Coronary Artery Disease

Ankle-brachial Index Measured by an Automated Oscillometric Method as a Predictor of Cardiovascular Events in Patients with Coronary Artery Disease

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Background: Ankle-brachial index (ABI) measured by conventional Doppler method has been reported to be an independent predictor of adverse cardiovascular events in patients with coronary artery disease (CAD). Recently, a clinical device has been developed to measure ABI by an oscillometric method. It is unclear whether ABI measured by this device can serve as a significant predictor of cardiovascular events in patients with CAD.

Materials and Methods: We included 82 patients from our outpatient clinic, who had received coronary angiography examination. ABI was determined in all subjects using the ABI-form (Colin VP1000) device. The lower value of ABI in either of the right or left limbs was used for data analysis. We divided our subjects into two groups with either ABI < 0.9 or ABI ≥ 0.9 and compared basal characteristics between groups. We followed up these patients for 20.0 ± 3.6 months (range 10 to 26). We analyzed the relationship between ABI and cardiovascular events. Then, we used univariate analysis to determine the significant predictors of cardiovascular events. Finally, we utilized multiple logistic regression analysis to identify the independent predictors of cardiovascular events.

Results: There were 14 patients with ABI < 0.9 and 68 patients with ABI ≥ 0.9. The patients with ABI < 0.9 were older and had higher plasma level of uric acid. The prevalence of three-vessel CAD, diabetes mellitus, hypertension, diuretic use, and the risk of cardiovascular death and cardiovascular events were significantly higher in the group of patients with ABI < 0.9. In a univariate analysis, cardiovascular events were significantly related to ABI < 0.9 (odds ratio: 12.6), three-vessel CAD (odds ratio: 12.5) and DM (odds ratio: 4.7). After a multiple logistic regression analysis, ABI < 0.9 and three-vessel CAD were still significant predictors of cardiovascular events.

Conclusions: ABI measured by the automated oscillometric method, like three-vessel CAD, can serve as a useful parameter to predict cardiovascular events in patients with CAD.

Key Words: Ankle-brachial index • Coronary artery disease • Peripheral arterial occlusive disease • Cardiovascular events

INTRODUCTION

Ankle-brachial index (ABI) < 0.9 has been used in clinical practice and epidemiologic studies as an indictor of peripheral arterial occlusive disease (PAOD).[1-6] Previous studies have shown that patients with PAOD often present with coronary atherosclerosis,[7,8] and are at increased risk for adverse cardiovascular events.[1,9] ABI

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measured by conventional Doppler method has been reported to be an independent predictor of cardiovascular events in patients with coronary artery disease (CAD).[10] Recently, an ABI-form clinical device (Colin VP1000) was developed to simultaneously measure bilateral arm and ankle blood pressure by an automated oscillometric method. The blood pressures measured with the new device were proven to be highly correlated with those obtained with the conventional Doppler method (correlation coefficient 0.95).[11] We had utilized the device to measure the ABI in patients with CAD and found that ABI < 0.9 was a useful parameter to predict the severity of coronary atherosclerosis.[12] In the present study, we followed up our study subjects and analyzed whether the ABI could serve as a significant predictor of cardiovascular events in patients with CAD.

MATERIALS AND METHODS

We prospectively included 82 patients (mean age 64.5 ± 9.9 years), who had received coronary angiography (CAG), from our outpatient clinic. Subjects with a history of coronary artery bypass grafting or cancer were excluded from this study. Patients with uremia were also excluded because arteriovenous shunt may influence the measurement of ABI. Demographic data, history of diabetes mellitus (DM), hypertension, smoking and use of antihypertensive drugs were recorded from reviewing medical charts. Levels of total cholesterol, triglyceride and uric acid were checked before CAG. Angiographically significant CAD was defined as at least 50% diameter narrowing of a major coronary artery. Before ABI measurement, height and weight were measured and body mass index (BMI) was calculated. ABI, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were determined in all subjects using the ABI-form (Colin VP1000) device. It is a device with four cuffs that can automatically simultaneously measure blood pressure levels by an oscillometric method in both arms and ankles and calculate the ABI. The lower value of ABI in either limbs and left brachial SBP and DBP were used for data analysis.

We divided our subjects into two groups with either ABI < 0.9 or ABI ≥ 0.9. The basal characteristics of the patients were compared between groups. The follow-up period lasted for 20.0 ± 3.6 months (range 10 to 26). We analyzed the relationship of ABI and cardiovascular events. Cardiovascular events were defined as cardiovascular death, nonfatal myocardial infarction or unstable angina. Then, we analyzed clinically associated variables in predicting cardiovascular events using univariate analysis. Finally, we utilized multiple logistic regression analysis to identify the independent predictors of cardiovascular events.

Statistical analysis

All data were analyzed using SPSS 11.0 software. Results are presented as mean ± SD. Comparisons of continuous variables between groups were made with the independent-samples t-test. Categorical variables were compared by the Chi-square test or Fisher's exact test. To identify variables as independent predictors of cardiovascular events, those variables significantly correlated in univariate analysis were further analyzed by multiple logistic regression analysis. A value of $p < 0.05$ was considered statistically significant.

RESULTS

Basal characteristics of the patients are summarized in Table 1. There were 14 patients with ABI < 0.9 and 68 patients with ABI ≥ 0.9. ABI values in the two groups were 0.77 ± 0.09 and 1.06 ± 0.08, respectively ($p < 0.01$). The 14 patients with ABI < 0.9 were older and had higher plasma levels of uric acid. The prevalence of diabetes mellitus, hypertension, diuretic use and three-vessel CAD was significantly higher in the group of patients with ABI < 0.9.

The relationship between ABI and cardiovascular events is shown in Table 2. During this follow-up period, 7 patients died from cardiovascular cause, 1 patient had a nonfatal acute myocardial infarction and 4 patients were hospitalized for unstable angina. The event-free rate was 93% in patients with ABI ≥ 0.9 and 50% in patients with ABI < 0.9 ($p < 0.01$). The risk of cardiovascular death and cardiovascular events was significantly higher in the patients with ABI < 0.9.

In a univariate analysis, cardiovascular events were significantly related to ABI < 0.9 (odds ratio: 12.6), three-vessel CAD (odds ratio: 12.5) and DM (odds ra-

Table 1. Basal characteristics of patients

Variable	ABI ≥ 0.9 (n = 68)	ABI < 0.9 (n = 14)	*p* value
ABI	1.06 ± 0.08	0.77 ± 0.09	< 0.01
Age (years)	64.0 ± 10.2	69.0 ± 7.5	0.04
Sex (male)	54 (79%)	10 (71%)	0.50
BMI (kg/m^2)	25.2 ± 3.1	23.9 ± 3.1	0.14
SBP (mmHg)	135.7 ± 19.2	144.6 ± 20.1	0.16
DBP (mmHg)	80.0 ± 10.5	79.0 ± 10.8	0.80
Total cholesterol (mg/dL)	199.0 ± 49.8	193.2 ± 72.4	0.79
Triglyceride (mg/dL)	162.9 ± 89.4	125.0 ± 120.6	0.32
Uric acid (mg/dL)	6.8 ± 1.8	8.7 ± 2.7	0.03
Use of aspirin	46 (68%)	10 (71%)	1.0
Use of clopidogrel	26 (38%)	5 (36%)	1.0
Use of beta-blockers	44 (65%)	10 (71%)	1.0
Use of CCBs	24 (35%)	4 (29%)	0.76
Use of ACEIs	24 (35%)	5 (36%)	1.0
Use of ARBs	26 (38%)	7 (50%)	0.41
Use of nitrate	48 (71%)	11 (79%)	0.75
Use of nicorandil	21 (31%)	5 (36%)	0.72
Use of diuretics	10 (15%)	8 (57%)	< 0.01
Hypertension	43 (63%)	13 (93%)	0.03
Diabetes mellitus	19 (28%)	10 (71%)	< 0.01
Smoking	25 (37%)	9 (64%)	0.06
1-vessel CAD	24 (35%)	1 (7%)	0.05
2-vessel CAD	22 (32%)	4 (29%)	1.0
3-vessel CAD	21 (31%)	9 (64%)	0.02
PCI	46 (68%)	10 (71%)	1.0

ABI = ankle-brachial pressure index; ACEIs = angiotension-converting enzyme inhibitors; ARBs = angiotension II receptor blockers; BMI = body mass index; CAD = coronary artery disease; CCBs = calcium channel blockers; DBP = diastolic blood pressure; PCI = percutaneous coronary intervention; SBP = systolic blood pressure.

Table 2. The relationship of ABI and cardiovascular events (cardiovascular death, nonfatal myocardial infarction, unstable angina)

Variable	ABI ≥ 0.9 (n = 68)	ABI < 0.9 (n = 14)	*p* value
Cardiovascular death	3 (4%)	4 (29%)	0.01
Nonfatal myocardial infarction	0 (0%)	1 (7%)	0.17
Unstable angina	2 (3%)	2 (14%)	0.13
Cardiovascular events	5 (7%)	7 (50%)	< 0.01

Table 3. Univariate predictors of cardiovascular events

Variable	Pt's with CV events (n = 12)	Odds ratio	95% Confidence interval	*p* value
ABI < 0.9	7 (50%)	12.6	3.1 - 50.5	< 0.01
Age > 65	9 (22%)	3.6	0.9 - 14.3	0.12
3-vessel disease	10 (33%)	12.5	2.5 - 62.2	< 0.01
Hypertension	10 (18%)	2.6	0.5 - 12.9	0.32
Diabetes mellitus	8 (28%)	4.7	1.3 - 17.2	0.02
Cholesterol > 240 mg/dL	1 (6%)	0.5	0.1 - 4.4	1.00
Triglyceride > 200 mg/dL	2 (11%)	0.7	0.1 - 3.8	1.00
Smoking	7 (21%)	2.2	0.6 - 7.7	0.20

CV = cardiovascular; P'ts = patients.

Table 4. Multiple logistic regression analysis of cardiovascular events

Variable	Adjusted odds ratio	95% Confidence interval	*p* valve
ABI < 0.9	8.0	1.5 - 41.8	0.01
3-vessel disease	8.7	1.5 - 49.7	0.02
Diabetes mellitus	1.4	0.3 - 7.3	0.68

tio: 4.7) (Table 3). After multiple logistic regression analysis, ABI < 0.9 and three-vessel CAD were still significantly correlated with the cardiovascular events (Table 4).

DISCUSSION

ABI measured by a conventional Doppler method has been reported to be a useful indicator of PAOD, especially when its value was less than 0.9. In addition, ABI was reported to be a predictor of the extent of coronary atherosclerosis in patients with CAD.[1-6,10] Recently, an ABI-form device (Colin VP1000) was developed to measure ABI using an automated oscillometric method. The major advantage of this device is that it can measure bilateral arm and ankle blood pressures at the same time and can calculate the ABI by using ankle and brachial SBP simultaneously. Using this device, we had proven that ABI < 0.9 was a useful parameter to predict the severity of coronary atherosclerosis.[12]

Our patients with ABI < 0.9 were older and had higher plasma levels of uric acid. The prevalence of DM, hypertension and diuretic use was also significantly higher in our patients with ABI < 0.9. The significant association between DM and ABI < 0.9 is in accordance with the clinical notion that DM is usually accompanied with a more diffuse atherosclerosis.[13] The prevalence of three-vessel CAD in our patients with ABI < 0.9 (64%) was about twice higher than that in patients with ABI ≥ 0.9 (31%). These findings are in agreement with the report that the coexistence of PAOD in CAD patients is associated with more diffuse and severe CAD.[14]

Previous studies have shown that patients with PAOD are at increased risk for adverse cardiovascular events.[1,9] Prospective studies using the ABI have also shown that a low ABI predicts fatal and nonfatal cardiovascular disease and all-cause mortality in people with and without existing clinical CAD and among people with existing peripheral vascular disease.[4,15-23] Christos et al. have demonstrated that ABI measured by conventional Doppler method is a useful predictor of cardiovascular events in patients with CAD.[10] In our study, we used the new device to determine ABI and also found that the risk of cardiovascular death and cardiovascular events was higher in patients with ABI < 0.9. In our patients, the event-free rate was 93% in patients with ABI ≥ 0.9 and 50% in patients with ABI < 0.9. The event-free rate of ABI ≥ 0.9 was similar to Christos's result (90%), but the event-free rate of ABI < 0.9 was less than Christos's result (73%). This difference in event-free rate of ABI < 0.9 might cause by different follow-up period. The follow-up period (20.0 ± 3.6 months) in our patients was longer than Christos's series (14.5 ± 2.4 months).

In our study, ABI < 0.9, three-vessel CAD and DM were the major predictors of cardiovascular events in univariate analysis (Table 3). After multiple logistic regression analysis, ABI < 0.9 and three-vessel CAD were still the major determinants of cardiovascular events, but the significance of DM in predicting cardiovascular events had disappeared (Table 4). Three-vessel CAD has been reported to be one of the major determinants of risk in CAD.[24] In our patients, the odds ratio of ABI < 0.9 (12.6) and three-vessel CAD (12.5) in prediction of cardiovascular events were similar. This implies that ABI < 0.9, like three-vessel CAD, is a good determinant of cardiovascular events in patients with CAD.

Study limitations

We included our study subjects from our outpatient clinic, and CAG was performed several days to 6 months earlier than ABI measurement. Thus, coronary artery severity of some patients might have changed during ABI data collection. In addition, percutaneous coronary intervention was performed in 56 patients. Left ventricular ejection fraction was not performed in most of them. Hence, we had no data about the relationship of left ven-

tricular systolic function and cardiovascular events.

CONCLUSIONS

ABI measured by the automated oscillometric method, like three-vessel CAD, can serve as a useful parameter to predict cardiovascular events in patients with CAD.

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以自動化脈衝式的方法所測得的踝臂血壓比可當做冠狀動脈病人心血管不良事件的指標

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背景　以傳統都卜勒的方法所測得的踝臂血壓比已報告過可做為冠狀動脈病人心血管不良事件的指標。最近，有一個儀器，可用自動化脈衝式的方法來測量踝臂血壓比。但是用此種儀器測量的踝臂血壓比是否也可當做冠狀動脈病人心血管不良事件的指標，仍不清楚。

方法和結果　我們從門診收了 82 位已做過心導管檢查的病人。我們以 ABI-form (Colin VP1000) 的儀器為每一位病人測量踝臂血壓比，並以兩側較低一側的值當作分析的數值。我們將病人分為兩組，一組為踝臂血壓比大於或等於 0.9、另一組為踝臂血壓比小於 0.9，並比較這兩組病人的基本資料。我們追蹤這些病人 20.0 ± 3.6 個月。我們分析踝臂血壓比和心血管不良事件的關係。然後我們用單變項分析去決定心血管不良事件的主要預測因子。最後再用多變項分析去找出心血管不良事件的決定因子。82 位病人有 14 位病人的踝臂血壓比小於 0.9，有 68 位病人的踝臂血壓比大於或等於 0.9。踝臂血壓比小於 0.9 的病人，其年紀較大、尿酸較高；三條血管病變、糖尿病、高血壓和利尿劑使用的盛行率較高且因心血管病變而死亡和心血管不良事件的危險性也較高。在單變項分析時，踝臂血壓比小於 0.9、三條血管病變和糖尿病是心血管不良事件的預測因子。在多變項分析後，踝臂血壓比小於 0.9 和三條血管病變仍是心血管不良事件的主要決定因子。

結論　以此自動化脈衝式的方法所測得的踝臂血壓比，就像三條血管病變，可當做冠狀動脈病人心血管不良事件的指標。

關鍵詞：踝臂血壓比、冠狀動脈疾病、周邊動脈阻塞性病變、心血管不良事件。