the percentage of the LV mass affected by infarct on the MRI scans at 3 months, divided by the AAR according to the modified APPROACH score.

Long-term follow-up After 3 months, the clinical condition of the patients was again evaluated and a 2D echocardiography was performed to evaluate impaired myocardial segmental contractility and to establish LVEDV, LVESV, and LVEF, which allowed to evaluate any improvement related to LVEF and the occurrence of any adverse LV remodeling in long-term follow-up. The improvement of LVEF was defined as an increase in the LVEF of 5% or higher. LV remodeling was defined as a relative increase in the LVEDV of more than 20% during follow-up. Cardiac MRI was performed at 3 months.

The median onset time of major adverse cardiac events (MACEs) reached 2 years. The occurrence of death, reinfarction, or hospitalization due to heart failure was evaluated jointly. The study was approved by the local bioethics committee.

Statistical analysis A statistical analysis was performed using the Statistica 8.0 software. Continuous variables were expressed as means ± standard deviation, while dichotomous variables were expressed as a percentage.

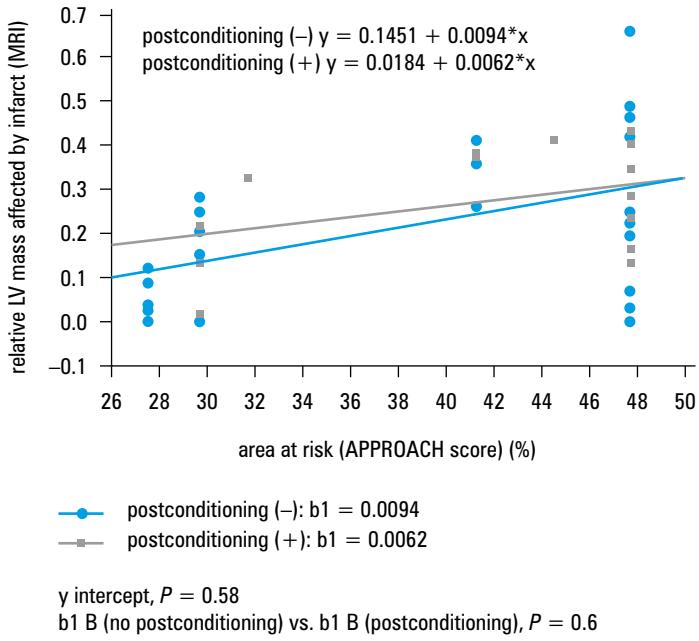

FIGURE 1 Analysis of covariance: linear regression of relative left ventricular mass affected by infarct against the area at risk by the APPROACH score depending on the use of postconditioning
Abbreviations: MRI – magnetic resonance imaging, others – see TABLE 2

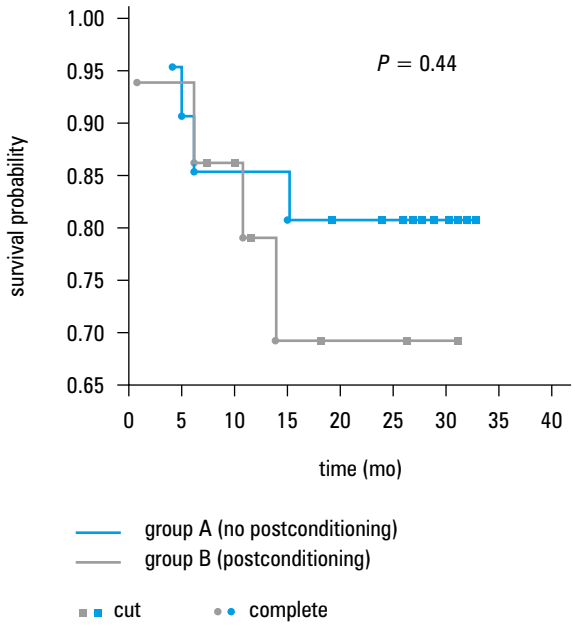

FIGURE 2 Kaplan–Meier survival curve

The analysis of normal distribution was performed using the Kolmogorov–Smirnov, Lilliefors, and Shapiro–Wilk tests. The homogeneity of variance within the groups was verified using the Levene's and Brown–Forsythe tests. A comparison of the values in the groups in relation to variables with normal distribution was made using the *t* test for unrelated variables. In the absence of normal distribution, a nonparameteric analysis was performed using a test for 2 groups: Kolmogorov–Smirnov test and Mann–Whitney *U* test. For qualitative variables, the level of significance was calculated using the χ^2 test with the Yates correction if necessary.

The predictive value of postconditioning for the final size of the infarction assessed by MRI, improvement of LVEF, the occurrence of LV remodeling during TTE, or the degree of regression in relation to the ST-elevation within 1 hour after angioplasty were evaluated using the univariate method of logistic regression with the implementation of estimation using the Rosenbrock and quasi-Newton method. All variables with a *P*-value of less than 0.1 were incorporated into a multivariate logistic regression analysis. The analysis of covariance (ANCOVA) was performed to examine the effect of independent covariates on the final myocardial size in the groups with and without postconditioning. The survival analysis was made using the Kaplan–Meier estimation.

RESULTS There were no significant differences between the groups in terms of age, sex, comorbidities, treatment (glycoprotein-IIb/IIIa inhibitors, statins, β-blockers, clopidogrel, angiotensin-converting enzyme inhibitors, or acetylsalicylic acid) and parameters of renal function (TABLE 1). The groups did not differ in terms of the parameters evaluated by MRI (TABLE 2). Moreover, intergroup differences in echocardiographic and angiographic parameters (AAR, collateral circulation, stent implantation) were not significant (TABLES 1 and 3). In group B, we observed a higher ST-elevation sum of all leads on output ECG compared with group A (10.61 ±5.16 mm vs. 17.25 ±9.5 mm; $P = 0.0089$; TABLE 3) and a trend towards shorter time to reperfusion (317.6 ±195.8 vs. 225.6 ±139.4; $P = 0.1$; TABLE 1). The ANCOVA analysis did not show any differences in the final myocardial size in any of the groups after adjusting for the following confounding variables: AAR (y-intercept $P = 0.58$), time to reperfusion (y-intercept $P = 0.25$), and ΣST prior to PCI (y-intercept $P = 0.28$). The linear regression plots for the above covariates and LV mass affected by infarct in groups A and B did not vary significantly: AAR, b1 A vs. b1 B; $P = 0.6$ (FIGURE 1); time to reperfusion, b1 A vs. b1 B; $P = 0.20$; and ΣST prior to PCI, b1 A vs. b1 B; $P = 0.27$; where b1 is the coefficient of linear equation.

None of the groups had any complications related to hemodynamic procedures (death, IRA occlusion, sustained ventricular arrhythmia), and the duration of hospitalization did not differ between the groups.

In the course of a 24-month follow-up, MACEs occurred in 8 patients (4 in group A [19%] and 4 in group B [22%]). A survival analysis using the Kaplan–Meier estimation did not reach statistical significance ($P = 0.44$) (FIGURE 2).

In a univariate logistic regression, postconditioning did not improve LVEF at 3 months (TABLE 4) or affect the development of adverse LV remodeling (TABLE 5). Moreover, a greater LVEDV and the presence of mitral regurgitation appeared to be independent risk factors of LV remodeling (TABLE 5).

TABLE 4 Univariate and multivariate analysis: improvement of left ventricle ejection fraction

	Univariate analysis				Multivariate analysis			
	OR	–95% CI	+95% CI	*P*	log OR	–95% CI	+95% CI	*P*
male sex	1.06	0.16	6.73	0.94				
age, y	1.05	0.97	1.14	0.17				
postconditioning	1.63	0.34	7.7	0.52				
time to reperfusion, min	0.999	0.995	1.00	0.98				
arterial hypertension	2.43	0.23	24.78	0.44				
diabetes	2.0	0.36	11.0	0.41				
smoking	0.38	0.07	1.92	0.23				
multivessel disease	0.43	0.087	2.19	0.3				
AAR, %	0.01	0.940	1.10	0.68				
MSI	0.45	0.070	2.95	0.40				
use of GP-IIb/IIIa inhibitor	1.27	0.2	7.91	0.79				
max troponin, ng/ml	1.1	1.01	1.2	0.02	1.054	0.944	1.178	0.34
CK-MB (4 h after PCI), U/l	1.008	1.0008	1.01	0.03	0.10	0.988	1.009	0.76
ΣST before PCI, mm	1.04	0.94	1.14	0.38				
LVEDV at discharge, ml	1.004	0.97	1.031	0.76				
LVESV at discharge, ml	1.006	0.96	1.04	0.75				
LVSV at discharge, ml	1.00	0.95	1.04	0.95				
LVEF at discharge, %	0.98	0.9	1.07	0.71				
GLS, %	1.17	0.94	1.44	0.13				
AGLS, %	1.17	0.98	1.39	0.07	0.95	0.807	1.130	0.58
WMSI at 3 months	5.19	0.57	46.9	0.13				
LVEDV at 3 months, ml	1.01	0.98	1.04	0.46				
LVESV at 3 months, ml	1.05	1.012	1.09	0.01	1.07	0.995	1.152	0.07
infarct mass on MRI, g	1.01	0.98	1.03	0.42				

Abbreviations: GP – glycoprotein, MRI – magnetic resonance imaging, LVSV – left ventricular stroke volume, WMSI – wall motion score index, others – see **TABLES 1**, **2**, and **3**

DISCUSSION Considering the contradictory data in the literature, this randomized and prospective study was designed to determine the effect of traditional angioplasty combined with the procedure of postconditioning on the size of the postinfarction scar as evaluated by MRI, the development of adverse remodeling, and any improvement in LVEF during a 3-month follow-up. Our study highlights the observation that postconditioning, though not associated with prolonged hospitalization or higher periprocedural risk, does not limit the infarction size as evaluated by MRI and does not determine any improvement in LVEF or the reduction of adverse LV remodeling as evaluated by 2D echocardiography. In the present study, the myocardium at risk was assessed angiographically with the modified APPROACH score, which is used to estimate the anatomical extent of the myocardium at risk in patients with acute STEMI. This estimation is independent of the presence of other perfusion defects related to other coronary lesions other than the IRA, but several factors, such as residual flow and collateral flow in the IRA can modulate the hypoperfused area. However, this method was demonstrated to correlate precisely with MRI.[11]

The first reports concerning the use of postconditioning, which were conducted in a nonrandomized fashion on small groups of patients, were promising. The first publications that underscored the advantage of postconditioning over traditional PCI in case of acute STEMI infarction were the studies by Staat et al.[14] and Laskey.[15] These reports indicated that postconditioning reduced the release of creatine kinase, which is a surrogate for the size of the infarction and improves the coronary flow reserve and resolution of ST-segment elevation. Other researchers indicated an improvement in LVEF or in the class of heart failure. Nevertheless, the examined groups were not only small but also heterogeneous (different locations of infarction or prior history of STEMI), while the endpoints were subjective (pertaining to the functional class) and with low reproducibility (coronary artery Doppler, release of myocardial injury markers).

In our study, patients had first anterior wall STEMI, and the outcomes of therapy were evaluated using contrast-enhanced MRI, which is a highly repeatable and precise technique that was first performed by Lønborg et al.[16] In the present study, the use of controlled reperfusion did not reduce the infarction size.

TABLE 5 Univariate and multivariate analysis: prediction of adverse left ventricular remodeling in a 3-month follow-up

	Univariate analysis				Multivariate analysis			
	OR	–95% CI	+95% CI	*P*	log OR	–95% CI	+95% CI	*P*
male sex (yes)	0.53	0.11	2.6	0.42				
age, y (constant value)	1.03	0.96	1.1	0.36				
postconditioning (yes)	0.62	0.15	2.53	0.5				
time to reperfusion, min (constant value)	1.002	0.99	1.006	0.27				
arterial hypertension (yes)	1.65	0.26	10.19	0.58				
diabetes (yes)	3.43	0.69	16.95	0.12				
smoking (yes)	0.73	0.18	2.92	0.65				
multivessel disease (yes)	1.36	0.34	5.41	0.65				
AAR, % (constant value)	0.99	0.909	1.070	0.73				
MSI (constant value)	0.24	0.032	1.831	0.16				
use of GP IIb/IIIa inhibitor (yes)	0.67	0.14	3.14	0.6				
max troponin, ng/ml (constant value)	1.03	0.96	1.1	0.33				
CK-MB (4 h after PCI), U/l (constant value)	0.99	0.98	1.0	0.31				
ΣST before PCI, mm (constant value)	1.01	0.92	1.1	0.81				
LVEDV at discharge, ml (constant value)	1.03	1.01	1.05	0.02	0.98	0.923	1,041	0.52
LVESV at discharge, ml (constant value)	0.95	0.89	1.00	0.08	0.97	0.864	1.085	0.57
LVEF at discharge, % (constant value)	0.98	0.91	1.06	0.75				
mitral valve incompetence, % (yes)	3.25	1.2	5.32	0.03	2.26	0.352	14.52	0.38
GLS, % (constant value)	1.02	0.87	1.19	0.76				
AGLS, % (constant value)	1.03	0.92	1.16	0.53				

Abbreviations: see **TABLES 1–4**

These results are contradictory to the results of Lønborg et al.[16] who reported an 18% reduction in the infaction size evaluated by contrast-enhanced MRI in a group of 118 patients treated by primary PCI followed by controlled reperfusion. The possible reason for this inconsistency should first and foremost be ascribed to the selection of patients. Patients suffering from multivessel disease were not excluded from the analysis. The coexistence of multivessel disease is related to a longer duration of atherosclerosis and the resultant development of collateral circulation, which, in specific anatomical conditions, may limit the final volume of necrosis during an acute occlusion of the IRA. The degree of stenosis of the IRA is yet another differentiating factor. In our patients, complete occlusion of the LAD was required while a high percentage of the subjects examined by Lønborg et al.[16] exhibited only a critical stenosis of the culprit coronary artery.

By applying methodology similar to that used in our study, Ortiz-Pérez et al.,[17] in a recently published paper, documented that the presence of collateral circulation and residual flow in the IRA determine a higher degree of myocardial recovery.[17] Moreover, according to Ortiz-Pérez et al.,[17] the target flow within the IRA was TIMI 3 after the procedure, and IRA stenting in all patients as well as the high percentage of abciximab use may explain the differences between the 2 studies.

In line with our observations, the studies by Freixa et al.[18] and Sörensson et al.[10] did not demonstrate any reduction in the infarction size as evaluated by contrast-enhanced MRI and suggested a possible and positive effect only in case of infarctions with a large AAR. The analysis done by Freixa et al.[18] is particularly interesting. It concerns the effect of controlled reperfusion on the infarction size at a particular time interval between the onset of symptoms and the beginning of PCI. Similarly to our study, Freixa et al.[18] did not exclude patients in whom the time between the onset of symptoms and PCI was between 6 to 12 hours. Patients did not benefit from the use of controlled reperfusion in any of the time intervals.

Simultaneously, the results of our research indicate high utility of peak longitudinal systolic strain evaluated using speckle tracking technique in the prediction of the final infarction size infarction as assessed by MRI. The peak value of the longitudinal strain of the LV for 16 segments as well as the one limited only to 9 segments connected with the vessel supplying the LAD artery appear to be independent predictors of a "major infarction" as evaluated at 3 months. This is, by far, the first study reporting that the evaluation of the longitudinal peak strain may serve as a predictor of the infarction size in patients treated with PCI. In our study, we clinically evaluated the relation between the implementation of controlled reperfusion and the occurrence of remodeling in the long-term follow-up. Even though the results

of the experimental research are encouraging, this relation has not been confirmed.[19,20]

The presence of comorbidities, such as diabetes and arterial hypertension, as well as advanced age have been reported to be factors that limit the efficiency of postconditioning in animal models.[21,22] The results of our research might have been affected by the application of primary stenting in selected patients. Primary stenting is a highly recommended strategy to decrease the risk of distal embolization.[23] The application of primary stenting in patients with STEMI with an occluded culprit artery is often not feasible due to the lack of a distal anatomical reference.

Our study has several limitations, the most important being the relatively low number of patients. Despite being limited only to the anterior location of myocardial infarction, the study population constitutes a relatively heterogenic group and any subanalysis of patients suffering from arterial hypertension, diabetes, multivessel disease, and collateral circulation could not have been done.

For the same reason, the analysis of patients suffering from a major infarction is difficult to conduct; however, this subgroup is assumed to benefit most from controlled reperfusion. In line with experimental studies on animals, the greatest benefits of postconditioning are derived within a short time after the occlusion of the culprit artery. Thus, it seems to be worth to stratify the study population in terms of the time to reperfusion and to the evaluation within a few days after the infarction using magnetic resonance performed when the area is at risk of necrosis, as in the study by Freixa et al.[18] Such an analysis was not feasible in our population due to a low number of patients. Regardless of the study limitations, our results correspond to those scarce data obtained by other investigators in the field. Moreover, in our study, we used MRI, which is the most reliable tool for evaluating infarction scar.

In conclusion, postconditioning after traditional primary angioplasty in extended myocardial infarction of the anterior wall appears to be a safe method. Nevertheless, the use of postconditioning failed to reduce the infaction size as evaluated by MRI and did not improve LVEF or prevent adverse LV remodeling as evaluated by 2D echocardiography during a 3-month follow-up.

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ARTYKUŁ ORYGINALNY

Wpływ modyfikowanej reperfuzji na wielkość zawału, rozwój niekorzystnej przebudowy oraz poprawę funkcji skurczowej lewej komory u chorych z pierwszym zawałem z uniesieniem odcinka ST ściany przedniej

Marek Elżbieciak, Krystian Wita, Marek Grabka, Jarosław Chmurawa, Anika Doruchowska, Maciej Turski, Artur Filipecki, Maciej Wybraniec, Katarzyna Mizia-Stec

I Klinika i Katedra Kardiologii, Śląski Uniwersytet Medyczny w Katowicach, Katowice

SŁOWA KLUCZOWE

martwica serca, modyfikowana reperfuzja, rezonans magnetyczny z kontrastem

STRESZCZENIE

WPROWADZENIE Najważniejszą metodą leczenia zawału z uniesieniem odcinka ST (*ST-elevation myocardial infarction* – STEMI) jest udrożnienie tętnicy dozawałowej, co jednak powoduje uszkodzenie reperfuzyjne mięśnia sercowego. Postulowaną metodą ograniczenia tego uszkodzenia jest modyfikowana reperfuzja. Dotychczasowe doniesienia dotyczące skuteczności tej metody są sprzeczne.

CELE Celem badania było określenie bezpieczeństwa wykonania modyfikowanej reperfuzji, a także jej znaczenia dla wielkości zawału, poprawy frakcji wyrzutowej lewej komory (*left ventricular ejection fraction* – LVEF) oraz rozwoju niekorzystnej przebudowy lewej komory w obserwacji 3 miesięcznej.

PACJENCI I METODY Do badania włączono 39 pacjentów z pierwszym zawałem typu STEMI ściany przedniej (wiek 58 ±10 lat) do 12 godzin od początku objawów. Chorych losowo przydzielono do grupy tradycyjnej reperfuzji (n = 21) oraz do grupy zmodyfikowanej reperfuzji (n = 18). Obszar zagrożony martwicą (AAR) oceniono angiograficznie. Niekorzystną przebudowę lewej komory oraz LVEF oceniono za pomocą badania echokardiograficznego w 6 dobie i po 3 miesiącach. Wielkość zawału oceniono za pomocą rezonansu magnetycznego (RM) po 3 miesiącach.

WYNIKI W analizie jednoczynnikowej metodą regresji logistycznej modyfikowana reperfuzja nie była predyktorem poprawy frakcji wyrzutowej (OR: 1,63; 95%CI: 0,34–7,7; p = 0,52) oraz rozwoju remodelingu LV (OR: 0,62; 95%CI: 0,15–2,53; p = 0,5). Nie stwierdzono również statystycznie istotnych różnic między grupami w wielkości zawału ocenianej po 3 miesiącach za pomocą RM w korelacji do AAR, czasu do reperfuzji oraz uniesienia odcinka ST przed angioplastyką.

WNIOSKI Modyfikowana reperfuzja jest metodą bezpieczną, ale jej zastosowanie nie wpłynęło na wielkość zawału, poprawę LVEF oraz rozwój niekorzystnej przebudowy lewej komory w obserwacji 3 miesięcznej.

Adres do korespondencji:
lek. med. Marek Elżbieciak,
I Klinika i Katedra Kardiologii,
Śląski Uniwersytet Medyczny,
ul. Ziołowa 45/47, 40-635 Katowice,
tel.: 32-359-88-90, fax: 32-252-36-58,
e-mail: elzbie20@gmail.com

Praca wpłynęła: 18.02.2013.
Przyjęta do druku: 14.05.2013.
Publikacja *online*: 14.05.2013.
Nie zgłoszono sprzeczności interesów.
Pol Arch Med Wewn. 2013;
123 (6): 268-276