

# UCLA

## UCLA Previously Published Works

### Title

Diagnostic Accuracy of Exercise Electrocardiogram in Women

### Permalink

<https://escholarship.org/uc/item/74s1g79r>

### Journal

Journal of Women's Health, 27(4)

### ISSN

1540-9996

### Authors

Shaikh, Kashif  
Budoff, Matthew J

### Publication Date

2018-04-01

### DOI

10.1089/jwh.2017.6864

Peer reviewed

## Diagnostic Accuracy of Exercise Electrocardiogram in Women

Kashif Shaikh, MD and Matthew J. Budoff, MD, FACC

CORONARY HEART DISEASE (CHD) is believed to be under-recognized in women due to substantial differences in the type, frequency, and quality of symptoms as compared with that in men.<sup>1,2</sup> CHD is the leading cause of mortality among women in industrialized nations.<sup>3,4</sup> Our understanding of sex-specific differences in initial presentation, diagnostic evaluation, and clinical outcomes has changed considerably for the past 2 decades.<sup>1,5-7</sup> Functional testing for patients with chest pain has been the diagnostic test of choice.

In this issue of *Journal of Women's Health*, Knol et al.<sup>8</sup> report on an important topic about the diagnostic accuracy of exercise electrocardiogram (ECG) in female patients with low-intermediate risk for coronary artery disease (CAD) compared with the diagnostic accuracy of coronary computed tomography angiography (CCTA) in contemporary times. They showed that for >50% stenosis on CCTA, exercise ECG was negative in 46%, inconclusive in 52%, and positive in only 2% of patients. Also, 64% of patients with positive exercise ECG had no CAD, whereas other 29% patients had a nonobstructive disease. This study shows even lower diagnostic accuracy than previous studies,<sup>9</sup> likely due to lower probability patients are being referred. Higher rates of inconclusive and false positive test results decrease the confidence in test and perhaps explain the higher number of invasive coronary angiography (ICA) in women, which consistently show majority cases with nonobstructive disease.<sup>9,10</sup> In current clinical practice, a majority of patients who undergo ICA after functional testing have normal or nonobstructive CAD.<sup>11</sup> The poor performance of exercise ECG overall and specifically in women calls for an alternative strategy to evaluate women with chest pain. Recent landmark trials including PROMISE<sup>12</sup> (Prospective Multicenter Imaging Study for Evaluation of Chest Pain), CRESCENT<sup>13</sup> (Calcium Imaging and Selective CT Angiography in Comparison to Functional Testing for Suspected Coronary Artery Disease), and SCOT-HEART<sup>14</sup> trial (Scottish Computed Tomography of the Heart) provide much needed data on the effectiveness of CTA versus functional stress testing for evaluation of patients with suspected CAD. The PROMISE trial comparing CCTA versus functional test showed CCTA provides more prognostic and discriminatory information than functional testing, with the greatest benefit in women.<sup>15</sup> Similarly, recent sex-focused analysis of CRESCENT trial<sup>16</sup> reported that

a higher number of women in the CCTA arm had chest pain resolution than women who underwent functional testing (40% CCTA vs. 22% stress:  $p=0.026$ ). Women in the CCTA arm more frequently reached a final diagnosis ( $p<0.001$ ) and had lower downstream diagnostic testing than women in the functional testing arm of the study (leading to lower costs [in euros] 326 vs. 478,  $p<0.001$ ).<sup>16,17</sup> This study reported that the CCTA led to 49% of patients having alterations in their medical management. More patients were started on statins (18%) and aspirin (8%), whereas in others statins and aspirins were discontinued. This is in accordance with previous studies, in the PROMISE trial there was higher proportion of patients newly initiated on aspirin (51%) and statins (110% increase).<sup>18</sup> More preventive therapies were reported in the CCTA arm of the SCOT-HEART trial as well.<sup>19</sup>

American College of Cardiology/American Heart Association and European Society of Cardiology guidelines recommend functional stress testing as the first line as an initial diagnostic test of IHD.<sup>20,21</sup> However, based on diagnostic accuracy and cost-effectiveness, 2016 United Kingdom National Institute for Health and Care Excellence (NICE) guidelines recommend CCTA as the initial diagnostic test of choice in the evaluation of patients with suspected CAD.<sup>22</sup>

Atypical symptoms, false positive treadmills, breast attenuation artifacts, and a greater rate of functional incapacity often make an evaluation of CAD in women more challenging.<sup>1</sup> Despite lower prevalence of obstructive CAD by coronary angiography and more often preserved ejection fraction (EF), women with CAD have more adverse outcomes than men.<sup>2,23</sup> CCTA has a much higher sensitivity and specificity to identify obstructive CAD, as well as ability to identify a nonobstructive disease, making it better suited in women as a first line test.

### Author Disclosure Statement

Dr. Matthew J. Budoff is a consultant for General Electric; the other authors have no conflict of interest.

### References

1. Shaw LJ, Bairey Merz CN, Pepine CJ, et al. Insights from the NHLBI-Sponsored Women's Ischemia Syndrome Evaluation (WISE) Study: Part I: Gender differences in traditional and novel risk factors, symptom evaluation, and

- gender-optimized diagnostic strategies. *J Am Coll Cardiol* 2006;47(3 Suppl):S4–S20.
2. Douglas PS, Ginsburg GS. The evaluation of chest pain in women. *N Engl J Med* 1996;334:1311–1315.
  3. Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart disease and stroke statistics—2017 update: A report from the American Heart Association. *Circulation* 2017;135:e146–e603.
  4. Stramba-Badiale M, Fox KM, Priori SG, et al. Cardiovascular diseases in women: A statement from the policy conference of the European Society of Cardiology. *Eur Heart J* 2006;27:994–1005.
  5. Mosca L, Barrett-Connor E, Wenger NK. Sex/gender differences in cardiovascular disease prevention: What a difference a decade makes. *Circulation* 2011;124:2145–2154.
  6. Mosca L, Benjamin EJ, Berra K, et al. Effectiveness-based guidelines for the prevention of cardiovascular disease in women—2011 update: A guideline from the American Heart Association. *J Am Coll Cardiol* 2011;57:1404–1423.
  7. Mosca L, Appel LJ, Benjamin EJ, et al. Evidence-based guidelines for cardiovascular disease prevention in women. *Circulation* 2004;109:672–693.
  8. Knol R, Kan H, Corneul J, Umans V, Van der P, Van der Zant F. Exercise ECG neither predicts nor excludes coronary artery disease in women with low to intermediate risk. *J Women's Health* 2017. [Epub ahead of print] DOI: 10.1089/jwh.2017.6433.
  9. Patel MR, Peterson ED, Dai D, et al. Low diagnostic yield of elective coronary angiography. *N Engl J Med* 2010;362:886–895.
  10. Shaw LJ, Shaw RE, Merz CN, et al. Impact of ethnicity and gender differences on angiographic coronary artery disease prevalence and in-hospital mortality in the American College of Cardiology-National Cardiovascular Data Registry. *Circulation* 2008;117:1787–1801.
  11. Neglia D, Rovai D, Caselli C, et al. Detection of significant coronary artery disease by noninvasive anatomical and functional imaging. *Circ Cardiovasc Imaging* 2015;8:e002179.
  12. Douglas PS, Hoffmann U, Patel MR, et al. Outcomes of anatomical versus functional testing for coronary artery disease. *N Engl J Med* 2015;372:1291–1300.
  13. Lubbers M, Dedic A, Coenen A, et al. Calcium imaging and selective computed tomography angiography in comparison to functional testing for suspected coronary artery disease: The multicentre, randomized CRESCENT trial. *Eur Heart J* 2016;37:1232–1243.
  14. The SCOT-HEART investigators. CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): An open-label, parallel-group, multicentre trial. *Lancet* (London, England) 2015;385:2383–2391.
  15. Pagidipati NJ, Hemal K, Coles A, et al. Sex differences in functional and CT angiography testing in patients with suspected coronary artery disease. *J Am Coll Cardiol* 2016;67:2607–2616.
  16. Lubbers M, Coenen A, Bruning T, et al. Sex differences in the performance of cardiac computed tomography compared with functional testing in evaluating stable chest pain: Subanalysis of the multicenter, randomized CRESCENT trial (Calcium Imaging and Selective CT Angiography in Comparison to Functional Testing for Suspected Coronary Artery Disease). *Circ Cardiovasc Imaging* 2017;10:e005295.
  17. Pagidipati NJ, Douglas PS. The puzzle of noninvasive testing in women: Filling in the pieces with the CRESCENT trial (Calcium Imaging and Selective CT Angiography in Comparison to Functional Testing for Suspected Coronary Artery Disease). *Circ Cardiovasc Imaging* 2017;10:e006085.
  18. Ladapo JA, Hoffmann U, Lee KL, et al. Changes in medical therapy and lifestyle after anatomical or functional testing for coronary artery disease. *J Am Heart Assoc* 2016;5:e003807.
  19. Williams MC, Hunter A, Shah ASV, et al. Use of coronary computed tomographic angiography to guide management of patients with coronary disease. *J Am Coll Cardiol* 2016;67:1759–1768.
  20. Fihn SD, Gardin JM, Abrams J, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: A report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *Circulation* 2012;126:e354–e471.
  21. Montalescot G, Sechtem U, Achenbach S, et al. 2013 ESC guidelines on the management of stable coronary artery disease: The Task Force on the management of stable coronary artery disease of the European Society of Cardiology. *Eur Heart J* 2013;34:2949–3003.
  22. Budoff MJ. The 2016 National Institute for Health and Care Excellence guidelines for chest pain: Better outcomes with cardiac CT. *BMJ J* 2017 [Epub ahead of print]; doi: 10.1136/heartjnl-2017-311776.
  23. Mieres JH, Gulati M, Bairey Merz N, et al. Role of non-invasive testing in the clinical evaluation of women with suspected ischemic heart disease: A consensus statement from the American Heart Association. *Circulation* 2014;130:350–379.

Address correspondence to:  
 Matthew J. Budoff, MD, FACC  
 Department of Cardiology  
 Los Angeles Biomedical Research Institute  
 Harbor-UCLA Medical Center  
 1124 W. Carson Street  
 Torrance, CA 90502-2006

E-mail: mbudoff@labiomed.org