Cardiomyopathies

Long-Term Follow-Up of Outcomes With F-18-Fluorodeoxyglucose Positron Emission Tomography Imaging—Assisted Management of Patients With Severe Left Ventricular Dysfunction Secondary to Coronary Disease

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Background—Whether viability imaging can impact long-term patient outcomes is uncertain. The PARR-2 study (Positron Emission Tomography and Recovery Following Revascularization) showed a nonsignificant trend toward improved outcomes at 1 year using an F-18-fluorodeoxyglucose positron emission tomography (PET)–assisted strategy in patients with suspected ischemic cardiomyopathy. When patients adhered to F-18-fluorodeoxyglucose PET recommendations, outcome benefit was observed. Long-term outcomes of viability imaging–assisted management have not previously been evaluated in a randomized controlled trial.

Methods and Results—PARR-2 randomized patients with severe left ventricular dysfunction and suspected CAD being considered for revascularization or transplantation to standard care (n=195) versus PET-assisted management (n=197) at sites participating in long-term follow-up. The predefined primary outcome was time to composite event (cardiac death, myocardial infarction, or cardiac hospitalization). After 5 years, 105 (53%) patients in the PET arm and 111 (57%) in the standard care arm experienced the composite event (hazard ratio for time to composite event =0.82 [95% confidence interval 0.62–1.07]; P=0.15). When only patients who adhered to PET recommendations were included, the hazard ratio for the time to primary outcome was 0.73 (95% confidence interval 0.54–0.99; P=0.042).

Conclusions—After a 5-year follow-up in patients with left ventricular dysfunction and suspected CAD, overall, PET-assisted management did not significantly reduce cardiac events compared with standard care. However, significant benefits were observed when there was adherence to PET recommendations. PET viability imaging may be best applied when there is likely to be adherence to imaging-based recommendations.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00385242.

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Key Words: fluorodeoxyglucose ■ heart failure ■ positron emission tomography ■ revascularization ■ viability imaging

Ischemic cardiomyopathy remains a significant cause of morbidity and mortality, despite advances in pharmacological and device therapy over the past 3 decades.1,2 There is a large body of predominantly observational data to demonstrate that restoration of blood flow to dysfunctional myocardium evaluated in a randomized controlled trial.

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in the territory of a stenosed coronary artery is beneficial,3,5 but controversies remain regarding surgical revascularization.

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*B. McArdle and Dr Shukla are joint first authors.

†The full list of participating sites in PARR-2 long-term follow-up is noted in the Appendix.

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particularly in the absence of an acute coronary syndrome or limiting angina.6

The STICH trial (Surgical Treatment for Ischemic Heart Failure) failed to show a mortality benefit among patients randomized to coronary artery bypass graft surgery (CABG) as compared with optimal medical therapy in the primary intention to treat analysis. Importantly, there was significant crossover between the 2 groups, and the as-treated analysis was in favor of improved outcomes with CABG.7

However, the decision whether to proceed with revascularization in these patients can be difficult, particularly in cases of repeat surgery or multiple comorbidities where both the risks and the potential benefits of revascularization are highest. Given the complexity of decision-making in these patients, multiple imaging modalities have been used to predict potential for left ventricular (LV) functional recovery by discerning between viable myocardium, which may recover function with revascularization, and scar, which will not.8–10

Positron emission tomography (PET) using 18F-fluorodeoxyglucose (FDG) has been shown in multiple observational studies to be a sensitive means for prediction of recovery of LV function post revascularization.11–13 There have also been several observational studies showing a relationship between the degree of mismatch on FDG PET and subsequent outcome in this patient population.11–13 This led to the PARR-2 study (PET and Recovery Following Revascularization), which remains the only randomized prospective study to evaluate outcome benefit of a PET-assisted management strategy in patients with severe LV dysfunction.

Results from the primary intention-to-treat analysis after 12 months of follow-up showed a trend toward improved outcome in the FDG PET–assisted cohort that did not reach statistical significance.16 However, a post hoc analysis, including only patients where there was adherence to the management strategy recommended on the basis of the FDG PET findings, showed a significant improvement in outcome with the FDG PET imaging–assisted approach when compared with standard care.16

Herein, we present the 5-year follow-up results from the PARR-2 study to evaluate whether a PET-guided approach to revascularization in patients with suspected ischemic cardiomyopathy results in a clinical benefit over the long term.

Methods

A complete description of the enrollment criteria and study protocol of the PARR-2 study, as well as comprehensive details of methods and design, have been previously published.16,17 In summary, patients were eligible for inclusion if they were over 18 years of age, had a LV ejection fraction of ≤35% documented on radionuclide ventriculography, LV angiogram, or echocardiography, and had a high suspicion for CAD based on at least one of the following: coronary angiography, previous percutaneous coronary intervention or CABG, previous myocardial infarction (MI), and positive stress perfusion imaging for scar and/or ischemia. Furthermore, patients included were those being considered for revascularization or revascularization work-up and heart failure and cardiac transplantation work-up or those in whom FDG PET viability imaging may have been considered useful by the attending physician. The study was approved by the institutional review board at each site, and all patients enrolled gave written informed consent.

Exclusion criteria were as follows: cases where the decision for revascularization or transplant had already been definitively made, patients who had previously undergone FDG PET viability imaging, as well as patients with recent MI; anatomy known to be unsuitable for revascularization; a need for emergent surgery; severe valvular disease requiring surgery; comorbidities that would likely adversely impact survival over 12 months; or patients who were geographically inaccessible.

Enrolled patients were then randomized to undergo either FDG PET viability imaging, with the results being made available to the treating physician afterward, or to proceed without FDG PET with alternate testing being performed at the discretion of the treating physician (standard care). Physicians and staff were unaware of the allocation before randomization. Block randomization was used and was prestratified according to site and according to whether the patient had prior angiography within 6 months. Outcomes were classified according to an adjudication process that was blinded to patient allocation.

PET Imaging and Decision Making

The methods are detailed in previous reports16,17 and summarized below. Patients in the PET arm underwent imaging at one of the 4 PET sites. Resting perfusion was evaluated with the use of either Rubidium-82 or N-13-Ammonia as previously described.17 An oral glucose load was administered to nondiabetic patients before the FDG scan, while an insulin–euglycemic clamp was used in diabetic patients.

All PET images were interpreted at a central core laboratory, and images were analyzed using an automated program to quantify the extent and severity of mismatch and scar in terms of a percentage of the LV. A computerized model incorporated these measurements, with clinical data to define a point estimate and 95% confidence interval (CI) for the likelihood of recovery of LV function.16,17 Low, moderate, or high likelihood of recovery were defined: low, upper confidence limit of the predicted ejection fraction change was 3% or less; high, lower confidence limit for predicted change was above 3%; moderate, confidence limits between high and low cut points. Images were also reviewed by an experienced physician, who considered the amount of scar and hibernation based on visual analysis, and classified patients accordingly. Cases where there was a discrepancy between the physician and the computer model were settled by consensus with another experienced physician. In addition to the standard clinical report, a report describing the defects and the extent of scar, hibernation, and viable myocardium (all as percent of the LV) and a recommendation based on the likelihood of LV recovery were faxed and delivered to the treating physician. With the FDG PET imaging data available for patients in the PET arm, the treating physician then made a decision regarding further management (ie, referral for angiography or revascularization or not).

For patients in the standard-care arm, the decision to refer for revascularization or revascularization work-up was made without FDG PET imaging.

Follow-Up and Outcomes

Once initial testing was complete, the treating physician would review the results for patients in either treatment group, in conjunction with the clinical context, and would make a decision whether or not to proceed with revascularization or revascularization work-up. If the decision was made to proceed, then procedures were performed within 8 weeks where possible. For protocol revascularizations, that is, revascularization driven by imaging results, the associated hospitalization was not counted as an event.

The predefined primary outcome of the long-term follow-up study was the time to occurrence of the composite of cardiac death, MI, or hospitalization for unstable angina or heart failure. Events were ascertained by telephone interview at 3-month intervals for 2 years and every 6 months for years 3 to 5 and based on best available data as of September 2013. All events were reviewed by an adjudication committee that was blinded to randomization allocation. Patients who underwent cardiac transplantation or suffered noncardiac death were censored at the time of transplantation or death, respectively.
the patients' status as alive or dead or where the cause of death could not be reliably determined, patients were censored at the time of their last follow-up. The definitions used for each event variable have been described previously.16

Statistical Analysis
We conducted an analysis of the 5-year follow-up from the PARR-2 trial. The original study had been powered at 80% for distinguishing between an event rate of 50% and 35% in the 2 arms after 1-year follow-up. The primary outcome in the 1-year study was occurrence of the composite of cardiac death, MI, or hospitalization for unstable angina or heart failure. Follow-up was continued ≤5 years (1825 days). Because 3 sites did not participate beyond 2 years, only patients randomized and enrolled at sites participating in long-term follow-up were included in this analysis.

An intention-to-treat framework was used for the primary analyses of the long-term data. Baseline characteristics of patients in the PET and standard care arm were compared using the t test for continuous variables and the χ² test for categorical variables. For the multivariable model, we included variables we considered relevant based on prior literature, whereby age, history of previous CABG, and diabetes mellitus were shown to be independent predictors.18 These were also the clinical parameters integrated with imaging measurements of scar and hibernation used to predict the likelihood of outcome benefit (as noted above). Thus, given the supporting literature, and their use in the model, these parameters were used for the adjusted hazard ratio (HR). We also adjusted for the site of enrollment. Adjusted survival curves were generated to illustrate differences in event-free survival between treatment groups.

As in the main PARR-2 study,16 because a patient’s course may not adhere to PET imaging recommendations, we performed an additional post hoc comparison of the optimal circumstances, where the patients’ management adhered to recommendations from FDG PET imaging, with those in the standard care arm. Similar to the 1-year analysis, patients were excluded from this post hoc analysis if they suffered events before FDG PET imaging or revascularization or revascularization work-up because these events may have partly driven revascularization or revascularization work-up. All analyses were performed using SAS software (SAS Institute Inc, Cary, NC).

Results
As described in the initial PARR-2 analysis, 430 patients were randomized across 9 sites. Patients were randomized to either FDG PET–assisted management (n=218) or standard care (n=212). There were 3 sites (21 PET patients and 17 standard care) that did not participate beyond 2 years of follow-up. Therefore, there were 392 patients randomized from 6 sites participating in long-term follow-up: 197 PET arm and 195 standard arm. Among these patients, there were 35 dropouts (20 in the PET arm and 15 in standard arm; Figure 1). The baseline characteristics between the 2 groups have been previously described in detail.16 Considering the patients randomized at sites participating in the 5-year long-term follow-up, age, sex, baseline ejection fraction, diabetes mellitus, prior MI, Canadian Cardiovascular Society (CCS) angina class, New York Heart Association dyspnea class, and serum creatinine were not significantly different between groups (Table 1). There was a higher prevalence of previous CABG at baseline in the PET arm (22%) compared with the standard care arm (16%: P=0.14). Medications were also similar between the 2 arms (Table 2). Comparing the 38 patients enrolled at sites that did not—with the 392 patients enrolled at sites that did—participate in long-term follow-up, there were no statistically significant differences in demographics except male sex (100% versus 83%, respectively; P=0.002).

Figure 1. Flow diagram showing patient randomization and subsequent follow-up. Of the 9 sites enrolled in the initial 2-year study, 6 participated in the 5-year follow-up. Patients who dropped out or had cardiac transplant or suffered noncardiac death before any cardiac event had occurred are noted at the bottom of the figure. These patients were censored in the survival analysis. PET indicates positron emission tomography; and STD, standard care.

In this long-term follow-up cohort, 96 patients (49%) in the PET arm underwent protocol revascularization compared with 65 patients (33%) in the standard care arm (P=0.002).16

Cardiovascular Events
After 5 years of follow-up, 105 (53% of enrolled patients) patients in the PET arm, and 111 (57%) patients in the standard care arm experienced the composite event (Figure 1). The adjusted HR for time to the composite event (FDG PET arm versus standard care) was 0.82 (95% CI 0.62–1.07; P=0.15; Figure 2). The rates of the individual components of the composite clinical end point are shown in Table 3.

Among the 201 patients with angiography in the preceding 6 months and among the 191 without, the adjusted HRs remained not significant between FDG PET and standard care for the time to composite event nor for the time to cardiac death.

Mortality
Overall, there were 62 deaths in the PET arm and 65 in the standard care arm, including those who may have had events
Table 1. Baseline Characteristics of Patients Randomized and Enrolled at Sites Participating in Long-Term Follow-Up

<table>
<thead>
<tr>
<th></th>
<th>STD (n=195)</th>
<th>PET (n=197)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>62±10</td>
<td>63±10</td>
<td>0.53</td>
</tr>
<tr>
<td>Sex, male (%)</td>
<td>162 (83%)</td>
<td>163 (83%)</td>
<td>0.93</td>
</tr>
<tr>
<td>Baseline EF, mean (SD)</td>
<td>26±8</td>
<td>27±7</td>
<td>0.40</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>69 (35%)</td>
<td>79 (40%)</td>
<td>0.34</td>
</tr>
<tr>
<td>Prior infarction, n (%)</td>
<td>154 (79%)</td>
<td>158 (80%)</td>
<td>0.76</td>
</tr>
<tr>
<td>Angiography in previous 6 mo, n (%)</td>
<td>98 (50%)</td>
<td>103 (52%)</td>
<td>0.69</td>
</tr>
<tr>
<td>Prior CABG, n (%)</td>
<td>32 (16%)</td>
<td>44 (22%)</td>
<td>0.14</td>
</tr>
<tr>
<td>Angina (CCS class II–IV), n (%)</td>
<td>92 (47%)</td>
<td>94 (49%)</td>
<td>0.92</td>
</tr>
<tr>
<td>Dyspnea (NYHA class II–IV), n (%)</td>
<td>163 (84%)</td>
<td>161 (82%)</td>
<td>0.63</td>
</tr>
<tr>
<td>Creatinine (μmol/L), mean (SD)</td>
<td>106±38</td>
<td>111±65</td>
<td>0.31</td>
</tr>
</tbody>
</table>

Table 2. Baseline Medications for Patients Randomized and Enrolled at Sites Participating in Long-Term Follow-Up

<table>
<thead>
<tr>
<th>Medication</th>
<th>STD (N=195)</th>
<th>PET (N=197)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin or Anticoagulant</td>
<td>179 (92%)</td>
<td>175 (89%)</td>
<td>0.32</td>
</tr>
<tr>
<td>ACE Inhibitor or ARB</td>
<td>179 (92%)</td>
<td>174 (88%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Beta Blocker</td>
<td>164 (84%)</td>
<td>152 (77%)</td>
<td>0.10</td>
</tr>
<tr>
<td>Digoxin</td>
<td>66 (34%)</td>
<td>65 (33%)</td>
<td>0.86</td>
</tr>
<tr>
<td>Nitrates</td>
<td>65 (33%)</td>
<td>80 (41%)</td>
<td>0.14</td>
</tr>
<tr>
<td>Diuretics</td>
<td>135 (69%)</td>
<td>143 (73%)</td>
<td>0.27</td>
</tr>
</tbody>
</table>

Discussion

The PARR-2 study remains the largest prospective randomized trial to evaluate the impact of FDG PET viability imaging on outcome in patients with ischemic cardiomyopathy.

The results of the primary-intention-to-treat analysis of patients randomized and enrolled in the 5-year long-term follow-up showed that the event-free survival in the PET arm did not reach a statistically significant difference compared with the standard arm. Therefore, the results of the primary analysis remain negative after 5 years of follow-up.

Similar to results after 1 year, when only patients for whom management adhered to the recommendations from the PET imaging were considered, there was a significant decrease in adverse cardiac events in the PET arm compared with standard care over the long term (HR=0.73, 95% CI 0.54–0.99; P=0.042). This result was driven primarily by the difference in cardiac rehospitalizations (see Table 3). Since the publication of the 1-year results of PARR-2, there has been only one other large prospective study correlating viability imaging with outcome after revascularization in this patient cohort, and this is the STICH viability substudy.19 This study included patients from the main STICH trial7 who had undergone viability imaging before the randomization to either medical therapy or CABG. The results showed no interaction between the presence or absence of significant viability and subsequent patient survival, irrespective of treatment strategy (CABG or medical therapy).

However, it is important to note that the imaging portion of the STICH viability substudy was not randomized, and the decision to perform viability imaging was at the discretion of the treating physician. Furthermore, the modalities used for imaging were dobutamine echocardiography and single photon emission computed tomography perfusion imaging which, although widely available, have lower sensitivity for hibernating myocardium than FDG PET, for which the extent of hibernating myocardium has also been shown to be a strong predictor of outcome benefit.12–15,20,21

Finally, the patient population in the STICH trial differed from those in the PARR-2 study, in that the STICH population was younger, and had lower prevalence of prior CABG, renal dysfunction, and 3-vessel CAD (among those with angiography).21 Therefore, the incremental value of the results of viability imaging was less because many of the patients in the STICH trial were already good candidates for CABG (having suitable anatomy was a requirement for inclusion). The PARR-2 patients likely represent a sicker cohort of patients where the decision on whether to proceed with revascularization is more
complex, and therefore, the results of PET imaging may be more likely to influence decision-making.22,23

As outlined in detail in the initial PARR-2 publication, approximately one fourth of patients did not adhere to the recommendation of the PET scan, despite the presence of high or medium levels of viability in 84% of these patients. The reasons for nonadherence are outlined in the original publication.16 In effect, this reflects real-world clinical practice where a multitude of factors are considered in the decision to proceed with revascularization, such as the patient’s comorbidities, symptoms, the suitability of the coronary anatomy, and whether the patient has had previous cardiac surgery.22 The improved outcomes demonstrated in this study in patients who adhered to PET recommendations suggest that this modality is best used in cases where there is clinical equipoise, such that the recommendation from the scan will have a real impact on the decision whether to perform revascularization or not.

Ling et al21 evaluated the impact of ischemia, hibernation, and scar on outcome in a cohort of 648 patients who underwent stress/rest Rb-82 and FDG PET at their center with a mean follow-up of 2.8±1.2 years. They found that revascularization reduced all-cause mortality compared with a propensity-matched group of patients undergoing medical therapy. They demonstrated that there is an association between all 3 parameters and all-cause mortality. They also found a significant interaction between hibernation and survival benefit from revascularization, with a cutoff of >10% being associated with superior outcomes when compared with medical therapy alone. The findings of the current study differed in that the composite event rate difference was driven primarily by cardiac rehospitalization rather than mortality as in the Ling et al’s study. The latter may have included sicker patients (patients were slightly older, had more diabetes mellitus, and more prior CABG), and indeed the mortality rate was higher (33% over a mean 2.8 years follow-up versus 32% over 5 years in the current study). Nevertheless, the findings are complimentary. Ling et al show that increased hibernating myocardium predicts increased likelihood of outcome benefit from revascularization, and the current study shows that when management adheres to imaging recommendations, outcome benefit can be achieved.

Study Limitations
As in the original PARR-2 publication,16 the principal limitation to this study was that only 76% of patients adhered to the management recommendation based on the PET results. Although this was in keeping with previous observational studies, it likely decreased the ability to detect a significant outcome difference between the 2 groups. However, it is reflective of real-world clinical practice where imaging results are not the sole determinant of subsequent patient management.

Only patients randomized at sites participating in long-term follow-up were included in this analysis. This represented 392 of the original 430 patients. Randomization was stratified according to sites. Thus, site exclusion should not impact the balance from randomization, but this may have reduced the power to detect a difference in the primary outcome. The post hoc analysis, including adherent patients, demonstrated a significant outcome benefit. However, while we adjusted for a history of previous CABG, diabetes mellitus, age, and site,

Table 3. Kaplan–Meier Rates for Components of the Composite Clinical End Point

<table>
<thead>
<tr>
<th>Components of CCE as First Events*</th>
<th>Standard, N=195 (K-M rates)</th>
<th>PET, N=197 (K-M rates)</th>
<th>Adjusted HR</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac death</td>
<td>26 (20.89%)</td>
<td>23 (17.46%)</td>
<td>0.80 (0.45, 1.43)</td>
<td>0.46</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>8 (6.69%)</td>
<td>15 (11.84%)</td>
<td>1.67 (0.69, 4.01)</td>
<td>0.25</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>2 (1.04%)</td>
<td>5 (3.93%)</td>
<td>2.25 (0.43, 11.76)</td>
<td>0.34</td>
</tr>
<tr>
<td>Cardiac rehospitalization</td>
<td>75 (45.77%)</td>
<td>62 (39.01%)</td>
<td>0.70 (0.50, 0.99)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

CCE indicates composite clinical end point; HR, heart rate; K-M, Kaplan–Meier; and PET, positron emission tomography.
*Note that if an MI occurred before death, MI would be the first recorded event. Hence, cardiac death as the first event is not equivalent to total cardiac-related deaths.
there may be bias that was not accounted for, and so this result must be interpreted with caution.

The recommendation from the PET images was based on a simplified approach of low, moderate, or high likelihood of recovery, which does not fully account for the often complex interplay of scar, hibernation, and viable tissue, particularly in cases with complex cardiac anatomy, and therefore, some patients may have been misclassified. In particular, the extent of hibernating myocardium has been demonstrated to be a more robust indicator of potential benefit from revascularization than simply viability alone.

In this study, we did not account for the impact of other testing in addition to viability imaging, such as stress perfusion scanning. Ischemia has been shown to be a predictor of outcome, and the interpretation of the FDG PET viability scan is augmented by this additional information. This was not considered in this study.24

The design of this study did not allow for comparison of FDG PET with different viability imaging modalities, such as single photon emission computed tomography, dobutamine echocardiography, or cardiac magnetic resonance imaging. However, the ongoing IMAGE-HF studies (Imaging Modalities to Assist With Guiding Therapy and the Evaluation of Patients With Heart Failure) to evaluate the role and impact of imaging in the management of patients with heart failure includes the project AIMI-HF (Alternative Imaging Modalities in Ischemic Heart Failure), that is randomizing patients with LV dysfunction who are highly likely to have significant CAD to either standard imaging (single photon emission computed tomography) versus advanced imaging using PET or magnetic resonance imaging. This study will hopefully provide further useful information to guide management decisions in this complex patient population.

Conclusions
After 5 years of follow-up, the overall results of the PARR-2 study did not detect a statistically significant benefit for PET-assisted management compared with standard care. On post hoc analysis including only patients who adhered to the recommendation from the PET scan, there was a statistically significant decrease in adverse cardiac events at 5 years compared with the standard care arm. This is also similar to the 12-month data. This seems to suggest that PET viability imaging may be best used in cases where the recommendation is likely to be followed by the treating clinician and the patient. However, this post hoc finding should be interpreted with caution and tested in future studies.

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Disclosures
Drs Beanlands and deKemp are consultants with Jubilant DRAXImage(JDI) and have received grant funding from GE Healthcare, Nordion, Lantheus Medical Imaging(LMI), and JDI. Dr

Table 4. Multivariable Survival Model for Adherence Analysis

<table>
<thead>
<tr>
<th></th>
<th>Hazard Ratio(95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adhere</td>
<td>0.728 (0.537, 0.989)</td>
<td>0.042</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.359 (1.010, 1.829)</td>
<td>0.043</td>
</tr>
<tr>
<td>Age</td>
<td>1.007 (0.992, 1.022)</td>
<td>0.384</td>
</tr>
<tr>
<td>CABG</td>
<td>1.779 (1.244, 2.543)</td>
<td>0.002</td>
</tr>
<tr>
<td>Site*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>01</td>
<td>0.748 (0.362, 1.544)</td>
<td>0.432</td>
</tr>
<tr>
<td>02</td>
<td>0.561 (0.201, 1.565)</td>
<td>0.270</td>
</tr>
<tr>
<td>04</td>
<td>0.423 (0.170, 1.052)</td>
<td>0.064</td>
</tr>
<tr>
<td>05</td>
<td>0.684 (0.261, 1.793)</td>
<td>0.440</td>
</tr>
<tr>
<td>08</td>
<td>0.426 (0.126, 1.440)</td>
<td>0.170</td>
</tr>
</tbody>
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CABG indicates coronary artery bypass grafting; and CI, confidence interval.

*One site is the reference site; the other 5 sites are considered versus this site.
deKemp receives revenues from a Rubidium-82 generator technology licensed to JDI and from sales of FlowQuant. Dr. Beanlands is a consultant for LMI. The other authors report no conflicts.

Appendix: PARR-2 Investigators
The full list of participating sites and coordinators is noted in the 1-year follow-up publication. The 5-year follow-up site investigators and PET Core Lab investigators are noted below. A detailed list of participants is noted in the Appendix in the Data Supplement.

University of Ottawa Heart Institute: R. Beanlands, MD, L. Garrard, RN, A.A. Davies, MD, T. Ruddy, MD, B. Chow, MD, L. Duchesne, MD, H. Haddad, MD, P. Hendry, MD, R. Masters, MD, L. Higginson, MD, T. Mesana, MD, R. deKemp, PhD, J. DaSilva, PhD, H. Ukkonen, MD, PhD, K. Yoshinaga, MD, PhD, B. McArdle, MB, BCH, T. Shukla, MD, J. Renaud, MS, R. Klein, PhD, M. Aung, CNMT, London Health Sciences Centre; D. Humen, MD, W. Kostuk, MD, G. Wisenberg, MD, R.G. Wells, PhD. Montreal Heart Institute: N. Racine, MD, M. White, MD. University Health Network: H. Ross, MD, R.M. Iwanochko, MD, L. Mickelborough, MD. St. Michael’s Hospital: M. Freeman, MD, B. Abramson, MD, D. Latter, MD. Hamilton Health Sciences Centre: A. Lamy, E. Fallen, MD, G. Coates, MD, K. Gulenchyn, MD.

References
2. Bonow RO, Mann JJ,将此文本转换为英文，然后在该英文文本中搜索关键词“PARR-2 Investigators”并突出显示。
3. Bonow RO, Mann JJ, 将此文本转换为英文，然后在该英文文本中搜索关键词“PARR-2 Investigators”并突出显示。
Ischemic cardiomyopathy remains a significant cause of morbidity and mortality, despite advances in pharmacological and device therapy over the past 3 decades. There is a large body of predominantly observational data to demonstrate that restoration of blood flow to dysfunctional myocardium in the territory of a stenosed coronary artery is beneficial, but controversies remain regarding surgical revascularization, particularly in the absence of an acute coronary syndrome or limiting angina. Whether viability imaging can impact long-term patient outcomes is uncertain and has not been studied using a randomized controlled trial design. PARR-2 (Positron Emission Tomography and Recovery Following Revascularization) randomized patients with severe left ventricular dysfunction and suspected CAD being considered for revascularization or transplantation to standard care versus F-18-fluorodeoxyglucose positron emission tomography–assisted management. The 1-year outcome data of PARR-2 have been previously reported; 6 sites participated in long-term follow-up. After 5 years follow-up, F-18-fluorodeoxyglucose positron emission tomography-assisted management did not significantly reduce cardiac events compared with standard care. However, on post hoc analysis, when only patients who adhered to positron emission tomography recommendations (76%) were included, the hazard ratio for the time to the primary outcome was significant (0.73 [95% confidence interval 0.54–0.99; \( P = 0.042 \)). These findings are also similar to the 1-year PARR-2 data. This suggests that positron emission tomography viability imaging is most predictive of outcome benefit and best used in cases where the recommendation is likely to be used to guide a revascularization decision by the treating clinician. Future studies are still needed, given the post hoc nature of these findings. Some such trials are underway.
Long-Term Follow-Up of Outcomes With F-18-Fluorodeoxyglucose Positron Emission Tomography Imaging–Assisted Management of Patients With Severe Left Ventricular Dysfunction Secondary to Coronary Disease

Brian Mc Ardle, Tushar Shukla, Graham Nichol, Robert A. deKemp, Jordan Bernick, Ann Guo, Siok Ping Lim, Ross A. Davies, Haissam Haddad, Lloyd Duchesne, Paul Hendry, Roy Masters, Heather Ross, Michael Freeman, Karen Gulenchyn, Normand Racine, Dennis Humen, Francois Benard, Terrence D. Ruddy, Benjamin J. Chow, Lisa Mielniczuk, Jean N. DaSilva, Linda Garrard, George A. Wells, Rob S.B. Beanlands and the PARR-2 Investigators

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SUPPLEMENTAL MATERIAL

Appendix: PARR-2 Investigators:

The full list of participating sites and co-ordinators is noted in the 1 year follow-up publication. The 5 year follow-up sites are noted below:

Clinical Coordinating Center for 5 year follow-up data
University of Ottawa Heart Institute:
R. Beanlands, T. Ruddy, R. deKemp, B. Chow, R. A. Davies, J. DaSilva, L. Garrard (Supervising Coordinator), A. Guo, C. Kelly, Judy Etele, M. Aung.

Data Coordinating Center for 5 year follow-up data
University of Washington - Harborview Center for Prehospital Emergency Care, Seattle, WA and the Cardiovascular Research Methods Centre, University of Ottawa Heart Institute:

Clinical Events Committee
Chair: Fraser Rubens; Members: Donald Beanlands, Marino Labinaz of University of Ottawa Heart Institute.

PARR-2 Follow-up Participating Sites: (Investigators and Research Co-ordinators); *indicates 5 year follow-up sites


*London Health Sciences Centre - D. Humen M.D., W. Kostuk M.D., G. Wisenberg M.D., M. Humen R.N.


*University Health Network - H. Ross M.D., R.M. Iwanochko M.D., L. Mickleborough M.D., A. Cymet R.N.

*St. Michael’s Hospital - M. Freeman M.D., B. Abramson M.D., D. Latter M.D., S. Freeman R.N.

Sunnybrook and Women’s College Health Sciences Centre - P. Bogaty M.D., J. Rodes M.D., L. Roy M.D., L. Boyer R.N.

Hopital Laval/Quebec City - P. Bogaty M.D., J. Rodes M.D., L. Roy M.D., L. Boyer R.N.

Centre hospitalier universitaire de
Sherbrooke - F Bernard M.D., S. Lepage M.D., H. Brown R.N.

RNA Core Lab
Toronto Western Hospital R.M. Iwanochko M.D., M. Hussain M.D., R Burke C.N.M.T., J. Reaney N.M.T.

PET Centers

Centre hospitalier universitaire de Sherbrooke: F. Benard M.D., J Rijo.

