Relation of Arterial Stiffness Assessed by Brachial-Ankle Pulse Wave Velocity to Complexity of Coronary Artery Disease

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Abstract: *Background:* The progression of atherosclerosis leads to increased arterial stiffness. The present study used brachial-ankle pulse wave velocity (baPWV) to evaluate the connection between arterial stiffness in patients with chest pain and the presence and extent of coronary artery disease (CAD). *Methods:* On a retrospective basis, we analyzed the data of 703 consecutive patients who had undergone baPWV and an elective coronary angiogram for suspected CAD, between June 2010 and July 2012, at a single cardiovascular center. *Results:* The baPWV was one of the statistically meaningful predictors of significant CAD (diameter of stenosis >50%) in addition to diabetes and dyslipidemia in a multivariate analysis. When the extent of CAD was classified into nonsignificant or significant CAD (ie, 1-, 2- and 3-vessel disease), there was a significant difference in baPWV between the significant and nonsignificant CAD groups, but there was no difference in baPWV among the 3 significant CAD groups. Linear regression analyses showed that baPWV was significantly associated with the SYNTAX (SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery) score. The cutoff value of baPWV at 1735 cm/s had a sensitivity of 55.6%, specificity of 62.4%, and area under receiver operating characteristic curve of 0.612 in predicting CAD. *Conclusions:* Arterial stiffness as determined by baPWV is associated independently with significant CAD in patients with angina. Arterial stiffness is related to CAD severity as assessed by the SYNTAX score. As a result, increased arterial stiffness assessed by baPWV is associated with the severity and presence of CAD.

Key Indexing Terms: Arterial stiffness; Brachial-ankle pulse wave velocity; Coronary artery disease; SYNTAX score. **[Am J Med Sci 2014;348(4):294–299.]**

Aortic stiffening is an independent predictor of cardiovascular events in patients with hypertension[1–3] and diabetes mellitus.[4] Elevated arterial stiffness is associated with a number of cardiovascular risk factors that include age, hypertension, diabetes mellitus and end stage renal disease.[5,6] Although arterial stiffness can be evaluated by various parameters, there is no consistent method. Several methods are currently used to evaluate the elasticity of arteries. Brachial-ankle pulse wave velocity (baPWV) to measure arterial stiffness is the gold standard.[7] This method allows a greater convenience of screening the general population than do other methods of measuring PWV. Some studies have directly shown that arterial stiffness measured through PWV is an independent predictor of cardiovascular mortality,[3,8] whereas others have suggested that a relationship exists between increased PWV and significant coronary artery disease (CAD).[7,9–13] One study found that arterial stiffness as determined by PWV is related to CAD severity as assessed by angiography and the "SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery" (SYNTAX) score.[12] But another study found baPWV has limited value for predicting the severity of CAD in patients with chest pain.[13] Furthermore, one study showed that baPWV might be of limited value in identifying patients at risk for CAD.[14] The SYNTAX score is a semiquantitative angiographic tool used to determine the extent and severity of CAD, on the basis of coronary anatomic risk factors. Although arterial stiffness and CAD are closely related, the correlation between arterial stiffness and the complexity of CAD should be reevaluated. On these grounds, we assessed, retrospectively, the association between arterial stiffness, as determined by baPWV, and the presence and extent of CAD, as detected by conventional coronary angiography (CAG) and SYNTAX score in patients who visited an outpatient clinic for chest pain without any history of ischemic heart disease.

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METHODS

Study Population

We retrospectively enrolled 851 individuals who were clinically suspected of having CAD at the Chiayi Chang Gung Memorial Hospital. The inclusion criteria for suspected CAD included symptoms suggestive of ischemic heart disease combined with an abnormal thallium myocardium perfusion scan or treadmill test. We excluded patients with a history of myocardial infarction, percutaneous coronary intervention (PCI) or coronary arterial bypass surgery. Patients with a history of congenital heart disease, severe valvular disease, cardiomyopathy, atrial fibrillation, impulse conduction disturbances or any other concurrent systemic illness were excluded from the study. Patients with serious medical problems requiring specific medical treatment were excluded. Also, the patients who had a history of peripheral artery disease, symptoms of intermittent claudication, limb ischemic signs or ankle brachial index <0.9 were excluded from this study. All patients underwent both baPWV measurements and angiography from 2010 to 2012. The baPWV measurement and echocardiography had been performed within at least 1 week before undergoing CAG as a part of the clinical pathway. All patients had a thorough physical examination and routine biochemical analysis of the blood and urine. After patients had fasted for at least 12 hours, the following parameters were measured: plasma triglycerides, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, fasting blood glucose, uric acid and serum creatinine. The final study population included 703 patients and the study was approved by the Institutional Review Board of Chiayi Chang Gung Memorial Hospital.

Assessment of Aortic Stiffness

BaPWV was measured using a volume-plethysmographic apparatus (Form/ABI; Colin Co., Ltd, Komaki, Japan). Details of the methodology have been described elsewhere.[15] In brief, this device simultaneously measures bilateral brachial and tibial arterial pressure waveforms, the lead I electrocardiogram and phonocardiogram. Occlusion cuffs, which were connected to both plethysmographic and oscillometric sensors, were placed around both arms and ankles with the patient in the supine position. All cuffs were inflated until the brachial and tibial arteries were completely occluded, and then deflated. The arterial pressure waveforms were digitized at 1200 Hz for the brachial arterial waves and at 240 Hz for the tibial arterial waves. The time difference between the brachial and ankle arterial pressure wave (ΔT) was examined in accordance with the wavefront velocity theory. The distance between the brachium and ankle (D) was calculated based on anthropometric data of the Japanese population. Finally, the baPWV was calculated as $D/\Delta T$. The baPWV reflects not only aortic stiffness, but also the stiffness of the muscular artery of the leg. Thus, the baPWV is a global measure for arterial stiffness reflecting both elastic and muscular arterial properties.

Echocardiographic Studies

The patients studied in the echocardiography laboratory were imaged in the left lateral decubitus position with a PHILIPS IE33 instrument (Philips Healthcare, the Netherlands) equipped with a multifrequency transducer. A complete echocardiographic study was performed using standard views and techniques. M-mode echocardiographies were obtained by 2-dimensional-guided echocardiography with a transducer having a frequency range of 3 to 5 MHz. The mean of 2 M-mode measurements obtained by 2 different investigators was used. The left ventricular mass was calculated by Devereux method.[16] The left ventricular mass index was calculated as the left ventricular mass divided by the body surface area.

SYNTAX Score and Angiographic Analysis

CAG was performed in all patients using a standard Judkins technique through the left radial artery at the physician's discretion. Two experienced physicians blinded to the study analyzed angiograms with a validated quantitative coronary angiographic system (Allura Xper FD10; Philips Healthcare the Netherlands). The opinions of 2 experienced physicians regarding the SYNTAX score completely agreed. Patients were assigned to the nonsignificant or significant (1-, 2-, or 3-vessel disease) group based on the presence of significant stenosis for each of the 3 main coronary arteries (the patients with left main disease were included in the 2-vessel disease group). A lesion was defined as significant if it caused a 50% reduction of the luminal diameter by visual estimation in vessels 1.5 mm. Each coronary lesion was separately scored and added to each coronary vessel to provide the vessel SYNTAX scores, which were then summed to provide the overall patient SYNTAX score.

Statistical Analysis

Numeric data are presented as mean and standard deviation, and categorical data are presented as frequencies and percentages. The independent *t* test and χ^2 tests were used for comparisons between the CAD and non-CAD groups. Furthermore, a multivariate logistic regression analysis was carried out to assess the odds ratios of factors related to significant CAD. A receiver operating characteristic (ROC) curve was used to show a positive correlation between the baPWV in patients with angina. Cutoff values were determined as the sum of sensitivity and specificity. Linear regression analyses were used to evaluate the associations between the SYNTAX score and baPWV while adjusting for potential confounders. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) 20.0 statistical package (SPSS Inc, Chicago, IL) and $P < 0.05$ was considered to indicate statistical significance.

RESULTS

Baseline characteristics of the study population and of each group of patients classified as "no CAD" versus "CAD" are summarized in Table 1. The sample was composed of 492 male and 211 female patients. The CAD group had a higher proportion of men, a higher mean age, higher proportion of diabetes mellitus, dyslipidemia than did the no-CAD group. There were no differences in body mass index, body surface area, proportion of smokers, hypertension, stroke, total cholesterol, low-density lipoprotein cholesterol, triglyceride levels, blood pressure, serum creatinine, uric acid, hemoglobin, left ventricular ejection fraction or left ventricular mass index between the 2 groups; however, high-density lipoprotein cholesterol was significantly lower in the CAD group than in the no-CAD group. In addition, mean (standard deviation) baPWV was significantly higher in the CAD group than in the no-CAD group (18.43 [4.58] m/s versus 17.01 [3.57] m/s, $P < 0.001$).

We carried out multivariate logistic regression analysis to detect the factors related to significant CAD. As shown in Table 2, diabetes, dyslipidemia and baPWV were meaningfully related to the existence of significant CAD.

Figure 1 shows the association between baPWV and the presence of CAD. With regard to the extent of CAD, we sorted patients into one of 4 groups: nonsignificant stenosis, 1-, 2- and 3-vessel disease. A significant difference of baPWV was observed between each group compared with the no-CAD group. However, no significant difference of baPWV was observed between CAD groups. A trend toward a positive association was found between the extent of CAD and baPWV. Figure 2 revealed that baPWV was significantly correlated with SYNTAX score ($R^2 = 0.525$, $P < 0.001$). The ROC curve analysis of the association between baPWV and CAD is shown in Figure 3.

Using the ROC curve, we determined the optimal cutoff value of baPWV and CAD that could predict the presence of coronary stenosis (Figure 3). The cutoff value of baPWV at 1735 cm/s had a sensitivity of 55.6%, specificity of 62.4% and area under ROC curve of 0.612 in predicting coronary artery stenosis. As shown in Table 3, using the cutoff value of baPWV at 1735 cm/s had a sensitivity of 55.6%, specificity of 62.4%, positive predictive value of 87.0% and negative predictive value of 23.6%.

DISCUSSION

In this cross-sectional study, baPWV was independently associated with significant CAD in patients who had no history of ischemic heart disease. Although it did not show a clinically relevant difference among groups of patients classified according to severity of CAD, we have demonstrated that baPWV was well correlated with a significant increase in the severity and complexity of CAD evaluated by the SYNTAX score, as detected by CAG.

According to previous studies, increased arterial stiffness hinders the hemodynamic buffering effect of the cardiovascular system, contributing to elevated systolic blood pressure and pulse pressure, CAD and left ventricular hypertrophy.[17,18]