Aortic Augmentation Index and Aging: Mathematical Resolution of a Physiological Dilemma?

To the Editor:

Aortic augmentation index (AIx) is frequently used to gauge arterial efficiency through effects of aortic stiffening and peripheral wave reflection. It is derived from the aortic pressure waveform and is calculated as aortic augmentation from the initial peak or shoulder to peak pressure divided by pulse pressure. It can be measured directly at cardiac catheterization from waves recorded in the ascending aorta or indirectly and noninvasively from radial artery pressure waves recorded by applanation tonometry at the wrist through use of a generalized transfer function.2

Sometimes the carotid AIx is used as a surrogate of aortic AIx.3 All of the published studies have reported that AIx increases with age. However, this change is not linear, and the curve relating AIx to age flattens beyond age 60 years.4–6 This curvilinear relationship lends itself to various explanations, which stem from the various physiological phenomena that contribute to AIx. From adolescence to middle age, aortic and carotid AIxs rise rapidly with age so that, by extrapolation, a value of 50% might be expected by age 60 years. Clearly, this is impossible, because the reflected wave (the numerator for AIx) cannot exceed amplitude of the incident wave (the major remaining component of the denominator). Another possibility is that, through decreasing myocardial contractility with age, wave reflection has a greater depressant effect on aortic flow from the heart in late systole and a lesser effect on pressure wave augmentation.7–9 Framingham investigators10 interpret this to represent decreased and delayed wave reflection, caused by increased proximal but not distal aortic stiffness.

We came to believe that all of the physiological mechanisms proposed may be moot and dominated by a mathematical phenomenon: a curvilinear relationship will result when 2 positively sloped linear equations (ie, increased augmented pressure [AP] with age and increased pulse pressure with age have different intercepts on the pressure axis), that is, their ratio (ie, AIx) will be curvilinear with age (Figure).

We evaluated whether the curvilinear increase in AIx with age may be attributed, at least partly, to the continued increases in aortic AP and aortic pulse pressure (PPao) with age. A total of 1601 cardiology outpatients from a previously described database11 from St. Vincent’s Clinic were analyzed. Data represent the first visit for each patient. All of the subjects gave informed consent, and all of the studies were approved by local ethics committees. Radial arterial sphygmography (pressure pulse waveform recording) was performed via applanation tonometry using a high-fidelity piezoelectric tonometer (SPT-301, Millar Instruments) with patients rested, supine, and in a temperature-controlled environment in accordance with consensus recommendations.12 Aortic pressure waveforms were then generated for all of the subjects using SphygmoCor (version 7.01, AtCor Medical), which applies a validated generalized transfer function (FDA Nos. K002742 and K012487).2 The waveforms were subsequently analyzed to yield measurements of AP, PPao, and AIx according to established protocols.12 Data were plotted to observe the changes in AP, PPao, and AIx with age. Least-squares regression was used to determine linear regressions for AP and PPao. For AIx, a logarithmic regression line was required. The equation representing the ratio between the 2 linear regression lines fitted for AP and PPao was calculated and was compared with the logarithmic regression line fitted for AIx. Regression lines and significance values were calculated using SPSS version 17.0 (SPSS Inc.).

In our cohort, AP and PPao were represented by linear regressions. For AP, the regression y=0.37x−9.04 gave an R2 of 0.27 and was highly significant (P<0.001). For PPao, the regression y=0.67x+10.07 gave an R2 of 0.28 and was also highly significant (P<0.001). The R2 values are high considering the number of subjects in the cohort. They were also the same as the R2 values obtained using second-order polynomials fitted to the same data for AP and PPao, which was calculated and was compared with the logarithmic regression line fitted for AIx. Regression lines and significance values were calculated using SPSS version 17.0 (SPSS Inc.).

The ratio of 2 linear equations (top left, dark-gray line and gray line) is a curve (top right, light-gray line). Bottom panel shows change in AIx with age from calculated ratio (black line) between linear regression equations for (AP vs age) and (PPao vs age) vs fitted logarithmic regression equation (gray line).

Figure. Mathematical principle underlying curvilinear AIx trend.
across the life span supports the observations in the ACCT (Anglo-Cardiff Collaborative Trial) cohort.\(^4\) Furthermore, our finding that AIx is better represented by a logarithmic regression line, because of its curvilinear pattern of change with age, supports the observations of the ACCT\(^4\) and others.\(^5,6\)

AIx is a widely used measure of central hemodynamics and a recognized surrogate indicator of cardiovascular risk,\(^1,12\) however, its interpretation is limited by the mathematical phenomenon discussed here. Reduced rate of AIx rise with age beyond 60 years is not necessarily attributed to any particular physiological phenomenon. It can be explained, at least partly, by the fact that the parameters used to derive it (namely, AP and PP\(_c\)) rise in a similar and approximately linear fashion across the life span.

The curvilinear pattern of AIx change with age has been proposed as evidence of decreasing wave reflection in older persons.\(^10\) However, wave reflection continues to increase with age across the life span and remains important to pulsatile pressure in the aorta in older persons.\(^13\) The mathematical concept presented here may partly explain the recent findings from Framingham that showed no association between wave reflection (measured by AIx) and cardiovascular risk in a longitudinal cohort,\(^14\) a finding that was inconsistent with those of another large longitudinal outcome study using non-AIx measures of wave reflection.\(^15\) It can also explain why the association between AIx and cardiovascular risk is seen primarily in persons under the age of 60 years as opposed to those who are older.\(^16\) AIx remains a valuable tool in assessing cardiovascular function. However, when quantifying vascular aging, cardiovascular risk, and wave reflection in research and practice with the AIx method, the concepts presented here need be considered.

Disclosures

M.F.O. is a director of AtCor Medical, a manufacturer of pulse wave analysis systems.

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