

## Sex-dependent impact of coronary microvascular dysfunction on long-term clinical outcomes in patients with no-obstructive coronary artery disease

T. Toya, A. Ahmad, M.T. Corban, J.D. Sara, I. Ozcan, L.O. Lerman, A. Lerman

Mayo Clinic, Rochester, United States of America

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**Background:** Coronary vasomotor response is different between males and females. However, the prognostic impact of this difference in coronary physiologic indices has not been characterized in patients with no obstructive coronary artery disease (NOCAD).

**Purpose:** We aimed to investigate the sex-specific differences of coronary vasomotor function in response to adenosine in a large cohort of patients with NOCAD and its impact on long-term clinical outcomes

**Methods:** We included 668 NOCAD patients who underwent invasive coronary vasoreactivity testing using intracoronary incremental doses of adenosine (18–72 µg) with available follow-up data. Indices of coronary vasomotor response were compared between males and females, and their prognostic impact on major adverse cardiovascular events (MACE: death, myocardial infarction, revascularization, and stroke) were analyzed based on sex.

**Results:** Females (N=461, mean age 54±12 years) had lower baseline microvascular resistance (BMR) and higher baseline average peak velocity (APV) than males (N=207, mean age 53±13 years), while hyperemic microvascular resistance (HMR) and hyperemic APV were similar between males and females. Consequently, coronary flow reserve (CFR: hyperemic/baseline APV) and resistive reserve ratio (RRR: BMR/HMR) were lower in females than males (Figure 1A). Lower CFR and RRR, as well as lower BMR and higher baseline APV were associated with MACE only in males, but not in females. Higher HMR was the only predictor for MACE in females (Figure 1B).

**Conclusions:** Sex-specific differences in coronary vasomotor response to adenosine may provide different prognostic values between males and females.

Figure 1A

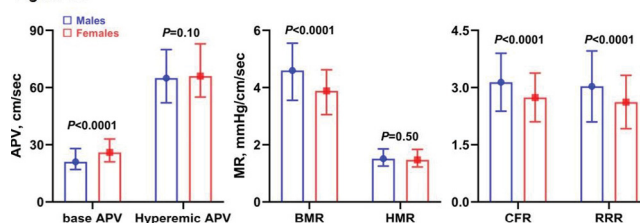


Figure 1B

**MACE (Univariate)**

**Baseline APV, cm/sec**

Total 1.00 [0.99, 1.02], P=0.57  
 Male 1.05 [1.01, 1.08], P=0.01  
 Female 1.00 [0.98, 1.02], P=0.92

**Hyperemic APV, cm/sec**

Total 1.00 [0.99, 1.00], P=0.31  
 Male 1.00 [0.98, 1.01], P=0.69  
 Female 1.00 [0.99, 1.01], P=0.52

**CFR**

Total 0.71 [0.55, 0.91], P=0.01  
 Male 0.43 [0.27, 0.67], P=0.0002  
 Female 0.72 [0.51, 1.02], P=0.06

**BMR, mm Hg/cm/sec**

Total 1.05 [0.94, 1.17], P=0.38  
 Male 0.83 [0.70, 0.99], P=0.04  
 Female 1.14 [0.98, 1.31], P=0.08

**HMR, mm Hg/cm/sec**

Total 1.56 [1.16, 2.08], P=0.03  
 Male 1.47 [0.90, 2.42], P=0.13  
 Female 1.58 [1.11, 2.28], P=0.01

**RRR**

Total 0.79 [0.64, 0.98], P=0.03  
 Male 0.50 [0.34, 0.72], P=0.002  
 Female 0.90 [0.67, 1.21], P=0.48

