Preoperative Prediction of the Outcome of Coronary Revascularization Using Positron Emission Tomography

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Background. Previous assessments of myocardial viability using positron emission tomography (PET) relied on demonstration of glucose metabolism in hypoperfused asynergic segments using the glucose analogue $[^{18}F]$2-fluoro-2-deoxyglucose (FDG). Recently, it was shown that myocardial viability could be assessed by calculating the water-perfusable tissue index (PTI) for the asynergic region. PTI represents the proportion of the myocardium that is capable of rapid transsarcolemmal exchange of water and thus perfusible by water. The aim of the present study was to assess myocardial viability by PET using PTI in patients undergoing coronary revascularization.

Methods and Results. Twelve patients with chronic coronary artery disease and previous myocardial infarction were studied. Analysis of transmission (tissue density) and $^{18}$O-labeled carbon monoxide (blood pool), and $^{18}$O-labeled water (myocardial blood flow [MBF]) emission PET data enabled the simultaneous quantification of MBF (ml·min$^{-1}$·g perfusible tissue$^{-1}$) and PTI (gram of perfusible tissue per gram of total anatomic tissue). In addition, PET imaging with FDG after 75-g oral glucose load was performed in eight patients. Preoperative echocardiography identified 33 hypocontractile and 26 control segments. Follow-up echocardiography performed 3 to 5 months later demonstrated 26 of 33 segments with improved wall motion (recovery) and seven of 33 segments without improvement (nonrecovery). MBF in the control segments (0.97±0.22 ml·min$^{-1}$·g perfusible tissue$^{-1}$) was significantly higher ($p<0.001$) than in both the recovery (0.73±0.18 ml·min$^{-1}$·g perfusible tissue$^{-1}$) and the nonrecovery (0.45±0.11 ml·min$^{-1}$·g perfusible tissue$^{-1}$) segments. PTI in the recovery regions (0.99±0.15) was ≥0.7 in all cases and slightly less than in control regions (1.10±0.15, $p<0.02$). FDG uptake in these regions was 92±17% ($n=13$) of the uptake in control segments with normal wall motion. In the nonrecovery group, PTI was 0.62±0.06 ($p<0.02$ versus control and recovery) and always <0.7. In the one patient in whom a comparison with metabolic imaging was made, FDG uptake was 46% of the uptake in a reference region with normal wall motion.

Conclusions. These data showed that contractile recovery occurred only in segments where PTI was ≥0.7, suggesting that ≥70% of myocardial tissue in a given asynergic segment should be perfusible by water to enable contractile recovery. There was good agreement between the PTI and FDG methods for predicting improvements in regional wall motion after revascularization. Although further studies should be performed in a larger patient group, the preliminary results are promising and suggest that PTI may be a good predictor of contractile recovery after coronary revascularization. (Circulation 1992;86:1738–1742)

Key Words • perfusible tissue index • positron emission tomography • myocardial viability • myocardial blood flow

Noninvasive preoperative prediction of an improvement in myocardial contractility after coronary revascularization would be of benefit in the management of patients with chronic ischemic coronary artery disease. A number of techniques have been developed for the detection of reversibly injured myocardium in such patients, in particular, reinjection of $^{99m}$Tc imaged with single-photon emission computed tomography (SPECT)$^{1,2}$ and positron emission tomography (PET).$^{3-5}$ Previously, assessment of myocardial viability using PET depended on the demonstration of sustained glucose metabolism in hypoperfused asynergic segments using the radiolabeled glucose analogue $[^{18}F]$2-fluoro-2-deoxyglucose (FDG)$^{3,4}$

It has recently been shown in patients who were successfully thrombolysed for an acute myocardial in-
This technique to preoperative assessment of myocardial viability in patients undergoing revascularization by either percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass graft surgery (CABG).

**Methods**

Twelve patients with chronic coronary artery disease and previous myocardial infarction who were due to undergo revascularization by PTCA or CABG were studied. Patient profiles are summarized in Table 1. From 3 to 6 days before revascularization, both PET scans and two-dimensional echocardiograms were recorded on the same day. Follow-up echocardiography was performed 3–5 months later to assess improvement in systolic function in the revascularized territory. All patients gave written informed consent to a protocol approved by the Hammersmith Hospital Research Ethics Committee and the United Kingdom Administration of Radioactive Substances Advisory Committee.

PET imaging was performed using an ECAT 931/08-12 tomograph (CTI/Siemens Inc., Knoxville, Tenn.), which allows data to be recorded from 15 parallel planes in an axial field of view of 10.5 cm. The scanning protocol was the same as that previously reported. Briefly, after placing the patient in the optimal imaging position, a transmission scan was performed by exposure of an external 67Ga ring source. The transmission scans are equivalent to low-resolution computed tomography scans and provide images of tissue density. The cardiac blood pool was then imaged after inhalation of 13O (150, 2.1 minutes). Venous blood samples were taken every minute during the 6-minute scan, and the 13O concentration in whole blood was measured using a NaI well-counter that was cross-calibrated with the scanner. After a 15-minute period to allow for decay of 15O radioactivity to background levels, MBF was measured by a previously validated protocol using 15O2, which was administered by 13O gas inhalation.

Metabolic imaging was performed in eight of 12 patients with FDG (150, 110 minutes). Study conditions were standardized by giving patients 75 g glucose orally, 90 minutes before the administration of FDG. FDG (185 MBq) was infused intravenously over 2 minutes, and one 10-minute data acquisition was performed 55 minutes after the end of tracer administration.

Two-dimensional echocardiography was performed using Toshiba SSH 65A and 160A ultrasound equipment and a 3.75-MHz transducer. Imaging was performed according to a standardized protocol. Regional wall motion was assessed from parasternal short-axis views and graded as normal, hypokinetic, akinetic, or dyskinetic. All echocardiographic analyses were performed by an investigator who was blinded to the results of the PET study.

Myocardial regions of interest (ROIs) were positioned on the PET images in areas that corresponded to hypocontractile and normally contracting segments identified on the echocardiograms. ROIs drawn on the transaxial PET images were matched with the regions on the short-axis echocardiographic images by using for guidance anatomic landmarks such as the papillary muscles and the junction of the right ventricular and the left ventricular wall. Values of MBF (ml/min · g perfusable tissue−1) and PTI (gram of perfusable tissue per...
TABLE 1. Patient Profiles Before and After Revascularization

<table>
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<tr>
<th>Age (years)</th>
<th>Sex</th>
<th>Preoperative CAG</th>
<th>Collaterals</th>
<th>Previous MI</th>
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CAG, coronary angiography; MI, myocardial infarction; LAD, left anterior descending coronary artery; LCx, left circumflex artery; RCA, right coronary artery; A, anterior; L, lateral; I, inferior; S, septal; PTCA, percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass graft surgery.

The recovery group consisted of seven akinetic and 15 hypokinetic segments that resumed fully normal contractile function in addition to four akinetic segments that became hypokinetic after surgery.

The mean value of MBF in control segments was 0.97±0.22 ml·min⁻¹·g perfusible tissue⁻¹ and was significantly higher than the values in the recovery (0.73±0.18, p<0.001) and nonrecovery (0.45±0.11, p<0.001) groups, respectively (Figure 2A).

The values of PTI in the recovery group were slightly reduced compared with those in the control segments (0.99±0.15 versus 1.10±0.15 g perfusible tissue/g total anatomic tissue, p=0.013). The value of PTI in each recovery segment was always ≥0.7 g perfusible tissue/g total anatomic tissue. FDG uptake in these segments was 92±17% (n=13) of the uptake in the corresponding control regions. However, PTI in the nonrecovery regions (0.62±0.06 g perfusible tissue/g total anatomic tissue) was significantly lower (p<0.02) than in both recovery and control segments (Figure 2B). In the one nonrecovery segment in which direct comparison of the FDG and PTI data was possible, there was a significant reduction (54%) in FDG uptake relative to the control region.

gram of total anatomic tissue) in these regions were calculated as previously described.6,7 In the cases where metabolic imaging was performed, the pixel counts on the FDG image were calculated in the same ROIs that were used for calculation of PTI and then expressed as a ratio of the activity in a normally contracting region. Asynergic myocardium was considered viable if it had an FDG uptake that was >50% of the uptake in a normally contracting region, as previously reported by Bonow et al.2

All data are presented as mean±SD. Comparison of multiple data sets was performed using a one-way ANOVA, and p<0.05 was considered statistically significant. Specific differences were identified by either a paired or unpaired Student’s t test corrected for multiple comparisons with the Bonferroni inequality adjustment.9

Results

On the preoperative echocardiograms, 17 akinetic, 16 hypokinetic, and 26 normally contracting control segments were identified. Of the 33 segments exhibiting wall motion abnormalities, 26 improved contractile function after surgery (recovery group), and seven segments showed no change (nonrecovery group). The
In this study, preliminary findings have been reported with the use of a new method to assess after surgery the presence of viable myocardium in patients undergoing coronary revascularization. It has been shown that improvement of myocardial contractility can be successfully predicted by calculating the PTI from transmission (tissue density) and C\textsuperscript{15}O (blood pool) and H\textsubscript{2}\textsuperscript{18}O (MBF) emission PET data sets. The findings are consistent with the hypothesis that the ability to exchange water rapidly from arterial blood into the myocyte across the sarcolemma is a property of viable myocardium. In addition to providing information on tissue viability, this method enables the simultaneous quantification of MBF.

Despite recent reports that have demonstrated a disproportionately high FDG uptake in myocardial regions that either are functionally compromised\textsuperscript{10} or contain significant fibrosis,\textsuperscript{11-13} there is considerable evidence to suggest that PET imaging with FDG can be used successfully to assess myocardial viability.\textsuperscript{2-5,14} Detection of myocardial viability using FDG relies on the demonstration of uptake of this tracer in hypoperfused asynergic segments, which is suggestive of sustained metabolic activity in these regions. In this study, the prediction of the reversal of wall motion abnormalities after revascularization using PTI was compared with the FDG technique in eight of 12 patients. In myocardial regions where PTI was preserved (i.e., \(\geq 0.7\)) and there was an improvement in regional wall motion after revascularization, FDG uptake was \(> 50%\) of that in a normally contracting reference region, which is indicative of viable myocardium.\textsuperscript{2} Similarly, in the one segment where FDG uptake was reduced to \(< 50%\) of the control territory, PTI was \(< 0.7\). Although these data are derived from a small number of patients, the preliminary observations suggest a good concordance between the two methods for assessing tissue viability.

PTI is defined as the proportion of the myocardial tissue within a given region of interest that is capable of rapidly exchanging water and therefore is perfusible by water. In normal myocardium, this ratio is close to the theoretically predicted value of unity, as all the myocardium is capable of rapidly exchanging water,\textsuperscript{15} whereas in patients with old myocardial infarctions, PTI was shown to decrease due to a fall in the mass of perfusable tissue (PTF in Figure 1).\textsuperscript{6,12} This could be explained by the presence of necrotic scar tissue in the infarcted zone, which could not exchange water rapidly and thus was nonperfusible tissue. In this study, it was observed that regional wall motion improved in asynergic segments only when PTI \(\geq 0.7\). These observations are entirely consistent with previous findings using this technique in patients who were successfully thrombolyzed for an acute myocardial infarction.\textsuperscript{6} These data indicate that for myocardial contractility to improve, \(\geq 70\%\) of the myocardial tissue within a functionally compromised segment should be perfusible by water (i.e., PTI \(\geq 0.7\)). The identification of a threshold value of PTI that is necessary for improvement in regional wall motion makes data interpretation significantly easier using PTI than when using the FDG technique. In addition, the findings of this study are consistent with the idea that the ability to rapidly exchange water across the sarcolemma is a property of viable myocardium. This concept may be extended to other modalities such as magnetic resonance imaging using deuterium oxide (D\textsubscript{2}O)\textsuperscript{16,17} for assessing myocardial viability. Although these data appear to be very promising, studies in a larger group of patients should be performed to confirm the validity of this technique.

Because H\textsubscript{2}\textsuperscript{18}O is a freely diffusible tracer that instantaneously equilibrates between arterial blood and myocardial tissue, the concentration of H\textsubscript{2}\textsuperscript{18}O in venous blood will be the same as in myocardium. Therefore, in the calculation of perfusable tissue fraction, only the H\textsubscript{2}\textsuperscript{18}O activity in arterial blood is corrected because the tracer concentration in myocardial tissue and venous blood cannot be distinguished.\textsuperscript{18} However, in the calculation of anatomic tissue fraction, the C\textsuperscript{15}O scan labels the arterial and venous circulations equally; hence, a larger blood pool correction is performed in extracting the tissue signal from the transmission scan compared with the extraction of the tissue signal in the kinetic analysis of the H\textsubscript{2}\textsuperscript{18}O data.\textsuperscript{15} Therefore, PTI, which is calculated as the ratio of perfusable tissue fraction to anatomic tissue fraction, is 1.1 in normal myocardium and is consistent with previous experimental data demonstrating that the venous vasculature represents approximately 10% of the total myocardial volume.\textsuperscript{19} In
this study, it was observed that in some regions, the values of PTI were >1.1. These regions predominantly were positioned in the interventricular septum. In the present study, H$_2^{15}$O was administered by inhalation of C$^{15}$O$_2$ gas. The blood in the right ventricular chamber is mixed venous; therefore, the concentration of H$_2^{15}$O is the same as in myocardial tissue. As a result, the measurement of perfusible tissue fraction in the septum is overestimated due to spillover of radioactive signal from the right ventricular blood pool into the tissue ROI due to the limited spatial resolution of the PET camera. This results in overestimation of PTI in septal regions. This phenomenon can be overcome by adopting an intravenous H$_2^{15}$O infusion protocol as an alternative to the C$^{15}$O$_2$ gas inhalation technique. In this situation, the concentrations of H$_2^{15}$O in both the right and left ventricles would be virtually identical, and the spillover from the chambers into the septal region would be adequately corrected by the kinetic model used in this study to analyze the H$_2^{15}$O data.

It was observed that values of MBF in both the recovery and nonrecovery groups were significantly lower than in control regions. In addition, MBF in the nonrecovery regions was significantly lower than in segments that recovered. Although this suggests that measurement of MBF alone should be sufficient for distinguishing viable from necrotic myocardium, this is not the case due to the significant overlap in the MBF values between recovery and nonrecovery regions (Figure 2A). There was no overlap in the PTI values between regions that did and those that did not subsequently improve contractile function after revascularization. Further evidence in support of the inadequacy of MBF measurement alone to assess tissue viability is provided from research that showed that in patients who were successfully thrombolysed for an acute myocardial infarction, there was no significant difference between the MBF values in regions that did and those that did not subsequently improve regional wall motion.

The use of PTI to assess myocardial viability has several practical advantages. First, the identification of a threshold value of PTI for predicting an improvement in regional wall motion makes data interpretation using this technique simple and direct. Second, scanning time, the radiation dose administered to the patient, and the cost of the imaging procedure are all less than with the FDG imaging approach. The advent of relatively inexpensive equipment dedicated to the production of radiotracers labeled with $^{15}$O may make this method more amenable to clinical centers.

In summary, it has been shown that the functional outcome of coronary revascularization may be accurately predicted by calculation of PTI. These findings support the hypothesis that the ability to exchange water rapidly across the sarcolemma is a property of viable myocardium and further suggest that $\geq 70\%$ of the tissue within a hypocontractile zone should be viable to enable improvement in contractile function. This approach provides further evidence to suggest that myocardial viability may be assessed by PET without metabolic imaging.

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References

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