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# Myocardial Perfusion Imaging Is a Strong Predictor of Death in Women

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**OBJECTIVES** We sought to assess the prognostic value and risk classification improvement using contemporary single-photon emission computed tomography myocardial perfusion imaging (SPECT-MPI) to predict all-cause mortality.

**BACKGROUND** Myocardial perfusion is a strong estimator of prognosis. Evidence published to date has not established the added prognostic value of SPECT-MPI nor defined an approach to detect improve classification of risk in women from a developing nation.

**METHODS** A total of 2,225 women referred for SPECT-MPI were followed by a mean period of 3.7 ± 1.4 years. SPECT-MPI results were classified as abnormal on the presence of any perfusion defect. Abnormal scans were further classified as with mild/moderate reversible, severe reversible, partial reversible, or fixed perfusion defects. Risk estimates for incident mortality were categorized as <1%/year, 1% to 2%/year, and >2%/year using Cox proportional hazard models. Risk-adjusted models incorporated clinical risk factors, left ventricular ejection fraction (LVEF), and perfusion variables.

**RESULTS** All-cause death occurred in 139 patients. SPECT-MPI significantly risk stratified the population; patients with abnormal scans had significantly higher death rates compared with patients with normal scans, 13.1% versus 4.0%, respectively ($p < 0.001$). Cox analysis demonstrated that after adjusting for clinical risk factors and LVEF, SPECT-MPI improved the model discrimination (integrated discrimination index = 0.009; $p = 0.02$), added significant incremental prognostic information (global chi-square increased from 87.7 to 127.1; $p < 0.0001$), and improved risk prediction (net reclassification improvement = 0.12; $p = 0.005$).

**CONCLUSIONS** SPECT-MPI added significant incremental prognostic information to clinical and left ventricular functional variables while enhancing the ability to classify this Brazilian female population into low- and high-risk categories of all-cause mortality. (J Am Coll Cardiol Img 2011;4:880–8) © 2011 by the American College of Cardiology Foundation

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Interest and emphasis on research concerning women and heart disease has grown substantially with increasing recognition of the importance of heart disease related to the female sex (1). However, a concerning gap in the knowledge, understanding, and general awareness of ischemic heart disease (IHD) in women still remains. Evidence-based guidelines for the prevention and treatment of IHD rely largely on the results of randomized clinical trials where women are usually underrepresented (2–4).

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The ability of single-photon emission computed tomography myocardial perfusion imaging (SPECT-MPI) to evaluate myocardial perfusion and left ventricular ejection fraction (LVEF) is well documented (5,6). Previous studies have determined the incremental prognostic value of myocardial perfusion and LVEF data to predict adverse outcomes in several subgroups, using different stress methods and radionuclide tracers (7–11). Most studies that evaluated the prognostic value of SPECT-MPI in women collected data before the year 2000 (12–14). In the following years, important changes in IHD treatment were introduced in clinical practice (15,16).

The spectrum of IHD varies across different ethnic populations and environments. Statistics from the World Health Organization reveal that IHD is the leading cause of death worldwide for adult women. Brazil, like other developing countries, has a highly variable racial, variable ethnical, and socioeconomically diverse population with a projected 40% increase in IHD mortality in young-to-middle-aged individuals (17). This study assessed the contemporary prognostic value of SPECT-MPI in women of a developing nation, with all-cause mortality as the main adverse outcome. We also evaluated the extent to which adding myocardial perfusion to a model based on traditional risk factors and LVEF correctly reclassified subjects in terms of risk of future all-cause mortality events.

## METHODS

**Study population.** The study cohort comprised 2,427 consecutive female patients between 55 and 75 years of age who underwent SPECT-MPI between March 2004 and October 2007 at Quanta Diagnostico Nuclear, Curitiba, Brazil. Reasons for SPECT-MPI referral included chest pain evaluation, systolic dysfunction investigation, surveillance of known IHD, diabetes mellitus workup, preoperative workup, and evaluation due to abnormal or inconclusive treadmill test. Clinical data were collected prospectively at study entrance. The only pre-specified exclusion criteria were sex and age, since males and older individuals have distinct IHD risk patterns and were out of the scope of the present investigation. The study was approved by the institutional review board, and all participants gave written informed consent.

**Imaging acquisition protocol.** All participants were submitted to stress (exercise or pharmacological protocols) and rest studies after intravenous injection of 20 to 25 mCi of $^{99m}$Tc-sestamibi, based on patient weight. Conventional image protocol acquisition using standard energy windows for $^{99m}$Tc in dual-head gamma cameras with a low-energy all-purpose collimator was performed. No attenuation or scatter correction was used. Images started 30 to 60 min after injection in the resting state and 15 to 30 min after injection at peak stress. An electrocardiography-gated SPECT acquisition was also performed.

**Image interpretation.** Semiquantitative visual interpretation of SPECT-MPI was performed by consensus of 2 experienced, board-certified observers using short-axis and vertical long-axis slices, divided into 17 standard segments for each patient (18). Each segment was scored based on the tracer uptake as: 0, normal; 1, mildly reduced; 2, moderately reduced; 3, severely reduced; and 4, absent tracer uptake in rest and stress images. A summed rest score (SRS) and summed stress score (SSS) were obtained by adding the scores of the 17 segments of the rest and stress images, respectively. The summed difference score (SDS) was determined by subtracting the SRS from the SSS. Studies were classified as normal (SSS $<4$) or abnormal (SSS $\geq 4$). Abnormal studies were further classified as having mild-to-moderate complete reversible perfusion defects (SSS = 4 to 12 and SRS $<4$), severe complete reversible perfusion defects (SSS $\geq 13$ and SRS $<4$), partial reversible perfusion defects (SSS $\geq 4$, SRS $>4$, and SDS $\geq 2$), or only fixed perfusion defects (SSS $\geq 4$ and SDS $<2$). The gated images were processed by quantified gated SPECT software (QGS, Cedars-Sinai, Los Angeles, California) to obtain post-stress LVEF.

**ABBREVIATIONS AND ACRONYMS**

**CI** = confidence interval
**HR** = hazard ratio
**IDI** = integrated discrimination index
**IHD** = ischemic heart disease
**LVEF** = left ventricular ejection fraction
**NRI** = net reclassification improvement
**SDS** = summed difference score
**SPECT-MPI** = single-photon emission computed tomography myocardial perfusion imaging
**SRS** = summed rest score
**SSS** = summed stress score