

Nascent Medical Therapies for Abdominal Aneurysms

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Efforts to identify medical therapies that halt the growth of aneurysms have been underway for at least 20 years.¹ Two studies published in this issue of the *Journal of the American Heart Association (JAHA)* give us some idea of how medical therapy will more often be considered a core component of the management of aortic abdominal aneurysms.

First, a meta-analysis by Al-Omran and colleagues² identifies an association between statin medications and significantly slower aneurysm growth rates, fewer aneurysm ruptures, and improved perioperative survival. The results are compelling and suggest that statin therapy may be beneficial for patients with abdominal aneurysms (including larger aneurysms) who do not otherwise meet indications for statin therapy indications.* With the favorable safety profile and the low cost of statins, it may be reasonable for clinicians to initiate high-intensity statin therapy for such patients, even without a confirmation from a randomized controlled trial. Perhaps even more important, clinicians should ensure statin therapy has been prescribed for all patients with abdominal aneurysm who *already do* meet typical indications. Several recent series report that only 60% to 70% of patients with peripheral artery disease receive statin therapy,^{7–9} and there

is no reason to expect that the rate would be any higher in patients with abdominal aneurysms.

Matrix metalloproteinases have been implicated in the pathogenesis of abdominal aneurysms through degradation of aortic wall elastin and collagen. Preclinical work had suggested the lipid-lowering agent fenofibrate downregulated matrix metalloproteinases. A small randomized trial, reported by Golledge and colleagues in this issue of *JAHA*,¹⁰ failed to demonstrate fenofibrate therapy significantly slowing growth of abdominal aneurysms. Aneurysm growth is typically a few millimeters per year, so it may not be surprising that no significant differences were found at 24 weeks. Follow-up of their cohort beyond 24 weeks may show a slowing of the growth rate not yet appreciated by these investigators.

Antibiotic use may merit more attention from clinicians managing abdominal aneurysms. Doxycycline has been investigated as a molecule to inhibit matrix metalloproteinase activity since the 1990s,^{1,11} and pooled results from several trials on doxycycline suggest this antibiotic may slow aneurysm growth.¹² In contrast to doxycycline, fluoroquinolones may potentiate aneurysm growth and rupture. Preclinical work from LeMaire and colleagues, demonstrating that increased matrix metalloproteinase activity is one of several effects of ciprofloxacin,¹³ provides an important piece of evidence that makes the association of ciprofloxacin and aneurysm rupture¹⁴ more compelling.

Population-level and preclinical studies suggest metformin may also slow aneurysm growth.^{15,16} Randomized trials of metformin therapy have been performed on nondiabetic populations (including, for example, nondiabetic subjects with coronary artery disease),¹⁷ so further studies of metformin as a potential medical therapy for abdominal aneurysms may be forthcoming.

While searching for medical therapies, we should not forget the impact of lifestyle on aneurysms. The aneurysm mortality incidence rate in the United States closely mirrors per capita cigarette consumption rates, and it is encouraging that rates of both are decreasing sharply.¹⁸ Clinicians must discuss tobacco use at each clinic visit, emphasize the health benefits of smoking cessation, and provide support to achieve complete abstinence (including free resources from smokefree.gov and 800-QUIT-NOW). We now know, from the work of Dalman and colleagues, that although exercise therapy does

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*Peripheral artery disease, “atherosclerotic disease of the lower extremity arteries,”³ is common among patients with abdominal aortic aneurysms.⁴ The pathogenesis of these 2 processes appears to share many features.⁵ By themselves, however, abdominal aortic aneurysms do not constitute peripheral artery disease, so the most recent guideline on cholesterol management⁶ does not seem to endorse statin therapy in patients who have abdominal aneurysms but do not have peripheral artery disease of presumed atherosclerotic origin or other listed indications for statin therapy.

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not halt growth, it is perfectly safe for people with aneurysms to exercise regularly.¹⁹

In summary, experimental studies evaluating medical therapies for abdominal aortic aneurysms suggest benefit from statins, doxycycline, and possibly metformin. Fluoroquinolones and tobacco seem harmful. Exercise does not adversely affect abdominal aneurysms and should be encouraged for the countless other benefits provided.

Disclosures

None.

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