Editorial

Positron Emission Tomography Fluorine-18-Labeled 2-Deoxy-2-Fluoro-d-Glucose Tells a Complicated Story in the Aortic Aneurysm Wall

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Abdominal aortic aneurysm (AAA) was first described in the second century by Antyllus, who surgically ligated the proximal and distal ends of the aneurysm. The modern treatment of AAA began with the first AAA replacement using a homograft in 1951. Since that time, the screening, diagnostic method, surveillance, and treatment of AAA have been very well studied and incorporated into a modern paradigm of care. The results of this work is the dramatic reduction in aneurysm-related mortality for patients who maintain care and contact with a healthcare provider. Indeed, in patients found to have an infrarenal aorta of 4 cm in diameter, aneurysm rupture or repair is the number 4 cause of death behind other cardiovascular, cancer, and lung disease, representing 6% to 8% of the total mortality.1,2

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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(Circ Cardiovasc Imaging, 2016;9:e005689.
DOI: 10.1161/CIRCCIMAGING.116.005689.)
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Circ Cardiovasc Imaging is available at http://circimaging.ahajournals.org
DOI: 10.1161/CIRCCIMAGING.116.005689

The maximal AP diameter of the aorta is strongly predictive of clinical outcomes, with small aortic aneurysms being clinically benign. Two large surveillance studies have identified a minimum aneurysm size for consideration of aneurysm repair.3,4 In both, subjects were enrolled with an aneurysm from 4.0 to 5.5 cm in diameter and randomly assigned to ultrasound surveillance until the aneurysm reached 5.5 cm or immediate repair. There was no difference in survival during long-term follow-up suggesting deferred repair was a safe strategy.5 Recent advances in the repair of AAA have also improved outcomes. Over the past 2 decades, AAA repair has largely transitioned from open surgical repair to endovascular stent-graft insertion. This less invasive procedure has significantly reduced the morbidity and mortality of the procedure while not diminishing the survival of these patients years later.6 Moreover, the investigations showing the efficacy of stent-grafting also reconfirmed the size criteria and made clear that treating patients too sick for open repair with an endovascular approach did not reduce mortality.7 Indeed, an important question in this field is can we improve upon these results?

Because the visionary investigator, M. David Tilson, recognized AAA as a pathological entity distinct from atherosclerosis, the understanding of the specific pathophysiological processes that result in aortic wall degeneration has been developed and refined. The unique histological features of AAA include remodeling of the medial and adventitial extracellular matrix and a transmural inflammatory infiltrate. Elaboration of matrix proteinases by the inflammatory infiltrate is hypothesized as one of the mechanisms of aortic matrix degeneration. This process provides many opportunities for the rational development of diagnostic and therapeutic techniques for this disease.

Fine histological analysis of aneurysm tissues demonstrates marked heterogeneity of the inflammation and structure of the aneurysm wall.8 One opportunity for (18)FDG-PET as used by Huang et al9 in this issue of Circulation: Cardiovascular Imaging is to refine our understanding of the heterogeneity of the degenerative process in vivo in small aortic aneurysms. The authors demonstrate a varied distribution of the (18)FDG uptake in the aortic wall and correlate those areas of increased metabolic activity to regions of high transmural stress using finite element analysis. It was particularly interesting that areas of high wall stress in association with thick intraluminal laminar thrombus are predictive of high uptake of FDG. This linkage is supported by previous observations associating intraluminal laminar thrombus volume with more rapid AAA growth.10

Of course, these results are the first step into the development of a clinically useful predictive test that will require...
validation and longitudinal study. The investigators analyzed >9000 data points (octants), which provided substantial statistical power, but these were generated through segmentation of the imaging, of only 21 patients. There was not a clear a priori rationale for the choice of a thrombus to wall ratio of 0.67, which was present in <12% of the octants analyzed (16 patients), but forms the most dramatic correlations between wall stress and inflammation. Finally, predictive features for growth need to be generated and longitudinally validated, which can identify patients who are at higher risk for progression and rupture. These may be areas where, for example, there is low stress, but inappropriately high 18FDG-PET activity suggesting degenerative activity.

Although these are important data, translating this information to enhance the care of patients with aneurysms is tempered by recent systematic reviews of 18FDG-PET in AAA, which suggest poor predictive value with respect to aneurysm growth and rupture. It may be overly simplistic to assume that all mural inflammation in an AAA is pathological, and advances that may permit phenotyping the inflammation may be necessary to distinguish between pathological and compensatory processes. Furthermore, the cells labeled by the 18FDG in vascular disease may not necessarily be inflammatory cells,13 as other imaging modalities for inflammation only correlate modestly with PET in the AAA wall.14

Nevertheless, there remains promise for PET imaging to both improve patient management and advance our understanding of this complex disease. As seen in this study, the predictive information obtained by PET with regard to wall stress was substantially enhanced by accounting for intraluminal laminar thrombus, suggesting a variety of inter-related factors are important to the pathological process. Future studies that include longitudinal evaluation, possibly in combination with circulating markers of disease, may extend the findings of this study to predict the expansion of small AAA.

The study of detection and treatment of AAA in large populations has substantially optimized the current patient management based on maximal diameter. However, there remains room for improvement. There are patients who have AAA rupture at a size smaller than that recommended and there are patients who do not rupture until reaching a much larger diameter. The decision to repair at 5.5 cm is based on a balancing of population risks and benefits of the aneurysm and repair. The question now is whether care can be further personalized to improve outcomes. This personalization may take on increased importance as medical therapy for small aortic aneurysms is developed. Ongoing research is investigating the role of determining outcomes based on patient size, aneurysmal rate of expansion, systemic inflammation, and biomarkers of extracellular matrix homeostasis or proteolysis. Novel imaging methods have also begun to expand our understanding of the pathophysiology of AAA and may provide an additional window into choosing the right timing and modality of repair. It is in this light that the report of Huang et al13 adds to our current understanding.

Sources of Funding
This work was supported by grants from the National Institutes of Health (Dr Curci: R01AG037120 and Dr Beckman: R01HL131977).

Disclosures
Dr Beckman is a consultant to Merck, Astra Zeneca, Bristol Myers Squibb, Sanofi, Abbott Vascular and received research grant from Bristol Myers Squibb and Merck. He is on the board of VIVA Physicians and has ownership in Janacare. The other author reports no conflicts.

References


**Key Words:** Editorials ■ aneurysm ■ aortic aneurysm ■ inflammation ■ mortality ■ positron emission tomography
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Circ Cardiovasc Imaging. 2016;9:
doi: 10.1161/CIRCIMAGING.116.005689
Circulation: Cardiovascular Imaging is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-9651. Online ISSN: 1942-0080

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circimaging.ahajournals.org/content/9/11/e005689

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