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Increasing Benefit From Revascularization Is Associated With Increasing Amounts of Myocardial Hibernation

A Substudy of the PARR-2 Trial

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OBJECTIVES We sought to determine: 1) whether F-18-fluorodeoxyglucose (FDG) positron emission tomography (PET) parameters identify high-risk patients who gain benefit from revascularization; 2) whether there is a cut point for such benefit; and 3) predictors of outcome in patients with severe left ventricular (LV) dysfunction due to coronary artery disease.

BACKGROUND Patients with ischemic LV dysfunction might benefit from revascularization but not without risk. The FDG PET imaging can detect viable myocardium that recovers after revascularization. In the PARR-2 (PET and Recovery Following Revascularization-2) trial, FDG PET imaging showed a nonsignificant trend for improved outcome compared with standard care. Understanding the predictors of outcome from this prospective trial should help better identify patients at risk and which patients most benefit from revascularization.

METHODS This post hoc analysis included 182 patients with left ventricular ejection fraction (LVEF) <35% and coronary artery disease, being considered for revascularization work-up, and randomized to the PET arm of PARR-2. The primary outcome was a composite of cardiac death, myocardial infarction, or cardiac repeat hospital stay at 1 year.

RESULTS There is an interaction between PET mismatch and protocol revascularization such that higher mismatch, when combined with revascularization, yields fewer primary outcome events ($p = 0.02$). On the basis of adjusted Cox modeling, with reduced mismatch (<7%), the risk is not significantly different with or without revascularization. As mismatch increases above this mark, risk is reduced with revascularization. Increasing creatinine (for a 10-μmol/l increase: hazard ratio: 1.03, 95% confidence interval: 1.01 to 1.06, $p = 0.010$) is also associated with increased risk, whereas decreasing LVEF (for a 2% decrease: hazard ratio: 1.08, 95% confidence interval: 0.99 to 1.18, $p = 0.087$) trends toward an association with increased risk.

CONCLUSIONS In this post hoc analysis, patients with ischemic cardiomyopathy with larger amounts of mismatch have improved outcome with revascularization. Renal function was also an independent predictor of outcome. The FDG PET seems to define high-risk patients that gain benefit from revascularization. (PET and Recovery Following Revascularization [PARR 2]; NCT00385242) (J Am Coll Cardiol Img 2009;2:1060–8) © 2009 by the American College of Cardiology Foundation

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Patients with ischemic cardiomyopathy might benefit from revascularization but have significant perioperative risk (1–3). Previous studies have shown that surgical mortality can vary from 5% to 37% (1,4–6). Therefore it is crucial to identify those patients who would benefit from revascularization. F-18-fluorodeoxyglucose (FDG) positron emission tomography (PET) imaging has long been regarded as the most sensitive method for the detection of viable recoverable myocardium (7). Outcome data from retrospective and/or observational studies have indicated that FDG PET can define viable myocardium in patients with left ventricular (LV) dysfunction, and if these patients do not undergo early revascularization they are at high risk for death and further cardiac events (4,8–17). This is supported by 2 meta-analyses that showed that patients with viable myocardium who received revascularization had better survival compared with those receiving medical therapy (7,18).

See page 1069

The aforementioned studies were observational in nature and could not determine whether clinical decisions guided by FDG PET imaging data altered patient outcome. Until recently data from randomized controlled trials were lacking.

The PARR-2 (PET and Recovery Following Revascularization) trial was the first randomized controlled trial to determine whether management assisted by FDG PET achieves a better clinical outcome than standard care without FDG PET available, in patients with severe LV dysfunction (19).

The results at 1 year showed that there was a trend toward benefit in the PET group compared with the standard care group, but this was not statistically significant. However, there was a 25% nonadherence rate to PET management recommendations. When adherence to PET recommendations for revascularization or revascularization work-up was considered, significant benefits were observed in the FDG PET arm.

The utility of FDG PET might be best realized in this subpopulation that adhered to PET imaging recommendations. In this post hoc analysis we sought to identify: 1) whether FDG PET parameters could identify high-risk patients who would gain significant benefit from revascularization; 2) at what cut point this benefit might be realized; and 3) to better define imaging predictors of outcome in patients with severe ischemia and LV dysfunction.

METHODS

The methods of the PARR-2 trial have been published separately (19,20). Details of methodology relevant to the patients included the current study are described in the following text.

Patients. Included in this substudy were patients randomized to the FDG PET arm of the PARR-2 trial. Candidates for the PARR-2 trial were: 1) patients being considered for revascularization or revascularization work-up; 2) patients being considered for transplantation work-up; 3) patients being considered for heart failure work-up; or 4) any patient for whom FDG PET viability imaging might be considered useful by the attending physician for decision-making and who met other inclusion criteria. Eligible patients were included if they were over 18 years of age; had an LVEF ≤35% documented by radionuclide angiogram (RNA), LV angiogram, or echocardiography; and had a high suspicion of coronary artery disease on the basis of coronary angiography, previous revascularization, previous myocardial infarction (MI) (≥4 weeks) verified by chart review, and/or positive stress perfusion imaging for scar with or without ischemia. Excluded were patients: in whom a therapy decision had already been determined such that the attending physician would not alter management on the basis of any potential viability findings; and those who had already had FDG viability imaging. Also excluded were those: with comorbidities that would affect survival; <4 weeks post-MI; already identified to be unsuitable for revascularization; requiring emergency revascularization;

ABBREVIATIONS AND ACRONYMS

CKD = chronic kidney disease
FDG = F-18-fluorodeoxyglucose
ICD = implantable cardioverter-defibrillator
LV = left ventricle/ventricular
EF = ejection fraction
MI = myocardial infarction
PET = positron emission tomography
RNA = radionuclide angiogram

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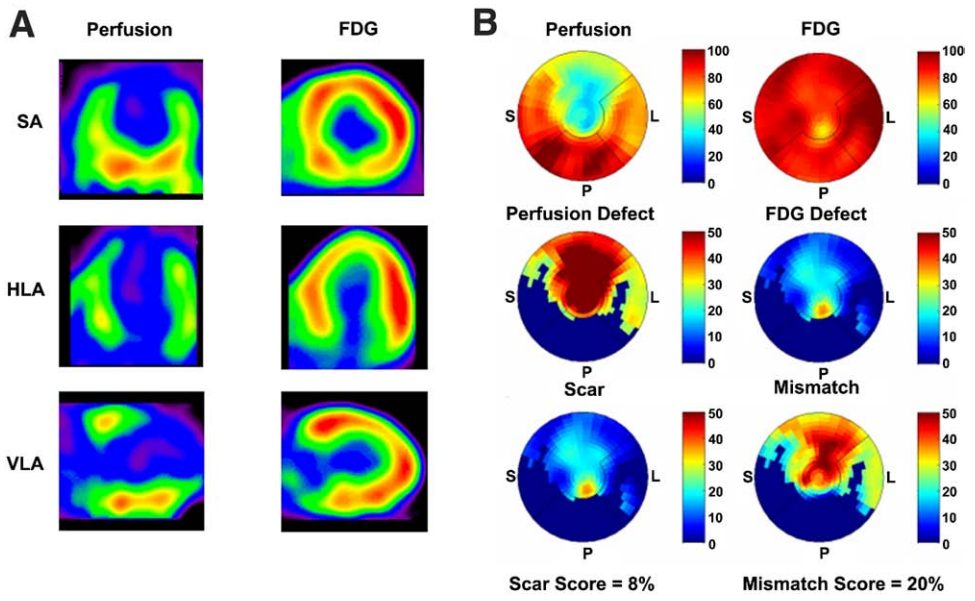

Figure 1. Examples of Images and Reconstructed Polar Maps in an Enrolled Patient

(A) Perfusion **(left)** and F-18-fluorodeoxyglucose (FDG) **(right)** imaging in the short-axis (SA), vertical-long-axis (VLA), and horizontal-long-axis (HLA) planes. Reduced perfusion with predominately maintained FDG uptake (mismatch) is noted in the anterior, septal, and lateral walls of the left ventricle (LV). **(B)** Polar maps (scale is %): **top row** showing the raw perfusion **(left)** and raw FDG uptake **(right)** polar maps; **middle row** is the normalized perfusion defect and FDG defect; **lowest row** is the scar score **(left)** and mismatch score **(right)**. Of the total LV myocardium, 8% was scar, and 20% was mismatch. The interpretation was that there was a large amount of mismatch and that the patient would be expected to improve after revascularization. The patient was referred for revascularization but died within 1 week, awaiting surgery.

with valvular disease that required surgery; or who were geographically inaccessible.

Data from the patients randomized to the PET arm of the PARR-2 trial were included in the present analysis if the patient had complete baseline data available, including: baseline RNA, baseline blood work, and having undergone FDG PET. Patients were excluded if they were found in work-up to not have coronary stenoses >50% or if they had poor-quality uninterpretable FDG PET imaging. Patients who had events before PET imaging were also excluded from this analysis; because such patients would not have had complete baseline data before the event.

Imaging. Patients underwent RNA imaging at baseline. The RNAs were acquired with a standard electrocardiogram-gated equilibrium Technetium-99m-red blood cell blood pool imaging protocol (19,21). The PET perfusion imaging was acquired at rest with a standard protocol with rubidium-82 or N-13-ammonia (19–22). Full details of PET imaging protocols are provided elsewhere (19–23). The images were analyzed to assess myocardial perfusion-metabolism mismatch and match (scar) expressed as a percentage of the LV, with our previously described scoring method (19–21) as illustrated in Figure 1.

FDG PET-ASSISTED MANAGEMENT ARM. As per the PARR-2 trial, these PET parameters were included with clinical parameters in a previously derived model that yielded a point estimate and 95% confidence interval for predicted LV function recovery after revascularization (20,21). Patients were classified as having low, moderate, or high likelihood of recovery if adequate revascularization could be achieved. Interpreting physicians considered the extent of scar and mismatch in their interpretation. A standard clinical report detailing the extent of scar (20), total viable myocardium, and mismatch (all as a percent of the left ventricle); the likelihood for recovery was faxed and delivered to the treating physician (20).

PROTOCOL REVASCULARIZATION VERSUS MEDICAL THERAPY. Once initial testing and evaluation were completed, the treating physician would then consider the PET imaging data in the context of the individual patient and make a decision to proceed or not with revascularization (or revascularization work-up in those without recent angiography).

Such revascularizations were considered protocol revascularization. These management plans were reviewed and confirmed at 8 weeks after enrollment. Hospital stays associated with protocol revascularization were not counted as events. Those patients without protocol revascularization were considered as having medical therapy.

Patients were censored at the time of events (see the Statistical Analysis text). As such, patients with events before a scheduled revascularization (having been censored at the time of the event) were considered to be in the nonrevascularized (medical) group. Given that decisions for aneurysm surgery might be different than revascularization alone, patients who underwent aneurysm resection were excluded.

Cardiac event variable definitions and measurement. The primary event of interest was the occurrence of any of the following within 1 year of randomization: cardiac death, MI, cardiac transplantation, or hospital stay due to cardiac cause such as unstable angina or heart failure. Elective admissions for procedures such as primary prevention implantable cardioverter-defibrillator (ICD) were not counted as events. Noncardiac deaths were not counted as events. Events were reviewed and verified by an adjudication committee blinded to the results of the FDG PET scan (19). The definitions of each variable and the timing of their measurement have been described previously in the PARR-2 trial design (19,20).

Table 1. Patient Characteristics

Variable	PET Arm (n = 182)	95% Confidence Interval
Age, mean (SD)	63 (10)	(61–64)
Male, n (%)	155 (85)	(80–90)
Baseline ejection fraction, mean (SD)	26 (6)	(25–27)
Diabetes, n (%)	72 (40)	(32–47)
Prior infarction, n (%)	150 (82)	(76–88)
Angiography in previous 6 months, n (%)	94 (52)	(44–59)
Prior coronary artery bypass grafting, n (%)	39 (21)	(16–28)
Angina (CCS class II–IV), n (%)	81 (45)	(37–52)
Dyspnea (NYHA functional class II–IV), n (%)	151 (83)	(77–88)
Creatinine (μmol/l), mean (SD)	112 (66)	(102–122)
FDG PET imaging scar score %, mean (SD)	18 (9)	(16–19)
FDG PET imaging mismatch score %, mean (SD)	5 (6)	(4–6)
Protocol revascularization, n (%)	83 (46)	(38–53)

CCS = Canadian Cardiovascular Society; FDG = F-18-fluorodeoxyglucose; NYHA = New York Heart Association; PET = positron emission tomography.

Table 2. Multivariable Cox Proportional Hazard Model

Variable	Parameter Estimate	Standard Error	p Value
Protocol revascularization	0.428	0.396	0.280
Mismatch size	0.050	0.036	0.161
Revascularization/mismatch interaction	−0.171	0.074	0.020
Creatinine (10 μmol/l increase)	0.032	0.013	0.011
Ejection fraction (2% increase)	−0.075	0.044	0.087

Statistical analysis. Continuous measures are presented as mean ± SD. Categorical measures are presented as frequencies with percentages. Because the primary objective of this substudy was to determine whether FDG PET parameters could identify high-risk patients who would gain significant benefit from revascularization, multivariable Cox proportional hazard models were used to assess the independent prognostic value of the protocol revascularization and PET parameters (mismatch and scar), including all 2-way interactions. Other baseline characteristics included in Table 1 with p values <0.20 on the basis of univariable Cox proportional hazard models were added to control for confounding with stepwise selection methods resulting in the final model given in Table 2.

To illustrate the observed interaction of revascularization and mismatch, hazard ratios were determined for mismatch levels with the interaction estimates from the adjusted Cox model with mismatch as a continuous variable (Fig. 2). Previous studies have defined mismatch as dichotomous variable. We therefore also performed secondary analyses evaluating mismatch as a dichotomous variable in the adjusted Cox model with an interaction test. A p value <0.05 was considered statistically significant. Statistical calculations were carried out with SAS software (SAS Institute Inc., Cary, North Carolina).

RESULTS

Clinical characteristics. Among the 218 patients who were enrolled in the PET arm, 182 met the substudy inclusion criteria and had complete and interpretable data (Table 1). Excluded were: 11 patients allocated to the PET group but who did not undergo PET imaging; 9 patients who initially seemed to meet inclusion criteria but were found to have an EF >35% on the RNA done at the time of enrollment (2 patients had EF >35% and did not

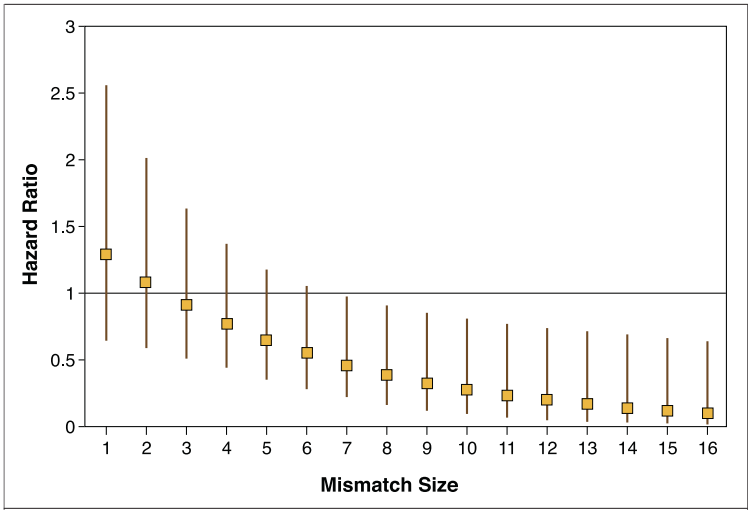

Figure 2. Interaction Hazard Ratios and 95% Confidence Interval at Various Levels of Mismatch Measured as a Continuous Variable

The figure is a derivation from the multivariable model. For those with mismatch of <7% there is no significant difference in the risk of the primary outcome if revascularization is done compared with not done. As mismatch increases (i.e., ≥7%), there is a decreased risk of the primary outcome for those who undergo revascularization. For those with mismatch of 7%, there is a 0.46 times lower risk for the primary outcome if revascularization is done.

undergo PET imaging); 6 patients were subsequently found to not have any significant coronary stenoses; 4 patients had poor-quality PET imaging data whereby no scar or mismatch score could be accurately determined (1 of these patients was also a patient without significant coronary artery disease on angiography); 2 patients had events preceding PET imaging (1 such patient had an EF >35%); 5 patients had no baseline RNA for EF or no creatinine measurement; and 3 patients underwent aneurysm resection. In all, 36 patients had 40 exclusion criteria, leaving 182 patients with complete and interpretable data for analysis.

The baseline characteristics of these patients are provided in Table 1. Patients were, on average, 63 ± 10 years of age with a mean EF of 26 ± 6% and a mean creatinine of 112 ± 66 μmol/l. The mean mismatch score in the total population was 5 ± 6%, and mean scar score was 18 ± 9%. Of the 182 patients, 83 (46%) patients underwent protocol revascularization, of whom 55 (66% of protocol revascularizations) underwent coronary artery bypass grafting. The mean mismatch and scar scores were 6 ± 7% and 15 ± 8%, respectively, in the patients who underwent revascularization compared with 4 ± 4% and 20 ± 9%, respectively, in those treated with medical therapy. Among those who underwent protocol revascularization, 3 (4%) had ICD device therapy compared with 8 (8%) in the medical group during the 1-year follow-up period. During the course of the trial the American College of Cardiology/American Heart Association guidelines for ICD therapy were published that recommended ICD for primary prevention in severe LV dysfunction as a Level I indication (24). As such, a recommendation was sent to the treating physicians of enrolled patients to consider device therapy, if the patient met appropriate criteria. Table 3 shows the medical therapy in each group.

Table 3. Medications Used by Patients in the Revascularization and Medical Therapy Groups

Medication	Medical Therapy	Protocol Revascularization
Antiplatelet and/or anticoagulation	91 (92%)	72 (87%)
Nitrates	39 (39%)	36 (43%)
Beta-blockers	77 (78%)	62 (75%)
ACE inhibitors or ARB	90 (91%)	71 (86%)
Digoxin	37 (37%)	24 (29%)
Diuretics	78 (79%)	59 (71%)

ACE = angiotensin-converting enzyme; ARB = angiotensin-receptor blocker.

Cardiovascular events. Fifty-four patients had a primary outcome. Of these 54 patients, cardiac death was first event in 11, MI in 5, transplantation in 2, and repeat hospital stay because of a cardiac cause in 36 patients (Tables 4 and 5). Eighteen patients had a cardiac death within 1 year of enrollment, 11 as a first event and 7 as a subsequent event. There were 2 noncardiac deaths (not counted as cardiac events), 1 of which occurred later than the patient's first cardiac event.

Multivariable analysis. When the interaction of mismatch and protocol revascularization was considered in the multivariable Cox proportional hazard model, there was a statistically significant effect on the primary outcome ($p = 0.020$) (Table 2). Increasing creatinine (for a 10-μmol/l increase: hazard ratio = 1.03, 95% confidence interval: 1.01 to 1.06, $p = 0.010$) is also associated with increased risk, and decreasing EF (for a 2% decrease: hazard ratio: 1.08, 95% confidence interval: 0.99 to 1.18, $p = 0.087$) trends toward an association with increased risk. The adjusted model in Table 2 summarizes that the interaction of mismatch and protocol revascularization is still statistically significant, even after adjusting for creatinine and EF.

To illustrate the observed interaction of revascularization and mismatch, in Table 2, hazard ratios were determined for mismatch levels with the interaction estimates from the adjusted Cox model with mismatch as a continuous variable (Fig. 2). In

Table 4. Distribution of First Events Between Medical Therapy and Protocol Revascularization Groups

	No Event	Cardiac Death	MI	Transplant	Repeat Hospital Stay	Total First Events
Medical therapy	66	6 (+5)	3	2	22	33
Protocol revascularization	62	5 (+2)	2	0	14	21
Total	128	11 (+7)	5	2	36	54

+ = number of cardiac deaths that were not the first event for the patient; MI = myocardial infarction.

patients with lower levels of mismatch (<7%), the risk of the primary outcome is not significantly different with or without revascularization. At higher levels of mismatch, ≥7%, the risk of the composite event decreases if the patient undergoes revascularization. When mismatch = 7, there is a 0.46 (95% confidence interval: 0.22 to 0.97) times lower risk of the primary outcome if the patient undergoes revascularization compared with not being revascularized (Fig. 2).

In response to this finding we analyzed the cut point of 7% as a dichotomous variable (Fig. 3). Those with mismatch ≥7% had a significantly reduced incidence of the primary outcome with revascularization compared with medical management (3 [13%] vs. 9 [56%], p = 0.015). No patients (0%) with mismatch ≥7% who received revascularization died, compared with 2 (13%) who were medically managed. The small number of deaths does not allow analysis of this end point. Those patients with a mismatch of <7% had no significant difference in the primary outcome when revascularization was undertaken, compared with not undertaken (18 [31%] vs. 24 [29%], p = 0.923). Nine (11%) patients suffered cardiac death in the medically managed group with mismatch <7% compared with 7 (12%) patients in the revascularized group.

Given that previous published reports have suggested a cut point of 5% for predicting adverse outcome without revascularization (4), we analyzed 5% and 6% in addition to the 7% cut point identified in the preceding text. Statistically significant effects of revascularization were observed with mismatch ≥6% (p = 0.036) or ≥7% (p = 0.015) but not with mismatch ≥5% (p = 0.216), although the overall interaction of mismatch and protocol revascularization was only significant for the cut point of 7% (p = 0.020) and not 5% (p = 0.771) or 6% (p = 0.054, a trend).

Table 5. Cardiac Repeat Hospital Stay Due to Cardiac Arrest, Angina, and CHF in Medical Therapy and Protocol Revascularization Groups

	Medical Therapy (n = 22)	Protocol Revascularization (n = 14)
Cardiac arrest	1 (5%)	1 (7%)
CHF	14 (64%)	8 (57%)
Angina	3 (14%)	4 (29%)
CHF and angina	2 (9%)	0
CHF with others	2 (9%)	1 (7%)

Others were severe mitral regurgitation, ventricular tachycardia, or atrial fibrillation.
CHF = congestive heart failure.

DISCUSSION

In this post-hoc observational analysis of the PARR-2 trial we found that, as the amount of myocardial perfusion-metabolism mismatch (as a measure of hibernation) increases, there is a progressive increase in a patient's benefit from revascularization. To our knowledge this is the first study to consider the relationship among mismatch as a continuous variable, revascularization, and outcomes and to use this relationship to determine a mismatch cut point for revascularization outcome benefit. In this prospective study, patients with ischemic cardiomyopathy with larger amounts of mismatch—specifically those with mismatch ≥7%—had an improved outcome with revascularization. Also of relevance is that there was no significant interaction between PET-defined scar and revascularization, suggesting that mismatch is the relevant parameter for determination of these outcome benefits of revascularization. Other parameters in the adjusted model, namely creatinine and EF, were predictors or trended toward being predictors of outcome regardless of whether the patient had revascularization or not. Even after adjusting for creatinine and EF, increasing amounts of mismatch defined by PET predicted increasing benefit from revascularization.

FDG PET imaging predictors of outcome. In a recent meta-analysis, of observational and predominately retrospective data, Schinkel et al. (7) have shown that using PET and other viability imaging methods can identify high-risk patients at greater risk of

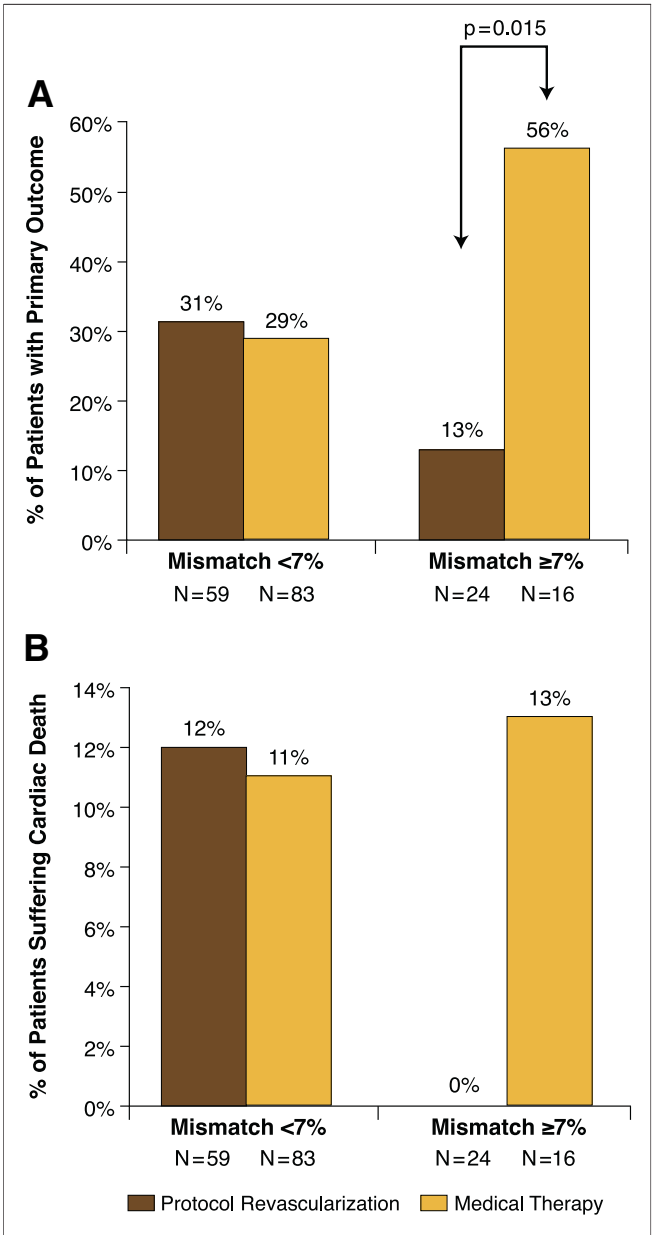

Figure 3. Effect of Revascularization or Medical Therapy

The effect of revascularization or medical therapy on primary outcome **(A)** and cardiac death **(B)** in patients with mismatch dichotomized to either <7% or ≥7%. In **A** for patients with mismatch of <7%, there is no significant difference in the primary outcome if revascularization is done compared with not done (p = 0.923). In patients with mismatch ≥7%, there is a significantly lower percentage of patients who experience the primary outcome if revascularization is undergone compared with not undergone (p = 0.015). In **B** for patients with mismatch of <7%, the percent of cardiac deaths when revascularization is done compared with not done is not very different. No patients with mismatch ≥7% who received protocol revascularization died compared with 2 (15%) who were medically managed.

cardiac events if they do not undergo revascularization. This meta-analysis report also pointed out the need for prospective data in this field, as was acquired in this study. The authors also report that there is a wide heterogeneity in dichotomous viability criteria for mismatch and viability that are used from study to study—often arbitrarily defined without definitive support for a given cut point.

Previous data evaluating the relationship of viability extent and the outcome response to revascularization are limited. Our prospective study is unique in that we evaluated mismatch as a continuous variable in a multivariable Cox model that yielded a cut point of 7%. There was an increase in the benefit of revascularization as mismatch increased. In analysis of a mismatch of 7% as a dichotomous variable, those patients with a mismatch of ≥7% gain significant outcome benefit when revascularization is undertaken compared with medical therapy (p = 0.015) (Fig. 2). This cut point requires prospective evaluation in another patient population.

Our findings are consistent with previous cohorts: in patients with mismatch, revascularization reduces undesirable clinical events compared with medical management alone. One previous study reported a cut point of 1 of 13 (7.6%) segments of the left ventricle, but this was arbitrarily selected, and there was no analysis of the relationship between the presence of mismatch and impact of revascularization on clinical outcomes (9). Di Carli et al. (4) showed that patients with a mismatch of at least 5% had a higher event rate when treated medically. In another study, with FDG SPECT, Desideri et al. (14) showed that the risk of death is significantly increased when the extent of mismatch exceeds 20%. These studies were retrospective. As such, it was unclear what role FDG PET imaging had in decision-making. The current study used a prospective design where FDG PET was applied in decision-making as part of the primary design of the PARR-2 trial.

In the current study, another predictor of outcome in the adjusted model was creatinine, and EF showed a trend toward increased risk. Previous studies have been variable as to whether EF was a predictor of outcome. Lee et al. (9) reported that patients with low EF <30% had higher cardiac mortality compared with those with an EF >30%. Likewise, Yoshida and Gould (12) reported a lower mortality rate for patients with an EF >43%. Previous studies where EF was not a predictor of outcome attributed this finding to the fact that the majority of patients included had severely depressed LVEF with mean EFs between 25% and 34% (4,8,14). Ejection fraction had a trend toward being

an independent predictor of outcome in our study, despite our patient population having severely reduced LVEF (26 ± 6%). That our study demonstrated a trend, whereas others did not, might be due to the fact that we considered a composite end point including death, MI, and cardiac repeat hospital stay and a larger sample size than previous studies (4,8,9,12,14).

No previous viability imaging studies have reported creatinine as a predictor of outcome. This might prove to be a useful clinical parameter to help distinguish a subgroup of patients who are at higher risk. This is increasingly relevant, due to the rising incidence of chronic kidney disease (CKD) in patients with heart failure. In addition viability assessment with other techniques, including cardiac magnetic resonance and computed tomography, carry risks for the patient with CKD (25,26). As such, in patients with CKD, FDG PET is the preferred advanced imaging approach for viability assessment.

Study limitations. First, this is a substudy, and hence it has all of the inherent limitations of a post hoc analysis and warrants confirmation in a larger study. However, this study's prospective design as part of a randomized controlled trial has advantages over previous retrospective studies. The sample size, although small, was powered to detect the interaction and also an absolute difference of 35% or greater on the basis of post hoc influence analysis with the Fisher exact test. Therefore, a delta of 39% would be statistically significant. Nevertheless, because of the overall small number of events, small changes in events could affect the difference between the groups or the cut point, further emphasizing the need for verification in a larger study.

Second, our overall number of fatal events was low, which hinders definitive conclusions regarding mortality with statistical techniques. Lower mortality likely reflects patient selection and/or improvements in medical therapy for heart failure. Third, the multivariable Cox proportional hazard models are limited by the number of events. Accordingly, to prevent overfitting of the multivariable Cox proportional hazard models, only baseline variables that were significant at a 0.20 significance level or lower were considered (i.e., creatinine and EF).

CONCLUSIONS

In this prospective observational analysis with a composite outcome, there is a progressive increase in patient benefit from revascularization as the amount of mismatch (a measure of hibernating myocardium) increases. Patients with ischemic cardiomyopathy with larger amounts of mismatch, specifically those with mismatch ≥7%, might have improved outcome with revascularization. Another independent predictor of outcome was impaired renal function, whereas lower EF demonstrated a trend toward an association with increased risk. These parameters seem useful in defining high-risk patients. The FDG PET imaging is useful in defining a subset of patients with myocardial perfusion-metabolism mismatch that could gain significant outcome benefit from revascularization.

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Key Words: fluorodeoxyglucose ■ heart failure ■ ischemic heart disease ■ viability.

▶APPENDIX

The other participating sites in the PARR-2 trial included the Divisions of Cardiology and Cardiac Surgery, Hamilton Health Sciences, Hamilton, Ontario, Canada; Division of Cardiology, Toronto Hospital, University of Toronto Health Sciences Network, Toronto, Ontario, Canada; Division of Cardiology, Toronto Western Hospital, University of Toronto, Ontario Canada; Division of Cardiology, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada; Division of Cardiology, Hopital Laval, Universitaire de Laval, Québec City, Québec, Canada. Full details of the participating teams from all sites have been published elsewhere.