

Expedient protocol for myocardial viability assessment with 18 F-FDG positron emission tomography

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Abstract

Background

We assessed image quality by applying an expedient metabolic preparation period (eMPP) combining simultaneous intravenous insulin and ^{18}F -fluorodeoxyglucose (^{18}F -FDG) administration without requiring a specific plasma glucose target for PET myocardial viability imaging in patients with ischemic cardiomyopathy.

Methods

Expedient MPP for cardiac ^{18}F -FDG uptake was assessed from the time of intravenous infusion of 12.5 or 25 gram of 50% dextrose to the time of ^{18}F -FDG injection. Cardiac ^{18}F -FDG image quality was analyzed according to a 5-point scoring system (5 = excellent to 1 = non-diagnostic) by two independent observers where consensus was achieved in joint reading for cases of disagreement. Further, 58 patients, who underwent the prior standard and MPP (sMPP) for i.v. glucose loading and insulin administration for ^{18}F -FDG PET, served for comparison.

Results

Eighty-nine consecutive patients (age: 62.5 ± 12.1 yrs, men $n = 74$ and women $n = 15$) underwent rest $^{99\text{m}}\text{Tc}$ -tetrofosmin SPECT/CT and ^{18}F -FDG PET/CT for the evaluation of myocardial viability. Comparing eMPP and sMPP, the quality scores were excellent in 48% vs. 48%, very good in 26% vs. 24%, good in 16% vs. 10%, fair in 6% vs. 5%, and non-diagnostic in 3% vs. 5%. The mean quality score was not significantly different between eMPP and sMPP (4.10 ± 1.10 vs 4.13 ± 1.17 ; $p = 0.810$). As regards the eMPP in diabetic and non-diabetic patients, the quality scores were excellent in 50% vs. 46%, very good in 25% vs. 27%, good in 10% vs. 27%, fair in 10% vs. 0%, and non-diagnostic in 5% vs. 0%, while the quality score was widely comparable among groups (4.05 ± 1.23 vs 4.18 ± 0.87 ; $p = 0.731$). The average MPP was significantly less in the eMPP than in the sMPP group (35 ± 12 vs. 68 ± 19 min; $p < 0.0001$).

Conclusions

Using an eMPP after intravenous infusion of dextrose by combining “simultaneous” intravenous insulin and ^{18}F -FDG administration without requiring a specific plasma glucose target, reduces the MPP by 52% compared to prior standard protocol, while maintaining image quality.

Introduction

The prevalence of ischemic cardiomyopathy (CMP) is on a continuous rise due to an increasing elderly population and improved survival in patients with acute coronary syndrome [1]. Restoration of coronary flow may improve left ventricular function, heart failure symptoms and cardiovascular outcomes in those high-risk patients who have evidence of ischemic, jeopardized viable myocardium [2, 3]. For more than two decades, it has been widely recognized that ischemic left ventricular dysfunction may be caused by repetitive ischemic insults during times of increased metabolic demand or exercise. This myocardial “stunning” may advance to myocardial ischemia at rest and is then referred to as myocardial “hibernation” [4–8]. In this respect, positron emission tomography (PET) with ^{18}F -fluorodeoxyglucose (^{18}F -FDG) and $^{99\text{m}}\text{Tc}$ single-photon emission computed tomography (SPECT) yield a high diagnostic accuracy for the detection and characterization of a perfusion-metabolism mismatch signifying a condition of hibernation-stunned myocardium in the presence of segmental severe hypokinesis/akinesis [2, 7, 9]. Numerous clinical investigations [3, 9] have demonstrated that a timely restoration of coronary flow of ischemic, jeopardized viable myocardium may indeed improve recovery in left ventricular function, heart failure symptoms and outcomes [2, 7, 10, 11].

Although that ^{18}F -FDG PET is the most sensitive and accurate imaging method for the identification and characterization of viable and/or hibernating myocardium, the preparation protocol may require a tedious, time-consuming glucose loading and insulin application protocol to succeed in adequate myocardial ^{18}F -FDG uptake necessary for optimal diagnostic yield [12]. Notably, in patients with clinically manifest insulin resistance and/or diabetes, frequent blood glucose measurements and supplemental insulin administration may cause a significant delay in PET image acquisition and, thereby, logistical challenges in a high-volume clinical PET facility

Several protocols of glucose loading with insulin administration have been proposed for ^{18}F -FDG PET myocardial viability assessment in patients with ischemic CMP [12, 13]. Based on prior work with sequential application of insulin and ^{18}F -FDG application after intravenous glucose challenge [13], we developed a straighter forward expedient metabolic preparation protocol with combined “simultaneous” intravenous insulin administration and ^{18}F -FDG injection without requiring a specific plasma glucose target for PET myocardial viability imaging. In this respect, we evaluated a more simplified and thus expedient metabolic preparation protocol and determined the quality of cardiac ^{18}F -FDG PET images for viability assessment in diabetic and non-diabetic patients with ischemic CMP.

Materials and methods

Patient population and imaging

Patients’ characteristics are denoted in Table 1, while the application of cardiac SPECT/CT and PET/CT are described in detail in prior publication [13].

Ethical approval

The study was approved by the Washington University in St. Louis (No.201911079), and each participant signed a clinical approved informed consent form.

Metabolic preparation protocol

Patients were grouped into those with known and treated diabetes mellitus (n=51; with oral antidiabetic medication and/or insulin) (Table 1). The remaining 38 patients without diabetes mellitus but with cardiovascular risk factors were assigned to the non-diabetic group studies (Table 1). All patients were investigated after an overnight fasting state. The metabolic preparation protocol was performed by a highly skilled nurse in a dedicated preparation room, and patients were moved and positioned in the PET/CT scanner about 10 min before starting the scan. In this regard, the metabolic preparation period (MPP) was defined as the period between intravenous infusion of 12.5 or 25g of 50% dextrose in 50mL water and ^{18}F -FDG injection. In the first step, the blood glucose levels were measured at the start of the MPP (Figure 1). With baseline serum glucose levels <125mg/dL, 25g of 50% dextrose in 50mL water solution was slowly infused intravenously. Conversely, when baseline serum glucose was between $\geq 125\text{mg/dL} - 140\text{mg/dL}$, only 12.5g of 50% dextrose in 50mL water solution was slowly infused intravenously. After the glucose challenge, serum glucose levels were determined again after a period of 20 min to identify the peak of the serum glucose increase for optimal dose application of insulin intravenously. If the serum glucose, after the glucose loads, yielded values between 140-200mg/dL, insulin was administered i.v. according to the insulin protocol shown in Figure 1 and followed immediately by i.v. injection of $\approx 10\text{ mCi } ^{18}\text{F}$ -FDG. In this lower range of post-challenge serum glucose levels, sufficient insulin sensitivity can be assumed so that insulin administration commonly leads to a marked decrease in serum glucose levels and effectively drives the ^{18}F -FDG into the myocardium. In case that no appropriate decline in serum glucose by $\geq 20\text{ mg/dL}$ was observed, an additional 1-2 U insulin were injected i.v. to stimulate an appropriate drop in serum glucose and, thus, cardiac ^{18}F -FDG uptake (Figure 1). If the serum glucose after glucose challenge was $\geq 180\text{mg/dL}$ (Figure 1), insulin was applied i.v. according to the insulin protocol (Table 2) and serum glucose measurement was repeated. Thus, the updated protocol involved omitting a prior 10-min interval following insulin injection to allow for ^{18}F -FDG administration during the peak uptake into the myocardium which follows immediately after insulin injection. In patients with diabetes mellitus and baseline serum glucose $\geq 150\text{ mg/dL}$ (Figure 1), no i.v. glucose load was conducted and intravenous insulin was directly applied according to the insulin protocol (Table 2). If after 10min, the serum glucose had then decreased by $\geq 20\text{mg/dL}$, $\approx 10\text{mCi } ^{18}\text{F}$ -FDG were injected. If the decrease in serum glucose was not $\geq 20\text{mg/dL}$, another 3 U of insulin were applied i.v. and serum glucose measurement was repeated again after another 10 min. If serum glucose had then declined by $\geq 20\text{mg/dL}$, $\approx 10\text{mCi } ^{18}\text{F}$ -FDG were injected. Following ^{18}F -FDG injection, serum glucose was monitored every 15-20 minutes, and before and after the 10-min PET/CT image acquisition. If a patient developed symptomatic or asymptomatic hypoglycemia (serum glucose <70mg/dL) after insulin application, the protocol allowed for administration of 2-3 ounces of apple juice orally to preserve normal

blood glucose levels. If symptomatic or asymptomatic hypoglycemia developed, necessitating the supplementation with apple juice to maintain normal blood glucose levels, within 20 min of the ^{18}F -FDG cardiac uptake period, the study was aborted as ^{18}F -FDG PET images most likely would have been of non-diagnostic image quality. Patients on oral antidiabetic medication were asked not to use oral antidiabetic medication in the morning. Patients with insulin-dependent diabetes mellitus were instructed to comply with their regular diet and baseline insulin regimen the day before the study but fasting after midnight and to withhold insulin until the metabolic preparation of the ^{18}F -FDG PET study began. If a diabetic patient developed symptomatic or asymptomatic hypoglycemia, despite fasting state, appropriate food or juice intake at the discretion of the patient was permitted; while this was followed by a 6-hour fasting period before starting the metabolic preparation or glucose challenge for the FDG-PET examination.

Processing of cardiac image data

As described in prior publication [13], the relative distributions of $^{99\text{m}}\text{Tc}$ -tetrofosmin and ^{18}F -FDG uptake were evaluated quantitatively, using the standard American Heart Association recommended 17-segment model and the Corridor 4DM software. In line with the American Society of Nuclear Cardiology recommendations [14], myocardium with the highest $^{99\text{m}}\text{Tc}$ -tetrofosmin uptake on the rest perfusion images (5 % of the sectors with the highest activity) was defined as 100% and served as reference for normalization of regional $^{99\text{m}}\text{Tc}$ -tetrofosmin and ^{18}F -FDG uptake. The Corridor 4DM software was applied and corresponding $^{99\text{m}}\text{Tc}$ -tetrofosmin and ^{18}F -FDG images were automatically scored quantitatively in all 17 segments. A 5-point scoring system was used to indicate segmental $^{99\text{m}}\text{Tc}$ -tetrofosmin and ^{18}F -FDG uptake: 0 = normal, 1 = mildly reduced, 2 = moderately reduced, 3 = severely reduced, and 4 = absent. Myocardium was defined as normal (and, thus, viable) when the $^{99\text{m}}\text{Tc}$ -tetrofosmin uptake on SPECT images yielded a score of 0, regardless of the ^{18}F -FDG uptake on PET. A concordant decrease in $^{99\text{m}}\text{Tc}$ -tetrofosmin and ^{18}F -FDG activity scores was labeled as a perfusion-metabolism match, signifying predominant non-viable myocardium. A decrease in $^{99\text{m}}\text{Tc}$ -tetrofosmin uptake, which was more severe than the decrease in ^{18}F -FDG uptake by ≥ 1 point was defined as a perfusion-metabolism mismatch, denoting predominant viable myocardium. The total myocardial extent of match or mismatch patterns was determined as N/17, where N was the number of segments demonstrating match or mismatch, respectively, as previously defined [7,13,15].

Quality evaluation of ^{18}F -FDG PET images

The quality of ^{18}F -FDG PET images was assessed visually by two independent experienced nuclear medicine physicians. Three cases of minor disagreement were settled by joint consensus reading. Cardiac ^{18}F -FDG image quality was determined according to a 5-point scoring system (5=excellent, 4=very good, 3=good, 2=fair, and 1=non-diagnostic) [13]. As resting hypoperfusion may induced a disproportionate increase in ^{18}F -FDG uptake in ischemic compromised but viable myocardium, likely

related to an increase in Glut-4 receptors and other yet unknown factors, the ^{18}F -FDG uptake in the ischemic region may overcome that in the remote and normally perfused myocardium. Furthermore, this ischemic region with disproportional high myocardial ^{18}F -FDG uptake, then defines the 100% uptake that again may cause a relative downscaling of FDG signal in the remote myocardium. Apart from the intensity of the homogenous or heterogenous myocardial ^{18}F -FDG uptake, the residual ^{18}F -FDG blood activity served as a second evaluation criterion. According to this, excellent image quality (score 5) was appreciated as homogenous/heterogenous ^{18}F -FDG signal and no blood pool activity; very good image quality (score 4) as homogenous/heterogenous ^{18}F -FDG-signal and mild blood pool activity; good image quality (score 3) as homogenous/heterogenous ^{18}F -FDG-signal and moderate blood pool activity; fair image quality (score 2) as homogenous/heterogenous moderate ^{18}F -FDG-signal and high blood pool activity; and non-diagnostic image quality (score 1) with low homogenous/heterogenous or no ^{18}F -FDG-signal and high blood pool activity, respectively.

Statistical analysis

Data are presented as mean $\pm$ SD for quantitative and absolute frequencies for qualitative variables. Comparison between the different groups was performed by two-way analysis of variance (ANOVA), followed by BH correction for Scheffe's multiple comparison tests. Statistical significance was assumed if a null hypothesis could be rejected at $p < 0.05$. All statistical analyses were performed with SPSS.

Results

Clinical and study characteristics

The characteristics of the study population are demonstrated in Table 1. Invasive coronary angiography conducted in all patients unraveled coronary lesions, as defined as $\geq 50\%$ epicardial arterial narrowing of one vessel in 7 (7.87%), two in 29 (32.58%), and three in 43 (48.31%). The baseline serum glucose levels (mg/dL) for sMPP patients were significantly lower than eMPP ($p < 0.003$), while peak serum glucose levels after glucose challenge did not significantly differ among both groups (Table 3). As expected, the MPP was significantly less in eMPP than in sMPP group ($p < 0.001$), whereas the ^{18}F -FDG uptake and preparation period were comparable, respectively (Table 3). When patients were sub-grouped into diabetes and non-diabetes, baseline serum glucose was significantly higher in the diabetes versus non-diabetes groups in both protocols with sMPP ($p < 0.002$) and eMPP ($p < 0.001$), respectively. The group comparison of peak serum glucose alterations and administered doses of insulin between sMPP and eMPP proved to be significant (Table 4). As regards the MPP, it tended to be longer in diabetes mellitus than in non-diabetes mellitus group in the sMPP, while it was the opposite in for the eMPP. The group comparison of MPP, ^{18}F -FDG uptake and preparation period was significant (by ANOVA).

Imaging Results and Quality Assessment

^{99m}Tc -SPECT/ ^{18}F -FDG PET unraveled ischemic, jeopardized myocardium in the majority of patients 61% (n=54) with ICM (Figure 2a-b). Of the 89 patients who were studied, standard quantitative polar map analysis demonstrated perfusion-metabolic mismatches (viable myocardium) in 54 (61%), and 12 (14%) had perfusion metabolic matches (non-viable myocardium). Both patterns of mismatches and matches coexisted in 23 patients (25%). In the whole study population, the total mismatch score in viable myocardium was 17.65 ± 9.5 . When analyzed and assigned to the three main coronary arterial distribution, the regional mismatch score was 7.10 ± 5.22 for the LAD, 5.97 ± 4.38 for the LCX, and 4.94 ± 3.59 for the RCA territory, respectively. In respect of the myocardial ^{18}F -FDG image quality assessment, the mean quality score in the eMPP population was 4.10 ± 1.11 , and in the sMPP population was 4.13 ± 1.11 with no significant difference (p=0.76) and no significant difference in image quality between diabetic and non-diabetic populations (p=0.73). Myocardial ^{18}F -FDG PET images were scored for the total study population as excellent in 51.69% (n=46), very good in 25.84% (n=23), good in 12.36% (n=11), fair in 5.61% (n=5), and non-diagnostic in 4.49% (n=4) (Figure 3a). Comparing diabetic and non-diabetic patients, the quality scores were excellent in 54.90% (n=28) vs. 57.89% (n=22), very good in 25.49% (n=13) vs. 23.68% (n=9), good in 7.84% (n=4) vs. 16.13% (n=5), fair in 5.88% (n=3) vs. 6.45% (n=2), and non-diagnostic in 5.88% (n=3) vs. 0% (n=0) (Figure 3b). Overall, the majority of diagnostic FDG image quality in diabetic patients proved to be excellent with 54.90% and in non-diabetic patients, it was predominantly excellent with 57.89%.

Discussion

The current provides first results that using an eMPP after intravenous infusion of dextrose by combining “simultaneous” intravenous insulin administration and ^{18}F -FDG injection without requiring a specific plasma glucose target leads indeed to a reduction in the MPP by 53% compared to prior standard protocol [13], while maintaining image quality. Notably, applying this novel and very time-efficient protocol for intravenous glucose loading with simultaneous intravenous insulin injection and subsequent ^{18}F -FDG injection yields a good-to-excellent image quality of ^{18}F -FDG PET/CT in 91% of patients with ischemic CMP.

In prior work [13], we reported on a practical and time-efficient protocol for intravenous glucose loading and insulin administration before ^{18}F -FDG injection that reduces the MPP by 61% as compared with an oral glucose challenge, while it afforded good-to-excellent image quality in 95% of ischemic CMP patients. We now expand these prior observations [13] to an even faster or expedient metabolic preparation period (eMPP) by combining simultaneous intravenous insulin administration and ^{18}F -FDG injection without requiring a specific plasma glucose target for PET myocardial viability imaging. Compared to the prior reported standard protocol [13], the average MPP was markedly less in the eMPP compared to the sMPP group (35 vs. 68 minutes). Given comparable cardiac ^{18}F -FDG PET image quality across the five-point score evaluation scale using either eMPP or sMPP, the eMPP after

intravenous infusion of dextrose by combining simultaneous intravenous insulin administration and ^{18}F -FDG injection may offer indeed a viable option to further fasten MPP for more flexible cardiac image PET/CT acquisition in a busy imaging laboratory, faster patient throughput and comfort.

Following the intravenous dextrose glucose challenge, the eMPP is performed by combining simultaneous intravenous insulin administration and ^{18}F -FDG injection without requiring a specific plasma glucose target compared to the sMPP with sequential insulin application, 10min interval to verify $\geq 20\text{mg/dL}$ drop in plasma glucose, followed by intravenous injection of 370 MBq ^{18}F -FDG. In particular, in diabetic patients the eMPP proved to be very effective by overcoming the shortcomings of a time-consuming and very tedious sMPP if there was no sufficient drop in serum glucose $\geq 20\text{mg/dL}$ with initial insulin application according to the sliding so that another 2-3 U of insulin needed to be injected. This again then was followed by another 10 min interval to verify a sufficient drop in serum glucose allowing for the intravenous injection of ^{18}F -FDG.

Admittingly, in 19% of patients undergoing the eMPP no sufficient drop in plasma glucose levels ($\geq 20\text{mg/dL}$) were observed, necessitating the additional injection of 1-3 U of insulin to further optimize the myocardial glucose and thus the ^{18}F -FDG uptake, but not delaying the protocol as ^{18}F -FDG had been injected already. Another advantage of this novel eMPP protocol is that it does not separate between diabetic and non-diabetic patients, albeit more units of insulin according to the sliding scale need to be applied. An expedited protocol for myocardial viability assessment with ^{18}F -FDG PET is likely to have important practical implications for a widespread clinical use as it is commonly seen as the most sensitive approach among cardiac imaging modalities for the identification and characterization of viability in regions of dysfunctional myocardium in ischemic CMP [2,9,16]. In the past, the metabolic preparation protocol for viability assessment with ^{18}F -FDG PET required substantial time with repeat measurements of plasma glucose and insulin injections to acquire optimal myocardial ^{18}F -FDG uptake and, thus, image quality, that rendered this test logistically quite unsuitable for a busy PET laboratory [2,11].

Initial protocols have commonly applied involved oral administration of 50–100 g of dextrose solution to fasting patients with subsequent intravenous injection of ^{18}F -FDG intravenously 60–120 min later [12]. Thus, the relatively long MPP with oral glucose loading due to a certain portion of patients with subclinical insulin resistance, diabetes mellitus, and/or a variability in the rate of intestinal glucose absorption may have also caused difficulties in the prediction of plasma glucose peak for optimal timing of the intravenous insulin injection and subsequent application ^{18}F -FDG. Given these challenges, oral glucose MPP with oral glucose loading has been reported with suboptimal ^{18}F -FDG PET images for viability assessment ranging between 2 and 33% of patients [12,17].

Current eMPP after intravenous infusion of dextrose by combining simultaneous intravenous insulin administration and ^{18}F -FDG injection an average MPP of only ≈ 35 min as compared to ≈ 68 min when compared to sMPP with subsequent insulin and ^{18}F -FDG injection administration. Notably, the eMPP

time was quite comparable among diabetic and non-diabetic patients with intravenous glucose loading presumably related to the higher insulin doses applied in diabetic patients with higher plasma glucose peak after intravenous glucose challenge. For practical reasons, some protocols have suggested delaying ^{18}F -FDG injection until the serum glucose level decreases below 125-140mg/dL after insulin injection [12]. Yet, such an approach requires repeat assessments of plasma glucose levels, and it implies an inherent risk of missing the maximal insulin effect required to drive the FDG into the myocardium associated with suboptimal image quality. Conversely, the proposed eMPP affords the advantage that the insulin injection and myocardial uptake of ^{18}F -FDG are taking place when the effect of insulin is likely to be maximal that ascertains good to excellent images quality of viability ^{18}F -FDG images in about 91% of patients as current results outline.

After FDG-injection, we commonly strived for 60min cardiac uptake periods in both non-diabetic and diabetic patients, respectively. The mean ^{18}F -FDG uptake period between was commonly higher in diabetic- than in non-diabetic patients within each group applying sMPP or eMPP, respectively, while it did not differ significantly between both MPP groups. The difference from our planned goals, however, represents predominantly the scanner availability in routine clinical practice, deserving further investigations.

Given the eMPP combining straightforward simultaneous intravenous insulin and ^{18}F -FDG administration without requiring a specific plasma glucose target for PET myocardial viability imaging, the implemented protocol allowed administering about 2-3 ounces of orange juice orally after an ^{18}F -FDG uptake period of at least 20 min if serum glucose levels dropped below 70mg/dL after insulin administration. In fact, this intervention was needed in 5 (16.13%) of our patients. Importantly, none of the patients had severe side effects that outline the safety profile of the proposed eMPP.

Conclusion

Using an eMPP after intravenous infusion of dextrose by combining simultaneous intravenous insulin administration and ^{18}F -FDG injection without requiring a specific plasma glucose target, reduces the MPP by 53% compared to prior standard protocol, while maintaining image quality.

The proposed eMPP may further advance the application and efficacy of the assessment of myocardial viability with ^{18}F -FDG in routine clinical practice deserving further investigations.

Abbreviations

CAD
coronary artery disease
eMPP

expedient metabolic preparation period

^{18}F -FDG

^{18}F -fluorodeoxyglucose

CT

computed tomography

PET

positron emission tomography

sMPP

standard metabolic preparation period

SPECT

single photon emission tomography

$^{99\text{m}}\text{Tc}$

$^{99\text{m}}$ Technetium

Declarations

Author contributions

All authors contributed to the study design. Material preparation and data collection: JM, EO, MA, SJ, AP, TS. Imaging analysis: JM, EO, AP, supervised by TS. Data analysis: JM, EO, SJ, AP, TS. Data interpretation: JM, EO, MA, SJ, AP, TS. Draft of the manuscript: JM, EO, MA, SJ, AP, TS.. All authors read and approved of the final manuscript.

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Data availability

The data underlying this article will be shared at reasonable request to the corresponding author.

Ethics approval and consent to participate

The study was approved by the Washington University in St. Louis (No.201911079) and was in accordance with the Helsinki Declaration. All participants gave written informed consent.

Consent for publication

All patients offered the informed consents for their images in Figures to be published.

Competing interests

The authors declare no competing interests.

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References

1. Ezekowitz JA, Kaul P, Bakal JA, Armstrong PW, Welsh RC, McAlister FA (2009) Declining in-hospital mortality and increasing heart failure incidence in elderly patients with first myocardial infarction. *J Am Coll Cardiol* 53:13–20. <https://doi.org/10.1016/j.jacc.2008.08.067>
2. Schindler TH, Valenta I, Dilsizian V (2024) Viability assessment in an evolving field of heart failure treatment: still needed? *Int J Cardiovasc Imaging* 40:1823–1825. <https://doi.org/10.1007/s10554-024-03252-2>
3. Allman KC, Shaw LJ, Hachamovitch R, Udelson JE (2002) Myocardial viability testing and impact of revascularization on prognosis in patients with coronary artery disease and left ventricular dysfunction: a meta-analysis. *J Am Coll Cardiol* 39:1151–1158. [https://doi.org/10.1016/s0735-1097\(02\)01726-6](https://doi.org/10.1016/s0735-1097(02)01726-6)
4. Marshall RC, Tillisch JH, Phelps ME, Huang SC, Carson R, Henze E, Schelbert HR (1983) Identification and differentiation of resting myocardial ischemia and infarction in man with positron computed tomography, ^{18}F -labeled fluorodeoxyglucose and $\text{N-}^{13}\text{ammonia}$. *Circulation* 67:766–778. <https://doi.org/10.1161/01.cir.67.4.766>
5. Tillisch J, Brunken R, Marshall R, Schwaiger M, Mandelkern M, Phelps M, Schelbert H (1986) Reversibility of cardiac wall-motion abnormalities predicted by positron tomography. *N Engl J Med* 314:884–888. <https://doi.org/10.1056/NEJM198604033141405>
6. Bax JJ, Schinkel AF, Boersma E, Schinkel AFm Rizello V, Elhendy A, Maat A, Roelandt JRTC, van der Wall EE, Poldermans D (2003) Early versus delayed revascularization in patients with ischemic cardiomyopathy and substantial viability: impact on outcome. *Circulation* 08 Suppl 11I39–42. <https://doi.org/10.1161/01.cir.0000089041.69175.9d>
7. Jain S, Jain A, Schindler TH (2024) Different Functional Outcome After Coronary Revascularization in Subacute and Chronic Hibernating Myocardium. *JACC Cardiovasc Imaging* 17:96–97. <https://doi.org/10.1016/j.jcmg.2023.06.021>
8. Mikhail S, Ozkan E, Valenta I, Parihar AS, Jain S, Schindler TH (2026) Classical and endogen type of coronary microvascular dysfunction and potential association with cardiovascular events in a cardiometabolic disease population. *Int J Cardiovasc Imaging* 42:601–612. <https://doi.org/10.1007/s10554-025-03574-9>

9. Valenta I, Quercioli A, Ruddy T, Schindler TH (2013) Assessment of myocardial viability after the STICH trial: still viable? *Cardiovasc Med* 16:289–298 doi: not available
10. Di Carli MF, Asgarzadie F, Schelbert HR, Brunken RC, Laks H, Phelps ME, Maddahi JJ (1995) Quantitative relation between myocardial viability and improvement in heart failure symptoms after revascularization in patients with ischemic cardiomyopathy. *Circulation* 92:3436–3444. <https://doi.org/10.1161/01.cir.92.12.3436>
11. Lu Y, Wang Y, Liu Z, Meng J, Yun M, Dong R, Zhnag XL (2025) Predict value of ratio of hibernating myocardium in TPD on reverse remodeling and MACEs in HFrEF patients post-revascularization. *Int J Cardiovasc Imaging* 41:2219–2228. <https://doi.org/10.1007/s10554-025-03529-0>
12. Lima BB, Kronenberg MW, Carr CM, Duran J, Chareonthaitawee P (2026) How to prepare patients for fluorine-18 fluorodeoxyglucose positron emission tomography myocardial viability assessment. *J Nucl Cardiol* 57:102480. <https://doi.org/10.1016/j.nuclcard.2025.102480>
13. Mhlanga J, Derenoncourt P, Haq A, Bhandiwad A, Laforest R, Siegel BA, Dehdashti F, Gropler RJ, Schindler TH (2022) (18)F-FDG PET in Myocardial Viability Assessment: A Practical and Time-Efficient Protocol. *J Nucl Med* 63:602–608. <https://doi.org/10.2967/jnumed.121.262432>
14. Dilsizian V, Bacharach SL, Beanlands RS, Bergmann SR, Delbeke D, Dorbala S, Gropler RJ, Knuuti J, Schelbert HR, Travin MI (2023) Correction to: ASNC imaging guidelines/SNMMI procedure standard for positron emission tomography (PET) nuclear cardiology procedures. *J Nucl Cardiol* 30:2186. <https://doi.org/10.1007/s12350-023-03357-6>
15. Valenta I, Alavi M, Parihar AS, Jain S, Schindler TH (2026) Prevalence of impaired flow-mediated epicardial vasodilation among different types of coronary flow regulation. *Int J Cardiovasc Imaging* 2026;42:1749–1763. <https://doi.org/10.1007/s10554-026-03736-3>
16. Wu YW, Tadamura E, Yamamuro M, Kanao S, Marui A, Tanabara K, Komeda M, Togashi K (2007) Comparison of contrast-enhanced MRI with (18)F-FDG PET/201TI SPECT in dysfunctional myocardium: relation to early functional outcome after surgical revascularization in chronic ischemic heart disease. *J Nucl Med* 48:1096–1103. <https://doi.org/10.2967/jnumed.106.038596>
17. Eitzman D, al-Aouar Z, Kanter HL, von Dahl J, Kirsh M, Deeb GM, Schwaiger M (1992) Clinical outcome of patients with advanced coronary artery disease after viability studies with positron emission tomography. *J Am Coll Cardiol* 20:559–565
18. [https://doi.org/10.1016/0735-1097\(92\)90008-b](https://doi.org/10.1016/0735-1097(92)90008-b)

Tables

Table 1 Patients and study characteristics

	All	sMPP	eMPP
<i>Patients' characteristics</i>			
N	59	58	31
Age (yrs)	62 ± 10	65 ± 10	62.5 ± 12
Male/female	48/11	16/12	28/3
Prior MI	60 (67%)	42 (72%)	18 (58%)
Heart Failure	73 (82%)	45 (78%)	28 (90%)
Angina	17 (19%)	15 (26%)	2 (6%)
Diabetes	51 (57%)	31 (53%)	20 (65%)
HTN	75 (84%)	48 (83%)	27 (87%)
Dyslipidemia	70 (79%)	44 (76%)	26 (84%)
Smoker	24 (27%)	12 (21%)	12 (39%)
COPD	14 (16%)	8 (14%)	6 (19%)
LVEF (%)	60 ± 13.5	32 ± 12	28 ± 15
CAD>50%	85 (96%)	54 (93%)	31 (100%)
One vessel	7 (8%)	4 (7%)	3 (10%)
Two Vessels	29 (33%)	18 (31%)	11 (35%)
Three vessels	43 (48%)	26 (45%)	17 (55%)
Left Main	34 (38%)	24 (41%)	10 (32%)

Values are mean ± standard deviation (SD). Numbers (%). MI: myocardial infarction; HTN: hypertension, COPD: chronic obstructive pulmonary disease; LVEF: left ventricular ejection fraction; CAD: coronary artery disease

Table 2

Insulin dosage in response to glucose challenge after intravenous infusion of 25g or 12.5g of 50% dextrose in 50mL water in non-diabetic and diabetic patients, respectively.

Serum Glucose (mg/dL)	Non-Diabetic	Diabetic
	i.v. Insulin Dose (Regular Insulin, U)	i.v. Insulin Dose (Regular Insulin, U)
130–140	1	2
> 140–150	2	3
> 150–160	3	4
> 160–170	4	5
> 170–180	5	6
> 180–200	6	7
> 200	7	8
Abbreviations: i.v. = intravenous; mg=milligram; dL=deciliter; and U=unit		

Table 3

Study characteristics across protocols

Study characteristics	sMPP	eMPP
Glucose at baseline (mg/dL)	116 ± 34	142 ± 41*
Glucose peak (mg/dL)	190 ± 28	182 ± 29
Glucose before imaging (mg/dL)	98 ± 25	111 ± 25*
Insulin (U)	6.7 ± 3.5	5.8 ± 2.57
FDG dose (mCi)	11.0 ± 0.7	11 ± 0.6
MPP (min)	68 ± 19	35 ± 12*
¹⁸ F-FDG uptake period (min)	82 ± 21	85 ± 21
Preparation period (min)	149 ± 27	120 ± 20
*p ≤ 0.05 vs sMPP using Student's T-Test; values are mean ± SD or n (%); MPP: metabolic preparation period. FDG-uptake period: time from FDG-injection and start of imaging; preparation period: time from start of MPP and start of imaging.		

Table 4
Study characteristics stratified by diabetes

	sMPP		eMPP	
	Diabetes	Non-Diabetes	Diabetes	Non-Diabetes
n	31	27	20	11
Study characteristics				
Glucose at baseline (mg/dL) ^{†,‡}	129 ± 42	102 ± 15	164 ± 32	103 ± 25
Glucose peak (mg/dL) [†]	194 ± 27	185 ± 30	176 ± 22	192 ± 38
Glucose before imaging (mg/dL) [†]	105 ± 26	92 ± 21	121 ± 22	94 ± 21
Insulin (U) [‡]	7.9 ± 4.2	5.3 ± 1.9	6.5 ± 2.3	4.6 ± 1.8
FDG dose (mCi) [‡]	10.7 ± 0.8	11.3 ± 0.6	11 ± 0.6	10.9 ± 0.6
MPP (min) [†]	69 ± 23	66 ± 13	30 ± 10	44 ± 9
18F-FDG uptake period (min) [‡]	90 ± 20	71 ± 18	97 ± 13	65 ± 15
Preparation period (min) ^{†,‡}	159 ± 28	138 ± 21	126 ± 19	108 ± 16
† Significant main effect of Protocol (sMPP vs. eMPP), Two-Way ANOVA.				
‡ Significant main effect of Diabetes Status (Diabetes vs. Non-Diabetes), Two-Way ANOVA.				
Values are mean ± SD. MPP: metabolic preparation period. FDG-uptake period: time from FDG-injection and start of imaging; preparation period: time from start of MPP and start of imaging.				

Figures

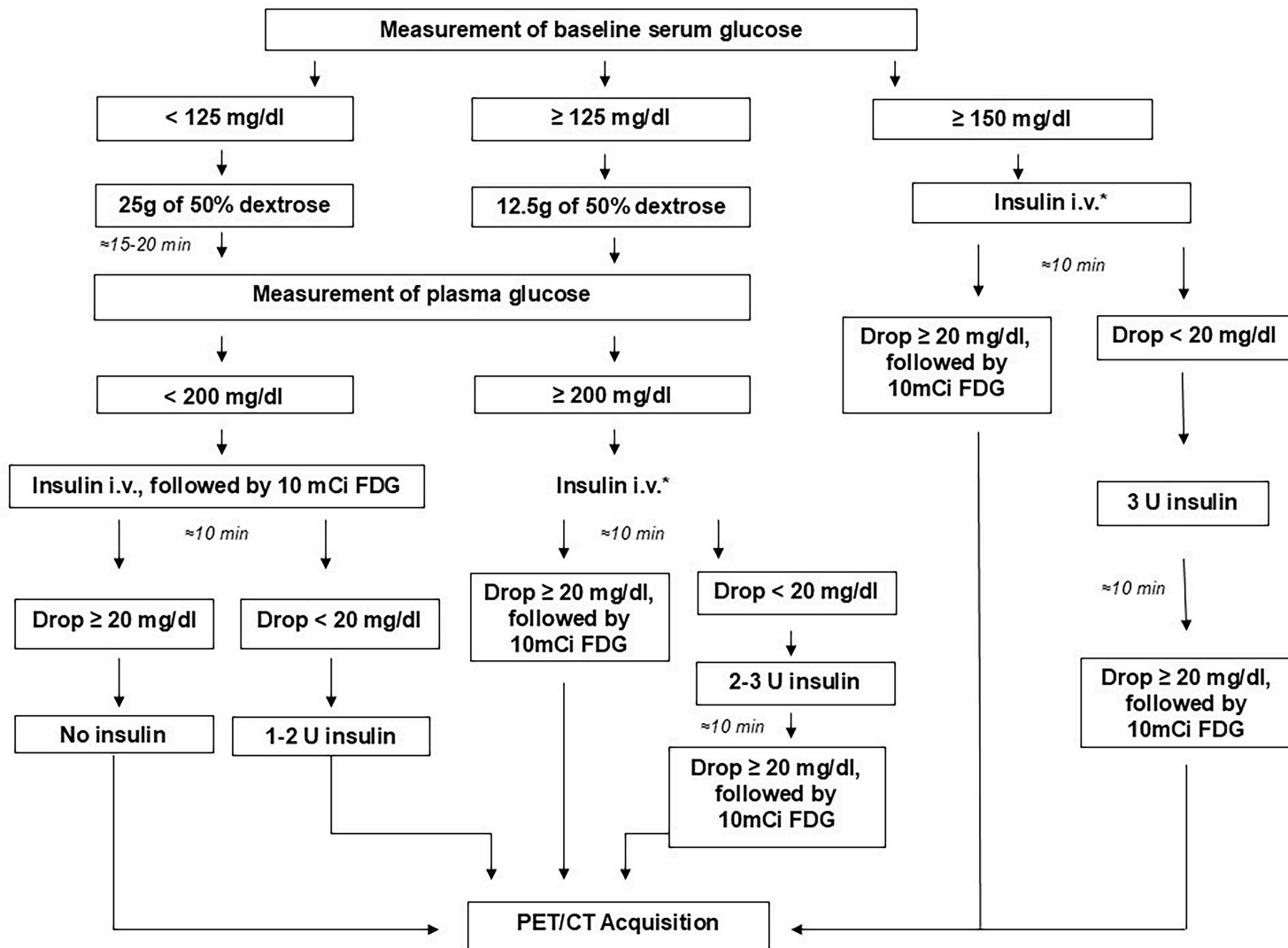


Figure 1

Expedient Metabolic Preparation Protocol. Schematic illustration of the metabolic preparation protocol based on initial serum glucose levels.

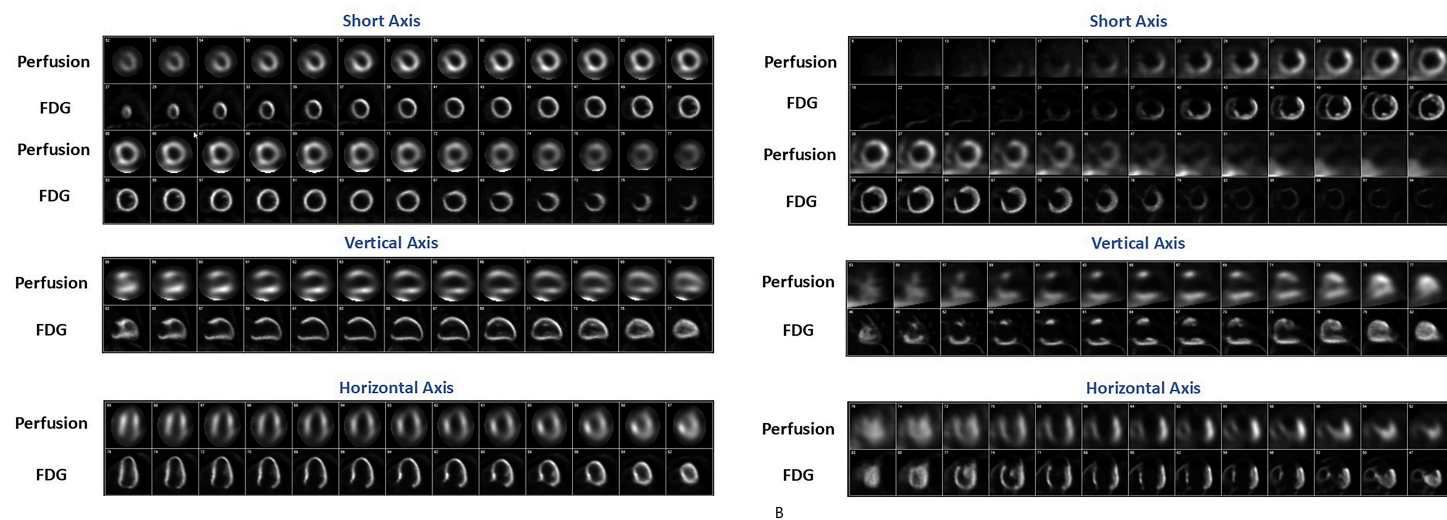


Figure 2

a. Case Example of "Mismatch" or Viable Myocardium as determined with ^{99m}Tc -SPECT/CT and ^{18}F -FDG PET/CT. Rest myocardial perfusion with SPECT/CT images with ^{99m}Tc -tetrofosmin and ^{18}F -FDG PET/CT in a patient with ischemic cardiomyopathy, demonstrating a "mismatch". ^{99m}Tc -SPECT/CT rest perfusion with short, vertical, and horizontal long axis images demonstrates a severe perfusion defect in the antero-septo-apical, and apical, as well as the basal- and mid-segments of the inferolateral walls that is accompanied by normal or upregulated ^{18}F -FDG-uptake on the PET images, consistent with hibernating-stunned myocardium.

b. Case Example of "Match" or Non-Viable Myocardium as determined with ^{99m}Tc -SPECT/CT and ^{18}F -FDG PET/CT. Rest myocardial perfusion SPECT/CT images with ^{99m}Tc -tetrofosmin and ^{18}F -FDG-PET/CT images in a patient with ischemic cardiomyopathy, demonstrating a "match". ^{99m}Tc -SPECT/CT rest perfusion with short, vertical, and horizontal long axis images demonstrate a severe perfusion defect involving the anterior, antero-septal, apical, and some extension into the infero-septal wall that is associated with predominant absence of ^{18}F -FDG-uptake on the PET images. Thus, there is widely a "match" finding with concordant absence of perfusion and viability to signify predominant transmural necrosis in LAD distribution.

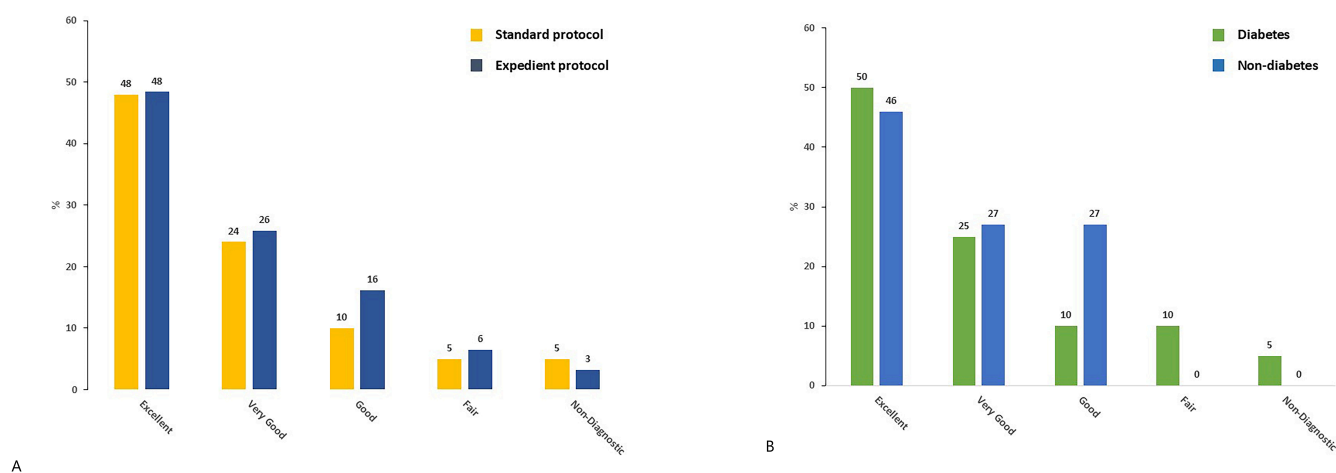


Figure 3

- a. Comparison of ^{18}F -FDG image quality score distribution among Protocols.** Myocardial ^{18}F -FDG image quality score distribution (%) in patients undergoing standard or expedited protocol, respectively.
- b. ^{18}F -FDG image quality score distribution for Expedient Metabolic Preparation Protocol among Diabetic- and Non-Diabetic Individuals.** Myocardial ^{18}F -FDG image quality score distribution (%) of the study population with expedited protocol and comparison among those with diabetes mellitus and non-diabetes mellitus, respectively.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Graphicalabstract.jpg](#)