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Ankle-brachial index as a predictor of one-year prognosis in ischemic stroke patients

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Abstract

Objective: Peripheral arterial disease (PAD) reduces functional activity and increases the rate of cardiovascular death in the elderly. Our study aimed to determine whether the presence of PAD in stroke patients affected the progression of disability or death one year after discharge. *Methods:* From April 2012 to March 2013, consecutive first stroke patients above 50 years of age without known PAD were enrolled. PAD was defined as a low ankle-brachial index (less than 0.9) measured by an automatic device. Clinical data associated with the stroke were collected from medical records. Disability in stroke patients was evaluated with the modified Rankin scale (mRS) on discharge day and one year after the index stroke. Progression of disability was defined as an increase in mRS more than one level at one year. *Results:* Among the 526 patients, 238 had ischemic strokes and underwent ankle-brachial index (ABI) measurement. Of them, 192 patients were included. In univariate analysis, age, dyslipidemia, discharge mRS, low-density lipoprotein cholesterol, D-dimer, homocysteine, internal carotid artery stenosis, posterior cerebral artery stenosis, and PAD were factors associated with worsening mRS. After adjustment for these factors in the logistic regression analysis, PAD was an independent factor associated with worsening mRS. In the analysis of one-year mortality, patients with PAD had a higher death rate, but PAD was not an independent factor after adjusting for other variables.
Conclusions: The presence of PAD in stroke patients suggests a chance of disability progression, but may not be a predictor of death after one year.

INTRODUCTION

Atherosclerosis is an important pathophysiological cause of stroke, myocardial infarction (MI), angina pectoris, and peripheral arterial disease (PAD).[1,2] Since atherosclerosis is a systemic condition, one vascular disease is commonly accompanied by another, or is a predictor of atherosclerosis-related disease in other sites.[3-6]

The ankle-brachial index (ABI) is the ratio of the ankle systolic pressure to the brachial systolic pressure. The ABI is a screening test that can readily and noninvasively be used to diagnose PAD; the test is regarded as positive for PAD when the ABI $\leq$ 0.9. The ability of the ABI to detect stenosis of over 50% in the femoral artery is remarkably high, with a sensitivity of 90% and a specificity of 98%.[7,8] In addition, an ABI $\leq$ 0.9 is related to other vascular diseases, such as MI, stroke, and left ventricular hypertrophy.[9] In addition, a lower ABI is associated with increased total mortality, mortality related to cardiovascular disease, morbidity of MI, and cerebral infarction. Therefore, ABI is useful for determining the morbidity or prognosis of any vascular disease.[10,11] However, its utility has mostly been studied in healthy people or patients with cardiovascular disease, and it has rarely been examined in patients with stroke. The ABI is not even mentioned in the stroke treatment guidelines.[12]

This study aimed to evaluate the characteristics of acute stroke patients with PAD and to determine whether ABI can predict the degree of physical limitation or death within one year of discharge.

METHODS

1. Subjects

Patients admitted to the Department of Neurology at Chosun University Hospital from April 2012 to March 2013 for a first ischemic stroke within seven days of onset were prospectively and consecutively registered to a database. Ischemic stroke was confirmed with MRI brain diffusion-weighted imaging (DWI).

All patients were 50 years of age or older and did not have a history of PAD. Patients who did

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not undergo an evaluation of the intracranial or extracranial arteries, patients diagnosed with a transient ischemic attack or without a confirmed stroke on MRI brain DWI, patients with an atypical cause of ischemic stroke (such as antiphospholipid syndrome, arterial dissection, arteriovenous malformation, or moyamoya disease), and patients unlikely to survive for one year due to concurrent critical disease (e.g., cancer patients) were excluded. The protocol was approved by a suitably constituted Ethics Committee of the institution where the study took place and it conformed to the provisions of the Declaration of Helsinki. The subjects all gave informed consent and patient anonymity was preserved.

2. Data collection

Clinical data were retrospectively collected from the database. The data included age, sex, medical history, National Institutes of Health Stroke Scale (NIHSS) at the time of presentation and at discharge, and the modified Rankin Scale (mRS) at the time of discharge.

All patients were examined for hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, alcohol use, and smoking habits. Hypertension was defined as blood pressure more than 140 mm Hg systolic or 90 mm Hg diastolic, or treatment with medications for hypertension. Diabetes was defined as fasting serum glucose level over 126 mg, or a 2-h blood glucose level over 200 mg/dL on an oral glucose tolerance test. Dyslipidemia was defined as fasting low-density lipoprotein (LDL) cholesterol over 160 mg/dL, total cholesterol over 240 mg/dL, or triglycerides greater than or equal to 200 mg/dL. Smokers were defined as patients who had smoked and drinkers were defined as patients who consumed two glasses of alcohol a day on average.

Electrocardiography and transthoracic echocardiography were performed on all patients. Patients with cardiovascular disease included individuals who had atrial fibrillation, mechanical heart valves, akinetic left ventricular segments, dilated cardiomyopathy, cardiac myxoma, sick sinus syndrome, MI history within 4 weeks, infectious endocarditis, or left ventricular or atrial thrombosis. The etiologic stroke subtypes were categorized by two neurologists (H.G.K. and I.S.C.) according to the Trial of Org 10172 and the Acute Stroke Treatment (TOAST) classification.

3. Image Analysis

The carotid and intracranial arteries of all patients were examined with MR angiography. Two neurologists (H.G.K. and I.S.C.) measured the degree of stenosis. The degree of stenosis was calculated by subtracting the measurement of the vessel at the distal part of the stenosis from the measurement of the adjacent normal vessel, and then dividing it by the size of the normal vessel. The result was multiplied by 100, in order to obtain the percentage of stenosis. Patients were classified into two groups: those with greater than or equal to 50% stenosis or obstruction, and those with less than 50% stenosis. The cut-off for the distal blood vessel was considered a stenosis of 50% or higher. When the two neurologists did not agree, the degree of stenosis was confirmed by another neurologist (S.H.A.).

4. ABI measurement

One skilled nurse practitioner in the Department of Vascular Surgery consistently used an instrument (IMEXLAB 9100, IMEX Medical Systems, USA) to measure the ABI of all the subjects during the hospitalization. The patient remained in the supine position for 5 min or more, and then the nurse practitioner concurrently measured systolic blood pressures in the left and right dorsalis pedis and the brachial arteries using the instrument. The ratio of the ankle systolic pressure to the brachial systolic pressure was calculated automatically. An ABI value on either side <0.9 was defined as PAD. An ABI value ≥ 1.4 or zero was excluded, due to the probability of a test error.

5. Follow-up

To assess the degree of recovery after one year (± 3 months) from the index stroke, the mRS was used. One trained stroke research practitioner interviewed the patients and their families to determine the mRS one year after discharge, the occurrence of cardiovascular event, neurologic worsening, or death. If the value of the mRS was 6 or the value increased by 2 points or more from the baseline score, or if the patient died within one year after discharge, the patient was included in the worse prognosis group.

6. Statistical analysis

The stroke patients were classified into groups with or without PAD. The demographic, clinical, and laboratory data were compared between the two groups. Pearson's chi-square test, Fisher's exact test, and Student's *t*-test were used for categorical and continuous variables, as appropriate. To avoid

variable selection caused by multicollinearity correlations, only variables that showed an association with and without worse prognosis with $p < 0.1$ in univariate analysis were included as potential independent prognostic factors in the multivariate logistic regression model. A 2-sided p value of <0.05 was considered statistically significant. All statistical analyses were performed using SPSS 19 (IBM Corp., Armonk, NY, USA).

RESULTS

During the study period, 526 patients were admitted to Chosun University Hospital with stroke symptoms. Of these patients, 12 (2.3%) had no acute ischemic lesion on MRI and were diagnosed as having a transient ischemic attack (TIA). Patients younger than 50 years old and patients who did not undergo an ABI measurement were excluded. A total of 238 patients (45.2%) had an acute ischemic stroke and underwent ABI measurement (Figure 1). Patients with atypical causes of ischemic stroke were also excluded: 4 with arterial dissection, 2 with moyamoya disease, 3 with arteriovenous malformation, and 2 with antiphospholipid syndrome. Two patients did not undergo MRI brain DWI or carotid artery studies. The discharge mRS scores were not obtained on 3 patients, and 30 patients did not attend consecutive appointments during the study. Of the total number of patients screened, 192 were included in the analysis (Figure 1). The mean age of patients was 70.1 years (range, 50–91 years). A total of 34 (17.7%) patients were diagnosed with PAD (Figure 1). Statistically significant factors associated with both stroke and PAD were age, dyslipidemia, and one-year mRS scores. However, PAD was not correlated with neurological severity (initial NIHSS, discharge NIHSS) (Table 1).

Within one year of discharge, 36 patients (18.8%) were found to have worsening mRS. In the PAD group, the causes of worsening were death in 6 subjects (infection 3, intracranial hemorrhage 1, asphyxia 1, and cardiovascular death 1), unexplained worsening in 5, lumbar pain in 1, and recurrent nonfatal stroke in 2. In the patients without PAD, the causes of worsening were death in 10 (infection 4, cardiovascular or sudden cardiac arrest 5, and recurrent fatal stroke 1), unexplained worsening in 9, aggravation of dementia in 1, and recurrent nonfatal stroke in 1. A total of 16 patients died (8.3%) and 6 of those patients (17.6%) were in the PAD group (Figure 2).

In the univariate analysis, age, dyslipidemia, LDL cholesterol, D-dimer, homocysteine, initial NIHSS, discharge mRS, and PAD were factors associated with worsening mRS (Table 2). After adjustment for these factors in the logistic regression analysis, PAD was found to be an independent factor associated with worsening mRS within one year (odds ratio [OR] = 3.149 (1.090–9.099); p= 0.034) (Table 3).

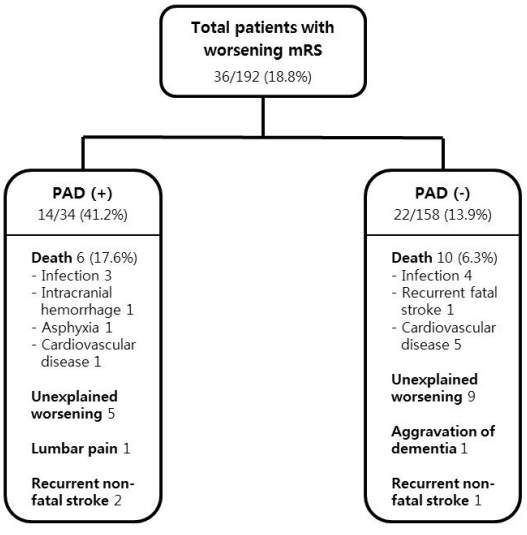

Figure 1. A selection of ischemic strokes with ankle-brachial index (ABI) in the study cohort

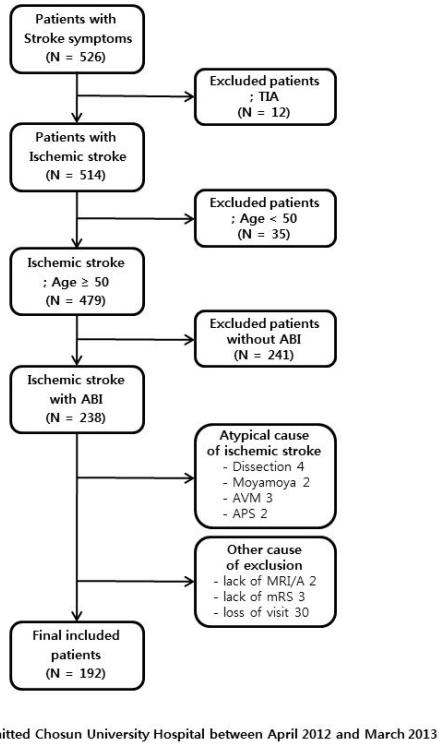

Figure 2. Total patients who have worsening mRS (1 year after discharge).

Table 1: Demographics and characteristics of ischemic stroke patients with and without peripheral arterial disease (PAD)

Variables	PAD (+) (n=34)	PAD (-) (n=158)	*p* value
Demographics			
Age	73.1±7.4	69.4±9.1	*0.026*
Male sex	18 (51.3)	81 (52.9)	*0.859*
Past History			
Hypertension	25 (73.5)	95 (60.1)	*0.143*
Diabetes mellitus	16 (47.1)	52 (32.9)	*0.118*
Dyslipidemia	25 (73.5)	83 (52.5)	*0.025*
Smoking	10 (29.4)	36 (22.8)	*0.412*
Alcohol	6 (17.6)	33 (20.9)	*0.670*
Cardiac disease	7 (20.6)	25 (15.8)	*0.499*
Vascular Status (>50% stenosis or occlusion)			
ICA	17 (50)	52 (32.9)	*0.060*
MCA	15 (44.1)	58 (36.7)	*0.419*
ACA	8 (23.5)	26 (16.5)	*0.327*
PCA	3 (8.8)	14 (8.9)	*1.000*
BA	2 (5.9)	8 (5.1)	*0.692*
VA	7 (20.6)	22 (13.9)	*0.325*
TOAST classification			
Cardioembolism	6 (17.6)	23 (14.6)	*0.648*
Large artery atherosclerosis	16 (47.1)	49 (31)	*0.073*
Small vessel occlusion	3 (8.8)	31 (19.6)	*0.135*
Undetermined (two causes)	2 (5.9)	9 (5.7)	*1.000*
Negative evaluation	7 (20.6)	46 (29.1)	*0.313*
Laboratory			
ESR (mm/hr)	21.4±15.6	16.9±15.8	*0.134*
CRP (mg/dl)	1.5±2.6	1.2±2.6	*0.550*
Total cholesterol (mg/dl)	189±49	176±37	*0.101*
LDL cholesterol (mg/dl)	117±47	107±29	*0.245*
Fibrinogen (mg/dl)	367±84	338±91	*0.089*
D-dimer (ng/ml)	429±293	352±283	*0.201*
Homocysteine (μmol/l)	13.7±8.2	11.5±3.9	*0.139*
Stroke scale			
Initial NIHSS	3 [0–21]	3 [0–23]	*0.831*
Discharge NIHSS	3 [0–18]	2 [0–29]	*0.815*
Discharge mRS			
0~1	19 (55.9)	99 (62.7)	
2~3	4 (11.8)	26 (16.5)	*0.149*
4~5	11 (32.4)	33 (20.9)	
One year prognosis (mRS)			
0~1	13 (38.2)	102 (64.6)	
2~3	5 (14.7)	24 (15.2)	*0.035*
4~5	10 (29.4)	22 (13.9)	
6 (death)	6 (17.6)	10 (6.3)	
Clinical worsening	14 (41.2)	22 (13.9)	*<0.001*
Cardiovascular events	4 (11.8)	10 (6.3)	*0.278*

Values are number of patients (%) or mean ± SD unless otherwise indicated.
ICA= internal carotid artery; MCA= middle cerebral artery; ACA= anterior cerebral artery; PCA= posterior cerebral artery; BA= basilar artery; VA= vertebral artery; ESR= erythrocyte sedimentation rate; CRP= C-reactive protein; LDL cholesterol= low-density lipoprotein cholesterol; NIHSS= National Institute of Health Stroke Scale; mRS= modified Rankin Scale

Table 2: Factors associated with worsened mRS within one year after ischemic stroke

Variables	Clinically worse (n=36)	Clinically stable (n=156)	*p* value
Demographics			
Age	72.9±8.6	69.4±8.9	*0.033*
Female sex	18 (50)	75 (48.1)	*0.835*
Past History			
Hypertension	23 (63.9)	97 (62.2)	*0.849*
Diabetes mellitus	13 (36.1)	55 (35.3)	*0.923*
Dyslipidemia	26 (72.2)	82 (52.6)	*0.032*
Smoking	6 (16.7)	40 (25.6)	*0.255*
Alcohol	6 (16.7)	33 (21.2)	*0.546*
Cardiac disease	8 (22.2)	24 (15.4)	*0.321*
Vascular status (>50% stenosis or occlusion)			
ICA	18 (50)	51 (32.7)	*0.051*
MCA	16 (44.4)	57 (36.5)	*0.378*
ACA	8 (22.2)	26 (16.7)	*0.431*
PCA	6 (16.7)	11 (7.1)	*0.097*
BA	0 (0)	10 (6.4)	*0.213*
VA	8 (22.2)	21 (13.5)	*0.186*
TOAST classification			
Cardioembolism	7 (19.4)	22 (14.1)	*0.420*
Large artery atherosclerosis	14 (38.9)	51 (32.7)	*0.479*
Small vessel occlusion	1 (2.8)	33 (21.2)	*0.009*
Undetermined (two causes)	2 (5.6)	9 (5.8)	*1.000*
Negative evaluation	12 (33.3)	41 (26.3)	*0.394*
Laboratory			
ESR (mm/h)	19±16	17±16	*0.477*
CRP (mg/dl)	1.8±3.15	1.1±2.5	*0.210*
Total cholesterol (mg/dl)	189.6±42.7	175.7±38.7	*0.059*
LDL cholesterol (mg/dl)	121.1±35.3	105.6±32.0	*0.011*
D-dimer (ng/ml)	453±297	344±280	*0.041*
Homocysteine (μmol/l)	14.9±7.5	11.2±4.0	*0.009*
Fibrinogen (mg/dl)	367±80	338±92	*0.073*
Stroke scale			
Initial NIHSS	4 [0–25]	3 [0–23]	*0.623*
Discharge NIHSS	4 [0–23]	2 [0–19]	*0.125*
Discharge mRS			
0~1	15 (41.7)	103 (66.0)	
2~3	13 (36.1)	17 (10.9)	*0.014*
4~5	8 (22.2)	36 (23.1)	
PAD (+)	14 (38.9)	20 (12.8)	*<0.001*

Values are number of patients (%) or mean ± SD unless otherwise indicated.

ICA= internal carotid artery; MCA= middle cerebral artery; ACA= anterior cerebral artery; PCA= posterior cerebral artery; BA= basilar artery; VA= vertebral artery; PAD= peripheral artery disease; ESR= erythrocyte sedimentation rate; CRP= C-reactive protein; LDL cholesterol= low-density lipoprotein cholesterol; NIHSS= National Institute of Health Stroke Scale; mRS= modified Rankin Scale

Table 3: Independent factors associated with worsened mRS within one year

	OR	95% CI	*p* value
Age	1.017	(0.964–1.074)	*0.533*
Dyslipidemia	0.605	(0.230–1.593)	*0.605*
PAD	3.149	(1.090–9.099)	*0.034*
Homocysteine	1.089	(1.001–1.185)	*0.048*
D-dimer	1.001	(0.999–1.002)	*0.338*
ICAS	1.332	(0.542–3.270)	*0.532*
PCAS	2.859	(0.796–10.263)	*0.107*

p value by multivariable logistic regression

OR= odds ratio; CI= confidence interval; PAD= peripheral artery disease; ICAS= internal carotid artery stenosis; PCAS= posterior cerebral artery stenosis

In the univariate analysis of one-year mortality, PAD was also associated with death within one year. Although patients with PAD had a higher death rate, PAD was not an independent factor after adjustment for other factors (age, mRS at discharge, LDL, D-dimer, internal carotid artery stenosis [ICAS], and posterior cerebral artery stenosis [PCAS]) in the Cox regression analysis (Table 4).

DISCUSSION

In this study, PAD was predictive of worsening stroke-related disability within one year, independent of stroke severity or age. Previous studies have identified several predictors of stroke outcomes.[13,14] Consistent factors for subsequent death and disability are mainly related to the presenting severity of the stroke and patient age; these factors were also identified in our study. Additionally, PAD and ICAS have borderline significance associated with poorer outcomes after an ischemic stroke. The systemic vascular status of stroke patients may affect clinical outcomes after an index stroke.

The presence of PAD suggests the likelihood of another major vascular stenosis or occlusion, such as in the coronary or cerebral arteries. In the Oxford Vascular Study (OXVASC), PAD was related to carotid stenosis.[15] However, there are only a few studies that have investigated the association between PAD and cerebral vascular stenosis or occlusion. In our study, PAD was accompanied by ≥50% stenosis or obstruction in the internal carotid artery and was correlated with dyslipidemia, which was closely related to atherosclerosis. PAD was not associated with intracranial stenosis or obstruction. In other words,

Table 4: **Independent Factors Associated with Death within One Year after Ischemic Stroke**

Variables	OR	95% CI	*p* value
Age	1.061	(0.983–1.146)	*0.128*
PAD	2.511	(0.762–8.274)	*0.130*
D-dimer	1.001	(0.999–1.003)	*0.319*
ICAS	3.451	(1.062–11.213)	*0.039*
PCAS	2.621	(0.806–8.527)	*0.109*
Discharge mRS	1.844	(0.606-5.613)	*0.281*

p value by Cox regression analysis

OR= odds ratio; CI= confidence interval; PAD= peripheral artery disease; ICAS= internal carotid artery stenosis; PCAS= posterior cerebral artery stenosis

PAD in the stroke patient is related to stenosis or obstruction in the larger carotid vessels rather than in the intracranial arteries. Large vascular strokes suggest large ischemic lesions and higher recurrence rates. Consequently, PAD patients may have poor outcomes one year after the initial stroke.

On the other hand, PAD itself may affect stroke outcomes. In acute stroke patients, early rehabilitation, including early walking, reduces the occurrence of complications, including deep phlebothrombosis, gastroesophageal reflux, aspiration pneumonia, urinary tract infection, joint contracture, pressure sores, and orthostatic hypotension.[16] Moreover, early mobilization can help stroke recovery and decrease the length of the hospitalization.[16] However, stroke patients with PAD may be restricted in active rehabilitation due to claudication or decreased motor function of the lower limbs.[17,18] In addition, even if the patient has not experienced or recognized any symptoms related to PAD in the past, a low ABI is closely related to deterioration of motor function.[19] Thus, PAD may aggravate stroke complications, and ultimately affect one-year prognosis after discharge.

An association between low ABI and the risk of cardiovascular disease has been reported in community-based research in individuals without a history of vascular disease, and in some studies of patients with cardiovascular disease.[20,21] A similar result could be expected from studies on patients with cerebral infarction.[22] However, there are only a few studies that have examined the association between PAD and cerebrovascular disease. In PATHOS (Polyvascular ATHerothrombosis Observational Survey), which studied the prognosis (morbidity and mortality) of patients with cardiovascular and cerebrovascular diseases, PAD was related to the occurrence of cardiovascular events and death, but there was no statistically significant association between PAD and the occurrence of cerebrovascular disease, as was shown in our study. [22] PAD suggests systemic atherosclerosis, and as shown in our study, patients with PAD often have large artery atherosclerosis (according to the TOAST classification), such as ICAS. [4,23]

Some limitations exist in this study. First, although this was based on a prospectively registered database, half of the subjects were contacted through phone calls to determine the one-year mRS, with only a moderate level of accuracy. The causes of death were confirmed from the patients' guardians, not death certificates.[24] The proportion of recurrent cerebrovascular events in our study was low compared to that in other population-based studies, which ranged from 4.5 to 8.6%. Our patients were given antiplatelet drugs or anticoagulants and medications to control the risk factors according to the individual stroke pathophysiology. This treatment may have contributed to the low stroke rate in the study. Our study exclude many patients who cannot conduct ABI and under 50 years old. It may affects the generalizability of our result. However, we considered patient under 50 years could have different etiology with patient over 50 years. And we cannot conduct ABI to all subject patients because limited number of test equipment. However, we believe that it would not affect data interpretation because there was a little difference in the baseline characteristics among patient over 50 years. And also, we cannot use HbA1c as a variable for PAD. Because, health insurance policy of our country allow HbA1c test for patient with diabetes. Therefore, it makes difficult to test HbA1c for all patients. Finally, there were relatively few subjects in this study. There are nearly no large-scale cohort studies on cerebrovascular disease in patients with PAD; in contrast, in the large community or population-based studies, there are usually over 1,000 vascular disease-free subjects. Therefore, additional data as well as further studies on stroke patients are needed to determine how to prevent deterioration after stroke through early PAD management.

DISCLOSURES

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Conflict of interest: None

REFERENCES

1. Petty GW, Brown RD, Jr., Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO. Ischemic stroke subtypes: a population-based study of incidence and risk factors. *Stroke* 1999; 30(12):2513-6.
2. Nagai Y, Kitagawa K, Sakaguchi M, *et al*. Significance of earlier carotid atherosclerosis for stroke subtypes. *Stroke* 2001; 32(8):1780-5.
3. Marek J, Mills JL, Harvich J, Cui H, Fujitani RM. Utility of routine carotid duplex screening in patients who have claudication. *J Vasc Surg* 1996; 24(4):572-7;discussion 7-9.
4. de Virgilio C, Toosie K, Arnell T, *et al*. Asymptomatic carotid artery stenosis screening in patients with lower extremity atherosclerosis: a prospective study. *Ann Vasc Surg* 1997; 11(4):374-7.
5. Zheng ZJ, Sharrett AR, Chambless LE, *et al*.

Associations of ankle-brachial index with clinical coronary heart disease, stroke and preclinical carotid and popliteal atherosclerosis: the Atherosclerosis Risk in Communities (ARIC) Study. *Atherosclerosis* 1997; 131(1):115-25.
6. Newman AB, Shemanski L, Manolio TA, *et al*. Ankle-arm index as a predictor of cardiovascular disease and mortality in the Cardiovascular Health Study. The Cardiovascular Health Study Group. *Arterioscler Thromb Vasc Biol* 1999; 19(3):538-45.
7. Kaiser V, Kester AD, Stoffers HE, Kitslaar PJ, Knottnerus JA. The influence of experience on the reproducibility of the ankle-brachial systolic pressure ratio in peripheral arterial occlusive disease. *Eur J Vasc Endovasc Surg* 1999; 18(1):25-9.
8. Matzke S, Franckena M, Alback A, Railo M, Lepantalo M. Ankle brachial index measurements in critical leg ischaemia--the influence of experience on reproducibility. *Scand J Surg* 2003; 92(2):144-7.
9. Murabito JM, Evans JC, Larson MG, Nieto K, Levy D, Wilson PW. The ankle-brachial index in the elderly and risk of stroke, coronary disease, and death: the Framingham Study. *Arch Int Med* 2003; 163(16):1939-42.
10. Newman AB, Sutton-Tyrrell K, Vogt MT, Kuller LH. Morbidity and mortality in hypertensive adults with a low ankle/arm blood pressure index. *JAMA* 1993; 270(4):487-9.
11. Criqui MH, Langer RD, Fronek A, *et al*. Mortality over a period of 10 years in patients with peripheral arterial disease. *N Engl J Med* 1992; 326(6):381-6.
12. Pearson TL. Correlation of ankle-brachial index values with carotid disease, coronary disease, and cardiovascular risk factors in women. *JCN* 2007; 22(6):436-9.
13. Demchuk AM, Buchan AM. Predictors of stroke outcome. *Neurol Clin* 2000;18(2):455-73.
14. Kenmuir CL, Hammer M, Jovin T, Reddy V, Wechsler L, Jadhav A. Predictors of Outcome in Patients Presenting with Acute Ischemic Stroke and Mild Stroke Scale Scores. *J Stroke Cerebrovasc Dis* 2015; 24(7):1685-9.
15. Marquardt L, Kuker W, Chandratheva A, Geraghty O, Rothwell PM. Incidence and prognosis of > or = 50% symptomatic vertebral or basilar artery stenosis: prospective population-based study. *Brain* 2009; 132(Pt 4):982-8.
16. Sorbello D, Dewey HM, Churilov L, *et al*. Very early mobilisation and complications in the first 3 months after stroke: further results from phase II of A Very Early Rehabilitation Trial (AVERT). *Cerebrovasc Dis* 2009; 28(4):378-83.
17. McDermott MM, Fried L, Simonsick E, Ling S, Guralnik JM. Asymptomatic peripheral arterial disease is independently associated with impaired lower extremity functioning: the women's health and aging study. *Circulation* 2000; 101(9):1007-12.
18. Scott-Okafor HR, Silver KK, Parker J, Almy-Albert T, Gardner AW. Lower extremity strength deficits in peripheral arterial occlusive disease patients with intermittent claudication. *Angiology* 2001; 52(1):7-14.
19. McDermott MM, Greenland P, Liu K, *et al*. Leg symptoms in peripheral arterial disease: associated clinical characteristics and functional impairment. *JAMA* 2001; 286(13):1599-606.
20. Papamichael CM, Lekakis JP, Stamatelopoulos KS, *et al*. Ankle-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(6):615-8.
21. Tsai AW, Folsom AR, Rosamond WD, Jones DW. Ankle-brachial index and 7-year ischemic stroke incidence: the ARIC study. *Stroke* 2001; 32(8):1721-4.
22. Agnelli G, Cimminiello C, Meneghetti G, Urbinati S. Low ankle-brachial index predicts an adverse 1-year outcome after acute coronary and cerebrovascular events. *J Thromb Haemost* 2006; 4(12):2599-606.
23. Hayashi C, Ogawa O, Kubo S, Mitsuhashi N, Onuma T, Kawamori R. Ankle brachial pressure index and carotid intima-media thickness as atherosclerosis markers in Japanese diabetics. *Diabetes Res Clin Pract* 2004; 66(3):269-75.
24. Quinn TJ, Dawson J, Walters MR, Lees KR. Reliability of the modified Rankin Scale: a systematic review. *Stroke* 2009; 40(10):3393-5.