弘 前 医 学 57 : 65—70, 2006

ORIGINAL ARTICLE

CLINICAL SIGNIFICANCE OF THE ANKLE-BRACHIAL INDEX (ABI) AND PULSE WAVE VELOCITY (PWV) IN PATIENTS WITH RETINAL VASCULAR OCCLUSION

Hiroshi Ohguro, Ryoichi Shimokawa, Ikuyo Ohguro, Futoshi Ishikawa, Hitoshi Yamazaki, and Mitsuru Nakazawa

Abstract Purpose: To report the clinical significance of ankle-brachial index (ABI) and pulse wave velocity (PWV) in retinal vascular occlusion.
Method: We measured the ABI and PWV, which are used as clinical indicators of arteriosclerosis, of 106 patients with retinal vascular occlusion (RVO) as well as hypertensive retinopathy (HR) and diabetic retinopathy (DR), and 100 age-matched healthy control subjects.
Results: ABI decreased with advancing age in patients with RVO, whereas no age-related changes were observed in non-RVO patients and control subjects. Furthermore, ABI was significantly lower in patients having combined presence of HR, DR and RVO than it was in patients with either HR, DR, RVO, HR+DR, HR+RVO or DR+RVO. Five out of six patients with abnormally low ABI values (less than 0.9) had associated central retinal artery occlusion (CRAO). In contrast, no such associations were observed in PWV among the groups.
Conclusion: Our present data provide the first evidence that measurement of ABI may be a clinical marker for management for retinal vascular occlusion, especially for CRAO.

Hirosaki Med. J. 57 : 65—70, 2006

Key words: ankle-brachial index (ABI); pulse-wave velocity (PWV); arteriosclerosis; retinal vascular occlusion; central retinal artery occlusion.

原 著

網膜血管閉塞症における足関節上腕血圧比 (ABI) と脈波速度 (PWV) の臨床的意義

大黒 浩　下川良一　大黒幾代
石川 太　山崎仁志　中沢 満

抄録 目的：網膜血管閉塞症における足関節上腕血圧比 (ankle-brachial index：ABI) と脈波速度 (pulse wave velocity：PWV) の臨床的意義について報告する.
対象と方法：網膜血管閉塞症，高血圧網膜症および糖尿病網膜症患者 106 例と年齢・性別をマッチさせた健常対照者 100 例を対象に，動脈硬化の指標である ABI および PWV を測定し，病態との関連につき検討した.
結果：網膜血管閉塞症を有する患者では加齢により ABI 値の減少がみられたが，他の網膜血管疾患患者や対照者ではみられなかった．ABI 値は三眼疾患すべてを合併している患者では他の患者に比べて有意に低かった．また，ABI 値が 0.9 以下の異常値を示した 6 例中 5 例は網膜中心動脈閉塞症を発症または発症していた．一方，PWV 値は疾患間で差はみられなかった.
結論：今回の結果は ABI 値が網膜血管閉塞症特に網膜中心動脈閉塞症の臨床マーカーとなり得ることを最初に示した研究である.

弘前医学 57 : 65—70, 2006

キーワード: 足関節上腕血圧比 (ABI); 脈波速度 (PWV); 動脈硬化; 網膜血管閉塞症; 網膜中心動脈閉塞症.

Department of Ophthalmology, Hirosaki University School of Medicine
弘前大学医学部眼科
別刷請求先：大黒 浩
Received for publication, September 16, 2005
Accepted for publication, December 20, 2005
平成17年9月16日受付
平成17年12月20日受理

Introduction

The ankle-brachial index (ABI), which measures the rate of hemodynamic change in the lower limbs by comparing the pressures found in the distal arteries of the leg with systemic pressure in arm, and pulse wave velocity (PWV) are simple, non-invasive and reliable methods to evaluate arteriosclerosis[1-4]. These methods are clinically utilized for diagnosis of peripheral arterial occlusive diseases and as a predictor of cardiovascular disease and mortality[5-9].

In our survey of the literature, no study could be found that specifically correlated these clinical measurements in terms of retinal vascular occlusion. Therefore, in the present study, to study the clinical significance of ABI and PWV in retinal vascular occlusion, we measured ABI and PWV in patients with several retinal vascular diseases accompanied by retinal vascular occlusion.

Patients and Methods

We measured ABI and PWV in 106 patients with several retinal vascular diseases (58 females, 48 males, average age 68±10) who were referred to Hirosaki University Hospital during 2002 through 2003. As a control, a total of 100 age- and sex-matched patients with cataract (54 females, 46 males, average age 65±7) who had no history of systemic diseases and retinal vascular diseases, such as hypertensive retinopathy (HR), diabetic retinopathy (DR) and retinal vascular occlusion (RVO), were used. After obtaining baseline ABI measurements, fundi of patients and control subjects were examined prospectively every 2 or 3 months during the 12-month follow-up period. HR was defined as having systemic hypertension and its ocular manifestations including arterial narrowing, cross phenomenon, retinal bleeding and retinal exudates. DR was defined as requiring systemic medications or diet for control of diabetes mellitus and its ocular manifestations of retinopathy. HR+DR was defined as having both systemic and ocular manifestations described above. Among these, a total of 44 eyes of 43 patients were diagnosed as having RVO such as central retinal artery occlusion (CRAO, n=5 eyes), branch retinal artery occlusion (BRAO, n=1 eye), central retinal venous occlusion (CRVO, n=12 eyes), and branch retinal venous occlusion (BRVO, n=26 eyes) at the time of ABI and PWV measurements. These types of retinal vascular occlusion were diagnosed based upon funduscopy appearance and fluorescein angiogram findings. No history of coronary artery diseases and cerebrovascular diseases were evident in the study groups.

The ABI and PWV were simultaneously measured using ABI-form (Japan Colin, Japan), which measures bilateral arm and ankle (brachial and posterior tibial arteries, respectively) blood pressure (BP) by oscillometric method according to the protocol described by manufacturer.

Significant differences between groups were found using Kruskal-Wallis test with a significant level of $P<0.05$. Linear regression analysis was applied to determine the effect of aging on the values of ABI or PWV using Spearman's rank correlation coefficients.

Results

ABI and PWV values of patients with or without RVO, and age-matched control subjects, were plotted against their ages. Spearman's rank correlation coefficients were calculated by linear regression analysis: ABI values for RVO ($y=1.457-0.005x$, $r^2=0.118$), non RVO patients ($y=1.083+0.001x$, $r^2=0.004$) (Figure 1A) and control subject

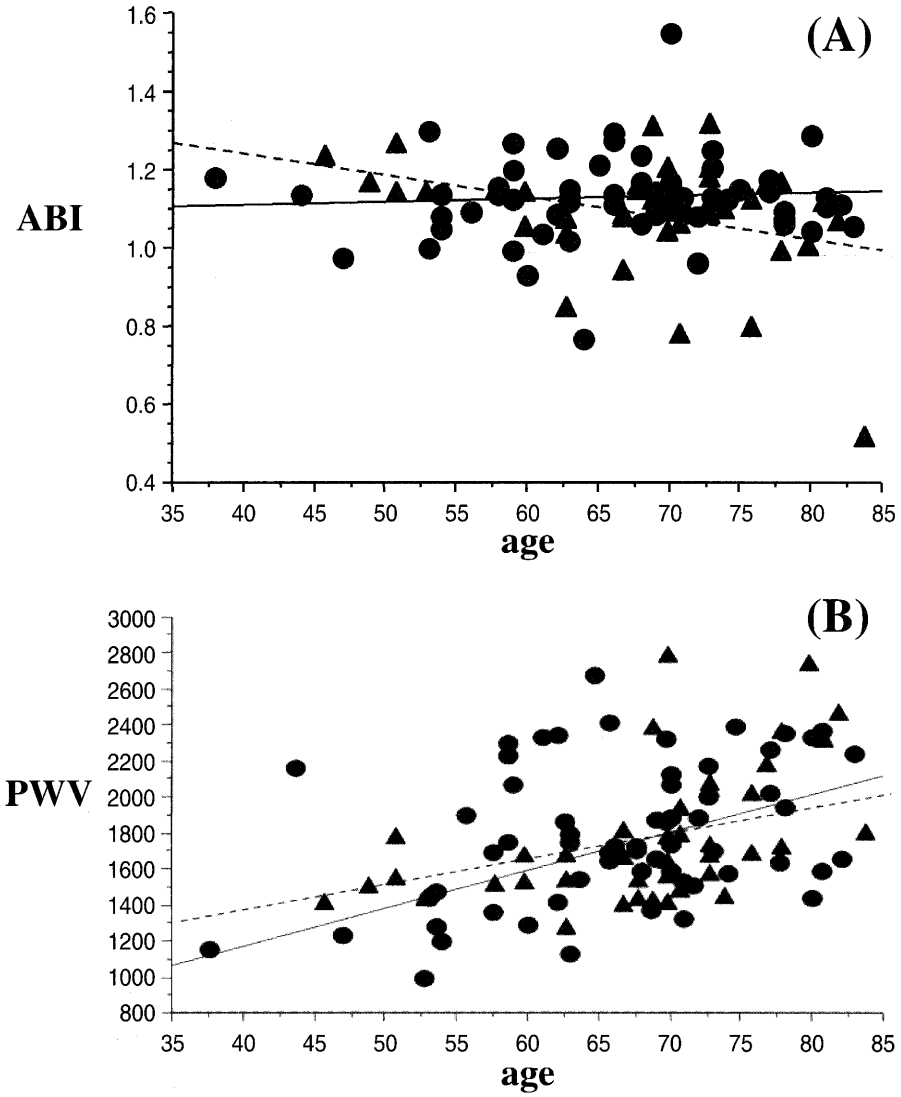

Figure 1 ABI and PWV indices in RVO and non-RVO patients.
ABI (A) and PWV (B) indices in RVO (filled triangles) and non-RVO patients (filled circles) were plotted against their ages. To examine correlations, Spearman's rank correlation coefficients were calculated by linear regression analysis: ABI measurements, RVO ($y=1.457-0.005x$, $r^2=0.118$, dotted line), non RVO patients ($y=1.083+0.001x$, $r^2=0.004$, solid line); PWV measurements, RVO ($y=326.4+20.9x$, $r^2=0.264$, dotted line), non RVO patients ($y=863.44+14.2x$, $r^2=0.122$, solid line).

($y=1.055+0.008x$, $r^2=0.007$); PWV values for RVO ($y=326.4+20.9x$, $r^2=0.264$), non RVO patients ($y=863.44+14.2x$, $r^2=0.122$) (Figure 1B). ABIs decreased relative to advancing ages in patients with RVO ($\rho=-0.302$, $p=0.049$), whereas such age related change was not observed in patients without RVO ($\rho=0.132$ $p=0.18$), or in control groups ($\rho=0.140$ $p=0.16$). No significant changes were observed in PWV values between RVO and non-RVO patients ($\rho=0.08$ $p=0.42$).

To further elucidate the clinical significance of ABI and PWV in retinal vascular diseases, patients were categorized into the following 7 groups: A, HR (31 cases); B, DR (17 cases); C, RVO (10 cases);

D, HR+DR (15 cases); E, HR+RVO (19 cases); F, DR+RVO (6 cases); G, HR+DR+RVO (8 cases). As shown in Table 1, ABIs in group G (HR+DR+RVO) were significantly lower than the other groups ($p<0.05$). In contrast, no significant correlation was observed in PWV values among these groups.

Several clinical studies have revealed that ABI less than 0.9 indicate significantly high risk for arteriosclerosis[1-3]. In the present study, we found 6 patients (1 in group B, 1 in group D, 1 in group E and 3 in group G) demonstrating less than 0.9 in ABIs (Table 2) out of total 43 patients with RVO (14.0 %). These patients all had relatively higher blood pressures, but their levels of blood pressures and PWV values were not statistically different (>0.05). Among these, three patients had CRAO at the time of ABI measurements and CRAO occurred in two other patients during the 12-month follow-up period after the ABI measurements. On the other hand,

Table 1 Mean ABI and PWV values in patients with several ocular vascular diseases

Group	Type of RVO*	Age	ABI	PWV
A) HR (n=31)		69±9	1.12±0.07	1736.4±349.4
B) DR (n=17)		63±13	1.09±0.13	1833.8±421.2
C) RVO (n=10)	BRVO n=6 CRVO n=3 CRAO n=1	71±6	1.12±0.11	1686.6±223.2
D) HR+DR (n=15)		66±7	1.18±0.13	1892.5±395.2
E) HR+RVO (n=19)	BRVO n=12 CRVO n=6 BRAO n=1 CRAO n=1	65±9	1.11±0.11	1815.4±409.0
F) DR+RVO (n=6)	BRVO n=4 CRVO n=1 CRAO n=1	69±10	1.12±0.15	1702.7±389.3
G) HR+DR+RVO (n=8)	BRVO n=4 CRVO n=2 CRAO n=2	73±11	0.90±0.20*	1892.1±475.8

HR, hypertensive retinopathy; DR, diabetic retinopathy; RVO, retinal vascular occlusion; BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; BRAO, branch retinal artery occlusion; CRAO, central retinal artery occlusion. *$P<0.05$. ABI was measured by ABI FORM (Japan Colin Co., Japan) and their data of each patient is mean value of both left and right sides as according to the manufacturer's protocol. *Type of RVO in each group was shown the profile at the time of ABI and PWV measurements. In group E, 71 year-old patient showed combined presence of CRVO and CRAO.

Table 2 Types of retinal vascular diseases in patients with low ABI values (less than 0.9)

Patient	ABI values[a]	PWV values[b]	Blood pressure (mmHg)[c]	Group	RVO at ABI measurement	RVO occurred after ABI measurement*
1) 65M	0.77	1261	127/94	B (DM)		
2) 63M	0.85	1565	151/109	D (HR+DM)		**CRAO**
3) 71M	0.78	1532	144/108	E (HR+RVO)	**CRAO**, CRVO	
4) 84M	0.52	1792	148/107	G (HR+DM+RVO)	BRVO	**CRAO**
5) 76M	0.78	1667	216/110	G (HR+DM+RVO)	**CRAO**	
6) 75F	0.88	2307	145/110	G (HR+DM+RVO)	**CRAO**	

[a,b]ABI and PWV values (mean of left and right). [c]Blood pressure (systolic/diastolic pressures at initial visit to our clinic). *Occurrence of RVO is indicated during the 12-month follow-up period after the ABI measurements.

100 other patients demonstrating more than 0.9 in ABIs as well as 100 control subjects did not develop any retinal vascular occlusions during the 12-month follow-up period.

Discussion

ABI is a non-invasive method to assess the patency of the lower extremity arterial system and to detect the presence of arterial occlusion disease, and PWV is also a non-invasive test to reflect arterial stiffening in elastic arteries and muscular arteries[1-4]. Several clinical studies have revealed that both ABI and PWV are valuable methods not only for diagnosis of peripheral arterial obstructive diseases but also for predicting mortality and morbidity among elderly or hypertensive patients[5-9]. However, in contrast to extensive evidences for the usefulness of ABI and PWV in systemic arterial obstructive diseases, no study has been available concerning the clinical significance of ABI and PWV in RVO. In our present study, to elucidate the clinical significance of these indices we performed ABI and PWV measurements in 106 patients with retinal vascular diseases that included RVO and 100 control subjects. The range of normal values for ABI is 0.9-1.2 and less than 0.9 suggests significant risk for arteriosclerosis with high sensitivity and specificity[1-4]. In our present study, the ABI index showed an age-related decrease in RVO patients but not in non-RVO patients. In addition, ABI index in group G (HR+DR+RVO) was significantly lower than in any of the other groups. However, in contrast, no significant differences were observed in PWV index between RVO and non-RVO, nor among these 7 groups. These observations suggested that low ABIs in severe cases involving a combination of HR, DR and RVO are at additional risk for systemic arterial obstructive diseases and this should be monitored carefully as part of their clinical management. Patients who have systemic atherosclerosis disease with low ABI values should also be alerted to the potential risk of ocular complications of RVO, especially in elderly patients.

Among our 43 patients with RVO, 6 patients (14%, 1 in group B, 1 in group D, 1 in group E, and 3 in group G) demonstrated less than 0.9 in ABI index. Interestingly, among these, three patients already had CRAO associated with this ABI measurement and new CRAO complications occurred in two other patients during the 12-month follow-up period after the ABI measurements. By contrast, however, the remaining 100 patients have not had any evidence of additional RVO manifestations so far. At present, there are seven CRAO patients in the study group. Five of the patients were diagnosed at the time of the initial ABI measurements and the other two developed CRAO after the initial measurements. It is noteworthy that three patients in group E or G who initially presented with evidence of CRAO showed significant low ABI values and two additional patients with low ABI values in group D and G developed CRAO manifestation during the 12 months follow-up after the ABI measurements. Therefore, CRAO patients with low ABI values therefore all had evidence of HR. In contrast, the other two CRAO patients in group C (73F patient, ABI = 1.03) or F (71M patient, ABI = 1.00) had ABI values in the normal range and showed no manifestation of HR. In terms of the significance of this data, low ABI values in patients with HR appear to indicate a high risk for the development of CRAO and measurement of ABI can be potentially clinically helpful for monitoring and management of retinal vascular occlusion, especially for CRAO.

References

1) Pearson TA. New tools for coronary risk assessment: what are their advantages and limitations? Circulation 2002;105:886-92.

2) Hirsch AT, Criqui MH, Treat-Jacobson D, Regensteiner JG, Creager MA, Olin JW, Krook SH et al. Peripheral arterial disease detection, awareness, and treatment in primary care. JAMA 2001;286:1317-24.

3) McDermott MM, Greenland P, Liu K, Guralnik JM, Criqui MH, Dolan NC, Chan C et al. Leg symptoms in peripheral arterial disease. JAMA 2001;286:1599-1606.

4) Theodoridou A, Bento L, D'Cruz DP, Khamashta MA, Hughes GR. Prevalence and associations of an abnormal ankle-brachial index in systemic lupus erythematosus: a pilot study. Ann Rheum Dis 2003;62:1199-1203.

5) Blacher J, Guerin AP, Pannier B, Marchais SJ, Safar ME, London GM. Impact of aortic stiffness on survival in end-stage renal disease. Circulation 1999;99:2434-9.

6) Matzke S, Franckena M, Alback A, Railo M, Lepantalo M. Ankle brachial index measurements in critical leg ischemia- the influence of experience on reproducibility. Scand J Surg 2003;92:144-7.

7) Murabito JM, Evans JC, Larson MG, Nieto K, Levy D, Wilson PW. The ankle-brachial index in the erderly and risk of stroke, coronary disease, and death. Arch Intern Med 2003;163:1939-42.

8) Papamichael CM, Lekakis JP, Stamatelopoulos KS, Papaioannou TG, Alevizaki MK, Cimponeriu AT, Kanakakis JE et al. Ankel-brachial index as a predictor of the extent of coronary atherosclerosis and cardiovascular events in patients with coronary artery disease. Am J Cardiol 2000;86:615-8.

9) Koji Y, Tomiyama H, Ichihashi H, Nagae T, Tanaka N, Takazawa K, Ishimaru S et al. Comparison of ankle-brachial pressure index and pulse wave velocity as markers of the presence of coronary artery disease in subjects with a high risk of atherosclerotic cardiovascular disease. Am J Cardiol 2004;94: 868-72.

10) Ono K, Tsuchida A, Kawai H, Matsuo H, Wakamatsu R, Maezawa A, Yano S et al. Ankle-brachial blood pressure index predicts all-cause and cardiovasucular mortality in hemodialysis patients. J Am Soc Nephrol 2003;14:1591-8.