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The comparison of contrast echocardiography and tissue Doppler imaging for evaluation of reperfused myocardium in patients with acute anterior myocardial infarction

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Abstract

Background: *Prediction of functional myocardial recovery post acute myocardial infarction should be based not only on flow patency of the infarct related artery (IRA) but also on the quality of microcirculation in at-risk segments. Myocardial blush grade (MBG) is a method of perfusion assessment which has an established value in prediction of both ventricular remodelling and prognosis. However, its invasive character encourages the search for other methods able to reflect myocardial recovery following successful reperfusion. Echocardiography is an imaging modality which has the potential to assess, noninvasively, myocardial perfusion and, quantitatively, the loss of contractile function. The aim of this study was to compare the values of myocardial contrast echocardiography (MCE), MBG and tissue Doppler imaging (TDI) in the assessment of microcirculation in patients with first acute myocardial infarction of the anterior wall.*

Methods: *The study group consisted of 39 patients (15 female and 24 male, mean age 58.8 ± ± 12.2 years) with first anterior infarction within 6 hours of chest pain onset. All patients underwent angioplasty of the anterior descending artery (LAD). Myocardial blush grade was assessed directly after angioplasty, whereas MCE using SonoView contrast accompanied by TDI study was performed 4 days thereafter.*

Results: *Neither of the quantitative MCE parameters showed significant correlation with perfusion assessed by MBG. Significant negative correlation of MBG was found with maximal systolic strain (ε) ($R = -0.51$, $p = 0.003$) and post systolic shortening ($R = -0.49$, $p = 0.007$) in infarcted segments, but this was not the case with the unaffected segments.*

Conclusions: *Use of MCE in the assessment of myocardial perfusion in myocardial infarction is limited, as shown by poor correlation with MBG. The presence of impaired contractile function by TDI corresponds better with myocardial perfusion than MCE does.* (Cardiol J 2008; 15: 548–554)

Key words: myocardial perfusion, myocardial blush grade, echocardiography

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Introduction

The fundamentals of modern treatment of myocardial infarction are based on the restoration of normal flow in the infarct related artery. Such a strategy is supported by many observations demonstrating that the presence of impaired flow is associated with significantly worse left ventricular function recovery and prognosis. It is estimated that less than 60% of patients with acute ST-segment elevation myocardial infarction (STEMI) undergoing thrombolytic therapy achieve normal flow in the infarct related artery (Thrombolysis In Myocardial Infarction [TIMI] grade 3) [1]. Therefore, it is essential to assess the patency of the infarct related artery since it may influence further treatment for STEMI, including the invasive approach, which is also reflected by current standards in myocardial infarction.

The information regarding the restoration of flow in infarct related artery may be drawn from various observations, such as: cessation of chest pain, ST-segment elevation resolution, assessment of serum concentration of biochemical markers of cardiac tissue necrosis and others [2]. However, it delivers only crude information, which, in some cases, can even be confounding. The ischemic episodes often brake down the coronary microvasculature, and therefore the flow to the infarct related artery may be markedly decreased despite the patent epicardial artery. This defect of perfusion within reperfused myocardium following acute ischemia and/or infarction is known as a no-reflow phenomenon [3].

A very promising method for the assessment of myocardial perfusion is contrast echocardiography (MCE). Some studies have shown that MCE performed after reperfusion can accurately demonstrate no reflow, and predict recovery of left ventricular function [4–6]. However, a direct comparison of MCE with dobutamine stress echocardiography (DSE) in patients with fully restored flow and no residual stenosis shows that reperfused segments at MCE often did not present functional improvement, whereas functional recovery could be more accurately determined by DSE [7]. It is hypothesized that MCE, due to hyperemic flow after reperfusion, can underestimate the infarct size and overestimate myocardial salvage. Moreover, no comparison between MCE and myocardial blush grade (MBG) was performed which is fundamental for a diagnosis of no reflow.

These ambiguous results raise the question of whether other echocardiographic techniques can be superior to MCE in the diagnosis of no reflow and its consequences. It was shown that the regional function of myocardium can be quantitatively assessed by tissue Doppler imaging (TDI) echocardiography. Moreover, this modality demonstrates different patterns for the diagnosis of nonischemic, ischemic and necrotic myocardium [8, 9].

Thus the aim of this study was to compare the results of MCE and TDI in respect to myocardial perfusion assessed by MBG directly post PCI in patients with acute myocardial infarction.

Methods

Patient characteristics

The study group consisted of 39 patients, 15 female and 24 male, admitted to the hospital with first acute anterior myocardial infarction within 6 hours from the onset of chest pain. Mean age was 58.8 ± 12.2 years. All patients had the indication for percutaneous angioplasty (PCI). Fourteen of them had non-ST-segment elevation myocardial infarction (NSTEMI), and 25 patients had STEMI. The diagnosis of STEMI and NSTEMI was established according to European Society of Cardiology (ESC) criteria based on the electrocardiogram changes and elevation of biochemical markers: concentration of creatine kinase MB-fraction (CK-MB) and troponin T (TnT). The mean of maximal serum concentration of CK-MB was 195.8 ± 158.7 UI/L and TnT 4.67 ± 4.98 UI/L.

The study protocol was approved by the local medical ethics committee and all patients provided informed consent.

Study protocol

All patients enrolled to the study had angiography performed shortly after admission to the hospital, followed by PCI. In the acute phase, all patients received the pharmacological regimens according to ESC standards adjusted to individual clinical presentation. On the fourth day of infarction echocardiographic examination was performed including: standard transechocardiographic echocardiography, TDI imaging and MCE.

Angiography

Coronary angiography was performed in standard views. The angiograms before and after PCI were digitally recorded to assess the flow and myocardial perfusion. The assessment of flow in the infarct-related vessel was done using the TIMI scale, and myocardial perfusion was evaluated according to MBG. The analysis was done by the angiographer blinded to the echocardiographic and ECG data.

Two-dimensional, M-mode and Doppler echocardiography

Standard transthoracic echocardiography was performed in all patients followed by TDI imaging and MCE by an experienced echocardiographer using a VIVID 5 (General Electric) machine equipped with a 2.5 MHz wideband transducer. Images were captured in 5 standard views (parasternal, long- and short axis, and apical 4-, 2- and 3-chamber). The data were digitally recorded, stored and then analyzed with ECHOPAC software. The dimensions of the left ventricle were measured in M-mode according to the recommendations of the American Society of Echocardiography (ASE). Based on these measurements, fractional shortening was derived. Left ventricular (LV) biplane ejection fraction (EF) was calculated based on the Simpson formula in apical 4- and 2-chamber views. M-mode presentation was also used for the assessment of mitral annulus plane systolic excursion (MAPSE) by the placement of the M-mode line perpendicular to the plane of the mitral valve in four chamber view.

Myocardial contrast echocardiography

Myocardial contrast echocardiography was performed using pulse inversion harmonic imaging (mechanical index about 0.9). The gain setting controls were adjusted at the beginning of each study and kept unchanged throughout the study. Time and lateral gain compensation adjustments were also made in order to have a homogenous myocardial brightness. Focal zone depth was set at about 1/3 of the image. Slow boluses of 2.5 mL of SonoView (Bracco, Italy) were injected intravenously followed by a saline flush over 60 s, and then images were captured over 10 consecutive cardiac cycles. The recordings were done in standard apical 4- and 2-chamber views, stored digitally and later analyzed using ECHOPAC software including the most affected walls based on two-dimensional wall motion analysis and ECG. Quantitative assessment of perfusion was performed offline, including plateau myocardial intensity (A, representing capillary blood volume), rate of rise of slope (β, representing mean myocardial red blood cell velocity) and their product ($A \times \beta$, representing myocardial blood flow) at end-systole, respectively, for infarcted, border zone and non-infarcted areas.

Tissue Doppler imaging echocardiography

All the images in TDI mode were recorded during a short period of apnea, during one ECG cycle with pulse repetition frequency exceeding 120 frames per second. Special attention was paid to obtaining the narrowest angle between the ultrasound beam and the long axis of the analyzed wall. TDI data were analyzed for the following areas of selected myocardial segments: infarcted (apical segments), border zone and non-infarcted (basal segments) area. Adequate localization of sample volume within these areas was based upon tissue tracking in 2-dimensional (2-D) presentation. The basic intervals of cardiac cycle were established according to the ECG tracings. The maximal velocity (VEL), maximal strain (ε) and maximal strain rate (SR) were calculated for the ejection period, end-systole and during diastole intervals. The post systolic shortening (PSS) was defined as the difference between maximal strain in diastole and end-systolic strain.

Statistical analysis

Statistica 6 software (StatSoft, Tulsa, USA) was used for statistical analysis. All the values were presented as arithmetic mean values and standard deviations. The differences in echocardiographic parameters in respect to MBG were assessed by ANOVA test. Spearman correlation was used to determine the relationship between MBG and echocardiographic parameters. The correlations were considered to be significant if the significance level (p) was < 0.05.

Results

Before PCI only 6 patients had a normal flow in the infarct related artery (TIMI 3), but normal myocardial perfusion (MBG 3) was observed only in 1 case. After PCI, in the majority of the study group, TIMI 3 arterial flow was achieved (26 patients); however, it was accompanied by MBG 3 only in 7 cases (Fig. 1). The results of 2-D and

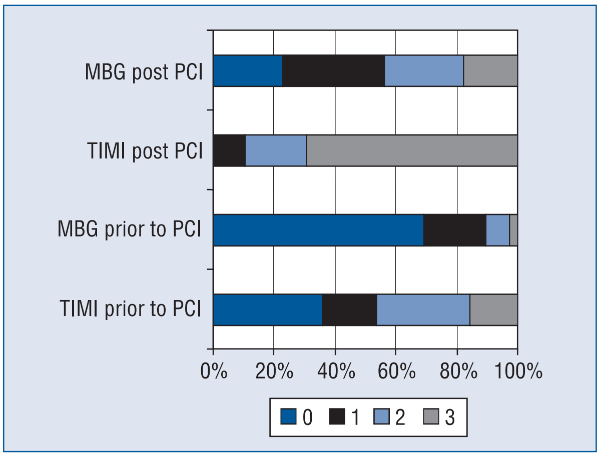

Figure 1. Thrombolysis In Myocardial Infarction (TIMI) and myocardial blush grade (MBG) prior and post percutaneous transluminal intervention (PCI).

Table 1. The results of 2-dimensional and M-mode assessment of left ventricle and Spearman correlation with myocardial blush grade (MBG) in the study group.

	Mean	SD	Minimal	Maximal	Correlation with MBG (Spearman r)	P
Left ventricular mass [g]	242.68	62.89	151	435	0.13	0.49
End diastolic dimension [mm]	50.96	5.12	41	60	0.09	0.60
End systolic dimension [mm]	35.68	4.95	24	46	0.22	0.20
Shortening fraction [%]	30.24	7.74	16	43	0.27	0.79
Posterior papillary muscle to fibrous annulus dimension [mm]	41.63	7.21	28	57	0.01	0.97
Tenting area [cm^2]	2.62	0.78	1.08	4.3	0.18	0.31
Diastolic LV area in 4CH [cm^2]	26.92	5.99	16.09	41	–0.04	0.81
Systolic LV area in 4CH [cm^2]	18.11	5.42	6	28.6	0.03	0.83
End diastolic volume [mL]	79.18	25.7	37	144	0.06	0.73
End systolic volume [mL]	41.42	16.74	13	84	0.06	0.72
Ejection fraction [%]	47.78	12.13	15	74	0.14	0.42
Mitral annulus plane systolic excursion [cm]	1.09	0.72	0.5	5	0.18	0.29

LV — left ventricle; CH — chamber

Table 2. The results of tissue Doppler imaging assessment of non-infarcted, border zone and infarcted myocardium and Spearman correlation with myocardial blush grade (MBG) in the study group.

	Mean	SD	Minimal	Maximal	Correlation with MBG (Spearman r)	P
$VEL_{non\ infarcted\ myocardium}$ [cm/s]	3.73	1.49	0.3	6.08	–0.03	0.8824
$VEL_{border\ zone}$ [cm/s]	2.75	1.49	0.2	6.73	0.06	0.7499
$VEL_{infarcted\ myocardium}$ [cm/s]	1.95	1.69	0.12	6.44	0.15	0.3927
$SR_{non\ infarcted\ myocardium}$ [s^{-1}]	–1.12	0.60	–2.2	–0.03	–0.05	0.7801
$SR_{border\ zone}$ [s^{-1}]	–0.69	0.47	–1.9	0.2	–0.29	0.1077
$SR_{infarcted\ myocardium}$ [s^{-1}]	–0.36	0.42	–1.8	0.13	–0.22	0.2111
$\varepsilon_{non\ infarcted\ myocardium}$ [%]	–14.78	7.87	–30.0	–1.6	–0.11	0.5500
$\varepsilon_{border\ zone}$ [%]	–9.0	7.63	–25.0	7.8	–0.32	0.0665
$\varepsilon_{infarcted\ myocardium}$ [%]	–2.4	8.2	–29.0	19.3	–0.51	0.0029*
$PSS_{non\ infarcted\ myocardium}$ [%]	2.37	7.14	–16.3	19.9	–0.15	0.4101
$PSS_{border\ zone}$ [%]	–9.8	6.95	–25.0	–1.3	–0.31	0.0825
$PSS_{infarcted\ myocardium}$ [%]	–3.5	7.06	–29.0	7.5	–0.49	0.0068*

VEL — myocardial velocity; SR — strain rate; ε — strain; PSS — post systolic shortening; *statisticaly significant

M-mode assessment of the LV are shown in Table 1. The comparison of these parameters did not reveal any significant differences among patients in respect to MBG achieved after PCI. Nevertheless, no correlation was found between MBG and standard 2-D and M-mode parameters (Table 1).

The results of TDI, including the maximal systolic VEL, SR, ε and PSS, respectively, for infarcted area, border zone and non infarcted myocardium, are given in Table 2. Strain curves for both the infarcted segment with a pronounced PSS and the referral segment are illustrated on Figure 2. The significant differences in maximal systolic strain ($\chi^2 = 8.21$; $p = 0.042$), and in PSS ($\chi^2 = 8.49$; $p = 0.037$), were found regardless of MBG achieved after PCI in infarcted segments. Also, the negative correlations of MBG with maximal systolic ε and PSS were found in infarcted myocardium, whereas no such relation was detected for other segments.

Figure 3 shows the wash-in curve of echocardiographic contrast for the infarcted segment. The mean, maximal and minimal, and standard deviation for quantitative MCE parameters and their correlation with MBG are shown in Table 3. None of

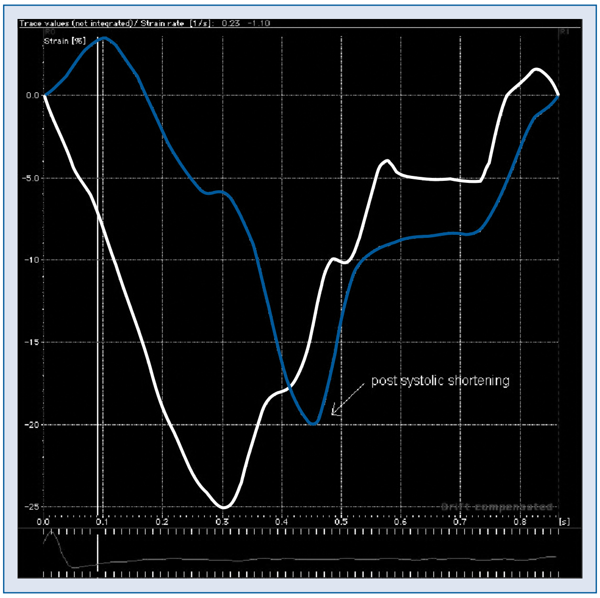

Figure 2. Strain curves for infarcted segment (blue line) and referral segment (white line). The systolic strain is decreased, and significant post-systolic shortening is present in the infracted area.

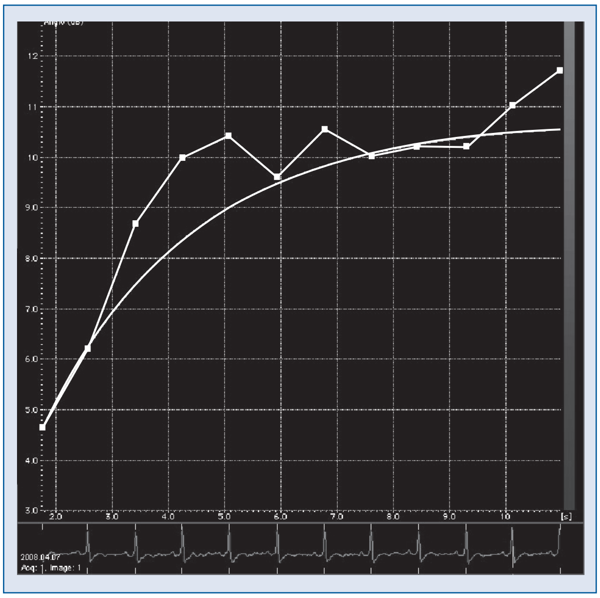

Figure 3. Wash-in curve of echocardiographic contrast for the infarcted segment.

Table 3. The results of myocardial contrast echocardiography assessment of non-infarcted, border zone and infarcted myocardium and Spearman correlation with myocardial blush grade (MBG) in the study group.

	Mean	SD	Minimal	Maximal	Correlation with MBG (spearman r)	P
$\beta_{\text{non infarcted myocardium}}$ [1/s]	0.15	0.43	–0.0002	2.28	0.097	0.57
$\beta_{\text{border zone}}$ [1/s]	0.11	0.48	–0.0005	2.87	–0.08	0.63
$\beta_{\text{infarcted myocardium}}$ [1/s]	0.04	0.08	–0.019	0.32	0.06	0.73
$A_{\text{non infarcted myocardium}}$ [dB]	58.15	19.04	26.20	96.00	–0.12	0.51
$A_{\text{border zone}}$ [dB]	55.52	22.17	10.10	96.20	0.15	0.39
$A_{\text{infarcted myocardium}}$ [dB]	51.05	21.72	0.00	89.00	0.09	0.58
$\beta \times A_{\text{non infarcted myocardium}}$	3.34	5.55	0.016	27.50	0.13	0.47
$\beta \times A_{\text{border zone}}$	2.23	3.44	0.004	13.90	–0.07	0.68
$\beta \times A_{\text{infarcted myocardium}}$	2.83	5.50	0.00	22.80	0.16	0.35

β — rise of slope of replenishment curve; A — myocardial plateau

these parameters showed a significant difference by ANOVA test regarding the final MBG. No significant correlation was found between MBG and A, β or A $\times$ β in the studied group.

Discussions

The course of LV remodelling, as well as the mortality of patients post myocardial infarction, depends on the success of reperfusion in infarcted myocardium as was proved in respect to either STEMI or NSTEMI [10, 11]. Traditionally, the procedural success of PCI was related to TIMI flow in infarcted artery; however, it is already known that the ischemic episodes may result in serious damage to coronary microvasculature resulting in a decrease of flow in infarcted myocardium ("no-reflow phenomenon"). MBG is a simple angiographic marker of microvascular reperfusion. Patients showing improved final MBG have reduced infarct size as judged by cardiac enzyme release, higher EF and lower mortality [12–14]. Despite its value, MBG has some disadvantages. First, it requires an invasive procedure, which in some centres is unavailable. Second, adequate prognosis may require a repetitive assessment of myocardial perfusion [15]. Some data suggest that echocardiography may successfully determine perfusion in myocardium. Especially promising results in the assessment of myocardial perfusion were presented with the use of ultrasound contrast [16]. An important finding of this study was to demonstrate that in patients presenting with first acute myocardial infarction, the contractile pattern of myocardium assessed by tissue Doppler imaging corresponds better with MBG than with quantitative parameters derived from MCE. Most of the studies documenting good results in detecting "no-reflow phenomenon" with MCE did not use any referral method to assess myocardial perfusion, whereas the validation of this method by comparison with SPECT varied from an almost perfect concordance to a limited correlation [17, 18]. Moreover, no SPECT analysis was performed in patients with acute myocardial infarction treated invasively. Consequently, this is, to the knowledge of the authors, the first study to compare MCE results with MBG perfusion in this group of patients. On the other hand, in this study the perfusion by MBG and MCE was not performed simultaneously. The MCE study was postponed by up to 4 days due to the latest safety recommendation of SonoView. The current safety policy states that contrast agents should not be used in the acute phase of myocardial infarction. Thus, as was shown by Kamp et al. [19], the perfusion defect dynamically changes during the time after restoration of the flow, and in this study the results of MCE could be different from those evaluated early post PCI.

The second very important finding was the correlation of TDI pattern with MBG. TDI has an established position in the quantitative regional assessment of the contractile function of myocardium. It successfully differentiates ischemic from non-ischemic, as well as viable from non-viable, myocardium. This means that MBG potentially can better predict the functional recovery of infarcted myocardium than is possible with MCE. This is in contrast to the conclusions of the studies performed by Swinburn et al. [5] and Brochet et al. [20]. However, both studies were based only on qualitative analysis of both myocardial perfusion with echocardiographic contrast and contractile function of myocardium. From a pathophysiological point of view, it is also important that perfusion by MCE can improve in the infarct related area due to patent microcirculation despite the lack of functional integrity of the cell membrane, which is necessary for functional recovery. Thus MCE can overestimate residual viability. As a consequence, MBG assessed directly after PCI can better correspond to functional recovery, which is presented by TDI parameters.

Other methodological factors could also influence our results. Performing the MCE may generate practical difficulties in setting up the optimal parameters. Moreover, we used a single bolus of echocardiographic agent, whereas more repetitive results could be expected with continuous injection of SonoView.

Conclusions

The study showed that disturbances in the microvascular flow in infarcted myocardium may persist despite successful PCI. The use of MCE in the assessment of myocardial perfusion in myocardial infarction is limited, as shown by poor correlation with MBG. The presence of impaired contractile function by TDI better corresponds to myocardial perfusion than MCE does.

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