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R_2CHADS_2 score is significantly associated with ankle–brachial index <0.9 in patients without atrial fibrillation

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ABSTRACT

Objective: Previous studies demonstrated $CHADS_2$ score and impaired renal function were both associated with ankle–brachial index (ABI) < 0.9 in patients without atrial fibrillation (AF). Hence, we hypothesized the R_2CHADS_2 score had a significant correlation with ABI < 0.9 and the aim of this study was to validate this association in non-AF patients.
Methods: A total of 1482 patients without AF were included. ABI was measured using an ABI-form device. Peripheral arterial occlusive disease (PAOD) was defined as ABI < 0.9 in either leg.
Results: Of the 1482 subjects, the prevalence of ABI < 0.9 was 5.6%. Multivariate analysis showed that increased age (odds ratio [OR], 1.049; $P < 0.001$), decreased estimated glomerular filtration rate (OR, 0.978; $P = 0.006$), and increased R_2CHADS_2 score (OR, 1.738; $P < 0.001$) were associated with ABI < 0.9. In addition, in patients with $CHADS_2$ score $\geqq$ 2, the presence of chronic kidney disease (CKD) was significantly associated with ABI < 0.9 ($P \leqq 0.006$), but in patients with CHADS2 score < 2, there was no such association ($P = 0.357$).
Conclusions: Our study demonstrated R_2CHADS_2 score was positively correlated with ABI < 0.9. In addition, the presence of CKD was a risk factor of ABI < 0.9 in patients with $CHADS_2$ score $\geqq$ 2. Hence, increased R_2CHADS_2 score in non-AF patients and the presence of CKD in non-AF patients with $CHADS_2$ score $\geqq$ 2 were useful parameters in identifying the high risk group of PAOD.
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1. Introduction

The ankle–brachial index (ABI) is a simple and reliable diagnostic tool for peripheral arterial occlusive disease (PAOD) [1,2]. An ABI < 0.9 has not only been established as a diagnostic method for PAOD, but also a strong predictor for cardiovascular and all-cause mortality [3–5].

PAOD is a systemic atherosclerotic disease with similar risk factors to coronary artery disease (CAD) and cerebrovascular disease [6]. Major risk factors for PAOD include advanced age, diabetes mellitus, hypertension, dyslipidemia, and cigarette smoking [6,7]. In addition, races, obesity, chronic kidney disease (CKD), chronic heart failure, and stroke were also reported to be associated with PAOD formation [6–12].

The $CHADS_2$ (chronic heart failure, hypertension, age $\geqq$ 75 years, diabetes, prior stroke) score is a simple and popular clinical score to assess the risk of stroke in patients with atrial fibrillation (AF) [13,14]. Because chronic heart failure, hypertension, old age, diabetes, and stroke are all risk factors for PAOD [6–12], we recently investigated the association between $CHADS_2$ score and ABI < 0.9 and found that $CHADS_2$ score was significantly associated with ABI < 0.9 in non-AF patients [15]. In addition, decreased estimated glomerular filtration rate (eGFR) was also independently associated with ABI < 0.9 in our previous study [15]. Impaired renal function was previously reported to be a predictor of stroke and systemic embolism in non-valvular AF patients and R_2CHADS_2 score exhibited discriminant power for stroke and improved net stroke

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risk reclassification than $CHADS_2$ score in ROCKET AF study [16]. Because all the six components of R_2CHADS_2 score were correlated with PAOD and there was no study to evaluate the relationship between R_2CHADS_2 score and PAOD, the aim of the present study was to investigate whether R_2CHADS_2 score was positively associated with PAOD and whether this score had an important impact on the relationship between $CHADS_2$ score and PAOD in non-AF patients.

2. Methods

2.1. Study subjects

This was a cross-sectional study. Study subjects were randomly included from a group of patients arranged for echocardiographic examinations in a local hospital because of suspected coronary artery disease, heart failure, hypertension, abnormal cardiac physical examination, and so on. Patients with significant aortic or mitral valve diseases, AF, significant ankle edema, and inadequate image visualization were excluded. Finally, a total of 1482 patients (mean age 61.4 ± 13.6 years, 837 males/645 females) were included. The study protocol was approved by the institutional review board of the Kaohsiung Medical University Hospital (KMUH-IRB). Informed consents have been obtained in written form from patients and all clinical investigation was conducted according to the principles expressed in the Declaration of Helsinki. The patients gave consent for the publication of the clinical details.

2.2. Assessment of ABI

The values of ABI were measured by using an ABI-form device (VP1000; Colin Co. Ltd., Komaki, Japan), which automatically and simultaneously measured blood pressures in both arms and ankles using an oscillometric method [17,18]. The ABI was calculated by the ratio of the ankle systolic blood pressure divided by the higher systolic blood pressure of the arms. After obtaining bilateral ABI values, the lower one was used for later analysis. The ABI measurement was done once in each patient. In addition, PAOD in our study was defined as ABI <0.9 in either leg.

2.3. Assessment of blood pressure

In our study, the bilateral arm and ankle blood pressure measurements were done simultaneously and automatically using the ABI-form device. The systolic and diastolic blood pressures were measured by an appropriate cuff and the average of systolic and diastolic blood pressures of bilateral arms were used for later analysis.

2.4. Calculation of $CHADS_2$ and R_2CHADS_2 score

The $CHADS_2$ score was calculated for each patient based on a point system in which 2 points were assigned for a history of stroke and 1 point was assigned for age ≧ 75 years, the presence of congestive heart failure, hypertension, and diabetes. The R_2CHADS_2 score was calculated for each patient based on a point system in which 2 points were assigned for renal dysfunction implicated by eGFR <60 ml/min/1.73 m^2 and a history of stroke, and 1 point was assigned for age ≧75 years, the presence of congestive heart failure, hypertension, and diabetes. Congestive heart failure was defined according to Framingham criteria. Hypertension was defined as systolic blood pressure ≧ 140 mmHg or diastolic blood pressure ≧ 90 mm Hg or anti-hypertensive drugs were prescribed. Diabetes was defined as fasting blood glucose level greater than 126 mg/dL or hypoglycemic agents were used to control blood glucose levels. Prior stroke was defined as history of cerebrovascular accident including cerebral bleeding and infarction.

2.5. 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). Blood sample was obtained within 1 month of enrollment. The value of eGFR was calculated using the 4-variable equation in the Modification of Diet in Renal Disease (MDRD) study [19]. CKD was defined as eGFR < 60 ml/min/1.73 m^2. In addition, information regarding patient medications including aspirin, angiotensin converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), β-blockers, calcium channel blockers, and diuretics, during the study period was obtained from medical records.

2.6. Statistical analysis

All data were expressed as mean (±standard deviation). The SPSS 15.0 (SPSS, Inc., Chicago, Illinois, USA) was used for statistical analysis. Data are expressed as percentages or mean ± standard deviation. Continuous and categorical variables between groups were compared by independent samples *t*-test and Chi-square test, respectively. The relationship between two continuous variables was assessed by a bivariate correlation method (Pearson's correlation). Subsequently, significantly correlated variables in the univariate analysis were further analyzed by forward multiple logistic regression analysis to identify the factors associated with ABI < 0.9. All tests were 2-sided, and the level of significance was established as $P < 0.05$.

3. Results

The mean age of the 1482 patients was 61.4 ± 13.6 years. The prevalence of ABI < 0.9 was 5.6%. Table 1 shows the comparison of clinical characteristics between patients with and without ABI < 0.9. Compared with patients with ABI ≧ 0.9, patients with ABI < 0.9 were found to have an older age, higher prevalence of

Table 1
Comparison of clinical characteristics between patients with ABI < 0.9 and ≧ 0.9.

Characteristics	ABI < 0.9 (n = 83)	ABI ≧ 0.9 (n = 1399)	P value
Age (year)	73.1 ± 13.3	60.7 ± 13.3	<0.001
Male gender (%)	55.4	56.5	0.909
Smoking history (%)	11.0	15.5	0.400
Heart failure (%)	25.3	7.9	<0.001
Hypertension (%)	84.3	69.1	0.003
Diabetes Mellitus (%)	59.0	26.9	<0.001
Cerebrovascular disease (%)	15.7	5.5	0.001
$CHADS_2$ Score	2.58 ± 1.14	1.30 ± 1.01	<0.001
R_2CHADS_2 score	4.17 ± 1.64	2.15 ± 1.58	<0.001
Laboratory parameters			
Triglyceride (mg/dl)	150.1 ± 88.4	153.2 ± 147.2	0.866
Total cholesterol (mg/dl)	195.0 ± 50.1	191.2 ± 42.9	0.510
Uric acid (mg/dl)	7.6 ± 2.2	6.9 ± 4.2	0.294
eGFR (ml/min/1.73 m^2)	38.5 ± 19.5	58.3 ± 20.7	<0.001
Medications			
Anti-platelet drugs (%)	53.4	34.6	0.002
Anti-hypertensive drugs (%)	86.6	75.6	0.023

Abbreviations. ABI, ankle–brachial index; eGFR, estimated glomerular filtration rate.

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