Ambulatory arterial stiffness index: determinants and outcome

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Objectives **We hypothesized that one minus the slope of diastolic on systolic blood pressure in individual 24-h ambulatory blood pressure recordings (ambulatory arterial stiffness index) might reflect arterial stiffness and predict cardiovascular mortality.**

Methods **In volunteers and a population recruited in China, we studied concordance between ambulatory arterial stiffness index and established indexes of arterial stiffness. We assessed the predictive value of ambulatory arterial stiffness index in relation to cardiovascular outcome in Irish hypertensive patients.**

Results **In 166 healthy volunteers, aged 22–83 years, the correlation coefficient between ambulatory arterial stiffness index and pulse wave velocity was 0.51 ($P<0.001$). In 348 randomly recruited Chinese, the correlations between ambulatory arterial stiffness index and both the central and peripheral systolic augmentation indexes were significantly stronger than those for 24-h ambulatory pulse pressure, particularly in study participants younger than 40 years. Among normotensive participants, the 95th percentile of the ambulatory arterial stiffness index was 0.55 in 234 Chinese and 0.57 in 1617 Europeans enrolled in the International Database on Ambulatory Blood Pressure Monitoring. The upper boundary of the 95% prediction interval of the ambulatory arterial stiffness index in relation to age ranged from 0.53 at 20 years to 0.72 at 80 years. In 11 291 patients enrolled in the Dublin Outcome Study, both ambulatory arterial stiffness index and 24-h ambulatory pulse pressure significantly predicted cardiovascular mortality. Ambulatory arterial stiffness index was a strong predictor of fatal stroke in normotensive participants, whereas pulse pressure better predicted heart attack in hypertensive patients.**

Conclusion **Ambulatory arterial stiffness index is a novel measure of arterial stiffness, which can be readily determined from ambulatory blood pressure recordings and which independently predicts cardiovascular mortality. *Blood Press Monit* 11:107–110**

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Keywords: ambulatory blood pressure monitoring, arterial stiffness, cardiovascular mortality, pulse pressure

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Introduction

Arterial stiffness is a strong predictor of cardiovascular morbidity and mortality [1–5]. Although several indexes of arterial stiffness are currently used, there is an ongoing debate with regard to their strengths and limitations [6–8]. They remain underused in routine clinical practice for cardiovascular risk stratification, possibly because with the exception of pulse pressure, measurement of most indexes requires special equipment and highly trained observers. We hypothesized that the regression slope of diastolic on systolic blood pressure in individual ambulatory blood pressure recordings might reflect the elasticity of the large arteries and predict cardiovascular mortality. The purpose of this short review paper is to summarize our recent findings on the ambulatory arterial stiffness index (AASI) in Chinese [9] and European [10] populations.

Methodology and results

Computation of ambulatory arterial stiffness index

We programmed oscillometric SpaceLabs 90202 and 90207 monitors (SpaceLabs Inc., Redmond, Washington, USA) to obtain blood pressure readings [11]. From unedited 24-h recordings, we computed for each individual the regression slope of diastolic on systolic blood pressure. AASI was defined as one minus this regression slope. This has previously been described [9,10,12].

Determinants of ambulatory arterial stiffness index

In a Chinese population sample [9,13], which included 348 participants (mean age, 46 years; 189 women), stepwise regression analysis showed that sex, age, mean arterial pressure and body height were independent determinants of AASI. AASI was 15.2% higher in women

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than in men, and increased with age at a rate of 0.055 units per 10 years. Furthermore, AASI rose by 0.015 units for each 10 mmHg increment in mean arterial pressure, but decreased by 0.026 units for each 10 cm increase in body height. AASI was not significantly correlated with the 24-h heart rate ($P = 0.24$). With these five aforementioned variables in the model, serum cholesterol, smoking and alcohol intake did not contribute to the variability of AASI.

Distribution of ambulatory arterial stiffness index in an International Ambulatory Blood Pressure Monitoring Database

We studied the distribution of AASI in 348 randomly recruited Chinese and 1062 Belgian and 902 Irish participants enrolled in the International Database of Ambulatory Blood Pressure Monitoring [14]. In these three study groups, AASI was normally distributed. In normotensive Chinese ($n = 234$) and Europeans ($n = 1617$), the 95th percentiles of AASI were 0.55 and 0.57, respectively. In the 1851 normotensive individuals of the three populations combined, the upper boundary of the 95% prediction interval in relation to age ranged from 0.50 at 20 years to 0.70 at 80 years [9].

Ambulatory arterial stiffness index as a measure of arterial stiffness

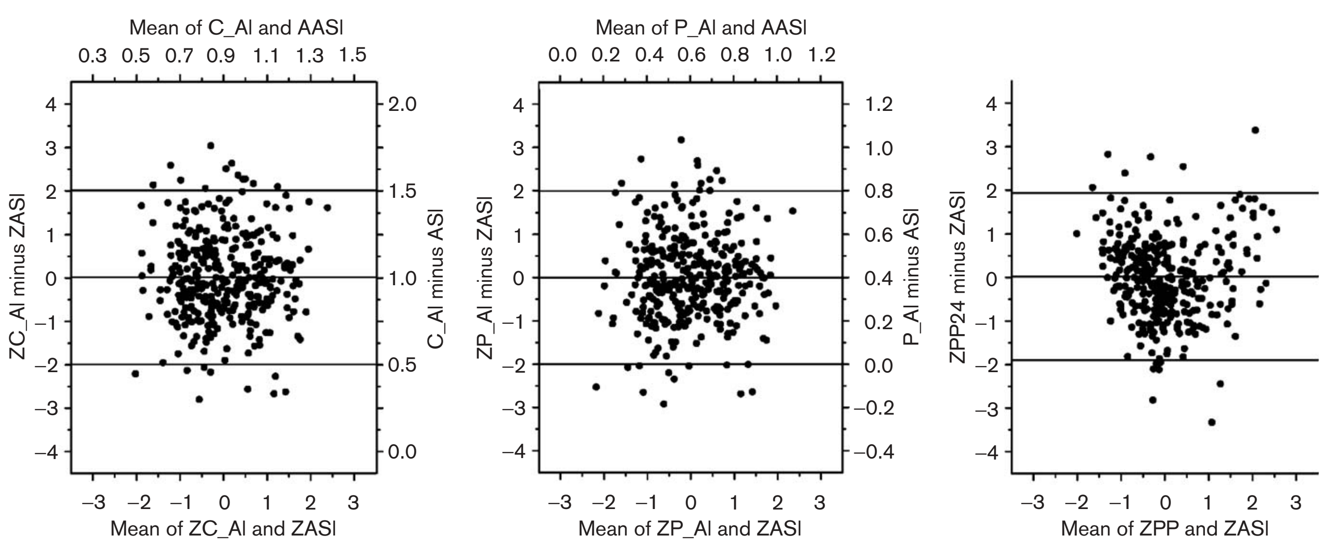
In 166 Chinese volunteers [9], who were not treated for hypertension (mean age, 48 years), we measured the carotid–femoral pulse wave velocity, using a high-fidelity SPC – 301 micromanometer (Millar Instruments Inc., Houston, Texas, USA) interfaced with a laptop computer running the SphygmoCor software, version 6.31 (AtCor Medical Pty. Ltd, West Ryde, New South Wales, Australia) [15]. Pulse wave velocity averaged 7.8 ± 2.1 m/s. AASI significantly correlated with pulse wave velocity in women ($r = 0.58$; $P < 0.001$) and in men ($r = 0.38$; $P = 0.002$). In all participants combined, the correlation coefficient was 0.51 ($P < 0.001$).

We also used the SphygmoCor device to measure the central and peripheral systolic augmentation indexes and the central pulse pressure in the participants in the Chinese population study [9]. Both before and after adjustment for body height and the 24-h pulse rate, we observed close correlations ($P < 0.001$) of AASI with the central and peripheral systolic augmentation indexes and the central pulse pressure. Figure 1 shows Bland–Altman plots for AASI versus the other measures of arterial stiffness [16]. Moreover, compared with the 24-h pulse pressure, AASI correlated more closely with the central ($r = 0.34$ versus 0.48; $P < 0.001$) and the peripheral ($r = 0.36$ versus 0.50; $P < 0.001$) augmentation indexes. In individuals younger than 40 years, there was no correlation of the augmentation indexes with the 24-h pulse pressure ($r = -0.00$; $P > 0.99$), whereas the correlation with AASI remained significant ($r = 0.18$, $P < 0.05$).

Ambulatory arterial stiffness index as a predictor of cardiovascular mortality

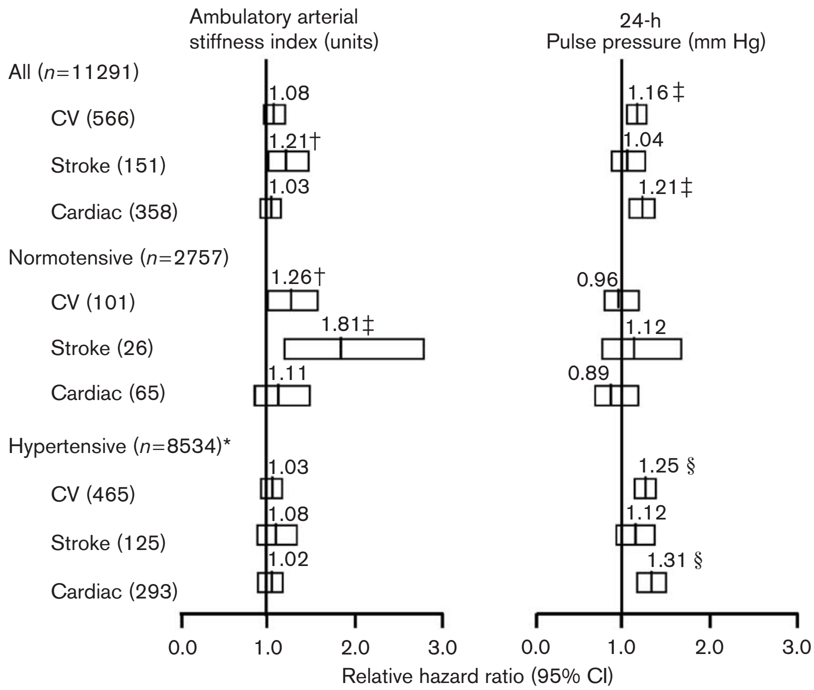
We explored the predictive value of AASI for fatal cardiovascular outcomes among a large cohort of patients referred to a single centre in Dublin, Ireland [10]. At

Fig. 1



Bland–Altman plots of three arterial stiffness indexes: AASI, ambulatory arterial stiffness index; ZASI, normalized 24-h ambulatory stiffness index; C_AI, central augmentation index; ZC_AI, normalized central augmentation index, P_AI, peripheral augmentation index; ZP_AI, normalized peripheral augmentation index; ZPP24, normalized 24-h pulse pressure. Normalization of the data involved calculating the deviation of each individual observation from the population mean in standard deviation units.

Fig. 2



Point estimates and 95% confidence intervals (95% CI) of the relative hazard ratios associated with a 1 SD increase in the ambulatory arterial stiffness index or the 24-h pulse pressure after adjustment for sex, age, mean arterial pressure, body mass index, smoking, diabetes mellitus and a history of cardiovascular disease. The ambulatory arterial stiffness index was additionally adjusted for pulse pressure and vice versa. *Hypertension was a daytime ambulatory blood pressure of at least 135 mmHg systolic and 85 mmHg diastolic. Significance of the relative hazard ratios: $^{\dagger}P<0.05$; $^{\ddagger}P<0.01$, $^{\S}P<0.001$.

baseline, while not on antihypertensive medication, 11 291 patients (mean age, 54.6 years; 5965 women) underwent ambulatory blood pressure monitoring. Over a median follow-up of 5.3 years, 566 cardiovascular deaths occurred – 151 from stroke and 358 from cardiac disorders. After adjustment for other cardiovascular risk factors including sex, age, mean arterial pressure, body mass index, smoking, diabetes mellitus and a history of cardiovascular disease, a 1 SD increase in AASI was associated with a 14% increased risk of cardiovascular mortality [10]. Further analysis showed that AASI was a stronger predictor than pulse pressure for stroke with the opposite trend for cardiac mortality (Fig. 2). In individuals with normal daytime ambulatory blood pressure (< 135/ < 85 mmHg), AASI was more predictive than pulse pressure of cardiovascular mortality, and of stroke mortality (Fig. 2).

Conclusions

We identified a novel index of arterial stiffness, which can be easily measured under ambulatory conditions by means of regular devices for ambulatory blood pressure monitoring. We validated AASI as a prognostic indicator of cardiovascular mortality. Pending further physiologic and clinical studies and validation in outcome studies, AASI might add to the risk stratification on the basis of ambulatory blood pressure monitoring [17].

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