Relationship between tissue reperfusion and postinfarction left ventricular remodelling in patients with anterior wall myocardial infarction treated with primary coronary angioplasty

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Abstract

Introduction: Pathological left ventricular remodelling is considered the main cause of heart failure in patients after myocardial infarction.

Aim: The purpose of this study was to evaluate correlations between the degree of coronary microvascular reperfusion assessed by means of the angiographic myocardial blush grade (MBG) scale and adverse left ventricular remodelling in patients with acute myocardial infarction treated with primary coronary angioplasty.

Methods: This study involved 92 consecutive patients, hospitalised because of their first anterior wall myocardial infarction, who underwent successful (TIMI-3 grade flow) primary coronary angioplasty. Angiographic myocardial reperfusion parameters (MBG, corrected TIMI Frame Count) were assessed. Three days and 6 months after the index PCI all patients underwent an echocardiographic examination and such parameters as end-diastolic volume (EDV), left ventricular ejection fraction (EF) and contractility index (WMSI) were calculated.

Results: The patients were divided into two groups: group 1 with impaired myocardial reperfusion (MBG 0-1) (n=32) and group 2 with adequate tissue reperfusion (MBG 2-3) (n=60). Negative left ventricular remodelling was observed more frequently in group 1 than in group 2 (28.1% *vs* 10%, p=0.029). More patients in group 1 presented heart failure symptoms (56.3% *vs* 25%, p=0.013).

Conclusions: Failure of tissue reperfusion assessed by means of angiographic indices (MBG 0-1) in patients with myocardial infarction treated with primary coronary angioplasty is associated with a higher rate of adverse myocardial remodelling and heart failure at 6 months after myocardial infarction.

Key words: remodelling, acute myocardial infarction, reperfusion

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Introduction

Pathological left ventricular (LV) remodelling is a major cause of chronic heart failure (CHF) and is associated with the worsening of prognosis in patients after myocardial infarction (MI) [1]. The most important factors influencing LV remodelling are the following: delay time of reperfusion therapy, location and extent of myocardial infarction, and – most of all – the degree of infarct-related artery (IRA) patency [2]. According to the *open vessel* theory, efficiency (of about 90%) in the restoration and maintenance of adequate flow in IRA as a result of primary coronary angioplasty should be associated with a reduction of the number of patients with adverse LV remodelling [3]. However, studies conducted by Bolognese et al. did not confirm this opinion [4]. Patients with LV dilation were observed equally frequently among those with MI treated with primary coronary angioplasty as with thrombolysis

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(30% *vs* 34%) [4, 5]. It has been also shown that LV remodelling was associated not only with patency and appropriate flow in IRA but also with the degree of myocardial reperfusion [6, 7].

Lack of reperfusion in the coronary microcirculation – the *no-reflow* phenomenon – is a result of ischaemic damage of the coronary circulation network, granulocyte infiltration, and also peripheral micro- or macro-embolisation, as well as a reflex spasm of afferent arterioles [8, 9]. *No-reflow* is seen in about 30% to 40% of patients with MI treated successfully with invasive methods or thrombolysis [8, 10]. It was shown that disturbances in myocardial reperfusion were related to a significant worsening of prognosis and a higher rate of postinfarction CHF [6, 7].

The purpose of our study was to evaluate remodelling in patients with anterior wall MI and the relationship between LV dilatation and tissue reperfusion failure (reperfusion in coronary microcirculation) evaluated by means of the angiographic myocardial blush grade (MBG) scale.

Methods

One hundred and nine consecutive patients admitted to hospital for invasive treatment of their first anterior wall MI between October 2001 and January 2003 were enrolled into this study. The study inclusion criteria were as follows: 1) a typical anginal pain lasting at least 30 min. from the onset of symptoms less than 12 hours before the procedure, 2) ST-segment elevation ≥0.2 mV on admission in at least two precordial leads, 3) successful primary percutaneous coronary intervention (PCI) (TIMI 3 flow grade, residual stenosis less than 30%). The following patients were excluded from the study: 1) patients with left bundle branch block, 2) signs of infarct evolution in ECG (negative T waves), 3) coexistence of other significant cardiac (valvular lesions, cardiomyopathies) or extracardiac diseases (neoplasms), 4) inadequate technical quality of angiographic images (excluded 3 patients) and 5) a poor *acoustic window* for echocardiographic evaluation (2 subjects excluded).

Each patient gave written informed consent to participate in the study. The study protocol was approved by the Local Bioethical Committee at Poznań University of Medical Sciences.

Of 104 patients initially enrolled in the study, echocardiographic examination on day 3 and at 6 months was performed in 92 subjects (12 patients died before the scheduled time of control follow-up examination). Thus, those patients represented the final study group.

Each patient received aspirin 150 mg/day and clopidogrel in a loading dose of 300 mg followed by a maintenance dose of 75 mg/day on the consecutive days and also unfractionated heparin in a dose dependent on the patient's body weight. Abciximab was used in patients with extensive infarction, in those with severe clinical status and in cases with a large thrombus impairing flow through the vessel. All patients, except those with absolute contraindications, received beta-blockers, angiotensin-converting enzyme inhibitors (ACEI) and statins. A clinical evaluation and chest X-ray when indicated were performed after 6 months. The following findings were considered as CHF symptoms: dyspnoea (>NYHA I), third cardiac sound, crepitations over the base of the lungs and radiologic signs of congestion on chest X-ray.

Coronary angiography and angioplasty, angiographic assessment

Coronary angiography was performed by means of the Judkins technique and was recorded digitally on a Hicor angiograph (Siemens, Germany) with a speed of 25 frames/s. Angiograms were analysed off-line using Acom PC computer software. Primary angioplasty was carried out in the typical manner in patients with TIMI flow grade <3 and/or stenosis >50%. Intracoronary stents were implanted in 86% of patients. The infarct-related artery (always the left anterior descending artery – LAD) was the subject of intervention.

TIMI flow (Thrombolysis In Myocardial Infarction) was calculated from the baseline angiogram and a second time from angiographic images taken after PCI.

CTFC calculation (corrected TIMI frame count) was performed by counting the number of frames necessary for the acquisition of the contrast medium path through IRA from its ostium (left anterior descending artery) to the reference point located at the distal end of the vessel. Then, the obtained number of frames was divided by 1.7 (correcting index).

The myocardial blush grade was estimated after procedure completion and was defined as follows: 0 – no contrast medium in the myocardium supplied by IRA or no outflow of the contrast medium; 1 – minimal myocardial blush; 2 – moderate myocardial blush (less than in the reference area); 3 – normal myocardial blush, comparable with the contralateral or ipsilateral coronary artery.

Echocardiographic examination

On in-hospital day 3 and at 6 months after MI, all patients underwent an echocardiographic examination (Sonos 5500 equipped with electronic 2.5 MHz probe, Hewlett Packard, USA). The study was performed employing standard 2D four-chamber apical, two-chamber long- and short-axis projections and was each time recorded on VHS tape. Left ventricular

Table I. Clinical characteristics of the studied groups

	Whole group N=92	Group 1 MBG 0-1 n=32	Group 2 MBG 2-3 n=60	p
Age [years]	61±13	64.6±11.1	59.2±13.5	0.01
Male [n]	66 (71.7%)	22 (68.8%)	44 (73.3%)	0.41
Arterial hypertension [n]	51 (55.4%)	23 (71.9%)	28 (46.7%)	0.02
Diabetes [n]	19 (20.7%)	12 (37.5%)	7 (11.7%)	0.005
Smoking [n]	40 (43.5%)	11 (34.4%)	29 (48.3%)	0.94
Hypercholesterolaemia [n]	57 (62%)	18 (56.3%)	39 (65%)	0.41
Delay in reperfusion therapy time [min]	270.4±161.4	361±197.4	221±113.1	<0.001
CK max (V/L)	3508.6±2687.2	3517.4±2398	3503.9±2849	0.29
CK-MB max (V/L)	347.8±231	388.6±250.2	326±211	0.16
Killip class >1 [n]	24 (26.1%)	12 (37.5%)	12 (20%)	0.06
ACE-I 6 months after MI [n]	72 (78.3%)	26 (81.3%)	46 (76.7%)	0.78
β-blockers 6 months after MI [n]	69 (75%)	25 (78.1%)	44 (73.3%)	0.77
Abciximab [n]	43 (46.7%)	17 (53.1%)	26 (43.3%)	0.25

Abbreviations: CK – creatine kinase, CK-MB – MB fraction of creatine kinase, ACE-I – angiotensin converting enzyme inhibitors

Table II. Angiogarphic data of the studied groups

	Whole group n=92	Group 1 MBG 0-1 n=32	Group 2 MBG 2-3 n=60	p
CTFC (mean ± SD)	22.6±12.9	31.8±15.3	17.7±7.9	0.03
Proximal LAD [n]	48 (52.2%)	17 (53.1%)	31 (51.7%)	0.63
Multivessel disease [n]	34 (37%)	18 (56.2%)	16 (26.7%)	0.005
Stent [n]	83 (90.2%)	30 (93.8%)	53 (88.3%)	0.89

Abbreviations: CTFC – corrected TIMI Frame Mount, MBG – Myocardial Blush Grade, LAD – Left Anterior Descending Artery

contractility was assessed by means of increased systolic LV wall thickness analysis in a 17-segment model according to the American Echocardiographic Society Guidelines. The wall motion score index (WMSI) was calculated employing a 4-point contractility scale, scored as 1 (normal motion), 2 (hypokinesia), 3 (akinesia) and 4 (dyskinesia), and was derived by averaging the scores from each segment. Left ventricular end-systolic volume (ESV) and LV ejection fraction (EF) by means of simplified Simpson's method were evaluated by echocardiograph internal software. Increase in the end-diastolic volume (EDV) ≥20% between day 3 and 6 months was considered as a significant predictor of adverse LV remodelling.

Statistical analysis

Continuous variables are presented as the arithmetic mean ± standard deviation, nominal variables as the number and percentage in the group. The normal distribution of variables was verified by means of the Shapiro-Wilk test. Parameters expressed in the interval scale with normal distribution were compared employing Student's t-test, those not following normal distribution using the Mann-Whitney U test. Data expressed in the nominal scale were compared by means of Fisher's exact or χ^2 test. Discriminant function analysis was used for the multivariate analysis of factors having an impact on adverse LV remodelling. A value of p less than 0.05 was considered significant. Statistical analysis was performed using the Statistica 6.0 software package.

Results

Patients were divided into two groups: group 1 with inadequate myocardial reperfusion (MBG 0 and 1, n=32), and group 2 with appropriate reperfusion in the coronary microcirculation (MBG 2 and 3, n=60). The clinical characteristics of both groups are outlined in Table I. Patients in group 1 were significantly older and more frequently had diabetes and arterial hypertension. Moreover, the delay time from onset of symptoms to balloon inflation was also longer in this group. Angiographic data are presented in Table II. Higher mean CTFC as well as a higher rate of multivessel disease were observed in group 1.

Table III. Echocardiographic data in the studied groups

	Whole group n=92	Group 1 MBG 0-1 n=32	Group 2 MBG 2-3 n=60	p
EF on day 3 [%]	46.2±8.6	44.5±7.6	47.1±9	0.29
EF at 6 months [%]	51.8±14.6	46±13.2	54.9±14.5	0.005
WMSI on day 3	1.71±0.39	1.84±0.35	1.64±0.38	0.008
WMSI at 6 months	1.54±0.45	1.75±0.46	1.43±0.4	0.001
EDV on day 3 [mL]	116.7±37.3	121±36.6	114±37.6	0.23
EDV at 6 months [mL]	121.7±47.9	134.9±40.8	114.6±50.2	0.01
ESV on day 3 [mL]	63.12±26.5	67±25	61±27.2	0.21
ESV at 6 months [mL]	62.6±37.4	74.4±34.15	56.3±37.84	0.008
SV on day 3 [mL]	53.6±17.3	54.6±16.35	53.1±17.9	0.53
SV at 6 months [mL]	58.5±20.5	58.6±15.4	58.4±22.8	0.59

Abbreviations: see Methods section

Mean EF at 6 months, as well as WMSI either on day 3 or after 6 months, were significantly higher in group 2 in comparison to group 1. No difference in EDV after 3 days was noted between the studied groups, whereas after 6 months EDV was significantly higher in group 1. Echocardiographic data are shown in Table III.

In the whole studied group, dilatation of the LV ≥20% within the 6-month follow-up period was noted in 15 patients (16.3%). Negative remodelling was found in 9 out of 32 patients (28.1%) in group 1 *vs* 6 out of 60 patients (10%) from group 2, (p=0.029, Figure 1). In discriminant function analysis, MBG 0-1 was found to be an independent predictor of negative LV remodelling after 6 months (p=0.025). The following borderline factors were also noted: delay time of therapy exceeding 6 hours (p=0.062) and infarct extent assessed by means of the maximum creatine kinase level (p=0.095). In univariate analysis no influence on LV dilatation of such factors as arterial hypertension, diabetes, age, multivessel disease and flow according to the TIMI scale prior to PCI was noted.

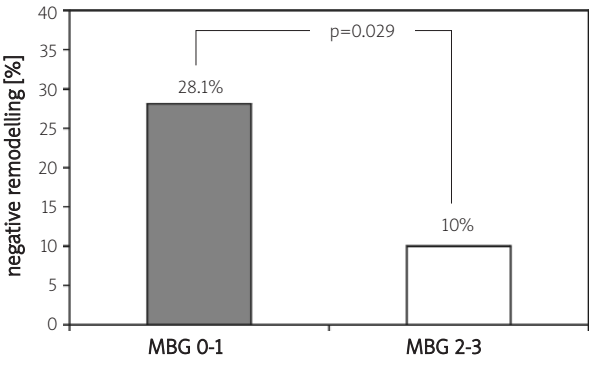

Figure 1. LV remodelling 6 months after AMI in the studied groups

Symptoms and signs of CHF were observed more often in group 1 than in group 2 (56.3% *vs* 25%, p=0.013). At the time of the 6-month follow-up, no significant differences in the ACEI or β-blockers administration were found between the studied groups.

Discussion

A number of reports confirmed a relationship between disturbances of tissue reperfusion evaluated by means of various diagnostic tools and no improvement in LV performance, as well as higher rate of adverse myocardial remodelling following MI [6, 7, 11]. Garber et al., in an experimental animal model employing magnetic resonance technology, evaluated relations between the presence of postreperfusion disturbances in the microcirculation and myocardial deformation, as well as distribution of LV mechanical strains that eventually led to its dilatation [11]. They noted that no reperfusion in the microcirculation increased the risk of remodelling independently from infarct extent and it was associated with load intensity on the myocardium both in the infarction area and in the adjacent segments. Many researchers stress that adequate blood supply is mandatory for the 'harmonious' process of adaptive mechanisms following MI (from mRNA expression to structural changes). An adverse ratio of vascular bed capacity to myocardial mass (lower density of capillary vessels, for example as a result of no epicardial artery recanalisation or postreperfusion microcirculation damage) has a significant impact on remodelling and accelerates the onset of CHF [12, 13].

The rate of LV dilatation (16.3%) observed in our study is slightly lower than that reported by other authors (about 20 to 30%) despite the fact that patients involved in our study were subjects with anterior wall infarcts, i.e. more prone to adverse myocardial remodelling [4, 7]. However, they were patients with their first MI and all

underwent successful PCI (patency restoration of infarct-related artery).

We observed that no reperfusion in the coronary microcirculation measured by means of angiographic indices (MBG 0-1) was associated with adverse postinfarction myocardial remodelling in the studied group of patients. This confirms the earlier reports of other authors regarding a significant impact of disturbances in the coronary microcirculation on negative myocardial remodelling. In a study by Bolognese et al., which examined myocardial perfusion using contrast echocardiography, microcirculation dysfunction was the most important risk factor of LV negative remodelling (OR–0.61, 95%, CI–0.52–0.71, p <0.00001) [7]. Thus, it seems that in order to reduce the number of patients with postinfarction HF, one should aim not only at early and durable IRA patency restoration but also employment of therapeutic procedures leading to reperfusion in the coronary microcirculation.

Moreover, the results of our study confirm that an evaluation of reperfusion in the microcirculation by means of the MBG angiographic scale is an efficient diagnostic tool that enables the identification of patients at risk of adverse LV remodelling. A multivariate analysis confirmed that MBG 0-1 (impaired myocardial reperfusion) was an independent risk factor of negative postinfarction remodelling. The myocardial blush assessment, in contrast to other methods of myocardial reperfusion evaluation (such as MRI, MCE, SPECT), is simple, safe and may – and even should – be adopted as a standard therapeutic procedure during primary PCI [10, 14, 15].

At the time of the 6-month follow-up, as many as 30% of patients after MI treated with PCI had restenosis in IRA that might lead to an impairment in LV performance and adverse LV remodelling [16, 17]. No angiographic follow-up examination was carried out at 6 months in this study. A generally accepted indication for angiographic examination is the recurrence of chest pain, but there is no common agreement to carry out this study routinely as a control one after primary PCI. Thus, lack of angiographic follow-up study is the main limitation of our study.

Conclusions

Failure of tissue reperfusion assessed by means of angiographic indices (MBG) in patients with myocardial infarction treated with primary coronary angioplasty is associated with a higher rate of adverse myocardial remodelling and CHF at 6 months after MI.

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Reperfuzja tkankowa a pozawałowa przebudowa lewej komory serca u chorych z zawałem serca ściany przedniej leczonych pierwotną angioplastyką wieńcową

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Streszczenie

Wstęp: Patologiczna przebudowa (remodeling) lewej komory stanowi główną przyczynę niewydolności serca u chorych po zawale. Celem pracy była ocena zależności pomiędzy stopniem reperfuzji w mikrokrążeniu wieńcowym ocenianym przy użyciu angiograficznej skali myocardial blush grade (MBG) a niekorzystną przebudową lewej komory u chorych z ostrym zawałem serca leczonych pierwotną angioplastyką wieńcową.

Materiał i metody: Do badania włączono 92 kolejnych chorych hospitalizowanych z powodu pierwszego w życiu zawału serca ściany przedniej i poddanych skutecznej (TMI–3) pierwotnej angioplastyce wieńcowej. Oceniano angiograficzne (*MBG*, *corrected TIMI Frame Count*) parametry reperfuzji tkankowej. Po 3 dniach i 6 mies. wszyscy chorzy mieli wykonane badanie echokardiograficzne z oceną objętości końcoworozkurczowej (EDV), frakcji wyrzutowej lewej komory (EF) oraz wskaźnika kurczliwości (WMSI).

Wyniki: Chorych podzielono na grupę ze złą reperfuzją tkankową (MBG 0–1) – grupa 1 (n=32) oraz grupę 2 (n=60) – z dobrą reperfuzją tkankową (MBG 2–3). Istotnie częściej negatywny remodeling lewej komory serca obserwowano w grupie 1 niż grupie 2 (28,1% *vs* 10%, p=0,029). W grupie 1 częściej występowały także objawy niewydolności serca (56,3% *vs* 25%, p=0,013).

Wnioski: Brak reperfuzji tkankowej oceniany za pomocą wskaźników angiograficznych (MBG 0–1) u chorych z zawałem serca leczonych pierwotną angioplastyką wieńcową jest związany z częstszym występowaniem niekorzystnej przebudowy mięśnia sercowego oraz objawów niewydolności serca 6 mies. po zawale.

Słowa kluczowe: remodeling, ostry zawał serca, reperfuzja

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