

# Comparison of the Appropriateness of Myocardial Perfusion Imaging in Men Versus Women

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After a decade of appropriate use criteria publication, the degree and predictors of inappropriate use in women compared with men are not known. We conducted a retrospective cohort investigation comparing appropriateness categories (appropriate, maybe appropriate, and rarely appropriate) and cardiovascular outcomes in patients undergoing nuclear myocardial perfusion imaging (MPI) between June 2011 and September 2014 in predominantly inpatient setting. Of 1,475 cases reviewed, 747 (50.6%) were women, and they were more likely to have rarely appropriate use 118 (15.8%) than men 62 (8.5%),  $p < 0.01$ , but they were less likely to have an abnormal MPI 102 (13.6%) than men 183 (25.6%),  $p < 0.01$ . Subsequent angiography and revascularization rates were similar in women 38 (37.2%) and 5 (4.9%) and men 52 (28.4%) and 16 (8.7%),  $p = 0.12$ ,  $p = 0.23$ , respectively. After median follow-up of 6 months, myocardial infarction rates were similar in women 3 (2.9%) and men 7 (3.8%),  $p = 0.67$ . Death rates were similar in women 8 (7.8%) and men 18 (9.8%),  $p = 0.57$ . The most common clinical scenario designated as rarely appropriate was in those with low pretest probability of coronary artery disease, who have interpretable electrocardiogram and are able to exercise in women 58 (49.1%) and men 21 (33.8%). In conclusion, based on the most contemporary appropriate use criteria publication, rarely appropriate use of MPI remains higher in women than that in men. This phenomenon was mostly observed in low-risk patients who can exercise. © 2017 Elsevier Inc. All rights reserved. (Am J Cardiol 2017;■:■-■)

Appropriate use criteria (AUC) for radionuclide stress testing were first published over a decade ago.<sup>1</sup> Despite efforts to minimize unnecessary use, up to 14% of radionuclide stress tests are considered inappropriate using these criteria.<sup>2</sup> Some studies have suggested that inappropriate use of radionuclide myocardial perfusion imaging (MPI) is greater in women than in men.<sup>3-5</sup> It is unclear why women undergo more tests designated as inappropriate compared with men. Women who present with angina often have nonobstructive epicardial coronary artery disease (CAD). In contrast, there is more clear relation between angina and epicardial CAD in men. The discrepancy of this presentation in women has been dubbed due to the presence of microvascular disease, often nebulous to diagnose and treat.<sup>6</sup> The extent and contributors to inappropriate use (alternatively, rarely appropriate use) of MPI has not been well defined. We sought to examine the magnitude and predictors for rarely appropriate use of MPI in women and in men.

## Methods

We conducted a retrospective cohort investigation of patients who had a Single Photon Emission Computed Tomography (SPECT) MPI at the University of Florida Health Shands Hospital. The University of Florida Institutional Review Board waived the requirement for informed consent and approved this study. Subjects were identified from records using the Informatics for Integrating Biology at the Bedside database system, which provided 1,500 SPECT MPI tests. Of which, 25 were incomplete due to missing essential data such as date of the MPI or the reason for ordering the test. Study data were collected and managed in the Research Electronic Data Capture database (2016 Vanderbilt University, Nashville, Tennessee).<sup>7</sup> Subjects underwent SPECT MPI between June 2011 and September 2014 in a predominantly (>75%) inpatient setting. Patients who were hospitalized for chest pain were ruled out for acute coronary syndrome, and their symptoms were deemed to be stable per the referring provider. Clinical notes were reviewed from the hospitalization or clinic visit at the time a SPECT MPI was ordered to determine the rationale for testing, risk factors, and last follow-up date. Baseline patient demographics, cardiovascular risk factors, previous testing including other noninvasive cardiac testing, coronary angiography, and coronary revascularization before and after the index SPECT MPI were collected through manual review of electronic health records. CAD was defined as any angiographic evidence of atherosclerotic disease in any of the epicardial coronary arteries or previous myocardial infarction (MI) based on chart review. The interpretation of MPI results was performed by multiple readers (combination of

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See page 5 for disclosure information.

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Table 1  
Baseline characteristics

Characteristics	Women (n = 747)	Men (n = 728)	Total n = 1,475	P Value
Age, mean (SD) (years)	60.0±13.2	58.9 ± 13.1	59.5±13.2	0.11
Body mass index, mean (SD) (kg/m <sup>2</sup> )	31.5±12.3	30.4 ± 6.9	30.9±10	0.03
Coronary artery disease	175 (23.5%)	270 (37.1%)	445 (30.2%)	<0.01
Active smoking	117 (15.7%)	162 (22.3%)	239 (18.9%)	<0.01
Congestive heart failure or Left ventricular systolic dysfunction	91(12.2%)	127 (17.5%)	218 (14.8%)	<0.01
Estimated glomerular filtration rate <90 ml/min/1.73m <sup>2</sup>	93.0 (12.4%)	129 (17.8%)	222.0 (15.1%)	<0.01
Hypertension	546 (73.2%)	564 (77.6%)	1111(75.4%)	0.05
Hyperlipidemia	415 (55.9%)	440 (60.5%)	855 (58.2%)	0.06
Diabetes Mellitus	234 (35.0%)	245 (33.8%)	479 (32.6%)	0.33
Family history of premature coronary artery disease	121 (16.2%)	98 (13.5%)	219 (14.9%)	0.14

SD = standard deviation.

radiologists and cardiologists) before collection of data; therefore, the investigators reported the predetermined report.

The 2013 AUC for Multimodality Imaging report was used to evaluate the indication and appropriateness of each MPI scan.<sup>1</sup> The appropriateness category was determined by multiple adjudicators, and 800 studies were allocated to the primary investigator (A.A.) and the remaining studies were divided equally among the rest of investigators (internal medicine hospitalists). Before data collection, a senior cardiologist met all investigators to explain the 80 clinical scenarios and each of the AUC categories (appropriate, maybe appropriate, and rarely appropriate). A smartphone application (2014 Astellas Pharma US, Inc., Northbrook, Illinois) was used to facilitate the process, and a monthly meeting was held to review the determination of the indication and corresponding appropriateness. The application is an electronic version of the 2013 AUC and uses a hierarchical algorithm based on specific information such as preoperative cardiac assessment for noncardiac surgery, previous noninvasive procedures and revascularizations, presence of angina or angina equivalence, other cardiovascular conditions, or for exercise prescription. The pretest probability was determined using the Diamond and Forrester criteria for symptomatic patients and by the Framingham 10-year global cardiovascular risk for asymptomatic patients.<sup>8,9</sup> In addition, the metabolic equivalents level was calculated from the history of maximum capacity of activity, or when unobtainable, was considered as unknown.

The primary outcome was appropriateness rates based on gender. Secondary outcomes were gender differences in (1) abnormal test results, defined by summed stress score >3; (2) subsequent angiography and revascularization; and (3) myocardial infarction and death from any cause. We also ranked the most commonly observed AUC scenarios for men and women in the rarely appropriate subgroups. Statistical analysis was performed using SPSS IBM version 22 (IBM, Armonk, New York). Chi-square or Fisher's exact tests were used to compare categorical variables; the Student *t* test was used to compare continuous variables. Univariate analysis was used to compare baseline characteristics, as well as primary and secondary outcomes in women and men. A multivariate logistic regression model was created to

Table 2

Appropriateness of myocardial perfusion imaging for both men and women

Variable	Women 747	Men 728	Total 1475
Appropriate	581 (77.8%)	596 (81.8%)	1177 (79.8%)
Maybe appropriate	48 (6.4%)	70 (9.6%)	118 (8.0%)
Rarely appropriate	118 (15.8%)	62 (8.5%)	180 (12.2%)

Test of heterogeneity *p* <0.01.

determine factors associated with rarely appropriate testing (yes/no) as the dependent variable and gender and other covariates as the independent variables. Covariates included age, body mass index, CAD, active smoking, congestive heart failure or left ventricular systolic dysfunction, estimated glomerular filtration rate <90, hypertension, hyperlipidemia, diabetes mellitus, and family history of premature CAD. *p* Values less than 0.01, 2-sided, were considered statistically significant.

## Results

A total of 1,475 SPECT MPIs were analyzed, and half were performed in women 747 (50.6%). Table 1 lists a comparison of the cohort characteristics. Women had lower prevalence of key co-morbidities such as CAD, active smoking, congestive heart failure or left ventricular systolic dysfunction, estimated glomerular filtration rate <90, *p* <0.05. In contrast, the prevalence of diabetes mellitus, hyperlipidemia, and family history of premature CAD was not different between men and women. In the total cohort, 180 (12.2%) tests were rarely appropriate; women were more likely to have rarely appropriate MPI compared with men (15.8% vs 8.5%, respectively), *p* <0.01 (Table 2). After including covariates into a multivariate logistic regression model, women gender was one of the most significant predictors of rarely appropriate testing (odds ratio 2.4, 95% CI 1.6 to 3.4), *p* <0.01 (see Supplementary Table 1). Regardless of the appropriateness category, an abnormal MPI was less likely to occur in women 102 (13.6%) than in men 183 (25.6%; odds ratio 0.47, 95% CI 0.35 to 0.60), *p* <0.01. However, in the rarely appropriate category, the rates of abnormal MPI results were similar between women 118 (8.5%) and men 62 (9.7%), *p* = 0.78

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