Can Nitrogen-13 Ammonia Kinetic Modeling Define Myocardial Viability Independent of Fluorine-18 Fluorodeoxyglucose?

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Objectives. The hypothesis of this study was that evaluation of myocardial flow and metabolism using nitrogen-13 (N-13) ammonia kinetic modeling with dynamic positron emission tomographic (PET) imaging could identify regions of myocardial scar and viable myocardium as defined by fluorine-18 fluorodeoxyglucose (F-18 FDG) PET.

Background. Uptake of most perfusion tracers depends on both perfusion and metabolic retention in tissue. This characteristic has limited their ability to differentiate myocardial scar from viable tissue. The kinetic modeling of N-13 ammonia permits quantification of blood flow and separation of the metabolic component of its uptake, which may permit differentiation of scar from viable tissue.

Methods. Sixteen patients, >3 months after myocardial infarction, underwent dynamic N-13 ammonia and F-18 FDG PET imaging. Regions of reduced and normal perfusion were defined on static N-13 ammonia images. Patients were classified into two groups (group I [ischemic viable], n = 6; group II [scar], n = 10) on the basis of percent of maximal F-18 FDG uptake in hypoperfused segments. Nitrogen-13 ammonia kinetic modeling was applied to dynamic PET data, and rate constants were determined. Flow was defined by K_1; volume of distribution (VD = K_1/k_2) of N-13 ammonia was used as an indirect indication of metabolic retention.

Results. Fluorine-18 FDG uptake was reduced in patients with scar compared with normal patients with ischemic viable zones (ischemic viable 93 ± 27% [mean ± SD]; scar 37 ± 16%, p ≤ 0.01). Using N-13 ammonia kinetic modeling, flow and VD were reduced in the hypoperfused regions of patients with scar (ischemic viable flow: 0.65 ± 0.20 ml/min per g; scar: 0.36 ± 0.16 ml/min per g, p ≤ 0.01; VD: 3.9 ± 1.3 and 2.0 ± 1.07 ml/g, respectively, p ≤ 0.01). For detection of viable myocardium in these patients, the sensitivity and specificity were 100% and 80% for N-13 ammonia PET flow >0.45 ml/min per g; 100% and 70% for VD >2.0 ml/g; and 100% and 90% for both flow > 0.45 ml/min per g and VD > 2.0 ml/g, respectively. The positive and negative predictive values for the latter approach were 86% and 100%, respectively.

Conclusions. In this cohort, patients having regions with flow ≤0.45 ml/min per g or VD ≤ 2.0 ml/g had scar. Viable myocardium had both flow >0.45 ml/min per g and VD > 2.0 ml/g. Nitrogen-13 ammonia kinetic modeling permits determination of blood flow and metabolic integrity in patients with previous myocardial infarction and can help differentiate between scar and ischemic but viable myocardium.

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Ischemic but viable myocardium has potential for recovery, whereas nonviable myocardium (scar) does not. Hence, defining viable myocardium is critical in predicting recovery of

function after revascularization. The accuracy of static imaging with positron emission tomography (PET) using a flow tracer (nitrogen-13 [N-13] ammonia or rubidium-82 [Rb-82]) and a metabolic agent (usually, fluorine-18 fluorodeoxyglucose [F-18 FDG]) for defining ischemic but viable myocardium has been well demonstrated in a number of studies (1–3). These studies suggest that prediction of viability requires assessment of both flow and metabolic integrity. More recently, Gewirtz et al. (4) showed that blood flow determined by N-13 ammonia kinetics may predict viability. In contrast, data from vom Dahl et al. (3) indicated that assessment of perfusion alone was insufficient and that the reliability of any viability data depends on the evaluation of metabolism in relation to perfusion.

The uptake of most perfusion radiotracers depends both on delivery (flow) and retention in the tissue (metabolic component). These two factors typically cannot be separated by static imaging approaches. Nitrogen-13 ammonia is one agent whose

kinetics depend on both flow and myocardial metabolism. Recently, modeling approaches have been used to separate flow from the metabolic component of N-13 ammonia uptake (5–7). These and similar approaches have been applied for flow quantification (5–11). However, because N-13 ammonia is metabolized by the myocardium, its kinetics could also be used as a reflection of metabolic integrity.

The hypothesis of the present study was that evaluation of myocardial flow and metabolism using the N-13 ammonia kinetic modeling approach (6) could identify myocardial scar as defined by F-18 FDG PET.

Methods

Patients. Sixteen male patients between 45 and 68 years old with a previous myocardial infarction were studied >3 months after infarction (non-Q wave in 2, Q wave in 14). One patient had previous coronary artery bypass graft surgery, and two had non–insulin-dependent diabetes mellitus.

Positron emission tomography. After an overnight fast, each patient received a 50-g oral glucose load. Dynamic PET imaging was performed using the ECAT 953/31 (Siemens/CTI) at McMaster University Medical Centre. This scanner has an axial field of view of 10.8 cm and a spatial resolution of 6-mm full width half maximum in all three dimensions. A total of 31 planes were reconstructed for each time frame using a Hann filter with a cutoff frequency of 0.5 cycles/pixel. A 30-min transmission scan using a germanium-68 ring source was obtained before each study, to correct for attenuation.

The scan protocol consisted of a 24-min dynamic scan (12 × 5 s, 4 × 20 s, 2 × 60 s, 1 × 1,200 s) started simultaneously with a bolus injection of 12 to 16 mCi of N-13 ammonia. After the N-13 ammonia scan, subjects received an injection of 8 to 10 mCi of F-18 FDG. A static image of FDG uptake was acquired 45 min after injection.

Region selection. Regions of interest were defined over the left ventricular myocardium with 1) visually apparent reduced N-13 ammonia uptake in the known or suspected territory of previous infarction; and 2) contralateral zones with normal uptake. Regions were defined in a given transaxial plane on the last frame of the N-13 ammonia sequence. The regions were large and contained 100 ± 20 2 × 2-mm pixels. Region placement was similar to previously described approaches (6,7,12). The regions of interest were applied to the corresponding images in the dynamic sequence, and myocardial time-activity curves were generated. A region of interest over the left ventricular cavity was also defined, and the time-

activity curve used as the arterial input function [$C_a(t)$] (Fig. 1). To define F-18 FDG uptake, the myocardial regions of interest from the N-13 ammonia images were applied to the corresponding transaxial plane of the static F-18 FDG image.

Tracer kinetic modeling. Myocardial blood flow was estimated using a two-compartment model (one vascular compartment and one extravascular compartment) with two rate constants fit to the time-activity N-13 ammonia data. Under rest conditions, the time-activity curves are adequately described by this model configuration, and the two rate constants have been shown to represent 1) the N-13 ammonia uptake rate (K_1 = Flow × Extraction [ml/min per g]); and 2) the N-13 ammonia washout rate (k_2 [min^{-1}]) (6). Under rest conditions, the initial extraction fraction for N-13 ammonia approaches 100% (5); thus, K_1 estimates flow (6,7).

The *volume of distribution* (VD) of the extravascular compartment was used as an indirect indicator of the metabolic retention of N-13 ammonia and is expressed as the uptake rate constant K_1 (ml/min per g) over the washout rate constant k_2 (min^{-1}): VD = K_1/k_2 (ml/g). The metabolic retention of N-13 ammonia (in the form of N-13 glutamine) decreases the apparent washout rate (k_2), thereby increasing the volume of distribution of the extravascular compartment (6). Thus, a high volume of distribution (K_1/k_2) indirectly reflects retention of N-13 ammonia activity and implies intact N-13 ammonia metabolism. A low volume of distribution is consistent with decreased N-13 ammonia retention, which may reflect decreased myocardial N-13 ammonia metabolism or greater washout of N-13, or both, as may occur in scar tissue.

The regional concentration of N-13 ammonia, $C_{meas}(t)$ (nCi/ml), is measured by the PET scanner and includes both tissue and blood activity. The time course of radioactivity was decay corrected to the middle time of each frame. The arterial blood pool concentration, $C_a(t)$ (nCi/ml), measured in the left ventricular cavity, was used as the arterial input function. The predicted myocardial concentration, $C_p(t)$, is given as follows:
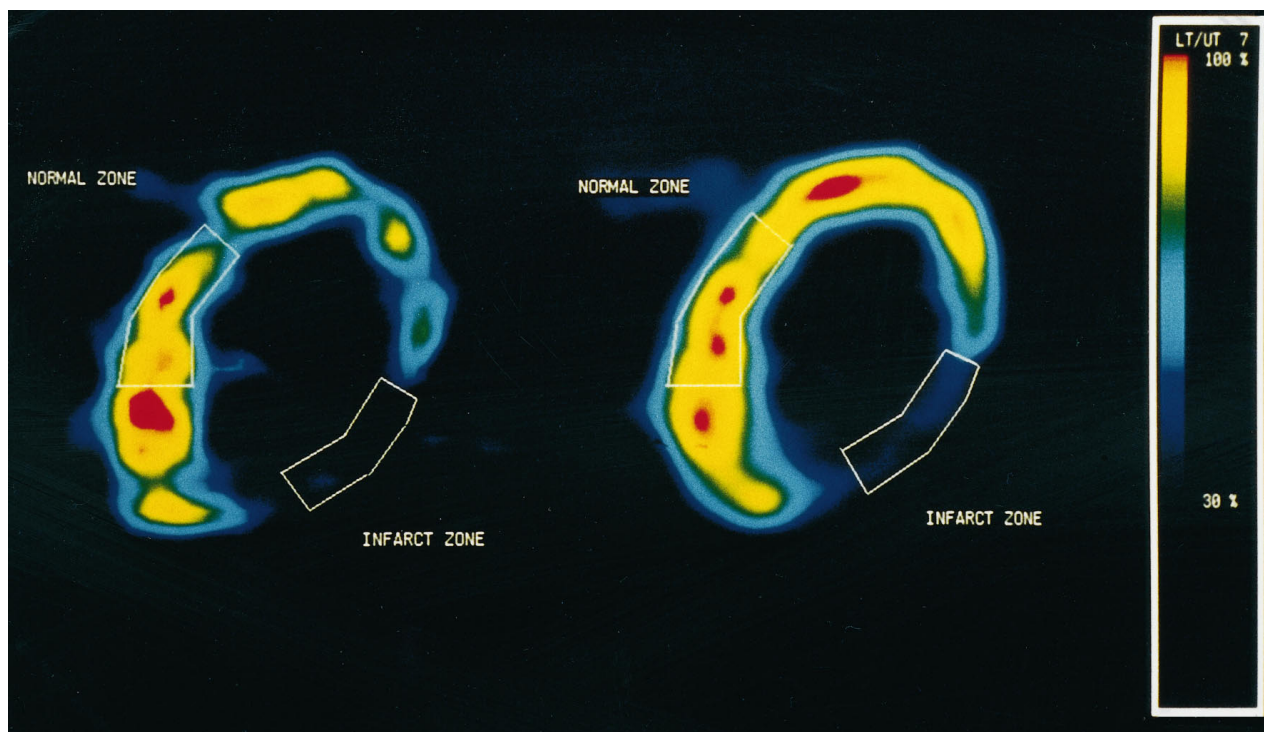
$$C_p(t) = C_a(t) \otimes K_1 e^{-k_2 t} \qquad [1]$$

The modeled regional concentration of N-13 ammonia, $C_{mod}(t)$, is then given by

$$C_{mod}(t) = F_a C_a(t) + (1 - F_a)C_p(t) \qquad [2]$$

and includes a correction for the blood volume fraction (F_a) in the myocardial region. This fraction comprises both the vascular component and blood spillover within the myocardial region and, in addition, accounts for partial volume effect (6). The model parameters (K_1, k_2, F_a) are estimated by minimizing the weighted residual sums of squares between $C_{meas}(t)$ and $C_{mod}(t)$. The residual sums of squares are weighted by the scan time of each frame. The minimization is implemented using the simplex method (MATLAB, Mathworks).

Statistical analysis. Patients were classified into two groups on the basis of F-18 FDG data in the abnormal region: group I (ischemic viable, n = 6) and group II (scar, n = 10). *Viable myocardium* was defined as a region having >60% of

Figure 1. Distribution of myocardial radioactivity at the last time frame of the N-13 ammonia acquisition **(left)** and the static F-18 FDG images **(right)**. Images are at the same level. Myocardial regions of interest were defined over the "infarct zone" (the zone with most reduced perfusion corresponding to the known inferolateral infarct) and the "normal zone" on the N-13 ammonia image. The myocardial regions of interest were applied to the F-18 FDG scan for definition of viability. In this example, there is a severe matched perfusion/F-18 FDG defect that, by F-18 FDG criteria, was scar.

peak normal zone F-18 FDG activity, as previously described (13).

Myocardial blood flow (K_1), N-13 ammonia washout (k_2), volume of distribution (VD = K_1/k_2) and F-18 FDG uptake were compared between the two patient groups by unpaired *t* testing. Abnormal segments were compared with normal segments within the same group by paired Student *t* testing (p < 0.02 was considered significant to account for multiple comparisons). Using the model for N-13 ammonia kinetics, the accuracy for defining viability in a given patient using different N-13 ammonia parameters, was determined by 1) K_1 (flow); 2) VD; and 3) combined K_1 and VD. Receiver operating characteristic curve analysis was used to determine the optimal cutoff for methods 1 and 2. (i.e., K_1 > 0.45 ml/min per g; VD >2.0 ml/g). For the combined approach, both K_1 > 0.45 ml/g per min and VD >0.2 ml/g were considered to define viability.

Results

Fluorine-18 FDG uptake. Among the 16 patients, 6 had ischemic but viable zones (group 1), and 10 had scar (group II) (Table 1). As expected, relative F-18 FDG uptake (percent of peak normal myocardial activity) in group I abnormal zones was significantly higher than that in group II (ischemic viable [mean ± SD] 93 ± 27%, scar 37 ± 16%, p ≤ 0.01). Of interest in group I, the relative F-18 FDG activity in the ischemic but viable zones showed a trend to be higher than the corresponding normal zones, consistent with tendency to increased glucose utilization in ischemic but viable tissue.

Myocardial blood flow (K_1). Flow was greater in the abnormal regions of patients with ischemic viable myocardium than in those with scar (ischemic viable 0.65 ± 0.20 ml/min per g, scar 0.36 ± 0.16 ml/min per g, p < 0.01) (Table 1).

Nitrogen-13 ammonia washout rate (k_2). No statistically significant difference was observed between ischemic viable and scar patient groups (0.20 ± 0.12 vs. 0.21 ± 0.10 min^{-1}); however, in both groups washout (k_2) showed a trend to be higher in the abnormal zones than their respective normal zones.

Volume of distribution. Volume of distribution was significantly greater in the ischemic viable group than the scar group (ischemic viable 3.9 ± 1.3 ml/g, scar 2.03 ± 1.07 ml/g, p < 0.01).

Viability detection. Among the abnormal regions of patients with F-18 FDG–defined scar, 8 (80%) of 10 had flow ≤0.45 ml/min per g; 7 (70%) of 10 had VD ≤2.0 ml/g; and 9 (90%) of 10 had either flow ≤0.45 ml/min per g or VD ≤2.0 ml/g. However, all regions with either flow ≤0.45 ml/min per g or VD ≤2.0 ml/g were scar by FDG. Consequently, the sensitivity and specificity for detecting F-18 FDG–viable myocardium in infarct zones for flow >0.45 ml/min per g were 100% and 80%; for VD >2.0 ml/g were 100% and 70%; and

Table 1. Regional Fluorine-18 Fluorodeoxyglucose Uptake and Nitrogen-13 Ammonia–Determined Flow, Washout and Volume of Distribution

Pt No.	F-18 FDG Uptake Region Mean/Myoc Peak (%) N	D	Flow (K_1) (ml/min per g) N	D	NH_3 Washout Rate (k_2) (min^{-1}) N	D	NH_3 Volume of Distribution (ml/g) N	D
				Group I: Ischemic Viable				
1	82	85	1.02	0.93	0.11	0.19	9.27	4.89
2	71	145	0.95	0.50	0.12	0.11	7.92	4.55
3	76	82	0.83	0.86	0.29	0.42	2.85	2.06
4	78	67	0.74	0.46	0.08	0.09	9.25	5.11
5	76	93	0.62	0.56	0.09	0.13	6.89	4.31
6	71	84	0.64	0.58	0.15	0.24	4.27	2.42
Mean	76	93	0.80	0.65	0.14	0.20	6.74	3.89*
SD	4	27	0.16	0.20	0.08	0.12	2.66	1.31
				Group II: Scar				
7	81	11	1.00	0.32	0.15	0.42	6.67	0.76
8	82	40	0.87	0.35	0.25	0.18	3.48	1.94
9	81	42	1.06	0.35	0.13	0.13	8.15	2.69
10	75	39	0.55	0.19	0.22	0.15	2.50	1.27
11	68	29	1.06	0.24	0.18	0.27	5.89	0.89
12	77	25	0.73	0.24	0.22	0.17	3.32	1.41
13	83	20	0.69	0.59	0.10	0.15	6.90	3.93
14	83	52	0.80	0.36	0.17	0.19	4.71	1.89
15	70	57	0.66	0.68	0.18	0.35	3.67	1.94
16	83	59	0.55	0.32	0.06	0.09	9.17	3.56
Mean	78	37†	0.80	0.36†	0.17	0.21	5.44	2.03†
SD	6	16	0.19	0.16	0.06	0.10	2.25	1.07

*$p \leq 0.01$ versus corresponding normal zone. †$p \leq 0.01$ versus group I and versus corresponding normal zone. D = defect zone; FDG = fluorine-18 fluorodeoxyglucose; Myoc = myocardium; N = normal zone; NH_3 = nitrogen-13 ammonia; Pt = patient.

for both flow >0.45 ml/min per g and VD >2.0 ml/g were 100% and 90%, respectively (Table 2).

The positive predictive value of flow criteria alone for defining F-18 FDG–viable tissue in patients with a zone of reduced perfusion was 75%, with a negative predictive value of 100% (all regions defined as scar by N-13 ammonia were scar by F-18 FDG). The positive predictive value for VD alone was 67%, with a negative predictive value of 100%. For the combined approach, positive predictive value increased to 86%, with a negative predictive value of 100%.

Fluorine-18 FDG uptake versus flow. To better understand how N-13 ammonia kinetics can predict F-18 FDG–defined

Table 2. Accuracy of Nitrogen-13 Ammonia Kinetic Methods for Predicting Viability Defined by Fluorine-18 Fluorodeoxyglucose in Abnormal Regions of 16 Patients

	Method		
	Flow (>0.45 ml/min per g)	VD (>2.0 ml/g)	Flow + VD*
Sensitivity	100%	100%	100%
Specificity	80%	70%	90%
Positive predictive value	75%	67%	86%
Negative predictive value	100%	100%	100%

*Flow > 0.45 ml/min per g and VD >2.0 ml/g. VD = volume of distribution.

viability, the relation between F-18 FDG activity and parameters of N-13 ammonia kinetics are displayed in Figure 2. Figures 2 and 3 show relative F-18 FDG uptake versus flow (K_1 of the N-13 ammonia kinetics model). Of note, all regions with flow <0.45 ml/min per g were F-18 FDG scar. One patient had very high F-18 FDG activity but borderline flow. The volume of distribution of N-13 ammonia in this region was also well within the normal range.

There were two patients with a region of F-18 FDG–defined scar but flow >0.45 ml/min per g. One patient had normal coronary anatomy with a large anterior wall myocardial infarction due to vasospasm (Patient 15). Volume of distribution was also <2.0 ml/g, consistent with infarction in this region. The second patient (Patient 13) had reduced F-18 FDG uptake but only mildly reduced flow and a volume of distribution >2.0 ml/g.

Discussion

In this study, regions with myocardial scar had reduced flow and a reduced N-13 ammonia volume of distribution. In addition, all the infarct zones with flow ≤0.45 ml/min per g and all the segments with volume of distribution for N-13 ammonia ≤2.0 ml/g were scar. These data support the hypothesis that
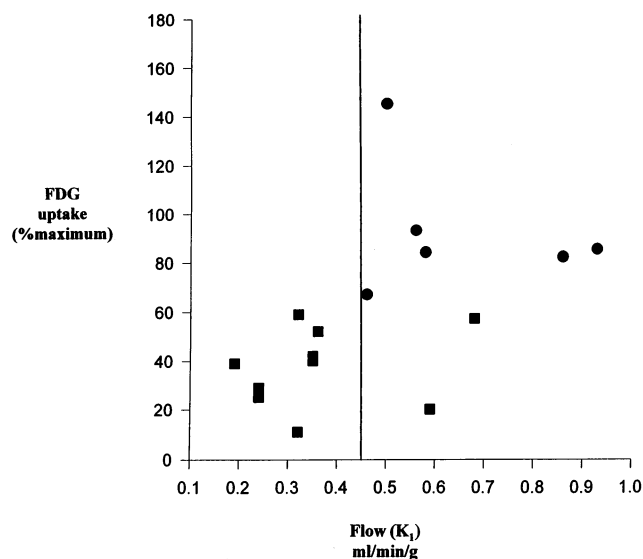
Figure 2. Relative FDG uptake versus K_1 for the abnormal regions in the 16 patients; cutoff is drawn at 0.45 ml/min per g. **Squares** = scar regions by FDG; **circles** = viable regions by FDG. Note two regions with reduced FDG but flow >0.45 ml/g (see text for further details).

N-13 ammonia kinetic modeling can be used to define myocardial scar. With this approach, the volume distribution data complement flow data. This allows the determination of both flow and metabolic integrity of the myocardium—a necessity for defining myocardial viability (3)—using a single radiotracer.

Nitrogen-13 ammonia kinetics and myocardial blood flow. The accuracy of N-13 ammonia kinetic modeling with PET for the determination of myocardial blood flow is well established (5–8). We applied the two-compartment model described by Hutchins et al. (6), who noted that a two-compartment model approach is adequate for quantification of myocardial blood flow at rest and that a third compartment is only necessary when states of high flow are induced. Because we studied our patients at rest, we selected the simpler approach, reducing the likelihood for errors in parameter determination. This approach also simplified the calculation for volume of distribution to a ratio of K_1/k_2. The myocardial blood flow measurements in normal segments of the current study (0.80 ± 0.18 ml/min per g) are comparable to blood flow measurements in normal myocardium from previous studies (4,6,8,9,14,15).

Metabolism and retention of N-13 ammonia. As with other myocardial perfusion radiotracers, it is the retention of N-13 ammonia that permits visualization of the myocardium on static imaging. Nitrogen-13 ammonia is delivered to myocardial tissue in relation to blood flow. However, in the myocyte, N-13 ammonia is converted to N-13 glutamine through the glutamine synthetase reaction (5,16–18). Nitrogen-13 glutamine becomes essentially trapped in the myocardium (5,17–19). However, metabolic changes, including pH, ischemia, hypoxia, temperature change and L-methiamine solfoximine (glutamine synthetase inhibitor) (5,16–18) can alter the myo-

cardial retention of N-13 ammonia. Reduced retention may be the result of changes in membrane permeability that occur with loss of cellular integrity in irreversibly injured cells. This could lead to the washout of N-13 ammonia or N-13 glutamine, which otherwise would have been retained. Alternatively, the replacement of necrotic myocytes by fibrosis would preclude the retention of N-13 ammonia.

The volume of distribution of N-13 ammonia represents the extent to which ammonia is taken up in the myocardial tissue. It is a function of both the delivery and washout of N-13 activity. If the uptake of N-13 ammonia depended only on flow, then the relation between K_1 and k_2 would be relatively fixed and the volume of distribution constant (as flow decreased, washout would decrease). However, as demonstrated in this study, washout did not decrease with reduction in flow; k_2 is the denominator for the volume of distribution, and its increase will lead to reduction in the extent of N-13 ammonia uptake. In the current study, a low volume of distribution (<2.0 ml/g) was highly predictive of myocardial scar.

The volume of distribution measurement in this study assumed that a two-compartment model describes N-13 ammonia kinetics at rest, as shown by Hutchins et al. (6). As noted earlier, this is a simpler approach than the three-compartment model because the number of parameters to solve is reduced. However, k_2 incorporates both clearance of N-13 and metabolic retention. This does not permit determination of the level of the derangement in N-13 ammonia metabolism, which occurs in myocardial scar, that might be achieved with more complex models. This may in part explain the lack of statistically significant differences in k_2 between scar and other tissue. However, the simpler two-compartment model does yield useful parameters of flow (K_1) and an indirect indicator of metabolism (volume of distribution).

Detection of myocardial viability with N-13 ammonia kinetics: comparison with previous studies. Evaluation of N-13 ammonia kinetic modeling for detection of myocardial viability has been limited. A range of N-13 ammonia uptake measurements with unpredictable patterns of F-18 FDG uptake was initially suggested by Schelbert (20). However, this work did not report myocardial blood flow quantification. vom Dahl et al. (3) suggested that perfusion imaging alone could not be used for detection of viability. However, these investigators also did not quantify myocardial blood flow or VD.

Gewirtz et al. (4) evaluated 22 infarct zones using a three-compartment kinetic model to quantify blood flow. However, the relation between k_2 and K_1 was fixed, and a third rate constant (k_3) was solved. In contrast, the current study applied a two-compartment model and solved for K_1 and k_2 without fixing their relation. Gewirtz et al. noted that myocardial blood flow <0.25 ml/min per g predicted myocardial scar, and flows >0.39 ml/min per g suggested viable myocardium on the basis of wall motion analysis. However, there was an overlap range between these two cutoffs. In the current study, a combined approach, considering both volume of distribution and myocardial blood flow to define viable myocardium, was correct in 86% of patients, and to define myocardial scar was

correct in 100% of segments. This combined approach may help to complement N-13 ammonia flow data for the definition of myocardial viability.

The current study supports the previous work by Gewirtz et al. (4), indicating that there is a blood flow level below which myocardial viability is less likely. However, the two studies differ in the level of myocardial blood flow at which this occurred and also in the use of volume of distribution data. The discrepancy in the cutoff blood flow level for viability is most likely related to differences in the modeling approaches. In contrast to Gewirtz et al. (4), the current study used a two-compartment model and also applied volume of distribution data; the K_1/k_2 ratio was not fixed. Of note, previous studies (15) have suggested that calculating myocardial blood flow <0.25 ml/min per g is extremely difficult because of the significant partial volume effect that occurs at this level of tracer activity in areas of myocardial thinning in infarct zones.

Gould et al. (21) used early (<2 min) and late (>2 min) Rb-82 imaging to assess perfusion and membrane integrity. Infarct size measured by this method was correlated with infarct size on F-18 FDG imaging (r = 0.82 for an automated analysis approach). A cohort of 35 patients was also followed up for 3 years. The Rb-82 washout approach for viability detection was shown to be predictive of mortality and helpful in patient selection for revascularization. Approximately 50% of the patients in these studies (21,22) were within 1 month of infarction when flow and metabolism may be evolving in the infarct zone. In the current study, only patients >3 months after myocardial infarction were included. Although the method described by Gould et al. (23) used Rb-82 and did not quantify blood flow, the concept is similar to the approach in the current study; that is, an independent assessment of flow and a measure of metabolic integrity using a myocardial perfusion tracer whose kinetics depend on both flow and metabolism (or in the case of Rb-82 on membrane integrity). Given the current difficulties in quantifying myocardial F-18 FDG uptake (23) and the length of time to acquire F-18 FDG data, approaches that use a single tracer, such as N-13 ammonia or Rb-82, to quantify flow and assess myocardial viability become attractive.

It is of interest to consider the two patients with F-18 FDG–defined scar and myocardial blood flow >0.45 ml/min per g. One of these patients (Patients 15) had normal coronary anatomy with a large anterior myocardial infarction, attributed to vasospasm. The volume of distribution was also low in this patient, consistent with infarction in this region. An alternative explanation for Patient 15 is a nontransmural scar with some residual viable myocardium. The F-18 FDG values were slightly below cutoff at 57%.

The second patient (Patient 13) had reduced F-18 FDG but only mildly reduced flow and maintained volume of distribution. Recently, Di Carli et al. (24) described reverse mismatch pattern with maintained perfusion but reduced F-18 FDG uptake. Their data suggested that this tissue was viable but represented stunned myocardium. This may explain the findings in Patient 13 and points out the problem of using F-18

FDG as a reference standard in some patients. The N-13 ammonia kinetic modeling approach may offer potential advantages for these patients. It remains to be seen whether the N-13 ammonia approach could also be helpful in other situations where F-18 FDG evaluation is difficult, such as diabetes (21,25,26), and requires further investigation.

Technical considerations and study limitations. The standard for confirming myocardial viability has been the improvement in wall motion abnormalities and ventricular function after revascularization. However, in many patients revascularization is not clinically indicated. In such situations, the level of F-18 FDG activity has been used as an indicator of myocardial viability (13,21,27). We selected the cutoff of 60% of peak activity used by Sawada et al. (13) because their N-13 ammonia/F-18 FDG imaging protocol was similar to our own. A limitation of the single-threshold approach could be the underestimation of viability in some myocardial regions. However, in the current study the 60% of peak F-18 FDG activity level was >2 SD below the mean normal zone F-18 FDG activity level.

The principles of defining absolute flow and metabolism with a single radiotracer may not be confined to PET imaging. The potential for quantitative dynamic single-photon emission computed tomographic data acquisitions may permit simultaneous evaluation of flow and metabolism using radiotracers whose uptake depend on both perfusion and metabolic integrity of the myocardium (13,28–31). Further investigations are necessary to evaluate whether this approach would improve viability detection methods which use SPECT myocardial perfusion tracers.

Conclusions. Nitrogen-13 ammonia kinetic modeling, derived from PET imaging studies, permits quantification of myocardial blood flow and assessment of metabolic integrity of the myocardium. In regions with previous myocardial infarction, N-13 ammonia kinetics can differentiate between scar and ischemic but viable myocardium, as defined by relative F-18 FDG uptake. This approach may permit a more rapid means for defining recoverable myocardium independent of F-18 FDG uptake. This would shorten scan time for patients and provide complementary physiologic data on absolute myocardial blood flow and metabolic integrity of the myocardium. Further large-scale clinical studies are now required to define the potential role of the N-13 ammonia kinetic imaging approach for defining myocardial scar and viability in patients with a previous myocardial infarction.

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