Adjusting the Aortic Augmentation Index for the Resting Heart Rate

In their recent review article, Stoner and colleagues address the important issue of whether the aortic augmentation index (AIX) should be adjusted for the resting heart rate (RHR) and evaluated the scientific basis for doing so. The review also correctly emphasised the strong influence of age, sex, mean arterial pressure (MAP) and height on AIX. These are important issues, as pulse wave analyses (PWAs) are increasingly being used in both research and clinical practice.

SphygmoCor is currently the most widely used device for performing non-invasive PWA; it measures and calculates the AIX standardised to a heart rate of 75 beats-per-minute, bpm (AIX75). SphygmoCor calculates the AIX75 by adjusting the AIX by \(-4.8\) for each 10 bpm above (and \(+4.8\) for each 10 bpm below) a RHR of 75 bpm. This adjustment is derived from the average values of two cardiac pacemaker studies that observed a linear decline of \(-3.9\) and \(-5.6\) in AIX for each pacemaker induced 10-bpm increment in RHR. The review raises appropriate concerns regarding the wider generalisability of these findings, as the two cardiac pacemaker studies included a combined total of only 42 participants (27 men) from a single centre. I have investigated these concerns by utilising baseline data obtained from the ‘Central Aortic Augmentation Study’ (CAAS), which was conducted in the north east region of Scotland in 2009.

The CAAS is a prospective cohort study of 546 consecutive ambulatory patients in sinus rhythm who underwent SphygmoCor radial applanation PWA in the supine position prior to elective coronary angiography over a 12-month period (mean age: 62 years, RHR: 61 bpm, MAP: 99 mmHg, height: 1.68 m, 64% men, 37% never-smokers, 59% coronary artery stenosis \(\geq 50\%\) on angiography). The study is funded by the Chief Scientists’ Office of Scotland and was approved by the local research ethics committee. All participants provided their informed written consent. At baseline, the overall mean AIX was 27.7 (SD 12.6) and the mean AIX75 was 21.2 (SD 11.1), with an absolute (paired) difference of 6.5 (95%CI 6.1 to 7.0). The cross-sectional relationship between AIX and RHR is shown in Fig. 1. Among the total patient population, the RHR explained 23% of the variability (‘variance’) in AIX, and a 10-bpm increase in RHR was associated with a \(-5.0\) (95%CI \(-4.3\) to \(-5.8\)) reduction in AIX: men \(-5.3\) (95%CI \(-4.5\) to \(-6.2\)); women \(-4.7\) (95%CI \(-3.4\) to \(-6.0\)). The pattern of AIX and AIX75 according to age and sex is shown in Fig. 2. Both indices generally increased with age and were higher in women than in men. The absolute difference between the two indices (AIX minus AIX75) did not vary substantially with increasing age, although, for men, the difference was lowest for those \(<55\) years of age and highest for those \(\geq 70\) years of age (4.9 and 8.1, respectively).

The review attempted to assess whether the selection of AIX or AIX75 influenced the interpretation of the results of 12 studies reporting both indices; however, this analysis was limited by the fact that nine of the studies included \(\leq 100\) participants. Among 542 CAAS participants with complete data available for a multivariable analysis, I have assessed the relationship between having ‘never-smoked’ (one or more cigarettes a day for more than a year) and aortic augmentation (AIX and AIX75). A multiple linear regression analysis (IBM-SPSS, version 21) was used to adjust for the four key variables highlighted in the review (age, sex, MAP and height), with the additional inclusion of RHR, for the relationship between AIX and smoking. The assumptions of linearity, normal distribution and equal variance for multiple linear regression were met.

Almost identical results were obtained irrespec-
tive of whether AIX or AIX75 was selected as the dependant variable. On the adjusted multivariable analysis, having ‘never-smoked’ was found to be associated with a $-2.33$ (95%CI $-0.68$ to $-3.98$; $p=0.006$) lower AIX and a $-2.29$ (95%CI $-0.63$ to $-3.94$; $p=0.007$) lower AIX75. In addition, according to the unadjusted analysis, having ‘never-smoked’ was associated with a $-0.70$ (95%CI $-2.64$ to $1.24$; $p=0.48$) lower AIX75, and the AIX value (adjusted only for RHR as a dependant covariate) was $-0.71$ (95%CI $-2.66$ to $1.23$; $p=0.47$) lower.

The Stoner review identified only one previous study concerning the repeatability of both AIX and AIX75, although the cited study is limited to the within-observer agreement of a single operator$^4)$. We have previously reported findings regarding the within-observer and between-observer repeatability of both indices (AIX and AIX75) using the Bland-Altman ‘95% limits of agreement’ (LoA) approach (mean difference ± 2 SD$^5$) within a single study$^6$, $^7$). Two research nurses performed SphygmoCor PWA in 20 participants (16 men) in sinus rhythm (mean: age 56 years, RHR: 64 bpm, MAP: 98 mmHg) on a single occasion after the participants had rested in the supine position for 15 minutes. In the hands of our nurses, we found the AIX and AIX75 values to have comparable levels of clinical repeatability: between-observer LoA for AIX = $0.7 ± 3.9$ (within-observer LoA $0.9 ± 5.3$ and $0.6 ± 7.3$); between-observer LoA for AIX75 = $1.0 ± 3.9$ (within-observer LoA $1.5 ± 7.0$ and $0.1 ± 8.0$).

In conclusion, the linear relationship between AIX and RHR observed in two previous cardiac pacemaker studies was replicated in a much larger study of patients attending the hospital for elective coronary angiography. In relation to smoking, a well-established cardiovascular risk factor, almost identical results were obtained from analyses based on AIX75 or AIX (with adjustment of AIX for RHR as a covariate). AIX and AIX75 also have comparable levels of clinical repeatability. Our findings suggest that a $-4.8$ reduction in AIX for each 10-bpm increase in RHR is an appropriate assumption for calculating AIX75. The available evidence suggests that it is ‘physiologically and epidemiologically’ appropriate to adjust AIX for RHR. The main precaution regarding the ‘clinical’ use of such adjustment is that a higher RHR is itself an independent risk factor for adverse cardiovascular events$^8$).

Future prognostic research will need to assess whether the composite index of AIX75 compares favourably to the separate assessment of AIX and RHR.

Conflicts of Interest

None.

References

2) Wilkinson IB, MacCallum H, Flint L, Cockcroft JR,


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