

NEWS

Symptomatic Myocardial Ischemia but No Obstructive CAD: Some Drugs Work, Others Don't, Review Finds

While the quality of evidence is low overall, ACE inhibitors and statins stand out as the best choice in this challenging subset, authors say.



By [Caitlin E. Cox](#) January 18, 2018



What to do with a patient who has angina and shows signs of ischemia on stress testing, but doesn't have obstructive coronary artery disease? Although the overall evidence base in these patients is sparse, ACE inhibitors and statins can improve quality of life and may even curtail angina, a new review suggests.

Results were mixed or lackluster for a host of other options, including beta-blockers, calcium-channel blockers, nicorandil, ranolazine, nitrates, and hormone therapy.

“This is sort of where it’s the art of medicine alongside the science of medicine. So, if at first you don’t succeed, try another drug,” senior author Michelle M. Graham, MD (University of Alberta, Edmonton, Canada), explained to TCTMD. But the “first roadblock,” she added, lies in “recognizing that this is an actual clinical problem and the patient you’re seeing in your office does not have noncardiac chest pain.”

Ischemia on stress testing with no obstructive coronary artery disease (INOCA) is found in half of women and one-third of men who present with angina and are referred for angiography. Sometimes these patients “are just patted on the head and told there’s nothing wrong with them,” Graham said. Proper diagnosis is important, she stressed. “Equally, you don’t want people with noncardiac chest pain being treated with cardiac medications, because it’s not going to help their symptoms and it’s going to impair their quality of life because of the side effects of the antianginal medications.”

Commenting for TCTMD, Carl J. Pepine, MD (University of Florida, Gainesville), said the problem now is that most clinicians “don’t do anything” for patients with INOCA.

“The literature indicates that once a person, particularly a woman, has an angiogram or a CTA that does not show obstructive disease, they are [usually] dismissed from specialty care with their cardiologist and oftentimes even from general care,” Pepine explained. Under these conditions, the treatments that are reviewed in the current paper, even the ACE inhibitor/statin combination, “in general are not deployed,” he said.

This undertreatment arises from the perception among clinicians that “these symptoms are inconsequential and not likely to be related to their heart, even though most of these patients have some objective evidence of ischemia,” Pepine said, adding, “There’s overwhelming evidence that most of these individuals have atherosclerosis even though it’s nonobstructive.”

A Mixed Bag

In their paper published online last week in the American Journal of Cardiology, Graham, along with Ricky D. Turgeon, PharmD, and Glen J. Pearson, PharmD (University of Alberta), dig through data from 35 randomized controlled trials on the pharmacological treatment of INOCA. The primary outcome measure was quality of life, whether general or angina-related.

“All studies had high or unclear risk of bias,” the researchers point out. “Quality of evidence was generally very low or low.”

Beta-blockers, calcium-channel blockers, and ACE inhibitors alone or in combination with a statin all showed signs of improving quality of life. For ranolazine, the largest study showed no significant gains but smaller trials of longer duration were positive. “Hormone therapy, ivabradine, nitrates, omega-3 fatty acids, and statins alone did not demonstrate improvement in [quality of life],” Graham et al report.

In terms of efficacy, the researchers found that beta-blockers, ACE inhibitors, nicorandil, and statins came out on top for reducing angina, while “conflicting” results were found for ranolazine and hormone therapy. Calcium-channel blockers weren’t consistently efficacious, and symptoms were not improved with metformin or trimetazidine.

“Few trials reported on safety outcomes,” they note.

Addressing Endothelial Dysfunction

For Graham, the flawed evidence base means that it’s too early to draw firm conclusions. “I don’t think you can rule out really any of these medications yet,” she said, adding, “These aren’t your big landmark 40,000-patient trials that show a 25% reduction in mortality. Even the inclusion criteria for these studies were challenging. So, we need to better identify these patients and go from there.”

Overall, “the evidence would suggest that statins and ACE inhibitors are reasonable and beta-blockers seem to work better than calcium-channel blockers. There’s also some potential benefit of ranolazine noted here,” Graham observed, adding that the ability of ACE inhibitors and statins to treat endothelial dysfunction sets them apart.

Pepine, too, cited this advantage, noting, “Many of these patients have endothelial dysfunction and/or smooth muscle dysfunction when they’re tested in the laboratory, and that’s

their mechanism of ischemia.” Additionally, statins can prevent atherosclerosis progression and thus may help forestall “either obstructive disease or . . . vulnerable plaque that would cause myocardial infarction or acute coronary syndromes,” he said.

Only solid research will clarify how patients with INOCA should be managed, Graham stressed. “We need better studies with higher-quality evidence before we can really nail down what we should be doing.”

WARRIOR, a trial that Pepine said has just received US Department of Defense funding, could provide some answers. He and others plan to enroll around 4,400 clinically stable women with symptoms of ischemia and nonobstructive CAD on diagnostic angiography or coronary CTA. The women will be randomized to intensive medical care (high-potency statin and ACE inhibitor plus aspirin) or usual care, with an average follow-up of 3 years. The primary outcome will be first occurrence of death, MI, stroke, or hospitalization for heart failure or angina.

Sources

Turgeon RD, Pearson GJ, Graham MM. [Pharmacological treatment of patients with myocardial ischemia with no obstructive coronary artery disease \(INOCA\)](#). Am J Cardiol. 2018;Epub ahead of print.

Disclosures

Graham and Pepine report no relevant conflicts of interest.