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Impact of systolic time intervals on the relationship between arterial stiffness and left ventricular hypertrophy

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ABSTRACT

Objectives: Arterial stiffness is correlated with left ventricular hypertrophy (LVH) and is susceptible to left ventricular performance. Therefore, if left ventricular systolic function is unknown, the relationship between arterial stiffness and LVH is controversial. This study was to assess the impact of the ratio of brachial pre-ejection period (bPEP) to brachial ejection time (bET), a marker of left ventricular systolic function, on the relationship between brachial-ankle pulse wave velocity (baPWV) and LVH.
Methods: A total of 1146 patients were included in the study. The baPWV and bPEP/bET were measured using an ABI-form device. Patients were classified into four groups. Groups 1, 2, 3, and 4 were patients with bPEP/bET $\leq$ 0.38 and baPWV below the median, bPEP/bET $>$ 0.38 but baPWV below the median, bPET/bET $\leq$ 0.38 but baPWV above the median, and bPET/bET $>$ 0.38 and baPWV above the median, respectively.
Results: Patients in groups 3 and 4 (high baPWV) and patients in group 2 (low baPWV but high bPEP/bET) were associated with increased left ventricular mass index (LVMI) and LVH (all $P < 0.001$). In a multivariate model, baPWV was significantly associated with LVMI ($P = 0.007$) and LVH ($P = 0.025$). Further adjustment for bPEP/bET made the association between baPWV and LVMI ($P = 0.150$) and LVH ($P = 0.173$) disappear.
Conclusions: The bPEP/bET has an important impact on the relationship between baPWV and LVH. Therefore, the value of bPEP/bET obtained from the same examination should be considered while interpreting the relationship between baPWV and LVH.

1. Introduction

Arterial stiffness may contribute to left ventricular hypertrophy (LVH) independently of blood pressure [1,2]. Some studies have reported a positive correlation between pulse wave velocity (PWV), a marker of arterial stiffness, with increased left ventricular mass index (LVMI) and LVH [3–5]. However, others have failed to identify the correlation [6–8]. Weber et al. [9] had evaluated the relationship between aortic PWV and left ventricular systolic function. They found a significant positive correlation between aortic PWV and left ventricular ejection fraction (LVEF) in cardiomyopathy patients, thus concluding that aortic PWV was susceptible to left ventricular systolic function [9]. Therefore, if left ventricular systolic function is unknown, the relationship between arterial stiffness and LVH is difficult to determine.

A clinical device, ABI-form (Colin VP1000, Komaki, Japan), has been developed to automatically and simultaneously measure blood pressures in both arms and ankles and record pulse waves of the brachial and posterior tibial arteries using an automated oscillometric method. Using this device, we can easily and automatically calculate the brachial-ankle PWV (baPWV), brachial pre-ejection period (bPEP), and brachial ejection time (bET) values by analyzing the signals of electrocardiogram, phonocardiogram, and brachial pressure volume waveform [10]. We have recently found that bPEP/bET has a significant correlation with LVEF and is a useful marker in prediction of impaired left ventricular systolic function [6,11]. As impaired left ventricular systolic function may affect baPWV, bPEP/bET may influence the relationship between baPWV

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and LVH. It is uncertain whether arterial stiffness is related to LVH independent of left ventricular systolic function. The aim of this study was to ascertain this impact of the bPEP/bET on the relationship between baPWV and LVH.

2. Subjects and methods

2.1. Study patients and design

Study subjects were randomly included from a group of patients who arranged for echocardiographic examinations at a regional hospital in southern Taiwan. Patients with significant aortic or mitral valve diseases, atrial fibrillation, significant ankle edema and inadequate image visualization were excluded. We did not include all patients consecutively because baPWV and bPEP/bET must be measured within 5 min after the completion of an echocardiographic examination. In total, 1146 patients were randomly included in this study.

The area under the curve for bPEP/bET in prediction of LVEF $< 50\%$ was 0.794 and the sensitivity and specivity of bPEP/bET > 0.38 (the optimal cutoff value) in prediction of LVEF $< 50\%$ were 73.5% and 73.5% in the study patients. The receiver operating characteristic curve for bPEP/bET in prediction of LVEF $< 50\%$ was shown in Fig. 1. The study population was further classified into four groups according to bPEP/bET > 0.38 or ≤ 0.38 and median value of baPWV. Groups 1, 2, 3 and 4 were made up of patients with bPEP/bET ≤ 0.38 and baPWV below the median, bPEP/bET > 0.38 but baPWV below the median, bPET/bET ≤ 0.38 but baPWV above the median, and bPET/bET > 0.38 and baPWV above the median, respectively. All patients were in sinus rhythm. The protocol was approved by our Institutional Review Board and all enrolled patients gave written, informed consent.

2.2. Evaluation of cardiac structure and function

The echocardiographic examination was performed by one experienced cardiologist with a VIVID 7 (General Electric Medical Systems, Horten, Norway), with the participant respiring quietly in the left decubitus position. The cardiologist was blind to the other data. Two-dimensional and two-dimensionally guided M-mode images were recorded from the standardized views. The echocardiographic measurements included left ventricular internal diameter in diastole (LVIDd), left ventricular posterior wall thickness in diastole (LVPWTd), and interventricular septal wall thickness in diastole (IVSTd). Left ventricular systolic function was assessed by LVEF. Left ventricular mass was calculated using Devereux-modified method, i.e. left ventricular mass $= 1.04 \times [(\text{IVSTd} + \text{LVIDd} + \text{LVPWTd})^3 - \text{LVIDd}^3] - 13.6$ g [12]. LVMI was calculated by dividing left ventricular mass by body surface area. LVH was defined as suggested by the 2007 European Society of Hypertension/European Society of Cardiology guidelines [13].

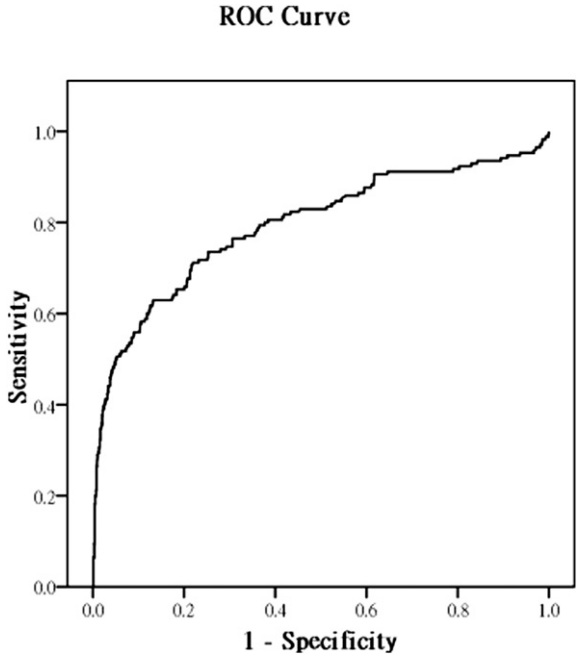

Fig. 1. Receiver operating characteristic curve for the ratio of brachial pre-ejection period to brachial ejection time (bPEP/bET) in prediction of left ventricular ejection fraction $< 50\%$.

2.3. Assessment of bPEP, bET, and baPWV

Both bPEP and bET were measured by an ABI-form device, which automatically and simultaneously measures blood pressures in both arms and ankles using an oscillometric method [10,14]. The bET was automatically measured from the foot to the dicrotic notch (equivalent to the incisura on the downstroke of the aortic pressure wave contour produced by the closure of aortic valve) of the pulse volume waveform. The total electromechanical systolic interval (QS_2) was measured from the onset of the QRS complex on the electrocardiogram to the first high-frequency vibration of the aortic component of the second heart sound on the phonocardiogram. The bPEP was also automatically calculated by subtracting the bET from the QS_2. The baPWV values were also measured and the measurement method has been reported and validated in previous studies [10,14,15].

2.4. Collection of demographic, medical, and laboratory data

Demographic and medical data including age, gender, smoking history (ever *versus* never), and comorbid conditions were obtained from medical records or interviews with patients. The body mass index (BMI) was calculated as the ratio of weight in kilograms divided by square of height in meters. Laboratory data were measured from fasting blood samples using an autoanalyzer (Roche Diagnostics GmbH, D-68298 Mannheim COBAS Integra 400). Serum creatinine was measured by the compensated Jaffé (kinetic alkaline picrate) method in a Roche/Integra 400 Analyzer (Roche Diagnostics, Mannheim, Germany) using a calibrator traceable to isotope-dilution mass spectrometry [16]. The value of estimated glomerular filtration rate (eGFR) was calculated using the 4-variable equation in the Modification of Diet in Renal Disease (MDRD) study [17]. Blood samples were obtained within 1 month of enrollment. In addition, information regarding patient medications including aspirin, angiotensin converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), non ACEI/ARB antihypertensive drugs, and HMG-CoA reductase inhibitors (statins) during the study period was obtained from medical records.

2.5. Statistical analysis

Statistical analysis was performed using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA) for windows. Data are expressed as percentages, mean $\pm$ standard deviation or median (25th–75th percentile) for triglyceride. Multiple comparisons among the study groups were performed by one-way analysis of variance (ANOVA) followed by post hoc test adjusted with a Bonferroni correction. The relationship between two continuous variables was assessed by a bivariate correlation method (Pearson's correlation). Multiple linear regression analysis was used to identify the factors