Angiology
http://ang.sagepub.com/

Photoplethysmography and Continuous-Wave Doppler Ultrasound as a Complementary Test to Ankle–Brachial Index in Detection of Stenotic Peripheral Arterial Disease

Du Hyun Ro, Hyuk Ju Moon, Ji Hyeung Kim, Kyoung Min Lee, Sung Ju Kim and Dong Yeon Lee

ANGIOLOGY published online 15 November 2012
DOI: 10.1177/0003319712464814

Angiology
00(0) 1-7

DOI: 10.1177/0003319712464814
http://ang.sagepub.com
SAGE

Photoplethysmography and Continuous-Wave Doppler Ultrasound as a Complementary Test to Ankle–Brachial Index in Detection of Stenotic Peripheral Arterial Disease

Du Hyun Ro, MD[1], Hyuk Ju Moon, MD[1], Ji Hyeung Kim, MD[2], Kyoung Min Lee, MD[3], Sung Ju Kim, MS[1], and Dong Yeon Lee, MD[1]

Abstract

Purpose: We evaluated the sensitivity and specificity of ankle–brachial index (ABI), photoplethysmography (PPG), and continuous-wave Doppler ultrasound (CWD) in the detection of anatomically stenotic peripheral arterial disease (PAD). Methods: Ninety-seven patients (194 legs) patients who had coincidentally undergone computed tomography angiography (CTA), ABI, PPG, and CWD for the evaluation of PAD were retrospectively reviewed. Sensitivity and specificity were measured. Results: Among 194 legs, 163 (84%) legs had stenotic PAD on CTA. Overall sensitivity of ABI, PPG, and CWD was 69.3%, 81.6%, and 90.8% and specificity was 96.8%, 77.4%, and 64.5%, respectively. Ankle–brachial index showed a statistically significantly decreased sensitivity (14.8%) for below trifurcation level stenosis compared with CWD (92%) and PPG (67%). The sensitivity of ABI was also significantly decreased in single level and moderate stenosis (45.1% and 42.1%, respectively). In contrast, the sensitivity of CWD and PPG was not significantly decreased. Conclusion: The ABI showed significantly decreased sensitivity especially in stenosis below the trifurcation level. Both PPG and CWD were complementary to ABI in these groups of patients.

Keywords

peripheral arterial disease, ankle–brachial index, photoplethysmography, continuous-wave Doppler, sensitivity, specificity

Introduction

Peripheral arterial disease (PAD) can be defined as a range of noncoronary arterial syndromes that are caused by the altered structure and function of the arteries that supply the brain, visceral organs, and the limbs.[1,2] Overall prevalence of PAD based on objective testing has been reported to be 3% to 10%, increasing to 15% to 20% in persons over 70 years in several epidemiologic studies.[2-5] The majority of patients with PAD are asymptomatic and the ratio of patients with symptomatic and asymptomatic[2,3,5,6] PAD is in the region of 1:2 to 1:4. Patients with symptomatic PAD have a significantly high risk of death from cardiovascular disease.[1,2,7] They have approximately a 28% 5-year mortality rate which is higher than the 5-year mortality rates of breast cancer and Hodgkin disease in the United States.[8] However, even in patients with PAD without typical symptoms such as intermittent claudication or critical limb ischemia, the risk of subsequent cardiovascular morbidity, myocardial infarction, and internal carotid artery stenosis is substantially higher than that in the average population.[6,8-11] Therefore, early detection and management of patients with asymptomatic PAD may be indicated. To date, ankle–brachial index (ABI) is the most widely used initial evaluation method for screening PAD.[1,2] It is relatively simple, noninvasive, inexpensive, and is more than 90% sensitive and specific compared to angiography, the gold standard test.[1,2,12] Although ABI provides several benefits, it has limitations. Ten percent of the general population has congenital absence of the dorsalis pedis or posterior tibial artery meaning that ABI would not be accurate.[13] And ABI may not be accurate in noncompressible pedal arteries, as in diabetic and elderly patients.[1,14,15] Furthermore, several authors have recently questioned the sensitivity of ABI and reported its sensitivity at 60%

[1] Department of Orthopaedic Surgery, Seoul National University College of Medicine, Seoul, South Korea
[2] Department of Orthopedic Surgery, Boramae Medical Center, Seoul National University College of Medicine, Seoul, South Korea
[3] Department of Orthopedic Surgery, Seoul National University, Bundang Hospital, Seongnam, South Korea

Corresponding Author:
Dong Yeon Lee, Department of Orthopaedic Surgery, Seoul National University Hospital, 28 Yeongeon-dong Jongno-gu, Seoul 110-744, South Korea
Email: leedy@snu.ac.kr

to 70%, compared with angiography.[16-18] Several noninvasive vascular diagnostic tools have been tried to overcome the shortcomings of ABI, which includes toe–brachial index,[19] segmental pressure examination,[20,21] continuous-wave Doppler ultrasound (CWD),[7] postexercise ABIs,[14] and photoplethysmography (PPG). Photoplethysmography is an optical measurement technique to measure blood volume changes.[22,23] Changes in blood volume, blood vessel wall movement, and the orientation of red blood cells can affect the amount of light received by the photodetector.[22] In patients with PAD, the signal becomes damped and loses its wave pattern.[22,23] Continuous-wave Doppler ultrasound is used to obtain velocity waveforms and to measure systolic blood pressure at sequential segments of the extremities. This technique allows estimation of disease location and severity, follow-up of disease progression, and quantification of the effects of interventional therapies.[1,2,7] Although CWD and PPG were originally introduced decades ago, there has been no report that directly compares the diagnostic value of ABI, CWD, and PPG.

The goals of this study are (1) to assess the sensitivity and specificity of ABI, PPG, and CWD in the detection of anatomically stenotic PAD, (2) to determine whether combining these tests would improve the sensitivity and specificity, and (3) to determine a complementary role of PPG and CWD in the detection of stenotic PAD.

Methods

Patient Selection

This study was approved by our local institutional review board. A total of 225 patients who had coincidentally undergone computed tomography angiography (CTA), PPG, ABI, and CWD in a 2-year period (2007-2008) for the evaluation of PAD were retrospectively reviewed. Among the 225 patients, 127 patients were excluded according to the exclusion criteria. Finally 97 patients (194 legs) were included in present study. Exclusion criteria were (1) patients who had undergone prior interventional procedures before tests, (2) patients who had undergone interventional procedures between tests, and (3) patients in whom the interval between tests was more than 14 days. Basic characteristics such as height, weight, history of hypertension, diabetes mellitus, and cardiovascular accident were collected from electronic medical records. Follow-up data of each individual patient were not included in this study.

Diagnostic Test

Computed tomography angiography was performed with a 64-channel MDCT (Brillance 64, Philips, the Netherlands and SOMATOM definition, Siemens AG., Germany) scanner using contrast dye. Precontrast phase, arterial phase, and venous phase images were taken. Results were interpreted by a vascular interventional and divided into 3 segments (iliac artery, femoral artery/popliteal artery, and below trifurcation level). Severity was categorized into mild stenosis (50%-69% diameter reduction), moderate stenosis (70%-89% of diameter reduction), and severe stenosis (more than 90% diameter reduction). In this study, moderate or severe stenosis was considered as significant anatomically stenotic PAD on CTA. The ABI, PPG, and CWD were measured according to the protocol at the same time. Patients were preconditioned at room temperature (24°C) for 20 minutes before evaluations. A single technician performed all the tests sequentially without disruption. The ABI was measured with a computer based diagnostic kit that includes 8 MHz continuous-wave Doppler (Vasoguard P84, VIASYS Healthcare) and sphygmomanometer with a blood pressure cuff to measure blood pressure. The ABI was derived for each leg by dividing the ankle pressure by the higher of the upper extremity pressures. Ankle pressures were determined as a higher pressure between pressures measured at posterior tibial artery and dorsalis pedis artery. An abnormal ABI was defined as less than 0.9. The CWD was subsequently measured with same equipment. Wave forms were obtained at both sides of femoral, popliteal, posterior tibial, and dorsalis pedis arteries. The probe was placed at the midportion of the femoral and popliteal artery. The posterior tibial pulse was detected at the posterior aspect of the medial malleolus. The dorsalis pedis pulse was detected at the dorsum of the foot.

The CWD wave form was interpreted by a single physician using the following criteria: (1) loss of triphasic pattern, (2) decreased amplitude of more than 50% compared with the contralateral side, or (3) loss of reverse flow component. The presence of any of these findings was considered as positive. As the normal Doppler arterial wave has a triphasic pattern composed of initial steep peak (representing systolic flow), dipping down second portion (representing reverse flow in early diastole) and last small peak (representing late diastole forward flow), loss of any component which lead to biphasic or monophasic pattern was considered as "loss of triphasic pattern."

The PPG was measured subsequently. The clips which have light emitting and receiving part were attached at toes to obtain waves. At least 60 heartbeats were obtained for the averaging period. The PPG wave form was interpreted by the same physician with the criteria listed as follows: (1) loss of dicrotic notch, (2) decreased amplitude of more than 50% compared with contralateral side, or (3) rounding of peaks compared with contralateral side. The presence of any of these findings was considered as positive (Figure 3).

Statistical Analysis

Statistical analysis was performed using Microsoft Excel (Microsoft Inc, Redmond, Washington) software. Results were systemically collected by a single researcher (D.H.R.). We considered CTA as the gold standard. Sensitivity, specificity, and 95% confidence interval (95% CI) values were calculated with the Wilson score method without continuity correction.[24] Ninety-five percent CI was used to compare between tests (if 95% CI of sensitivity of test A was higher than test B without overlapping, test A was considered to have statistically higher sensitivity than test B). The sensitivity of subgroups was calculated by grouping patients with the

Table 1. Demographics of the Study Population

Variable	Value
Total patients/legs	97/194
Age	67 (22-89)
Sex (male)	88 (91%)
Diabetes mellitus[a]	44 (45%)
Hypertension[a]	56 (58%)
Smoker (ex-smoker included)	53 (55%)
Coronary artery disease[b]	20 (21%)
Carotid artery disease[c]	16 (16%)

[a] Hypertension and diabetes mellitus documented in patient's medical record and treated with medicines.
[b] Coronary artery disease diagnosed by cardiac stress testing or angiography and documented in patient's medical record.
[c] Carotid artery disease diagnosed by ultrasound examination or angiography and documented in patient's medical record.

underlying disease and using CTA findings (number of involved segment, location of involved segment, and severity of stenosis). Pearson chi-square test was performed to compare the prevalence of PAD in subgroups. *P* value <.05 was considered as statistically significant. In every statistical analysis, each leg was considered independent of each other as each test (ABI, PPG, CWD, and CTA) was separately (ie, left and right) performed and interpreted.

Results

Among the 194 legs of 97 patients, 163 (84%) legs were diagnosed with stenotic PAD on CTA. The demographic data of the study population are described in Table 1. Mean age was 67 years (range 22-89) and males were predominant (approximately 9:1). Prevalence of comorbidities such as hypertension (58%), smoking history (55%), diabetes (45%), coronary artery disease (21%), and cerebrovascular disease (16%) were recorded. All patients were Korean.

Of the 163 legs anatomically diagnosed with stenotic PAD on CTA, single-segment occlusion was observed in 71 cases (43.6%) and multiple segmental involvement was found in 92 cases (56.4%). Iliac artery stenosis was observed in 76 cases (46.6%), femoral/popliteal artery stenosis was found in 60 cases (36.8%), and below trifurcation level stenosis in 27 cases (16.6%). By stenosis severity, mild stenosis (50%-69% diminution of diameter) was observed in 11 cases (6.7%), moderate stenosis (70%-89% diminution of diameter) was in 19 cases (11.6%), and severe stenosis (more than 90% diminution of diameter) was found in 133 cases (81.6%).

The overall sensitivity of ABI, PPG, and CWD for CTA-proven PAD was 69.3%, 81.6%, and 90.8%, respectively. The specificity of ABI, PPG, and CWD was 96.8%, 77.4%, and 64.5%, respectively. The overall sensitivity of ABI was statistically significantly lower than CWD. However, the specificity of ABI was significantly higher than CWD (Table 2). Accordingly about 30% of CTA-proven patient with PAD could be misdiagnosed by ABI criteria.

Table 2. Sensitivity and Specificity of PPG, CWD, and ABI in Patients With PAD

Modality	Sensitivity, % (95% CI)	Specificity, % (95% CI)
ABI	69.3% (61.9%-75.9%)	96.8% (83.8%-99.4%)
PPG	81.6% (74.8%-87.2%)	77.4% (58.9%-90.4%)
CWD	90.8% (85.3%-94.8%)	64.5% (45.4%-80.8%)

Abbreviations: ABI, ankle–brachial index; CI, confidence interval; PPG, photoplethysmography.

Subgroup Analysis of Sensitivity and Specificity

We subsequently performed subgroup analysis. Patients were grouped by underlying disease (diabetes mellitus, hypertension, and smoking history) and CTA findings (number of involved segment, location of involved segment, and severity of stenosis). As the sensitivity of diagnostic tests (ABI, CWD, and PPG) could be affected by prevalence of disease, we performed Pearson chi-square test to the null hypothesis that there is no significant difference in the number of patients with PAD in the subgroup. *P* value <.05 was considered as statistically significant. There was no statistical difference in the number of patients with PAD by smoking history and hypertension subgroup (*P* value .676 and .052, respectively). However, the number of patients with PAD in the group with diabetes mellitus was statistically significantly (*P* value .046) higher (79 of 88 patients, 89.8%) than the nondiabetic groups (84 of 106, 79.2%), though it was not strong. Subgroup analysis of sensitivity by underlying disease showed no statistically significant differences between groups (95% CI of sensitivity was compared). As summarized in Table 3, underlying disease did not affect the sensitivity of diagnostic test.

Subgroup analysis by stenosis severity, number of segments involved, and anatomical location by CTA findings was performed. The ABI showed statistically significantly lower sensitivity in both the moderate and severe group when compared with PPG and CWD (Figure 1A). Similarly, in single-segment stenosis, the sensitivity of ABI was statistically significantly lower than that of PPG and CWD (Figure 1B). By stenosis level, sensitivity of ABI was only 14.8% (95% CI: 5.9%-32.5%; Figure 1C), which means ABI could misdiagnose about 85% of CTA-proven below trifurcation level stenosis. As ABI was not sensitive in specific groups of patients, we combined the result of PPG and CWD with ABI to evaluate their combined value. When we re-define PAD positive as "either positive PPG or ABI value of less than 0.9," the sensitivity increased from 69.3% to 87.1% (95% CI: 81.1%-91.4%). When we combine CWD instead of PPG, the sensitivity increased up to 92% (95% CI: 86.8%-95.3%). In the below trifurcation level stenosis, the sensitivity increases more dramatically. Combination of PPG with ABI could increased sensitivity up to 77.8% (95% CI: 59.2%-89.4%) and combination of CWD with ABI could increase sensitivity up to 92.5% (95% CI: 76.6%-97.9%; Figure 2).

Table 3. Subgroup Analysis of Sensitivity and Specificity

Variables	Sensitivity (95% CI)	Specificity (95% CI)
DM (n = 88, PAD = 79)		
ABI	74.7% (64.1%-82.9%)	88.9% (56.5%-98%)
PPG	78.5% (68.2%-86.1%)	89% (56.5%-98.1%)
CWD	97.5% (91.2%-99.3%)	66.7% (35.4%-87.9%)
Non-DM (n = 106, PAD = 84)		
ABI	64.3% (53.6%-73.7%)	100% (85.1%-100%)
PPG	84.5% (75.3%-90.7%)	72.7% (51.9%-86.9%)
CWD	84.5% (75.3%-90.7%)	63.6% (43%-80.3%)
Smoker (n = 106, PAD = 88)		
ABI	65.9% (55.5%-75%)	100% (82.4%-100%)
PPG	86.4% (77.6%-92%)	77.8% (54.8%-91%)
CWD	87.5% (79%-92.9%)	55.6% (33.7%-75.4%)
Nonsmoker (n = 88, PAD = 75)		
ABI	73.3% (62.4%-82%)	92.3% (66.7%-98.6%)
PPG	76.0% (65.2%-84.3%)	76.9% (49.7%-91.8%)
CWD	94.7% (87.1%-97.9%)	76.9% (49.7%-91.8%)
Hypertension (n = 112, PAD = 99)		
ABI	70.7% (61.1%-78.8%)	100% (77.2%-100%)
PPG	79.8% (70.9%-86.5%)	76.9% (49.7%-91.8%)
CWD	88.9% (81.2%-93.7%)	76.9% (49.7%-91.8%)
Nonhypertension (n = 82, PAD = 64)		
ABI	67.2% (55%-77.4%)	94.4% (74.2%-99.1%)
PPG	84.4% (73.6%-91.3%)	77.8% (54.8%-91%)
CWD	93.8% (85%-97.5%)	55.6% (33.7%-75.4%)

Abbreviations: ABI, ankle–brachial index; CI, confidence interval; CWD, continuous-wave Doppler; DM, diabetes mellitus; PPG, photoplethysmography.

Discussion

This study demonstrated that the overall sensitivity of ABI for detecting PAD was lower than CWD and PPG. In stenosis with below trifurcation level, single level, and moderate degree, the sensitivity of ABI was statistically significantly lower than that of PPG and CWD. However, the specificity of PPG and CWD was lower than that of ABI. Both PPG and CWD were complementary to ABI so that combining these tests improved sensitivity in diagnosing anatomically stenotic PAD.

Traditionally, clinical symptoms are considered to be important in diagnosing PAD. However, the presence of intermittent claudication largely depends on the activity level of patients. In chronic debilitating condition such as diabetes mellitus and chronic renal failure, PAD may manifest as a critical limb ischemia even in patients without claudication.[1,2] As PAD is closely associated with ischemic cardiovascular disease, early detection and early intervention (such as risk reduction medication and exercise programs) for PAD have become more important.[1,2] And with rapid progression in the technology of interventional endovascular procedures, timely intervention in selected patients could decrease amputation, procedural morbidity, and mortality.[25]

Computed tomography angiography is usually indicated in patients with symptomatic PAD to check the anatomic location of disease before any interventional procedure.[1,2] It is considered as accurate as digital subtraction angiography, a gold standard diagnostic method in PAD.[1,26] However, as CTA needs a bolus injection (usually >100 mL) of iodine-contained contrast agent, and potential serious complication such as nephrotoxicity and anaphylaxis limits its usage as a primary diagnostic method, especially in patients with decreased renal function. Magnetic resonance angiography can be an alternative option in this particular situation however it may not be available in usual clinical settings. Ankle–brachial index is a standard noninvasive diagnostic method for detecting PAD.[1,2] It is a relatively simple, noninvasive, inexpensive test and has been reported to have good sensitivity and specificity when compared with CTA or angiography.[1,2,27] However, the limitations of ABI have been highlighted by many authors. Reich reported that 10% of the general population has congenital absence of the dorsalis pedis artery or posterior tibial artery and ABI may not be accurate in noncompressible pedal arteries.[1,13-15] Schroder et al recently reported that a high ankle pressure ABI had a sensitivity of 68% and a specificity of 99%, while low ankle pressure ABI had a sensitivity of 89% and specificity of 93%.[16] Lijmer et al reported a 79% sensitivity and 96% specificity of ABI for detecting 50% or more stenosis that was confirmed by angiography.[17] Nam et al also reported a 61% sensitivity and 87% specificity of ABI by the same angiographic criteria above.[18] These reports showed a lower sensitivity than previous reports which suggested a 95% of sensitivity and specificity.[1,2,12] Such inconsistent findings for sensitivity is likely based on a lack of clear definition of PAD in terms of anatomical location. Khan et al reported that several studies in which ABI has been shown to be >90% sensitive and >95% specific to diagnose 50% stenosis of lower arteries are inaccurate, because of their lack of the definition of PAD in terms of the diameter stenosis of the arteries concerned.[28]

Our report differs from the ones cited above by directly comparing CTA findings with noninvasive studies (ABI, PPG, and CWD) in terms of anatomic location. Our definition of PAD on CTA was more than 70% of diminution at least one segment (from iliac artery to below trifurcate level). With direct comparison, we demonstrated that the sensitivity of ABI decreases in stenosis below trifurcate level, single level stenosis, and moderate stenosis groups. Therefore, early diagnosis of PAD would not be feasible with ABI in these specific groups. Many efforts have been tried to overcome limitations of ABI. Ramsey et al criticized ABI in that it fails to reflect the severity of peripheral ischemia when underlying vessels are calcified or when there is extensive pedal or digital arterial disease.[19] Instead of ABI, authors proposed the toe–brachial index for detecting PAD. In this article, the toe–brachial index was well correlated with ankle pressure and the sensitivity for detecting PAD was 85% to 90%.[19] However, the toe–brachial index is not as popular in practice as ABI. It is more difficult to measure and its accuracy has also been questioned.[1,2,29] Allen et al have proposed PPG as an alternative test for ABI in a primary care

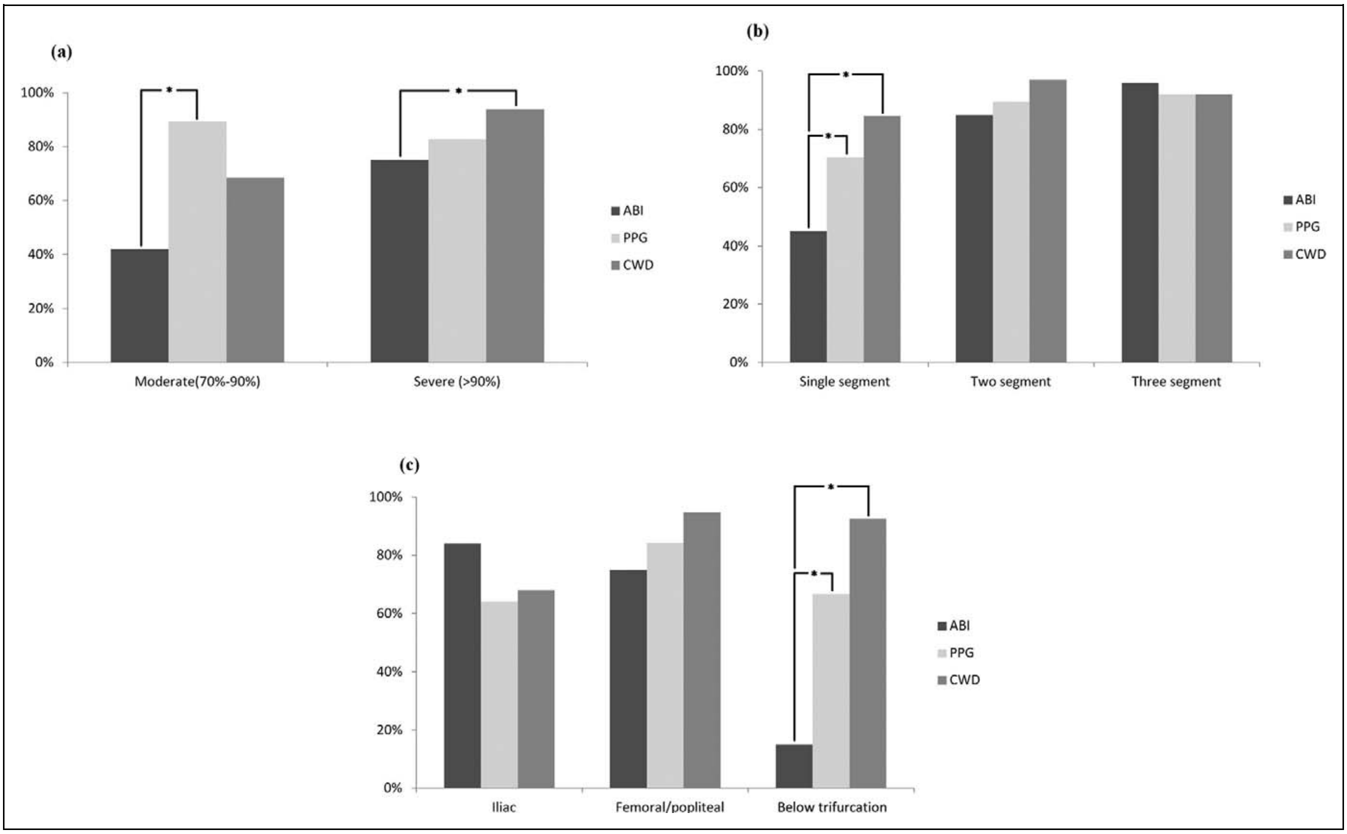

Figure 1. Sensitivity of subgroup analysis. A, Analysis by stenosis severity level shows significant decreased sensitivity of ABI both in moderate and in severe stenoses. B, Analysis by number of involved segment shows significantly decreased sensitivity in single segment involvement. C, Analysis by involved anatomic location shows extremely low sensitivity of ABI in below trifurcation level stenosis. A statistically significant difference in sensitivity was marked with the asterisk (95% confidence interval was compared). ABI indicates ankle–brachial index; PPG, photoplethysmography; CWD, continuous-wave Doppler.

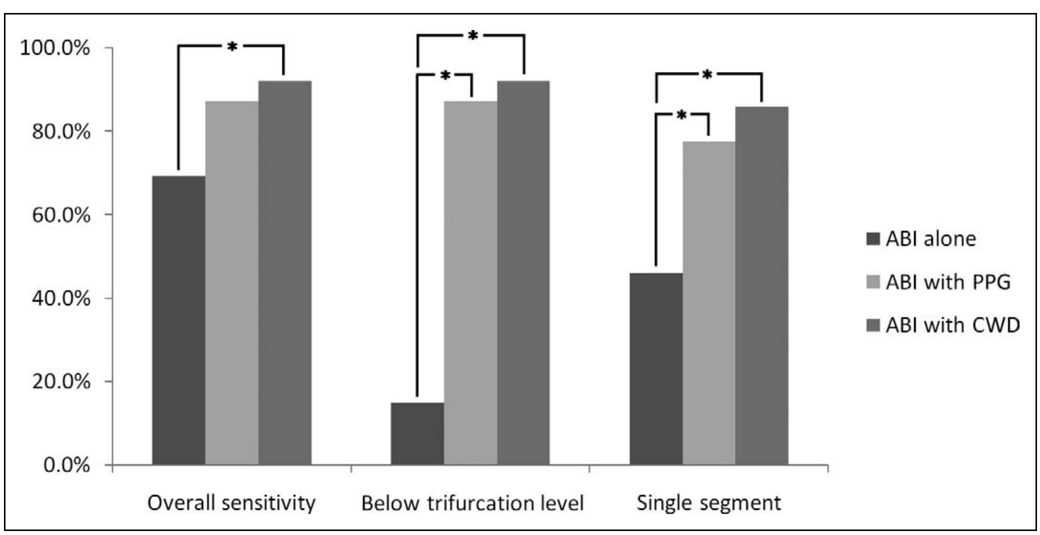

Figure 2. Sensitivity of combined use of PPG and CWD shows increased sensitivity. The ABI alone in below trifurcation level, single segment disease was not reliable, whereas combined use could increase sensitivity dramatically. A statistically significant difference in sensitivity was marked with the asterisk (95% confidence interval was compared). ABI indicates ankle–brachial index; PPG, photoplethysmography; CWD, continuous-wave Doppler.

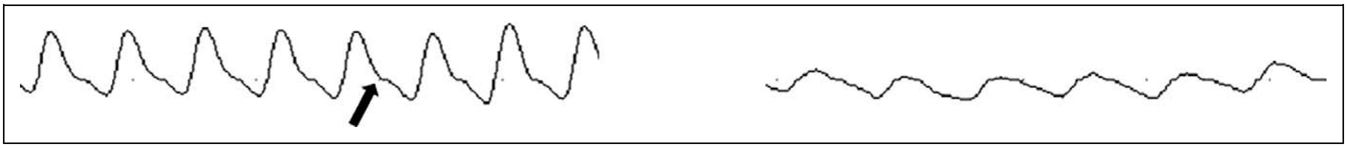

Figure 3. Configuration of PPG waves. Figure on left side shows normal PPG wave that has dicrotic notch (arrow) and narrow peak. Figure on right side shows abnormal PPG where the loss of dicrotic notch and rounding of peak are observed.

setting.[22,30] The authors advocated PPG as it has 91% sensitivity and 93% specificity compared with ABI, while it takes less time and does not need a trained specialist. Gale et al proposed segmental pressure measurements in addition to ABI.[21] However, compared with ABI, the addition of segmental pressure to waveform data failed to improve the accuracy.[21] Despite these efforts, none of these authors have demonstrated which test could improve the sensitivity of ABI in terms of anatomical location.

As early detection and early intervention of PAD is becoming more important in community health care, the need for a more sensitive test is becoming more important. In this study, we have analyzed the limitations of ABI in terms of location, severity, and number of involved segments and demonstrated that the sensitivity of ABI could increase with combining CWD and PPG.

This study has limitations as follows: (1) as this study is based on a retrospective review, confounding factors could not be controlled effectively. For example, we could not clearly check current smoking status but only record smoking history. (2) Vessel wall calcification that might have had an effect on ABI had not been assessed. However, only 1 leg had an ABI of more than 1.3, which indicates noncompressible calcified vessel. (3) The prevalence of PAD, especially severe PAD, was substantially high in the study population (80 legs were less than 0.6 for ABI) and males were predominant (female to male ratio was 1:9). This may have been a result of the retrospective nature of this study. This study retrospectively reviewed cases that had needed CTA for evaluation of vascular status in high-risk patients. A demographic study has shown a male predominance pattern of PAD in South Korea.[31] Furthermore, Criqui et al also reported that although the prevalence of PAD is similar between sexes, male patients tend to be more severely affected compared with women.[9] Therefore, we feel a male predominance in this study would not invalidate our conclusions. (4) Though we have demonstrated the limitations of ABI in below trifurcation level disease, the clinical significance of early detection and interventional treatment for the stenosis below trifurcation required further evaluation.[1,2] However, as several studies have demonstrated improvement in claudication symptom and foot ulcer by endovascular intervention at below trifurcation level, we expect that intervention therapy or exercise programs would be helpful in selected groups of patient.[32,33] (5) The possibility of qualitative interpretation of pulse waves, especially in PPG interpretation may affect the result of our study. More objective measures such as computerized interpretation of waveforms could increase the diagnostic value of PPG[34] (Figure 3).

In conclusion, ABI showed statistically significantly decreased sensitivity in detection of anatomically stenotic PAD especially in stenosis below trifurcation level. Both PPG and CWD were complementary to ABI in these groups of patients. Early detection of stenotic PAD can be facilitated by combination of ABI with PPG or CWD. This may enable timely intervention in patients with PAD without typical claudication symptoms.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: grant from Seoul National Hospital Research Fund (SNUH 04-2009-0300) and Seoul National University Fund (800-20110020).

References

1. Hirsch AT, Haskal ZJ, Hertzer NR, et al. ACC/AHA 2005 guidelines for the management of patients with PAD (lower extremity, renal, mesenteric, and abdominal aortic): executive summary a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease) endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. *J Am Coll Cardiol.* 2006;47(6):1239-1312.
2. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *J Vasc Surg*. 2007;45(suppl S):S5-S67.
3. Criqui MH, Fronek A, Barrett-Connor E, Klauber MR, Gabriel S, Goodman D. The prevalence of peripheral arterial disease in a defined population. *Circulation*. 1985;71(3):510-515.
4. Selvin E, Erlinger TP. Prevalence of and risk factors for peripheral arterial disease in the United States: results from the National Health and Nutrition Examination Survey, 1999-2000. *Circulation*. 2004;110(6):738-743.
5. Meijer WT, Hoes AW, Rutgers D, Bots ML, Hofman A, Grobbee DE. Peripheral arterial disease in the elderly: the Rotterdam study. *Arterioscler Thromb Vasc Biol*. 1998;18(2):185-192.

6. Hooi JD, Stoffers HE, Kester AD, et al. Risk factors and cardiovascular diseases associated with asymptomatic peripheral arterial occlusive disease. The Limburg PAOD Study. Peripheral Arterial Occlusive Disease. *Scand J Prim Health Care.* 1998; 16(3):177-182.
7. Leng GC, Lee AJ, Fowkes FG, et al. Incidence, natural history and cardiovascular events in symptomatic and asymptomatic peripheral arterial disease in the general population. *Int J Epidemiol*. 1996;25(6):1172-1181.
8. Belch JJ, Topol EJ, Agnelli G, et al. Critical issues in peripheral arterial disease detection and management: a call to action. *Arch Intern Med*. 2003;163(8):884-892.
9. Criqui MH, Denenberg JO. The generalized nature of atherosclerosis: how peripheral arterial disease may predict adverse events from coronary artery disease. *Vasc Med*. 1998;3(3): 241-245.
10. Simons PC, Algra A, Eikelboom BC, Grobbee DE, van der Graaf Y. Carotid artery stenosis in patients with peripheral arterial disease: the SMART study. SMART study group. *J Vasc Surg.* 1999;30(3):519-525.
11. House AK, Bell R, House J, Mastaglia F, Kumar A, D'Antuono M. Asymptomatic carotid artery stenosis associated with peripheral vascular disease: a prospective study. *Cardiovasc Surg*. 1999;7(1):44-49.
12. Hirsch AT, Criqui MH, Treat-Jacobson D, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. *JAMA*. 2001;286(11):1317-1324.
13. Reich RS. The pulses of the foot: their value in the diagnosis of peripheral circulatory disease. *Ann Surg*. 1934;99(4):613-622.
14. Stein R, Hriljac I, Halperin JL, Gustavson SM, Teodorescu V, Olin JW. Limitation of the resting ankle-brachial index in symptomatic patients with peripheral arterial disease. *Vasc Med*. 2006; 11(1):29-33.
15. Guo X, Li J, Pang W, et al. Sensitivity and specificity of ankle-brachial index for detecting angiographic stenosis of peripheral arteries. *Circ J*. 2008;72(4):605-610.
16. Schroder F, Diehm N, Kareem S, et al. A modified calculation of ankle-brachial pressure index is far more sensitive in the detection of peripheral arterial disease. *J Vasc Surg*. 2006;44(3): 531-536.
17. Lijmer JG, Hunink MG, van den Dungen JJ, Loonstra J, Smit AJ. ROC analysis of noninvasive tests for peripheral arterial disease. *Ultrasound Med Biol*. 1996;22(4):391-398.
18. Nam SC, Han SH, Lim SH, et al. Factors affecting the validity of ankle-brachial index in the diagnosis of peripheral arterial obstructive disease. *Angiology*. 2010;61(4):392-396.
19. Ramsey DE, Manke DA, Sumner DS. Toe blood pressure. A valuable adjunct to ankle pressure measurement for assessing peripheral arterial disease. *J Cardiovasc Surg (Torino)*.. 1983; 24(1):43-48.
20. Lynch TG, Hobson RW, 2nd, Wright CB, et al. Interpretation of Doppler segmental pressures in peripheral vascular occlusive disease. *Arch Surg*. 1984;119(4):465-467.
21. Gale SS, Scissons RP, Salles-Cunha SX, et al. Lower extremity arterial evaluation: are segmental arterial blood pressures worthwhile? *J Vasc Surg*. 1998;27(5):831-838.
22. Allen J. Photoplethysmography and its application in clinical physiological measurement. *Physiol Meas*. 2007;28(3):R1-R39.
23. Alnaeb ME, Boutin A, Crabtree VP, Mikhailidis DP, Seifalian AM, Hamilton G. Assessment of lower extremity peripheral arterial disease using a novel automated optical device. *Vasc Endovascular Surg*. 2007;41(6):522-527.
24. Newcombe RG. Two-sided confidence intervals for the single proportion: comparison of seven methods. *Stat Med*. 1998; 17(8):857-872.
25. Egorova NN, Guillerme S, Gelijns A, et al. An analysis of the outcomes of a decade of experience with lower extremity revascularization including limb salvage, lengths of stay, and safety. *J Vasc Surg*. 2010;51(4):878-885.
26. Shareghi S, Gopal A, Gul K, et al. Diagnostic accuracy of 64 multidetector computed tomographic angiography in peripheral vascular disease. *Catheter Cardiovasc Interv*. 2010;75(1):23-31.
27. Yao ST, Hobbs JT, Irvine WT. Ankle systolic pressure measurements in arterial disease affecting the lower extremities. *Br J Surg*. 1969;56(9):676-679.
28. Khan TH, Farooqui FA, Niazi K. Critical review of the ankle brachial index. *Curr Cardiol Rev*. 2008;4(2):101-106.
29. Brooks B, Dean R, Patel S, Wu B, Molyneaux L, Yue DK. TBI or not TBI: that is the question. Is it better to measure toe pressure than ankle pressure in diabetic patients? *Diabet Med*. 2001; 18(7):528-532.
30. Allen J, Overbeck K, Nath AF, Murray A, Stansby G. A prospective comparison of bilateral photoplethysmography versus the ankle-brachial pressure index for detecting and quantifying lower limb peripheral arterial disease. *J Vasc Surg*. 2008;47(4):794-802.
31. Yu JH, Hwang JY, Shin MS, et al. The prevalence of peripheral arterial disease in korean patients with type 2 diabetes mellitus attending a university hospital. *Diabetes Metab J*. 2011;35(5): 543-550.
32. Durham JR, Horowitz JD, Wright JG, Smead WL. Percutaneous transluminal angioplasty of tibial arteries for limb salvage in the high-risk diabetic patient. *Ann Vasc Surg*. 1994;8(1):48-53.
33. Feiring AJ, Wesolowski AA, Lade S. Primary stent-supported angioplasty for treatment of below-knee critical limb ischemia and severe claudication: early and one-year outcomes. *J Am Coll Cardiol*. 2004;44(12):2307-2314.
34. Allen J, Oates CP, Lees TA, Murray A. Photoplethysmography detection of lower limb peripheral arterial occlusive disease: a comparison of pulse timing, amplitude and shape characteristics. *Physiol Meas*. 2005;26(5):811-821.