# Sex Differences in Advanced Cardiac MRI Assessment

*Karen Ordovas, MD, MAS*

**Karen Ordovas, MD, MAS,** is a professor in residence, director of cardiac imaging in the department of radiology and biomedical imaging at the University of California, San Francisco. She specializes in cardiac and pulmonary imaging, in particular cardiovascular CT and MRI at the UCSF Imaging Center. She received her medical degree from Universidade Federal do Rio Grande do Sul, Brazil, and completed her residency in radiology at the Instituto de Cardiologia do Rio Grande do Sul, Brazil. She has completed research and clinical fellowships in cardiothoracic radiology at UCSF and earned a master's degree in clinical research from the department of epidemiology and biostatistics at UCSF. Dr Ordova's research interests include establishing evidence-based applications for coronary CT angiography and cardiac MRI in several clinical settings. Her articles have appeared in *Radiology*, *American Journal of Cardiology*, *JACC: Cardiovascular Imaging*, and *Stroke: A Journal of Cerebral Circulation*.

It is of ultimate importance that physicians understand sex and gender differences in cardiovascular disease presentation and response to interventions (1). More specifically, the classic medical knowledge of cardiovascular diseases derives primarily from experimental models and clinical studies with underrepresentation of female subjects (2). Awareness of the historical gender-biased approach to cardiovascular disease has led to many initiatives from professional societies and funding agencies to ensure sex differences are captured in basic and clinical research in the field (3).

Following this new norm in biomedical research, the current study by Rutkowski et al (4) investigates sex differences in cardiac imaging parameters obtained from advanced cardiac MRI technology for in vivo assessment of cardiac efficiency and flow dynamics: four-dimensional (4D) flow MRI. The investigators present the first study comparing kinetic energy as measured by using 4D flow cardiac MRI between healthy male and female volunteers and show that there is significant difference in left ventricular vorticity between male and female subjects. The study findings introduce the concept that there are cardiac efficiency discrepancies between sexes that can be measured by advanced cardiac MRI and should be taken into account when assessing cardiac health.

The field of 4D cardiac MRI has developed significantly in the past few years. Most studies have focused on comparison of 4D flow–derived cardiac MRI parameters between healthy volunteers and a small sample of patients with known cardiovascular disease (5–7). In addition, some groups have proposed normal ranges for 4D flow parameters, with particular emphases in differences between age groups (8,9). Very few previous publications have highlighted sex or gender differences in 4D flow parameters. Föll et al have documented sex-related differences in ventricular flow vorticity which were not explained by ventricular geometric differences (10). Garcia et al have shown that peak flow velocity of the aorta measured by 4D flow was significantly different between male and female sexes, even when controlling for heart rate (11).

When looking at different advanced cardiac MRI techniques such as multiparametric imaging, several investigators have documented sex differences in T1, T2, T2*, and extracellular volume (ECV) parameters in healthy volunteers. Roy et al have shown that mean myocardial T1 and ECV at 3 T were significantly greater in age-matched women than in men, whereas T2 and T2* values were not different between the sexes (12). Similarly, Liu et al have analyzed data from the Multi-Ethnic Study of Atherosclerosis (MESA) cohort and showed that women had significantly greater ECV and native T1 compared to men, as well as lower post-contrast T1 values (all $P < .05$) (13). However, there are no large data sets to date to determine sex-specific normal ranges for these parameters.

In the clinical arena, sex-specific standards of reference for cardiac MRI parameters are available, including cardiac volumes, function, and mass (14,15). More recently, the European Association of Cardiovascular Imaging has published an expert consensus on classification of cardiac MRI abnormal values into mild, moderate, and severe ranges, including sex-specific recommendations (16). In addition, cardiology guidelines for imaging diagnosis and disease management include some sex-specific recommendations, such as on cardiac MRI diagnosis of arrhythmogenic right ventricular cardiomyopathy (17) and adults with congenital heart diseases (18).

In summary, the work by Rutkowski et al is a small hypothesis-generating study applying advanced cardiac MRI to better understand sex difference in cardiac efficiency. However, the data presented in this article can be extremely useful to guide future study designs and to inform important research questions for subsequent clinical studies in the field.

**Disclosures of Conflicts of Interest: K.O.** Activities related to the present article: disclosed no relevant relationships. Activities not related to the present article: consultant for Arterys. Other relationships: disclosed no relevant relationships.

From the Department of Radiology, University of California–San Francisco Ringgold Standard Institution, 550 Parnassus Ave, Box 0628, San Francisco, CA 94143. Received December 19, 2019; revision requested December 23; revision received January 31, 2020; accepted February 4. **Address correspondence to** the author (e-mail: *karen.ordovas@ucsf.edu*).

See also the article by Rutkowski et al in this issue. Conflicts of interest are listed at the end of this article.

## References


1. Mosca L, Barrett-Connor E, Wenger NK. Sex/gender differences in cardiovascular disease prevention: what a difference a decade makes. Circulation 2011;124(19):2145–2154.
2. Dougherty AH. Gender balance in cardiovascular research: importance to women's health. Tex Heart Inst J 2011;38(2):148–150.
3. Pilote L, Raparelli V. Participation of Women in Clinical Trials: Not Yet Time to Rest on Our Laurels. J Am Coll Cardiol 2018;71(18):1970–1972 [Published correction appears in J Am Coll Cardiol 2018;71(23):2716.].
4. Rutkowski DR, Barton GP, François CJ, Aggarwal N, Roldán-Alzate A. Sex Differences in Cardiac Flow Dynamics in Healthy Volunteers. Radiol Cardiothorac Imaging 2020;2(1):e190058.
5. Hope MD, Hope TA, Crook SE, et al. 4D flow CMR in assessment of valve-related ascending aortic disease. JACC Cardiovasc Imaging 2011;4(7):781–787.
6. Browning JR, Hertzberg JR, Schroeder JD, Fenster BE. 4D Flow Assessment of Vorticity in Right Ventricular Diastolic Dysfunction. Bioengineering (Basel) 2017;4(2):E30.
7. Jeong D, Anagnostopoulos PV, Roldan-Alzate A, et al. Ventricular kinetic energy may provide a novel noninvasive way to assess ventricular performance in patients with repaired tetralogy of Fallot. J Thorac Cardiovasc Surg 2015;149(5):1339–1347.
8. Barker AJ, Roldán-Alzate A, Entezari P, et al. Four-dimensional flow assessment of pulmonary artery flow and wall shear stress in adult pulmonary arterial hypertension: results from two institutions. Magn Reson Med 2015;73(5):1904–1913.
9. Crandon S, Westenberg JJM, Swoboda PP, et al. Impact of Age and Diastolic Function on Novel, 4D flow CMR Biomarkers of Left Ventricular Blood Flow Kinetic Energy. Sci Rep 2018;8(1):14436.
10. Föll D, Taeger S, Bode C, Jung B, Markl M. Age, gender, blood pressure, and ventricular geometry influence normal 3D blood flow characteristics in the left heart. Eur Heart J Cardiovasc Imaging 2013;14(4):366–373.
11. Garcia J, Barker AJ, van Ooij P, et al. Assessment of altered three-dimensional blood characteristics in aortic disease by velocity distribution analysis. Magn Reson Med 2015;74(3):817–825.
12. Roy C, Slimani A, de Meester C, et al. Age and sex corrected normal reference values of T1, T2 T2* and ECV in healthy subjects at 3T CMR. J Cardiovasc Magn Reson 2017;19(1):72.
13. Liu CY, Liu YC, Wu C, et al. Evaluation of age-related interstitial myocardial fibrosis with cardiac magnetic resonance contrast-enhanced T1 mapping: MESA (Multi-Ethnic Study of Atherosclerosis). J Am Coll Cardiol 2013;62(14):1280–1287.
14. Maceira AM, Prasad SK, Khan M, Pennell DJ. Normalized left ventricular systolic and diastolic function by steady state free precession cardiovascular magnetic resonance. J Cardiovasc Magn Reson 2006;8(3):417–426.
15. Kawel-Boehm N, Maceira A, Valsangiacomo-Buechel ER, et al. Normal values for cardiovascular magnetic resonance in adults and children. J Cardiovasc Magn Reson 2015;17(1):29.
16. Petersen SE, Aung N, Sanghvi MM, et al. Reference ranges for cardiac structure and function using cardiovascular magnetic resonance (CMR) in Caucasians from the UK Biobank population cohort. J Cardiovasc Magn Reson 2017;19(1):18.
17. Marcus FI, McKenna WJ, Sherrill D, et al. Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the task force criteria. Circulation 2010;121(13):1533–1541.
18. Stout KK, Daniels CJ, Aboulhosn JA, et al. 2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2019;73(12):e81–e192 [Published correction appears in J Am Coll Cardiol 2019;73(18):2361–2362.].