The feminine mystique of AUC

Regina S. Druz, MD, FACC, FASNC[a,b]

[a] Integrative Cardiology Center of Long Island, Mineola, NY
[b] Hofstra NSLIJ School of Medicine, Hempstead, NY

Received Aug 10, 2015; accepted Aug 10, 2015
doi:10.1007/s12350-015-0271-8

See related article, pp. 695–705

In her well-known book, ''The Feminine Mystique'' (1963), psychologist Betty Friedan argues that biased portrayal of women in the media created a perception that women were naturally fulfilled by domestic duties and risked unhappiness in choosing career path over family.[1] Coining the term ''feminine mystique'' to describe this phenomenon, the author convincingly showed how it precluded many women from self-actualization beyond their biological role, and stunted their growth. Mrs. Friedan book is widely credited with ushering a second wave of feminism in the 1970s, and advancing opportunities for women in all spheres of American life.

Betty Friedan died of congestive heart failure in 2006, at the age of 85. In 2003, forty years after the ''Feminine Mystique,'' the National Heart, Lung and Blood Institute, the American Heart Association, and other organizations joined forces to raise awareness with a goal to educate and unravel gender disparities in pathophysiology, presentation, and prognosis of heart disease. It is ironic, however, that we still have our own case of ''feminine mystique'' in myocardial perfusion imaging (MPI). Several recent studies suggested that women are more likely to receive inappropriate (rarely appropriate) testing, and some questioned if the use of the appropriateness use criteria (AUC, 2009) for SPECT MPI in women is justified given lower age-adjusted prevalence of CAD, and differences in pathophysiology and clinical presentations.[2-6] The use of AUC is impactful on referral and reimbursement, as well as downstream resource utilization.

In this issue of the journal, Doukky et al. investigated the appropriateness of AUC SPECT for women, dispelling the ''feminine mystique'' of MPI observed in prior studies.[7] Doukky et al. report on a sub-study of the prospectively recruited cohort of 1511 patients, all undergoing clinically indicated SPECT in the office-based setting, with the majority referred by primary care physicians. The primary end-point was a composite of major adverse cardiac events (MACE), defined as cardiac death, non-fatal myocardial infarction, or coronary revascularizations triggered by MPI findings, while the secondary end-point was a similarly defined composite MACE for early ($\leq$6 months) or late (>6 months) post-MPI events. Revascularization procedures performed within 6 months of SPECT were considered to be triggered by the MPI findings while those beyond the 6 months were deemed to be due to a clinical change. Using regression models, authors investigated gender association of observed outcomes with the clinical and imaging predictors across the AUC spectrum, with AUC category assigned by a computer-based logic.

As may be expected, women undergoing SPECT MPI were older but at a lower 10-year Framingham risk, with lower likelihood and lower prevalence of obstructive CAD, and less likely to exercise. Women were more likely to be tested for chest pain syndromes, and had greater association for inappropriate SPECT MPI (OR 27.86, $P < .001$) even after adjustment for the clinical covariates of AUC determination (age, risk factors, ischemic equivalent symptoms, interpretable ECG, ability to exercise). Women had significantly lower prevalence of abnormal MPI, including ischemia and left ventricular dysfunction, in the entire cohort, and across all AUC subgroups (Figure 1). After adjusting for the clinical covariates, no interaction was observed between gender and the AUC categories as determinants of abnormal MPI findings, indicating that women had similar relative risk of abnormal MPI irrespective of the AUC group (Figure 2). Predictably, less abnormalities

Reprint requests: Regina S. Druz, MD, FACC, FASNC, Integrative Cardiology Center of Long Island, 121 Jericho Turnpike, Mineola, NY; *rdruzmd@aol.com, md@iccli.com*

J Nucl Cardiol 2016;23:706–9.
1071-3581/$34.00

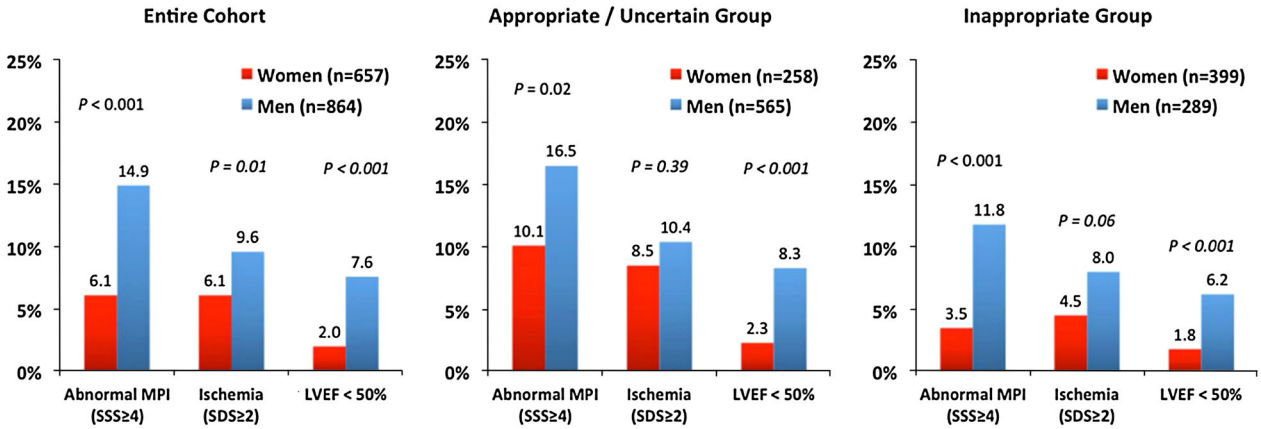

Figure 1. Myocardial perfusion imaging findings according to gender and appropriateness. *SSS*, Summed stress score; *SDS*, summed difference score; *LVEF*, left ventricular ejection fraction.

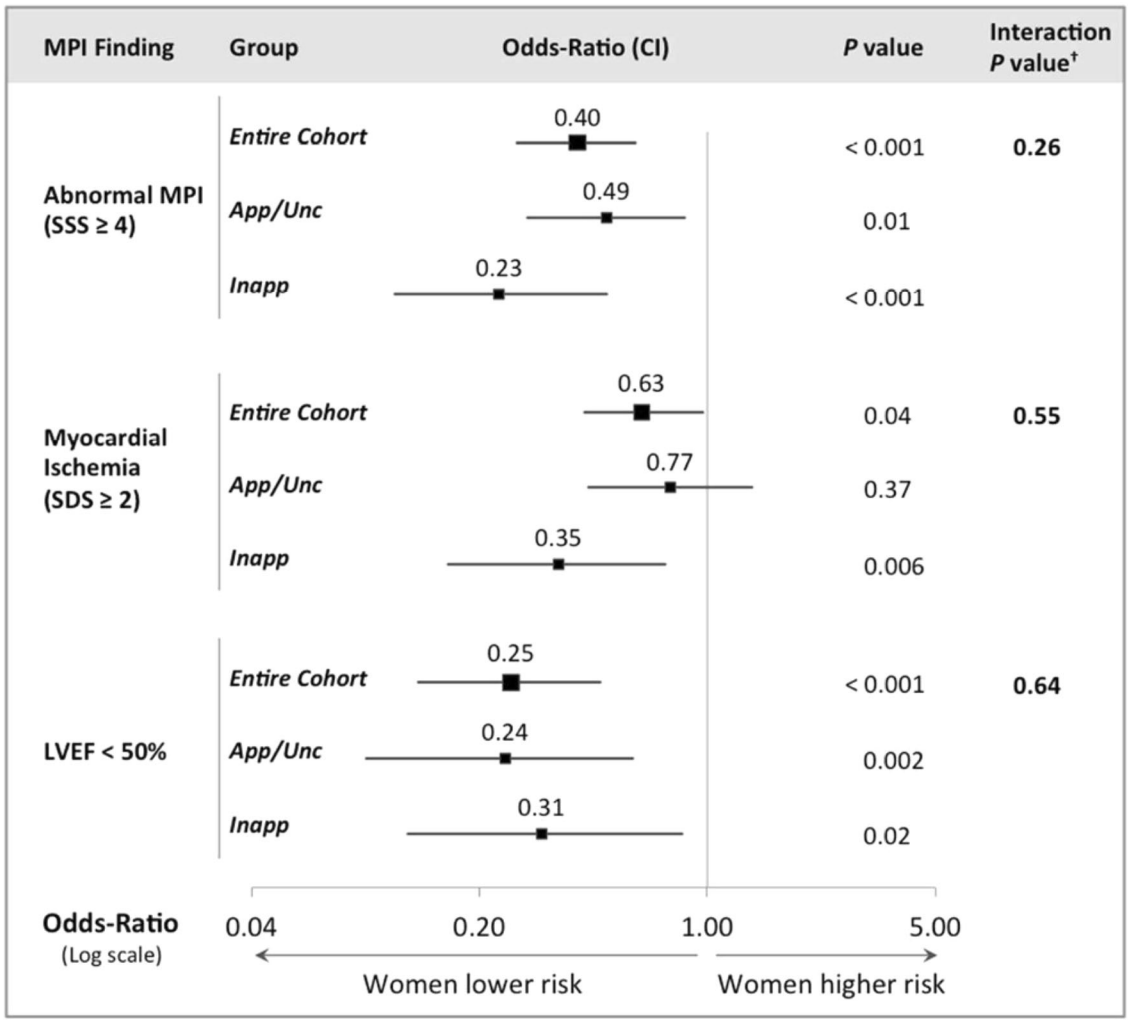

Figure 2. Impact of gender on myocardial perfusion imaging findings according to appropriateness. Subgroups—adjusted for clinical covariates.

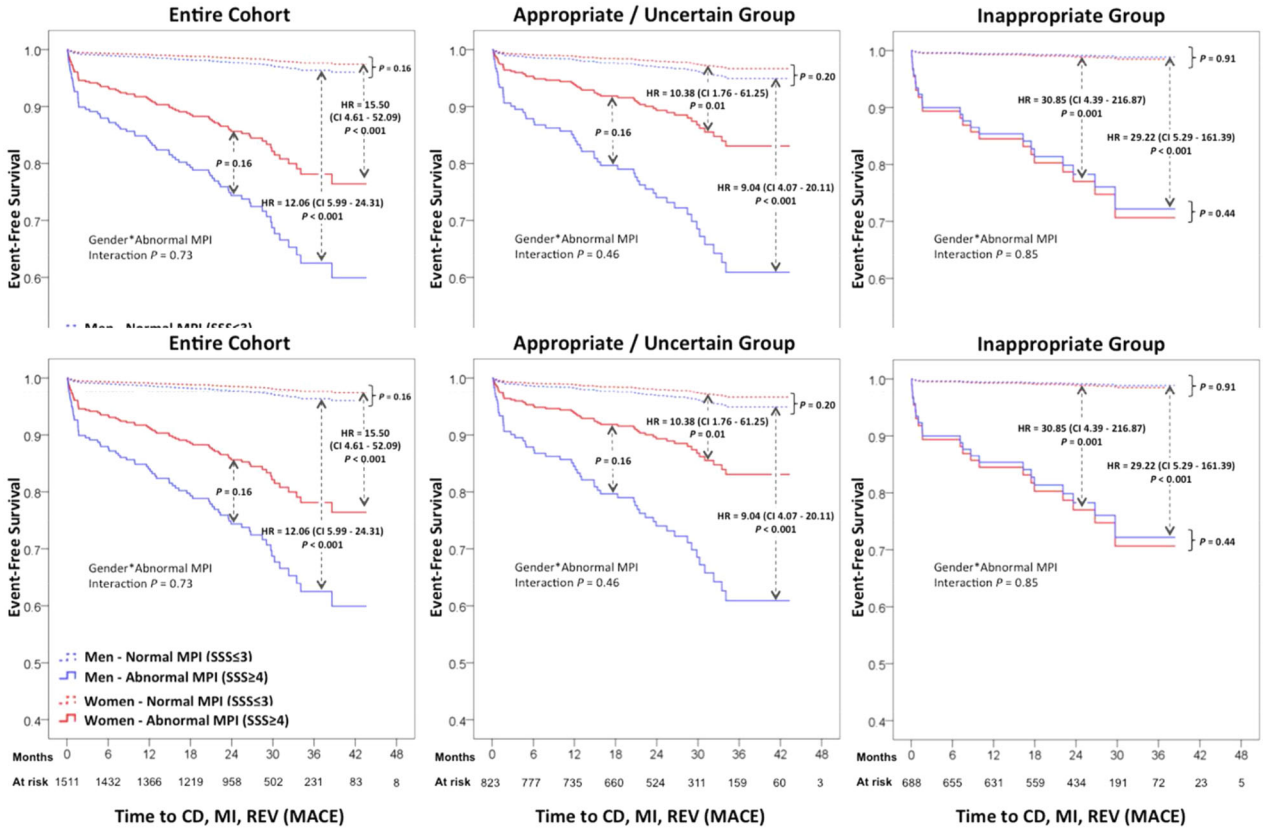

Figure 3. Major adverse cardiac events according to gender, perfusion imaging, and appropriateness Group. *HR*, Hazard ratio; *CI*, 95% confidence interval; *MPI*, SPECT myocardial Perfusion Imaging; *SSS*, summed stress score; *CD*, cardiac death; *MI*, non-fatal myocardial infarction; *REV*, coronary revascularization.

on the MPI resulted in less adverse outcomes for women, with no interaction observed between gender and AUC as predictors of MACE. Thus, the outcomes in women, while more favorable than in men, were not associated with AUC subgroups after adjustment for clinical and imaging covariates. Abnormal MPI, not gender or AUC subgroup, was the most powerful predictor of MACE (Figure 3).

So, does the study indeed dispel the case of ''feminine mystique'' for SPECT MPI? It certainly validates that AUC is a gender-neutral mechanism that does not adversely impact women in regard to abnormal MPI, or outcomes. However, a clinician is left with a sense of unease as yet another study found that despite more symptoms and less exercise, women were at a lower risk of obstructive CAD and its complications.

Perhaps, the power of feminine mystique is in making us look beyond the obvious, rudimentary definition of coronary artery disease as an obstructive entity? Newer risk determinants, including genetic and inflammatory markers and their relationship to endothelial dysfunction, are showing gender specificity, and may shed more light on risk prediction in women.[8,9] Until such markers are validated, we have to contend with the fact that the current methods may underestimate the true burden of CAD in women, specifically the non-obstructive CAD that manifests as a sudden clinical event. The understanding of the gender-specific pathophysiology and the differential influences of genetic, environmental, hormonal, and inflammatory predictors will undoubtedly re-shape our practice of cardiac imaging in the future.

Disclosure

No conflicts to disclose.

References

1. Friedan B. The feminine mystique. New York: WW Norton and Company; 1963.
2. Hendel RC, Berman DS, Di Carli MF, Heidenreich PA, Henkin RE, Pellikka PA, et al. ACCF/ASNC/ACR/AHA/ASE/SCCT/SCMR/SNM 2009 Appropriate Use Criteria for Cardiac Radionuclide Imaging: A Report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, the American

Society of Nuclear Cardiology, the American College of Radiology, the American Heart Association, the American Society of Echocardiography, the Society of Cardiovascular Computed Tomography, the Society for Cardiovascular Magnetic Resonance, and the Society of Nuclear Medicine. Endorsed by the American College of Emergency Physicians. J Am Coll Cardiol 2009;53:2201-29.

3. Mehta R, Ward RP, Chandra S, Agarwal R, Williams KA. Evaluation of the American College of Cardiology Foundation/American Society of Nuclear Cardiology appropriateness criteria for SPECT myocardial perfusion imaging. J Nucl Cardiol 2008;15:337-44.
4. Hendel RC, Cerqueira M, Douglas PS, Caruth KC, Allen JM, Jensen NC, et al. A multicenter assessment of the use of single-photon emission computed tomography myocardial perfusion imaging with appropriateness criteria. J Am Coll Cardiol 2010;55:156-62.
5. Gupta A, Tsiaras SV, Dunsiger SI, Tilkemeier PL. Gender disparity and the appropriateness of myocardial perfusion imaging. J Nucl Cardiol 2011;18:588-94.
6. Mehta R, Williams KA. AUC for SPECT: Is gender bias inappropriate. J Nucl Cardiol 2011;18:538-40.
7. Doukky, R, Hayes, K, Frogge, N. Appropriate use criteria for SPECT myocardial perfusion imaging: Are they appropriate for women? J Nucl Cardiol 2015. doi:10.1007/s12350-015-0233-1.
8. Ridker PM, Buring JE, Cook NR, Rifai N. C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events: An 8-year follow-up of 14,719 initially healthy American women. Circulation 2003;107:391-7.
9. Daniels LB, Maisel AS. Cardiovascular biomarkers and sex: The case for women. Nat Rev Cardiol. 2015. doi:10.1038/nrcardio.2015.105.