Abdominal Aorta Dilatation and Cardiovascular Outcomes
Another Dimension of Arterial Age?

Ahmad Masri, MD; João L. Cavalcante, MD

Aortic aneurysm is defined as having a permanent localized dilatation of the aorta, with at least 50% increase in diameter compared with the expected normal diameter of that aortic segment.[1] The same guidelines do not offer a definition for a localized aortic dilatation of <50% of the expected normal diameter, commonly referred to in clinical practice as mild aortic dilatation. Further, this definition does not specify what represents a normal diameter. It has been recognized that aortic diameters are affected by age, sex, body size, and imaging modality.[1] Thus, without taking these factors into account, normal diameters can be misclassified as abnormal.

See Article by Qazi et al

The lack of standardized cutoffs for the aorta represented a challenge in which normal needed to be defined before defining what is abnormal but nonaneurysmal. Many smaller studies attempted to address this,[1–4] but it was not until a landmark study using the Framingham Heart Study Offspring and Third Generation cohorts data took a comprehensive approach defining sex-specific normal diameters of the aorta at multiple segments stratified by age and body surface area, using noncontrasted multidetector computed tomography (CT) in a community-based cohort.[5] However, the question remained, what is the clinical significance of having a dilated, nonaneurysmal aorta?

Abdominal aortic aneurysm has been recognized to be associated with atherosclerotic risk factors, supported by an abundance of prospective studies from national screening programs which showed increased mortality in patients with mild aortic aneurysms.[6–9] Years later, the Tromsø study was published.[10] This was a population-based study of 6295 men and women aged 25 to 84 years and followed up for 10 years who did not have aneurysmal abdominal aorta using ultrasonography. In the study, subjects with age- and sex-adjusted infrarenal aortic diameter 27 to 29 mm had mortality risk ratio of 1.92 (95% confidence interval, 1.16–3.19) when compared with a referent group with aortic diameter of 21 to 23 mm.[10] However, the Tromsø study did not account for body size and used ultrasound instead of multidetector CT to measure aortic diameters. Furthermore, in the case of thoracic aorta diameter, there are no prior large community-based data that have shown an association between nonaneurysmal dilated thoracic aorta and mortality, after adjusting for age, sex, body size, and risk factors.

In this issue of *Circulation: Cardiovascular Imaging*, Qazi et al[11] studied the association between increased aortic diameters and incident adverse cardiovascular events. The study evaluated 3318 subjects enrolled in the Framingham Heart Study Offspring and Third Generation cohorts who underwent a noncontrast multidetector CT and were free of cardiovascular disease. Aortic diameter was measured at 4 prespecified anatomic locations: ascending, descending, infrarenal, and lower abdominal (LAA) as was previously described by the same group and published by Rogers et al.[5] The primary outcome was a composite of cardiovascular death, myocardial infarction, coronary insufficiency (described as an equivalent of unstable angina), index admission for heart failure, and stroke. According to the reference values published by Rogers et al,[5] aortic diameters were dichotomized into normal versus abnormal (>90th percentile for age, sex, and body surface area). Despite being free of cardiovascular disease and younger, males had a greater burden of CAD risk factors profile and coronary artery calcium (CAC) than females. After a mean follow-up of 8.8 years, there were 177 events (71% of them being either myocardial infarction and stroke). After adjusting for baseline traditional cardiovascular risk factors, enlarged infrarenal aorta (hazard ratio, 1.57; 95% confidence interval, 1.06–2.32) and LAA (hazard ratio, 1.53; 95% confidence interval, 1.00–2.34) were associated with increased risk of cardiovascular events. These results persisted even after adjusting for CAC in addition to traditional cardiovascular risk factors.

Further, the authors took a deep dive into their data and used the same aortic diameters as continuous variables. After adjusting for traditional cardiovascular risk factors and CAC, descending aorta and LAA were statistically associated with a higher incidence of cardiovascular events but not infrarenal aorta. Subsequently, aortic diameter was replaced by the number of dilated aortic segments, and after adjusting for traditional risk factors and CAC, having 2 dilated aortic segments was associated with incident cardiovascular events, whereas having 3 or 4 dilated segments was not after multivariate adjustment. Furthermore, there was a significant sex interaction noted for LAA dilatation suggesting that its association with outcomes varies in males versus females. Rather, these results are likely the result of multiple subgroup analyses and lack of power to detect a difference in small subgroups of patients, and as such these findings should be considered as hypothesis generating.

From the Department of Medicine, Division of Cardiology, University of Pittsburgh/UPMC, Pittsburgh, PA (A.M., J.L.C.).

Correspondence to João L. Cavalcante MD, Heart and Vascular Institute, UPMC, University of Pittsburgh, 200 Lothrop St, Scaife Hall, S-558, Pittsburgh, PA 15213. E-mail cavalcantejl@upmc.edu

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This study has many strengths that make it the first study to meticulously show an association between dilated nonaneurysmal aortic segments and incident cardiovascular events. First, this is a large community-based cohort without history of cardiovascular diseases yet showing that sex differences persist despite the best effort to account for all known confounders. Second, this is the first study that used aortic diameters stratified by age, sex, and body surface area to define dilated segments. Third, aortic diameter was measured in each patient at 4 predefined segments using anatomic landmarks after a consistent methodology. Fourth, comprehensive evaluation for traditional cardiovascular risk factors was done for all participants, as well as measuring CAC, which is another objective measure of the individual participant's risk for incident cardiovascular events.[12]

The authors report their primary outcome by dichotomizing aortic diameter into normal versus abnormal (>90th percentile for age, sex, and body surface area). Dichotomizing a continuous variable has drawbacks.[13–15] From a practical standpoint, it is unlikely that the risk associated with a dilated aortic segment is linear. It might well be that such risk only starts beyond the 90th percentile. Whether this should be the threshold to define what is considered abnormal cannot be answered by this study, but needs to be verified by other investigators to help refine the risk stratification proposition based on aortic diameters. The resultant disagreement between linear versus dichotomous variable is nicely shown by the authors, where they presented secondary analysis using continuous aortic diameters. Not surprisingly, the results were different from when aortic diameter was dichotomized (when continuous diameter used, descending aorta and LAA were associated with incident cardiovascular events, whereas when aortic diameter was dichotomized, infrarenal aorta and LAA were associated with incident cardiovascular events). Given the beforementioned limitations to dichotomizing a continuous variable, we are more confident drawing conclusions from the models where aortic diameter was entered as a continuous variable.

An important limitation of this study is the lack of mechanistic link between abdominal aorta dilatation and adverse cardiovascular outcomes. Is this in part mediated by a greater burden of atherosclerosis and hypertension? The extent of the abdominal aorta calcification has been shown to be a marker of coronary atherosclerosis,[16] its progression,[17] and also associated with greater incidence of cardiovascular events.[18] Would it be possible that individuals with both dilatation and calcification of the abdominal aorta would be at even a greater cardiovascular risk than having either condition alone? Unfortunately, the present study does not address that. Another limitation is the lack of external validity and applicability to other non-white ethnic and racial groups.[5] In MESA (Multi-Ethnic Study of Atherosclerosis),[19] Chinese participants had larger ascending aorta by 1.5 mm, and blacks had smaller ascending aorta by 0.5 mm, when compared with whites. Although such small differences are unlikely to produce clinically meaningful difference in the outcome of patients, further studies of a diverse population are needed before generalizing this current study findings to the whole population. Although the aortic diameter differences between noncontrast CT versus CT angiography for the evaluation of the aorta have not been systematically compared, an important limitation acknowledged by the authors is the use of axial images for aortic measurements instead of the recommended multiplanar reconstructions, which accounts for the eccentricity of the dilatation and tortuosity of the vessel. Nonetheless, this lack of accuracy is traded by the better reproducibility, although future studies should investigate the impact of data acquisition and standardization of aortic measurements.[20]

In conclusion, Qazi et al[11] provide important insights from this large community-based study by demonstrating the association between dilated, nonaneurysmal abdominal aortas, and incident cardiovascular events seem to extend beyond traditional cardiovascular risk factors and CAC. Sex differences are to be respected and clinical decisions individualized. This forgotten condition of dilated nonaneurysmal aorta deserves our attention as it provides an opportunity to better understand the mechanisms by which it modulates cardiovascular risk. Is this another subclinical marker of atherosclerosis or does the clinical impact extend beyond that? This work should stimulate further research in this area allowing a thoughtful approach for how to improve and personalize cardiovascular risk assessment.

Disclosures

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