Myocardial perfusion assessed by contrast echocardiography correlates with angiographic perfusion parameters in patients with a first acute myocardial infarction successfully treated with angioplasty

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BACKGROUND: Angiographic flow in an epicardial artery does not define perfusion at the microvascular level.

AIM: To compare myocardial contrast echocardiography (MCE) with angiographic methods of assessing microvascular reperfusion in patients with acute myocardial infarction (AMI).

METHODS: One hundred consecutive patients with a first ST segment elevation myocardial infarction and single-vessel disease were successfully treated with primary percutaneous coronary intervention. Regional contrast score index (RCSI), corrected Thrombolysis In Myocardial Infarction (TIMI) frame count (cTFC), TIMI myocardial perfusion grade (TMPG) and myocardial blush grade were evaluated.

RESULTS: Among 717 asynergic segments on MCE, 168 revealed a lack of perfusion. TMPG and cTFC correlated significantly with RCSI ($P=0.031$ and $P=0.027$, respectively). Myocardial blush grade did not correlate with RCSI ($P=0.067$). Patients with anterior AMI had significantly more segments with a perfusion defect on MCE than patients with inferior AMI ($P=0.0001$).

CONCLUSIONS: MCE results correlate with angiographic methods of perfusion assessment such as TMPG and cTFC. Anterior AMI is associated with a greater extent of perfusion defect. MCE results correlate also with recovery of systolic left ventricular function and clinical outcome at six month follow-up.

Key Words: Contrast echocardiography; Coronary angiography; Myocardial infarction; Myocardial perfusion

Corrélation entre la perfusion myocardique évaluée par l'échocardiographie de contraste et les paramètres angiographiques de perfusion chez des patients ayant subi un premier infarctus aigu du myocarde, traité par angioplastie

CONTEXTE : Le flux sanguin à l'angiographie dans une artère épicaudique ne détermine pas la perfusion au niveau microvasculaire.

BUT : L'étude avait pour but de comparer l'échocardiographie de contraste myocardique (ECM) avec des techniques angiographiques d'évaluation de la reperfusion microvasculaire chez des patients ayant subi un infarctus aigu du myocarde (IAM).

MÉTHODE : Cent patients consécutifs, ayant subi un premier infarctus aigu du myocarde accompagné d'un sus-décalage du segment ST et associé à une lésion monotronculaire ont été traités par une intervention coronarienne percutanée pratiquée d'emblée, qui a porté fruit. Différents paramètres ont été évalués : l'indice de contraste régional (ICR), le nombre corrigé d'images TIMI (thrombolyse dans l'infarctus du myocarde) (TIMIc), le degré de perfusion myocardique TIMI (PMT) et le degré de voile myocardique (VM).

RÉSULTATS : Cent soixante-huit segments asynergiques à l'ECM sur 717 ont révélé une insuffisance de perfusion. La PMT et la TIMIc se sont montrées en forte corrélation avec l'ICR ($P=0,031$ et $P=0,027$ respectivement). Par contre, on n'a pas établi de corrélation entre le VM et l'ICR ($P=0,067$). Enfin, les patients ayant subi un IAM antérieur présentaient un nombre significativement plus élevé d'images lacunaires à l'ECM que les patients ayant subi un IAM inférieur ($P=0,0001$).

CONCLUSIONS : Les résultats de l'ECM sont en corrélation avec ceux des techniques angiographiques d'évaluation de la perfusion comme la PMT et la TIMIc. L'IAM antérieur est associé à des images lacunaires étendues. Il y a également une corrélation entre les résultats de l'ECM et le rétablissement du fonctionnement systolique ventriculaire gauche et les résultats cliniques au bout de six mois.

Angiographic flow in an epicardial artery does not accurately define perfusion at the microvascular level. The lack of myocardial reperfusion despite restored flow, the 'no-reflow' phenomenon, was initially revealed by myocardial contrast echocardiography (MCE) and confirmed by other imaging techniques such as positron emission tomography (1-3). In acute myocardial infarction (AMI), the lack of myocardial perfusion despite recanalization of an infarct-related artery (IRA) is associated with an increased rate of left ventricular (LV) dysfunction, complications and impaired survival (4-7).

There is a need for applying techniques for assessing flow at the tissue level at the bedside. MCE in AMI provides information regarding the adequacy of myocardial tissue perfusion, as well as the spatial extent of microvascular obstruction.

Several techniques can be easily and reproducibly used for no-reflow phenomenon assessment. Among these are angiographic methods, such as myocardial blush grade (MBG), Thrombolysis In Myocardial Infarction (TIMI) myocardial perfusion grade (TMPG) and the corrected TIMI frame count (cTFC) (8-10). MBG relates to the contrast opacification of the myocardial bed subtended by the infarct artery, and TMPG relates to the contrast opacification of myocardium according to the speed of this process. The cTFC is a quantitative index of the coronary flow in the IRA. Few data exist that compare perfusion assessed by contrast echocardiography with myocardial perfusion on angiography.

The aim of the present study was to compare intravenous MCE with angiographic methods of assessing microvascular reperfusion in

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TABLE 1
Patient clinical characteristics

Evaluated parameter	Patients without a perfusion defect (n=53)	Patients with a perfusion defect (n=47)	P
Age, years*	58.3±11.33	60.8±12.82	0.31
Male sex, %	56.9	58.2	0.68
Hypertension, %	64.2	65.2	0.91
Diabetes mellitus, %	37.7	26.1	0.22
Dyslipidemia, %	60.4	63.1	0.79
Smoking, %	17.3	21.7	0.58
CK-MB*†, U/L	197.8±129.2	244.2±161.9	0.13
Patients with anterior MI, %	24.5	63.6	0.000014
Time from pain onset to balloon*, min	270.7±171.4	288.6±223.5	0.68

*Values presented as mean ± SD; †Maximum value. CK-MB Creatine kinase (muscle-brain); MI Myocardial infarction

patients with a first AMI successfully treated with primary percutaneous coronary intervention (PCI).

METHODS

Study population

Between May 2004 and December 2004, 100 consecutive patients with a first AMI who were admitted within 12 h of the onset of chest pain and treated with primary PCI were enrolled in the present study. Only patients with single-vessel disease were included in the study. Exclusion criteria included cardiogenic shock at the time of MCE, unsuccessful angioplasty, lower than grade 3 TIMI flow post-PCI and a residual lesion of less than 30%, clinical history of congestive heart failure or valve disease, pregnancy or breastfeeding, life-threatening conditions other than AMI or an inadequate thoracic window for echocardiography. No upper age limit was defined.

The study complied with the Declaration of Helsinki. The study protocol was approved by the local ethics committee, and informed consent was obtained from all subjects participating in the study. Clinical characteristics are shown in Table 1.

Almost all patients received acetylsalicylic acid, nitroglycerine and heparin intravenously. Beta-blockers and angiotensin-converting enzyme inhibitors were given after one or two days of hospitalization, unless contraindications were present. All patients received statins from the first day of treatment. In case of stent implantation (90% of patients), either clopidogrel or ticlopidine was administered.

Patients were divided into two groups according to absence (group 1) or presence (group 2) of perfusion disturbances on MCE.

Echocardiographic analysis

All studies were performed using the Philips Ultrasound System Sonos 5500 (Philips Medical, The Netherlands) equipped for harmonic imaging and a 3.6 MHz transducer. The instrument setting for MCE was optimized for maximum sensitivity and ideal conditions for visual myocardial contrast detection. The recommended dynamic range was in the medium or middle range (45 dB to 55 dB); the focal zone depth was set at approximately two-thirds of the image, and gain was adjusted so that myocardial tissue speckle details could be seen on baseline images (this resulted in homogenous grey backscatter throughout the entire wall of the left ventricle). The mechanical index was set between 0.3 and 0.9. Thereafter, all settings were kept constant during acquisition of the images. The dysfunctional area was visualized using harmonic imaging in either the four- or the two-chamber view. Electrocardiogram (ECG) triggering was performed in late end-systole at every third heart beat, with image acquisition at the T wave of the ECG signal.

The baseline regional wall motion score index (WMSI) and regional contrast score index (RCSI) were calculated at least 48 h after PCI. The Optison contrast agent (Amersham Health, USA) was administered via a peripheral vein. MCE was performed using a modality of subsequent data acquisition of triggered end-systolic images. The criterion for good perfusion on MCE was defined as homogenous enhancement in 50% of wall thickness in each segment. Patients were then divided into two groups, according to the presence of a perfusion defect assessed by MCE.

Echocardiographic images were digitally stored in a cine loop format for off-line analysis by two experienced observers. Discrepancies were resolved by consensus. Baseline fundamental imaging, including two parasternal (long- and short-axis) views, was used to evaluate baseline regional and global wall motion score indexes using the 16-segment model before MCE (11). For each wall segment, motion was scored as 1 (normal), 2 (hypokinetic), 3 (akinetic) or 4 (dyskinetic). LV ejection fraction (LVEF) and WMSI were obtained for all echo scans. WMSI was obtained by dividing the sum of the segment scores by the number of segments scored.

LVEF was derived using the modified biplane Simpson's method, from orthogonal apical long-axis projections (four-chamber view and two-chamber view). All measurements were derived in a blinded fashion by two experienced operators. The mean three measurements of the best visualized cardiac cycles were calculated for each echo study.

Application of contrast agent

After preinjection recordings, the ultrasound contrast agent Optison was injected intravenously. This contrast agent consists of perfluorocarbon-filled microbubbles with a median diameter of 3 µm to 4 µm. A dose of 1 mL of contrast agent was injected, followed by 10 mL of saline. This was chosen following the results of pilot studies. One bolus injection was administered for each echocardiographic view (12). At least five beats before and 30 beats after the injection were recorded for each view.

Definitions

Myocardial perfusion of each segment was assessed using the following grading scheme: poor or no opacification, partial opacification, adequate opacification or artifacts. Adequate opacification was scored when the segment showed homogeneous opacification in at least one view. Partial opacification was scored as inadequate myocardial enhancement in any view relative to adjacent segments with adequate opacification. Lack of opacification was scored as low myocardial enhancement. Artifacts were differentiated from perfusion defects before final analysis. Based on MCE results, patients were categorized according to the presence of myocardial perfusion defect in at least one segment in the dysfunctional area.

The presence of myocardial perfusion was defined as adequate opacification in that segment. Areas of no or poor myocardial opacification were regarded to be myocardial perfusion defects.

The RCSI was calculated by dividing the sum of perfusion assessment of every asynergic segment by the number of evaluated segments. For each segment, good myocardial perfusion was scored as 1. Segments with partial, poor or no opacification were scored as 0. The range of RCSI was 0 to 1 (13). In cases of normal perfusion, the RCSI was 1.

Primary PCI

In all patients, coronary angiography and intervention were performed by an experienced invasive cardiologist within 12 h of the onset of symptoms. Ninety patients underwent primary stent implantation. Arterial access was by the right femoral artery. Selective coronary arteriography and left ventriculography were performed using standard techniques (14). The IRA was identified based on coronary anatomy, regional LV dysfunction and ECG changes.

The PCI procedure was considered to be successful when the residual stenosis was less than 30% in the absence of dissection and

TABLE 2
Patient angiographic characteristics

Evaluated parameter	Patients without a perfusion defect (n=53)	Patients with a perfusion defect (n=47)	P
TIMI grade before PCI	0.8±1.2	0.9±1.2	0.93
Number of stents	1.1±0.4	1.0±0.4	0.22
Tirofiban administration, n (%)	9 (16.9)	4 (7.5)	0.019
cTFC	21.3±8.7	30.9±19.1	0.007
Myocardial blush grade	2.27±1.2	2.12±1.1	0.57
TMPG	2.20±0.9	1.83±1.0	0.08

Values are presented as mean ± SD unless otherwise indicated. cTFC Corrected Thrombolysis In Myocardial Infarction (TIMI) frame count; PCI Percutaneous coronary intervention; TMPG TIMI myocardial perfusion grade

thrombosis. The infarct-related vessel was analyzed before and after primary coronary angioplasty to assess the residual stenosis. Contrast flow through the epicardial vessel was graded using the standard TIMI flow grade scale of 0 to 3. All angiograms were analyzed by two observers blinded to clinical and echocardiography results. In a case of disagreement, a third observer reviewed the film, and discrepancies were resolved by consensus.

Pharmacological treatment in the catheterization laboratory included intravenous heparin 6000 U to 10,000 U at the beginning of the procedure.

Coronary angiograms after PCI were evaluated for the cTFC, TMPG and MBG.

Thirteen patients were treated with the glycoprotein IIb/IIIa blocker (tirofiban) at the discretion of the PCI operator. Perfusion assessment was qualitative (three perfusion patterns).

MBG

Myocardial blush was graded on the angiograms performed immediately after the primary coronary angioplasty procedure by two experienced investigators who were blinded to all data other than the coronary angiograms.

Grading was performed on cine film at 25 frames/s recorded in a digital coronary imaging catheterization laboratory. In each patient, the best projection was selected to assess the myocardial region perfused by the IRA.

Angiographic runs had to be long enough to allow some filling of the venous coronary system, and backflow of the contrast agent into the right atrium had to be present to be certain of adequate contrast filling of the epicardial coronary artery.

All angiograms were performed with 6 Fr guiding catheters in a standardized fashion after 400 µg nitroglycerine (intracoronary) was given immediately after PCI; this procedure allowed quantitative coronary artery analysis.

MBGs were defined according to the van't Hof et al study (9).

TMPG

The duration of cine filming was required to exceed three cardiac cycles in the washout phase to assess washout of the myocardial blush. TMPGs were defined according to the Gibson et al study (15).

TIMI frame count

The cTFC is the number of cine frames required for the contrast to first reach the standardized distal coronary landmarks in the culprit artery and was measured by use of a frame counter on a cine viewer. A frame count of 100, a value that is the 99th percentile of patent vessels, was imputed to an occluded vessel. The cTFC is a measure of time, based on a filming speed of 30 frames/s. Definitions of the first and last frames used for TIMI frame counting are based on those in the Gibson et al study (10).

Figure 1 Perfusion defects on echocardiography in patients divided into groups according to Thrombolysis In Myocardial Infarction (TIMI) myocardial perfusion grade (TMPG). Vertical columns indicate 95% CI. * $P < 0.05$ compared with TMPG 0 group (Tukey's post hoc test). Wilks' $\lambda = 0.82599$, $F(6,162) = 2.7082$; $P = 0.01561$

Statistical analysis

Continuous variables were expressed as mean ± SD and compared by means of two-tailed unpaired *t* tests. Discrete variables were expressed as percentages of the study population and compared by the χ^2 test or Fisher's exact test. To assess the correlation between the number of segments with a perfusion defect and the clinical, laboratory, echocardiographic and angiographic variables, the Spearman rank correlation test was used. Perfusion defects assessed by echocardiography were compared in various groups of patients established according to tissue perfusion on angiography using ANOVA with the post hoc Tukey test. Analysis of EF during follow-up was also performed using ANOVA for repeated measures. $P < 0.05$ was considered to be statistically significant. Statistical analyses were performed with Statistica 6.0 for Windows (StatSoft, New Zealand).

RESULTS

A total of 100 consecutive patients were included, all of whom were available for angiographic and echocardiographic analysis.

Group 1 consisted of 53 patients without a perfusion defect on MCE, while segments with perfusion disturbances were found in 47 patients (group 2). The mean RCSI in groups 1 and 2 were 1 and 0.56 ± 0.4 , respectively ($P = 0.0064$). There were no significant differences between groups with respect to age, sex, heart rate, arterial pressure, pharmacological treatment or mean pain-to-balloon time (Table 1).

Comparison between MCE and angiographic methods of reperfusion assessment

From 1600 segments in all enrolled patients, 717 asynergic segments were analyzed. Among the 717 segments assessed by MCE, 168 (22%) revealed partial or total lack of perfusion. Sixteen segments had inadequate MCE images due to difficulties with imaging of the medial and basal segments of the lateral wall. These 16 segments were not included in the analysis. Medial and basilar segments of lateral wall were assessed only in lateral and anterolateral infarctions.

The results of angiographic reperfusion assessment techniques were as follows: mean cTFC was 25.2 ± 14.5 , mean TMPG was 2.02 ± 0.97 and mean MBG was 2.2 ± 1.16 (Table 2). Both cTFC and TMPG differed distinctly between group 1 and group 2 ($P = 0.007$ and $P = 0.08$, respectively). The RCSI was also significantly different ($P = 0.0064$). TMPG and cTFC correlated significantly with RCSI ($P = 0.031$ and $P = 0.027$, respectively) (Figure 1), while MBG did not correlate with the RCSI ($P = 0.067$) (Figure 2). TMPG and cTFC were significant predictors of perfusion disturbances as defined by MCE,

Figure 2) Perfusion defects on echocardiography in patients divided into groups according to myocardial blush grade (MBG). Vertical columns indicate 0.95% CI. * $P < 0.05$ compared with MBG groups 1 and 2 (Tukey's post hoc test). Wilks' lambda = 0.77123, $F(6,162) = 3.7448$; $P = 0.00162$

TABLE 3
Patient echocardiographic characteristics

Evaluated parameters	Patients without a perfusion defect (n=53)	Patients with a perfusion defect (n=46)	P
Ejection fraction, biplane	49.5±7.0	45.2±7.4	0.004
ESV, biplane	52.5±20.8	67.3±24.3	0.001
EDV, biplane	110.1±38.6	121.0±35.6	0.15
Wall motion score index	1.4	1.6	0.0009
Number of asynergic segments	5.3±2.7	9.5±2.6	0.0001

EDV End-diastolic volume; ESV End-systolic volume

whereas MBG was not predictive. MCE perfusion results correlated significantly with TMPG ($P = 0.01$). Using the Spearman rank correlation test, it was demonstrated that TMPG and cTFC correlated in both groups of patients with the number of segments without a perfusion defect on MCE. P values are shown in Table 3.

TMFG and MBG correlated with the WMSI ($P = 0.025$ and $P = 0.038$, respectively).

The relationship between myocardial perfusion defects assessed by MCE and clinical and laboratory parameters

Patients from the group with a perfusion defect had more segments with impaired contractility ($P = 0.0001$) and higher WMSI ($P = 0.0009$) (Table 3). The mean number of segments with contractility disturbances was five in group 1 and nine in group 2. Regional WMSI were 1.4 and 1.6 in group 1 and group 2, respectively ($P = 0.0009$).

In group 1, the IRA was the left anterior descending coronary artery in 16 patients (30.1%), the right coronary artery in 31 patients (58.5%) and the circumflex coronary artery in six patients (11.4%).

In group 2, the IRA was the left anterior descending coronary artery in 29 patients (63.0%), the right coronary artery in 12 patients (26.1%) and the circumflex coronary artery in five patients (10.9%).

More anterior infarcts were found and, consequently, the IRA was more often the left anterior descending coronary artery in patients with a perfusion defect (group 2). Of 53 patients from group 1, only 13 had an anterior myocardial infarction, whereas there were 29 anterior myocardial infarctions in group 2 ($P = 0.00014$).

Patients with an anterior AMI had significantly more segments with a perfusion defect evaluated with MCE than patients with inferior myocardial infarction ($P = 0.0001$).

Group 1 had higher EF (EF biplane), lower end-systolic volume and lower WMSI than patients in group 2 (Table 3).

Figure 3) Ejection fraction (EF) during the index hospitalization and after a six-month follow-up in patients with perfusion defects on myocardial contrast echocardiography (MCE) (dotted line, squares) or with proper perfusion (solid line, circles). Data are presented as mean ± 95% CI. ANOVA for repeated measures revealed statistically significant interaction between the presence of perfusion defects on echocardiography and change in EF during follow-up ($F(1,91) = 5.8554$; $P = 0.0175$)

In a multivariate analysis, the absence of an anterior myocardial infarction ($P = 0.0017$), high EF on echocardiography ($B = -0.31$, $P = 0.006$), low TMPG ($B = -0.33$, $P = 0.01$) and the use of glycoprotein IIb/IIIa blockers ($B = -0.31$, $P = 0.004$) were the only predictors of reperfusion on MCE.

Only 13 patients from the whole study group received tirofiban: 16.9% of patients from the group without a perfusion defect and 7.5% from the group with a perfusion defect. Patients treated with tirofiban had a significantly lower RCSI than those who did not receive tirofiban ($P = 0.003$).

Smoking was more frequent in patients with a perfusion defect on MCE, but the difference was at the limit of significance ($P = 0.053$). In multivariate analysis, smoking ($B = 0.2$, $P = 0.053$) and maximum level of creatine kinase (muscle-brain) ($B = 0.21$, $P = 0.037$) were predictors of a perfusion defect on MCE. Peak creatine kinase (muscle-brain) correlated well with WMSI ($P = 0.037$) and with RCSI in group 2 ($P = 0.037$).

During the in-hospital stay, no serious cardiovascular events were observed, which is not surprising when one considers the single-vessel coronary disease population.

Six-month clinical follow-up

Ten patients were unavailable for follow-up: two from group 1 and eight from group 2. In group 1, LVEF increased significantly from 52.1% on admission to 55.9% at the six-month follow-up ($P = 0.026$ by Student's *t* test); in group 2, it decreased from 45% on admission to 43% at follow-up. The difference in LVEF between both groups was statistically significant ($P = 0.0175$). There was a statistically significant interaction between the presence of perfusion defects in the initial contrast echo and the change in EF on follow-up (ANOVA for repeated measures) $F(1,91) = 5.8554$ ($P = 0.0175$) (Figure 3).

Generally, in the majority of cases, patients who had good MCE results also had long-term improvement of ventricular function.

Patients from group 2 had a higher incidence of death during the six-month follow-up period. Two of 39 patients (5%) died, whereas there were no deaths in the group with good perfusion on MCE. Two patients (5%) in group 2 had a nonfatal myocardial infarction, while no patients sustained a subsequent myocardial infarction in group 1. The combined end point (death and reinfarction) was significantly lower in patients without a perfusion defect ($P = 0.039$). Moreover, the combined end point occurred only in patients with impaired perfusion

on both MCE and angiography (MCE plus TFC defects, $P=0.0076$; MCE plus MBG defects, $P=0.0076$; and MCE plus TMPG defects, $P=0.034$).

DISCUSSION

Our study showed that in patients with a first AMI with single-vessel disease who were successfully treated with primary PCI, perfusion assessed by contrast echocardiography correlates well with angiographic parameters of reperfusion, such as cTFC and TMPG. There was no such correlation between MCE and MBG in our group of patients.

Recent studies have demonstrated that myocardial perfusion and metabolism are often abnormal, despite restoration of TIMI grade 3 flow in the IRA (1,2,4,16). This no-reflow phenomenon is thought to be the result of microvascular obstruction (17-19). This phenomenon is a marker of more extensive myocardial tissue damage and has been proven to be associated with poorer functional recovery, an increased frequency of heart failure and poor survival (4,20). This is why there is a growing need to establish a reliable marker of myocardial perfusion. Several markers of myocardial perfusion have been proposed. Among these are electrocardiographic (ST segment elevation resolution), echocardiographic (MCE) and angiographic methods (TMPG, MBG, CTFC). What they have in common is that they give information about perfusion and, at the same time, patient prognosis. In the present study population, despite TIMI grade 3 flow, more than 40% of patients had some degree of perfusion defect detected by MCE and/or angiography.

MCE, actively studied and compared with many diagnostic tools, appears to have feasibility and accuracy comparable with technetium-99m sestamibi single photon emission computed tomography (SPECT) imaging. Myocardial uptake using SPECT depends largely on myocardial microvascular volume. MCE detects not only microvascular volume, but also blood flow. These differing mechanisms may affect the relative accuracies of MCE and SPECT for detecting myocardial viability and perfusion early after AMI.

Hickman et al (21) recently published a paper in which they compared MCE with SPECT early after first AMI. In this study, 56 patients underwent resting transthoracic echocardiography, low-power MCE and SPECT 7±2 days following a first AMI and thrombolysis. Contractile reserve was assessed three months following revascularization. The sensitivity and specificity of MCE and SPECT were 83% and 78% (P not significant), and 78% and 45% ($P=0.01$), respectively. MCE was the only multivariate predictor of global recovery of function and contractile reserve ($OR=3.5$, $P=0.01$). The different physiological mechanisms used in MCE and SPECT translate into different relative accuracies for the detection of myocardial perfusion and viability. Our findings showed that the presence of myocardial perfusion on MCE from either collateral or antegrade flow provided information on the extent of infarction and was associated with recovery of resting wall motion.

Our study compared simple-to-determine invasive and noninvasive markers of reperfusion (Table 4). The principal findings were that MCE results correlated with angiographic methods of perfusion assessment, such as TMPG and cTFC assessed following primary PCI; MCE results also correlated with the recovery of systolic LV function and clinical outcome at the six-month follow-up; anterior AMI was associated with a greater extent of perfusion defect in patients treated with primary PCI; treatment with a glycoprotein IIb/IIIa blocker was associated with better myocardial tissue perfusion in patients with AMI.

In our study, serious adverse events (two deaths and two nonfatal myocardial infarctions) occurred only in the group with a perfusion defect on both MCE and angiography (Table 5). We assume that a combination of two or more perfusion markers is more predictive than a single marker, giving additional information about clinical prognosis. MBG has an established position among angiographic perfusion markers. The myocardial blush scale has been found to relate to enzymatic infarct size in patients after primary PCI in AMI (9,22). According to Haager et al (23), a combination of MBG and number

TABLE 4
Correlations between angiographic parameters of reperfusion and the number of asynergic segments and segments without reperfusion on myocardial contrast echocardiography (MCE) using the Spearman rank correlation test

Correlation	R	P
cTFC and the number of asynergic segments	0.27	0.027
TMPG and the number of asynergic segments	-0.24	0.026
TMPG and the number of asynergic segments without reperfusion on MCE	-0.24	0.025
MBG and the number of asynergic segments	-0.22	0.038
MBG and the number of assessed segments without reperfusion on MCE	-0.20	0.068

cTFC Corrected Thrombolysis In Myocardial Infarction (TIMI) frame count; MBG Myocardial blush grade; TMPG TIMI myocardial perfusion grade

of ECG leads with persistent ST segment elevation after PCI is highly predictive of patient outcomes. MBG has better predictive value for long-term mortality than Killip class, TIMI flow grade and LVEF. Nevertheless, in our study, the correlation between contrast echocardiography and MBG was much poorer than with TMPG.

Gibson et al (8) showed that TMPG correlates well with TIMI flow in the IRA. Among patients with TIMI grade 3 flow, TMPG helps to identify patients at highest risk of 30-day mortality. In addition, TMPG correlates with cTFC. cTFC of fewer than 14 frames and TMPG 3 in AMI predicts a favourable clinical outcome. Despite its similarity to the MBG scale, TMPG classification also takes into account the period of time the contrast stays in microvasculature (8).

It has been suggested that cTFC on the 90 min angiogram after thrombolytic therapy reflects myocardial reperfusion and could be an independent predictor of in-hospital and one-month clinical outcome (10,24,28). However, cTFC determined in the epicardial artery is only an indirect parameter of the microvascular function. Using the Spearman rank correlation test, we demonstrated that MBG, TMPG and cTFC correlated in both studied groups of patients with the number of myocardial segments without reperfusion.

Contrast echocardiography has previously been validated as a reference technique for the evaluation of myocardial perfusion (1,25-27). The most significant advantage is that it can be applied in the setting of AMI. The no-reflow phenomenon is detected by contrast echocardiography in 16% of patients with TIMI grade 3 flow (29). Contrast echocardiography was chosen by Agati et al (29) as a tool to prove superiority of primary PCI over thrombolytic therapy. Kamp et al (12) carried out serial MCE in patients after primary PCI, showing that a significant reduction in size of the initial perfusion defect predicts functional recovery after four weeks; these findings underscore the potential diagnostic value of the method. In AMI treated with PCI, it may have not only therapeutic implications, but also prognostic significance, because no-reflow is associated with LV dysfunction at follow-up (30,31).

We believe that our main division of the study population into one group with and one group without perfusion defects assessed by MCE was well-founded and reasonable; almost all echocardiographic and angiographic parameters, as well as clinical outcomes, turned out to be better in the group without perfusion defects on MCE.

Despite its potential to assess myocardial perfusion in a noninvasive way, MCE has not become a routine clinical tool thus far. An important limitation is that the underlying pathophysiology is complex. Moreover, appropriate interpretation of MCE requires experience and training. Furthermore, sophisticated software is needed to perform the studies optimally and to acquire accurate data.

As demonstrated in the present study, as well as in numerous previous studies, reperfusion markers correlate with clinical outcomes at follow-up and can be used as surrogate study end points in clinical

TABLE 5

The number of deaths and nonfatal myocardial infarctions at the six-month follow-up according to agreement between myocardial contrast echocardiography (MCE), corrected Thrombolysis In Myocardial Infarction (TIMI) frame count (cTFC), myocardial blush grade (MBG) and TIMI myocardial perfusion grade (TMPG) abnormalities on admission

	cTFC		MBG		TMPG	
	Good perfusion	Impaired perfusion	Good perfusion	Impaired perfusion	Good perfusion	Impaired perfusion
MCE without a perfusion defect	0/47 (0)	0/9 (0)	0/46 (0)	0/8 (0)	0/46 (0)	0/7 (0)
MCE with a perfusion defect	0/9 (0)	4/26 (15.4)*	0/11 (0)	4/26 (15.4)*	0/4 (0)	4/34 (11.8)*

Values represent the number of people from the group who had a perfusion defect. *Included two deaths and two myocardial infarctions

trials to assess the effect of therapeutic strategies in AMI (8,32). We believe that patients with perfusion defects assessed both on echocardiography and angiography (especially by TMPG and cTFC) can be easily selected as a high-risk population and benefit from additional pharmacological or interventional therapy.

Limitations

Regional wall thickening and motion were evaluated with echocardiography by semiquantitative analysis. We did not study the possible influence of collaterals on LV function. It was not possible to evaluate the exact role of various drugs, particularly angiotensin-converting enzyme inhibitors, which were given in the majority of cases. In our study, treatment with tirofiban was not randomized. Thirteen patients were treated with tirofiban at the discretion of the PCI operator. In those who received tirofiban, AMI was prevalent. Nevertheless, patients treated with tirofiban had fewer perfusion defects with MCE

than those who did not receive this glycoprotein IIb/IIIa blocker. The follow-up period in our study was very short and was confined to in-hospital observation. The results presented cannot be applied to patients with complicated myocardial infarction or multivessel disease, who were excluded from the study.

CONCLUSIONS

MCE results correlate with angiographic methods of perfusion assessment such as TMPG and cTFC following primary PCI. Anterior AMI is associated with larger perfusion defects in patients treated with primary PCI. MCE perfusion results correlate with recovery of systolic LV function and clinical outcome at six-month follow-up. MCE is an uncomplicated bedside method of perfusion assessment at a microvascular level in patients with AMI and gives additional information about actual infarct size, enabling early evaluation of the success of primary PCI results.

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