Universiteit
Leiden
The Netherlands

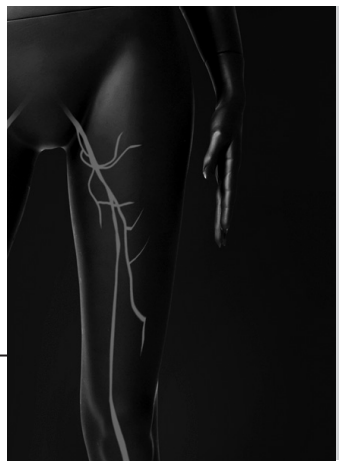
Experimental therapeutic strategies in restenosis and critical limb ischemia

Tongeren, B. van

Citation
Tongeren, B. van. (2010, April 22). *Experimental therapeutic strategies in restenosis and critical limb ischemia*. Retrieved from https://hdl.handle.net/1887/15290

Version:	Corrected Publisher's Version
License:	Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden
Downloaded from:	https://hdl.handle.net/1887/15290

Note: To cite this publication please use the final published version (if applicable).



Chapter 08

A comparison of the Doppler-derived maximal systolic acceleration versus the ankle-brachial pressure index for detecting and quantifying peripheral arterial occlusive disease in diabetic patients

Accepted for publication J Cardiovasc Surg

R.B.M. van Tongeren
A.J.N.M. Bastiaansen
R.C. van Wissen
S. le Cessie
J.F. Hamming
J.H. van Bockel

Abstract

Aim: To assess the diagnostic accuracy of the Doppler derived maximal systolic acceleration (ACC_{max}) as a novel technique for evaluating peripheral arterial occlusive disease (PAOD) in patients with diabetes mellitus, who are known for a falsely elevated ankle-brachial index (ABI).

Methods: In this retrospective analysis ACC_{max} was measured at ankle level in a series of 163 consecutive patients referred to the vascular laboratory for initial assessment of PAOD. Patients were classified according to the presence or absence of diabetes. In the non-diabetic patients PAOD was defined as ABI ≤0.90. This group was used to establish the association between ACC_{max} and ABI in a linear regression model. The result was then used to predict the presence or absence of PAOD in the diabetic patients.

Results: 301 lower limbs were examined. The study group consisted of 166 limbs of patients without diabetes and 135 limbs of patients with diabetes. PAOD was present in 52% of limbs in the nondiabetic group versus 59% of limbs in the diabetic group (ABI ≤0.90, or in case of non-compliant vessels toe-brachial index (TBI) ≤0.70). An ACC_{max} cut-off value of >10 m/s^2 was found to be highly predictive for the exclusion of PAOD (negative predictive value 95%). In addition, the ACC_{max} cut-off value of <6.5 m/s^2 was highly predictive for the detection of PAOD (positive predictive value 99%). A strong quadratic association was found between ACC_{max} and ABI in the non-diabetic group (R^2=0.85). In the diabetic patients R^2 values were 0.81 and 0.79 after ABI and TBI measurement respectively.

Conclusion: DUS-derived ACC_{max} is an accurate marker that could offer significant benefits for the diagnosis of PAOD, especially in diabetic patients.

Introduction

Measuring the pressure in the ankle arteries has become a standard in the initial evaluation of patients with suspected peripheral arterial occlusive disease (PAOD). The diagnosis PAOD is generally considered at an ankle-brachial index (ABI) less than or equal to 0.90 is associated with a 3-6 fold increased risk of cardiovascular mortality.[1] This risk is proportionally related to the degree of ABI reduction, i.e. a lower ABI predicts a higher mortality risk. In patients with diabetes, PAOD is even more aggressive and the cardiovascular event rates are higher than in comparable non-diabetic populations.[2] At least 20% of patients with PAOD have diabetes[3,4] while the prevalence of PAOD in diabetic patients is as high as 29%.[5] The number of patients with diabetes has significantly increased during the past 20 years and it is likely that this number will double in the next 20 years.[6]

ABI measurement provides functional information about the presence and severity of PAOD. Patients with diabetes however, may have stiffer or even densely calcified arteries (Monckeberg's sclerosis) that are less or even not compressible resulting in falsely elevated ankle pressures.[7] Pressure measurements therefore may under-appreciate disease severity and renders ABI of limited use in a large group of patients with diabetes.[8,9] An ABI ≥1.30 is considered as unreliable, but more misleading is that also lower values (ABI <1.30) may be overestimated.[10]

Since the mid-1970s several authors have reported good results using qualitative or quantitative waveform parameters for the assessment of peripheral arteries.[11-18]. However, most methods have not gained extensive clinical use, mainly due to their complexity or need for additional equipment. Furthermore, most techniques were adopted to evaluate the presence or absence of a significant stenosis in the aortoiliac segment.

More recently, Bardelli et al. suggested the maximal systolic acceleration (ACC_{max}) measured by duplex ultrasound as a new velocimetric parameter to assess renal artery stenosis with simple and accurate test characteristics.[19] Where distal arterial pressure measurements tend to be unreliable in diabetic patients, duplex assessment is very well feasible.[8] We aimed at Doppler measurements to evaluate ACC_{max} as new instrument for revealing the presence and severity of PAOD in diabetic patients in whom ABI measurement is anticipated to be misleading.

Methods

Patients. During a 12-months period, we reviewed all patients referred to our vascular laboratory for ABI and arterial duplex ultrasound (DUS) assessment of the lower limb. All evaluations were performed at the Leiden University Medical Center by a single vascular technologist (R.W.). Patients were classified based on the presence or absence of diabetes that was identified by a fasting plasma glucose value of 7 mmol per L or higher or the

use of diabetes medication. In case of diabetes and 'non-compressible' vessels (ABI≥1.30), toe pressures were measured according to international guidelines.[1,10] Toe-brachial index (TBI) values ≤0.70 are considered abnormal. Thus a non-diabetic group was used to establish the association between ACC_{max} and ABI. The diabetic patients were divided in two subgroups: diabetic patients in whom ABI outcome was lower than 1.30, and diabetic patients in whom TBI measurement was performed.

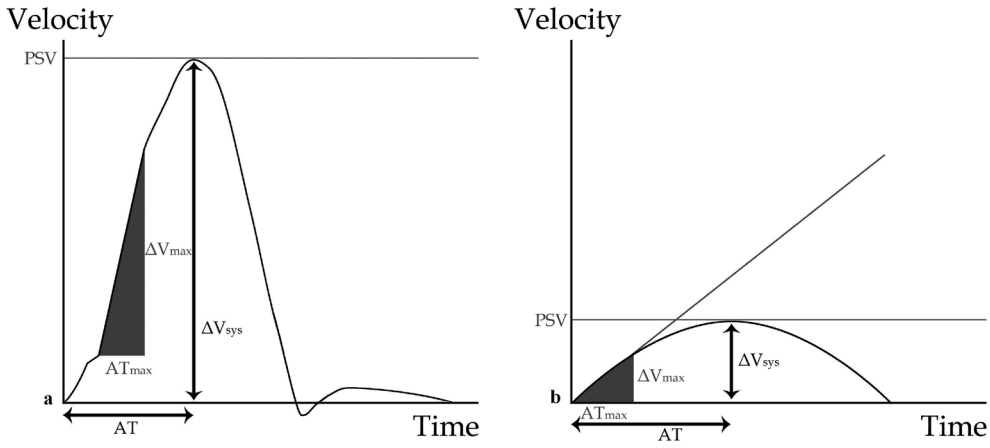
Ankle-brachial index measurement. Resting ABI measurement served as reference standard for the presence or absence of PAOD and was performed with the patient in supine position. In case of ABI≥1.30, toe pressures were used to calculate TBI. The absolute pressures in both arms and legs were measured by sphygmomanometry, using an 8 MHz continuous wave Doppler probe (Imexdop CT+, Nicolet Vascular Inc., Golden, USA) and a calculating cuff inflator (Hokanson TD 312, P.E. Hokanson Inc., Bellevue, USA) with a 12 cm cuff. The cuff was wrapped around the arm or ankle and inflated above the systolic pressure. The cuff was then slowly deflated until the signal returned. The point at which the signal returned was taken as the systolic pressure for the specific artery. The ABI for each leg was calculated as the ratio of the higher of two systolic ankle pressures (posterior tibial or dorsalis pedis) and the higher of the left and right brachial artery systolic pressures. The ABI ≤0.90 was taken as denoting the presence of significant PAOD in accord with the Trans-Atlantic Inter-Society Consensus Document on Management of Peripheral Arterial Disease (TASC).[1]

Toe pressures were measured by photoplethysmography (PPG) (VasoGuard XP 84, VIASYS Healthcare Inc., Germany). The cuff was wrapped around the toe and inflated above the systolic pressure. The cuff was then slowly deflated until the signal returned. The point at which the signal returned was taken as the systolic pressure for the specific artery. The TBI for each toe was calculated as the ratio of systolic toe pressures and the higher of the left and right brachial artery systolic pressures.

Duplex ultrasound. DUS was performed using a 5-7,5 MHz transducer (Aloka SSD-5500, Aloka, Tokyo, Japan) at <60° Doppler insonation angles. Doppler waveforms were obtained at the level of the ankle from the posterior tibial artery and anterior tibial artery and were stored on hard disc. ACC_{max} was defined according to Bardelli et al.[19] as the maximal slope of the Doppler curve in the early systolic phase (figure 1). The ACC_{max} was obtained and computer-based calculated from the same artery that provided the higher of the two systolic ankle pressures. The investigator performing these calculations (A.B.) was blinded for the results of ABI measurements.

Data analysis. In the non-diabetic patient group, sensitivity and specificity for various thresholds of ACC_{max} were calculated using receiver operating characteristic curve (ROC) analysis to define cut-off values for establishing PAOD. Subsequently, linear regression was used to determine the association between ACC_{max} and ABI in the non-diabetic and

Figure 1. *Analysis of the Doppler spectrum.*



(a) Normal (triphasic) Doppler waveform with *peak systolic velocity* (PSV), *acceleration time* (AT) from the beginning to the peak of the systole and the *systolic velocity gradient*
(ΔVsys). The *maximal systolic acceleration* (ACC_{max}) is defined as the maximum slope of the acceleration phase in the Doppler curve. ATmax is the elapsed time and ΔVmax is the velocity gradient between the beginning and end of the maximal acceleration phase (grey area). ACC_{max} = ΔVmax/ATmax.
(b) Example of an abnormal (monophasic) Doppler waveform. The *maximal systolic acceleration* (ACC_{max}) in the more uniform initial part of the systolic Doppler
curve (grey area) is higher than the *mean systolic acceleration* (ACCsys), which is the slope of curve from the beginning of the systolic upstroke to the peak of the systole (ACCsys=ΔVsys/AT).

diabetic group separately. Again, if ABI was ≥1.30 in the diabetic group, TBI was used to assess the relationship with $ACC_{max.}$ We studied a linear, a quadratic and a logarithmic relation, using $ACC_{max,}$ $ACC_{max} + (ACC_{max})^2$ and $\log(ACC_{max})$ respectively, as predictors. Since the number of regression parameters is not the same in these three models the adjusted R^2 was used to determine the optimal form of association. Further, in a multiple linear regression model with patient group (non-diabetic, diabetic with ABI and diabetic with TBI) as complementary predictor, it was studied whether the corresponding ABI (or TBI) in the diabetic group was systematically higher or lower. Tests were performed using SPSS 14.0 for windows (SPSSinc., Illinois, CA, USA).

Results

A total of 163 consecutive patients were referred to the vascular laboratory for non-invasive arterial assessment of the lower extremity during the 12-months period. Three patients were excluded because no reliable distal pressure measurements could be obtained: ABI values were higher than 1.30 and TBI was technically not feasible. The severity of ischemic disease, vascular risk factors and relevant comorbidity of the patients

are summarized in Table I. Due to the presence of ulcers or a history of amputation exclusively unilateral assessment was performed in 19 cases. In 71% of limbs the higher ABI was obtained from the posterior tibial artery and 29% from the dorsal pedal artery. In the group of non-diabetic patients, 166 limbs were examined. ABI ranged from 0.26 to 1.26. Values were found to be within the definition of PAOD in 87 of the 166 limbs (52%). The group of patients with diabetes consisted of 73 patients. ABI ranged from 0.19 to 1.23 in 75 limbs. In 60 limbs with ABI values ≥1.30, TBI ranged from 0.23 to 0.98. Seventy-nine of 135 examinations revealed a value indicating PAOD (59%). Distribution of corresponding ACC_{max} values for the several patient categories is shown in Figure 2.

Table I. *Patient characteristics and severity of ischemic disease.*

Characteristic	N = 160 (%)
Age (yrs, mean ± SD)	66 ± 17
Male sex	107 (67)
Smoking	99 (62)
Hypertension	60 (38)
Hyperlipidemia	41 (26)
Cardiac disease	36 (22)
Diabetes mellitus	50 (31)
Fontaine classification:	
I: asymptomatic	25 (16)
II: claudication	90 (56)
III: ischemic rest pain	23 (14)
IV: tissue loss	22 (14)

Table II. *Probability values of various thresholds of ACC_{max} for the establishment of peripheral arterial disease, defined as ABI ≤0.90.*

ACC_{max} (m/s^2)	Se (%)	Sp (%)	PPV (%)	NPV(%)	Ac (%)
≤5.85	76	100	100	81	88
≤6.45	81	99	99	84	90
≤8.45	92	87	87	91	89
≤10.1	96	63	72	95	80

Se=Sensitivity; Sp=Specificity; PPV=Positive predictive value; NPV=Negative predictive value; Ac=Accuracy

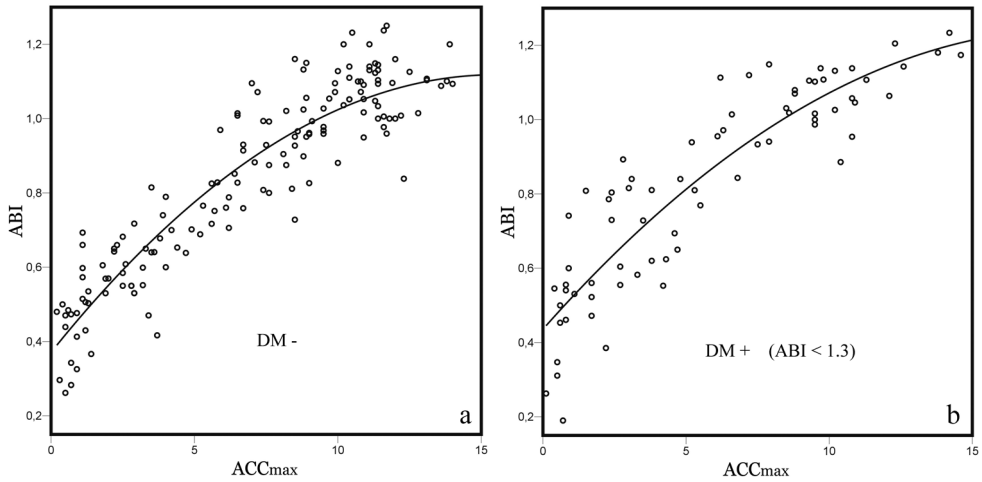
Receiver operating characteristic analysis

Including all 166 legs of patients without diabetes, sensitivities, specificities, PPV, NPV and accuracies of various ACC_{max} cut-off values for the detection of PAOD (ABI ≤0.90) are shown in Table II. Values were calculated by ROC curve analysis (Figure 4). The highest accuracy (90%) was provided by an ACC_{max} ≤6.45. The highest negative predictive value (95%) was provided by an ACC_{max} ≥10.1 where ACC_{max} ≤6.45 provides a positive predictive value of 99% and adequately predicts PAOD. Practical thresholds useful for screening purposes are ACC_{max} >10 and <6.5. Table III shows how these intervals relate to the ABI cut-off value

for the presence of PAOD. Measuring an ACC_{max} >10 practically excludes the presence of PAOD and patients with an ACC_{max} <6.5 are very likely to have PAOD.

Association between ABI and ACC_{max}

Figure 2. *Association between ACC_{max} and ABI.*



(a) In patients without diabetes, a quadratic model demonstrated the strongest association with an adjusted R^2 of 0.85. (b) In diabetic patients (ABI <1.30), a quadratic model also revealed the strongest association with an adjusted R^2 of 0.81. **(c)** In diabetic patients (ABI ≥1.30 and therefore TBI measurement), a quadratic model revealed the strongest association with an adjusted R^2 of 0.79.

ACC_{max} =Maximal systolic acceleration; ABI=Ankle-brachial index; TBI=toe-brachial-index.

The association between ABI and ACC_{max} in the non-diabetic patient group was assessed by linear regression. Adjusted coefficient of determination (R^2) values of 0.76, 0.79 and 0.85 were obtained for respectively linear, logarithmic and quadratic associations. So, the strongest association was established by a quadratic relationship. In diabetic patients the quadratic association also produced the best adjusted R^2 value: 0.81 and 0.79 in case of ABI and TBI measurement respectively. (Figure 2). Assuming a parallel course of the 3 curves, a multiple regression model with ACC_{max} and the 3 patient groups as predictors, showed that the diabetic patients presented for a given ACC_{max} value on average a 0.053 higher ABI value, supporting falsely elevated ABI also when values are lower than 1.3 ($p<0.001$, figure 3). Furthermore, in the diabetic subgroup of patients with TBI measurements, for any given ACC_{max} on average a 0.27 lower TBI value was obtained ($p<0.0001$).

Discussion

In case of reduced vessel compliance, an accurate, simple, and rapid alternative technique which can reliably determine the presence or absence of significant PAOD and predict its severity is highly desirable. The current study shows that ACC_{max} seems to be a useful technique for the diagnosis of PAOD in diabetic patients, especially since we confirm ABI measurements to be significantly elevated in diabetic patients over the whole range. The clinical relevance of ACC_{max} is provided by the strong association with ABI values, as pressure measurement is important in the detection of significant PAOD, and offers prognostic data that are primarily useful to predict (limb) survival.[1,20] Furthermore ABI can be used to monitor efficacy of therapeutic interventions.[10]

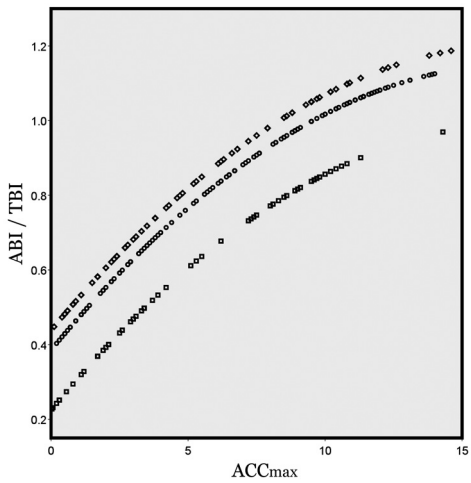
As long as ABI is not obviously falsely elevated (i.e. ≥ 1.3), it provides as much information as TBI and can be relied upon in clinical decision making.[22] Toe pressures and the toe-brachial indices are commonly advocated in diabetic patients if ABI is greater than 1.3 because digital arteries are assumed to be less affected by medial calcification.[10,22] However, certainly in case of concomitant neuropathy, digital arteries may also be calcified in diabetic patients and consequently have reduced compressibility to some extent.[21] Moreover, measurement of toe pressure is technically more demanding, time consuming and even may be impossible due to inflammatory lesions, ulceration or tissue loss.[22] Kröger et al. reported that toe pressure assessment was not feasible with Doppler technique in even 21 of 50 diabetic patients and still in 5 patients after measurement with optical sensors.[23] In the present study TBI assessment appeared technically not possible in 6 of 72 limbs (36 diabetic patients with ABI ≥1.30). Regarding other non-invasive alternative modalities that might be used in individuals with noncompressible vessels, pulse volume recording (PVR) lacks accuracy in distal segments[10] and transcutaneous oximetry (TcPO2) has been questioned because of its reproducibility, accuracy and the controversy about the influence of medial calcification on TcPO2 measurements.[24,25]

Since the introduction of DUS into the field of PAOD, criteria used for diagnosing PAOD are usually based on direct assessment of the peak systolic velocity (PSV) and ratio between PSV upstream and downstream from a stenosis. These velocity parameters are highly accurate for assessing PAOD in angiographic controlled studies, but also time-consuming, not always assessable and less sensitive in the presence of multiple lesions.[26-29] Various strategies to improve the accuracy have been evolved by proposing other velocimetric parameters derived from distal Doppler waveforms. This indirect assessment of vascular segments has been studied for both qualitative[11-14] and quantitative parameters such as pulsatility index[15,30], maximum reverse flow[15,30,31], resistance index[16], acceleration time[16,17,30,32], end-diastolic velocity[15] and mathematical techniques, i.e. Laplace[33] and Fourier transform.[34] Despite good agreement, only few of these methods are embodied in the routine clinical practice, probably because of complexity or need for additional equipment. Furthermore, the assessed segment in these studies was the aortoiliac

region. In fact few studies have analyzed Doppler spectral analysis obtained from distal arteries for evaluating PAOD. Bishari et al. found a good correlation (R=0.77) between PSV values at the ankle and clinical presentation (Rutherford classification) in 25 patients.[35] Furthermore, wide variations of the ankle-brachial acceleration ratio in comparison with ABI were reported by Forsberg, however using *mean systolic acceleration*.[36]

Doppler-derived *maximal systolic acceleration* (ACC_{max}) of the crural/pedal arteries has not been studied earlier. Bardelli et al. found ACC_{max} values to be highly predictive in the assessment of renal artery stenosis.[19] Analogous to his method we measured the acceleration in the more uniform initial part of the systolic Doppler curve because the shape of the Doppler curve even varies between normal arteries (figure 1).[37]

Figure 3. *Association between ACC_{max} and ABI / TBI in patients with and without diabetes.*



The o-line representing non-diabetic group and ◊ and □-lines representing the diabetic group. In a multiple regression model, diabetic patients had for any given ACC_{max} value on average a 0.053 higher ABI value ($p<0.001$). If ABI≥1.30 and therefore TBI was used, for any given ACC_{max} on average a 0.27 lower TBI value was obtained ($p<0.0001$).
ACC_{max} =Maximal systolic acceleration; ABI=Ankle-brachial index; TBI=toe-brachial-index. (◊ = ABI ; □= TBI).

When ACC_{max} is considered for identifying PAOD, a high negative predictive value is very important. Calculating the ideal cut-off value by means of ROC curve, an ACC_{max} >10 was found highly predictive (95%) for selecting individuals without significant PAOD. Table III shows a discrepancy in only 3 patients by applying an ACC_{max} >10, all having a borderline ABI value of respectively 0.84, 0.87 and 0.90. In addition, ACC_{max} <6.5 identifies individuals suffering from PAOD with high certainty (99%).

Patients can be initially evaluated by ACC_{max}. In the present study, patients with an ACC_{max} value between 6.5 and 10 still have a 30% risk of having an ABI ≤0.90. A strategy of screening patients by means of ACC_{max} and subjecting only those to complete DUS scanning if ACC_{max} is not definitive, will be more effective and time-saving. As noted before the current noninvasive tests for assessing the severity of PAOD in the diabetic population are less reliable. The results in the present study confirm the view that arteries of patients with diabetes are less compressible than the arteries of their non-diabetic counterparts. Moreover, ABI values in diabetic patients are falsely elevated due to some degree of arterial calcifications over the whole range, not only if ABI ≥1.30. The clinical consequence can be that in patients with diabetes significant PAOD is missed or assessed more optimistically. In our study only one non-diabetic patient had a normal ABI value with a corresponding ACC_{max} <6,5 (Table III) and would thus potentially be missed. In the diabetic group however, in 39 of 135 limbs ACC_{max} <6,5 was paralleled by an ABI value > 0.90.

Table III. *Two-way contingency table comparing the presence or absence of PAD defined as ABI ≤ versus > 0.90 with the suggested ACC_{max} cut-off values.*

	ABI		
ACC_{max} (m/s^2)	≤0.90	>0.90	Total
<6.5	66	1	67
6.5-10	13	30	43
>10	3	53	56
Total	82	84	166

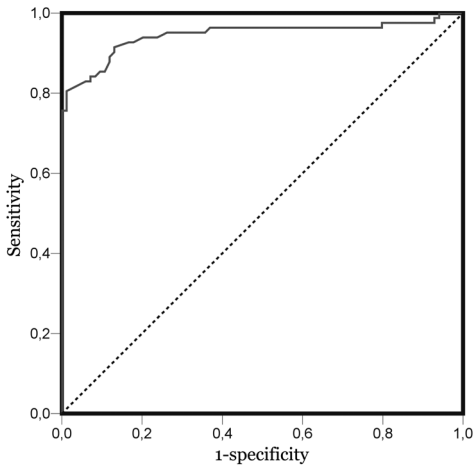
The association between ACC_{max} and the ABI provides an accurate method to predict the ABI by curve interpolation, as shown in figure 2a. Because the same association is found in patients with diabetes (with a higher constant due to higher degrees of medial calcification) ACC_{max} measurement is very suitable to assess the severity of PAOD in patients with diabetes. The same criteria as in patients without diabetes are applicable. In theory, when ACC_{max} drops, ABI should approximate zero and the curve should cross the origin of both axes. This discordance in our data could possibly be explained by lacking sensitivity of the ABI measurement in the lower zone.

The present study has several limitations that need to be addressed. Using ABI as gold standard reference can be criticised because of its well documented variation and the fact that stiffened arteries due to calcification can also be observed in non-diabetic patients.[42] However, indirect pressure measurements with Doppler correlate well with intra-arterial measurements [38] and angiographic extent of lower limb atherosclerosis in large series of cases [39,40]. Besides, Doppler waveforms have the ability to recover if sufficient collaterals have developed.[11,41] So, assessing distal waveform parameters might underestimate angiographic proven stenoses. However, this restriction also applies to ABI measurement,

providing functional information about the presence and severity of PAOD rather than anatomical information provided by angiography.
Since single measurements were accomplished by a single vascular technologist, no data can be provided on the variation of ACCmax. In general, the reproducibility of duplex scanning is moderate to good whereas variation in ABI measurement can be approximately 15%.[42,43]

In conclusion, ACC_{max} can serve as an accurate marker of peripheral arterial occlusive disease. In absence of reliable ABI measurement, ACC_{max} is a useful technique in diabetic patients. In view of the strong association between ACC_{max} and ABI, the severity of PAOD can be reliably estimated by this parameter. In addition to being non-invasive, inexpensive and accurate this new acceleration parameter is easily obtained from the ankle arteries without need for additional equipment, technical skills or difficult mathematical calculations, reducing time needed for assessing the entire lower limb for PAOD independent of the presence of diabetes.

Figure 4. *ROC curve to show the predicted ability of ACCmax.*



References

1. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). Eur J Vasc Endovasc Surg 2007;33 Suppl 1:S1-75.
2. American Diabetes Association. Peripheral arterial disease in people with diabetes. Diabetes Care 2003;26:3333-41.
3. Murabito JM, D'Agostino RB, Silbershatz H, Wilson WF. Intermittent claudication. A risk profile from The Framingham Heart Study. Circulation 1997;96:44-9.
4. Marso SP, Hiatt WR. Peripheral arterial disease in patients with diabetes. J Am Coll Cardiol 2006;47:921-9.
5. Lange S, Diehm C, Darius H, Haberl R, Allenberg JR, Pittrow D et al. High prevalence of peripheral arterial disease and low treatment rates in elderly primary care patients with diabetes. Exp Clin Endocrinol Diabetes 2004;112:566-73.
6. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27:1047-53.
7. Weitz JI, Byrne J, Clagett GP, Farkouh ME, Porter JM, Sackett DL, Strandness DE Jr, Taylor LM. Diagnosis and treatment of chronic arterial insufficiency of the lower extremities: a critical review. Circulation. 1996;94:3026-49. Review.
8. Williams DT, Harding KG, Price P. An evaluation of the efficacy of methods used in screening for lower-limb arterial disease in diabetes. Diabetes Care 2005;28:2206-10.
9. 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;11:29-33.
10. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL et al. ACC/AHA 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): 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. Circulation 2006;113:e463-e654. Review.
11. Sensier Y, Bell PR, London NJ. The ability of qualitative assessment of the common femoral Doppler waveform to screen for significant aortoiliac disease. Eur J Vasc Endovasc Surg 1998;15:357-64.
12. Shaalan WE, French-Sherry E, Castilla M, Lozanski L, Bassiouny HS. Reliability of common femoral artery hemodynamics in assessing the severity of aortoiliac inflow disease. J Vasc Surg 2003;37:960-69.
13. Spronk S, den Hoed PT, de Jonge LC, van Dijk LC, Pattynama PM. Value of the duplex waveform at the common femoral artery for diagnosing obstructive aortoiliac disease. J Vasc Surg 2005;42:236-42.
14. Eiberg JP, Jensen F, Gronvall Rasmussen JB, Schroeder TV. Screening for aortoiliac lesions by visual interpretation of the common femoral Doppler waveform. Eur J Vasc Endovasc Surg 2001;22:331-6.
15. Currie IC, Wilson YG, Baird RN, Lamont PM. Postocclusive hyperaemic duplex scan: a new method of aortoiliac assessment. Br J Surg 1995;82:1226- 9.
16. van Asten WN, Beijneveld WJ, Pieters BR, van Lier HJ, Wijn PF, Skotnicki SH. Assessment of aortoiliac obstructive disease by Doppler spectrum analysis of blood flow velocities in the common femoral artery at rest and during reactive hyperemia. Surgery 1991;109:633-9.
17. Burnham SJ, Jaques P, Burnham CB. Noninvasive detection of iliac artery stenosis in the presence of superficial femoral artery obstruction. J Vasc Surg 1992;16:445-451.
18. Harward TR, Bernstein EF, Fronek A. The value of power frequency spectrum analysis in the identification of aortoiliac artery disease. J Vasc Surg 1987; 5(6):803-13.
19. Bardelli M, Veglio F, Arosio E, Cataliotti A, Valvo E, Morganti A. New intrarenal echo-Doppler velocimetric indices for the diagnosis of renal artery stenosis. Kidney Int 2006;69:580-7.
20. Raines JK, Darling RC, Buth J, Brewster DC, Austen WG. Vascular laboratory criteria for the management of peripheral vascular disease of the lower extremities. Surgery. 1976;79:21-9.
21. Young MJ, Adams JE, Anderson GF, Boulton AJ, Cavanagh PR. Medial arterial calcification in the feet of diabetic patients and matched nondiabetic control subjects. Diabetologia 1993;36:615-21.
22. 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;18:528-32.

23. Kröger K, Stewen C, Santosa F, Rudofsky G. Toe pressure measurements compared to ankle artery pressure measurements. Angiology. 2003;54:39-44.
24. de Graaff JC, Ubbink DT, Legemate DA, Tijssen JG, Jacobs MJ. Evaluation of toe pressure and transcutaneous oxygen measurements in management of chronic critical leg ischemia: a diagnostic randomized clinical trial. J Vasc Surg 2003;38:528-34.
25. Rooke TW, Osmundson PJ. The influence of age, sex, smoking, and diabetes on lower limb transcutaneous oxygen tension in patients with arterial occlusive disease. Arch Intern Med 1990;150:129-32.
26. Sensier Y, Hartshorne T, Thrush A, Nydahl S, Bolia A, London NJ. A prospective comparison of lower limb colour-coded Duplex scanning with arteriography. Eur J Vasc Endovasc Surg 1996;11:170-5.
27. Sensier Y, Fishwick G, Owen R, Pemberton M, Bell PR, London NJ. A comparison between colour duplex ultrasonography and arteriography for imaging infrapopliteal arterial lesions. Eur J Vasc Endovasc Surg 1998;15:44-50.
28. Karacagil S, Lofberg AM, Granbo A, Lorelius LE, Bergqvist D. Value of duplex scanning in evaluation of crural and foot arteries in limbs with severe lower limb ischaemia--a prospective comparison with angiography. Eur J Vasc Endovasc Surg 1996;12:300-3.
29. Pinto F, Lencioni R, Napoli V, Petrucci R, Vignali C, Armillotta N et al. Peripheral ischemic occlusive arterial disease: comparison of color Doppler sonography and angiography. J Ultrasound Med 1996;15:697-704.
30. Breslau PJ, Jorning PJ, Greep JM. Assessment of aortoiliac disease using hemodynamic measures. Arch Surg 1985;120:1050-2.
31. Baker JD. Hemodynamic assessment of aortoiliac segment. Surg Clin North Am 1990;70:31-40.
32. Johnston KW, Kassam M, Koers J, Cobbold RS, MacHattie D. Comparative study of four methods for quantifying Doppler ultrasound waveforms from the femoral artery. Ultrasound Med Biol 1984;10:1-12.
33. Baker JD, Skidmore R, Cole SE. LaPlace transform analysis of femoral artery Doppler signals: the state of the art. Ultrasound Med Biol 1989;15:13-20.
34. Lee HG, Yum MK. Fourier transformation of arterial Doppler waveforms of the lower extremity. J Clin Ultrasound 2004;32:277-85.
35. Bishara RA, Taha W, Alfarouk MO, Abdel AK, Wasfy S. Duplex detected ankle peak systolic velocity: a new parameter for the assessment of degree of peripheralischemia. Int Angiol 2004;23:368-72.
36. Forsberg L, Norgren L, Sjoberg T. Acceleration ratio measurements with ultrasound Doppler in patients with occlusive arterial disease. A prospective investigation. Acta Radiol Diagn 1985;26:121-7.
37. Stavros AT, Parker SH, Yakes WF, Chantelois AE, Burke BJ, Meyers PR et al. Segmental stenosis of the renal artery: pattern recognition of tardus and parvus abnormalities with duplex sonography. Radiology 1992;184:487-92.
38. Bollinger A, Barras JP, Mahler F. Measurement of foot artery blood pressure by micromanometry in normal subjects and in patients with arterial occlusive disease. Circulation. 1976;53:506-12.
39. Carter SA. Indirect systolic pressures and pulse waves in arterial occlusive diseases of the lower extremities. Circulation. 1968;37:624-37.
40. Müller-Bühl U, Wiesemann A, Oser B, Kirchberger I, Strecker EP. Correlation of hemodynamic and functional variables with the angiographic extent of peripheral arterial occlusive disease. Vasc Med. 1999;4:247-51.
41. Bascom PA, Johnston KW, Cobbold RS, Ojha M. Defining the limitations of measurements from Doppler spectral recordings. J Vasc Surg 1996;24:34-44.
42. Koelemay MJ, Legemate DA, van Gurp JA, de Vos H, Balm R, Jacobs MJ. Interobserver variation of colour duplex scanning of the popliteal,tibial and pedal arteries. Eur J Vasc Endovasc Surg. 2001;21:160-4.
43. de Graaff JC, Ubbink DT, Legemate DA, de Haan RJ, Jacobs MJ. Interobserver and intraobserver reproducibility of peripheral blood and oxygen pressure measurements in the assessment of lower extremity arterial disease. J Vasc Surg. 2001;33:1033-40.