Pulsatile but Not Steady Component of Blood Pressure Predicts Cardiovascular Events in Coronary Patients

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Abstract—Although the differences between central and peripheral blood pressure (BP) values have been known for decades, the consequences of decision making based on peripheral rather than central BP have only recently been recognized. There are only a few studies assessing the relationship between intraaortic BP and cardiovascular risk. In addition, the relationship between central BP and the risk of cardiovascular events in a large group of coronary patients has not yet been evaluated. Therefore, the aim of the study was to determine the prognostic significance of central BP-derived indices in patients undergoing coronary angiography. Invasive central BPs were taken at baseline, and study end points were ascertained during over a 4.5-year follow-up in 1109 consecutive patients. The primary end point (cardiovascular death or myocardial infarction or stroke or cardiac arrest or heart transplantation or myocardial revascularization) occurred in 246 (22.2%) patients. Central pulsatility was the most powerful predictor of the primary end point (hazard ratio [HR] 1.30, 95% confidence interval [CI] 1.14 to 1.48). Central pulse pressure was also independently related to the primary end point (HR 1.25, 95% CI 1.09 to 1.43). Central mean BP as well as peripheral BP parameters were not independently related to the primary end point risk. Central pulsatility was also related to risk of cardiovascular death or myocardial infarction or stroke. The pulsatile component of BP is the most important factor related to the cardiovascular risk in coronary patients. It is more closely associated with cardiovascular risk than steady component of BP. (Hypertension. 2008;51:848-855.)

Key Words: blood pressure ▪ central pulse pressure ▪ pulsatility ▪ cardiovascular risk ▪ atherosclerosis ▪ coronary artery disease

Diastolic blood pressure (DBP) was previously believed to be the only meaningful predictor of cardiovascular events; however, systolic blood pressure (SBP) is now being considered an even more important cardiovascular risk factor.1 Recently, the prospective and retrospective epidemiological studies have demonstrated that elevated pulse pressure (PP, the difference between systolic and diastolic pressure) is independently related to the risk of cardiovascular events, especially in the elderly.1,2 Furthermore, new parameters (pulsatility and pulsatility index) of the pulsatile component of blood pressure (BP) have been developed.3,4 Pulsatility is calculated as PP divided by mean blood pressure (MBP).3 Unlike SBP, DBP, and PP, this new parameter is not correlated with MBP, and thus it may be very useful in research on atherosclerosis pathogenesis and its complications development.5,6 Pulsatility may be seen as indicator of the relative changes of blood pressure in opposition to pulse pressure which is an index of absolute blood pressure changes.

Although the differences between central and peripheral BP values have been known for decades, the consequences of decision making based on peripheral rather than central BP have only recently been recognized.6–9 As central BP directly affects heart and coronary as well as carotid arteries and is directly related to the incidence of major cardiovascular complications, more and more attention is being given to the ascending aortic BP measurements.6–7 There are only a few studies assessing the relationship between central BP and cardiovascular risk. The relationship between pulsatility (as measured invasively in the ascending aorta) and the risk of cardiovascular events has not yet been evaluated. Therefore, the present study was designed for the assessment of the relationship between prognosis and the steady and pulsatile components of central BP.

Methods

Study Population

Consecutive patients suspected of having coronary artery disease (CAD) who were undergoing nonemergency coronary angiography from December 1998 to November 2001 were eligible for our study.
We excluded from the analysis all patients with acute myocardial infarction (MI) within a week before angiography, patients in unstable hemodynamic conditions, and those with primary pulmonary hypertension. Patients with hemodynamically significant valvular heart disease as determined during catheterization or echocardiography and patients with congenital heart disease as well as those with atrial fibrillation and atrial flutter at the time of examination were excluded. The institutional ethics committee approved the study protocol. The study procedures were in accordance with institutional guidelines.

The study group consisted of 1150 patients. Among them 299 (26.0%) were women and 851 (74.0%) were men. Study end points were ascertained for 1109 (96.4%) patients. Furthermore, only the cause and date of death was obtained for 3 participants whereas only date of death for one patient. Thirty seven (3.2%) patients were lost to follow-up.

We examined a possible bias in the formation of the analyzed population by comparing it with respect to age, gender, risk factors, heart failure, and values of BPs as well as mean value of ejection fraction (EF) with the data from a population consisting of 41 patients for which there was no whole follow-up information. These comparisons showed no statistically significant differences with respect to all of the above factors.

### Baseline Data Collection

Fasting blood samples were taken before coronary angiography for the analysis of lipids as well as glycemia and creatinine levels. Diabetes was defined as a fasting blood glucose level of 7.0 mmol/L or more or the use of an antidiabetic drug. No differentiation was made between type 1 and type 2 diabetes during analysis because of the low number of patients with type 1 diabetes. Participants with total cholesterol levels ≥5.2 mmol/L or being prescribed a lipid-lowering drug were considered as having hypercholesterolemia. Hypertension was defined as a high brachial BP (SBP ≥140 mm Hg or DBP ≥90 mm Hg) or prescription of a BP-lowering drug for high BP. Glomerular filtration rate (GFR) was calculated using abbreviated MDRD study equation. Present smokers were defined as those who smoked any tobacco in the previous month. EF was determined using contrast ventriculography.

Brachial BP was measured twice using a mercury sphygmomanometer (“STANDBY” Model, W.A. BAUM Co Inc). Measurements were made under standardized conditions, between 8 and 11 AM. Patients were seated for measurements, had not eaten or smoked for at least 30 min, and had rested for 10 min. BP for individual participants was calculated as the average of the 2 readings.

Central BP measurements were obtained in the supine position. Aortic SBP and DBP were measured in the ascending aorta using a low-compliance fluid-filled system (the natural frequency of the system was 17 Hz and the damping coefficient 0.35). The transducer was localized on the level of aortic valve. It was calibrated with mercury manometer. MBP was obtained by direct integration of the BP curve. PP was calculated as the difference between SBP and DBP. Pulsatility was calculated as PP divided by MBP.3

Cardiac catheterization was performed according to a standard technique. Coronary angiograms were scored using 2 techniques: NASCET and Oka.5

### Number of Diseased Arteries

The 3 major coronary vessels (left anterior descending artery, circumflex artery, and right coronary artery) and their branches were evaluated for the extent of coronary atherosclerosis. A diseased artery was defined as >50% stenosis in at least 1 of its segments. Significant left main artery stenosis was coded as 2-vessel disease.

### Mean Stenosis

The maximum stenosis was measured in 15 segments (as defined by the American Heart Association6)), and the mean stenosis was then calculated.

All physicians followed European Society of Cardiology guidelines when considering myocardial revascularization. All cardiovascular drugs taken within 24 hours before catheterization were analyzed. The following medication classes were considered in the analysis: antiplatelets, β-blockers, ACE-inhibitors, calcium antagonists, diuretics, nitrates, statins, fibrates, digoxin, oral hypoglycemics, and insulin.

### Study End Points

Study end points were assessed over a 4.5-year follow-up period. A standardized questionnaire was sent to every participant. In case of no response the second questionnaire was sent. If the answer was still not obtained family or neighbors were contacted. Every effort was made to determine the patients’ status. If the answer was obtained and the patient reported no health problems no further contact was made. However, in case of any health problem patient was contacted personally. The diagnosis of MI, stroke, percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), nonfatal cardiac arrest, and heart transplantation was made on the basis of medical documentation.

The primary end point was defined as cardiovascular death or nonfatal MI or nonfatal stroke or nonfatal cardiac arrest or PCI or CABG or heart transplantation. The secondary end point was defined as cardiovascular death or nonfatal MI or nonfatal stroke. Cardiovascular events which occurred within 24 hours after coronary angiography (stroke in 1 patient, ventricular fibrillation in 2 patients, and sustained ventricular tachycardia in 2 patients) were not included in the analysis as they were considered as procedure-related.

### Statistical Analysis

Categorical variables are reported as percentages and continuous variables as means±SD. Normally distributed continuous variables were compared using Student t test. Mann-Whitney U test was used in case of variables without normal distribution. The Pearson χ2 test was applied to all categorical variables. A 2-tailed probability value of less than 0.05 was considered to indicate statistical significance. Correlations between BP-related indices and coronary atherosclerosis measures were calculated using Spearman correlation. The standardized by age (in 5-year strata) and gender rates of primary end point according to quartiles of central and peripheral MBP, PP, and pulsatility were calculated.

Cox’s proportional hazards models were used to determine the effects of BP-derived indices and the other variables on the occurrence of primary and secondary end points in both univariate and multivariate analyses. Commencing with all variables presented in Table 1 and prescribed medications stepwise regression analysis was performed using probability value >0.05. To compare the prognostic value of BP-related indices, each index was included separately into the model containing all independent predictors of the end point. The risk associated with BP-derived indices is reported according to the standard deviation increase in the value of each index. This allows easy comparison of the prognostic value of these indices. As the next step we constructed 2 models: model 1 consisted of age, gender, and a BP-related index, whereas model 2 consisted of the above variables plus ejection fraction, mean coronary artery stenosis, heart failure, heart rate, risk factors, cardiovascular history, GFR, and prescribed drugs. Afterward we performed additional multivariate analysis: central MBP was forced to the above described models together with central PP, then with central pulsatility, and finally central PP together with central pulsatility were analyzed. We repeated the above analyses using calculated (from SBP and DBP) central and peripheral MBP.

Subgroup analysis examined the relationship between BP-derived indices and the risk of primary end point according to variables which were significant predictors of the event-free survival in multivariate analysis of the whole study group. Additionally, subgroup analysis according to age, previous myocardial revascularization procedures, heart failure, and hypertension was performed. Only BP-derived indices which were independent predictors of the primary end point occurrence in the whole study group were included in this part of the analysis. Test for interaction in the Cox model was used to compare hazard ratios between the analyzed subgroups. We also calculated Receiver Operator Characteristics curves. All data were analyzed using STATISTICA 6.0 software (StatSoft, Inc).
Table 1. Characteristics of the Analyzed Population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Men n=821</th>
<th>Women n=288</th>
<th>P</th>
<th>Overall n=1109</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>56.9±10.1</td>
<td>59.3±9.9</td>
<td>&lt;0.05</td>
<td>57.5±10.1</td>
</tr>
<tr>
<td>Smoking</td>
<td>111 (13.5%)</td>
<td>18 (6.3%)</td>
<td>&lt;0.05</td>
<td>129 (11.6%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>595 (72.5%)</td>
<td>242 (84.0%)</td>
<td>&lt;0.05</td>
<td>837 (75.5%)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>679 (82.7%)</td>
<td>241 (83.7%)</td>
<td>NS</td>
<td>920 (83.0%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>113 (13.7%)</td>
<td>47 (16.3%)</td>
<td>NS</td>
<td>160 (14.4%)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>53 (6.5%)</td>
<td>16 (5.6%)</td>
<td>NS</td>
<td>69 (6.2%)</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>470 (57.2%)</td>
<td>125 (43.4%)</td>
<td>&lt;0.05</td>
<td>595 (53.7%)</td>
</tr>
<tr>
<td>Previous myocardial revascularization</td>
<td>74 (9.0%)</td>
<td>18 (6.3%)</td>
<td>NS</td>
<td>92 (8.3%)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27.3±3.5</td>
<td>28.0±4.7</td>
<td>&lt;0.05</td>
<td>27.5±3.9</td>
</tr>
<tr>
<td>Left ventricular EF, %</td>
<td>55.2±12.6</td>
<td>59.7±11.3</td>
<td>&lt;0.05</td>
<td>56.4±12.4</td>
</tr>
<tr>
<td>Heart rate, per minute</td>
<td>65.9±10.6</td>
<td>69.1±13.9</td>
<td>&lt;0.05</td>
<td>66.6±11.5</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>5.4±1.1</td>
<td>5.6±1.1</td>
<td>&lt;0.05</td>
<td>5.5±1.1</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.2±0.3</td>
<td>1.4±0.3</td>
<td>&lt;0.05</td>
<td>1.2±0.3</td>
</tr>
<tr>
<td>LDL cholesterol, mmol/L</td>
<td>3.3±1.0</td>
<td>3.4±1.1</td>
<td>NS</td>
<td>3.3±1.0</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>2.1±1.2</td>
<td>1.8±0.9</td>
<td>&lt;0.05</td>
<td>2.0±1.2</td>
</tr>
<tr>
<td>Fasting glucose, mmol/L</td>
<td>5.5±1.4</td>
<td>5.5±2.0</td>
<td>NS</td>
<td>5.5±1.6</td>
</tr>
<tr>
<td>Creatinine, μmol/L</td>
<td>97.0±36.8</td>
<td>85.3±52.6</td>
<td>&lt;0.05</td>
<td>93.9±41.9</td>
</tr>
<tr>
<td>Glomerular filtration rate, mL/min/1.73 m²</td>
<td>79.8±19.8</td>
<td>94.5±24.8</td>
<td>&lt;0.05</td>
<td>83.7±22.2</td>
</tr>
</tbody>
</table>

EF indicates ejection fraction.

Results

The clinical characteristics of the study population is shown in Table 1. Obesity (body mass index ≥30.0 kg/m²) was found in 259 (23.4%) patients, whereas 557 (50.2%) participants were overweight (body mass index 25.0 to 30.0 kg/m²). Left ventricular EF ≥55% was observed in 739 (66.6%) patients, whereas 101 (9.1%) subjects had EF below 40%. The central BP values as well as pulsatility at baseline are shown in Table 2. The brachial BPs are presented in Table S1 (available in an online data supplement at http://hyper.ahajournals.org). The proportions of patients treated with cardiovascular drugs during 24-hours before catheterization are presented in Table S2. On the basis of coronary angiography, 1-vessel CAD was found in 271 (24.4%) patients, 2-vessel disease in 254 (22.9%), and 3-vessel disease in 349 (31.5%) participants, whereas 235 (21.2%) patients had no significant atherosclerotic lesion in the coronary tree. The mean stenosis of coronary artery segments was 19.3±13.1%. Of 874 patients with significant (>50%) lesions in coronary arteries, 323 (37.0%) were subsequently treated conservatively, 357 (40.8%) underwent PCI, and 194 (22.2%) underwent CABG.

Mean stenosis of coronary artery correlated better with BP-derived indices (data not shown) than the number of diseased arteries. Similarly, mean stenosis was correlated better with BPs as well as with pulsatility in patients with normal left ventricular EF (≥55%). In patients with left ventricular EF <55% BPs did not correlate with any coronary atherosclerosis measures. On the other hand the correlation between mean stenosis and central pulsatility only just reached statistical significance. On the basis of these observations, the mean stenosis was used as a measure of coronary atherosclerosis in the subsequent multivariate analyses.

During a mean follow-up time of 52.7±19.2 months 90 deaths were recorded. The mean follow-up time for those who survived until the end of the follow-up was 55.0±19.2 months. During the follow-up there were 71 (6.4%) cardiovascular deaths, 91 (8.2%) nonfatal myocardial infarctions, 28 (2.5%) nonfatal strokes, and 1 (0.1%) nonfatal cardiac arrest. One patient (0.1%) underwent heart transplantation, 116 (10.5%) underwent PCI, and 26 (2.3%) CABG, whereas 10 participants (0.9%) underwent both PCI and CABG.

The primary end point occurred in 246 (22.2%) patients (198 men and 48 women). The standardized by age and gender event rates according to quartiles of central MBP, PP, and pulsatility are presented on (Figure 1). The risk of the primary end point was not related to the quartiles of MBP. On the other hand it was significantly higher in the 4th quartile of central PP compared to 1st and 2nd. The risk was also significantly higher in 3rd and 4th quartiles of central pulsatility compared to 1st quartile. The event rates did not differ among quartiles of peripheral MBP, PP, or pulsatility. Independent predictors of the primary end point are shown in Table 3. According to the Wald statistics value the most powerful predictor of the primary end point was EF. When central pulsatility was added to the model consisting of all independent predictors (EF, mean coronary stenosis, previous

Table 2. Central BP Values at Baseline

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>135.3±23.1</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>71.6±11.0</td>
</tr>
<tr>
<td>Mean blood pressure, mm Hg</td>
<td>92.9±13.6</td>
</tr>
<tr>
<td>Pulse pressure, mm Hg</td>
<td>63.7±18.2</td>
</tr>
<tr>
<td>Pulsatility</td>
<td>0.68±0.15</td>
</tr>
</tbody>
</table>
MI, sex, GFR, diabetes) it occurred the most powerful predictor. When central PP was included instead of pulsatility it appeared to be more strongly related to the cardiovascular risk than any of non–BP-related variables. If other BP-related parameters were included into the model they were not independently related to the risk of the primary end point.

Table 4 shows hazard ratios of the primary end point according to MBP, PP, and pulsatility. MBP was not related to the risk of the primary end point. Central PP and central pulsatility were related to the cardiovascular risk both after age and gender adjustment as well as after adjustment for a number of other variables.

When central MBP and central PP were forced together into the above statistical models only central PP occurred significantly related to the cardiovascular risk (Table 5). Similarly, when central pulsatility was forced into the models together with MBP only the former variable occurred a predictor of the primary end point. When central PP and central pulsatility were analyzed together none of them reached the significance level. However, after adjustments for age and gender central pulsatility but not central PP was significantly related to the risk of primary end point. We repeated the above analyses using calculated central and peripheral MBP. The results did not differ significantly (Table S3). Subgroup analyses are presented on (Figures 2 and 3). We found no significant heterogeneity among analyzed subgroups. We also calculated ROC curves. The area under the curve was 0.52 (95% CI 0.47 to 0.56) for central

Table 3. Independent and BP-Related Predictors of the Primary End Point

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio (95% Confidence Interval)</th>
<th>Wald Statistics</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Independent non-BP related predictors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ejection fraction, per SD</td>
<td>0.80 (0.70 to 0.92)</td>
<td>9.57</td>
<td>0.002</td>
</tr>
<tr>
<td>Mean coronary artery stenosis, per SD</td>
<td>1.25 (1.08 to 1.44)</td>
<td>9.14</td>
<td>0.0055</td>
</tr>
<tr>
<td>Previous myocardial infarction (yes-1, no-0)</td>
<td>1.38 (1.03 to 1.86)</td>
<td>4.68</td>
<td>0.0305</td>
</tr>
<tr>
<td>Sex (male-1, female-0)</td>
<td>1.44 (1.03 to 2.02)</td>
<td>4.49</td>
<td>0.0341</td>
</tr>
<tr>
<td>Glomerular filtration rate, per SD</td>
<td>0.85 (0.73 to 0.99)</td>
<td>4.15</td>
<td>0.0416</td>
</tr>
<tr>
<td>Diabetes (yes-1, no-0)</td>
<td>1.39 (1.00 to 1.95)</td>
<td>3.85</td>
<td>0.0496</td>
</tr>
<tr>
<td>Invasive ascending aortic blood pressure*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean blood pressure, per SD</td>
<td>1.01 (0.89 to 1.16)</td>
<td>0.04</td>
<td>0.8362</td>
</tr>
<tr>
<td>Pulse pressure, per SD</td>
<td>1.25 (1.09 to 1.43)</td>
<td>10.07</td>
<td>0.0015</td>
</tr>
<tr>
<td>Pulsatility, per SD</td>
<td>1.30 (1.14 to 1.48)</td>
<td>14.64</td>
<td>0.0001</td>
</tr>
<tr>
<td>Sphygmomanometer brachial blood pressure*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean blood pressure, per SD</td>
<td>1.04 (0.92 to 1.18)</td>
<td>0.42</td>
<td>0.5194</td>
</tr>
<tr>
<td>Pulse pressure, per SD</td>
<td>1.03 (0.86 to 1.22)</td>
<td>0.08</td>
<td>0.7759</td>
</tr>
<tr>
<td>Pulsatility, per SD</td>
<td>1.07 (0.94 to 1.21)</td>
<td>0.91</td>
<td>0.3388</td>
</tr>
</tbody>
</table>

SD indicates standard deviation.

*BP-derived indices were added separately to the model consisting of independent non-BP related predictors of the primary end point.

Figure 1. The risk of primary end point according to quartiles of central mean blood pressure, pulse pressure, and pulsatility. All rates are standardized by age (in 5-year strata) and gender.
MBP, 0.57 (0.53 to 0.62) for central PP, and 0.58 (0.54 to 0.63) for central pulsatility.

Secondary end point consisted of cardiovascular death or nonfatal MI or nonfatal stroke occurred in 144 (13.0%) patients. The independent predictors of the end point are shown in Table S4. According to the Wald statistics value the most powerful predictor of the secondary end point was GFR. When central pulsatility was added to the model it occurred independently related to the end point. If other BP-related parameters were included into the model they were not independent predictors.

**Discussion**

In recent years, the pulsatile component of BP has been shown to be involved in the pathogenesis of atherosclerosis.6,11,12 Although many studies have demonstrated an independent relationship between the pulsatile component of BP and the risk of cardiovascular events, some studies have failed to show such an association, especially in younger subjects.13,14 This can be attributable to measurement of peripheral instead of central BP.6 Indeed, because central SBP and PP values differ significantly from peripheral values the consequences of decision making based on peripheral BP...
have been increasingly recognized in recent years. Central PP was related to the risk of the primary end point in our population of coronary patients. This finding is consistent with the previous studies. In the population of the CAFE Study central PP was proved to be related to the cardiovascular risk. Safar et al reported that central PP (measured noninvasively on carotid artery) was related to the risk of death in patients with renal insufficiency, but no such association could be shown for peripheral pressure. Roman et al studied patients with risk factors but without symptoms of CAD and concluded that central aortic pressure better predicts incident cardiovascular disease than brachial pressure. On the other hand Dart et al reported peripheral PP to be superior compared to central PP in predicting outcome in hypertensive women. However, it should be underlined that population studied by Dart et al was much older compared to the other studies. It is known that age is one of the major factors influencing the difference between peripheral and central BP. It should be also noted that only women were included in the analysis in this study. Although sex was not significantly related to the association between central PP and the cardiovascular risk in our study (Figure 2), it should be underlined that it cannot be excluded that sex in addition to age may explain the different results reported by Dart et al. Moreover, analytic methods in this study have been questioned. We would like to emphasize that all the above mentioned studies used noninvasive methods to assess central BP whereas direct invasive measurements were used in the present study.

Steady component of BP (represented by MBP) was not related to the cardiovascular risk in our study population. This finding agrees with some previous studies. In contrast, pulsatile components of BP parameters were significant predictors of cardiovascular risk. Our findings concur with the results of several small studies showing independent relationship between intra-aortic pulsatility and pulsatility index and the risk of restenosis in patients undergoing coronary angioplasty as well as with the results of Chirinos et al who showed a correlation between central PP and cardiovascular risk in men with angiographically confirmed CAD. Although these authors did not include the extent of the coronary atherosclerosis into the multivariable analysis, we did include it and therefore we were able to show that the relationship between central pulse pressure and cardiovascular risk is independent of the coronary atherosclerosis extent in subjects with CAD. Moreover, to our best knowledge, this is the first study to show that central pulsatility (a measure of relative changes of BP) is an independent predictor of event-free survival. These observations may suggest that in coronary patients relative changes in BP (represented by pulsatility) are at least as important as absolute changes (represented by PP) when prognosis determination is considered. The present findings are in concordance with the previously published results suggesting aortic pulsatility correlates better with coronary atherosclerosis than central PP. The suggestion that BP pulsatile component is one of the most powerful predictors of the prognosis is supported by studies indicating that cyclic strain on vascular wall takes part in the development of atherosclerosis. Safar and Smulyan have recently suggested the usefulness of the calculation of the pulsatility. Our results do not agree with the study of Darne et al who showed steady component of BP to be more closely correlated with cardiovascular risk compared to pulsatile component. However, Darne et al based their analysis on peripheral pressure whereas we analyzed central ones, they studied healthy untreated population whereas our study group consisted of coronary patients majority of whom was prescribed BP-lowering drugs. As the influence of most of these agents is more pronounced on steady rather than pulsatile component of BP it is possible that this effect could influence the lack of relationship between MBP and cardiovascular risk in our study population. These differences in the studied populations and methods used account for the different results. It should be underlined that at present time coronary patients are usually prescribed 1 or even more BP-lowering drug. Therefore, results obtained from untreated coronary population probably would be useless.

Classic risk factors such as smoking or hypercholesterolemia were not related to the event-free survival in our study population. This is consistent with reports showing no significant relationship between hypercholesterolemia or hypertension and cardiovascular risk in treated coronary population. Patients with higher cholesterol levels have greater probability of being prescribed a lipid-lowering agent. This can probably explain the mentioned findings. This phenomenon could probably also account for the lack of the relationship between peripheral BP and cardiovascular risk in our study, as physicians treat patients according to peripheral but not central BP and the effect of cardiovascular drugs on peripheral BP can differ from its effect on central BP. Importantly, we found no effect of both central and peripheral MBP on the outcome. It is known that the difference in MBP between ascending aorta and peripheral artery is small. The reason for the lack of the influence of smoking on the event-free survival could be relatively small proportion of active smokers, and maybe high cessation rate during the follow-up.

A number of studies have recently suggested the usefulness of invasive BP waveform measurements. However, it would be far more convenient to measure central BP parameters noninvasively. Recently, greater attention has been given to pulse wave analysis which allows central BP assessment. Indeed, it was suggested that inclusion of central instead of peripheral BP values in cardiovascular risk algorithms may improve their accuracy. Further studies are needed to prove this hypothesis. The present findings also suggest that studies aiming at assessment of the cardiovascular drugs influence on central BP wave will be probably continued in the near future. Although the value of central PP measurements has been studied in patients with multiple risk factors or renal failure, no previous study has examined the relationship between pulsatility and the prognosis in these or other patient groups. In addition, there is a need for studies aiming at explaining the role of BP pulsatile component in various patient subgroups, such as women, patients with heart failure, diabetes, etc.
Our study does have some limitations. Although the present study population was 3 times greater when compared with the single published study measuring central BP invasively and examining the relationship between central BP and cardiovascular risk, it is still possible that the results may have differed if a larger group was analyzed. We did not assess the left ventricular stroke volume. Because PP is determined directly by stroke volume, not by ejection fraction, stroke volume measurement would increase the precision of the analysis. Nevertheless, it is improbable that inclusion of stroke volume instead of EF in the multivariate analyses would significantly change our results. A fluid-filled system was used to record the ascending aortic pressure. The use of a high-fidelity pressure transducer would increase the accuracy of the recorded pressure waveform. Most study participants were prescribed cardiovascular drugs. Some of these agents have been shown to interfere with central SBP augmentation. However, the inclusion of cardiovascular drugs in the multivariate analysis did not influence the main results. Moreover, the majority of patients under consideration for coronary angiography in routine practice are taking cardiovascular drugs. It should be underlined that only patients undergoing routine nonemergency coronary angiography were included in the present study. Therefore, our results should not be applied to other patients, especially to those without CAD. On the other hand our results agree with the findings of Safar et al and Roman et al. Nevertheless, other studies are needed to explain the above doubt.

Perspectives
We showed in a large population undergoing coronary angiography that the pulsatile component of BP, measured in the ascending aorta, is one of the most important factors related to event-free survival and that it is more closely associated with cardiovascular risk than steady component. Pulsatility (a measure of relative changes of blood pressure) in the ascending aorta was also proved to be a major predictor of the cardiovascular risk. These results support prospective examination of the use of central pulsatility (especially estimated using pulse wave analysis) in future trials. Our findings may have a deep influence on the understanding of the nature of relationship between pressure wave and atherosclerosis complications development. Indeed, our results provide a rationale for a concept that rather antipulsatile than antihypertensive therapy might be of special effectiveness in coronary patients. This hypothesis should be tested in the near future. Upcoming studies will probably explain the effect of various classes of antihypertensive drugs on ascending aortic pulsatility.

Source of Funding
This work was supported by Jagiellonian University, Medical College (501/ZKL/27/L).

Disclosures
None.

References


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Piotr Jankowski, Kalina Kawecka-Jaszcz, Danuta Czarnecka, Małgorzata Brzozowska-Kiszka, Katarzyna Styczkiewicz, Magdalena Loser, Małgorzata Kłoch-Badelek, Jerzy Wilinski, Adam M. Curyło and Dariusz Dudek

on behalf of the Aortic Blood Pressure and Survival Study Group

_Hypertension_. 2008;51:848-855; originally published online February 11, 2008;
doi: 10.1161/HYPERTENSIONAHA.107.101725

_Hypertension_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:

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