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Coronary Microvascular Dysfunction, Microvascular Angina, and Treatment Strategies

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ABSTRACT

Angina without coronary artery disease (CAD) has substantial morbidity and is present in 10% to 30% of patients undergoing angiography. Coronary microvascular dysfunction (CMD) is present in 50% to 65% of these patients. The optimal treatment of this cohort is undefined. We performed a systematic review to evaluate treatment strategies for objectively-defined CMD in the absence of CAD. We included studies assessing therapy in human subjects with angina and coronary flow reserve or myocardial perfusion reserve <2.5 by positron emission tomography, cardiac magnetic resonance imaging, dilution methods, or intracoronary Doppler in the absence of coronary artery stenosis ≥50% or structural heart disease. Only 8 papers met the strict inclusion criteria. The papers were heterogeneous, using different treatments, endpoints, and definitions of CMD. The small sample sizes severely limit the power of these studies, with an average of 11 patients per analysis. Studies evaluating sildenafil, quinapril, estrogen, and transcutaneous electrical nerve stimulation application demonstrated benefits in their respective endpoints. No benefit was found with L-arginine, doxazosin, pravastatin, and diltiazem. Our systematic review highlights that there is little data to support therapies for CMD. We assess the data meeting rigorous inclusion criteria and review the related but excluded published data. We additionally describe the next steps needed to address this research gap, including a standardized definition of CMD, routine assessment of CMD in studies of chest pain without obstructive CAD, and specific therapy assessment in the population with confirmed CMD. (J Am Coll Cardiol Img 2015;8:210–20) © 2015 by the American College of Cardiology Foundation.

Patients with chest pain without obstructive coronary artery disease (CAD) have been a diagnostic and therapeutic challenge and have contributed to significant economic, social, and health care costs (1,2). At least 10% to 30% of patients presenting with angina have no significant CAD on invasive coronary angiography (3,4). As many as 50% to 65% of these patients with chest pain without obstructive CAD are believed to have coronary microvascular dysfunction (CMD), also known as microvascular angina (5–8). CMD is typically defined as impaired vasodilation of arterioles, leading to an inadequate increase in blood flow from rest to stress.

Patients believed to have CMD have a poor prognosis, with higher rates of hospitalization and increased rates of adverse cardiovascular events, including sudden cardiac death, myocardial infarction, congestive heart failure, and coronary revascularization (2,8–11).

Historically, the only practical methods available for the assessment of CMD have been invasive, such as intracoronary (IC) Doppler flow wire or thermodilution. This has likely impaired the objective evaluation of CMD in patients presenting with chest pain without obstructive CAD. Thus, the treatment of CMD has often been studied within imprecise clinical entities such as cardiac syndrome X (12). Moreover, a lack of consensus on diagnostic criteria and nomenclature for CMD has further obscured the evidence that sought to objectively define microvascular angina as a distinct clinical entity.

Given these challenges, it is unclear to what extent effective therapies have been identified in patients with CMD. Therefore, we performed a systematic review of the published data to evaluate treatment strategies for CMD using a rigorous definition with contemporary and accurate methods of microvascular assessment. We found little data that met these criteria. Accordingly, we analyze the challenges in studying therapies for CMD, present the results of our systematic review, discuss the excluded but related published data, and propose future research directions for this important field.

CURRENT CHALLENGES IN CMD TREATMENT RESEARCH

CMD VERSUS OTHER CAUSES OF CHEST PAIN WITHOUT OBSTRUCTIVE CAD. There are multiple diagnoses that may cause chest pain without obstructive CAD. These diagnoses include microvascular angina, gastroesophageal reflux disease, musculoskeletal chest pain, cardiac syndrome X, cardiac syndrome Y (slow coronary flow), coronary