Supplemental digital content 1

Supplemental Results

Tables S1. Relationship of systolic and diastolic augmentation indices with heart rate and pulse wave velocity, by age group.

The format is the same as used in Table 5 of the main text. sAix systolic augmentation index. dAix diastolic augmentation index. HR heart rate. PWV carotid-femoral pulse-wave velocity. β regression coefficient with units as indicated and explained in the main text. PP pulse pressure. SE standard error of the estimate of β.

Young

		unit for β	sAix	dAix
HR	β	% PP.beat^{-1}.min	-0.33	-0.03
	SE		0.11	0.07
	p		0.008	0.7
PWV	β	% PP.m^{-1}.sec	2.97	-1.22
	SE		0.88	0.55
	p		0.002	0.03

Middle-aged

		unit for β	sAix	dAix
HR	β	% PP.beat^{-1}.min	-0.22	0.005
	SE		0.1	0.04
	p		0.02	0.91
PWV	β	% PP.m^{-1}.sec	4.11	-1.69
	SE		0.82	0.38
	p		<0.0001	0.0002

Aged

		unit for β	sAix	dAix
HR	β	% PP.beat^{-1}.min	-0.52	-0.05
	SE		0.13	0.04
	p		0.0005	0.24
PWV	β	% PP.m^{-1}.sec	0.7	-0.1
	SE		0.7	0.2
	p		0.33	0.6

<u>Tables S2</u>. Analysis of variance regarding wave reflection parameters, with adjustment for height, weight, heart rate, mean central blood pressure and pulse wave velocity.
sAix systolic augmentation index, sAix@75 systolic augmentation index adjusted for a heart rate of 75 b/min, sT1r time to begin of systolic reflected wave, dAix diastolic augmentation index, dMTT mean transit time of diastolic reflected wave.
The model was the same as used for generating the rightmost part of Tables 2 and 4 in the main text, with the addition of the mentioned covariates, chosen because they significantly differed between genders. With the exception of dMTT, the effect of gender remained significant with this adjustment.

	gender	*age group*	*position*	*gender*age*	*gender* position*	*age* position*	*age*gender* position*
sAix	<.0001	<.0001	0.108	0.808	0.084	<0.001	0.500
sAix@75	<.0001	<.0001	0.120	0.779	0.060	0.000	0.494
sT1r	<.0001	<.0001	0.990	0.082	0.820	0.033	0.492
dAix	0.032	<.0001	0.356	0.652	0.140	<.0.001	0.637
dMTT	0.177	<.0001	<.0001	0.362	0.493	0.000	0.526

Supplemental Discussion

Effects of age and gender on standard indices of aortic stiffness

The gold standard for the noninvasive evaluation of aortic stiffness is the measurement of PWV, here accomplished with the Complior device, which is the one most frequently used for this purpose, as apparent from a recent systematic review [1]. In this sample of an apparently healthy european population, we obtained mean values of PWV in agreement with those found in studies carried out in similar groups and with the same method [2-6]. PWV increased with age, as uniformly reported by all authors [1], and was slightly higher in men than in women, an effect of gender also found in healthy subjects by some [4, 7], although not all studies [3, 8].

Another widely used index of central arterial stiffness is the sAix calculated from the pulse contour of aortic pressure, as estimated from tonometry of either the radial artery (followed by a mathematical transform with a transfer function) or the carotid artery (mathematical transform not required). Both methods for obtaining the sAix have been validated against direct invasive measurements [9, 10]. Studies using either have uniformly concluded that, in healthy subjects, the sAix increases with age and is higher in women, compared to men [11-14], as we indeed observed (Digital Supplemental Content 2, Tables S3 and S4). Interestingly, most of the age-related change in the sAix occurred between the young and the middle-aged, with only limited further increase from the middle-aged to the aged groups, in accord with the patterns described in similar populations by Mitchell et al [12], as well as by McEniery et al [13]. Considering that the systolic augmentation of aortic pressure is in part determined by the respective timing of forward and reflected waves, a shorter travel length for the latter, related to the smaller body size of women, could explain the effect of gender on the sAix. However, neither in any of the cited studies, nor in the present one was this effect removed by adjustment for body height, suggesting the contribution of other, yet unknown factors.

In summary, our observations regarding the effects of age and gender on both PWV and sAix are in accord with findings generally reported in healthy populations, supporting the generalizability of conclusions about to be drawn from the comparison of these standard arterial stiffness indices with the newly developed dAix.

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