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Transfer function-derived central pressure and cardiovascular disease events: the Framingham Heart Study

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Abstract

Background: Relations between central pulse pressure (PP) or pressure amplification and major cardiovascular disease (CVD) events are controversial. Estimates of central aortic pressure derived using radial artery tonometry and a generalized transfer function may better predict CVD risk beyond the predictive value of brachial SBP.

Methods: Augmentation index, central SBP, central PP, and central-to-peripheral PP amplification were evaluated using radial artery tonometry and a generalized transfer function as implemented in the SphygmoCor device (AtCor Medical, Itasca, Illinois, USA). We used proportional hazards models to examine relations between central hemodynamics and first-onset major CVD events in 2183 participants (mean age 62 years, 58% women) in the Framingham Heart Study.

Results: During median follow-up of 7.8 (limits 0.2–8.9) years, 149 participants (6.8%) had an incident event. Augmentation index ($P = 0.6$), central aortic systolic pressure ($P = 0.20$), central aortic PP (P = 0.24), and PP amplification (P = 0.15) were not related to CVD events in multivariable models that adjusted for age, sex, brachial cuff systolic pressure, use of antihypertensive therapy, total and high-density lipoprotein cholesterol concentrations, smoking, and presence of diabetes. In a model that included standard risk factors, model fit was improved ($P = 0.03$) when brachial systolic pressure was added after central, whereas model fit was not improved ($P = 0.30$) when central systolic pressure was added after brachial.

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Conflicts of interest

G.F.M. is owner of Cardiovascular Engineering, Inc., a company that designs and manufactures devices that measure vascular stiffness. The remaining authors report no conflicts of interest.

Conclusion: After considering standard risk factors, including brachial cuff SBP, augmentation index, central PP and PP amplification derived using radial artery tonometry, and a generalized transfer function were not predictive of CVD risk.

Keywords

aorta; augmentation index; cardiovascular disease; central pressure; prognosis; reflected wave

INTRODUCTION

Central and peripheral blood pressures (BPs) differ because of variable effects of reflected wave timing and amplitude and pressure amplification. The heart and brain are exposed to central rather than peripheral systolic pressure and pulse pressure (PP). Thus, central pressures and measures of wave reflection, such as carotid–brachial pressure amplification and augmentation index, may provide incremental or superior prediction of risk for major cardiovascular disease (CVD) events compared with conventional brachial BP [1–5]. It has been suggested that applanation tonometry, applied to the brachial and carotid arteries, as used in the Framingham Study [6] and others [7–9] may have limitations that obscure the prognostic value of central hemodynamic measures [10,11]. A recent meta-analysis of published and unpublished data suggested that there was a trend for central PP to predict CVD events better than brachial PP [12]. Subsequently, two larger studies that used carotid tonometry or radial artery tonometry and a generalized transfer function showed potential benefit of central aortic pressure indices, including PP, over brachial cuff pressure in prediction of outcome [13,14]. In contrast, recent data from the Framingham Heart Study found that central PP and pressure amplification were not predictive of CVD events in models that adjusted for standard risk factors, including conventional brachial SBP[6]. Thus, a goal of this analysis was to determine whether central pressure obtained by using a transfer function was predictive of events beyond the predictive value of brachial SBP in the Framingham cohort.

The proper approach to calibration of the radial pressure waveform prior to applying the transfer function is also controversial. The standard approach utilized by the SphygmoCor device (AtCor Medical, Itasca, Illinois, USA) uses brachial cuff pressure to calibrate the radial pressure waveform, which assumes that there is no additional amplification of the pressure waveform between brachial and radial arteries. However, several studies have suggested that additional amplification of the pressure waveform between brachial and radial sites will result in underestimation of central pressure if cuff pressure is used to calibrate the radial pressure waveform [15–18].

The present analysis sought to clarify these questions by using the generalized transfer function algorithms implemented in the SphygmoCor device to estimate central pressure, augmentation index, and pressure amplification from radial tonometry waveforms obtained during the previously reported Framingham Heart Study examination [6]. Radial waveforms were calibrated by using either cuff SBP and DBP, as recommended by the manufacturer of the SphygmoCor device, or brachial mean and diastolic pressure to examine the effects on central pressure estimation.

METHODS

Participants

The design and selection criteria for the Framingham Heart Study Original and Offspring cohorts have been detailed previously [19,20]. Participants attending the seventh examination of the Offspring cohort (N = 3539; 1998–2001) or the 26th examination of the Original cohort (N = 310; 1999–2001) were eligible for the present investigation. Tonometry measurements were implemented beginning in February 1999 as described previously [21]. Participants were excluded from the present analysis for the following reasons: attended the visit prior to implementation of tonometry (N = 879), bad or incomplete tonometry data (N = 209), prior CVD (N = 196), or missing covariate or follow-up information (N = 333), resulting in a sample of 2232 participants [1299 (58%) women] as previously reported [6]. For the present analysis, participants were further excluded if adequate radial artery tonometry or transfer function results were not available (N = 49), resulting in a final sample size of 2183 cases. All protocols were approved by Boston University Medical Center's Institutional Review Board and participants provided written informed consent.

Clinical evaluation and definitions

Medical history, physical examination, and electrocardiography were performed routinely at each Framingham Heart Study examination [20,19]. Clinic BPs represent the average of two auscultatory BPs obtained by the physician on seated participants at the time of each Framingham clinic examination using a standardized measurement protocol. Peripheral PP was calculated as the difference between brachial cuff systolic pressure and diastolic pressure. BMI was calculated by dividing weight in kilograms by the square of the height in meters. Criteria for diabetes mellitus were a fasting glucose level of 126 mg/dl (7.0 mmol/l) or greater, or use of medications used to treat hyperglycemia.

Outcomes

Major CVD events were defined as fatal or nonfatal myocardial infarction, unstable angina (prolonged ischemic episode with documented reversible ST segment changes), heart failure, and ischemic or hemorrhagic stroke. Medical records were obtained for all hospitalizations and physician visits related to CVD during follow-up and were reviewed by a committee of three investigators; events were adjudicated following established criteria [22,23].

Noninvasive hemodynamic data acquisition

Participants were studied in the supine position after resting for approximately 5 min. Supine brachial cuff SBP and DBP were obtained using an oscillometric device. Arterial tonometry with simultaneous electrocardiography was obtained from brachial, radial, femoral, and carotid arteries using a commercially available tonometer (SPT-301; Millar Instruments, Houston, Texas, USA). All recordings were performed on the right side of the body. Tonometry and electrocardiographic data were digitized (1000 Hz) during the primary acquisition and transferred to the core laboratory (Cardiovascular Engineering, Inc., Norwood, Massachusetts, USA) for analyses that were performed blinded to clinical data.

Tonometry data analysis

Tonometry waveforms were signal averaged using the electrocardiographic R wave as a fiducial point. Oscillometric systolic and diastolic cuff blood pressures obtained at the time of the tonometry acquisition were used to calibrate the peak and trough of the signal-averaged brachial pressure waveform. Diastolic and integrated mean brachial pressures were used to calibrate carotid pressure tracings [24]. Carotid PP was defined as the difference between the peak and trough of the calibrated carotid pressure waveform. Carotid–brachial PP amplification was defined as brachial PP divided by carotid PP. Augmentation index was computed from the carotid pressure waveform as previously described [25].

Transfer function-derived central aortic pressure was calculated from radial tonometry waveforms as previously described using algorithms implemented via the SphygmoCor device [4]. The radial tonometry waveforms were calibrated using two alternative approaches. The brachial tonometry calibration method used brachial cuff pressure to calibrate a signal-averaged brachial tonometry waveform and then used integrated brachial mean pressure and diastolic pressure to calibrate the radial waveform under the assumption that mean pressure and diastolic pressures are equal in large arteries free of flow-limiting stenoses. In contrast, the radial tonometry calibration method, which is the standard method used by the SphygmoCor device, assumes brachial and radial pressures are equal. Therefore, measured brachial cuff systolic and diastolic pressures were used to calibrate the peak and trough, respectively, of the signal-averaged radial tonometry waveform.

In a secondary analysis, we examined the effects of excluding cases based on screening measures recommended by the SphygmoCor device. Exclusion criteria included pulse height variations more than 5%, pulse diastolic variation more than 5%, pulse shape variation more than 4%, or an operator index less than 80. The operator index represents a composite of the foregoing individual criteria. Cases were further excluded for any of the following reasons: low pulse amplitude (<100 analog-to-digital converter units), augmentation index more than 50%, central or peripheral peak time (T1) outside the acceptable limits (80–150 ms), concordance of central and peripheral T1, or a low first derivative of the pressure waveform. The latter additional criteria are thought to indicate a nonphysiological waveform or a waveform in which tonometry has not been properly applied even when the waveforms are stable and repeatable.

Statistical analysis

Baseline characteristics for the entire study sample were tabulated. Carotid pressures derived using direct tonometry and central aortic pressures derived by using the two alternative calibration methods were tabulated; relations between values obtained by the various methods were examined using Pearson correlation coefficients.

We examined the association between pulsatile hemodynamic measures and time to a first major CVD event by using Cox proportional hazards regression, after confirming that the assumption of proportionality was met. Covariates were selected beginning with components of the Framingham risk score [26] as defined in the prior publication involving this sample [6] and included the following variables at the baseline examination: age, sex, seated SBP

obtained by the examining physician, use of anti-hypertensive therapy, total and high-density lipoprotein cholesterol concentrations, regular use of cigarettes in the prior year, and presence of diabetes mellitus. In addition, we evaluated the relative predictive power of concurrently acquired supine central aortic pressure and brachial cuff systolic pressures by examining improvement in model fit when central and peripheral systolic pressure were added sequentially to a risk factor model. To a base model that included standard risk factors except BP, we added the supine oscillometric brachial SBP obtained at the time of tonometry and then central aortic systolic pressure obtained by using the standard SphymoCor calibration methods, noting the change in −2 log likelihood on each step. Then we reversed the order of entry of central aortic and brachial systolic pressures and again noted the change in model fit at each step. The foregoing approach, which simply examines improvement in model fit as each variable is added to a model containing the other, is indifferent to the effects of collinearity between central and peripheral pressure. In secondary analyses, we examined the effects of screening measures implemented in the SphygmoCor device by comparing hemodynamic measures in cases that were included as compared with those that were excluded by the additional screening measures. In accordance with SphygmoCor recommendations, we reran the outcome models including only cases that fulfilled all screening criteria and used the oscillometric SBP obtained at the time of tonometry as a covariate instead of the BP obtained by the physician. All analyses were performed with SAS version 9.3 (SAS Institute Inc., Cary, North Carolina, USA). A two-sided $P < 0.05$ was considered statistically significant.

RESULTS

Baseline characteristics of the study sample are presented in Table 1. During a median follow-up period of 7.4 (limits0.2–8.9) years, 149 of 2183 participants (6.8%; 57% women) had a first major CVD event, including 56 fatal or nonfatal myocardial infarctions, four individuals with coronary insufficiency, 56 with new heart failure, and 33 strokes.

Central hemodynamic variables are presented in Table 2. There were modest differences between systolic pressures in the central aorta, carotid, brachial and radial arteries, with the expected pattern of generally increasing pressure moving away from the heart and toward the periphery (Tables 1 and 2), because of wave reflection and peripheral amplification. Transfer function central pressures were lower when assessed using the radial as compared with the brachial calibration method (Table 2). Conversely, PP amplification was higher when central pressure was assessed using the radial calibration method (Table 2). Values for central, brachial, and radial systolic pressure and PP were highly correlated ($r = 0.88–0.96$, Table 3). The correlation between the seated SBP obtained by the physician earlier during the visit and the supine oscillo-metric BP obtained at the time of tonometry was less strong ($r = 0.78$, $P < 0.001$).

Cox models for individual pulsatile hemodynamic measures are presented in Table 4. In models that adjusted for standard risk factors, including seated SBP obtained by the physician, augmentation index, central aortic PP, and PP amplification were not related to CVD events, regardless of the calibration method used (Table 4).

We next examined the relative predictive value of central aortic as compared with simultaneously acquired brachial systolic pressure. When added to the base model that included standard risk factors (excluding physician BP), brachial systolic pressure recorded at the time of tonometry was associated with events (hazard ratio = 1.30 per SD, 95% confidence interval: 1.12, 1.50, $P < 0.001$) and model fit was improved (−2 log likelihood 2096.8 vs. 2085.6, $P < 0.0001$).When central aortic systolic pressure was subsequently added to the model, there was no further improvement in model fit (−2 log likelihood 2085.6 vs. 2083.2, $P = 0.30$). When added first to the base model, central aortic systolic pressure was associated with events (hazard ratio = 1.25 per SD, 95% confidence interval: 1.08, 1.44, $P < 0.01$) and model fit was improved (−2 log likelihood 2096.8 vs. 2088.4, $P = 0.012$). When brachial systolic pressure was subsequently added to the model that included central aortic systolic pressure, model fit was improved (−2 log likelihood 2088.4 vs. 2083.2, $P = 0.03$), indicating that brachial pressure provided additional prognostic information even after considering simultaneous central BP assessed using the standard SphygmoCor method.

A comparison of cases that passed ($N = 1262$) as compared with those that were excluded ($N = 921$) by the recommended SphygmoCor screening measures is presented in Supplemental Table 1, http://links.lww.com/HJH/A625. The only measure that differed significantly was augmentation index, which was used as a criterion for exclusion (if the value was >50%). As expected, this exclusion resulted in lower augmentation index in the included cases. When models were repeated using the supine oscillometric SBP obtained at the time of tonometry as a covariate in the models instead of the physician BP and including only cases that passed SphygmoCor screening measures, only central aortic PP was associated with events, although the direction of the association was opposite to the hypothesis that higher central aortic pressure pulsatility is associated with increased events (Supplemental Table 2, http://links.lww.com/HJH/A625).

DISCUSSION

We utilized radial artery tonometry waveforms obtained in middle-aged and older participants in the community-based Framingham Heart Study to examine relations between central hemodynamic measures and risk for major CVD events. Central systolic pressure, central PP, augmentation index, and PP amplification were derived from radial artery waveforms using the generalized transfer function and analysis algorithms implemented via the SphygmoCor device. In our community-based sample, central BP, augmentation index, and pressure amplification were not associated with risk for a major CVD event in models that adjusted for established risk factors.

A limited number of longitudinal studies have suggested that central systolic pressure and PP and measures of wave reflection may provide incremental CVD risk stratification beyond that provided by standard risk factors including conventional brachial BP [1–5,27]. A recent meta-analysis identified a trend for central PP to predict CVD events better than brachial PP [12]. In addition, augmentation index was reported to predict CVD events independently of peripheral BP. Our results indicate that in a community-based sample, central systolic pressure and PP, augmentation index, and pressure amplification do not provide additional

prognostic information after accounting for standard risk factors, including conventionally measured seated brachial SBP obtained during the clinic visit by a physician.

We evaluated the relative predictive value of central and peripheral systolic pressure by entering one BP measure and then the other to a base model that included standard risk factors and assessing improvement in model fit when central pressure was added after vs. before peripheral pressure. When central systolic pressure was added to a model that included peripheral systolic pressure and standard risk factors, model fit was not improved. In contrast, when peripheral systolic pressure was added to a model that included central systolic pressure and standard risk factors, model fit was improved, indicating that peripheral systolic pressure is a better predictor of events in our community-based cohort. These analyses demonstrate that once peripheral systolic pressure has been considered, central systolic pressure offers no additional risk prediction in our cohort. Thus, our data do not support the hypothesis that higher central pressures and measures of central wave reflection provide clinically relevant, independent prognostic information after considering conventional BP recorded noninvasively in the arm using standard techniques that have been a staple of clinical practice for more than a century.

Prior studies have assumed that brachial systolic and diastolic pressures could be applied to the peak and trough of a radial waveform to assess mean arterial pressure, which is required to calibrate the carotid or central aortic pressure waveform [2,3]. However, others have shown that the implicit assumption of no amplification between brachial and radial arteries may be incorrect [15–18]. Pressure amplification between the brachial and radial arteries, if present, will cause overestimation of pressure amplification between central aortic and brachial cuff pressures. In our study, direct calibration of radial tonometry with brachial cuff pressure resulted in lower central systolic pressure and PP and higher pressure amplification (Table 2), consistent with our observation of modest additional amplification of the pressure waveform between the brachial and radial sites (Table 1).

The inability of central PP and measures of wave reflection to provide incremental risk prediction beyond that provided by standard CVD risk factors should be interpreted in light of the strong correlation between central and peripheral systolic pressure and PP in middle-aged and older adults who are at highest risk for CVD events [28,29]. We have demonstrated that independent of the method used to calibrate waveforms or estimate central pressure, there is a very high degree of correlation between central aortic, carotid, brachial, and radial systolic pressure and PP ($r = 0.88–0.98$). To illustrate the effect of correlation between a candidate predictor variable and other covariates in the model, we computed hazard ratios required to achieve 80% power when covariates accounted for a proportion of variance (R^2) in the predictor variable that varied from 25 to 90% [30]. Results are plotted in the Fig. 1. Panel A demonstrates that as R^2 approaches 90%, the hazard ratio required approaches 2.0. We also computed the number of events required to achieve 80% power with a fixed hazard ratio of 1.30 for various levels of R^2. We chose a hazard ratio of 1.30 because it corresponds to 80% power in a study with 149 events when $R^2 = 25\%$. As shown in panel B, to detect a hazard ratio of 1.30 when $R^2 = 90\%$, a sample with 1118 incident events would be required. As a result, the opportunity to demonstrate that central aortic or carotid pressure provides incremental prognostic information after considering conventional brachial cuff BP is

extremely limited. Differences between central and peripheral BP do occur, consistent with well documented physical principles associated with variable timing and amplitude of wave reflections. However, the very high degree of correlation between central and peripheral pressures, regardless of method used to estimate central pressure, indicates that variability in the difference between central and peripheral pressure is quite small in comparison with overall variability in BPs in our community-based sample.

To minimize the effects of collinearity between central and peripheral pressures, we also evaluated PP amplification, which assesses only the relative difference between central and peripheral PP. In addition, amplification depends only on relative differences in waveform shape between two sites, for example, carotid-to-brachial or carotid-to-radial, and is not dependent on the value of BP used to calibrate the waveforms. In multivariable risk factor-adjusted models, we found no relation of amplification to risk for events when amplification was assessed using a generalized transfer function as implemented via the SphygmoCor device. Our findings suggest that when considered in the context of the broad distribution of values for peripheral systolic pressure and PP found in middle-aged and older people, knowledge of the modest differences that may be seen between central and peripheral PP does not contribute substantively to CVD risk prediction in a sample such as ours.

Several limitations of our study should be considered. We acknowledge that a null finding in an observational study cannot definitively prove that there is no causal link between the differences in central and peripheral BP and risk for CVD events. Each of the methods assessed in our study provides only a noninvasive estimate of central pressure. A direct measure of central pressures may provide better risk discrimination. We cannot exclude the possibility that with more follow-up or a substantially larger sample, transfer function-derived vascular measures might be associated with risk for CVD events. We evaluated a middle-aged and older cohort of predominately white study participants. Therefore, our results may not be generalizable to younger individuals and other ethnicities. Strengths of our study include a large, community-based sample with routinely ascertained risk factors, and a comprehensive battery of measures of arterial stiffness and wave reflection.

In conclusion, over the past several decades, numerous researchers have proposed various methods in an effort to improve on the prognostic power of conventional BP as assessed in the brachial artery using techniques that have been standard in clinical practice for over a century. The observation that there can be differences between central and peripheral systolic pressure and PP raised hope that central BP would provide independent prognostic information for predicting CVD events. In addition, the observation that progressive augmentation of the central pressure waveform from early adulthood to midlife erodes the difference between central and peripheral PP and accelerates the rise in central BP suggested that augmentation index might be a clinically useful measure of CVD risk. These are reasonable hypotheses that have been vigorously pursued in various forums. Our study demonstrates that additional measures of modest differences between central and peripheral systolic pressure and PP are not sufficient to result in improved assessment of CVD risk in a large, well characterized, middle-aged, and older community-based sample such as ours.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

BP	blood pressure
CVD	cardiovascular disease
PP	pulse pressure

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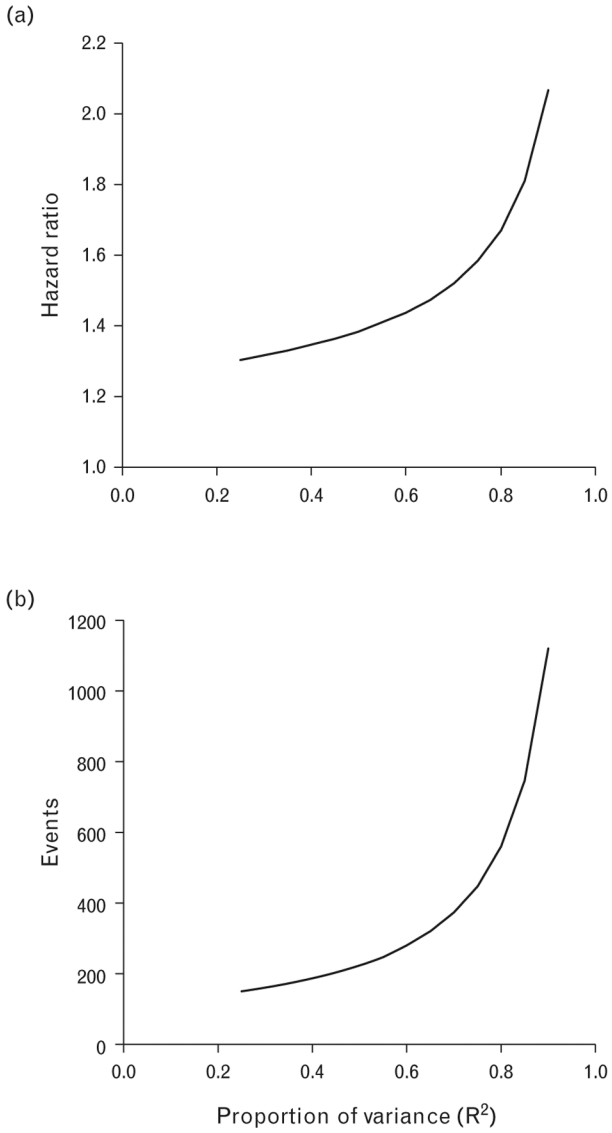

FIGURE 1.

Power analysis for models that include covariates that are correlated with a primary predictor variable. Panel A illustrates the minimum hazard ratio required to achieve 80% power to detect an effect with 149 events when covariates in the model explain a proportion of variance (R^2) in the primary predictor. Panel B illustrates the number of events required to achieve 80% power for a fixed hazard ratio of 1.30.

TABLE 1.

Characteristics of the sample at examination cycle seven ($N = 2183$)

Variable	Value
Age (years)	62 ± 12
Women, N (%)	1265 (58)
Height (cm)	167 ± 10
Weight (kg)	75 ± 16
BMI (kg/m^2)	27.2 ± 4.6
Heart rate (beats/min)	65 ± 11
Total cholesterol (mg/dl)	201 ± 36
High-density lipoprotein cholesterol (mg/dl)	56 ± 17
Triglycerides ln(mg/dl)	4.7 ± 0.5
Hypertension treatment, N (%)	697 (32)
Diabetes, N (%)	175 (8)
Smoker, N (%)	274 (13)
Clinic BP (mmHg)	
Systolic	127 ± 19
Diastolic	74 ± 10
Pulse	53 ± 17
Brachial tonometry pressures (mmHg)	
Systolic	124 ± 18
Diastolic	70 ± 11
Pulse	54 ± 15
Mean	92 ± 12
Radial tonometry pressures (mmHg)	
Systolic	128 ± 20
Pulse	58 ± 17

All values are mean ± SD except as noted.

BP, blood pressure.

TABLE 2.

Central pressure characteristics by direct carotid tonometry and generalized transfer function (N = 2183)

	Transfer function variables by calibration method		
Variable	**Carotid tonometry**	**Brachial calibration[a]**	**Radial calibration[b]**
Central systolic pressure (mmHg)	122 ± 20	118 ± 18	115 ± 17
Diastolic pressure (mmHg)	70 ± 11	71 ± 11	71 ± 11
Central PP (mmHg)	52 ± 17	47 ± 16	44 ± 15
PP amplification, ratio[c]	1.06 ± 0.12	1.17 ± 0.14	1.25 ± 0.14
Augmentation index, %	15 ± 13	31 ± 11	31 ± 11

Values are given as mean ± SD.

PP, pulse pressure.

[a]Brachial waveform calibrated using brachial cuff systolic and diastolic pressures; radial tonometry subsequently calibrated using brachial mean and diastolic pressures, which allows for variable amplification between brachial and radial artery.

[b]Radial waveform calibrated using brachial cuff systolic and diastolic pressures, which assumes that there is no amplification between brachial and radial artery and is the standard method employed by the SphygmoCor system.

[c]Defined as brachial PP divided by carotid (tonometry) or central (transfer function) PP.

TABLE 3.

Correlations between central and peripheral systolic pressure and pulse pressure estimated by various methods

		Central aortic pressure by calibration method			
Pressure		**Radial**	**Carotid**	**Brachial calibration[a]**	**Radial calibration[b]**
Brachial	SBP	0.96	0.96	0.96	0.97
	PP	0.95	0.95	0.94	0.96
Radial	SBP		0.95	0.97	0.91
	PP		0.93	0.95	0.88
Carotid	SBP			0.98	0.96
	PP			0.96	0.95
Central, brachial calibration	SBP				0.97
	PP				0.96

Values represent Pearson correlation coefficients. For each site, the SBP row compares the corresponding systolic pressures and the PP row compares the corresponding PPs. All P values are less than 0.001.

PP, pulse pressure.

[a]Brachial waveform calibrated using brachial cuff systolic and diastolic pressures; radial tonometry subsequently calibrated using brachial mean and diastolic pressures, which allows for variable amplification between brachial and radial artery.

[b]Radial waveform calibrated using brachial cuff systolic and diastolic pressures, which assumes that there is no amplification between brachial and radial artery and is the standard method employed by the SphygmoCor system.

TABLE 4.

Cox models for transfer function-based pulsatile hemodynamic measures as predictors of a major cardiovascular event during the follow-up period

Hemodynamic measure	Hazard ratio (95% confidence interval)	*P*
Augmentation index[a]	1.06 (0.85, 1.31)	0.60
Brachial calibration[b]		
Central systolic pressure	1.12 (0.89, 1.40)	0.35
Central PP	0.89 (0.73, 1.07)	0.22
PP amplification	1.10 (0.94, 1.27)	0.23
Radial calibration[c]		
Central systolic pressure	1.17 (0.92, 1.49)	0.20
Central PP	0.89 (0.73, 1.08)	0.24
PP amplification	1.13 (0.95, 1.35)	0.15

Hazard ratios expressed per 1 SD higher value, adjusted for age, sex, total cholesterol, HDL cholesterol, SBP obtained by the physician in the clinic, smoking, diabetes and hypertension treatment. Each hemodynamic measure was evaluated in a separate model.95% confidence interval, lower and upper limits of the 95% confidence intervals.

[a]Adjusted to a heart rate of 75 beats/min.

[b]Brachial waveform calibrated using brachial cuff systolic and diastolic pressures; radial tonometry subsequently calibrated using brachial mean and diastolic pressures, which allows for variable amplification between brachial and radial artery.

[c]Radial waveform calibrated using brachial cuff systolic and diastolic pressures, which assumes that there is no amplification between brachial and radial artery and is the standard method employed by the SphygmoCor system.