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ORIGINAL PAPER

The amount of dysfunctional but viable myocardium predicts long-term survival in patients with ischemic cardiomyopathy and left ventricular dysfunction

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Abstract To evaluate the prognostic significance of combined myocardial perfusion SPECT and [18F]FDG PET viability scanning for the prediction of survival in patients with ischemic cardiomyopathy (iCMP) and left ventricular dysfunction. 244 patients (64.0 ± 10.6 years, 86 % men) with iCMP and LVEF ≤45 % underwent SPECT/PET. Percent scar tissue and SPECT/PET-mismatch (%-mismatch) were calculated and correlated with event-free survival according to the type of therapy (medical therapy with/out revascularization) provided after imaging. Death from any cause was defined as the primary endpoint. Early revascularization (ER) was performed in 113/244 (46 %) patients within 32 ± 52 days (26 bypass surgeries and 87 percutaneous coronary interventions). 65 patients died during follow-up for a median of 33 months. Kaplan–Meier analysis showed that those patients with ≥5 % mismatch not undergoing ER had significantly higher mortality than did the group with similar mismatch who did receive ER. Cox analysis identified both SPECT/PET-mismatch and the interaction of SPECT/PET-mismatch with ER as independent predictors for death due to all causes. A threshold of ≥5 % SPECT/PET-mismatch predicted best which patients with iCMP and LV dysfunction would benefit from ER in terms of long-term survival.

Keywords Hibernation · Revascularization · Prognosis · Survival · Metabolism

Abbreviations

ACD	All cause death
AUC	Area under the curve
CABG	Coronary artery bypass graft
CD	Cardiac death
CR	Cardiac revascularization
ER	Early revascularization
iCMP	Ischemic cardiomyopathy
LVEF	Left ventricular ejection fraction
MI	Myocardial infarction
PCI	Percutaneous coronary intervention
PET	Positron emission tomography
SPECT	Single photon emission computed tomography

Introduction

There is an ongoing discussion about the efficiency of myocardial viability diagnostics in the prediction of recovery of left ventricular function after revascularization therapy. In particular, it remains uncertain if a decision about revascularization therapy based upon viability imaging leads to improvement in patients' individual outcome. The recently published substudy of 601 patients in the STICH trial [1] reported that, after adjustment for baseline variables, myocardial viability was not predictive

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of survival in groups receiving or not receiving CABG, as compared with medical therapy alone.

Given these unfavorable results, it is all the more important to clearly define the concept of myocardial viability. Of the several techniques available for assessing the presence of viable tissue, [18F]fluorodeoxyglucose (FDG) positron emission tomography (PET) studies of metabolism in combination with single photon emission computed tomography (SPECT) measurement of myocardial perfusion is the most sensitive in the prediction of functional recovery after revascularization [2–4] and improved survival [5, 6], as it uniquely detects dysfunctional but viable myocardium, in contrast to the total extent of viability (normal plus dysfunctional myocardium) acquired by other methods. It was a main criticism of the STICH trial, that viability assessment was restricted to perfusion SPECT alone and dobutamine echocardiography, both techniques which have well-known limitations in their ability to detect viability [2]. Another recently published multicenter trial, the PARR-2 study, indeed demonstrated significant outcome benefits in patients with an LVEF $\leq$35 % when clinicians adhered to SPECT/PET-based recommendations rather than standard care alone [7].

There is a general consensus that the increase in left ventricular ejection fraction (LVEF) following revascularization correlates with the number of viable segments [8–11]. However, although commercial software for the calculation of myocardial viability is widely available and gives highly reproducible results, in the planning of treatment strategies, it remains to be established just how much viable myocardium should be present in order to anticipate a significant improvement in patient survival after coronary revascularization.

Therefore, we conducted a retrospective study in a series of 244 patients with iCMP and left ventricular dysfunction in order to evaluate the prognostic significance of combined SPECT/PET viability imaging in the prediction of survival. We hypothesized that we could identify a specific post hoc threshold of mismatch between viability and perfusion serving to discriminate those patients who benefited from revascularization from those who did not. We further hypothesized that applying this threshold SPECT/PET could independently predict patients' outcomes.

Methods

Study population

We identified consecutive patients who had been referred by the departments of cardiology at the University of Munich for viability diagnostic testing between 11/2001 and 05/2010. Inclusion criteria were as follows: patients with previous myocardial infarction (MI) and/or stenosis $\geq$50 % of at least one coronary artery at coronary angiography, and resting LVEF $\leq$45 %. Patients with recent MI, percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery within less than 8 weeks, unstable angina, non-ischemic cardiomyopathy or valvular disease were excluded. All decisions concerning the choice of treatment were made by the referring physicians, rather than according to random assignment. For the purposes of the study, patients were separated on the basis of the treatment received within 90 days (31 $\pm$ 71) after viability imaging into the following two groups: [1] the medical therapy group (including both, patients with ongoing medical therapy and those who were initially referred to revascularization who could not be successfully revascularized and therefore had ongoing medical therapy), [2] the successful early revascularization group.

[Tc-99 m]sestamibi SPECT perfusion imaging

In the setting of viability testing, ECG-gated [^{99m}Tc]sestamibi SPECT was performed at rest in all patients, with administration of a weight-adjusted dose of 4 MBq/kg (>300 MBq). Gated emission images were acquired at least 45 min after tracer injection with a triple headed camera system (Philips (formerly Picker) Prism 3000 XP, Cleveland, USA) using a low energy, high resolution parallel-hole collimator with 360 degrees of rotation in continuous operation mode. An electrocardiogram R-wave detector provided gating to acquire 12 emission frames per cardiac cycle. LVEF calculation was carried out using the QGS® 2008 processing software (Cedars-Sinai Medical Center, Los Angeles, CA, USA).

FDG metabolic PET

All PET studies were acquired on a whole body PET or PET/CT scanner (ECAT exact HR + or Biograph 64, Siemens Medical Systems, Forchheim, Germany; Allegro or Gemini, Philips, Hamburg, Germany) after intravenous injection of 370 MBq FDG. In the standard protocol, all patients were pretreated with acipimox 120 min before FDG injection. Diabetic patients received FDG after hyperinsulinemic euglycemic clamping, whereas euglycemic patients received FDG at 60 min after oral glucose loading [12]. A PET acquisition was obtained starting at 45 min after FDG injection.

Image analysis and quantification

SPECT/PET images were evaluated by consensus of two experienced observers, who were aware of height, weight, and gender of the patients. Reconstructed image data sets

were imported to a dedicated software package (QPS with QPET plugin, Cedars-Sinai Medical Center, Los Angeles, California). 3D left ventricular contours derived from resting SPECT scans and FDG PET images were co-registered in 3D to correct for rotational and positional errors between the two scans, as previously described for stress/rest pairs [13]. Upon obtaining this registration, the contours derived from the SPECT data were applied to the spatially co-registered SPECT/FDG pairs. Quantification of the viability scores (mismatch and scar areas) was performed after direct image count normalization between the perfusion and viability scans. The method of assigning mismatch and scar scores was according to the PARR-1 study [14], with automatic registration and utilization of normal limits for resting perfusion. In brief, the analysis was performed in polar coordinates, with computation of scar and mismatch scores for each patient's polar map within the spatial domain of the resting perfusion defect, as defined by Total Perfusion Deficit (TPD) analysis [15]. When the normalized perfusion value at a given polar map location was lower than the normalized FDG uptake, the mismatch score was calculated from the difference of the two scores. The scar score was calculated relative to the normalized FDG uptake in each polar map segment. When normalized perfusion exceeded FDG uptake, the scar score was assigned a value equal to the normalized perfusion value in that segment. The total scar score in the entire polar map was computed as the sum of all segmental scar and mismatch scores, and reported as a percentage of the total area of the LV myocardium, and also as the normalized TPD (i.e. scar plus mismatch, Fig. 1).

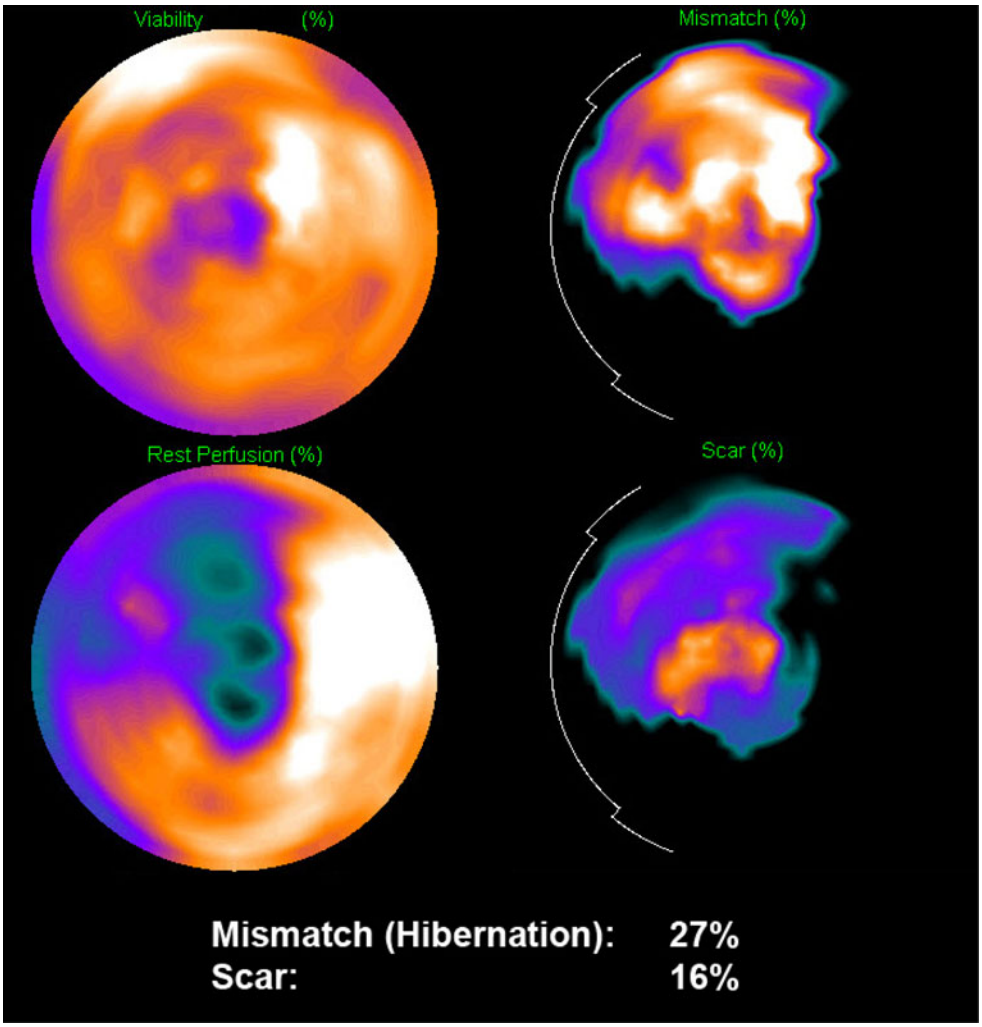

Fig. 1 Example for quantification of SPECT/PET-mismatch and scar tissue in percent of total left ventricular myocardium using QPS® software tool. Bull's-eyes of FDG-Metabolism (*upper left*) and Perfusion (*lower left*) are presented as well as the calculated areas of mismatch (*upper right*) indicating areas of hibernating myocardium and also areas of myocardial scar (*lower right*) where neither relevant perfusion nor FDG-Uptake is present

Invasive coronary angiography

Invasive coronary angiography was performed with a minimum of 2 projections of the right and five projections of the left coronary system using the transfemoral Judkins approach. All angiograms were digitally recorded, and quantitatively interpreted off-line (Quant-Cor QCA, Siemens Medical Systems, Forchheim, Germany or Digital Cardiac Imaging system, Philips, Eindhoven, The Netherlands) by two experienced readers.

Patient follow-up

For the assessment of individual outcomes, review of clinical records and telephone interviews with the patients or their relatives were conducted by an individual who was blind to the patients' test results. The primary study endpoint was death from any cause, as noted and confirmed by review of death certificate, hospital charts, or physician's record. In contrast to more specific cardiac endpoints, death from any cause is generally accepted as a more objective, clinically relevant and unbiased primary endpoint [5, 16, 17]. Death from any cause, along with occurrence of non-fatal myocardial infarction (as evidenced by signs, symptoms and enzyme elevation), late revascularizations (CABG or PCI administered more than 90 days after SPECT/PET imaging), cardiac transplantation, or hospital stay due to cardiac cause such as unstable angina or heart failure, were defined as the secondary endpoint. The follow-up period ended in November 2010.

Statistical analysis

Categorical variables are presented as absolute and relative frequencies, while continuous variables are presented as mean and SD. For between-group comparisons, unpaired Student's t-tests or Mann–Whitney U rank-sum tests were used, as appropriate. The Pearson's Chi square or Fisher's exact tests were performed to determine the significance of differences in proportions. For each individual, the date of entry into follow-up was defined as the date of whichever test (SPECT or PET) came second. The end of follow-up for the primary study endpoint was defined either as the date of death from any cause, or the end of the follow-up period. The end of follow-up for the secondary endpoint was defined either as the date of the first event (death, or non-fatal events specified above), or the end of the follow-up period. The analyses were conducted with the R statistical package (version 12.13.0), with P values less than 0.05 considered significant.

We structured the analysis of observational data to mimic a randomized clinical trial; i.e., a patient's assignment to a particular treatment was based on the therapy selected in the first 90 days after SPECT/PET to eliminate influences on therapy decision (medical vs. medical plus revascularization) for each patient a propensity score was calculated, which included as candidate variables the baseline age, gender, scar area, LVEF, diabetes, coronary angiography in the preceding 6 months, prior bypass surgery, present symptoms of angina, present dyspnea, creatinine levels and extent of coronary artery disease. These variables were considered in the context of logistic regression analysis using backward elimination.z

The threshold for the SPECT/PET mismatch was estimated using a time-dependent ROC-analysis for censored data. To this end, the linear predictor from a Cox regression, the endpoint was adjusted by the propensity score, and the interaction between revascularization and mismatch was used as a marker for testing various thresholds of the SPECT/PET mismatch (dichotomized). A threshold of $\geq$5 % proved to be optimal. In the next step, 95 % confidence intervals were calculated for the area under the curve (AUC) at 2, 3, 4 and 5 years for a mismatch $\geq$5 % using resampling techniques (999 replications). In addition, the Cox proportional hazards model was used to test the association between treatment and event-free survival time. Proportional hazards assumptions were fulfilled. Furthermore, Kaplan–Meier estimates were calculated with the optimal threshold of $\geq$5 %.

Results

Patient characteristics

The final study group consisted of 244 patients (age 64.0 $\pm$ 10.6 years, 86 % male) with a mean LVEF of 36 $\pm$ 14 % as calculated by gated SPECT. The mean scar burden was 16 $\pm$ 11 %, and the mean area of SPECT/PET-mismatch was 6 $\pm$ 5 %. All patients received optimized medical therapy at the time of SPECT/PET according to present guidelines [18]. Medication consisted of nitrates, beta-blockers, ACE inhibitors, digoxin and diuretics, as well as antiplatelet and/or anticoagulation agents, when appropriate. Mean creatinine level was 141 $\pm$ 123 µmol/l. 136/244 (56 %) patients were scheduled for early revascularization therapy, of which 26 (19 %) for CABG surgery and 110 (81 %) for PCI. 62 of these 136 patients (46 %) had a <5 % and 74 (54 %) had a $\geq$5 % SPECT/PET-mismatch. Revascularization procedure could be successfully performed within 90 days after SPECT/PET in 113/244 (46 %) patients, of which CABG surgery in 26 (23 %) and PCI in 87 (77 %) patients. The baseline clinical parameters and the results of SPECT/PET separated for patients with and without revascularization are summarized in Table 1. Patients who underwent early revascularization

Table 1 Baseline characteristics of study patients according to early intervention

Variable	All Patients (n = 244)	Medical therapy (n = 131)	Early revascularization (n = 113)	*P*
Demographic characteristics				
Age (years)	64 ± 11	64 ± 11	63 ± 10	0.39
Male gender	210 (88 %)	112 (86 %)	98 (87 %)	0.78
History of CAD				
1-Vessel disease	49 (20 %)	32 (24 %)	17 (15 %)	0.08
2-Vessel disease	49 (20 %)	27 (21 %)	22 (20 %)	0.87
3-Vessel disease	146 (60 %)	72 (55 %)	74 (66 %)	0.12
Diabetes	82 (34 %)	43 (33 %)	39 (35 %)	0.78
Prior angiography (<6 months)	142 (58 %)	70 (53 %)	72 (64 %)	0.10
Prior CABG	52 (21 %)	35 (27 %)	17 (15 %)	<0.05
Angina	122 (50 %)	72 (55 %)	50 (44 %)	0.10
Dyspnea	174 (71 %)	90 (69 %)	80 (74 %)	0.33
Creatinine (μmol/l)	141 ± 123	141 ± 123	141 ± 132	0.83
SPECT/PET findings				
Scar, percentage of the LV	16 ± 11	16 ± 11	16 ± 11	0.92
SPECT/PET-mismatch, percentage of the LV	6 ± 5	5 ± 5	7 ± 5	<0.05
Gated SPECT LVEF, percentage	36 ± 14	37 ± 14	36 ± 14	0.49
Time between SPECT and PET, in days	19 ± 72	20 ± 72	17 ± 72	0.77

Values are expressed as n (%) or mean ± SD

had greater SPECT/PET-mismatch and presented more frequently with bypass grafts. Furthermore, there was a trend towards present angina symptoms, and performance of angiography in the preceding 6 months in the group with early revascularization.

Propensity score

Significant or nearly significant influences in therapy decisions were detected using logistic regression with backward elimination for prior angiography, prior bypass surgery, present dyspnea and the extent of coronary disease (Table 2). These variables were used for calculating individual propensity scores, which were transformed into quintiles.

Table 2 Variables significantly influencing the physicians' decision undertake medical therapy in combination with early revascularization or medical therapy alone, which were adjusted using the propensity score

Coefficient	Estimate	Standard error	Z value	*P*
Intercept	−1.01	0.39	−2.61	0.009
Angiography (<6 months)	0.64	0.28	2.33	0.02
Prior CABG	−0.99	0.35	−2.83	0.005
Dyspnea	0.56	0.31	1.80	0.07
CAD-2	0.65	0.42	1.53	0.13
CAD-3	1.02	0.37	2.79	0.005

Outcome events and identification of SPECT/PET-mismatch threshold

During a mean follow-up period of 33 ± 29 months, 65/244 patients (27 %) reached the primary endpoint. In this group of patients we determined 40 cardiac deaths (16 % of all patients) and 25 non-cardiac deaths (10 % of all patients). The secondary endpoint was met by 128 (52 %) of the patients and consisted of 40 PCI, 12 CABG, two heart transplantations, 34 hospitalizations due to cardiac decompensation, 17 non-fatal MI, seven cardiac death and 16 non-cardiac death. For secondary endpoint analysis, patients who first had a non-fatal event and subsequently died were censored at the day of the non-fatal event. 116 (48 %) patients had no events during follow-up.

A cutoff value of 5 % mismatch discriminated best between patients benefiting from medical therapy in combination with early revascularization (≥5 %) and those who benefit from medical therapy alone (<5 % or no mismatch) in the propensity-adjusted model.

Survival analysis

To visualize the impact of early revascularization Kaplan–Meier survival curves for the primary endpoint of the

different patient groups combining the variables "mismatch <5 versus ≥5 %" and "medical therapy versus medical therapy plus early revascularization" were calculated. These curves revealed that those patients with SPECT/PET-mismatch of ≥5 % not undergoing revascularization had the highest mortality, followed by the patients with a mismatch <5 %, who received early intervention. Patients with mismatch ≥5 % who received early revascularization showed markedly lower mortality, falling in the range for patients without mismatch ≥5 % and without revascularization (log-rank test, $P = 0.065$, Fig. 2a). Corresponding Kaplan–Meier curves for the secondary endpoint indicated that the group of patients with ≥5 % SPECT/PET-mismatch and without early revascularization also presented with the lowest probability of event-free survival (log-rank test, $P = 0.002$, Fig. 2b). There was no difference in survival found for patients scheduled for revascularization who were revascularized compared to those who got medical therapy alone (log-rank test, $P = 0.54$, Fig. 3a) and also between patients who got PCI compared to those who got CABG (log-rank test, $P = 0.35$, Fig. 3b).

Cox regression analysis for the primary endpoint, showed an interaction between ≥5 % mismatch and early revascularization (i.e. patients with relevant mismatch but without revascularization) to be the strongest independent predictor for death from any cause ($P = 0.007$). Notably, the effect of early revascularization on event-free survival markedly increased for mismatch ≥5 % (Fig. 4). SPECT/PET-mismatch ≥5 % also predicted survival independently of subsequent revascularization ($P = 0.02$). In contrast, neither revascularization nor any of the variables comprising the propensity score, were identified as independent predictors (Table 3). Early revascularization was also a statistically significant predictor of the secondary endpoint.

Discussion

The availability of steadily improving interventional and medical therapies for the treatment of acute coronary events and stable coronary artery disease have in recent years markedly increased the number of long-term survivors, and consequently also the number of patients living with ischemic cardiomyopathy [2]. These patients frequently present with regional and/or global left ventricular dysfunction, progressive LV remodeling, and ultimately congestive heart failure, all of which contribute to the challenges faced by contemporary cardiovascular medicine. Treatment options include standard medical therapies, as well as interventional strategies; specifically, revascularization, resynchronization, transplantation, and also experimental cardiac stem cell therapy can be indicated in cases of left ventricular failure. However, the high morbidity risk associated with these procedures, as well as their high cost, complicate decision making, especially given the uncertain long-term benefits of some treatment strategies [19].

The main finding of the present study of 244 patients with ischemic cardiomyopathy and left ventricular dysfunction is that perfusion-metabolism mismatch observed by SPECT/PET was associated with the increased mortality if no revascularization was performed. In addition, there was a strong association between the amount of SPECT/PET-mismatch and the survival benefits derived from early revascularization. We found the optimal threshold for the amount of SPECT/PET-mismatch discriminating between patients who did or did not benefit from revascularization to be 5 % of the left ventricular myocardium. Furthermore, when including further events such as non-fatal myocardial infarction, late revascularization, cardiac decompensation

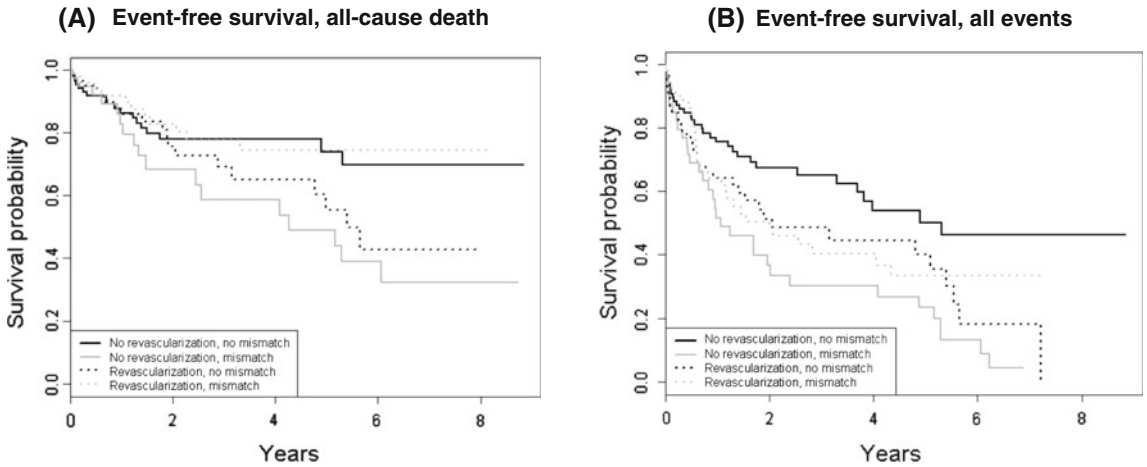

Fig. 2 Kaplan-Meier survival curves for **a** death due to all causes (primary endpoint, log rank test, $P = 0.065$) and **b** the composite of death and all soft events (secondary endpoint, $P = 0.002$) during long-term follow-up. Patients (n = 244) were stratified into four subgroups by combining the variables of early revascularization with the presence of ≥5 % or <5 % SPECT/PET-mismatch

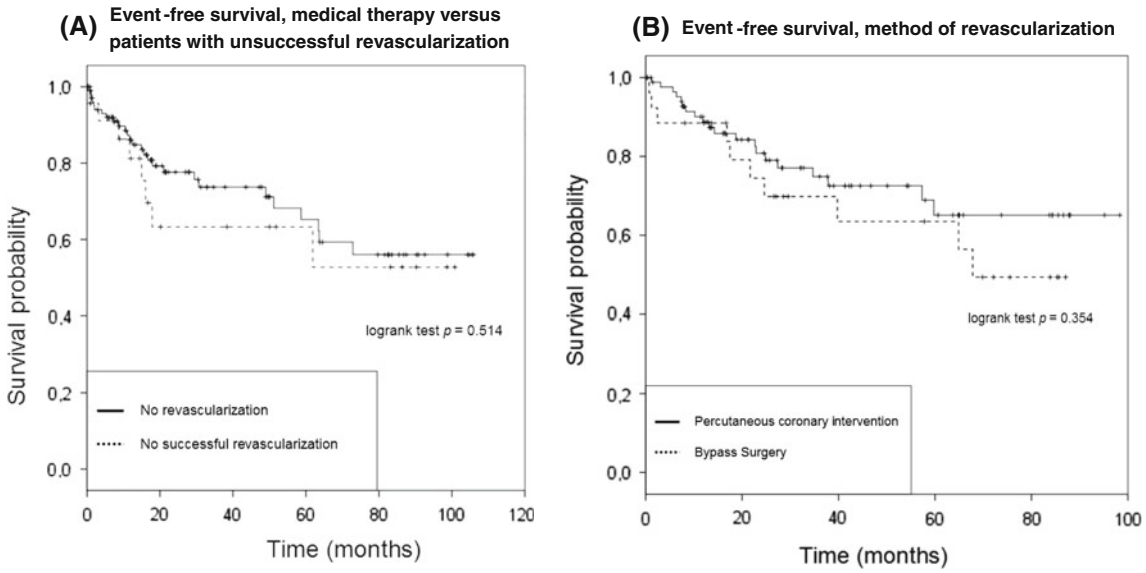

Fig. 3 Kaplan-Meier survival curves for death due to all causes (primary endpoint) comparing the patient subgroups **a** who got medical therapy (no revascularization) as a primary decision versus those who could not be sufficiently revascularized (log rank test, $P = 0.54$) and **b** who got PCI versus CABG for early revascularization (log-rank test, $P = 0.35$)

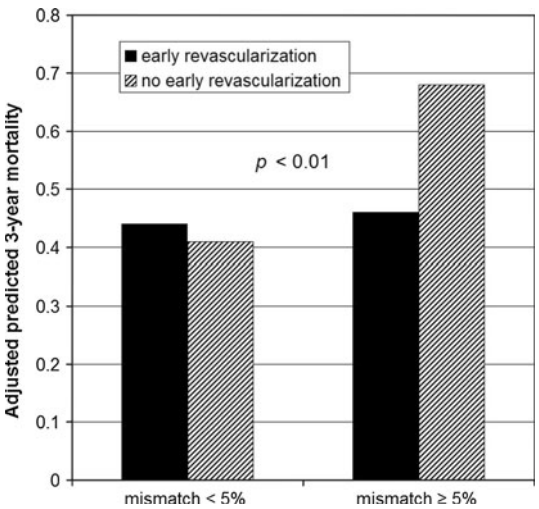

Fig. 4 Association between predicted mortality and the amount of SPECT/PET-mismatch when applying a 5 % threshold regarding the benefit derived from early revascularization. *Bars* were derived from a multivariable Cox regression model including the propensity score

or heart transplantation into the outcome analysis, the group of patients with mismatch ≥5 % who did not receive early revascularization still had the worst prognosis of all. We found only a minor protective effect of early revascularization against the appearance of non-fatal events during follow-up, suggesting that the patients with mismatch ≥5 % and early revascularization indeed had a lower probability for death from any cause, but still require attentive treatment in order to avoid repeat hospital stays.

A few earlier studies have sought to identify a threshold of hibernating myocardium discriminating between those patients who did or did not benefit from revascularization. In the post hoc analysis of the 182 patient PET arm of PARR-2 study [20], D'Egidio et al. found the threshold of perfusion-metabolism mismatch predicting reduced mortality after revascularization to be 7 %, only slightly higher than the present result. However, a number of methodological differences need to be considered in comparing these two studies. The follow-up period of 12 months in

Table 3 Cox proportional hazards model predicting survival

Parameter	Death from any cause			All events		
	HR	95 % CI	*P*	HR	95 % CI	*P*
Propensity score	0.94	0.75–1.19	0.62	1.10	0.94–1.29	0.24
Revascularization	1.55	0.81–2.97	0.19	1.70	1.04–2.78	0.04
SPECT/PET-mismatch ≥5 %	2.20	1.13–4.28	0.02	2.61	1.59–4.26	0.0001
Interaction between SPECT/PET-mismatch ≥5 % and revascularization	0.26	0.09–0.69	0.007	0.35	0.17–0.70	0.003

the earlier study was markedly briefer than the 33 month follow-up of the present study, such that a lower number of severe cardiac events (11 cardiac deaths and five MI), were encountered by D'Egidio et al. Consequently, heart transplantation and repeat hospital stays were included in the primary outcome, in contrast to our considerably more strict definition. However, the prospective setting must be considered as a particular strength of the PARR-2 trial. While our SPECT/PET mismatch analysis was necessarily retrospective, we used individual propensity scores to make a statistical correction for potential selection bias in the decision for attempting revascularization. This study design therefore emulates as closely as possible a prospective setting.

Other retrospective studies have reported thresholds for perfusion-metabolism mismatch ranging from 5 to 20 % of the LV myocardium [21–23], but these thresholds were estimated from visual evaluation, rather than the present software-based finding of ≥5 %. Furthermore, the earlier retrospective studies all suffer from a selection bias towards revascularization, or, as in D'Egidio et al., included soft events like repeated hospital stay because of cardiac cause in their outcome analysis. Despite these shortcomings, it emerges as a consistent finding of this and all preceding studies that the occurrence of cardiac events without revascularization correlated with the number of viable myocardial segments, i.e. hibernating myocardium.

As known from studies focusing on ischemia diagnostics, it is helpful for clinicians to have identified objective thresholds, so as to simplify decision making about the advisability of carrying out revascularization. This holds particularly for patients suffering from co-morbidities, or severely reduced left ventricular function, such that surgical interventions bring an additional risk of morbidity. Compared to the 10 % threshold described by Hachamovitch et al. [24] for optimized clinical decision-making in patients with stress-induced ischemia, the threshold in the present study with 5 % hibernating myocardium seems rather low. However, even small regional effects promoting cardiomyocyte survival in the setting of chronic repetitive ischemia may result in enhanced vulnerability to lethal arrhythmias and sudden cardiac death. Similarly, even small amounts of hibernating myocardium constitute a pathophysiological substrate for high risk of sudden cardiac death, independent of changes in functional stenosis severity, acute myocardial necrosis, or fibrotic scar [25].

The combined presence of considerable areas of ischemia (>15 %) and hibernation (>15 % perfusion-metabolism mismatch) was recently reported to be predictive for survival if no early intervention was performed [5]. Interestingly, improved survival was evident in that study irrespective of the degree of viability. In contrast, we now report that patients with <5 % SPECT/PET-mismatch, or indeed, without any mismatch, who received early revascularization had markedly higher mortality than did the patients without revascularization. This result again strengthens our claim that both detection and quantification of hibernating myocardium are essential for optimal clinical decision-making.

Limitations

First, due to the retrospective design of the present study not all patients had follow-up investigations in our hospital, so that no detailed data about functional recovery can be presented, which would have been of interest to prove success of revascularization.

Second, in the present study we compared non attenuation corrected (AC) SPECT data with AC PET for identification and quantification of hibernating and scar areas, so that one might assume that this protocol leads to an overestimation of myocardial hibernation due to larger areas of perfusion defects compared to AC-SPECT [26]. This is remedied by the algorithm applied by QPS. First QPS® calculates the SPECT TPD by comparing the perfusion polar map of the patient to the average perfusion polar map of a non AC normal database, which is implemented in the software. Second, after the TPD has been derived, FDG viability PET scan polar maps are normalized to the perfusion scan polar maps and mismatch (which is equal to hibernating myocardium with hypoperfusion, but sustained viability) and scar can be calculated within the area of the TPD similar to the PARR-1 trial method by assigning a perfusion and a viability score to each segment and looking for mismatches (reduced perfusion, sustained viability) and matches (reduced perfusion, no viability) [14]. This approach has been well established and yields excellent results [15].

Summarizing, in a retrospective analysis of 244 patients with ischemic cardiomyopathy and left ventricular dysfunction, a threshold of ≥5 % hibernating myocardium as determined by SPECT/PET-mismatch was found to discriminate best between patients who did or did not benefit from early revascularization during a prolonged follow-up.

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Conflict of interest Cedars-Sinai Medical Center receives royalties for the licensure of software used in the quantitative assessment of function, perfusion, and viability, a portion of which is distributed to some of the authors of this article.

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