

# Effect of Sex Differences on Invasive Measures of Coronary Microvascular Dysfunction in Patients With Angina in the Absence of Obstructive Coronary Artery Disease



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**CME Objective for This Article:** At the completion of this article, the learner should be able to: 1) appraise the current understanding of coronary microvascular function and its role in patients presenting with angina in the absence of obstructive coronary artery disease; 2) define coronary flow reserve in patients with angina in the absence of obstructive coronary atherosclerosis; and 3) define the index of microcirculatory resistance in patients with angina in the absence of obstructive coronary atherosclerosis.

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## ABSTRACT

**OBJECTIVES** This study investigated sex differences in coronary flow reserve (CFR) and the index of microcirculatory resistance (IMR) in patients with angina in the absence of obstructive coronary artery disease.

**BACKGROUND** Coronary microvascular dysfunction is associated with worse long-term outcomes, especially in women. Coronary flow reserve (CFR) and the index of microcirculatory resistance (IMR) are 2 methods of assessing the coronary microcirculation.

**METHODS** We prospectively enrolled 117 women and 40 men with angina in the absence of obstructive coronary artery disease. We performed CFR, IMR, fractional flow reserve, and quantitative coronary angiography in the left anterior descending artery. Coronary flow was assessed with a thermodilution method by obtaining mean transit time ( $T_{mn}$ ) (an inverse correlate to absolute flow) at rest and hyperemia.

**RESULTS** All patients had minimal atherosclerosis by quantitative coronary angiography (% diameter stenosis:  $23.2 \pm 12.3\%$ ), and epicardial disease was milder in women (fractional flow reserve:  $0.88 \pm 0.04$  vs.  $0.87 \pm 0.04$ ;  $p = 0.04$ ). IMR was similar between the sexes ( $20.7 \pm 9.8$  vs.  $19.1 \pm 8.0$ ;  $p = 0.45$ ), but CFR was lower in women ( $3.8 \pm 1.6$  vs.  $4.8 \pm 1.9$ ;  $p = 0.004$ ). This was primarily due to a shorter resting  $T_{mn}$  in women ( $p = 0.005$ ), suggesting increased resting coronary flow, whereas hyperemic  $T_{mn}$  was identical ( $p = 0.79$ ). In multivariable analysis, female sex was an independent predictor of lower CFR and shorter resting  $T_{mn}$ .

**CONCLUSIONS** Despite similar microvascular function in women and men by IMR, CFR is lower in women. This discrepancy appears to be due to differences in resting coronary flow between the sexes. The effect of sex differences should be considered in interpretation of physiological indexes using resting coronary flow. (J Am Coll Cardiol Intv 2015;8:1433-41) © 2015 by the American College of Cardiology Foundation.

Women are more likely than men to have angina in the absence of coronary artery disease (CAD) (1-3), and coronary microvascular dysfunction has been proposed as one of the explanations of this phenomenon (4). Invasively, coronary flow reserve (CFR) is typically used to interrogate microvascular function, and low CFR has been associated with major adverse outcomes, including myocardial infarction and death (5,6). Still, CFR is affected by epicardial influences and has a variability that limits its reproducibility. The index of microcirculatory resistance (IMR), on the other hand, is a direct measure of the microcirculation that has been shown to be largely independent of variations in hemodynamic state (7-9). Data remain limited on the use of CFR and IMR as measures of the coronary microvasculature, particularly between women and

men, where important sex differences in microvascular dysfunction have been reported (10). Therefore, we investigated the effect of sex differences on CFR and IMR in measuring coronary microvascular dysfunction in women and men with angina in the absence of obstructive CAD.

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## METHODS

**STUDY POPULATION.** We prospectively enrolled adult patients who were electively referred to the cardiac catheterization laboratory for coronary angiography because of a clinical suspicion of coronary ischemia based on the presence of angina, with or without an abnormal stress test. Typical angina was

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