The prognostic value of contrast echocardiography in the prediction of the recovery of left ventricular function in patients with acute anterior myocardial infarction

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Abstract

Introduction: The immediate and complete restoration of perfusion in patients with acute myocardial infarction (MI) leads to the survival of myocardial cells in the initially ischaemic risk area and makes the recovery of left ventricular contractile function possible.

Aim: The goal of the study was to assess the utility of contrast echocardiography (CE) in the prediction of left ventricular function recovery in patients with AMI treated by percutaneous coronary intervention (PCI).

Methods: Eighty six patients (aged 58.4±11.2) with anterior AMI, treated by PCI of the left anterior descending coronary artery, were included in the study. Two-dimensional and contrast (Optison) echocardiography were performed immediately before and after PCI, and three days post-PCI. Myocardial contrasting was assessed using the following criteria: 0 – lack of perfusion; 0.5 – partial perfusion; 1 – normal perfusion. On the third day post-PCI, the regional myocardial contrast index was evaluated as the mean value in dyssynergic left ventricular segments (LVRCstI). After three months, the left ventricular regional contractility index (LVRCtrctI) was calculated as the sum of points in the segments which were dyssynergic in the initial study, divided by their number.

Results: 90% of segments with perfusion defects three days post-PCI demonstrated contractility defects (hypokinesia or akinesia) three months post-PCI. LVRCstI three days post-PCI correlated strongly with LVRCtrctI three months post-PCI (R2=0.7696). The sensitivity, specificity and accuracy of EC three days post-PCI in the prediction of recovery of left ventricular function were 88%, 80% and 86%, respectively.

Conclusions: The presence of myocardial perfusion in the region supplied by the infarct-related artery three days post-MI is indicative of myocardial survival and predicts the recovery of contractile function in this region in long-term observation.

Key words: contrast echocardiography, myocardial perfusion

Kardiol Pol 2006; 64: 455-461

Introduction

The occlusion of an infarct-related artery leads to local left ventricular (LV) contractility disturbances, which can persist for a few days after the infarction despite successful revascularisation. The presence of akinetic segments may be related to myocardial stunning or extensive necrosis. Differentiation between these two states is difficult, but crucial, as it affects therapeutic decisions and has prognostic value in patients with acute myocardial infarction (MI). There are a few methods which are applied to solve this problem. Several authors have suggested that contrast echocardiography, which permits an evaluation of the microcirculation immediately after revascularisation procedures, may fulfil this role [1, 2]. Left ventricular contractile function is dependent on myocardial perfusion. Experimental studies indicate that the immediate and complete restoration of perfusion leads to the survival of myocardial cells in the initially ischaemic "risk area" and makes the recovery of LV contractile function possible [3].

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Received: 28 July 2005. **Accepted:** 25 January 2006

The aim of the study was to assess the utility of contrast echocardiography in the prediction of LV function recovery in patients with anterior-wall acute MI treated by percutaneous coronary intervention (PCI), three months after revascularisation.

Methods

The study group comprised 86 consecutive patients (18 women, 68 men) with anterior MI, aged 29-78 (mean, 58.44±11.2), referred for invasive treatment to the Department of Haemodynamics and Angiography of the Cardiology Institute at the Jagiellonian University in Kraków as part of the Małopolska Province Interventional Treatment in Myocardial Infarction Programme [4]. The diagnosis of MI was made based on chest pain lasting more than 30 min, ST-segment elevation by at least 2 mm in two consecutive ECG leads, and elevation of creatine kinase and troponin levels.

Following admission, immediate coronary angiography and subsequent PCI were performed in all the patients.

Two-dimensional echocardiography with harmonic imaging (emitted ultrasound frequency, 1.88 MHz; received ultrasound frequency, 3.75 MHz) and echocardiographic contrast, using an Aloka device, immediately prior to and after PCI of the infarct-related artery, and three days post-PCI, were performed. The dynamic range was set at 60 dB. The gain and depth were individually adjusted for each patient and were not modified during the study. The ultrasound beam was focused at the level of the mitral valve. Image acquisition was performed using standard 50-60 Hz temporal resolution. Regional LV contractility was assessed by an analysis of two-dimensional cardiac images in the long- and short-axis parasternal and four- and two-chamber apical views. The LV was divided into 16 segments, each of which was rated according to a four-point scale (normokinesis, 1; hypokinesis, 2; akinesis, 3; dyskinesis, 4) [5].

Second-generation Optison contrast was used for contrast echocardiography. The contrast was administered as a peripheral intravenous bolus of 0.3-0.5 ml. Myocardial perfusion was assessed in real time using a low mechanical index (0.3) and harmonic imaging. A semi-quantitative evaluation of segmental myocardial perfusion was conducted by a visual analysis of the grey-scale intensity of individual LV segments, based on a 16-segment model and three-point scale (0, lack of perfusion; 0.5, partial perfusion; 1, normal perfusion, Figure 1). Segments with perfusion disturbances prior to PCI were noted. An increase in contrast intensity in a given segment following PCI was considered evidence of reperfusion. If the perfusion defect post-PCI was less than 25% of the initial value, a given patient was considered to have improved perfusion (*reflow*); if it exceeded 25%, the patient was assigned to the *no-reflow* group [6, 7].

The regional myocardial contrast index (LVRCstI) was calculated in the segments which were dyssynergic in the initial (pre-PCI) echocardiographic examination, based on a three-point scale (the sum of points in each segment divided by the number of segments analysed), three days after the infarction. Segments with homogeneous contrast levels were considered viable (1, normal perfusion).

After three months, segmental LV contractility was examined and compared with the results of the perfusion study three days post-PCI. The LV regional myocardial

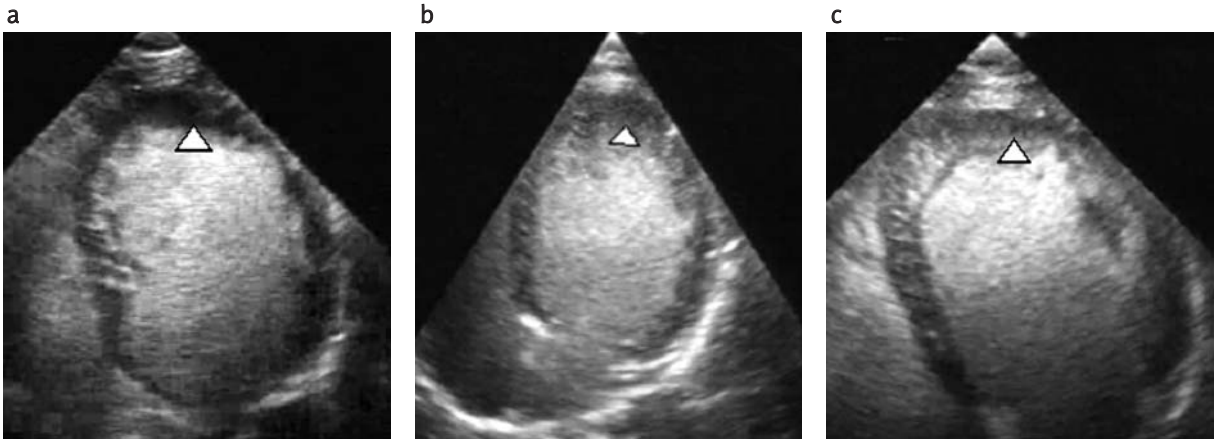

Figure 1. Evaluation of myocardial perfusion using a three-point scale: a: 0 – lack of perfusion, b: 0.5 – partial perfusion, c: 1 – normal perfusion

contractility index (LVRCtrctI) was calculated by an evaluation of contractility in the initially (pre-PCI) dyssynergic segments on a four-point scale (the sum of points in each segment divided by the number of segments analysed). Akinetic and hypokinetic segments were considered viable if, three months after PCI, contractility improved by one level (i.e. from akinesia to hypokinesia, or from hypokinesia to normokinesia); dyskinetic segments were considered viable if contractility improved by two levels (i.e. from dyskinesia to hypokinesia).

Statistical analysis

Continuous variables are presented as means ± standard deviation. The correlation between LV myocardial viability assessment by contrast echocardiography three days post-infarction and segmental viability assessment by conventional echocardiography (based on the recovery of contractility) after a three-month observation period was evaluated using Cohen's κ test. Kappa values >0.4, >0.6 and >0.8 represent poor, good and excellent correlation, respectively.

The relationship between the regional contractility index (LVRCtrctI) and regional contrast index (LVRCstI) was examined by linear regression analysis.

By comparing the results of myocardial perfusion analysis three days post-PCI by contrast echocardiography with LV contractility analysis three months post-PCI, we evaluated its sensitivity, specificity, accuracy, and positive and negative predictive values in the prediction of left ventricular contractile function recovery.

Results

Study population characteristics are presented in Table I.

Significant stenosis in the VI or VII segment of the left anterior descending coronary artery was found in all patients (mean, 92.3±12.6%). Forty five patients suffered from single-vessel coronary artery disease without lesions in other, 23 had two-vessel disease with haemodynamically insignificant stenosis (<50%) in another coronary artery, while 18 patients had significant (50-70% stenosis) atherosclerotic lesions in vessels other than the infarct-related artery.

On pre-PCI examination, 1293 of 1376 segments were successfully evaluated; contractility disturbances were present in 529 segments. Perfusion defects were demonstrated by contrast echocardiography in 478 of the 529 dyssynergic segments; 327 were akinetic, 10 were dyskinetic, and 141 were hypokinetic. Myocardial perfusion was normal in 51 dyssynergic segments (20 akinetic, 31 hypokinetic).

Post-PCI examination revealed an improvement in regional contractility and myocardial perfusion of LV – 442 dyssynergic segments were observed post-PCI. Perfusion

Table I. Characteristics of patients with and without an improvement of perfusion post-PCI.

	Study population (n=86)	Improved perfusion (n=54)	Unimproved perfusion (n=32)	p
Age [years]	58.4±11.2	55.7±11.9	63.04±9.7	0.0114
Female/Male [n]	18/68	11/43	7/25	0.5758
Time to angioplasty [h]	3.9±1.3	3.1±1.25	4.7±1.4	0.003
CK (U/L)	3973.32±3887.6	2940.4±3298.4	5694.7±4253.1	0.0034
CK/MB (U/L)	388.16±343.4	306.5±335.1	524.1±319.9	0.0033
Troponin (ng/ml)	57.5±85.7	37.9±74.1	87.2±94.9	0.0629
% arterial stenosis	92.3±12.6	90.1±13.8	95.9±9.0	0.0032
History of coronary artery disease [n]	18 (21%)	11 (20%)	7 (22%)	0.8935
No history of coronary artery disease [n]	68 (79%)	43 (80%)	25 (78%)	0.9548
Diabetes mellitus [n]	22 (26%)	12 (22%)	10 (31%)	0.4790
Hypertension [n]	52 (60%)	29 (54%)	23 (72%)	0.4143
Hyperlipidaemia a [n]	66 (77%)	44 (81%)	22 (69%)	0.6207
Tobacco smoking [n]	38 (44%)	14 (26%)	24 (75%)	0.0074
Family history of coronary artery disease [n]	31 (36%)	21 (39%)	10 (31%)	0.6222

Abbreviations: p – statistical significance of the difference between the groups with improved and unimproved perfusion; CK – creatine kinase; CK/MB, MB – fraction of creatine kinase

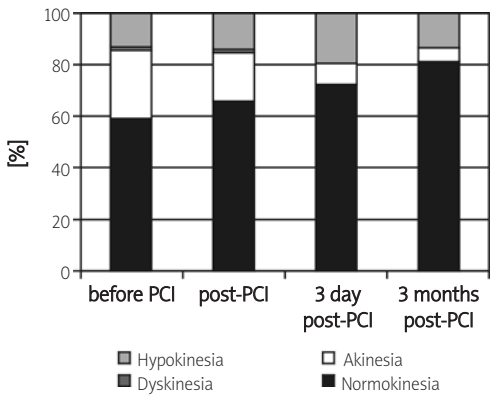

Figure 2. Percentage distribution of normokinetic and dyssynergic segments in the various observation periods

defects were present in 5 dyskinetic, 225 akinetic, and 119 hypokinetic segments. Perfusion was normal in 26 akinetic and 67 hypokinetic segments.

Perfusion disturbances were significantly decreased in 54 patients – the *reflow* group; perfusion did not improve significantly in 32 patients – the *no-reflow* group.

Three days post-infarction, both contractility and myocardial perfusion continued to improve in 35 patients; 233 of 358 dyssynergic segments (89 akinetic and 144 hypokinetic) demonstrated perfusion defects. Myocardial perfusion was normal in 16 akinetic and 109 hypokinetic segments.

After three months, echocardiography was performed in 84 patients (two subject from the *no-reflow* group died 5 and 6 days after MI respectively and 1263 of 1344 segments were successfully examined; 238 were dyssynergic (68 akinetic and 170 hypokinetic). Figure 2 presents the quantitative distribution of normokinetic and dyssynergic segments for each observation period.

Table II. Correlation between the assessment of myocardial viability in dyssynergic left ventricular segments three days post-PCI and the improvement of contractility of these segments after three months of observation

		LV contracility	
CE		Viable	Non-viable
	Viable	97	28
	Non-viable	23	210
	κ agreement	86% 0.72	

A further comparative analysis was performed on the segments which were initially dyssynergic (pre-PCI). A correlation analysis was performed based on echocardiographic examination results – LV myocardial viability assessment by contrast echocardiography three days post-infarction and evaluation of viable segments in which contractility improved in long-term observation.

Table II presents the correlation between myocardial viability analysis in dyssynergic LV segments three days post-PCI and contractility improvement in these segments three months post-PCI.

Of the 233 LV segments in which perfusion defects were observed three days post-infarction, 210 (90%) did not demonstrate improved contractility in long-term observation. Contractility improved after three months in 23 segments in which contrast echocardiography three days post-PCI revealed perfusion disturbances. 28 segments which did not improve contractility in long-term observation contained contrast on examination three days post-PCI.

The sensitivity, specificity, accuracy, and positive and negative predictive values of contrast echocardiography three days post-infarction for predicting the segmental recovery of LV contractile function were 88%, 80%; positive predictive value, 90%; 78%; and 86%, respectively.

Figure 3 depicts the correlation between LV regional myocardial contrast index (LVRCstI) three days post-PCI and the regional contractility index (LVRCtrctI) in long-term observation. Linear regression analysis revealed a significant correlation between LVRCtrctI and LVRCstI. Patients who demonstrated normal perfusion in relatively more of the initially dyssynergic segments three days post-PCI (i.e. higher LVRCstI) had a greater number of segments which regained their contractile function in long-term observation (i.e. lower LVRCtrctI).

Discussion

The prognostic assessment of patients with acute MI is extremely important, as it influences therapeutic decisions and allows for the identification of high-risk patients. Myocardial viability analysis plays a key role in this assessment. Contractile function of the infarct zone may be diminished for several days after reperfusion despite the preservation of myocardial viability. Several modalities can be used to identify viable myocardium, including low-dose dobutamine echocardiography, radionuclide studies, and magnetic resonance imaging. Magnetic resonance imaging is the most sensitive method (>90%), while positron emission tomography (PET) and dobutamine echocardiography are the most

specific in the identification of viable myocardium. The decision as to which method should be used for the assessment of myocardial viability must be based not only on their sensitivity and specificity, but also their availability and cost-effectiveness. The limited availability and high cost of magnetic resonance imaging and PET significantly limit their application in this field [8].

The prognostic role of contrast echocardiography in the assessment of myocardial viability in patients with acute MI has been underlined in recent years [9]. Ito et al. presented the first data on the value of reperfusion evaluation in patients with MI by contrast echocardiography in the prediction of LV contractile function recovery [10]. The authors were the first to administer echocardiographic contrast directly into the coronary arteries. The presence of a residual myocardial perfusion defect immediately after invasive treatment was a risk factor related to the lack of restoration of contractility in the infarction zone. Sabia et al. [11] observed the recovery of LV contractile function one month after reperfusion of an epicardial artery in patients in whom collateral circulation was visualised by the infusion of contrast into a non-infarct-related artery.

Contrast echocardiography is a useful method for the assessment of collateral blood flow, as angiography is limited to the assessment of vessels greater than 100 µm in diameter, while most collateral vessels are significantly smaller. Although other authors have confirmed the usefulness of this method, the optimal time for performing prognostic contrast echocardiography is yet to be determined. It is assumed that post-revascularisation hyperaemia, which could affect the accuracy of diagnosis, recedes within 24-48 hours after an infarction [12]. This does not, however, diminish the role of contrast echocardiography may play in making therapeutic decisions immediately after reperfusion, as well as identifying high-risk patients. The ability to perform several examinations, and thus to assess the dynamics of myocardial perfusion over time, is a further advantage of contrast echocardiography. Several data suggest that this is a dynamic process, and the effect observed immediately after PCI may change in response to various factors.

The first studies evaluating the prognostic significance of contrast echocardiography in the analysis of LV function recovery were published by Rocchi et al. [13]. The authors administered PESDA contrast intravenously in patients two days after an infarction. Left ventricular contractility was assessed six weeks after the infarction. Contractility was shown to have improved in LV segments which, despite being akinetic, demonstrated normal perfusion two days post-infarction. Dyssynergic segments without perfusion did not recover their contractile function. The authors

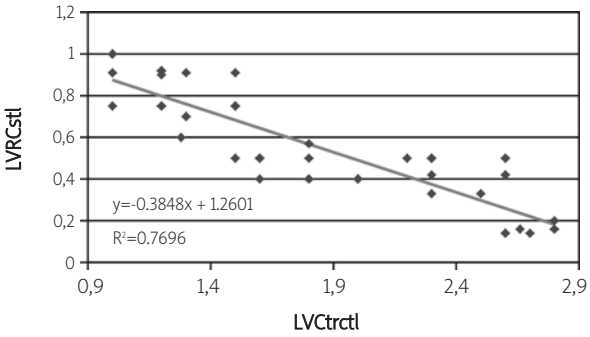

Figure 3. Linear correlation between LV regional myocardial contrast index (LVRCstI) three days post-infarction and regional contractility index (LVRCtrctI) after three months of observation

also demonstrated a strong correlation between myocardial perfusion assessment by contrast echocardiography and cardiac scintigraphy. Dynamic changes in microcirculatory perfusion were studied by other authors, using intravenous contrast. Kamp et al. [14] conducted serial examinations in patients with acute MI – immediately before PCI, and 1 and 12-24 hours after revascularisation. The extent of perfusion abnormalities in the examination 12-24 hours post-PCI predicted the recovery of contractile function in a given region four weeks after the infarction. In a multivariate analysis, the initial presence of TIMI 3 flow in the epicardial artery and the extent of the perfusion defect assessed after 12-24 hours were the independent predictors of restitution of LV contractile function.

Swinburn et al. [2], Lepper et al. [1], Brochet et al. [15], and Mengozzi et al. [16] suggested that contrast echocardiography may be useful in the prediction of LV contractility improvement. Main et al. [17] demonstrated that myocardial perfusion analysis two days after MI is a significant factor affecting the recovery of LV contractile function. According to the authors, 90% of segments which maintained perfusion two days post-infarction improved their contractility during long-term observation, whereas segments without perfusion failed to improve. The current study confirms this observation. Contractility did not improve in most segments with perfusion defects three days post-infarction. Similarly to previous authors, we demonstrated a strong correlation between LV regional contrast index three days post-infarction and LV regional contractility index during three-month observation [18, 19].

Greaves et al. [20] compared various methods applied in the analysis of myocardial perfusion, including contrast echocardiography and haemodynamic

parameters such as cTFC (corrected TIMI Frame Count) and MBG (Myocardial Perfusion Grade), and concluded that contrast echocardiography is most accurate in the prediction of recovery of contractile function.

Although our results appear promising, it is worth noting a few limitations. The study population consisted exclusively of patients with acute anterior MI due to the homogeneity of this group and the high accuracy of contrast echocardiographic examination of the anterior wall.

Conclusions

The presence of myocardial perfusion in the region supplied by the infarct-related artery three days after anterior MI is indicative of myocardial viability and allows the recovery of LV contractile function to be predicted.

The regional contrast index of the infarct zone, evaluated three days post-PCI, correlates with the regional contractility index of this area after three months of observation.

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Wartość prognostyczna echokardiografii kontrastowej w ocenie powrotu funkcji lewej komory u chorych z ostrym zawałem serca ściany przedniej

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Streszczenie

Wstęp: Natychmiastowe i całkowite przywrócenie perfuzji u chorych z ostrym zawałem serca (AMI) prowadzi do zachowania żywotności komórek miokardium w obszarze wyjściowego niedokrwienia – *risk area* i pozwala na powrót skurczowej funkcji lewej komory.

Cel: Celem pracy była ocena przydatności echokardiografii kontrastowej (EK) w przewidywaniu powrotu funkcji lewej komory u chorych z AMI leczonych przezskórną interwencją wieńcową (PCI).

Materiał i metody: Badaniami objęto 86 chorych (średni wiek 58,4±11,2 lat) z AMI ściany przedniej, u których wykonano PCI gałęzi przedniej zstępującej lewej tętnicy wieńcowej. Badanie echokardiograficzne dwuwymiarowe i z zastosowaniem echokardiograficznego kontrastu Optisonu wykonywano bezpośrednio przed i po PCI, a także w 3. dniu po PCI. Zakontrastowanie mięśnia serca oceniano w skali trójstopniowej: 0 – brak perfuzji, 0,5 – częściowa perfuzja, 1 – prawidłowa perfuzja. W 3. dobie po PCI oceniano regionalny wskaźnik zakontrastowania miokardium jako średnią wartość w dyssynergicznych segmentach lewej komory (RWKonLK).W ciągu 3 mies. obliczano regionalny wskaźnik kurczliwości lewej komory (RWKLK) w obszarze dyssynergicznych segmentów obecnych w badaniu wyjściowym jako sumę punktów poszczególnych segmentów podzieloną przez liczbę ocenianych segmentów.

Wyniki: W 90% segmentów z defektem perfuzji 3. dnia po PCI obserwowano zaburzenia kurczliwości lewej komory pod postacią hipokinezy lub akinezy w okresie 3 mies. po PCI. Stwierdzono wysoką korelację pomiędzy RWKonLK w 3. dobie po PCI a RWKLK ocenianym w okresie 3 mies. obserwacji (R^2=0,7696). Czułość, swoistość i dokładność EK wykonanej w 3. dobie po PCI w przewidywaniu powrotu funkcji skurczowej lewej komory wynosiła odpowiednio 88%, 80% i 86%.

Wnioski: Obecność perfuzji mięśnia sercowego w obszarze zaopatrywanym przez tętnicę dozawałową 3. dnia po zawale serca świadczy o jego żywotności i jest czynnikiem warunkującym poprawę funkcji skurczowej tego obszaru w odległej obserwacji.

Słowa kluczowe: echokardiografia kontrastowa, perfuzja mięśnia sercowego

Kardiol Pol 2006; 64: 455-461

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Praca wpłynęła: 28.07.2005. **Zaakceptowana do druku:** 25.01.2006.