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VIABILITY

Late Improvement of Regional Wall Motion After the Subacute Phase of Myocardial Infarction Treated by Acute PTCA in a 6-Month Follow-Up

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ABSTRACT

Background. The aim of this follow-up study was to investigate the late effects of acute coronary angioplasty (PTCA) on regional wall motion after the subacute phase of myocardial infarction (MI). *Methods and Results*. Seventeen patients were investigated initially at a median of 11 days and again at 6 months after acute PTCA for myocardial infarction (< 8 hours after onset of symptoms) by cardiac magnetic resonance imaging. Corresponding short-axis slices encompassing the left ventricle (LV) were acquired using a standard cine MR for regional wall motion analysis and using delayed contrast enhanced magnetic resonance imaging (ceMRI) for infarct size quantification. The infarct size was similar in the subacute phase and the 6 month follow-up (20.8 and 21.9%, respectively; n.s.). Regional wall motion improved significantly in the area of hyperenhancement [percentage wall thickening (PWT) 21.9% and 37.9%, $p < 0.05$] in contrast to remote normal myocardium (46.4% and 38.4%; n.s.). Regional wall motion was significantly poorer in transmural compared with nontransmural MI in the subacute stage, and a late improvement could only be observed in transmural MI. *Conclusion*. Transmural areas of hyperenhancement displayed significant late long-term improvement of regional wall motion after acute PTCA, possibly related to prolonged stunning compared with nontransmural areas.

Key Words: Contrast enhanced magnetic resonance imaging (ceMRI); Acute PTCA; Myocardial infarction; Global and regional myocardial function; Follow-up study.

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INTRODUCTION

Myocardial infarction (MI) is still a major health problem and the most frequent cause of mortality in Western countries (Mortality from coronary heart disease and acute myocardial infarction—United States, 2001). Early revascularization (thrombolysis, acute PTCA) minimizes infarct size and improves myocardial function (Liem, 1998; Ottervanger et al., 1999) and long term prognosis (Ito et al., 1996; Wu et al., 1998a).

Precise cardiac magnetic resonance imaging (MRI) can now be applied to study the long-term effects of acute PTCA not only on global myocardial function, but also on infarct size and regional myocardial function. We hypothesize a beneficial effect of acute PTCA on myocardial function over a follow-up period of 6 months, likely inversely related to the transmural extent of MI (Choi et al., 2001; Gerber et al., 2001; 2002; Kim et al., 2000). A long-term beneficial effect on regional myocardial function could partially be responsible for reduced mortality in earlier studies (Ito et al., 1996; Wu et al., 1998a).

Combining functional magnetic resonance imaging and delayed contrast enhanced magnetic resonance imaging (ceMRI), quantification of the area of hyperenhancement as the area of infarction (IA) at any stage of myocardial infarction and quantification of the regional and global left ventricular function is amenable noninvasively (Kim et al., 1999). With the implementation of T1-weighted contrast enhanced magnetic resonance imaging techniques, an identification of the area of infarction has become possible (Eichstaedt et al., 1986). Planimetry of the left ventricle and the area of hyperenhancement can be performed to measure the size and the transmural extent of MI (Kim et al., 2000). Previous studies determined the improvement of global ejection fraction and regional wall motion in patients with acute MI after direct coronary angioplasty in a 7-day follow-up period (O'Keefe et al., 1992). In a recent study, Choi et al. (2001) investigated the improvement of regional myocardial function after revascularization (not confined to acute PTCA) of acute myocardial infarctions over a 3-month follow-up.

In contrast to these studies, we compared regional wall thickening in the hyperenhanced areas of patients who underwent acute PTCA of the infarct-related artery. Comparisons were made by performing cardiac MR imaging in the subacute phase of MI and after remodeling and healing processes 6 months later. The aim of our study was to identify the influence of acute PTCA on regional myocardial function using a long-term cardiac MRI study design.

METHODS

Patients

Seventeen patients (13 males, 4 females), with a recent history of first myocardial infarction (< 21 days) treated by acute PTCA within 8 hours of symptom onset, were investigated. The same MR protocol was performed in the subacute phase of myocardial infarction and 6 months later.

Inclusion Criteria

Patients with first myocardial infarctions diagnosed by typical electrocardiogram (ECG) changes and/or elevated cardiac enzymes (CK > 2–2.5 fold, CK − MB/CK > 8%, or TnI higher than the given normal range) and acute coronary angioplasty of the infarct-related artery within 8 hours of symptom onset were included. All patients gave written informed consent to participate in this study, which had been approved by the local ethics committee.

Exclusion Criteria

Patients with unstable clinical conditions, claustrophobia, premature ventricular contractions, atrial fibrillation, former myocardial infarction, or pacemakers were excluded.

MR Imaging

Imaging was performed on a 1.5 Tesla whole body imager (Magnetom Vision MR scanner, Siemens Medical Systems, Erlangen, Germany) using the phased-array coil for signal detection.

For global and regional myocardial function analysis, an ECG-triggered segmented fast low angle shot (FLASH)-2D-sequence (TR/TE 100/4.8 ms, Echo-View-Sharing, Flip angle = 20°, 8 mm slice thickness with 10 mm slice distance) was used for acquisition of short-axis slices in a single breath-hold encompassing the left ventricle. The effective temporal resolution was 50 ms.

Delayed ceMRI technique was performed 15–20 minutes after administration of 0.2 mmol per kg body weight Gd-DTPA (Magnevist®, Schering, AG, Berlin, Germany) with a segmented inversion recovery TurboFLASH pulse sequence (TR/TE 250/3.4 ms, TI 150–250 ms, FoV 350 × 350 mm^2, in-plane resolution 1.37 × 1.85 mm^2, slice thickness 7 mm, slice gap 10 mm). Corresponding short-axis slices were acquired as for cine measurements.

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Data Analysis

Global and regional left ventricular function was analyzed using Argus-Software, Release 2.3 (Siemens, Erlangen, Germany). Epicardial and endocardial contours in end-systolic and end-diastolic images of each slice were drawn manually. End-systolic volume index (ESVI), end-diastolic volume index (EDVI), and stroke volume index (SVI) were used as variables for global left ventricular function. Percentage wall thickening [PWT (%)] as a regional myocardial function parameter and end-diastolic wall thickness [EDWT (mm)] were calculated for 40 segments in each slice. Percentage wall thickening was derived from the following formula (i):

(i) PWT (%) = 100 × (end-systolic thickness (mm) − end-diastolic thickness (mm))/end-diastolic thickness (mm).

Planimetrical determination of hyperenhanced areas (HE) and of the entire area of the left ventricle (LV) was done for each slice using Adobe®-Photoshop 5.0 (San Jose, CA, USA) in ceMRI images. Infarct size as a percentage of left ventricular mass was calculated for each patient [formula (ii)]:

(ii) Percentage size of infarction (PSI) (%) = hyperenhanced area × 100/area of left myocardium

The PWT (%) for hyperenhancing segments and six remote segments were calculated for each patient. If any of the contrast-enhanced short-axis slices showed a transmural extent of hyperenhancement, the patient was considered to have a transmural myocardial infarction.

Statistical Analysis

For statistical analysis and data presentation, distribution-free tests and parameters were used (Kusuoka and Hoffman, 2002), making assumptions on the data distribution unnecessary. Regional left ventricular function was tested for differences between area of hyperenhancement and the remote nonhyperenhanced myocardium using the signed rank test (Conover, 1980; Kusuoka and Hoffman, 2002; Siegal, 1988). The same test was used for analysis of differences between the two MR scans (subacute phase and follow-up). To compare parameters of patients with nontransmural and transmural myocardial infarction, the Mann–Whitney U test for untied variables was used (Conover, 1980; Kusuoka and Hoffman, 2002; Siegal, 1988). All p values to be presented in the following should be regarded as descriptive p values, since they were not formally adjusted for multiplicity (Dunn, 1993). A p value ≤ 0.05 therefore indicates statistical significance.

Data description was based on medians, quartiles, minimum, and maximum [median (Q1;Q3;Min;Max)], and graphical presentation on nonparametric box plots, accordingly. Numerical analysis was drawn out using SigmaStat (Release 2.03) (SPSS Inc., Chicago, IL, USA), and graphics were generated using SigmaPlot (Release 4.0) (SPSS Inc., Chicago, IL, USA).

RESULTS

Demographic Data, Cardiac Enzymes, Infarct-Related Artery, and Infarct Size

All 17 patients with a median age of 55 years (45, 61, 38, 77) underwent two MR investigations with the same protocol in the subacute and chronic phases of myocardial infarction. The first MR measurement was 11 days (6, 14, 4, 20) after acute PTCA and the second 195 days (171, 414, 152, 598) later. All images were of good quality and were included in analysis. In 8/17 cases the left anterior descending artery (LAD) was the infarct-related artery, in 5/17 the left circumflex artery (Cx), and in 4/17 the right coronary artery (RCA). Peak CK and peak TnI were 1235 U/l (725, 1819, 265, 4045) and 79 ng/ml (20.4, 146.6, 2.5, 489.4), respectively. In all 17 patients the hyperenhanced areas were found in myocardial regions of the infarct-related artery-dependent myocardium (Table 1). Infarct size was similar in the subacute phase and the follow-up—20.8 (12.2, 32.8, 0.0, 39.0) and 21.9 (12.3, 29.0, 4.7, 46.4), respectively (n.s.) (Table 1, Fig. 1). At follow-up patient 2 showed an occluded infarct-related artery. All other patients undergoing a control angiography showed thrombolysis in myocardial infarction (TIMI) III flow in the infarct-related artery. Four patients were asymptomatic and showed no sign of ischemia during exercise tolerance testing, and a second coronary angiogram thus was not performed.

Global Left Ventricular Function

In the first study during the subacute phase of myocardial infarction the end-diastolic volume index (ml/m^2) was 57.5 (41.8, 76.2, 34.0, 99.5) and 47.2 (40.6, 60.3, 27.6, 67.5) in the chronic phase (n.s.). Values for end-systolic volume index (ml/m^2) did not reveal a statistically significant difference (n.s.)

Table 1. Demographic data, infarct-related artery (IRA), transmural extent of MI, change of regional wall motion during the study period.

Patient	Age (years)	Sex	IRA	MRI extent	IA	Δ PWT (%)	Δ PSI (%)	Δ SVI (ml/m^2)	Δ EDVI (ml/m^2)	Δ ESVI (ml/m^2)
1	41	m	LAD	Transmural	Anterior	−25.8	−17.2	11.5	20.3	8.8
2	48	m	LAD	Transmural	Anterior	52.6	6.6	−18.9	−35.3	−16.3
3	41	f	LAD	Nontransmural	Anterior	31.1	5.5	2.3	13.6	11.3
4	46	m	LAD	Nontransmural	Anterior	106.4	22.1	3.1	21.0	17.9
5	70	m	LAD	Transmural	Anterior	−8.6	−14.3	5.3	2.5	−2.8
6	56	m	CX	Transmural	Posterolateral	35.6	0.3	−25.2	−41.7	−16.5
7	55	m	RCA	Nontransmural	Posterior	3.1	2.1	−15.5	−10.3	5.2
8	51	m	LAD	Nontransmural	Anterior	34.0	−10.5	−19.7	−37.3	−17.5
9	38	m	LAD	Transmural	Anterior	−12.1	10.5	−18.9	−37.2	−18.3
10	59	f	RCA	Transmural	Posterior	16.6	4.3	−1.1	−5.8	−4.8
11	41	m	LAD	Nontransmural	Anterior	63.8	0.0	−23.7	−33.1	−9.5
12	60	f	CX	Transmural	Posterolateral	40.5	9.8	−1.1	−15.9	−14.9
13	66	f	CX	Nontransmural	Posterolateral	−32.8	11.9	−2.5	−0.1	2.3
14	77	m	RCA	Transmural	Posterior	9.6	0.8	−25.1	−35.2	−10.1
15	54	m	RCA	Transmural	Posterior	58.3	−4.3	1.6	2.3	0.8
16	65	m	RCA	Nontransmural	Posterior	7.8	−11.7	12.6	5.7	−6.9
17	58	m	CX	Transmural	Posterolateral	22.0	−7.6	−1.2	2.2	3.0
Median	55					22.0	0.8	−1.2	−5.8	−4.8
(Q1;Q3)	(45;61)					(0.1;43.5)	(−7.6;6.6)	(−18.9;2.3)	(−35.2;2.5)	(−14.9;3.0)
(Min;Max)	(38;77)					(−32.8;106.4)	(−17.2;22.1)	(−25.2;12.6)	(−41.7;21.0)	(−18.3;17.9)
p value						$p < 0.001$	n.s.	n.s.	n.s.	n.s.

ΔPWT = change of percentage wall thickening, ΔPSI = change of percentage size of infarct, ΔSVI = change of stroke volume index, ΔEDVI = change of end-diastolic volume index, ΔESVI = change of end-systolic volume index.

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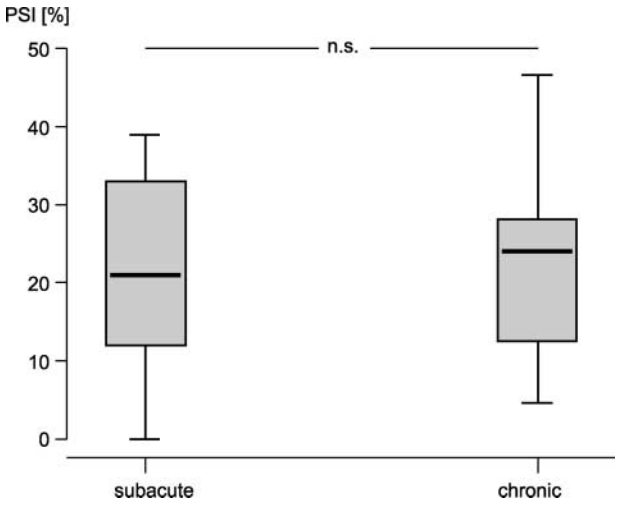

Figure 1. Percentage size of infarct [PSI (%)] in the subacute and chronic phases of myocardial infarction after acute PTCA shows no significant difference. Data are presented as median, Q1, Q3, minimum, and maximum.

between the subacute stage of MI, 26.8 (17.8, 36.9, 15.6, 60.1) and the follow-up, 26.9 (18.8, 31.6, 11.0, 41.8). Stroke volume index (ml/m^2) was 29.7 (22.5, 42.4, 1.5, 47.3) and 26.9 (18.8, 31.6, 11.0, 41.8) in the acute and chronic phases of myocardial infarction, respectively (n.s.) (Table 1).

Regional Wall Motion in Relation to Transmural Extent of Myocardial Infarction

Figure 2 shows the improvement of the regional wall motion (percentage wall thickening = PWT) in hyperenhanced myocardium of transmural myocardial infarction after acute PTCA in the follow-up MR investigation 6 months after intervention. PWT in hyperenhanced myocardium in the subacute phase of myocardial infarction was 8.0% (3.4, 19.1, −12.3, 40.7) and 28.2% (23.5, 30.4, 21.9, 40.6) in transmural and nontransmural extent of hyperenhancement, respectively ($p = 0.036$). In the chronic phase the values for PWT in transmural and nontransmural hyperenhancement were 41.1% (26.9, 61.3, 9.7, 123.0) and 28.5% (10.2, 61.0, −8.8, 81.7), respectively (n.s.).

End-Diastolic Wall Thickness in Relation to Transmural Extent of Myocardial Infarction

In hyperenhanced myocardium end-diastolic wall thickness (mm) in the subacute phase of MI was 12.4 mm (11.5, 13.9, 10.5, 15.3) and 13.4 (11.6, 15.2, 10.8, 16.6) with transmural and nontransmural hyperenhancement, respectively ($p = 0.3$). In these hyperenhanced areas end-diastolic wall thickness (mm) in the chronic phase of MI was 8.5 mm (7.1, 10.2, 6.5, 11.3) and 9.3 mm (7.1, 10.5, 6.7, 11.2) with transmural and nontransmural hyperenhancement, respectively ($p = 0.96$).

In remote nonhyperenhancing myocardium end-diastolic wall thickness was 11.3 mm (10.6, 11.8, 8.4, 14.1) and 11.2 mm (10.6, 11.9, 8.4, 14.1) for transmural and nontransmural subacute MI, respectively ($p = 0.96$). In chronic MI the remote nonhyperenhancing myocardium end-diastolic wall thickness was 10.3 mm (9.6, 11.7, 7.2, 13.2) and 10.4 mm (9.7, 10.7, 7.1, 11.8) for transmural and nontransmural MI, respectively ($p = 0.66$).

Corresponding p values for comparison between the subacute and chronic phases of transmural MI were significant for end-diastolic wall thickness in hyperenhanced ($p = 0.002$), but nonsignificant for remote myocardium ($p = 0.38$).

Corresponding p values for comparison between the subacute and chronic phase of nontransmural MI were significant for end-diastolic wall thickness in hyperenhanced ($p = 0.02$) and in remote myocardium ($p = 0.03$).

Change of Regional Wall Motion in Relation to Early Infarct Size and Regional Wall Motion

The change of regional myocardial function [Change of PWT (%) = (PWT chronic phase − PWT subacute phase)] in hyperenhanced myocardium did not correlate to

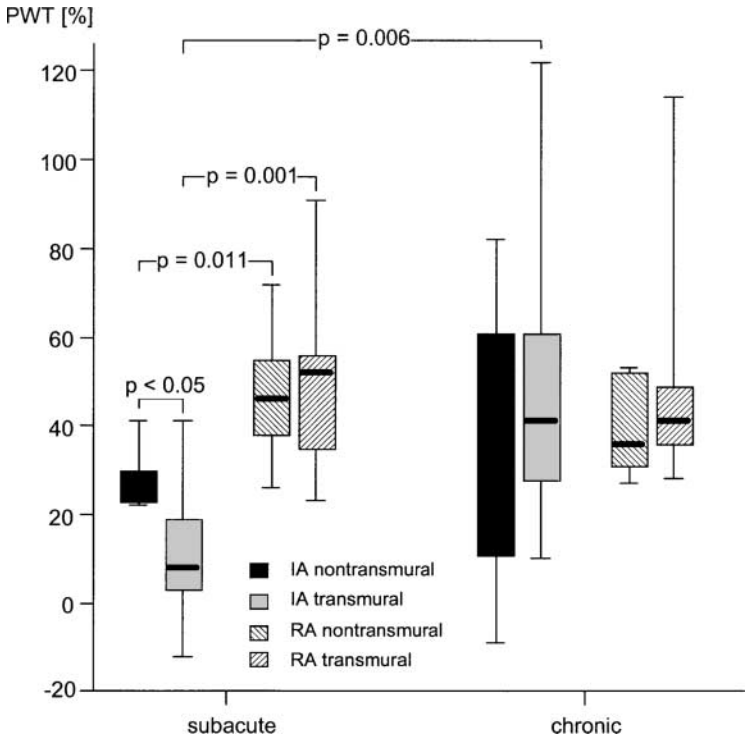

Figure 2. Percentage wall thickening (PWT) as a measure of regional myocardial function for nontransmural (n = 7) and transmural (n = 10) myocardial infarction in the area of injury (IA) and the remote area (RA) in the subacute and chronic phases of myocardial infarction after acute PTCA. Data are presented as median, Q1, Q3, minimum, and maximum. No change is observed in the remote regions. Note the significant improvement of PWT in patients with transmural infarcts in contrast to nontransmural infarcts. Data are presented as median, Q1, Q3, minimum, and maximum.

infarct size in the subacute phase of myocardial infarction. Comparing the change of regional wall motion for patients with percentage size of infarction PSI (%) $\leq$ 20 and PSI (%) $>$ 20, both groups did not differ significantly—34.8% (5.4, 46.5, $-$32.8, 63.8) and 16.5% ($-$9.5, 37.9, $-$25.8, 106.4), respectively (n.s.).

The change of regional wall motion (PWT) showed an inverse correlation ($r = -0.54$; $p = 0.03$) to baseline regional wall motion (PWT) in the subacute phase of myocardial infarction (Fig. 3). Comparing the change of regional wall motion PWT (%) for patients with baseline PWT (%) $\leq$ 20 and PWT $>$ 20 resulted in a statistically significant difference between those two groups—34.8% (26.6, 58.2, 7.8, 106.4) and 3.1% ($-$15.5, 22.5, $-$32.8, 58.3), respectively ($p = 0.03$).

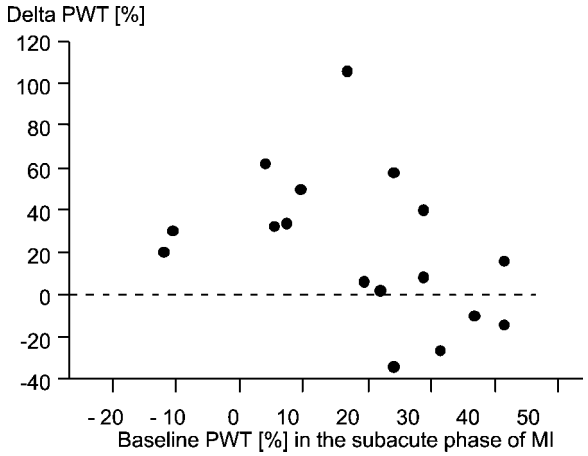

Figure 3. Change of regional wall motion in hyperintense areas between the subacute and chronic phase of myocardial infarction after acute PTCA in relation to baseline percentage wall thickening (PWT). The Difference Delta of percentage wall thickening is calculated using the formula: Delta PWT (%) = PWT chronic $-$ PWT subacute). Positive values indicate an improvement in regional myocardial function, negative values deterioration.

DISCUSSION

Our study showed a beneficial late long-term effect on regional wall thickening after acute PTCA

(< 8 hours of symptom onset) in the area of injury between the subacute phase (11 days post MI) and 6 months after myocardial infarction using a combined MR approach of cine MR and delayed-contrast enhanced magnetic resonance imaging. Global left ventricular function parameters did not improve over time in this study. However, earlier improvements within the first week (O'Keefe et al., 1992) would not have been detected with this study design. Previous studies showed that acute revascularizations (acute PTCA, thrombolysis) after acute MI reduce infarct size and the degree of left ventricular dysfunction (Lima et al., 1995; Ottervanger et al., 1999). This is of clinical importance, as a good left ventricular function correlates with better long-term prognosis (Ito et al., 1996; Wu et al., 1998b). O'Keefe et al. (1992) showed an improvement of global ejection fraction from 52.6% to 58.9% and of systolic function in the infarct zone by a mean of 30% in 323 patients with direct coronary angioplasty for acute MI preangioplasty and 7 days later.

Our study was designed to investigate the late long-term effects (i.e., after the subacute phase of MI) of acute PTCA (< 8 hours of symptom onset) during a 6-month follow-up. Surprisingly, the benefit of improved percentage wall thickening (PWT) could only be observed in patients with a transmural extent of hyperenhancement. The worse the regional wall motion during the subacute phase of myocardial infarction, the more regional wall motion recovered in the follow-up investigation at 6 months. There was no significant correlation between infarct size and the change of regional wall motion. At first sight our data of late improvement of regional wall thickening, especially in patients with transmural MI, seem to contradict the data published by other groups (Choi et al., 2001; Gerber et al., 2001; 2002; Kim et al., 2000). Gerber et al. (2001) have shown that radial thickening did not improve when using tagging for inotropic response assessment in areas of hyperenhancement (with and without early hypoenhancement). In the subepicardial layer of nontransmural infarcts, however, an inotropic response was observed in radial thickening, and the periphery of nontransmural infarcts showed an inotropic response in circumferential shortening. The results of our study could partly be explained by recruitment of viable layers in the periphery of transmural infarcts, though formal analysis and tagging were not part of our study protocol. Choi et al. (2001) state that the transmural extent of acute MI is inversely correlated to long-term improvement in contractile function, concluding that ceMRI has the potential to identify viable and nonviable myocardium. An explanation for some differences could be the study design. In our study a homogenous group of patients with acute PTCA (< 8 hours of symptom onset) was investigated. Choi et al. included all patients with successful revascularization after MI (thrombolysis or angioplasty) without a restricted time window after onset of symptoms. Recently published data examined the relationship of ischemic time and ceMRI of myocardial infarction. The duration of ischemia and the time window of imaging after administration of the contrast agent are crucial for quantification of the real infarct size. The shorter the time of ischemia, the later the area of hyperenhancement matches the real area of irreversible myocardial damage measured by 2,3,5-triphenyltetrazolium chloride (TTC) staining (Oshinski et al., 2001). In our study we acquired the images 15–20 minutes after contrast agent (CA) injection. Choi et al. did not state the exact timing of imaging. Additionally, subacute investigation after myocardial ischemia and reperfusion was performed at day 11 (median) in our patients vs. day 4.2 (mean) in the other study. The follow-up investigation was later in our patient population (6 vs. 2–3 months). Also, the two differing dosages of contrast agent might influence the results. We hypothesize that the late improvement of regional wall thickening in patients with transmural MI and acute PTCA is due to a prolonged stunning phase in comparison to patients with nontransmural MI (Choi et al., 1998; Rochitte et al., 1998; Wu et al., 1998b).

In our study, localization and size of areas of hyperenhancement did not change from the subacute stage to 6 months post MI, despite a reduction of end-diastolic wall thickness. There are conflicting data in the literature on the development of infarct size using the delayed-enhancement technique. In contrast to our data, Ingkanisorn et al. (2002) describe a reduction in infarct size due to a hypothesized overestimation during the acute phase of MI with myocardial edema. These conflicting data can probably be explained by the earlier first MR scan within two days after MI performed by this group. However, this also underlines the further need to identify the underlying pathophysiological mechanisms of the technique. According to the previous studies of Simonetti et al., who compared 10 imaging modalities for infarct detection (Simonetti et al., 2001), we used the technique that was found to have the best contrast-to-noise ratio. Further examinations of Judd et al. (1995) have shown a significant correlation between the area of necrosis (TTC negative areas) and hyperenhanced regions in a canine model of reperfused acute myocardial infarction ($r = 0.93$; $p < 0.035$). There is an ongoing discussion on the pathophysiological background of delayed ceMRI for identification of the area of injury

after acute and chronic ischemia. Gadolinium-DTPA (Gd-DTPA) is an extravascular contrast agent and can be found in infarcted myocardium due to a change of distribution volume. In the acute and subacute stage of MI this is due to edema, cell membrane rupture (Jennings et al., 1983; Steenbergen et al., 1985), and a change in wash-in/wash-out kinetics (Kim et al., 1996). In chronic MI, however, an increased extracellular space of the scar tissue might contribute to a change of distribution volume responsible for the hyperenhancement (Fedele et al., 1994; Kim et al., 1999; Ramani et al., 1998).

Conflicting data in literature leading to variable interpretation of hyperenhancing areas as viable, partially viable, or nonviable, may partly be explained by the pharmacological properties of Gd-DTPA (Weinmann et al., 1984) and many factors influencing the size of the hyperenhancing areas. Additional examinations are needed to investigate the impact of influencing factors like dosage of contrast agent, optimal inversion time, status of collaterals, extent of remaining stenosis in the infarct-related artery after coronary intervention, and the amount of microcirculation (and microvascular obstruction).

In conclusion, the results of our study reveal the importance of acute PTCA in myocardial infarction for cardio protection. Surprisingly, improvement of regional myocardial function was seen only in patients with transmural infarctions. The conflicting results in contrast to other studies imply the need for standardization of delayed-contrast enhanced magnetic resonance imaging and further clarification of whether or not hyperenhancement in this technique represents only nonviable myocardium.

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