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Original article

Heart rate significantly influences the relationship between atrial fibrillation and ankle-brachial index

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ABSTRACT

Objectives: Both atrial fibrillation (AF) and vascular disease share several risk factors and the two diseases often coexist. The patients with AF were reported to have a decreased ankle-brachial index (ABI). However, ABI was also reported to have an inverse relationship with heart rate (HR). Because AF patients often have a transiently or persistently rapid HR, this study aimed to assess whether AF was significantly associated with decreased ABI and whether HR could significantly influence the relationship between AF and ABI.
Methods: We included 166 AF and 1336 non-AF patients from subjects undergoing echocardiographic examinations. ABI was measured using an ABI-form device.
Results: Compared to non-AF patients, AF patients had a decreased ABI ($p < 0.001$). In a multivariate model, including covariates of age, sex, blood pressures, etc., the presence of AF was significantly associated with low ABI ($\beta = -0.069$, $p = 0.026$). However, further adjustment for HR made this association disappear ($p = 0.971$).
Conclusion: This study demonstrated that the presence of AF was associated with decreased ABI, but this association became insignificant after further adjustment for HR, which suggested HR could significantly influence the relationship between AF and ABI.

Introduction

Atrial fibrillation (AF) has been shown to be a major risk factor of vascular disease [1–3] and vascular disease similarly has been found to increase the risk of AF [1,4]. Both AF and vascular disease share several risk factors, including old age, obesity, heart failure, diabetes, and hypertension and the two diseases often coexist [4–6]. Therefore, the presence of AF may have an influence on vascular function as shown by ankle-brachial index (ABI).

ABI is an easy-to-use, non-invasive, and reliable diagnostic tool for peripheral arterial occlusive disease (PAOD) [7,8]. An ABI <0.9 has not only been established as a reliable diagnostic marker for PAOD, but also a strong predictor for overall and cardiovascular mortality [9–11]. A clinical device, ABI-form (VP1000; Colin Co. Ltd., Komaki, Japan), has been developed to automatically and simultaneously 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 ABI and brachial-ankle pulse wave velocity (baPWV) [12,13].

AF patients often have a transiently or persistently rapid heart rate (HR). Recently, we reported that HR significantly influences the relationship between AF and arterial stiffness [14]. Furthermore, several studies have demonstrated that HR has an inverse correlation with ABI [15–17]. Although tachycardia-induced cardiomyopathy is a well-known reason of cardiac dysfunction in patients with AF [18], whether HR may significantly influence the relationship between AF and ABI has not been studied. Hence, the first aim of this study was to compare ABI between patients with and without AF and to determine whether AF patients had a decreased ABI. The second aim of this study was to assess whether AF per se was a major determinant of decreased ABI and whether

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HR could significantly influence the relationship between AF and ABI.

Methods

Study subjects

This was a cross-sectional study. Study subjects were prospectively included from a group of patients who arranged for echocardiographic examinations at Kaohsiung Municipal Hsiao-Kang Hospital. Patients with inadequate image visualization were excluded. AF patients were consecutively included. However, non-AF patients were not consecutively included because ABI measurement must be performed within 10 min after the completion of echocardiographic examination. Finally, 166 patients with persistent or permanent AF and 1336 non-AF patients were included in this study. The study protocol was approved by the institutional review board of the Kaohsiung Medical University Hospital (KMUH-IRB). Informed consent was obtained in written form from patients and all clinical investigations were conducted according to the principles expressed in the Declaration of Helsinki. The patients gave consent for the publication of the clinical details.

Assessment of ABI, baPWV, and HR

The values of ABI, baPWV, and HR were measured by using an ABI-form device (VP1000), which automatically and simultaneously measured blood pressures in both arms and ankles using an oscillometric method [12,13]. The ABI was calculated by the ratio of the ankle systolic blood pressure (SBP) divided by the higher SBP of the arms. For measuring baPWV, pulse waves obtained from the brachial and tibial arteries were recorded simultaneously and the transmission time, which was defined as the time interval between the initial increase in brachial and tibial waveforms, was determined. The transmission distance from the arm to each ankle was calculated according to body height. The baPWV value was automatically computed as the transmission distance divided by the transmission time. In addition, for measuring HR, nine seconds of electrocardiographic signal were recorded and four consecutive beats if HR <120 beats/min or eight consecutive beats if HR ≧120 beats/min during this period was automatically analyzed and then averaged to get the mean HR for later analysis. In non-AF patients, the examination of ABI-form device was performed once. However, in AF patients, the examination of ABI-form device was performed thrice. The left and right ABI values were obtained by averaging three left and right ABI values acquired from the repeated examinations in AF patients. After obtaining bilateral ABI values, the lower one was used for later analysis. In addition, in AF patients, the six values of baPWV, the three values of HR, and the six values of SBP and diastolic blood pressure (DBP) from both arms obtained from the repeated examinations were averaged for later analysis.

Evaluation of left ventricular systolic 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. Left ventricular ejection fraction (LVEF) was measured using the modified Simpson's method. In non-AF patients, LVEF was measured and averaged from 3 consecutive beats. In AF patients, LVEF was determined using the index-beat method [19–21].

Collection of demographic, medical and laboratory data

Demographic and medical data including age, gender, and history of diabetes mellitus, hypertension, cerebrovascular accident (CVA), and chronic heart failure (CHF) were obtained from medical records or interviews with patients. CHF was defined according to Framingham criteria. Body mass index (BMI) was calculated as the ratio of weight in kilograms divided by the square of height in meters. Laboratory data including total cholesterol and triglyceride values were also collected. The value of estimated glomerular filtration rate (eGFR) was calculated using the 4-variable equation in the Modification of Diet in Renal Disease study [22]. In addition, information regarding patient medications including angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), β-blockers, calcium channel blockers (CCBs), and diuretics during the study period was obtained from medical records.

Statistical analysis

SPSS 18.0 software (SPSS, Chicago, IL, USA) was used for statistical analysis. Data were expressed as mean ± standard deviation or percentage. Continuous and categorical variables between groups were compared by independent samples *t*-test and Chi-square test, respectively. The multiple linear regression analysis was employed to identify the determinants of ABI. The impact of HR on the relationship between AF and ABI was assessed by a modified procedure in 3 modeling steps. The first model consisted of age and sex. The second model consisted of the significant variables in the univariate analysis except HR. The final step was adding HR. All tests were 2-sided and the level of significance was established as $p < 0.05$.

Results

Table 1 shows the comparison of baseline characteristics between patients with and without AF. Compared to patients without AF, patients with AF had a lower ABI, higher prevalence of ABI <1.0, older age, lower prevalence of female gender, higher HR, lower SBP and DBP, higher prevalence of CVA and CHF, lower total cholesterol and triglyceride, and higher percentage of ACEI and/or ARB and diuretic use.

In a univariate analysis, ABI had a negative correlation with the presence of AF, age, female gender, HR, SBP, diabetes, CVA, CHF, total cholesterol, LVEF <50%, baPWV, and use of ACEIs and/or ARBs and diuretics and positive correlation with DBP, BMI, and eGFR. Table 2 displays the standardized coefficient β estimates for ABI by the presence of AF with and without adjustment for demographic, clinical, LVEF <50%, baPWV, biochemical parameters, and HR. The presence of AF was associated with ABI in the age- and sex-adjusted model (standardized coefficient $\beta = -0.101$; 95% confidence interval (CI), −0.063 to −0.020; $p < 0.001$) and in the multivariate model adjusting for the significant variables in the univariate analysis except HR (standardized coefficient $\beta = -0.069$; 95% CI, −0.052 to −0.003; $p = 0.026$). This relation between AF and ABI disappeared after further adjustment for HR ($p = 0.971$). Because high value of ABI (ABI ≧1.3) could be related to poor arterial distensibility resulting from stiffness and calcification, we performed a subgroup analysis in the 1467 patients with ABI <1.3 (Table 3). The relation between AF and ABI still disappeared after further adjustment for HR ($p = 0.957$).

Table 4 shows the univariate and multivariate correlates of ABI in all study patients. After the multivariate analysis, old age, increased HR, decreased BMI, history of CVA and CHF, high total cholesterol, and use of diuretics were the major determinants of decreased ABI in all study patients. We also performed a subgroup