



Research Letter

Association of Coronary Artery Dominance With Long-term Outcomes in Female Patients With Suspected Ischemia but Nonobstructive Coronary Artery Disease



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Background

Coronary artery dominance, referring to the arterial supply of the posterior descending artery (PDA), significantly impacts clinical outcomes in cardiac patients. Typically, the PDA originates from the right coronary artery in the right-dominant pattern, the most common form found in individuals. The less prevalent left-dominant type sees the PDA deriving from the left circumflex artery, and balanced dominance involves both the right coronary artery and left circumflex artery supplying the PDA. Notably, left coronary dominance has been found to be linked to adverse outcomes in patients with acute coronary syndrome who undergo percutaneous coronary interventions.¹ Additionally, for patients referred for computed tomography angiography, a study found that a left-dominant system was an independent predictor of nonfatal myocardial infarction and all-cause mortality.² However, the clinical implications of coronary dominance in female patients with ischemia and nonobstructive coronary artery disease (INOCA) are poorly understood. To explore this, we conducted a study using data from female participants in the National Heart, Lung, and Blood Institute-sponsored Women's Ischemia Syndrome Evaluation, examining the correlation between coronary dominance and major adverse cardiovascular events (MACE).

Methods

We evaluated female participants enrolled between 1996 and 2000 in the National Heart, Lung, and Blood Institute-sponsored Women's Ischemic Syndrome Evaluation study (NCT00000554) who were undergoing evaluation for suspected ischemia. Angiograms of these

participants, displaying no obstructive coronary artery disease, were deemed suitable for determining coronary artery dominance. A core laboratory carried out both qualitative and quantitative angiographic studies, operating under blind conditions to ensure objectivity, remaining unaware of all patient characteristics, including sex and outcomes. Coronary dominance was determined by the coronary artery supplying the PDA: characterized as left, right, or balanced. Information on all-cause death at 8 years (mean) follow-up and MACE (all-cause mortality, nonfatal myocardial infarction, nonfatal stroke, heart failure hospitalization) at 5.4 years were analyzed. χ^2 tests were used for categorical variables and Wilcoxon rank sum tests for continuous variables. Cox proportional hazard regression was used to explore the impact of coronary dominance on MACE, cardiovascular events, angina hospitalization, and overall survival. Angina hospitalization survival probability was analyzed by the Kaplan-Meier method.

Results

Among 569 female participants, there was no significant difference in mean age, race, body mass index, and overall comorbidities. Patients with left-dominant circulation did not show an increased risk for MACE ($P = .7$), cardiovascular events ($P = .3$), and overall mortality ($P = .5$). However, patients with left-dominant circulation had an increased rate of hospitalizations for angina. At the end of follow-up, 14/44 (32%) patients with left-dominant circulations vs 99/438 (23%) of patients with right-dominant circulations had angina hospitalizations ($P = .041$, respectively) (Figure 1A). There was no significant difference found when globally comparing left-dominant, right-dominant, and balanced-dominant systems to one another ($P = .12$) (Figure 1B).

Keywords: coronary artery dominance; ischemia and nonobstructive coronary artery disease; Women's Ischemic Syndrome Evaluation; major adverse cardiovascular events; angina-related hospitalization.

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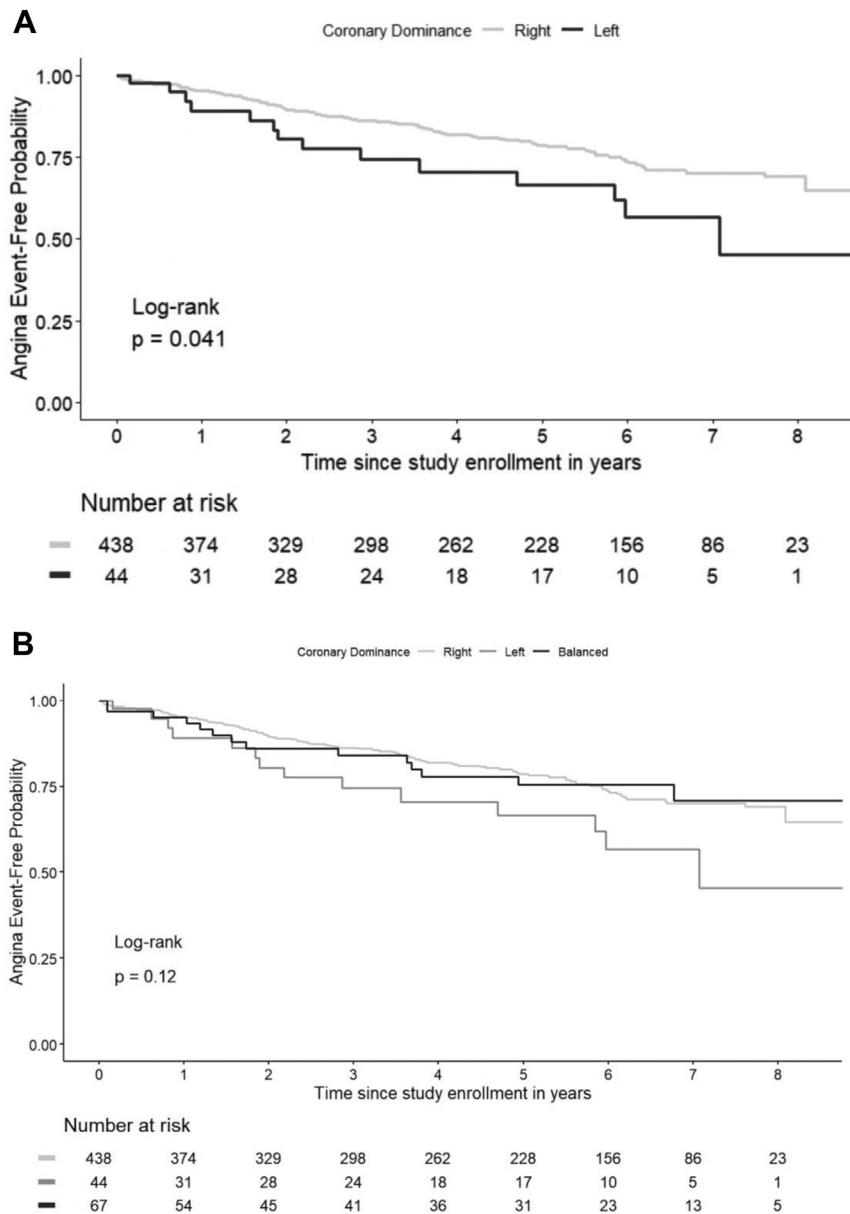


Figure 1.

Kaplan-Meier curve of angina hospitalizations over mean follow-up period of 8 years. (A) Top, left vs right-dominant circulations. (B) Bottom, left vs right vs balanced circulations.

Discussion and conclusions

Although left coronary dominance has been linked with a poorer prognosis in obstructive coronary artery disease (CAD), there is a knowledge gap regarding its impact on clinical outcomes in female patients with suspected INOCA. This study illuminates a potential link between left-dominant circulation and a heightened risk of angina-related hospitalization among these women. Our work builds on 2 prior studies; one demonstrated that a left-dominant circulation, determined by computed tomography angiography, was an independent predictor of nonfatal myocardial infarction and all-cause mortality, whereas a preceding case-control study accentuated a notably higher prevalence of nonobstructive CAD in females with left dominance.^{2,3} Our study advances this understanding by incorporating prognostic measures, suggesting that angina-related hospitalizations are more frequent in females with nonobstructive CAD with left-dominant circulations.

Risk factors for INOCA closely align with those for obstructive CAD, embodying common atherosclerosis inducers such as aging, hypertension, diabetes mellitus, and dyslipidemia.^{4,5}

Our study proposes the concept of coronary dominance as a new element in the INOCA risk schema, indicating a higher prevalence of angina hospitalizations for INOCA among female patients with left-dominant circulations. This advancement in understanding the interaction of coronary dominance with ischemic heart disease symptoms notably enriches our evolving knowledge of this disease in the female population.

A comprehensive strategy to manage patients with INOCA might entail developing a predictive model to identify those at risk based on clinical and lifestyle factors.⁶ Noninvasive tests such as cardiac magnetic resonance imaging and positron emission tomography would form the core of early diagnosis, with an emphasis on detecting often underdiagnosed conditions such as coronary microvascular dysfunction.^{7,8} Active management of diagnosed patients would involve adjusting

medications, which include antianginal drugs, calcium channel blockers, nitrates, statins, angiotensin-converting enzyme inhibitors, and aspirin.⁹ Concurrently, patients should be educated and encouraged to adopt heart-healthy lifestyle habits, such as a balanced diet, regular exercise, smoking cessation, and alcohol limitation.⁹ Finally, to ensure the effectiveness of the treatment and adherence to lifestyle modifications, regular follow-up appointments would be scheduled, allowing health care professionals to tailor the management plan as needed. This structured approach could potentially reduce hospitalizations due to angina in these high-risk patients.

Our study has limitations, particularly when it comes to comparing left-dominant circulation with both right and codominant types. Although we noted no substantial disparities when examining all 3 circulatory types on a global scale, meaningful distinctions were solely seen between left- and right-dominant circulations. Moreover, the question remains whether coronary dominance acts as an independent risk factor in both sexes, as our study primarily focused on females. The lack of significant MACE findings is possibly attributed to the limited sample size.

Our results may have implications for the management of women with INOCA. They suggest that left-dominant circulation may be a prognostic factor for angina-related hospitalizations in this female INOCA population, which contributes to the adverse quality of life and consumes health care resources. Further research is needed to fully understand the relationships between coronary dominance and clinical outcomes in suspected INOCA.

Declaration of competing interest

Noel Bairey Merz serves on advisory boards of iRhythm and SHL Telemedicine. Janet Wei reports honoraria paid to CSMC from Abbott Diagnostics. Carl Pepine declares grants from GE Healthcare GE-265-303; Merck MK-1242-001-01; Sanofi EFC11570; University of Florida Office of Research AGR DTD 04-26-2018; CSL Behring, LLC CSL112-3001; BioCardia BC-14-001-02; Mesoblast, Inc MSB-MPC-CHF001; Ventrix, Inc; Athersys, Inc AMI MultiStem; Verily Life Sciences LLC-Project Baseline OSMB; Ironwood MSB-MPC-CHF00-DMC, Imbria Pharmaceuticals, Inc; Milestone Pharmaceuticals, Inc; Caladrius Biosciences, Inc; Gatorade Trust through the University of Florida Department of Medicine; and the McJunkin Family Foundation. Amer Muhyieddeen, Yujie Cui, and Eileen Handberg reported no financial interests.

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Ethics statement and patient consent

The research conducted adhered strictly to the principles stipulated in the Declaration of Helsinki. It underwent thorough review and obtained endorsement from an established ethical review committee. The design and protocol of the study were carefully inspected to ensure maximal respect for patient autonomy, confidentiality, and safety.

Each participant provided their informed consent in writing, agreeing to partake in the research and allowing their medical records to be used for research purposes. Prior to any analysis, patient data were anonymized and deidentified to uphold the privacy and confidentiality of the participants.

In the event of required alterations to the research protocol during the study, the changes were subject to scrutiny and approval by a distinguished ethical committee. This institution is fully committed to the execution of high-quality research, all the while maintaining a firm ethical standpoint and abiding by the topmost standards of research ethics.

It is believed that the findings of this research may notably augment the current body of knowledge and aid in enhancing patient care in the future.

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