Aortic Root Dimension and Hypertension: A Chicken–Egg Dilemma

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The structural and functional characteristics of ascending aorta, receiving ejected volume at each beat, are important biological factors in the pathophysiology of arterial hypertension. Whatever cause is found in the background of hypertension, elevation of blood pressure (BP) occurs when the amount of blood pushed into the arterial tree is not offset by a corresponding reduction of the impedance load opposed to the outflow, as the interplay between elastic conduits and high resistance terminal arteries. Whereas a logical sequence of pathophysiologic alterations would consider high BP as one of determinants of enlarged aortic root dimension, most studies could not identify a close enough association to hypothesize a cause–effect relationship.1 One potential reason of the inconsistency between assumption and reality could lay on the different pathophysiology sustaining systolic and diastolic hypertension, as well as on the cross-sectional nature of the studies.

In this issue of the journal, Farasat et al.2 examine correlates of aortic root dimensions in well-defined sub-types of arterial hypertension, including normality (N), prehypertension (PH), isolated systolic (ISH), isolated diastolic (IDH), and combined systo-diastolic hypertension (SDH). This study proposes results that help understanding some method limitations, favor a better comprehension of the interplay between conductance arteries and hypertension, and eventually might track research in this field.

The body size confusion

As already highlighted in the Framingham Heart Study,3 age, sex, and especially body size are important factors potentially affecting identification of the relation between aortic root and BP. To account for the influence of body size, normalization of aortic root is traditionally obtained using body surface area (BSA).1,4 This approach is also used in the study by Farasat et al.2 The use of BSA might be further justified by the reported better univariate correlation found with aortic root compared to weight or height alone, in some, though not all3 studies. However, there are reasons that should suggest cautiousness when normalizing aortic diameter for BSA. The first reason, and perhaps the most important, is that BSA is a squared approximation empirically generated from weight and height, while aortic diameter is a linear dimension. This geometric difference is important for scaling body proportions.5 In fact, the relation between aortic root and BSA is not linear but quadratic. In other words, aortic root diameter is linearly related to the square root of BSA, not to its raw value. The consequence of this geometric error of assuming as linear relations that are not linear, can be also visually appreciable. Thus, in the right tail of a normal distribution, small differences in BSA are associated with disproportionately greater differences in aortic root, whereas in the left tail larger differences in BSA are associated with disproportionately smaller differences in aortic root dimension.

The investigators of the Framingham Heart Study3 compared body size correlates of aortic root in men and women, and reported inconsistent results, depending on what parameters were used to normalize for body size. Thus, the Framingham investigators found that the greater aortic root dimension in men was confirmed when normalization for body size was obtained by dividing for height or body mass index, whereas women exhibited unexpected greater aortic root dimension than men when dividing by body weight or BSA. Interestingly, no type of normalization could achieve similarity between genders. A possible explanation of this body size-related inconsistency might be found in the complex interrelations between body composition (i.e., fat-free mass and adipose tissue) and cardiac geometry and performance, highlighted in a number of studies, and suggesting that, similar to what is demonstrated for left ventricular (LV) mass or cardiac output, when BSA is used without accounting for the abnormal body composition in overweight and obese subjects, this normalization might underestimate the raw value by overadjusting for adipose mass.

Farasat et al.2 found that when only age was considered as a potential confounders, due to the well known effect of aging on arterial stiffness, only elevation of diastolic BP was associated with greater aortic root dimensions, evident both in the group with IDH and in that with combined SDH. This was evident especially in men, for the relevant statistical difference between subjects with ISH and both IDH and SDH. Interestingly, this difference was not seen in women.

When aortic root was normalized for BSA,2 the value was tracked down by the highest values of BSA in the groups with diastolic hypertension, which were more obese. This was more evident among women, who exhibited a prevalence of obesity of 27% in the IDH and of 19% in the SDH, compared with 3%
in normals (among men the prevalence was lower: 5 and 9% respectively, compared to 0% in normals). With the use of the estimated BSA, therefore, aortic root is also normalized for adipose body mass (since weight is included in the computation of BSA). This should not necessarily be considered a wrong choice, since weight is a relevant, independent determinant of aortic root dimension. In addition there is also evidence that, although non-influential for the variance of LV mass, adipose tissue is a predictor of stroke volume independently of other cofactors, including fat-free mass. The use of the combined confounders, age and BSA, completely offset all differences in the Farasat's study. In the absence of definite clarifications on the above issues, findings on aortic root normalized for BSA should be considered very carefully, before extracting pathophysiologic inference.

**Cause–effect relation between hypertension and aortic root dimension?**

The Framingham Heart Study adopted a different approach. Vasan et al. studied an unselected, large population over an extended age-span (20–89 years), including hypertensive and class I obese participants, and used height and weight (not BSA) as covariates in their models. Aortic root measurement was 2.4 mm smaller in women than in men of comparable age, height, and weight. Adjusting for age, height and weight, aortic root was positively associated with diastolic BP, whereas it was negatively related to systolic BP in both men and women, a result more similar to the Farasat's result once adjustment for age (but not BSA) was computed. In the Framingham Heart Study, clear-cut aortic root dilatation was ~30% less likely with high systolic BP, suggesting scenarios of potential reverse causations (small aorta—systolic hypertension: where is egg and where is chicken?).

Future research should help clarifying the apparent inconsistency of the relations of aortic root with diastolic and systolic BP, which might have opposite signs. Most probably, longitudinal studies on the evolution of hypertensive cardiovascular disease (including the classification reported in the study by Farasat et al.) will help reconciling these findings.

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