VILNIUS UNIVERSITY

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VALUE OF CARDIOVASCULAR MAGNETIC RESONANCE FOR THE PREDICTION OF LEFT VENTRICULAR FUNCTIONAL RECOVERY AFTER REVASCULARISATION

Summary of the Doctoral Dissertation
Biomedical Sciences, Medicine (06B)

Vilnius, 2011

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Summary of the dissertation was sent on the 23 of August 2011.

A full text of the dissertation is available at the Library of Vilnius University, Universiteto str. 3, LT-01122 Vilnius, Lithuania.

VILNIAUS UNIVERSITETAS

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ŠIRDIES MAGNETINIO REZONANSO VERTĖ, PROGNOZUOJANT KAIRIOJO SKILVELIO MIOKARDO KONTRAKCIJOS ATSISTATYMĄ PO REVASKULIARIZACIJOS

Daktaro disertacijos santrauka

Biomedicinos mokslai, medicina (06B)

Vilnius, 2011

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Disertacija bus ginama viešame Medicinos mokslo krypties tarybos posėdyje 2011 m. rugsėjo mėn. 29 d. 12 val. Vilniaus universiteto ligoninių „Santariškių klinikos“ Konferencijų salėje (Raudonojoje). Adresas: Santariškių 2, LT-08661, Vilnius, Lietuva.

Disertacijos santrauka išsiuntinėta 2011 m. rugpjūčio mėn. 23 d.

Disertaciją galima peržiūrėti Vilniaus universiteto bibliotekoje, Universiteto g. 3, LT-01122 Vilnius, Lietuva.

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LIST OF ABBREVIATIONS

ACC	American College of Cardiology
ACE	angiotensin-converting enzyme
AHA	American Heart Association
AUC	area under the curve
CABG	coronary artery bypass graft surgery
CAD	coronary artery disease
CCS	Canadian Cardiovascular Society
CMR	cardiovascular magnetic resonance
CR	contractile reserve
CRT	cardiac resynchronisation therapy
ECG	electrocardiography
EDWT	end-diastolic wall thickness
EF	ejection fraction
ESC	European Society of Cardiology
ESVI	end-systolic volume index
FOV	field of view
GFR	glomerular filtration rate
ICD	implantable cardioverter-defibrillator
LDD	low-dose dobutamine
LDD-CMR	low-dose dobutamine cardiovascular magnetic resonance
LIMA	left internal mammary artery
LGE	late gadolinium enhancement
LGE-CMR	late gadolinium enhancement cardiovascular magnetic resonance
LV	left ventricle
LVEF	left ventricular ejection fraction
LVD	left ventricular systolic dysfunction
LVddI	left ventricular diastolic diameter index
MI	myocardial infarction

MVRF	mitral valve regurgitation fraction
NPV	negative predictive value
NYHA	New York Heart Association
ONBEAT	on-pump beating heart coronary artery bypass graft surgery
ONSTOP	conventional cardioplegic arrest coronary artery bypass graft surgery
OR	odds ratio
QW/NQW	Q-wave/non-Q-wave
PCI	percutaneous coronary intervention
PPV	positive predictive value
RIM	thickness of the non-contrast-enhanced myocardial rim surrounding the scar
ROC	receiver operating curve
SD	standard deviation
SI	sphericity index
SVR	surgical ventricular reconstruction
TE	time of echo
TR	time of repetition
WHF	World Heart Federation
WMSI	wall motion score index

INTRODUCTION

Hibernating myocardium is normally defined as a viable and dysfunctional myocardium that improves in function following revascularisation. Revascularisation of the hibernating myocardium results in an improvement of regional and global left ventricular (LV) systolic function, remodeling is reversed, survival is increased, and there is a decrease in the composite end-point of myocardial infarction (MI), heart failure, and unstable angina. In contrast, patients with minimal or no evidence of myocardial viability appear to have no benefit from revascularisation compared to medical therapy. The invasive tests are of limited value in the diagnosis of hibernated myocardium. These findings have emphasized the need and importance of noninvasive tests to diagnose and quantify the viable myocardium in areas of LV systolic dysfunction (LVD). The below described clinical study is limited to the assessment of myocardial viability only in chronic LVD and will not attempt to differentiate between stunning and hibernation.

Previous studies have demonstrated that quantification of the transmural extent of late gadolinium enhancement (LGE) by cardiovascular magnetic resonance (CMR) can be used to predict the likelihood of a recovery of myocardial function after revascularisation. However, in non-transmural scars (LGE 1% to 75%), only an intermediate likelihood of functional recovery was found. When the low-dose dobutamine (LDD) stimulation was compared to scar imaging, LDD-CMR is superior to LGE-CMR in predicting the recovery of function after revascularisation. This observation was most pronounced in segments with 1% to 74% of infarct transmurality. It has been suggested that even though LGE-CMR depicts the area of myocardial fibrosis, it does not assess the functional state of the surrounding (potentially viable) myocardium, which can be normal, remodelled, hibernating, stunned or ischemic. Additionally, another study suggested that the thickness of the non-contrast-enhanced and potentially viable myocardial rim (RIM) surrounding the scar may be clinically useful for assessing myocardial viability. The functional state of non-contrast-enhanced myocardial rim can be assessed using LDD-CMR, whereas the critical thickness of the scar surrounding non-contrast-enhanced myocardial rim, which is needed to regain contractility after revascularisation, seems to be clinically useful in patients with an

ischemic cardiomyopathy and regional wall thinning. This hypothesis was elegantly tested in 35 patients with chronic dysfunctional myocardium due to a chronic total occlusion. The results of this study indicated that in segments with an intermediate LGE (i.e., LGE transmurality between 25% and 75%), the measurement of baseline contractility of the non-contrast-enhanced epicardial rim or simply baseline contractility of the wall (the authors assume that scar tissue does not contract) better identifies which segments maintain contractile reserve (CR) during LDD-CMR and recover after revascularisation than the LGE transmurality, end-diastolic wall thickness and the thickness of the non-contrast-enhanced rim. The study confirms that only the jeopardised dysfunctional myocardium of the unenhanced rim may have CR during LDD and recover after revascularisation; however, the normokinetic unenhanced rim has no CR and no recovery after successful percutaneous coronary intervention (PCI).

All the aforementioned studies advance the concept that a more comprehensive approach to defining viability by CMR is warranted in clinical practice when the recovery of LV function is the desired end-point.

GOAL AND OBJECTIVES OF THE RESEARCH

The primary goal of this research was to prospectively and directly compare CR during LDD-CMR with the RIM and LGE as predictors of segmental functional recovery in patients with LV systolic dysfunction undergoing surgical or percutaneous revascularisation. In the current research, we prospectively tested the hypothesis that the addition of LDD-CMR and quantification of CR or additional measurement of the RIM in segments with LGE 1 to 75% would improve the predictive value for the recovery of LV segmental function after revascularisation in patients with ischemic LV dysfunction.

The second goal of this research was to determine the optimal LDD-CMR- and LGE-CMR-based predictor of significant (≥5%) LVEF improvement 6 months after revascularisation.

OBJECTIVES OF THE RESEARCH

1. To prospectively and directly compare three different CMR viability parameters (CR during LDD-CMR, LGE transmurality and RIM both measured using LGE-

CMR) and their combinations as predictors of segmental functional recovery in patients with LVD undergoing surgical or percutaneous revascularisation.

2. To determine the optimal LDD-CMR- and LGE-CMR-based predictor of significant (≥5%) LVEF improvement 6 months after revascularisation.
3. To evaluate the influence of revascularisation on LV functional and morphological characteristics and patients' clinical course.
4. To evaluate the frequency and extent of new periprocedural/perioperative myocardial injury assessed by LGE-CMR in our patients' cohort.
5. To analyse the pathologic basis of Q-wave (QW) and non–Q-wave (NQW) myocardial infarction.

DEFENDED STATEMENTS

1. LGE-CMR and LDD-CMR provide complementary information regarding myocardial viability, and a combination of both techniques is valuable for more accurate prediction of viability irrespective of the degree of LVD.
2. LDD-CMR is superior to LGE-CMR as a predictor of segmental functional recovery, and the greatest advantage of LDD-CMR is in segments with LGE from 1% to 75%.
3. Measuring the non-contrast-enhanced myocardial rim surrounding the scar has no additional value in clinical practice, because its prognostic value is not superior to the prognostic values of other analysed viability parameters.
4. The best LDD-CMR- and LGE-CMR-based predictors of significant LVEF improvement after revascularisation are:
    - the percentage of viable segments from all dysfunctional and revascularised segments in a patient;
    - the variable, incorporating three different parameters: the percentage of viable segments, the LVEF measured during administration of LDD and the baseline LVEF.
5. There is a trend toward reverse LV remodeling and symptomatic improvement in patients with ischemic LVD after a successful revascularisation of the significant amount of viable myocardium.

6. LGE-CMR is a good method for the determination of the frequency and extent of new periprocedural/perioperative myocardial injury and also for the evaluation of the frequency, extent, and localization of myocardial injury that occurs late after revascularisation.
7. There is a week correlation between the presence of Q waves on electrocardiogram and the transmurality of LGE. Q wave is determined by the total size rather than transmural extent of underlying MI.

NOVELTY OF THE RESEARCH

1. On the basis of this research the combined CMR viability assessment method (incorporating LDD-CMR and LGE-CMR) was introduced and studied at the Vilnius University Hospital Santariškių Klinikos for the first time in Lithuania and in the three Baltic states as well.
2. According to the available medical literature, there are several, single-centre, small sample size studies (with a maximal sample size of 35 patients) that used the combined CMR method for the prediction of segmental functional recovery after revascularisation. The authors of those studies emphasized the need of further studies in other medical centres with larger sample sizes as well as randomised studies in this field.
3. To the best of our knowledge, the prospective and direct comparison of three different CMR viability parameters (CR, LGE and RIM) and their combinations as predictors of segmental functional recovery has not been studied in patients with LVD undergoing either surgical or percutaneous revascularisation.
4. To the best of our knowledge, the combined LDD-CMR- and LGE-CMR-based predictor of significant improvement of global LVEF has not been investigated thus far.
5. In contrast to the majority of CMR-based viability studies described in available medical literature, the patients in our cohort underwent either percutaneous or surgical revascularisation, what represents perfectly the real clinical practice.
6. On the basis of the below described research, the CMR-based algorithm of myocardial viability assessment is created and successfully introduced into clinical practice at the Vilnius University Hospital Santariškių Klinikos. We

believe that the use of this CMR-based algorithm will help to select the most suitable candidates for revascularisation, medical treatment, or LV reconstructive surgery.

METHODS

Patients and study design

A prospective evaluation of the different CMR parameters for predicting LV segmental and global functional recovery was performed in 55 patients (63 years old [SD, 10 years]), 6 women, 3 with previous coronary artery bypass graft surgery (CABG), 22 with previous PCI, 42 [76%] with three-vessel disease, 3 [5%] with one-vessel disease) with LVD (LVEF 35% [SD, 8%]) before they underwent surgical (n=43) or percutaneous (n=12) revascularisation. A total of 91 patients without contraindications for CMR were screened for the following inclusion criteria: 1) chronic coronary artery disease (CAD) (>70% stenosis in one or more major epicardial vessels), scheduled for a revascularisation procedure; 2) LVEF ≤45%; 3) at least two adjacent segments with wall motion abnormalities at rest; and 4) no infarction or revascularisation within the last two months. 74 patients were included in the study only after a successful and complete coronary revascularisation. Of the 19 patients who did not complete the study, 5 not to undergo the repeated CMR scan or were lost during follow-up; 3 died in early postoperative period after CABG; 7 had significant periprocedural injury (new LGE zones on repeated CMR scans and clinically proven periprocedural myocardial infarction (MI) or MI between both scans); 3 had pacemakers or defibrillators implanted in the period between the MR scans; and 1 was excluded because of dilated cardiomyopathy with secondary CAD. None of the patients were excluded from the study for technical reasons or image quality. The mean interval between CMR and revascularisation was 24 days, and none of the patients presented clinical evidence of infarction during this period. The mean interval between MI and the first CMR was 1322 days (3.6 years). In 55 patients, the extent of regional contractility and LGE were determined repeatedly by CMR 27 weeks [SD, 4] (6 months) after revascularisation.

Chemiluminescent, microparticle-based assay for troponin I was performed within 24 hours after revascularisation procedure in the patients with clinical suspicion of periprocedural injury. The ECG analysis was performed blindly without knowledge of

the CMR data by one investigator. Measurement for defining Q wave (QW) and localization of MI was undertaken according to the Minnesota Code and the ESC/ACCF/AHA/WHF universal definition of myocardial infarction.

The study was approved by the Lithuanian Bioethics Committee (21th of June 2007 Nr. 17), and informed written consent was obtained from each patient prior to inclusion in the study.

CMR protocol

All the CMR examinations were performed using a 1.5 T MR scanner (Avanto, Siemens Medical Solutions, Erlangen, Germany) using prospective gating. Steady-state free precession cine CMR was performed during breath holding, and 4-, 3-, and 2-chamber views, as well as a short-axis stack covering the left ventricle every 8 mm without a gap, were acquired at rest and at the end of each dose of dobutamine (5 and 10 10 μg/(kg·min)) (echo time (TE)/repetition time (TR)/flip angle, 1.22 ms/63 ms/65 degrees; field of view (FOV), 250 mm; voxel size, 1.9×1.3×8 mm, matrix size 109 × 192). After revascularisation, only rest images were acquired using the same technique.

Ten-to-fifteen minutes after infusion of 0.15 mmol/kg of the commercially available gadolinium-based contrast agent (gadopentetate dimeglumine or gadodiamide), an inversion recovery gradient-echo sequence (TE/TR/flip angle, 3.2 ms/700 ms/25 degrees; FOV, 400 mm, matrix size 156 × 256) was performed in the same planes as the cine images with an inversion time (240 to 330 ms) chosen to reduce the signal from normal myocardium. The typical voxel size was 2.1×1.6×8 mm. Angulation was kept constant for a short-axis and LGE imaging to enable a match between the LGE and wall motion images.

Post-processing Analysis

We analysed the cine images and contrast-enhanced images using a model in which the LV was divided into 17 segments. The wall motion was graded as 1 (normal), 2 (mild hypokinesia), 3 (severe hypokinesia), 4 (akinesia), or 5 (dyskinesia) by 2 investigators. Discordant assessments were jointly reviewed. For the patients undergoing percutaneous revascularisation, segments were considered to be undergoing revascularisation according to the scheme commonly used in stress echocardiography. The LV apical

segment was assigned to a specific coronary artery territory according to the vessel anatomy on a conventional angiogram. For the global LV functional analysis, all short-axis slices from the base to the apex at rest and during administration of dobutamine (10 μg/[kg·min]) were analysed with Argus software (Siemens) by two independent experienced observers. The wall motion score index (WMSI) was calculated by dividing the sum of scores by the number of segments per patient. The LV sphericity index (SI) was measured by dividing the length of the LV from the apex to the mitral annulus by the width of the LV at the basal aspect of the papillary muscles in the end-diastolic apical four-chamber view. An absolute change in LVEF ≥5% 6 months after revascularisation was considered to be significant. When predicting significant LVEF improvement, a segment was considered viable if it had no LGE or had any LGE and produced CR during LDD stimulation. The number of viable segments divided by the total number of dysfunctional and revascularised segments in a patient was expressed as a percentage that was used together with the absolute number of viable segments to predict a significant LVEF improvement. We compared two groups: responders (i.e., patients with significant LVEF improvement 6 months after revascularisation) and non-responders (i.e., patients without significant LVEF improvement [improvement of LVEF <5%]).

The extent of LGE within each segment and the RIM was also measured by the two investigators on short-axis, contrast-enhanced CMR images. Contrast-enhanced pixels were defined as those with image intensities of >2 SD above the mean of image intensities in a remote myocardial region in the same image. LGE was assessed on a 5-grade scale in which a score of 0 indicated no hyperenhancement; a score of 1, hyperenhancement of 1% to 25% of the tissue in each segment; a score of 2, hyperenhancement of 26% to 50% of the tissue; a score of 3, hyperenhancement of 51% to 75% of the tissue; and a score of 4, hyperenhancement of 76% to 100% of the tissue. LGE transmurality was analysed quantitatively by dividing the hyperenhanced area, as measured by computer-assisted tracings, by the total area in each segment before being expressed as a percentage. The thickness of the non-contrast-enhanced rim was defined as the mean wall thickness of the non-enhanced area of a segment. Only the dysfunctional segments detected on the first MR scan and those without an increase in

the LGE area on the second MR scan were analysed. The total LGE score per patient was calculated by dividing the sum of the LGE scores by the number of segments.

An improvement in wall motion at follow-up by at least 1 grade with the exception of improvement from grade 5 to grade 4 was regarded as functional recovery or viability of the segment. The LDD-CMR was regarded as indicative of viability or CR when there was an improvement of 1 wall motion grade at either the 5 or 10 μg/(kg·min) dose. The segmental wall motion, LDD-CMR, LGE, and functional recovery were assessed by two reviewers. All discordant assessments were jointly reviewed.

Statistical Analysis

To compare the values of different CMR parameters for predicting segmental functional recovery, the usual characteristics, such as sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), were calculated. Using a logistic regression model, the threshold values that produced the optimal sensitivities and specificities were identified. Being optimal did not mean that this threshold produced the highest accuracy. The difference between sensitivity and specificity was also considered (e.g., a threshold producing 99% sensitivity and 10% specificity was not treated as the best, even if its accuracy was the highest). Furthermore, several logistic regression models to predict myocardial viability using CR, LGE50, and RIM4 values were developed. For LGE50 and RIM4, the calculations were performed using binary variables, which were assigned a value of 1 if the measurement exceeded the threshold value and a value of 0 otherwise (e.g., LGE50=1 when LGE>50 and LGE50=0 when LGE≤50). As we wanted not only to test whether single parameters perform differently but also to find out whether there is a rationale for using a combination of several methods, 5 different logistic regression models were created. In all of the viability models, functional improvement after revascularisation acted as a dependent variable. Meanwhile, the other above-mentioned CMR parameters acted as independent variables. All independent variables were statistically significant (**Table 1**). To find out which method had the best predictive ability, the areas under the receiver operating curves (ROC) of the five different logistic regression models were compared.

Table 1. The independent variables, used in five different logistic regression models.

Model No.	List of independent variables	Model abbreviation
1*	RIM4 (*P*=0.001), CR (*P*=0.001)	RIM4+CR
2	LGE50 (*P*<0.001), CR (*P*<0.001)	LGE50+CR
3	LGE50 (*P*<0.001)	LGE50
4	CR (*P*<0.001)	CR
5*	RIM4 (*P*<0.001)	RIM4

* Models were created using only segments with any degree of LGE.

The different baseline and follow-up characteristics of patients with and without significant improvement in LVEF 6 months after revascularisation were compared. The values from both patient groups were expressed as the mean (SD). The effect of revascularisation was compared using a Wilcoxon signed-rank test. The continuous variables that were not distributed normally were compared by using a nonparametric test. The variables that differed significantly between groups were included in a forward stepwise (Wald) logistic regression analysis to determine the best independent predictor of significant LVEF improvement. The ROC analysis was performed to validate the variables with the best predictive ability. Additionally, several logistic and linear regression models for prediction of the absolute change in LVEF after revascularisation were developed using different number of variables in the models. The ROC analysis of the latter models was performed to validate the model with the best predictive ability. The predictor of global functional recovery was treated superior to the other methods if its area under the ROC curve (AUC) was significantly greater.

To ensure a statistical power of the prediction of segmental recovery, a required sample size of dysfunctional and successfully revascularised segments was calculated (n=276). All calculations were performed using the SPSS 16.0 and StAR software. A *P* value of <0.05 was considered statistically significant.

RESULTS

Baseline characteristics of the patients

Fifty-five patients underwent a successful and complete revascularisation procedure (the visual examples of the dynamical changes of LV function are presented in **Figure 1–3**). A significant improvement in LVEF ≥5% was demonstrated in 43 (78%) of the 55

patients, and the baseline characteristics of patients with and without significant improvement in LVEF are given in **Table 2**.

Only the functional LV parameters before revascularisation differed significantly between the groups (**Table 3**). Patients in the nonresponder group had significantly greater baseline LV volume indexes, LVSI and WMSI. Although the absolute number of viable segments differed nonsignificantly between groups (*P*=0.485), the percentage of viable segments was significantly greater in the responder group (*P*=0.006).

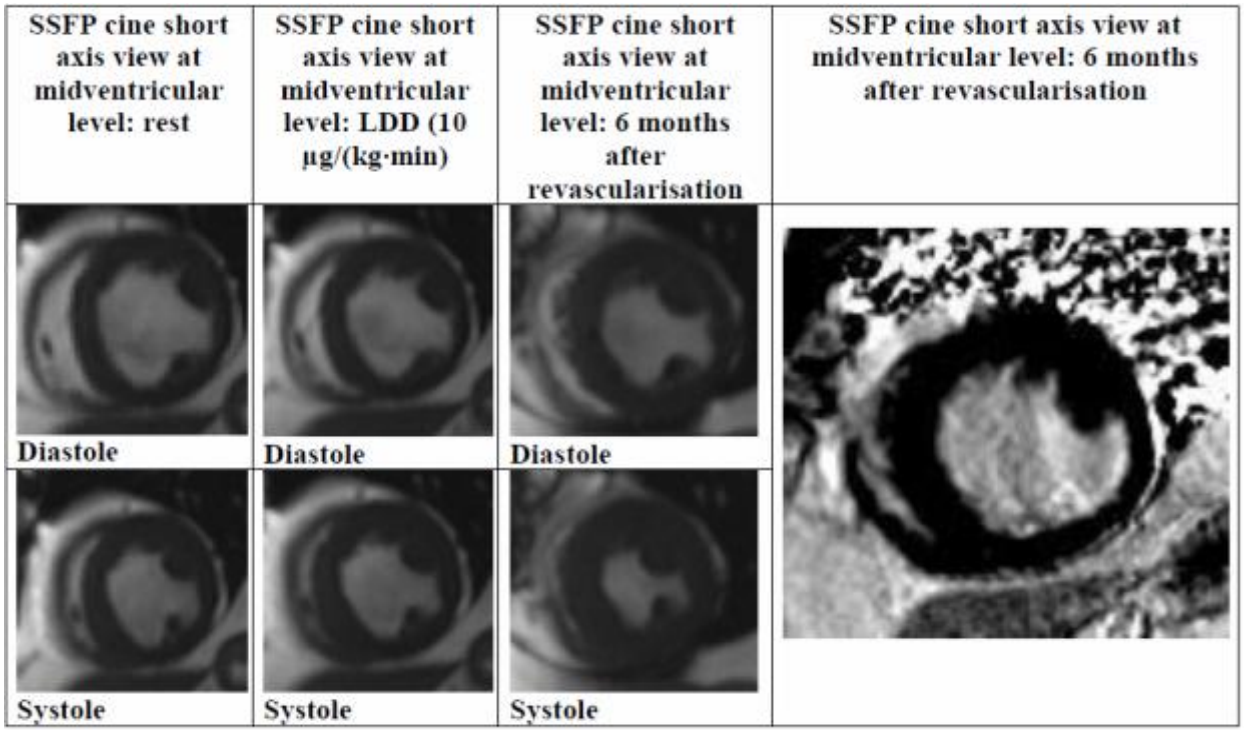

Figure 1. 49 year's old male; CMR viability study (patient without previous MI, LVEF at rest 30%, three-vessel disease).

There is mild hypokinesia in septal segments and severe hypokinesia in inferior and inferolateral segments at rest (first column). There is CR only in septal segments during LDD infusion (second column). 6 months after revascularisation (complete revascularisation after CABG, 5 distal anastomoses) there is functional recovery in all at rest dysfunctional segments with remaining mild hypokinesia in inferior and inferolateral segments (third column). There is an subendocardial LGE <25% in inferior and inferolateral segments (fourth column). LVEF 6 months after revascularisation is 42%.

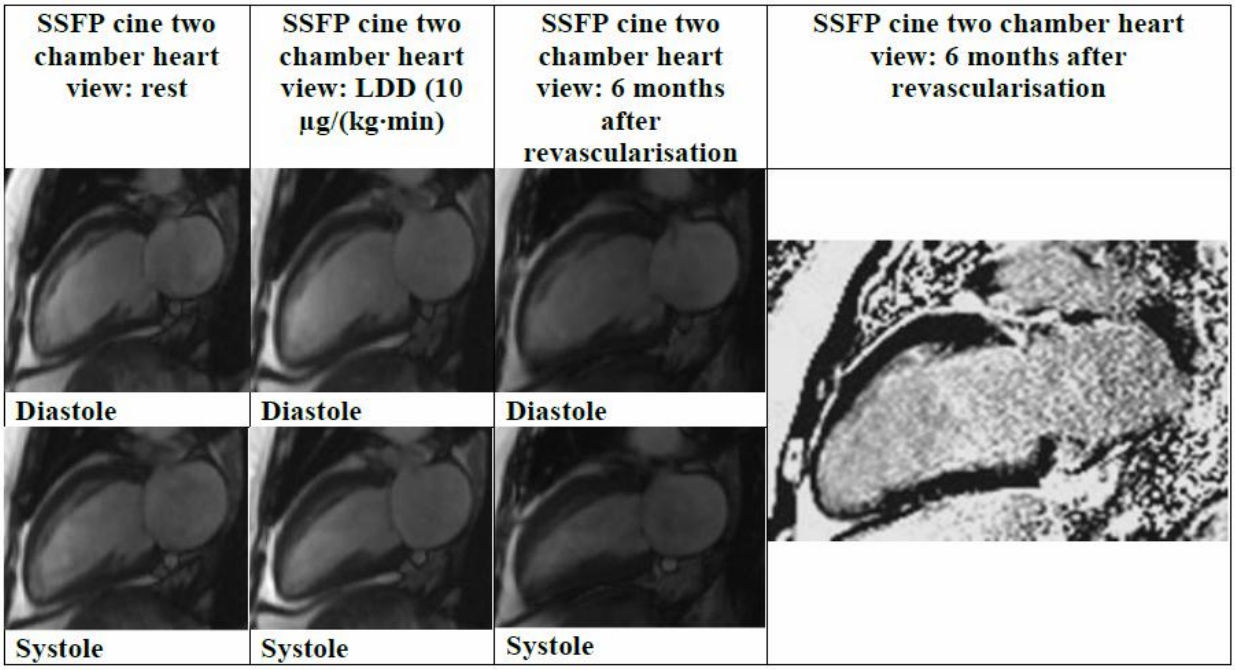

Figure 2. 52 year's old male; CMR viability study (patient without previous MI, LVEF at rest 24%, three-vessel disease).

There is severe hypokinesia in anterior and inferior walls (first column). There is CR in all segments of anterior and inferior walls during LDD infusion (second column). 6 months after revascularisation (complete revascularisation after CABG, 5 distal anastomoses) there is functional recovery in all segments of anterior and inferior walls (third column). There is no LGE in above-mentioned segments (fourth column). LVEF 6 months after revascularisation is 47%.

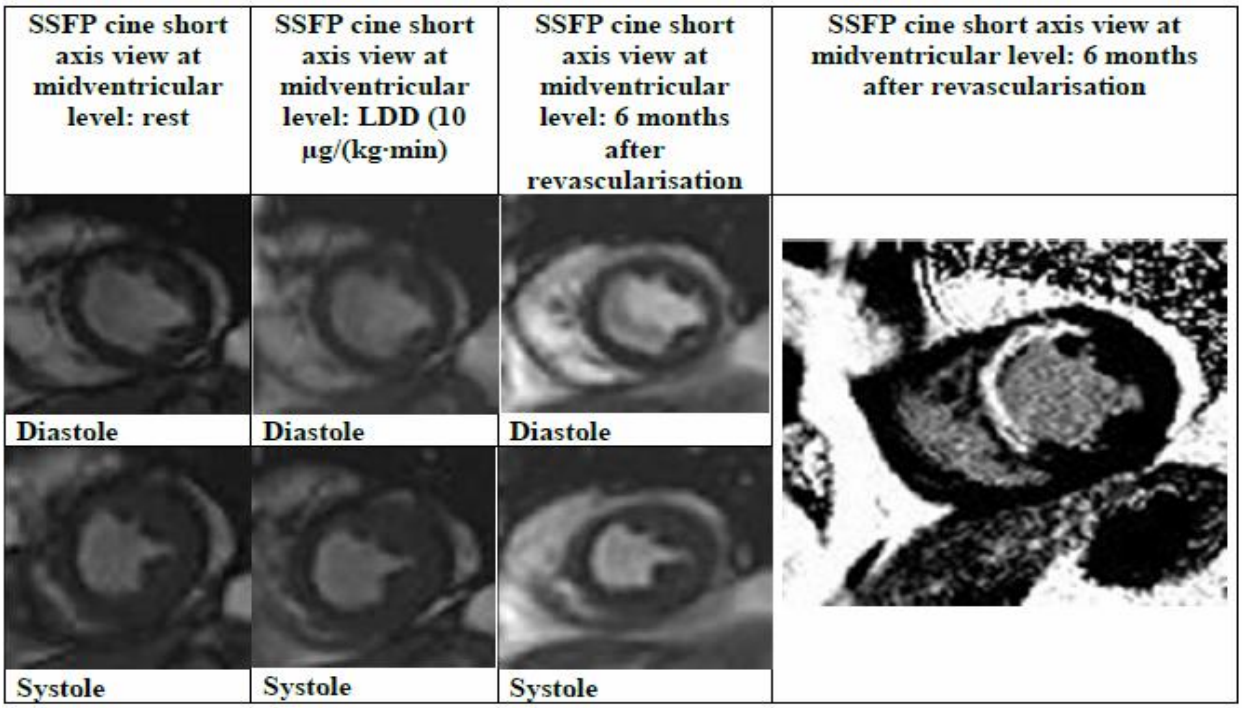

Figure 3. 62 year's old male; CMR viability study (patient with previous Q wave anteroseptal MI, LVEF at rest 41%, one-vessel disease).

There is mild hypokinesia in anterior and anteroseptal segments at rest (first column). There is no CR in anterior and anteroseptal segments during LDD infusion (second column). 6 months after revascularisation (complete revascularisation after LAD PCI) there is no functional recovery in anterior and anteroseptal segments (third column). There is an subendocardial LGE 76 to 100% in above-mentioned segments (fourth column). LVEF 6 months after revascularisation is 30%.

Table 2. The baseline characteristics of patients with and without significant improvement in LVEF.

Baseline characteristic	All patients n=55	Responders n=43	Nonresponders n=12	*P* value
Age, years	63 (10)	64 (10)	60 (8)	0.221
Men, n (%)	49 (89)	37 (86)	12 (100)	0.321
GFR, mL/min	91 (33)	88 (35)	101 (25)	0.175
Hypertension, n (%)	51 (93)	39 (91)	12 (100)	0.566
Smokers, n (%)	14 (26)	10 (23)	4 (33)	0.492
Diabetes mellitus, n (%)	12 (22)	10 (23)	2 (17)	1.000
Previous documented MI, n (%)	48 (87)	36 (84)	12 (100)	0.193
NYHA functional class	2.8 (0.8)	2.7 (0.8)	2.8 (0.9)	0.338
No. of diseased vessels	2.7 (0.6)	2.7 (0.6)	2.9 (0.3)	0.153
CABG, n (%)	43 (78)	33 (77)	10 (83)	0.717
ONBEAT, n (%)	12 (28)	9 (27)	3 (30)	1.000
ONSTOP, n (%)	31 (82)	24 (83)	7 (70)	
No. of distal anastomoses	2.57 (1.6)	2.4 (1.6)	2.8 (1.5)	0.455
LIMA, n (%)	36 (84)	29 (88)	7 (70)	0.325
PCI, n (%)	12 (22)	10 (23)	2 (17)	1.000
Beta-blockers, n (%)	49 (89)	38 (88)	11 (92)	1.000
ACE inhibitors, n (%)	40 (73)	33 (77)	7 (58)	0.274
Statins, n (%)	44 (80)	33 (77)	11 (92)	0.422
Diuretics, n (%)	41 (75)	31 (72)	10 (83)	0.709
Duration between revascularisation and 2nd CMR, weeks	27 (5)	27 (4)	28 (8)	0.501

Values are means (SD) unless otherwise indicated. A responder was defined as a patient with an improvement in LVEF ≥5% after revascularisation.

Table 3. The baseline LV parameters of patients with and without significant improvement in LVEF

LV parameter	All patients n=55	Responders n=43	Nonresponders n=12	*P* value
LVEF, %	35 (8)	36 (8)	32 (8)	0.100
LVEF <30%, n (%)	13 (24)	9 (21)	4 (33)	0.448
LVEDVI, mL/m^2	95 (37)	89 (37)	116 (33)	**0.013**
LVESVI, mL/m^2	63 (29)	58 (29)	79 (28)	**0.012**
LVWMSI	1.84 (0.40)	1.75 (0.35)	2.17 (0.38)	**0.002**
LVSI	0.57 (0.10)	0.56 (0.10)	0.61 (0.10)	**0.047**
Total LGE score	1.6 (5.3)	1.8 (6.0)	1.2 (0.6)	0.076
No. of viable segments*	4.5 (2.7)	4.9 (2.8)	4.4 (2.8)	0.485
% of viable segments**	66 (29)	72 (29)	46 (24)	**0.006**

Values are means (SD) unless otherwise indicated. The total LGE score per patient was calculated by dividing the sum of the LGE scores by the number of segments. *Segment was considered viable if it had no LGE or had any LGE and produced CR during LDD stimulation. **The number of viable segments divided by the total number of dysfunctional and revascularised segments in a patient and expressed as a percentage.

Prediction of regional left ventricular functional recovery after revascularisation

Overall, 410 (44%) of the 935 myocardial segments analysed had abnormal contractility and underwent successful revascularisation. A functional recovery was observed in 245 segments (60%), but the remaining 165 segments (40%) showed no signs of functional recovery after revascularisation. The functional recovery was documented in 75% of the segments with mild hypokinesia, 45% of those with at least severe hypokinesia, and only 18% of those with akinesia or dyskinesia before revascularisation. The functional recovery of the myocardium decreased with increasing LGE transmurality (82% of segments with functional recovery in LGE 0% to 25%, 67% in LGE 26% to 50%, 41% in LGE 51% to 75%, and 13% in LGE >75% were found) (**Figure 4**). Functional recovery of the segments with LGE from 0% to 25% is much more likely than the functional recovery of the segments with LGE >75% (odds ratio (OR), 30.4). A similar trend in segmental functional recovery was observed in 210 segments with severe hypokinesia, akinesia, or dyskinesia (92% segments with functional recovery in LGE 0% to 25%, 57% in LGE 26% to 50%, 37% in LGE 51% to 75%, and 9% in LGE >75%) (OR, 51.6) and in 95 segments with akinesia or dyskinesia

(67% of segments with functional recovery in LGE 0% to 25%, 42% in LGE 26% to 50%, 19% in LGE 51% to 75% and 3% in LGE >75%) (OR, 65.6) (**Figure 4**).

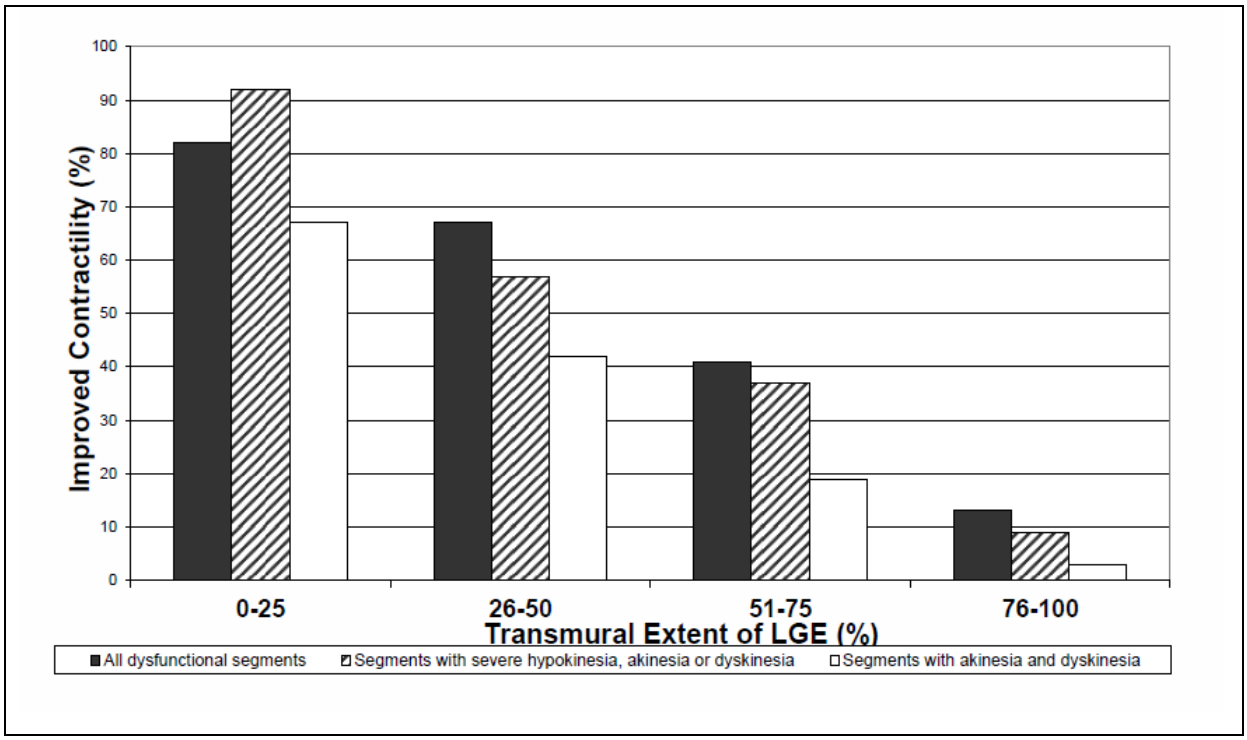

Figure 4. Relationship between LGE before revascularisation and the likelihood of improved segmental contractility after revascularisation

Data are shown for all 410 dysfunctional segments and separately for the 210 segments with at least severe hypokinesia and for the 95 segments with akinesia and dyskinesia before revascularisation. For all three analyses, there was an inverse relationship between the LGE and the likelihood of improvement in contractility.

The decreasing likelihood of functional recovery with more extensive scarring found in the present study confirms the prognostic importance of scarred myocardium, which is consistent with previous studies. The high percentage (82%) of segments with no or minimal scarring (LGE ≤25%) in our cohort recovered 6 months after revascularisation, and this fact confirms the hypothesis that 6 months after revascularisation was sufficient for almost complete recovery. The decreasing likelihood of functional recovery with more pronounced functional segmental abnormality (i.e., functional recovery was observed in 75% of the segments with mild hypokinesia and in only 18% of those with akinesia or dyskinesia before revascularisation) can be explained

by good relationship between functional segmental abnormality score and LGE transmurality (Pearson correlation coefficient (r) =0.58; P<0.0001).

Sixty-four per cent of segments (204 of the 318) with functional recovery were observed in the group with an end-diastolic wall diameter of ≥5.5 mm; however, only 45% of segments (41 of the 92) with an end-diastolic wall diameter of <5.5 mm recovered after revascularisation (OR, 2.17).

Based on segmental functional recovery 6 months after revascularisation, the prognostic values of different CMR parameters and threshold values for the LGE and the RIM that could be used in practice to distinguish between viable and nonviable segments were calculated (**Table 4**). Using an LGE threshold value of 50%, patients in whom recovery of regional myocardial function is likely or unlikely can be roughly differentiated with a sensitivity of 82% and a specificity of 65%. An RIM value of 4 mm can predict the recovery of hibernating myocardium with a sensitivity and specificity of about 78% and 71%, respectively. Although the sensitivities of LGE50 and CR were comparable (82% and 83%, respectively), the specificity of CR was the highest (78%), which is consistent with previous studies.

Table 4. The prognostic value of the four different CMR viability parameters

Parameter	Sensitivity, %	Specificity, %	PPV, %	NPV, %	Threshold value	No. of analysed segments
LGE	82	65	78	70	50%	410
RIM	78	71	69	80	4 mm	247
CR	83	78	85	75	–	410
EDWT	61	60	69	51	7.3 mm	410

The LGE, RIM, and EDWT threshold values were calculated using the logistic regression model. PPV, positive predictive value; NPV, negative predictive value; no, number.

To prospectively and directly compare the predictive value of CR, RIM, and LGE, binary variables for the LGE and the RIM (LGE50, 50% cut-off; and RIM4, 4-mm cut-off) were used. The areas under the ROC curves obtained using five different logistic regression models were compared (**Figures 5** and **6**): a) in all dysfunctional and revascularised segments (n=410), depending on LVEF (i.e., in patients with LVEF <30%

and LVEF ≥30%); b) in segments with any degree of LGE (n=247); c) in segments with LGE from 26% to 75% (n=180) and from 1% to 75% (n=186); and d) in segments with LGE >75% (n=61).

Comparing the three different viability prediction models (LGE50+CR, CR, LGE50) in patients with LVEF ≥30% and <30% (**Figure 5**), CR alone was observed to be superior to LGE50 alone in the group with LVEF ≥30% (*P*=0.026), but not in the group with LVEF <30% (*P*=0.16). The significant superiority of the combined viability prediction model (LGE50+CR) over the CR only model was noticed in both patient groups. In patients with LVEF <30%, using the combined viability prediction model (LGE50+CR), the percentage of correct predictions for hibernating myocardium was 84% compared with 82% for patients with LVEF ≥30%. The high percentage (84%) of correct predictions for hibernating myocardium in the patient group with LVEF <30% confirms the hypothesis that CMR is very suitable for viability prediction, especially in patients with severe LV dysfunction, in whom echocardiographic methods of viability prediction are less accurate.

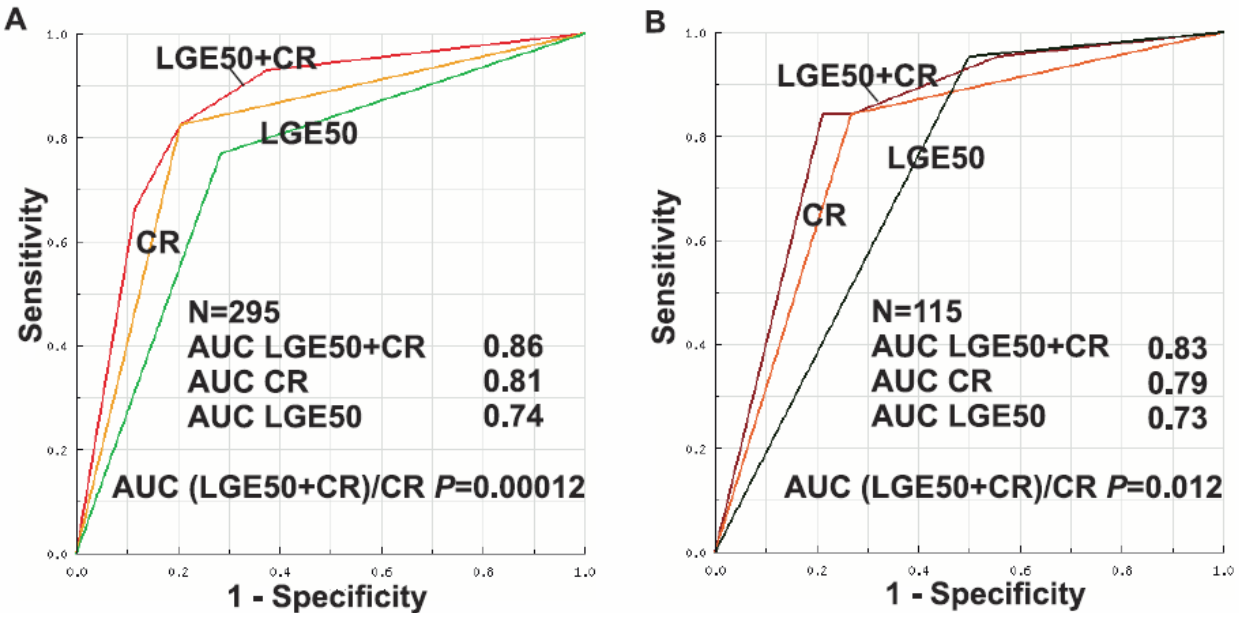

Figure 5. ROC curves: the logistic regression model combining LGE50 and CR compared to CR alone and LGE50 alone

The AUC value for LGE50+CR was significantly higher than CR alone or LGE50 alone in patients with LVEF ≥30% (A) and in patients with LV EF <30% (B).

The areas under the ROC curves of five different viability prediction models (RIM4+CR, LGE50+CR, CR, RIM4, and LGE50) were compared in segments with any degree of LGE (**Figure 6A**). The AUC of combined viability prediction model (RIM4+CR) was the highest and differed significantly from all other analysed viability prediction models except from the combined model (LGE50+CR) (P=0.712). Using only segments with LGE 26% to 75% (**Figure 6B**) and segments with LGE 1% to 75% (**Figure 6C**), the same significant superiority of combined model (RIM4+CR) over all other analysed models, except of LGE50+CR model was noticed (RIM4+CR versus LGE50+CR, P=0.172 and P=0.426, respectively). Additionally, the AUC of combined viability prediction model (LGE50+CR) differed significantly from RIM4 alone, LGE50 alone, and CR alone in all above-mentioned subsets of segments (**Figure 6A–C**). Using only segments with LGE >75% (**Figure 6D**), four different viability prediction models were compared: RIM4+CR, CR alone, RIM4 alone, and absolute values of LGE (the cut-off value of LGE50 was not used, because in this subset of segments there were no any segments with LGE less than 50%). In the latter subset of segments, differences between the ROC curves of analysed viability prediction models were insignificant.

CR alone had a significant superiority to LGE50 alone in segments with any degree of LGE (P=0.0076), in segments with LGE 26% to 75% (P=0.005), and in segments with LGE 1% to 75% (P=0.007). There was no significant difference between CR alone and LGE50 alone in the segments with LGE >75%. Taking into account only the segments with any degree of LGE (**Figure 6A–C**), the areas under the ROC curves for RIM4 alone and LGE50 alone differed insignificantly. In ischemic cardiomyopathy with regional wall thinning, the addition of RIM measures to LGE can be useful, but according to our findings, the RIM did not give much more information than LGE, especially in segments with LGE from 1% to 75% or from 26% to 75%. As we expected, the correlation coefficient between the RIM and LGE is high (r=-0.81), and the AUC values are comparable because these two parameters carry virtually the same information regarding scar transmurality.

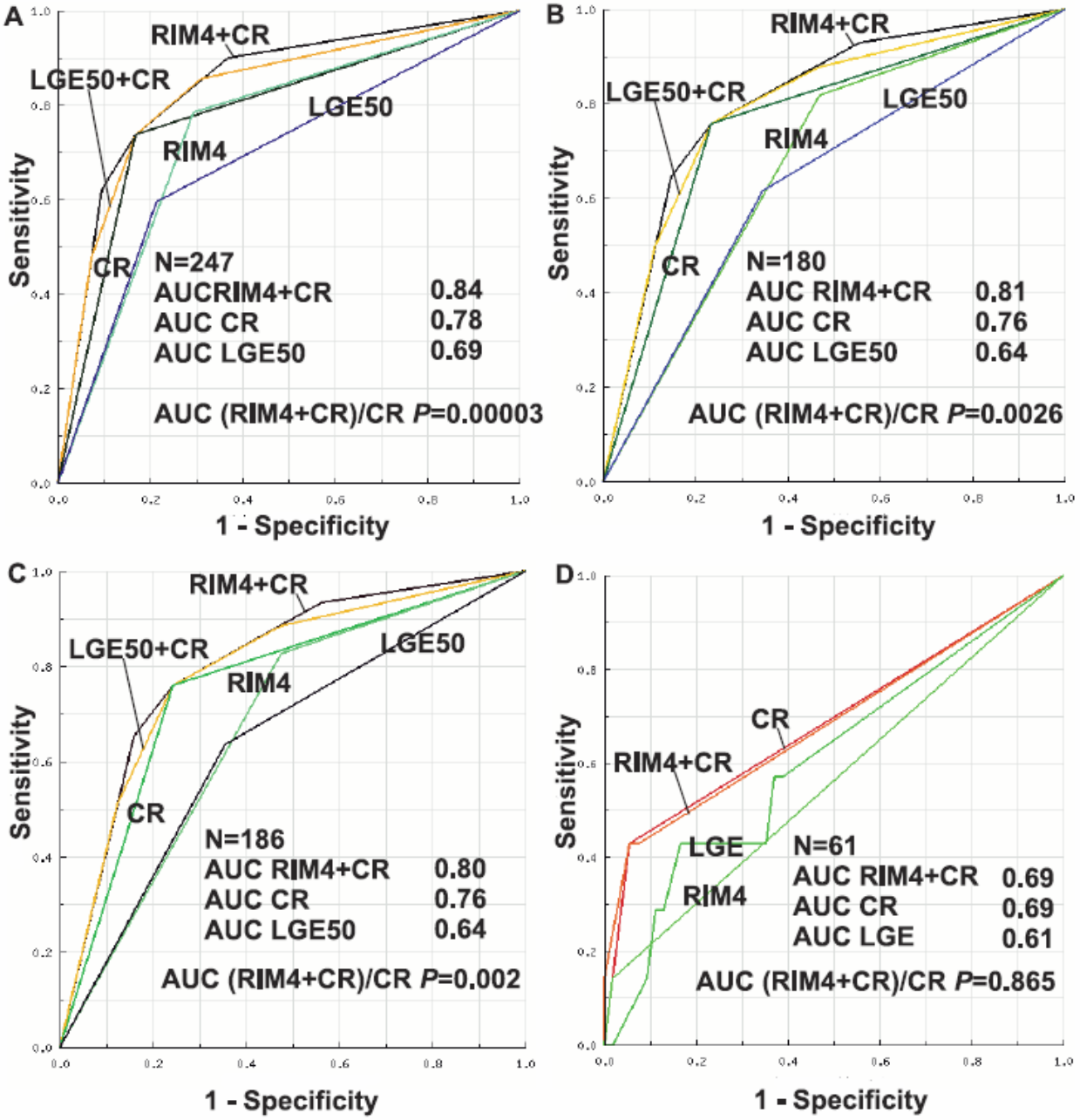

Figure 6. ROC curves: the logistic regression model combining RIM4+CR or LGE50+CR compared to CR alone, LGE50 alone, and RIM4 alone

The AUC values for RIM4+CR and LGE50+CR was significantly higher than CR alone, RIM4 alone or LGE50 alone in the segments containing any degree of LGE (A), in the segments with LGE from 26% to 75% (B), and in the segments with LGE from 1% to 75% (C). The differences between the AUC values of RIM4+CR, LGE alone, RIM4 alone, and CR alone were not significant in segments with LGE >75% (D).

The results of the aforementioned analysis indicate that the addition of LDD-CMR to LGE-CMR improves viability prediction when all dysfunctional segments, including

and excluding those without any contrast enhancement, are analysed. IR is superior to LGE50 in predicting hibernating myocardium in all sets of segments. Taking into account that most of the segments (around 82%) without any LGE recovered and that most of the segments (around 88%) with LGE >75% did not recover function after revascularisation, the evaluation of additional viability parameters besides LGE seemed to have little additional value in those subsets of segments. Thus, the addition of LDD-CMR seemed to have the greatest additional value in segments with 1% to 75% LGE, whereas measurement of the RIM thickness had no superiority over LGE50 in this LGE subset. In patients with intermediate LGE from 1% to 75% and from 26% to 75%, the addition of the CR improved the correct predictions of the hibernating myocardium from 64% to 76% and from 63% to 76%, respectively. Additionally, our findings confirm the fact that in segments with intermediate LGE, functional assessment of the RIM (i.e., assessment of the inotropic reserve during LDD) is more important than measuring RIM thickness.

Taking into account the higher predictive value of CR compared with LGE50, it is possible to use LDD-CMR instead of LGE-CMR to assess viability in selected patients with severely reduced renal function (GFR <30 ml/min) to avoid the risk of nephrogenic systemic fibrosis.

Prediction of global left ventricular functional recovery after revascularisation

Overall, the mean improvement in global ventricular function 6 months after revascularisation was 11% (SD, 8%). The improvement of CCS angina pectoris functional class was observed in both patients' groups: mean difference of 2.6 (SD, 0.9) (P<0.001) in the responders and 2.9 (SD, 0.3) (P=0.001) in the nonresponders. No patient at follow-up had angina pectoris of more than class I CCS. In the responders, the mean NYHA functional class was improved by 1 class (mean difference, 0.95 [SD, 1.15]; P<0.001), whereas in the nonresponders, the mean NYHA functional class remained almost unchanged (mean difference, 0.67 [SD, 1.61]; P=0.167). Successful revascularisation resulted in the improvement of angina pectoris symptoms; however, the improvement in heart failure symptoms depended on significant LVEF improvement, i.e., on successful revascularisation of the significant amount of viable myocardium.

There was a strong inverse correlation between baseline WMSI and LVEF 6 months after revascularisation (r=–0.72, P<0.0001) (**Figure 7A**), indicating that the greater WMSI at baseline was related to lower LVEF 6 months after revascularisation and lower LVEF improvement. However, the correlation between the area of LGE to LVEF change and the correlation between the area of LGE to LVEF after revascularisation was weak (r=–0.38, P=0.004 and r=–0.37, P=0.006; respectively). Interestingly, an excellent correlation between LVEF measured during administration of dobutamine (10 µg/[kg·min]) and LVEF 6 months after revascularisation was documented (**Figure 7B**). This finding suggests that by measuring LVEF by CMR during LDD administration, it is possible to predict the absolute LVEF 6 months after successful revascularisation.

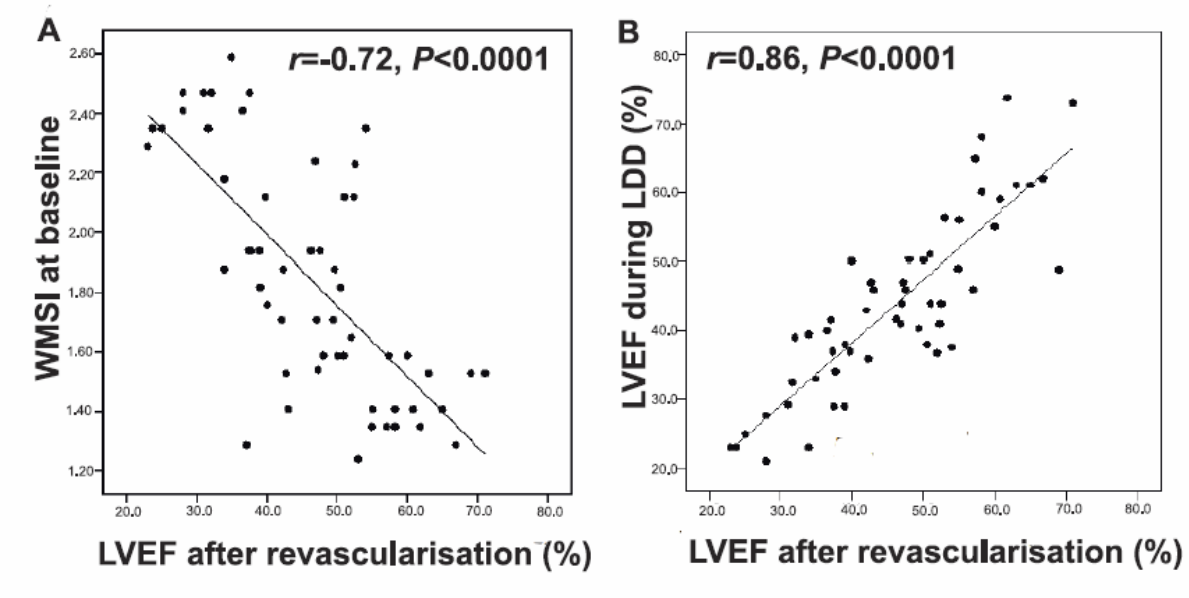

Figure 7. Correlation scatterplots

Correlation between WMSI at baseline and LVEF 6 months after revascularisation (A); correlation between LVEF measured during LDD administration and LVEF 6 months after revascularisation (B).

Six months after revascularisation, significant differences in LVEF (P<0.001), LV WMSI (P<0.001), LVSI (P=0.036), number of segments with functional recovery (P=0.045), and percentage of segments with functional recovery (P<0.001) comparing responder and nonresponder groups were documented (**Table 5**).

Table 5. The follow-up characteristics of the patients with and without significant improvement in LVEF

Follow-up characteristic	All patients n=55	ΔLVEF ≥5% n=43	ΔLVEF <5% n=12	*P* value
NYHA functional class	1.9 (0.9)	1.8 (0.8)	2.2 (1.02)	0.217
LVEF, %	46 (12)	50 (11)	34 (7)	**<0.001**
LVWMSI	1.55 (0.46)	1.43 (0.41)	1.97 (0.37)	**<0.001**
LVSI	0.56 (0.08)	0.55 (0.08)	0.61 (0.08)	**0.036**
No. of segments with functional recovery*	4.8 (2.8)	4.8 (2.8)	3.1 (2.2)	**0.045**
% of segments with functional recovery**	62 (31)	71 (28)	32 (17)	**<0.001**

Values are means (SD). *Improvement in wall motion at follow-up by at least 1 grade with the exception of improvement from grade 5 to grade 4 was regarded as functional recovery of the segment. **The number of segments with functional recovery at follow-up divided by the total number of dysfunctional and revascularised segments in a patient and expressed as a percentage.

Taking into account the changes of LV functional parameters within each group, both groups demonstrated a significant improvement in LVEF and WMSI; however, a significant decrease in ESVI (P<0.001) and LVddI (P=0.034) at follow-up was observed only in the responder group (**Table 6**). Changes in the other LV parameters (i.e., mitral valve regurgitation fraction, EDVI, and SI) after revascularisation were insignificant in both groups.

At baseline, significant differences regarding LV volume indexes, WMSI and SI, between the groups with and without significant LVEF improvement were determined. Patients in the nonresponder group had more remodelled left ventricles at baseline, higher LV volume indexes, LVSI and higher LVWMSI. These baseline LV parameters could contribute to the fact that the 6-month follow-up period could be too short for significant inverse remodelling in such ventricles. Insignificant changes in the LV volume indexes and sphericity index in this patients' group at follow-up were observed. Additionally, patients in the nonresponders group had not only a significantly lower percentage of viable segments, but also a significantly lower amount and percentage of segments with functional recovery after revascularisation. Thus, patients in the nonresponder group had a significantly lower amount of viable myocardium that was successfully revascularised comparing with the responder group. As a result, a trend toward reverse LV remodelling in patients with ischemic LVD after successful

revascularisation of the significant amount of viable myocardium was observed (LVESVI decreased by 22% in the responder group). The remodelled left ventricles have a lower amount of viable myocardium and/or more pronounced cellular and subcellular changes related to hibernation, thus, the significant reverse remodelling in such ventricles is less likely and/or takes much more time.

Table 6. The dynamic changes in LV function after revascularisation within groups of patients with and without significant improvement in LVEF

	Baseline	**Follow-up**	**Difference**	***P* value**
ΔLVEF ≥5%				
LVEF, %	36 (8)	50 (11)	–14 (6)	**<0.001**
LVEDVI, mL/m^2	89 (37)	87 (24)	2.3 (26)	0.296
LVESVI, mL/m^2	58 (29)	45 (20)	13 (14)	**<0.001**
LVWMSI	1.75 (0.35)	1.43 (0.41)	0.3 (0.3)	**<0.001**
LVSI	0.56 (0.10)	0.55 (0.08)	0.00 (0.1)	0.749
LVddI, cm/m^2	2.84 (0.55)	2.76 (0.5)	0.09 (0.37)	**0.034**
MVRF, %	21(11)	19 (10)	2.6 (14)	0.293
ΔLVEF <5%				
LVEF, %	32 (8)	34 (7)	–1.7 (2.3)	**0.038**
LVEDVI, mL/m^2	116 (33)	110 (25)	5.5 (28)	0.347
LVESVI, mL/m^2	79 (28)	74 (20)	4.7 (20)	0.347
LVWMSI	2.17 (0.38)	1.97 (0.37)	0.20 (0.19)	**0.009**
LVSI	0.61 (0.10)	0.61 (0.08)	0.00 (0.06)	0.894
LVddI, cm/m^2	3.0 (0.4)	3.0 (0.5)	–0.1 (0.4)	0.575
MVRF, %	22 (12)	17 (11)	4.2 (21)	0.388

Values are means (SD). The same abbreviations as used in Table 3.

To assess the best CMR-based predictors of significant LVEF improvement, the variables that differed significantly between the responders and nonresponders at baseline were used (**Table 3**). Forward stepwise logistic analysis revealed that EDVI (*P*=0.33), ESVI (*P*=0.74), and LVSI (*P*=0.19) were not good predictors of significant LVEF improvement. Meanwhile, WMSI was a significant predictor of LVEF ≥5% after revascularisation in a forward stepwise logistic analysis model (*P*=0.016; OR 0.074; 95% confidence interval, 0.009-0.617).

Additionally, two other parameters were compared: the absolute number of viable segments in a patient and the percentage of viable segments from all dysfunctional and revascularised segments in a patient. A viable segment was defined as a segment without

any LGE or with any LGE and having CR during LDD-CMR. The relationship between the percentage of viable segments and the change in LVEF was relatively close to linear, although the correlation between the absolute number of viable segments and the change in LVEF was rather week (**Figure 8**). The number of segments that recovered function at follow-up was significantly related to the number of viable segments identified by CMR at baseline (r=0.79, P<0.0001) and to the percentage of viable segments at baseline (r=0.51, P<0.0001).

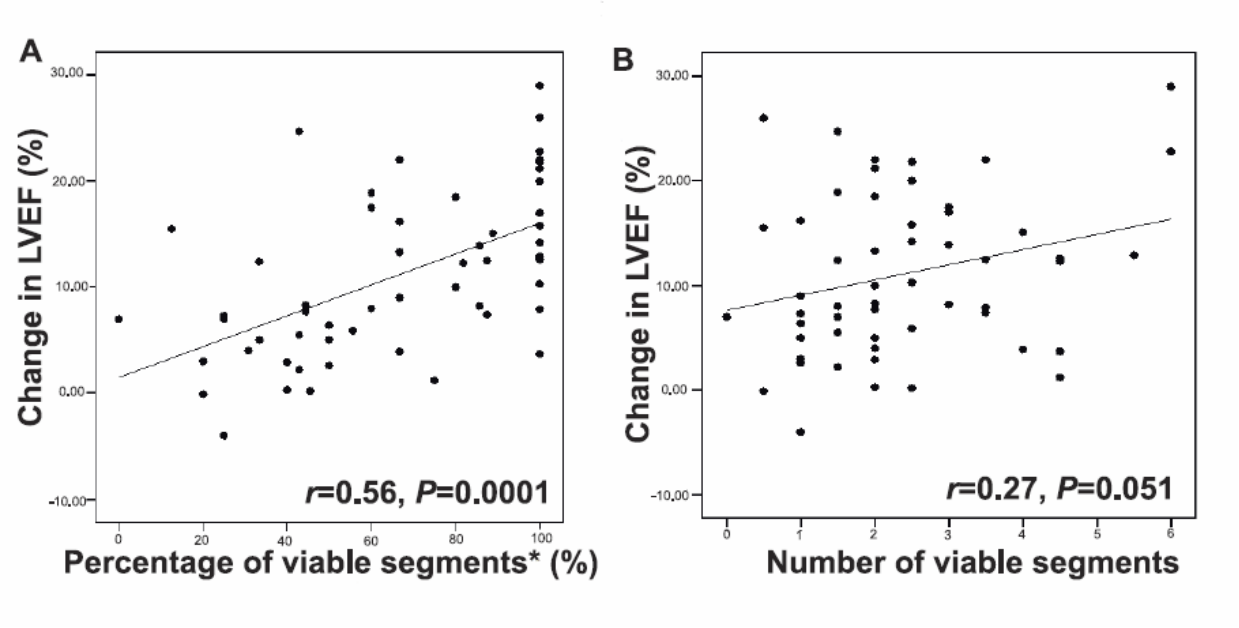

Figure 8. Correlation scatterplots

Correlation between the percentage of viable segments and the change in LVEF 6 months after revascularisation (A); Correlation between the absolute number of viable segments and the change in LVEF 6 months after revascularisation (B). *Percentage of viable segments is defined as the number of viable segments in a patient divided by all dysfunctional and revascularised segments and expressed as a percentage.

Using ROC analysis, the AUC for the percentage of viable segments was 0.76 (P=0.007) compared with the AUC of 0.57 for the number of viable segments (P=0.49) (**Figure 9**). This finding demonstrates that the absolute number of viable segments has a lower predictive value for significant global LV functional recovery than the percentage of viable segments. An additional ROC analysis was used to define a threshold for the percentage of viable segments in a patient that had the optimal sensitivity and specificity for predicting significant global LV functional recovery. The application of a cut-off

value of ≥50% viable segments yielded a sensitivity of 72% and a specificity of 75% for predicting a significant improvement in LVEF 6 months after revascularisation.

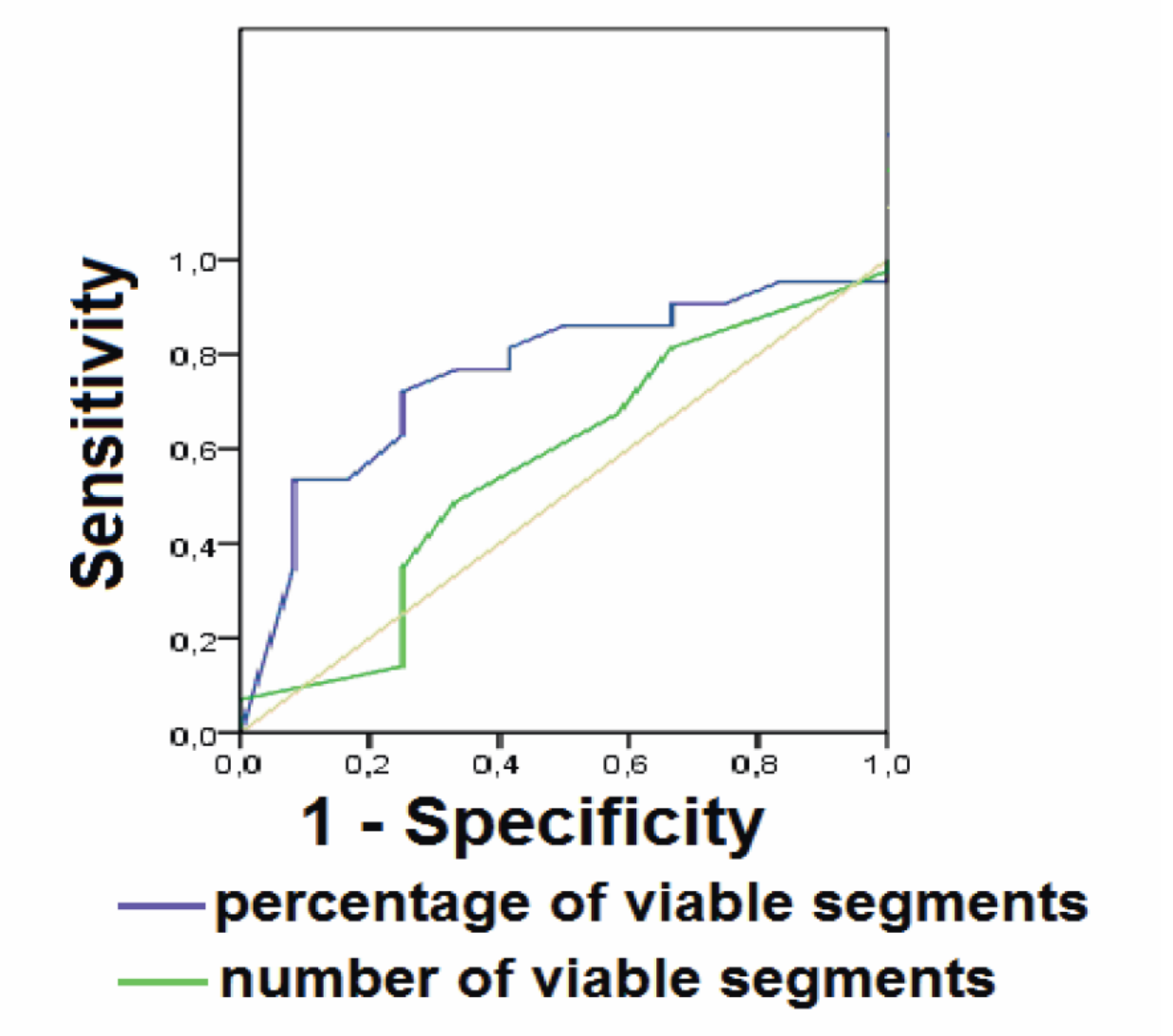

Figure 9. The areas under the ROC curves for the percentage of viable segments and the number of viable segments for predicting a significant improvement in global LV function after revascularisation

Taking into account an excellent correlation between LVEF measured during administration of dobutamine (10 μg/[kg·min]) (further in the text LDD LVEF) and LVEF 6 months after revascularisation, the LDD LVEF value for the prediction of significant LVEF improvement was used. ROC analysis showed that the AUC value of LDD LVEF was 0.74 (P=0.013), slightly lower than the AUC value of the percentage of viable segments (0.76, P=0.007).

For the prediction of LVEF change after revascularisation from the baseline LVEF, several models with different variables – baseline LVEF (further in the text LVEF), LDD LVEF, and the percentage of viable segments – were constructed. The best models were as follows:

1. Linear regression model for the prediction of the absolute change in LVEF using two independent variables: LDD LVEF and LVEF:
    - Absolute LVEF change = 0.630×LDD LVEF–0.482×LVEF;
    - R^2=0.787; R^2(adj.)= 0.779.
2. Linear regression model for the prediction of the absolute change in LVEF using three independent variables: LDD LVEF, LVEF, and the percentage of viable segments:
    - Absolute LVEF change = 0.427×LDD LVEF–0.393×LVEF+0.092×percentage of viable segments;
    - R^2=0.820; R^2(adj.)= 0.810.

Using above-mentioned linear regression models, different models for predicting a significant LVEF improvement were compared (**Figure 10**): a) logistic regression model, using LVEF and LDD LVEF as independent variables (AUC, 0.80; *P*=0.002); b) logistic regression model, using LVEF, LDD LVEF, and the percentage of viable segments as independent variables (AUC, 0.82, *P*=0.001); c) logistic regression model, using 0.630×LDD LVEF-0.482×LVEF as an independent variable, which is the prediction of the absolute change in LVEF from linear regression model 1 (AUC, 0.78; *P*=0.003); and d) logistic regression model, using 0.427×LDD LVEF–0.393×LVEF+0.092×percentage of viable segments as an independent variable, which is the prediction of the absolute change in LVEF from linear regression model 2 (AUC, 0.82; *P*=0.001).

Models including the percentage of viable segments (i.e., models with three independent variables) are better than models including two independent variables; however, in the logistic regression model b), the percentage of viable segments is a nonsignificant variable, and in the linear regression model d), the percentage of viable segments is a significant variable. Using the model d), a sensitivity of 74% and a specificity of 83% could be achieved, meanwhile using the model b), a sensitivity of

83% and a specificity of 75% could be achieved irrespective of the fact that the percentage of viable segments is an insignificant variable. Both the above-mentioned models are better than the model relying only on LDD LVEF.

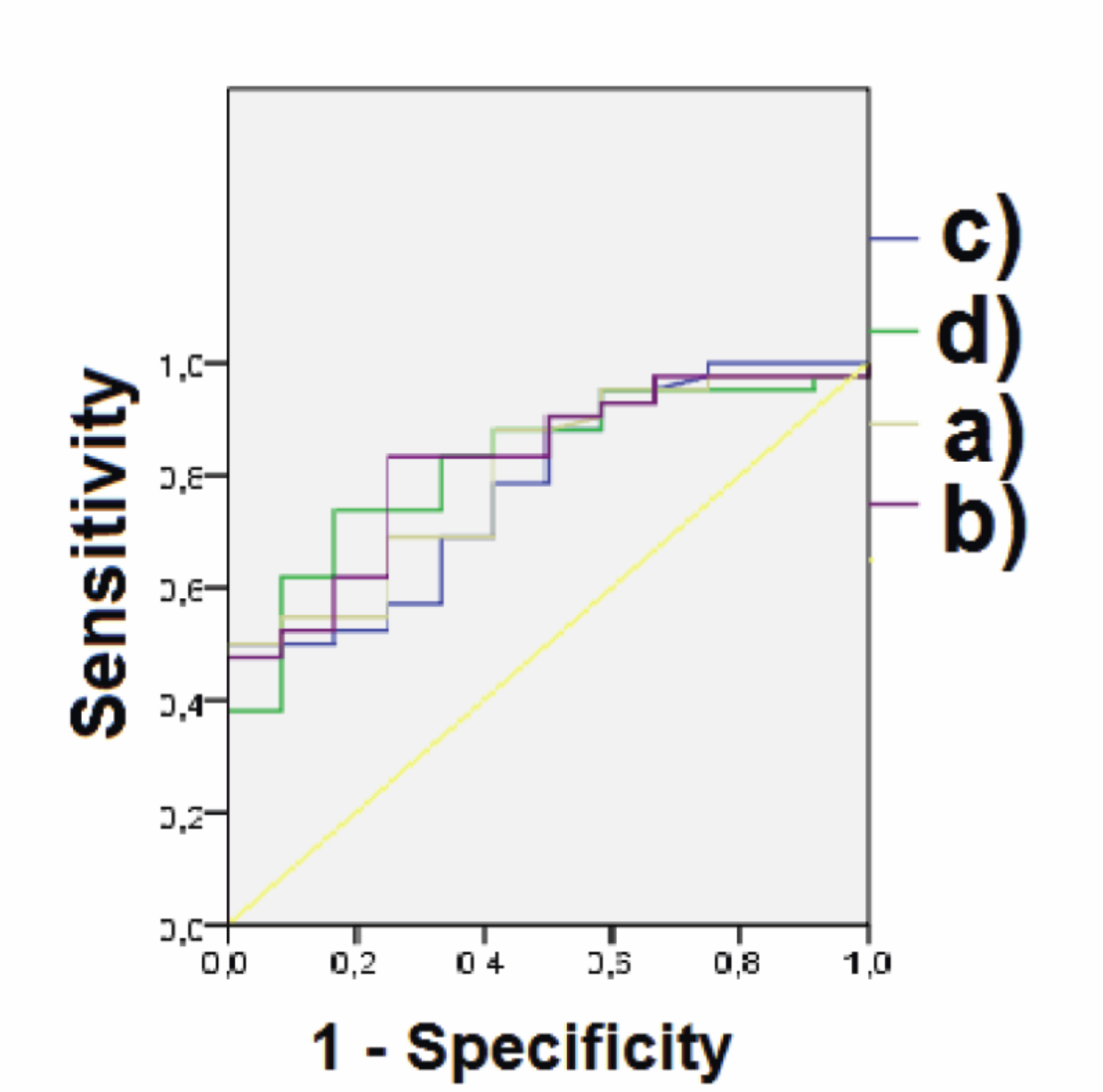

Figure 10. The areas under the ROC curves for the different models used for predicting a significant improvement in global LV function after revascularisation
Definitions of the models are in the text.

Models including the percentage of viable segments (i.e., models with three independent variables) are better than models including two independent variables;

however, in the logistic regression model b), the percentage of viable segments is a nonsignificant variable, and in the linear regression model d), the percentage of viable segments is a significant variable. Using the model d), a sensitivity of 74% and a specificity of 83% could be achieved, meanwhile using the model b), a sensitivity of 83% and a specificity of 75% could be achieved irrespective of the fact that the percentage of viable segments is an insignificant variable. Both the above-mentioned models are better than the model relying only on LDD LVEF.

Previous studies have demonstrated that a substantial amount of the jeopardised myocardium needs to be present to result in an improvement of LVEF after revascularisation. In previous studies, the setting of a cut-off level of ≥4 dysfunctional and viable segments (representing approximately 25% of the left ventricle) assessed by echocardiography yielded the highest diagnostic accuracy to predict improvement in LVEF. The present study demonstrates that the absolute number of viable segments has a lower predictive value for global LV functional recovery than the percentage of viable segments. The weak predictive value of the number of viable segments was recently reported by other investigators. As we were basing our experiments on a different study design and relying on our segmental functional recovery prediction results, we incorporated LGE-CMR and LDD-CMR data. Our results concerning global functional recovery prediction indicate that the best predictor of significant LVEF improvement 6 months after revascularisation in our cohort was the percentage of viable segments from all dysfunctional and revascularised segments in a patient.

In summary, further studies are warranted to confirm our findings. However, using a cut-off value of ≥50% viable segments from all dysfunctional and revascularised segments in a patient, it is possible to predict a significant improvement in LVEF 6 months after revascularisation with a sensitivity of 72% and a specificity of 75%. Using the variable 0.427×LDD LVEF–0.393×LVEF+0.092×percentage of viable segments, it is possible to predict the absolute change in LVEF after revascularisation and also to predict a significant improvement in LVEF with a sensitivity of 74% and a specificity of 83%. The above-mentioned findings could be relevant for clinicians making decisions about revascularisation in patients with impaired LV function in everyday practice. Additionally, our findings raise questions regarding the definition of substantial myocardial viability in further clinical viability studies.

CMR for the determination of the frequency and extent of new periprocedural/perioperative myocardial injury

Sixty-three patients underwent the second CMR scan. New LGE zones were identified in 7 patients (11%) (in 5 patients after CABG and in 2 patients after PCI). New LGE zones in those patients involved an average of 3.9 segments and the mean area of 14.3 cm^2. A significant elevation in troponin I concentration (mean concentration, 30 μg/L) within 24 h after revascularisation was found in 5 patients. The concentration of specific cardiac markers was not examined in the remaining 2 patients because they had not any clinical signs of perioperative myocardial injury. The definite time of perioperative myocardial injury in the latter 2 patients remains unclear, and the injury could be determined rather by the late graft occlusion than by the perioperative injury. The direct relationship between the amount of injured segments and the troponin I concentration was noticed: 3 patients with new LGE zones involving an average of 6 segments had the mean troponin I concentration of approximately 59.5 μg/L.

The primary goal of our study was to evaluate the predictive value of different CMR parameters, and we believe that the exclusion of the patients with new LGE zones from the analysis improved the reliability of our research.

LGE-CMR is a good method for the determination of the frequency and extent of new periprocedural/perioperative myocardial injury as well as for the evaluation of the frequency, extent, and localization of myocardial injury that occurs late after revascularisation.

The pathologic basis of Q-wave and non-Q-wave myocardial infarction

In order to evaluate the pathological basis of QW and NQW myocardial infarction, the data of 44 patients were analysed (**Table 7**). Nine patients were excluded from the analysis because of the presence of left bundle-branch block that prevents the interpretation of QW. Two patients were not analysed because of the absence of LGE zones on LGE-CMR and QW on ECG.

Table 7. Baseline characteristics of the patients included in the ECG analysis

Baseline characteristic	Value
Age, years	62 (10)
Men, n (%)	40 (91)
Main location of MI*	
Anterior, n (%)	15 (34)
Inferior, n (%)	5 (11)
Lateral, n (%)	6 (14)
Multiple, n (%)	18 (41)
Ventricular function	
EDVI, mL/m^2	92 (32)
ESVI, mL/m^2	59 (25)
LVEF, %	35 (8)
Mass, g	193 (56)

Values are mean (SD) unless otherwise indicated. *Location of MI was established from LGE-CMR scans according the above-mentioned post-processing analysis. The same abbreviations as used in Table 3.

Of all MIs, 45% were at some point transmural, and 73% of all MIs at some point nontransmural. QW on ECG was present in 31 patients (70%). Transmural MI showed NQW in 3 (16%) of the 19 patients and subendocardial MI showed QW in 15 (60%) of the 25 patients. There was a perfect match between the location of QW on ECG and LGE on CMR in 29 (94%) of the 31 patients and a mismatch between LGE location and QW in respective ECG leads only in 2 patients (16%).

The relationship between the presence of QW on ECG and MI transmurality was not significant (r=0.26, P=0.85), but the correlation between the presence of QW and infarct area was significant (r=0.59, P<0.0001). Using the ROC analysis, the LGE transmurality and the LGE area as predictors of the presence of QW on ECG were compared (**Figure 11**). Although the difference in AUC values was of borderline significance (P=0.057), but the LGE area was a better predictor of the presence of QW than the LGE transmurality (AUC values of 0.84 and 0.63, respectively). The borderline difference between AUC values of the abovementioned predictors could be influenced by the small sample size. The threshold value of the LGE area of 19 cm^2 produced a sensitivity of 88% and a specificity of 71%, meanwhile the threshold value of 24 cm^2 produced a sensitivity of 76% and a specificity of 86% for predicting the presence of the QW on ECG.

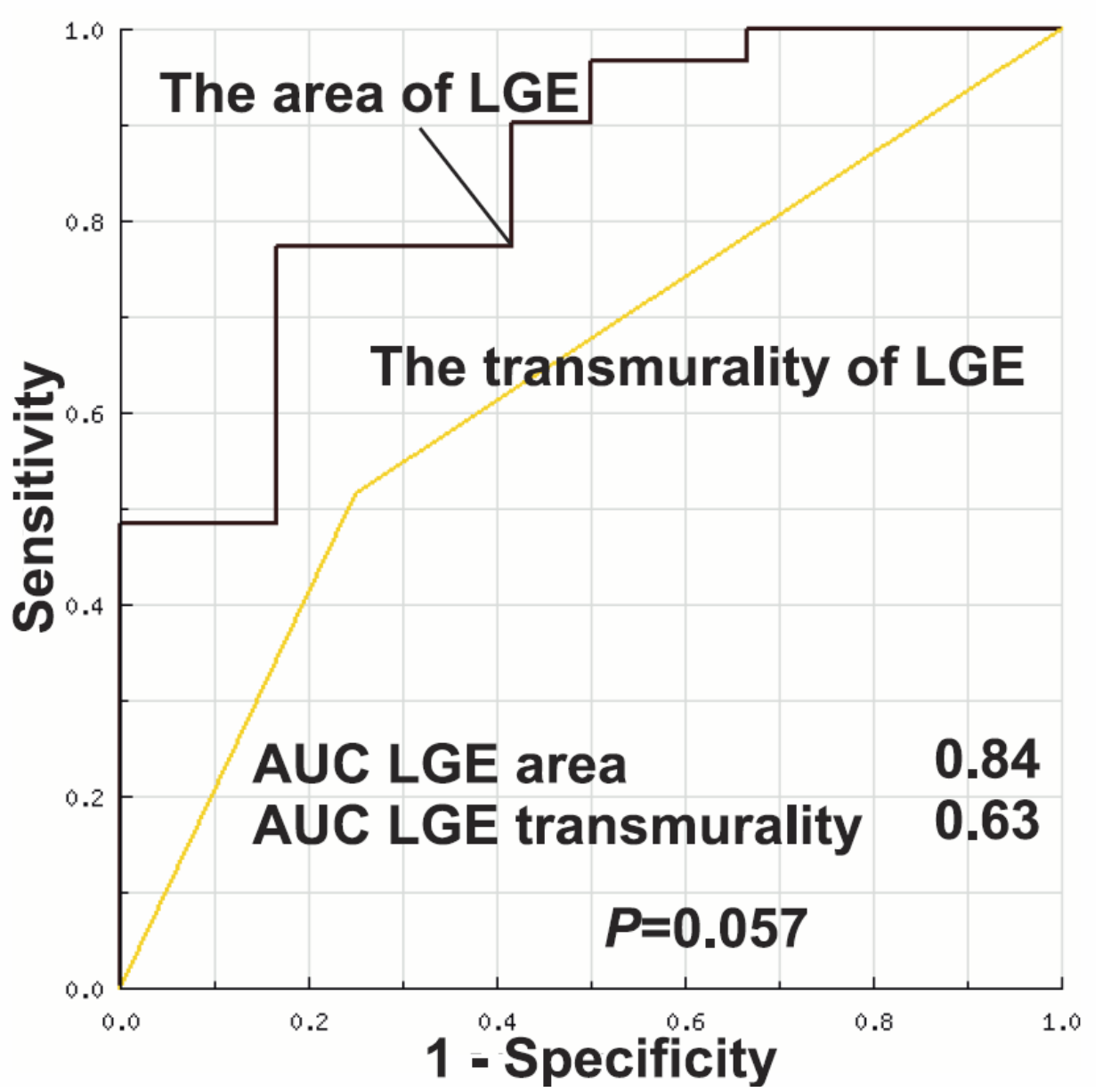

Figure 11. The areas under the ROC curves for the area of LGE and the transmurality of LGE for predicting the presence of the Q wave on ECG

The QW/NQW distinction is useful clinically; however, CMR findings show that MIs have a complex structure with a varying transmural extent, making a transmural/non-transmural division over-simplistic. Additionally, the transmural MI is not a necessary condition for QW. According our results, the QW/NQW distinction is determined by the total size rather than transmural extent of underlying MI.

CONCLUSIONS

1. Late gadolinium enhancement- and low dose dobutamine cardiovascular magnetic resonance provide complementary information regarding myocardial viability, and a combination of both techniques is valuable for more accurate prediction of segmental and global recovery irrespective of the degree of left ventricular dysfunction.
2. The best predictor of segmental recovery after revascularisation is contractile reserve. Its sensitivity and specificity is superior to the respective values of the late gadolinium enhancement threshold value of 50% and the non-contrast-enhanced myocardial rim threshold value of 4 mm.
3. The greatest advantage of low dose dobutamine cardiovascular magnetic resonance is in segments with late gadolinium enhancement transmurality from 1% to 75%.
4. Measuring the non-contrast-enhanced myocardial rim surrounding the scar has no additional value in clinical practice, because its prognostic value is not superior to the prognostic values of other analysed viability parameters.
5. For the prediction of significant (≥5%) left ventricular ejection fraction improvement after revascularisation, is possible to use two variables:
    - the cut-off value ≥50% of viable segments from all dysfunctional and revascularised segments in a patient;
    - the variable 0.427×LVEF measured during LDD administration–0.393×baseline LVEF+0.092×percentage of viable segments.
6. There is a trend toward reverse left ventricular remodelling and symptomatic improvement in patients with ischemic left ventricular dysfunction after successful revascularisation of the significant amount of viable myocardium.
7. Late gadolinium enhancement cardiovascular magnetic resonance is suitable for the determination of the frequency and extent of new periprocedural/perioperative myocardial injury after revascularisation and myocardial injury that occurs late after revascularisation.

8. There is a week correlation between presence of Q waves on electrocardiogram and late gadolinium enhancement transmurality. Q wave is determined by the total size rather than transmural extent of underlying myocardial infarction.

CLINICAL IMPLICATIONS

1. For clinical use, we propose to initially perform LGE-CMR and add the LDD-CMR just after the LGE-CMR only in patients with LGE from 1% to 75%, as the addition of LDD significantly improves viability prediction in this subset of patients.
2. The measurement of RIM thickness in the segments with LGE from 1% to 75% does not give more information than the measurement of LGE transmurality and is not recommended in the routine clinical practise.
3. On the basis of above-described research created clinical CMR based viability assessment algorithm is presented in **Figure 12**.
4. Revascularisation, in cases when patients have no angina pectoris and the target is the improvement of heart failure symptoms, should be performed when there is a substantial amount of viable myocardium, (50% or more viable segments from all dysfunctional and revascularised segments).
5. Taking into account the higher predictive value of CR compared with LGE50, it seems possible to use LDD-CMR instead of LGE-CMR to assess viability in selected patients with severely reduced renal function (GFR <30 mL/min) to avoid the risk of nephrogenic systemic fibrosis.

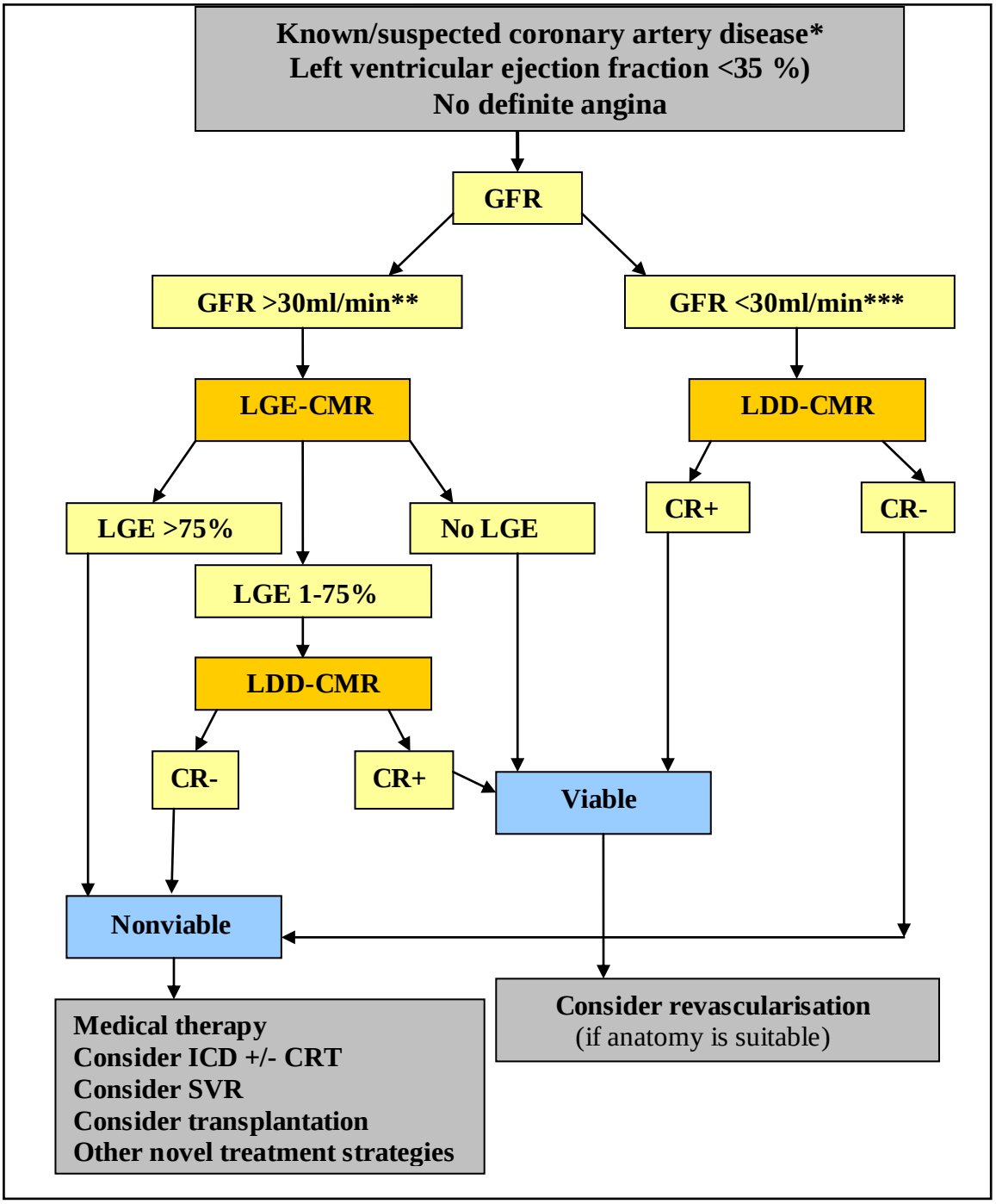

Figure 12. Proposed clinical CMR based viability assessment algorithm.

*All patients should be treated with the modern medical therapy; **In case GFR is between 30 and 60 mL/min, LGE-CMR should be performed on individual basis, taking into account the exact value of GFR and the contrast agent used. Thus, LGE-CMR should be performed only after evaluation of the patients' risk and benefit profile; *** – gadolinium-based contrast agent is contraindicated because of the high risk of nephrogenic systemic fibrosis.

SUMMARY IN LITHUANIAN

ĮVADAS

Hibernuojantis (arba žiemojantis) miokardas paprastai apibrėžiamas kaip gyvybingas ir disfunkcinis miokardas, kurio funkcija po revaskuliarizacijos pagerėja. Žiemojančio miokardo revaskuliarizacija lemia kairiojo skilvelio (KS) bendros bei segmentinės funkcijos pagerėjimą, atgalinę KS remodeliaciją, pagerėjusį paciento išgyvenamumą bei sumažėjusią tokių komplikacijų, kaip miokardo infarktas, širdies nepakankamumas bei nestabili krūtinės angina, riziką. Tuo tarpu, pacientams, neturintiems miokardo gyvybingumo požymių ar turintiems juos minimalius, revaskuliarizacijos nauda neviršija medikamentinio gydymo naudos. Kadangi invazinių tyrimo metodų vertė nustatant miokardo gyvybingumą yra minimali, būtina neinvazinių tyrimo metodų pagalba išeminės kilmės KS sistolinę disfunkciją turintiems pacientams nustatyti žiemojantį miokardą bei jo kiekį.

ŠMRT yra sparčiai besivystantis, jonizuojančiosios spinduliuotės neturintis tomografinis tyrimo metodas, kuriuo gaunami vaizdai bet kurioje pageidaujamoje plokštumoje. ŠMRT vėlyvojo kontrastinės medžiagos kaupimo (VKMK) metodika yra unikali, siekiant nustatyti tikslų anatominį randinio audinio dydį ir jo išplitimo KS sienelėje laipsnį. Ši metodika suteikia tikslios informacijos apie anatominį rando išplitimą, tačiau nesuteikia informacijos apie likusio (kontrastinės medžiagos (k/m) nekaupiančio) miokardo funkcinę būklę. Pavyzdžiui, lieka neaišku, ar k/m nekaupiantis miokardas yra nepakitęs, tuomet jokio funkcijos atsistatymo po revaskuliarizacijos neverta tikėtis, ar k/m nekaupiantis miokardas yra pakitęs (priblokštas, žiemojantis, išeminis ar visos šios būklės kartu), tuomet miokardo funkcija po revaskuliarizacijos gali atsistatyti [6]. Todėl miokardo gyvybingumui tiksliau įvertinti, reikia ne tik nustatyti anatominį rando dydį, bet ir turėti papildomos informacijos, t. y. įvertinti miokardo funkcinę būklę – kontraktilinį rezervą (KR) adrenerginės stimuliacijos metu, ir nustatyti epikardinio sienelės storio (ESS) virš netransmuralinės vėlyvojo k/m kaupimo zonos diametrą.

TYRIMO TIKSLAS

Pagrindinis tyrimo tikslas yra tiesiogiai ir prospektyviai palyginti trijų miokardo gyvybingumo parametrų (KR nustatyto mažų dobutamino dozių metu, VKMK

transmuralumo bei ESS) bei jų derinių vertę, prognozuojant KSSD turinčių pacientų segmentinės KS funkcijos atsistatymą/pagerėjimą po perkutaninės ar chirurginės revaskuliarizacijos. Tyrimu siekiama prospektyviai patikrinti hipotezę, kad mažų dobutamino dozių MRT atlikimas ir miokardo KR nustatymas arba ESS matavimas segmentuose, kurių VKMK procentas yra nuo 1 % iki 75 %, pagerins segmentinės ir bendrosios KS sistolinės funkcijos atsistatymo/pagerėjimo po revaskuliarizacijos prognozavimą.

Antrasis tyrimo tikslas yra nustatyti optimalų MDDMR bei VKMKMR metodikų duomenimis besiremiantį reikšmingo KSIF pagerėjimo (t. y. KSIF pagerėjimo ≥5 %) prognozinį veiksnį.

TYRIMO UŽDAVINIAI

1. Nustatyti trijų miokardo gyvybingumo parametrų (kontraktilinio rezervo MDD metu bei VKMK metodika nustatomų k/m kaupimo transmuralumo bei ESS) bei jų derinių vertę, prognozuojant lėtine KŠL sergančių bei KSSD turinčių pacientų miokardo segmentinės kontrakcijos pagerėjimą po revaskuliarizacijos.
2. Remiantis sudėtine MRT metodika (MDDMR bei VKMKMR), nustatyti optimalų reikšmingo KSIF pagerėjimo (t. y. KSIF pagerėjimo ≥5 %) praėjus 6 mėnesiams po revaskuliarizacijos prognozinį veiksnį.
3. Ištirti revaskuliarizacijos įtaką KS funkciniams ir morfologiniams rodikliams bei pacientų klinikiniams simptomams.
4. VKMKMR metodu įvertinti periprocedūrinių/perioperacinių miokardo nekrozės zonų dažnį ir dydį.
5. Ištirti priklausomybę tarp VKMK transmuralumo ir Q bangos buvimo elektrokardiogramoje.

GINAMIEJI TEIGINIAI

1. Vėlyvojo k/m kaupimo ir mažų dobutamino dozių magnetinio rezonanso metodikų derinys leidžia labai tiksliai prognozuoti tiek bendros, tiek ir segmentinės kairiojo skilvelio kontrakcijos pagerėjimą, ar net pilną jos atsistatymą, nepriklausomai nuo kairiojo skilvelio sistolinės funkcijos sutrikimo laipsnio.

2. Didžiausia verte, prognozuojant miokardo segmentinės kontrakcijos atsistatymo tikimybę po revaskuliarizacijos, pasižymi kontraktilinio rezervo nustatymas, ypač širdies raumens segmentuose, kurių k/m kaupiančio rando transmuralumas siekia nuo 1% iki 75%.
3. Prognozuojant segmentinės miokardo kontrakcijos pagerėjimą ar atsistatymą po revaskuliarizacijos, epikardinio sluoksnio virš k/m kaupiančio rando matavimas neduoda jokios praktinės naudos, nes jo prognozinė vertė neviršija kitų analizuotų parametrų prognozinių verčių.
4. Reikšmingą kairiojo skilvelio išstūmimo frakcijos pagerėjimą po revaskuliarizacijos, galima tiksliai prognozuoti, apskaičiuojant:
    - gyvybingų segmentų procentą pacientui;
    - vertę kintamojo, susidedančio iš trijų parametrų: mažų dobutamino dozių metu išmatuotos kairiojo skilvelio išstūmimo frakcijos, pradinės kairiojo skilvelio išstūmimo frakcijos bei gyvybingų segmentų procento.
5. Reikšmingo gyvybingo miokardo kiekio revaskuliarizacija išeminės kilmės kairiojo skilvelio sistolinę disfunkciją turintiems pacientams lemia atgalinės KS remodeliacijos tendenciją bei širdies nepakankamumo simptomų sumažėjimą.
6. Vėlyvojo k/m kaupimo magnetinio rezonanso tyrimas yra tinkamas metodas tiksliai nustatyti naujų periprocedūrinių ar perioperacinių miokardo pažeidimo zonų bei zonų, atsiradusių vėlyvuoju laikotarpiu po revaskuliarizacijos, dydį, dažnį ir vietą.
7. Elektrokardiografiniai transmuralumo žymenys (Q banga, ne Q banga) yra silpnai susiję su tikru vėlyvojo k/m kaupimo išplitimu ir Q bangos buvimas elektrokardiogramoje labiau priklauso nuo bendro randinio audinio ploto negu nuo randinio audinio transmuralumo.

TYRIMO METODIKA

Aprašomas tyrimas – prospektyvus, dviejų MR metodikų (mažų dobutamino dozių indukuojamo kontraktilinio rezervo ir vėlyvojo k/m kaupimo transmuralumo) lyginamasis tyrimas, prognozuojant lėtine KŠL sergančių bei KSSD turinčių pacientų bendrosios bei segmentinės kontrakcijos atsistatymą po revaskuliarizacijos (PKI ar AKJO). Lyginant šių MR metodikų bei jų derinių diagnostinę vertę remtasi trimis

parametrais: kontraktiliniu rezervu mažų dobutamino dozių metu, vėlyvojo gadolinio turinčios k/m kaupimo transmuralumu bei k/m nekaupiančios sienelės storiu virš k/m kaupiančios zonos. Palyginimas atliktas vienoje pacientų grupėje.

Tyrimas buvo atliktas Vilniaus universiteto ligoninės „Santariškių klinikos“ Kardiologijos ir angiologijos centre nuo 2008 m. lapkričio iki 2011 m. gegužės, pasitelkiant „1.5 T Siemens Avanto“ (Vokietija, Erlangen) MR aparatą. Iš viso buvo ištirtas 91 pacientas, tačiau į galutinę analizę buvo įtraukti 55 pacientai (amžius 63 ± 10 metai, 6 moterys, 3 anamnezėje turėję AKJO, 22 anamnezėje turėję PKI, 42 (76 proc.) turintys trijų vainikinių arterijų ligą, 3 (5 proc.) vienos vainikinės arterijos ligą), turintys KS sistolinę disfunkciją (vidutinė KSIF 35 ± 8 proc.) ir kuriems buvo atlikta chirurginė (n=43) ar perkutaninė (n=12) revaskuliarizacija. Vidutinis intervalas tarp MR tyrimo ir revaskuliarizacijos buvo 24 dienos ir nė vienam iš įtrauktų į tyrimą pacientų per šį laikotarpį nebuvo klinikinių miokardo infarkto požymių. Prieš revaskuliarizaciją atlikto širdies magnetinio rezonanso tyrimo (ŠMRT) metu buvo vertinami morfologiniai bei funkciniai KS ertmės bei sienelių parametrai ramybėje bei MDD (5 ir 10 μg/kg/min.) skyrimo į veną metu, tėkmė per aortos bei dviburį vožtuvus ir vėlyvojo kontrastinės medžiagos (k/m) kaupimo miokarde pobūdis. Praėjus 27 ± 4 savaičių (vidutiniškai 6 mėnesiams) po revaskuliarizacijos, tik ramybės vaizdai buvo gaunami, naudojant tuos pačius MR principus ir parametrus. Gyvybingumo matu laikytas segmentinės ir bendrosios kontrakcijos pagerėjimas/atsistatymas, praėjus 6 mėnesiams po revaskuliarizacijos. Analizuojami gyvybingumo parametrai buvo vertinti dviejų tyrėjų, vertinimo skirtumai buvo bendrai aptariami. Statistinės analizės metodai buvo taikyti 410 išeityje disfunkcinių segmentų (iš 276 reikalingų segmentų tyrimo statistiniam patikimumui užtikrinti).

TYRIMO REZULTATAI

Reikšmingas KSIF pagerėjimas ≥5 proc. buvo nustatytas 43/55 (78 proc.) pacientams. Reikšmingo KSIF pagerėjimo ir nepagerėjimo pacientų grupių pradiniai ypatumai reikšmingai nesiskyrė. Pacientai, kurių KSIF pokytis buvo <5 %, turėjo reikšmingai didesnius pradinius KS tūrių indeksus, sienelės judesio balų bei kairiojo skilvelio sferiškumo indeksus. Nors absoliutus gyvybingų segmentų skaičius tarp grupių

reikšmingai nesiskyrė (p=0,485), tačiau gyvybingų segmentų procentas buvo statistiškai reikšmingai didesnis tų pacientų, kurių KSIF pokytis buvo ≥5 % (p=0,006).

Iš viso 410 (44 %) iš 935 analizuotų miokardo segmentų turėjo sutrikusią pradinę kontrakciją ir buvo sėkmingai revaskuliarizuoti (analizuotų segmentų skaičius gerokai viršijo statistiškai apskaičiuotą minimalią segmentų imtį, t. y. 276 segmentus). Segmentinė kontrakcija po revaskuliarizacijos pagerėjo/atsistatė 245 (60 %) segmentuose, o kitų 165 (40 %) segmentų funkcija po revaskuliarizacijos nepagerėjo. Funkcinio miokardo atsistatymo/pagerėjimo dažnis mažėjo, didėjant VKMK transmuralumui (82 % segmentų atsistatė, jei VKMK transmuralumas buvo nuo 0 % iki 25 %, 67 % segmentų – jei VKMK nuo 26 % iki 50 %, 41 % segmentų – jei VKMK nuo 51 % iki 75 %, ir 13 % segmentų – jei VKMK >75 %). Funkcinio atsistatymo galimybių santykis tarp segmentų, kurių VKMK nuo 0 % iki 25 %, ir segmentų, kurių VKMK >75 %, lygus 30,4.

Naudodami VKMK transmuralumo 50 % slenkstinę vertę (toliau VKMK50), galime apytikriai atskirti segmentus, kurių funkcijos atsistatymas po revaskuliarizacijos yra tikėtinas, nuo segmentų, kurių kontrakcijos pagerėjimo tikimybė yra daug mažesnė. Šios slenkstinės vertės jautrumas siekia 82 %, o specifiškumas 65 %. ESS 4 mm slenkstinė vertė 78 % jautrumu ir 71 % specifiškumu padeda prognozuoti žiemojančio miokardo atsistatymą. Nors VKMK50 bei KR jautrumas yra panašus (t. y. siekia 82 % VKMK50 atveju ir 83 % KR atveju), tačiau KR specifiškumas yra didžiausias (78 %), palyginti su kitų analizuotų parametrų specifiškumais. GDSD jautrumas ir specifiškumas yra reikšmingai mažesni už kitų trijų parametrų analogiškas vertes.

Siekiant prognozuoti segmentinės kontrakcijos atsistatymą po revaskuliarizacijos, buvo lyginti penkių skirtingų logistinės regresijos modelių plotai po ROC kreivėmis: a) visuose disfunkciniuose bei revaskuliarizuotuose segmentuose (n=410), priklausomai nuo KSIF (t. y. pacientams, kurių KSIF <30 % ir kurių KSIF ≥30 %); b) segmentuose, turinčiuose bet kokio transmuralumo VKMK (n=247); c) segmentuose, kurių VKMK buvo nuo 26 % iki 75 % (n=180), taip pat nuo 1 % iki 75 % (n=186); d) segmentuose, kurių VKMK buvo ≥76 % (n=61).

Trys skirtingi gyvybingumo prognozavimo modeliai (VKMK50+KR, KR ir VKMK50) buvo lyginti analizuojant visus disfunkcinius bei revaskuliarizuotus segmentus (n=410), priklausomai nuo pacientų pradinės KSIF (t. y. pacientams, kurių

KSIF buvo <30 %, ir pacientams, kurių KSIF ≥30 %). Lyginant plotus po ROC kreivėmis, KR buvo pranašesnis negu VKMK50 tiems pacientams, kurių KSIF ≥30 % (p<0,026), bet ne tiems, kurių KSIF <30 % (p=0,16). Sudėtinio modelio (VKMK50+KR) reikšmingas pranašumas prieš vien tik KR besiremiantį segmentinės kontrakcijos pagerėjimo modelį išryškėjo abiejose pacientų grupėse (p=0,012 ir p=0,00012, atitinkamai grupėje su KSIF <30 proc. ir grupėje su KSIF ≥30 proc.).

Penki skirtingi segmentinės kairiojo skilvelio kontrakcijos atsistatymo prognozavimo modeliai (ESS4+KR, VKMK50+KR, KR, ESS4, VKMK50) buvo lyginti, analizuojant segmentus, turinčius bet kokį VKMK transmuralumą. Sudėtinio modelio (ESS4+KR) plotas po ROC kreive buvo didžiausias bei reikšmingai skyrėsi nuo visų kitų modelių plotų po kreivėmis, išskyrus sudėtinį (VKMK50+KR) modelį (p=0,712). Analizuojant tų pačių penkių modelių plotus po kreivėmis segmentuose, turinčiuose VKMK nuo 26 % iki 75 % ir VKMK nuo 1 % iki 75 %, nustatyta ta pati tendencija: reikšmingas sudėtinio modelio (ESS4+KR) pranašumas prieš kitus analizuotus modelius, išskyrus sudėtinį (VKMK50+KR) modelį (atitinkamai, p=0,172 ir p=0,426). Be to, sudėtinio modelio (VKMK50+KR) plotai po kreivėmis buvo statistiškai reikšmingai didesni už ESS4, VKMK50 bei KR modelių plotus po ROC kreivėmis visose pirmiau minėtose segmentų grupėse. Analizuojant segmentus, kurių VKMK transmuralumas buvo ≥76 %, lyginti keturi modeliai (ESS4+KR, KR, ESS4 bei absoliučios VKMK vertės (VKMK50 slenkstinė vertė šiai segmentų grupei netenka prasmės, nes imtyje nėra nė vieno segmento, kurio VKMK būtų <50 %). Pastarojoje segmentų grupėje reikšmingų skirtumų tarp analizuotų modelių po ROC kreivėmis nerasta.

Vien tik KR besiremiančio modelio plotas po ROC kreive reikšmingai skyrėsi nuo VKMK50 ploto po ROC kreive segmentuose, turinčiuose bet kokio transmuralumo kontrastinės medžiagos kaupimą (p=0,0076), taip pat segmentuose, kurių VKMK buvo nuo 26 % iki 75 % (p=0,005) bei nuo 1 % iki 75 % (p=0,007). Statistiškai reikšmingo skirtumo tarp vien tik VKMK50 bei vien tik ESS4 besiremiančių modelių plotų po ROC kreivėmis nebuvo nė vienoje iš analizuotų grupių.

Praėjus 6 mėn. po revaskuliarizacijos, vidutinis bendrosios KS funkcijos pagerėjimas buvo 11 ± 8 %. KA CCS funkcinės klasės pokytis po revaskuliarizacijos buvo reikšmingas tiek reikšmingo KSIF pokyčio pacientų grupėje, tiek pacientų be reikšmingo KSIF pokyčio grupėje. Vertinant ŠN NYHA funkcinės klasės pokytį,

pacientų, kurių KSIF pagerėjo reikšmingai, vidutinė NYHA funkcinė klasė sumažėjo 1 klase ($p<0,001$), o pacientų be reikšmingo KSIF pagerėjimo vidutinė NYHA funkcinė klasė išliko beveik nepakitusi ($p=0,167$).

Lyginant pacientų grupių su ir be reikšmingo KSIF pagerėjimo ypatumus praėjus 6 mėnesiams po revaskuliarizacijos, buvo pastebėti reikšmingi KS parametrų skirtumai tarp grupių (4.4 lentelė): KSIF ($p<0,001$), KS SJBI ($p<0,001$), KS SI ($p=0,036$), pagerėjusios kontrakcijos segmentų skaičiaus ir šių segmentų procento (šiuo atveju pagerėjusios kontrakcijos segmentų procentas buvo apskaičiuotas pirmiau aprašyta metodika, tik imti ne tikėtinai gyvybingi segmentai, o realiai atsistatę po revaskuliarizacijos segmentai) (atitinkamai $p=0,045$ ir $p<0,001$).

Vertinant su revaskuliarizacija susijusį KS funkcinių parametrų kitimą abiejose grupėse, buvo nustatytas reikšmingas KSIF bei SJBI pokytis abiejose grupėse, o, reikšmingas (siekiantis vidutiniškai 22 proc.) KS GSTI sumažėjimas ($p<0,001$) bei KS ddI sumažėjimas ($p=0,034$), praėjus 6 mėnesiams po revaskuliarizacijos, buvo stebimas tik toje pacientų grupėje, kurių KSIF pagerėjo reikšmingai.

Siekdami nustatyti reikšmingo KSIF pagerėjimo ŠMRT prognozinius veiksnius, mes detaliau analizavome du parametrus: absoliutų gyvybingų segmentų skaičių pacientui bei gyvybingų segmentų procentą nuo visų prieš revaskuliarizaciją buvusių disfunkcinių bei revaskuliarizuotų segmentų. Segmentas buvo laikomas gyvybingu, jeigu jis nekaupė k/m arba pasižymėjo kontraktiliniu rezervu MDDMR metu, esant bet kokio transmuralumo k/m kaupimui. Naudojant logistinės regresijos modelius, tik gyvybingų segmentų procentas buvo reikšmingas KSIF pagerėjimo ≥ 5 % prognozinis rodiklis ($p=0,013$), o štai absoliutus gyvybingų segmentų skaičius nebuvo reikšmingas ($p=0,588$). Papildoma ROC kreivių analizė pateikė analogiškus rezultatus. Plotas po kreive gyvybingų segmentų procentui buvo 0,76 ($p=0,007$), palyginti su plotu po kreive 0,57 absoliučiam gyvybingų segmentų skaičiui ($p=0,49$). Papildoma logistinės regresijos modelio analizė buvo atlikta siekiant nustatyti gyvybingų segmentų procento slenkstinę vertę, kuri pasižymėtų optimaliu jautrumu ir specifiškumu prognozuojant reikšmingą bendrosios kairiojo skilvelio kontrakcijos atsistatymą po revaskuliarizacijos. Paciento gyvybingų segmentų procento slenkstinė vertė ≥ 50 % buvo optimali, pasižymėjo 72 % jautrumu ir 75 % specifiškumu prognozuojant reikšmingą KSIF pagerėjimą, praėjus 6 mėnesiams po revaskuliarizacijos.

Kadangi buvo gauta puiki koreliacija tarp KSIF, išmatuotos MDDMR metu, bei KSIF absoliučios vertės, praėjus 6 mėnesiams po revaskuliarizacijos, mes pabandėme įtraukti pastarąjį parametrą į reikšmingo KSIF pagerėjimo prognozavimo modelius. Analizuojant KSIF, išmatuotos MDDMR metu, plotą po ROC kreive reikšmingam KSIF pagerėjimui, plotas po kreive buvo 0,738 ir jis statistiškai reikšmingai skyrėsi nuo 0,5 (p=0,013).

Siekdami prognozuoti absoliutų KSIF pokytį po revaskuliarizacijos, mes sukūrėme keletą modelių, į kuriuos įtraukėme kelis kintamuosius: pradinę KSIF (toliau KSIF), KSIF, išmatuotą MDDMR metu (toliau MDDKSIF), bei gyvybingų segmentų procentą. Praktiniame darbe reikšmingą KSIF pokytį galima prognozuoti 74 % jautrumu ir 83 % specifiškumu, naudojant nepriklausomą kintamąjį, lygų 0,427×MDDKSIF-0,393×KSIF+0,092×gyvybingų segmentų procentas. Šis kintamasis leidžia gana tiksliai apskaičiuoti numatomą po revaskuliarizacijos absoliutų KSIF pokytį. Pastarasis modelis buvo pasirinktas kaip geriausias, nes visi šio modelio kintamieji pasižymėjo statistiniu reikšmingumu.

Septyni pacientai (11 %) (5 atlikta AKJO, 2 atlikta PKI) iš 63 pacientų, kuriems buvo atlikta antroji ŠMRT, buvo pašalinti iš tyrimo, nustačius reikšmingas naujas VKMK zonas. Naujos VKMK zonos šiems pacientams apėmė vidutiniškai 3,9 segmento ir jų plotas vidutiniškai siekė 14,3 cm^2. Penkiems pacientams reikšmingai padidėjo troponino I koncentracija per 24 valandas po AKJO ar PKI (troponino I koncentracija vidutiniškai siekė 30 µg/l), kitiems dviem pacientams širdies pažeidimo žymenys nebuvo tirti, nes nebuvo klinikinių perioperacinio pažeidimo požymių. Pastariesiems dviem pacientams (abiem atlikta AKJO) miokardo pažeidimo laikas nėra aiškus ir pažeidimą galėjo lemti vėlyva apeinamųjų vainikinių arterijų jungčių okliuzija, o ne perioperacinis pažeidimas.

Analizuodami ryšį tarp Q bangos buvimo elektrokardiogramoje ir VKMK dydžio, vietos bei transmuralumo, vertinome 44 pacientų duomenis. Devyni pacientai buvo pašalinti iš analizės dėl kairės Hiso pluošto kojytės blokados elektrokardiogramoje, nes šis laidumo sutrikimas neleidžia adekvačiai vertinti Q bangos buvimo. Dviejų pacientų duomenys neanalizuoti, kadangi neturėjo VKMK zonų ŠMRT vaizduose bei Q bangos EKG. Vertinant visus pacientus, 45 % miokardo infarktas nors viename segmente buvo transmuralinis ir 73 % bent viename segmente buvo netransmuralinis. 31 (70 %)

pacientui buvo nustatyta elektrokardiografinė Q banga. Trims iš 19-os (16 %) transmuralinį MI turinčių pacientų Q bangos EKG nebuvo, o penkiolikai iš 25-ių (60 %) subendokardines VKMK zonas turinčių pacientų Q banga buvo. Nagrinėjant Q bangos vietą EKG bei VKMK zonų išplitimą konkrečios vainikinės arterijos baseine, nustatyta puiki atitiktis: 29 pacientams iš 31 (94 %) lokalizacija atitiko ir tik 2 (16 %) pacientams neatitiko.

Prognozuojant Q bangos buvimą EKG, analizuoti dviejų parametrų (VKK transmuralumo bei VKK ploto pacientui) plotai po ROC kreivėmis. Nors p reikšmės statistinis patikimumas yra ribinis (p=0,057), tačiau VKMK plotas pacientui yra geresnis Q bangos buvimo EKG prognozinis veiksnys nei VKMK transmuralumas (AUC atitinkamai 0,84 ir 0,63).

IŠVADOS

1. Vėlyvojo kontrastinės medžiagos kaupimo ir mažų dobutamino dozių magnetinio rezonanso metodikų derinys leidžia labai tiksliai prognozuoti tiek bendrosios, tiek segmentinės kairiojo skilvelio kontrakcijos pagerėjimą, ar net visišką jos atsistatymą, nepriklausomai nuo kairiojo skilvelio sistolinės funkcijos sutrikimo laipsnio.
2. Didžiausia verte prognozuojant miokardo segmentinės kontrakcijos atsistatymo tikimybę po revaskuliarizacijos pasižymi kontraktilinio rezervo nustatymas. Jo jautrumo ir specifiškumo parametrai pranoksta 50 % vėlyvojo k/m kaupimo trasmuralumo bei 4 mm epikardinio (k/m nekaupiančio) sienelės storio virš k/m kaupiančio rando slenkstinius parametrus.
3. Didžiausia mažų dobutamino dozių magnetinio rezonanso atlikimo ir kontraktilinio rezervo nustatymo nauda yra širdies raumens segmentams, kurių kontrastą kaupiančio rando transmuralumas yra nuo 1 % iki 75 %.
4. Prognozuojant segmentinės miokardo kontrakcijos pagerėjimą ar atsistatymą po revaskuliarizacijos, epikardinio sluoksnio virš kontrastinę medžiagą kaupiančio rando matavimas neduoda jokios praktinės naudos, nes jo prognozinė vertė neviršija kitų analizuotų parametrų prognozinių verčių.

5. Prognozuojant reikšmingą kairiojo skilvelio išstūmimo frakcijos pagerėjimą (≥5 %) po revaskuliarizacijos, galima taikyti du parametrus:
    - gyvybingų segmentų procento pacientui slenkstinę vertę ≥50 %;
    - kintamąjį: 0,427 × mažų dobutamino dozių metu išmatuota kairiojo skilvelio išstūmimo frakcija – 0,393 × pradinė kairiojo skilvelio išstūmimo frakcija + 0,092 × gyvybingų segmentų procentas. Šis kintamasis pasižymi dideliu jautrumu ir specifiškumu prognozuojant absoliutų KSIF pokytį po revaskuliarizacijos.
6. Reikšmingo gyvybingo miokardo kiekio revaskuliarizacija išeminės kilmės kairiojo skilvelio sistolinę disfunkciją turintiems pacientams lemia ne tik reikšmingą širdies nepakankamumo NYHA funkcinės klasės sumažėjimą, bet ir atgalinės kairiojo skilvelio remodeliacijos tendenciją. Praėjus 6 mėnesiams po revaskuliarizacijos, reikšmingai sumažėja kairiojo skilvelio diastolinio diametro indeksas bei galutinio sistolinio kairiojo skilvelio tūrio indeksas. Atgalinės remodeliacijos tendencija yra būdingesnė skilveliams, kurių morfologiniai ir funkciniai pakitimai prieš revaskuliarizaciją yra lengvesni, o sėkmingai revaskuliarizuoto gyvybingo miokardo kiekis didesnis.
7. Vėlyvojo kontrastinės medžiagos kaupimo magnetinio rezonanso tyrimas yra tinkamas metodas naujų periprocedūrinių ar perioperacinių miokardo pažeidimo zonų bei zonų, atsiradusių vėlyvuoju laikotarpiu po revaskuliarizacijos, dydžiui, dažniui ir vietai tiksliai nustatyti.
8. Elektrokardiografiniai transmuralumo žymenys (Q banga, ne Q banga) yra silpnai susiję su tikru vėlyvojo kontrastinės medžiagos kaupimo išplitimu ir Q bangos buvimas elektrokardiogramoje labiau priklauso nuo bendro randinio audinio ploto negu nuo randinio audinio transmuralumo.

PUBLICATIONS

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