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LETTERS TO THE EDITOR

Reclassification of Severe Ischemia on PET Versus SPECT MPI Using a Same-Patient Simultaneous Imaging Protocol

Severe ischemia on myocardial perfusion imaging (MPI) serves as a gatekeeper for further downstream invasive testing to identify candidates who derive symptomatic benefit with revascularization.[1] Positron emission tomography (PET) and single-photon emission computed tomography (SPECT) may provide differing assessments of ischemia in the same patient caused by underlying technological differences. Previous intermodality comparisons have been limited by the lack of the simultaneous, same-patient acquisition of PET and SPECT, and use of semiquantitative or visual perfusion assessment.[2] We performed a post hoc analysis of a randomized study where patients underwent near-simultaneous PET and SPECT MPI to assess possible reclassification of severe ischemia between the 2 modalities and its effect on downstream resource use.[3]

A total of 322 symptomatic patients with known coronary artery disease who were referred for clinically indicated pharmacological stress MPI underwent near-simultaneous rest and stress (89% dipyridamole, 11% regadenoson) technetium 99m SPECT and rubidium 82 PET imaging from June 2009 to August 2013. The study protocol has been previously published.[3] The perfusion images were displayed and quantified using commercial software (Cedars Sinai Cardiac Suite). Ischemia was determined from automated perfusion quantitation using ischemic total perfusion defect (TPD) (stress TPD-rest TPD), which was verified by blinded core-lab readers, and categorized into none (0%), mild (1% to 4.9%), moderate (5% to 9.9%), and severe (≥10%). It was compared between paired PET and SPECT studies using Mc-Nemar Bowker's symmetry test. Post-test clinical management was left at the discretion of the referring physician, who had access to the randomized study report (PET or SPECT). Effect of ischemia reclassification on outcomes was assessed by comparing rates of 12-month downstream revascularization between: 1) patients with severe ischemia on both; 2) severe ischemia on PET, but not SPECT; 3) severe ischemia on SPECT but not PET; and 4) less than severe ischemia on both using Fisher exact and/or chi square tests. To assess how ischemia reclassification between PET and SPECT would affect eligibility for revascularization based on the ISCHEMIA (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches) trial, we estimated the number of patients with severe ischemia on PET who had obstructive disease on angiogram (any epicardial stenosis ≥70%) within 6 months who had less than severe ischemia on SPECT.[1] The study was approved by Saint Luke's Hospital Institutional Review Board. All patients signed written informed consent.

The mean age of the study cohort was 66.3 ± 9.7 years, 64.9% were men, 27.3% had diabetes, and 78.0% were on ≥3 coronary artery disease medications at baseline. Patients were symptomatic, with mean respective Seattle Angina Questionnaire (SAQ) Angina Frequency and Summary Scores of 78.5 ± 19.0 and 76.6 ± 17.0 at baseline, improving by a mean of 11.8 and 10.1 points to 90.6 ± 16.8 and 87.2 ± 16.4 at 12 months. Medical therapy was intensified in 78 patients (25.4%) by 3 months, 61 (19%) had coronary angiogram within 6 months, and 49 (15%) underwent revascularization within 12 months.

Of 322 patients, 0 (0%), 26 (8%), 67 (21%), 135 (42%), and 94 (29%) were classified by PET as nondiagnostic and having no, mild, moderate, and severe ischemia, respectively. Similar classification using SPECT for the same patients was 2(1%), 79 (25%), 96 (30%), 114 (35%), and 31 (10%), respectively ($P < 0.001$). Among 94 patients with severe ischemia on PET, only 19% (n = 18) had severe ischemia when measured with SPECT. Conversely, among 31 patients with severe ischemia on SPECT, 42% (n = 13) had less than severe ischemia on PET ($P < 0.001$) (**Figure 1A**). Rates of 12-month revascularization were similar between patients with severe ischemia on both and severe ischemia on PET but not SPECT, but significantly lower in patients with severe ischemia on SPECT but not PET and those with less than severe ischemia on both (**Figure 1B**). Obstructive disease was present in 45 of 61 patients (74%), 30 (67%) of whom had severe ischemia with PET vs 9 (20%) with SPECT ($P < 0.001$). Among patients with severe ischemia on PET and obstructive disease who may derive symptomatic benefit with revascularization, 73% (22 of 30) had less than severe ischemia on SPECT. Our study further expands upon how the superior diagnostic performance of PET vs SPECT translates into classification of high-risk ischemia in patients, potentially influencing post-test decision making. It raises the possibility that a significant proportion of patients enrolled using nuclear imaging criteria in the ISCHEMIA trial may have less than severe ischemia when measured with PET; conversely, patients with severe ischemia may not have been enrolled caused by underestimation of severity on

SPECT. Our study is limited by lack of myocardial blood flow information on patients who underwent PET. Ancillary nonperfusion information was used for clinical report, but this study focused on blinded automated relative perfusion reads alone. Images were acquired on 3 different types of SPECT and PET cameras, which could introduce noise in the intermodality comparison. However, this was done to reflect real-world practice, improving the generalizability of the study findings. Moreover, attenuation-correction software was routinely used for SPECT studies to ensure high-quality images. As post-test management was not dictated by the protocol, coronary angiography was not performed in all patients.

Our study suggests a need for separate risk thresholds with PET and SPECT while selecting a high-risk population as the target of an intervention. Equivalency of risk thresholds on other stress imaging modalities, as a function of subsequent management, remains to be studied in the future.

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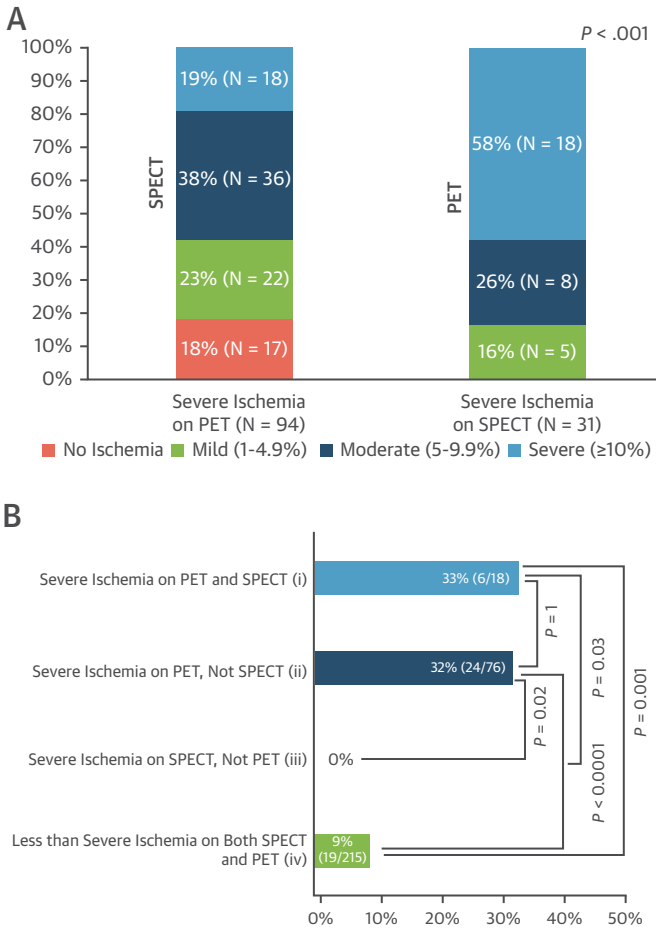
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

FIGURE 1 Assessment of Severe Ischemia on SPECT Versus PET MPI Performed Simultaneously



(A) Reclassification of severe ischemia on automated perfusion assessment between positron emission tomography (PET) and single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI). **(B)** Rate of 12-month downstream revascularization among patients with concordant vs discordant assessments of severe ischemia on PET and SPECT.

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