Fasting and Nonfasting Iodine-123-Idophenylpentadecanoic Acid Myocardial SPECT Imaging in Coronary Artery Disease

Gary V. Heller, Ami E. Iskandrian, Cesare Orlandi, Alan W. Ahlberg, Jackyeong Heo, April Mann, Michael P. White, Andre Gagnon and Raymond Taillefer

Nuclear Cardiology Laboratory, Division of Cardiology, Hartford Hospital, Hartford, Connecticut, and the Divisions of Medicine and Nuclear Medicine, University of Connecticut School of Medicine, Farmington, Connecticut; Nuclear Cardiology Laboratory, Allegheny University of the Health Sciences, Philadelphia, Pennsylvania, and Hôtel-Dieu de Montréal, Canada

Iodine-123-labeled idophenylpentadecanoic acid (IPPA) metabolic imaging has been shown to be clinically useful for the identification of myocardial viability in patients with coronary artery disease and left ventricular dysfunction. Imaging is usually performed under fasting conditions since nonfasting conditions may affect myocardial uptake of ^{123}I-IPPA. The purpose of this study was to examine the impact of dietary condition on ^{123}I-IPPA metabolic imaging. **Methods:** Forty patients with stable coronary artery disease underwent, in randomized order and on separate days, ^{123}I-IPPA SPECT myocardial imaging under fasting and nonfasting conditions. Patients were injected with ^{123}I-IPPA (4–5 mCi) at rest with imaging performed at 4 (initial) and 30 (delay) min. For each image (initial and delay images), 10 segments were analyzed by three experienced observers without knowledge of patient identity or dietary condition using a 5-point grading system (0 = no uptake to 4 = normal uptake). A summed global score was obtained for each image by adding the scores for all 10 segments. Image quality was assessed using a 3-point grading system. **Results:** Visual agreement for normal and abnormal segments between fasting and nonfasting conditions was 82% (kappa = 0.63). There were no significant differences in the summed global scores for both conditions. Image quality was equivalent for both conditions in 65% of cases and superior under the nonfasting condition in 25% of cases. **Conclusion:** Image quality as well as the presence, location and severity of defects are similar under fasting and nonfasting conditions with ^{123}I-IPPA. Therefore, fasting is not necessary before ^{123}I-IPPA SPECT imaging for the assessment of myocardial viability.

Key Words: iodine-123-idophenylpentadecanoic acid; SPECT; myocardial viability; fasting

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In patients with coronary artery disease and left ventricular dysfunction, prognosis is partially based on the severity of impairment in resting ejection fraction (*1*). However, it is recognized that patients with dysfunctional but viable myocardium may benefit from revascularization with improvement in prognosis (*2–10*). Several methods have been described to identify viable myocardium including PET, MRI, echocardiography and myocardial perfusion imaging (*8,9*). Assessment of viability using myocardial perfusion imaging has generally been performed with blood flow tracers including ^{201}Tl and ^{99m}Tc-sestamibi (*8,11,12*). However, the metabolic status of myocardial cells is also an accurate measure of viability. As long-chain free fatty acids are the preferred substrate of cardiac muscle (*13–16*), radiolabeled free fatty acids have been studied as potential probes of viability (*17–21*). One such compound, ^{123}I-labeled idophenylpentadecanoic acid (IPPA), has been shown to have uptake proportional to myocardial blood flow (*19–21*), and redistribution of defects between initial and delay rest images may indicate viability (*22–25*). In previous studies, patients were imaged under fasting conditions due to concerns that a fatty meal may affect myocardial uptake of ^{123}I-IPPA. Such a requirement may limit the use of this radiopharmaceutical. Despite theoretical concerns, the impact of dietary condition on ^{123}I-IPPA imaging has not been evaluated. The purpose of this study was to compare ^{123}I-IPPA tomographic myocardial imaging under fasting and nonfasting conditions in the same patients with coronary artery disease.

MATERIALS AND METHODS

Study Design

This was a prospective, open-label, randomized, crossover, multicenter trial in which patients with evidence of coronary artery disease underwent ^{123}I-IPPA tomographic myocardial imaging under fasting and nonfasting conditions.

Patient Selection

Male and female patients who had at least one of the following inclusion criteria were eligible for participation in this study: (a) documentation of a coronary artery stenosis ≥70% by cardiac catheterization within 3 mo of enrollment; (b) previous coronary artery bypass surgery; (c) documented history of prior myocardial infarction ≥6 wk before enrollment; (d) or a previously positive stress myocardial perfusion imaging study. Patients who met entry criteria signed informed consent approved by the Institutional Review Boards from participating institutions and a negative urine human chorionic gonadotropin test was required in women of child-bearing potential. Patients were excluded for the following: <21 yr of age, untreated metabolic disorder (diabetes or thyroid disease), documented nonischemic cardiomyopathy or allergy to human serum albumin or iodine.

Iodine-123-IPPA Injection

Each patient received two intravenous injections of ^{123}I-IPPA (Medco Research, Inc., Research Triangle Park, NC) at rest separated by an interval of 4–14 days. Doses of 0.039–0.096 mCi per/kg were administered as a bolus. The dose administered ranged from 3.88 to 5.30 mCi.

Dietary Protocol

Patients were instructed to remain in a fasting state after midnight before each ^{123}I-IPPA injection. Three to five drops of

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For correspondence or reprints contact: Gary V. Heller, MD, PhD, Director, Nuclear Cardiology Laboratory, Division of Cardiology, Hartford Hospital, 80 Seymour St., Hartford, CT 06102.

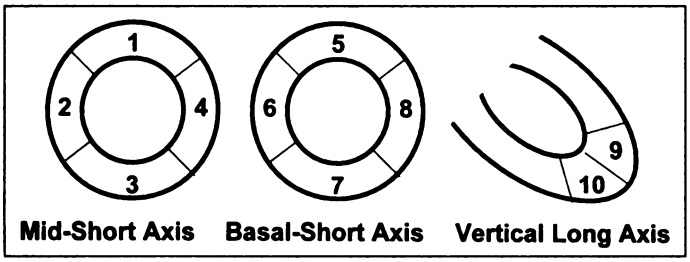

FIGURE 1. Schematic of interpretation of ^{123}I-IPPA images under fasting and nonfasting conditions.

saturated solution of potassium iodine or 8–10 drops of Lugol's solution were administered 1 hr before the ^{123}I-IPPA injections. Patients remained in a fasting state until completion of ^{123}I-IPPA imaging. During the nonfasting condition, patients were instructed to consume a low-fat meal 30–65 min before the ^{123}I-IPPA injection. The order of dietary condition was determined by a central laboratory randomized code.

Image Acquisition

For ^{123}I-IPPA imaging during both dietary conditions, the patient was positioned under a gamma camera and injected with radiopharmaceutical while supine. SPECT images during both dietary conditions were acquired 4 (initial) and 30 (delay) min after ^{123}I-IPPA injection. Image acquisition parameters consisted of 32 views (40 sec/projection) over a circular 180° orbit progressing anteriorally from the 45° right anterior oblique to the 45° left posterior oblique angle. Imaging was performed using a low-energy, all-purpose collimator.

Processing Details

Filtered backprojection was performed using a low-pass Butterworth filter with a frequency cutoff of 0.35 and an order of 5.0 for reconstruction of transaxial slices to a thickness of 6.6 mm. Azimuth definition (from apex-to-base or anterior-to-posterior) was obtained from the midtransverse and sagital slices for reconstruction of the short-axis, horizontal long-axis and vertical long-axis slices. No preprocessing filtration or attenuation correction was used.

Image Interpretation

Images were evaluated by three experienced study investigators without knowledge of patient identity or dietary condition. All images were interpreted using a semiquantitative assessment of 10 segments (Fig. 1). Each segment was scored using a 0–4 scale

TABLE 1
Demographics of 40 Patients Undergoing Fasting and Non-Fasting Iodine-123-IPPA SPECT Imaging

Male	32 (80%)
Caucasian	30 (75%)
Age (yr)	58.8 ± 10.2 (range 40–76)
Cardiac history:	
s/p PTCA	10 (25%)
s/p MI	30 (75%)
s/p CABG	14 (35%)
Risk factors:	
Hypertension	21 (53%)
Diabetes	13 (33%)
Smoking	19 (48%)
Family history	19 (48%)
Hyperlipidemia	17 (43%)

s/p = status post; PTCA = percutaneous transluminal coronary angioplasty; MI = myocardial infarction; CABG = coronary artery bypass surgery; IPPA = idophenylpentadecanoic acid.

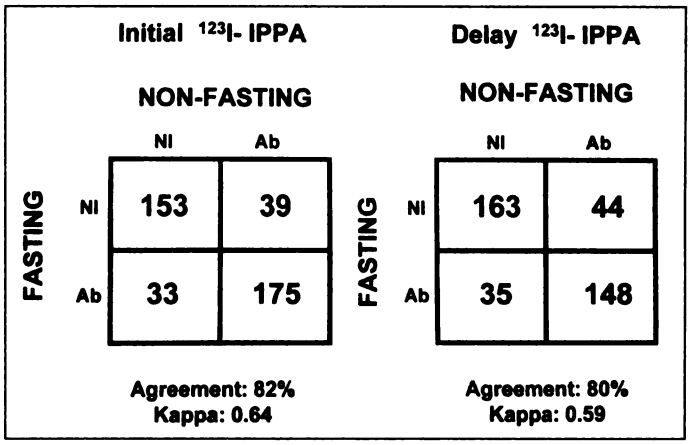

FIGURE 2. Consensus agreement of initial and delay ^{123}I-IPPA images under fasting and nonfasting conditions for normal and abnormal segments.

(0 = no activity; 1 = severe defect; 2 = moderate defect; 3 = mild defect; and 4 = normal activity) and agreement was by consensus. A summed global score was determined for each image (initial and delay images) by adding the scores for all 10 segments. A summed global score < 4 was considered normal. In addition, image quality was assessed using a side-by-side evaluation of the paired images without knowledge of patient identity or dietary condition. Images were categorized as: (a) equivalent quality of images during both dietary conditions; or (b) superior quality of images during one dietary condition over the other.

Statistical Analysis

Assessment of ^{123}I-IPPA distribution between fasting and nonfasting conditions was performed using linear regression, with agreement by Cohen's kappa statistic (*26*). Comparison of image quality was performed using McNemar's test of correlated proportions (*27*). Significant differences were predetermined at $p \leq 0.05$.

RESULTS

Patient Demographics

In the 40 patients who completed the protocol, all had evidence of coronary artery disease by study design (Table 1). There was also a high incidence of prior myocardial infarction and revascularization.

Imaging Results

Image segments (10 per image) were classified as normal or abnormal for both fasting and nonfasting conditions. There was excellent agreement between both conditions for the initial (4 min) and delay (30 min) image segments with exact agreement of 82% (K = 0.64) and 80% (K = 0.59), respectively (Fig. 2).

Images were further classified by the location and severity of defects for both fasting and nonfasting conditions (Fig. 3).

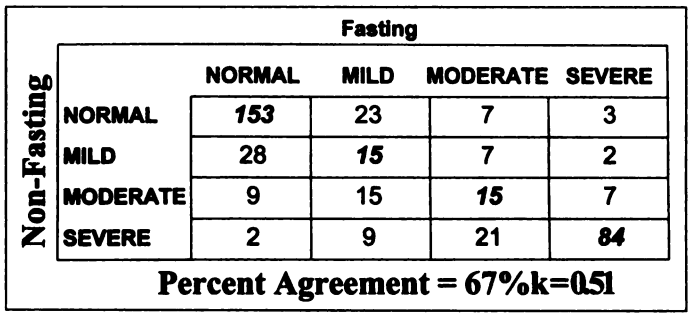

FIGURE 3. Consensus agreement of initial ^{123}I-IPPA images under fasting and nonfasting conditions for defect severity (normal, mild, moderate and severe photon reduction).

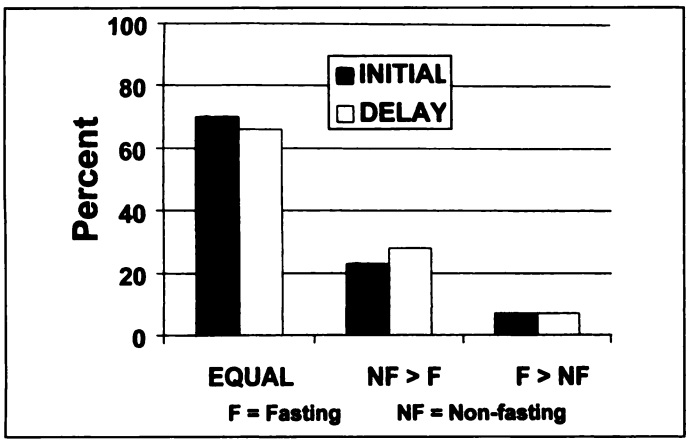

FIGURE 4. Comparison of image quality of 40 patients undergoing fasting and nonfasting ^{123}I-IPPA imaging.

Exact agreement between both conditions for defect severity of the initial (4 min) imaging segments was good (67%, K = 0.51). Defect location by vascular territory was also similar between fasting and nonfasting conditions (left anterior descending coronary artery: 19 versus 20; circumflex coronary artery: 12 versus 12; and right coronary artery: 25 versus 27, respectively; p = ns for all three coronary artery distributions). There was no systematic under- or overestimation of defect location or severity between both dietary conditions.

Comparison of Image Quality Between Fasting and Nonfasting Conditions

A visual assessment of image quality for both dietary conditions was also performed (Fig. 4). The majority of initial and delay images during both dietary conditions were found to be of equivalent quality and interpretable. However, 9/40 (23%) of the initial and 11/40 (28%) of the delay images under the nonfasting condition were considered to be superior to those under the fasting condition. Furthermore, only 3/40 (8%) patients had initial and delay images under the fasting condition, which were considered to be superior to those under the nonfasting condition. An example of ^{123}I-IPPA image quality in a patient during both the fasting and nonfasting condition is shown in Figure 5. In this patient, initial image quality was slightly worse during the fasting condition, but delay image quality was equivalent during both dietary conditions. Initial and delay imaging defect location and severity were similar during both dietary conditions and overall image quality was such that image interpretation was of high confidence.

DISCUSSION

This multicenter trial demonstrated that initial and delay ^{123}I-IPPA imaging results under fasting and nonfasting conditions yield similar diagnostic information. In fact, image quality was found to be superior in 25% of cases with nonfasting conditions. Thus, dietary restrictions are not necessary for optimal ^{123}I-IPPA imaging.

Use of Iodine-123-IPPA for the Identification of Ischemic Coronary Artery Disease and Viability

It has been demonstrated that fatty acids constitute a primary fuel source for the normal myocyte (*8*). The myocyte extraction of free fatty acids is regulated by such conditions as stress-induced cardiac energy states as well as the presence of chronic ischemia and injury. The use of radiolabeled fatty acids as a measure of myocardial cellular conditions was first proposed over 30 yr ago. The use of IPPA as a substrate was developed much later and avoided the rapid deiodination encountered with the earlier alkyl fatty acids (*13–19*). Clinical applications of ^{123}I-IPPA imaging have included identification of patients with ischemic coronary artery disease as well as viability. Several previous studies with ^{123}I-IPPA using both planar and SPECT imaging have demonstrated a high sensitivity and specificity for coronary artery disease (*20,21*) and compared favorably with ^{201}Tl (*21,24*). This imaging technology has also been applied to the assessment of myocardial viability (*22,23,25*). Murray et al. (*22,23*), in two separate studies, demonstrated a sensitivity of 92% and specificity of 86% for detecting biopsy-proven viable segments. In the latter study, an excellent correlation with ^{201}Tl reinjection was found, and when disagreement occurred, ^{123}I-IPPA correctly identified viable segments (*23*). These findings demonstrate the important clinical value of ^{123}I-IPPA imaging in the identification of myocardial viability. The results from our study demonstrate that a nonfasting condition does not affect ^{123}I-IPPA image quality as well as the presence, location and severity of defects. This has important clinical implications for patients requiring assessment of myocardial viability who are unable to fast before imaging. Since image acquisition can be completed in 1–1.5 hr, ^{123}I-IPPA imaging may have an

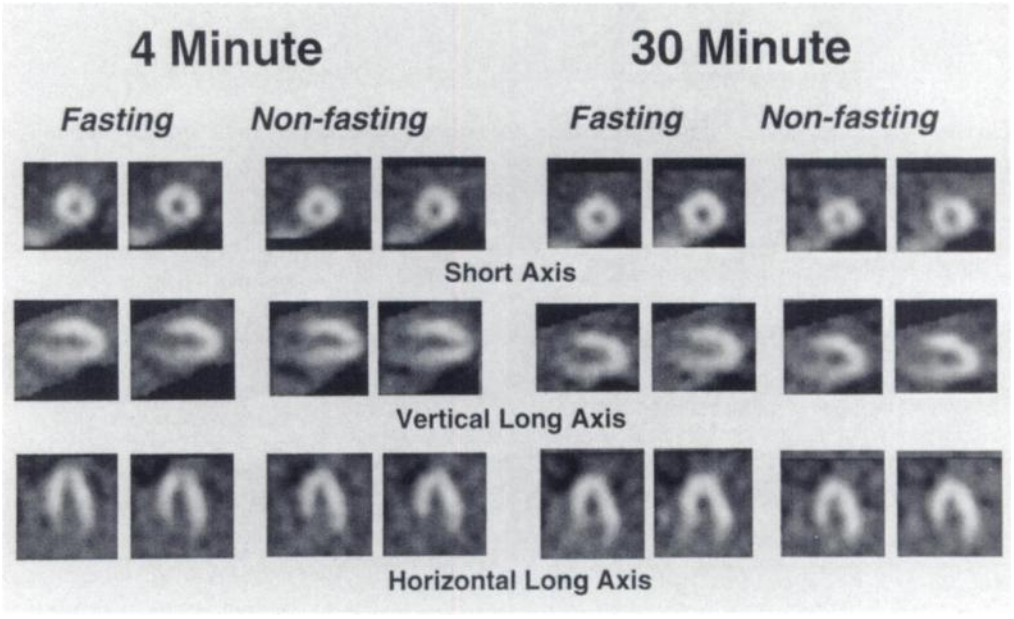

FIGURE 5. Example of image quality under fasting and nonfasting conditions with ^{123}I-IPPA imaging in the same patient for initial (4 min) and delay (30 min) SPECT acquisition.

advantage over rest-redistribution ^{201}Tl imaging, which requires 4–24 hr for delayed imaging.

CONCLUSION

Image quality as well as the presence, location and severity of defects are similar under fasting and nonfasting conditions with ^{123}I-IPPA. Therefore, fasting is not necessary before ^{123}I-IPPA SPECT imaging for the assessment of myocardial viability.

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High-Resolution Cardiac PET in Rabbits: Imaging and Quantitation of Myocardial Blood Flow

Kazuhiro Shimada, Katsuya Yoshida, Hiroyuki Tadokoro, Shinobu Kitsukawa, Akira Takami, Kazutoshi Suzuki, Shuji Tanada and Yoshiaki Masuda

Division of Advanced Technology for Medical Imaging, National Institute of Radiological Sciences, and Third Department of Internal Medicine, Chiba University School of Medicine, Chiba, Japan

A high-resolution PET system for small animals was tested for its applicability to the investigation of regional myocardial blood flow (MBF) in rabbits. **Methods:** Nineteen measurements were performed in 10 closed-chest anesthetized rabbits at baseline and during infusions of adenosine (0.2 mg/kg/min) and propranolol (0.20–1.20 mg slow infusion) to obtain a wide range of MBF. Myocardial blood flow was assessed both by dynamic ^{13}N-ammonia PET and by colored microspheres. Blood was withdrawn directly from the femoral artery, and arterial ^{13}N activity was measured by coincidence type gamma detection system for the input function. Nitrogen-13 myocardial uptake was calculated by dividing the myocardial ^{13}N activity by the integral value of the input function. **Results:** Three or four contiguous cross-sectional myocardial images were obtained after ^{13}N-ammonia injection. The left ventricular wall and cardiac cavity were clearly visualized. Moreover, initial passage of the tracer through the heart was obtained with serial 10-sec PET images. Nitrogen-13 myocardial uptake correlated well with flow measured with microspheres ($r = 0.88$). **Conclusion:** Our cardiac PET system can be used for in vivo imaging and quantitation of MBF in small animals and may play an important role in the future study of animal models of cardiovascular diseases.

Key Words: PET; rabbits; myocardial blood flow

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For correspondence or reprints contact: Katsuya Yoshida, MD, Division of Advanced Technology for Medical Imaging, National Institute of Radiological Sciences, Anagawa 4-9-1, Inage-ku, Chiba-shi, 263, Japan.