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Non-invasive vascular assessment in people with type 2 diabetes: Diagnostic performance of Plethysmographic-and-Doppler derived ankle brachial index, toe brachial index, and pulse volume wave analysis for detection of peripheral arterial disease

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ABSTRACT

Objective: There is evidence that standard assessment techniques for detecting PAD might be of less diagnostic accuracy in people with type 2 diabetes. The aim of this study was to examine diagnostic performance of Plethysmographic-and-Doppler derived ankle brachial index, toe brachial index, and Pulse volume waveform analysis for detecting PAD in people with T2DM.

Methods: In this cross-sectional study 303 patients with T2DM were included in the study. The participants underwent ABI measurement, applying both Plethysmographic and Doppler derived devices, as well as TBI, PVW was also recorded for each patient. Diagnostic performance of each test for detecting PAD, applying ultrasound Doppler scan as the reference standard, was measured. Moreover, the best cut-off point for each method to detect PAD was determined.

Results: PVW showed the highest sensitivity (81.8%) for detecting PAD, followed by ABI_{DOP} (72.7%), and ABI_{PLE} (20%). However, all devices showed an excellent specificity for detecting PAD. The optimal cut-off point for diagnosis of PAD was 0.9 for ABI_{DOP}, 1.2 for ABI_{PLE}, and 0.38 for TBI.

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Conclusion: Within this population of patients with T2DM, TBI less than 0.38 provided the best sensitivity for detection of PAD followed by PVW, $ABI_{DOP} \leq 0.9$, and $ABI_{PLE} < 1.2$.

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1. Introduction

Peripheral arterial disease (PAD) is a highly prevalent, yet underdiagnosed, condition [1]. Although frequently asymptomatic, it is a leading cause of leg pain, claudication, ulceration, gangrene, and even amputation. On the other hand, patients with type 2 diabetes (T2DM) are more likely to develop PAD than do the non-diabetic subjects. Furthermore, they are affected by more severe and extensive form of the disease that tends to involve more distal arteries, progress more quickly, and also it is more likely to lead to ischemic ulceration and amputation [2]. Ankle brachial index (ABI) measured by hand-held or automated devices has been the foundation of non-invasive vascular assessments for several years. Toe brachial index (TBI) and analysis of pulse volume waveform (PVW) are further used in certain conditions.

ABI is widely used as an initial non-invasive tool for detection of PAD. However, the diagnostic accuracy of ABI varies according to the studied population, cut-off points, and the techniques used to detect flow to ankle arteries. Doppler ultrasound, despite some limitations, is primarily used for measuring the ABI. The sensitivity and specificity of Doppler-derived-ABI (ABI_{DOP}) have been reported to widely range from 17% to 100% and 18% to 100%, respectively, with a lower sensitivity among patients with diabetes [3]. Although an $ABI \leq 0.90$ has been recommended by the American Heart Association (AHA) and European Society of Cardiology (ESC) as the best cut-off point both for detection of PAD and prediction of cardiovascular disease (CVD) [3,4], studies conducted among various populations proposed higher level of ABI as an optimal cut-off [5,6]. Furthermore, with regard to the threshold of ≤ 0.90 , ABI detection in patients with diabetes yielded the sensitivity even as low as 70%, suggesting this test may be affected by diabetic calcified arteries [7]. On the other hand, automated devices for measurement of ABI have been recently used to overcome such limitations of Doppler ultrasound as being time-consuming and operator-dependent. However, plethysmographic-based ABI (ABI_{PLE}) has been reported to have a specificity of $>90\%$ but a moderate sensitivity of $<80\%$ for detection of PAD [8,9]. Moreover, the optimal cut-off point for diagnosis of PAD is considerably higher than the threshold of ≤ 0.90 , traditionally used for ABI_{DOP} [8,9].

The fact that ABI has considerable limitations including inability to detect distally located PAD and being falsely elevated and non-diagnostic in the presence of medial artery calcification (MAC) necessitates the need for a secondary mode of assessment for diagnosis of PAD, especially in patients with diabetes in whom both conditions are frequently seen. As TBI is measured distally, it is more likely to detect more distal stenosis. Furthermore, digital vessels are less likely to be affected by MAC [10]. These factors make the TBI a more sensitive test than ABI for detection of PAD

in patients with diabetes [11]. However, there are varying levels of diagnostic accuracy and no strictly evidence-based cut-off is recommended for TBI to diagnose PAD across the current literature. Moreover, analysis of PVW is another non-invasive diagnostic procedure utilized as an adjunct to ABI measurement to identify PAD in patients suspected to MAC [9]. However, there is limited evidence regarding diagnostic accuracy of this method as well as feasibility of incorporating it into routine practice for detection of PAD in patients with diabetes.

Due to the high prevalence of PAD in patients with diabetes and the fact that a large proportion of patients with PAD are asymptomatic, accurate non-invasive vascular assessment of lower limbs for timely diagnosis of PAD is essential in these patients. Diagnostic accuracy of various methods as well as specific cut-off point for diagnosis of PAD in patients with diabetes is not well-established. To the best of our knowledge, no clinical study was performed to explore diagnostic performance of various methods and cut-offs for detection of PAD in people with T2DM. Thus, we conducted this study to examine and compare individual diagnostic performance of Plethysmographic-and-Doppler derived ABI, TBI, and PVWs analysis for detecting PAD in people with T2DM and also to determine the best cut-off point for each method, using ultrasound Duplex scan (UDS) as the gold standard.

2. Method

We conducted a cross-sectional study to determine the diagnostic performance of common non-invasive lower limb vascular assessment techniques in people with T2DM for detecting PAD. This study was carried out at Institute of Endocrinology and Metabolism, on diabetic patients who conformed with the criteria for assessment of PAD according to American Diabetes Association (ADA) guidelines [12]. The following subjects were included: patients 50 years of age and older, patients under 50 years of age who had other PAD risk factors (namely smoking, hypertension, dyslipidemia, or duration of diabetes >10 years), and patients with symptoms or signs of PAD including history of decreased walking speed, leg fatigue, claudication, and abnormal pedal pulses [12]. Exclusion criteria were: inability to lay supine, cellulitis, lymphedema, thrombophlebitis, history of deep vein thrombosis (DVT) during the preceding 6 months, congestive heart failure, history of Raynaud's phenomenon, any known allergy to applying gel, presence of a wound preventing Doppler probe or ankle cuff placement, as well as previous bilateral mastectomy preventing measurement of brachial blood pressure. All participants provided a written informed consent prior to participation. The study was approved by the local ethics committee according to the Declaration of Helsinki.

Prior to the arterial assessment procedures, participants were asked to complete a brief questionnaire including demo-

graphic data (age, sex, duration of diabetes, smoking status), and drug history. Moreover, documented medical outcomes, such as coronary artery disease (CAD), stroke, hypertension (HTN), and retinopathy, were recorded. In the same session measurement of blood pressure (BP), weight, and height as well as assessment for the presence or absence of neuropathy were performed by an experienced nurse. Moreover, blood sample was obtained for measurement of glycated hemoglobin (HbA1C), triglyceride (TG), total cholesterol (chol), low density lipoprotein (LDL), high density lipoprotein (HDL), and creatinine (cr). Estimated glomerular filtration rate (e GFR) was calculated according to Cockcroft and Gault formula "CCr = $\{((140 - \text{age}) * \text{weight}) / 72 * \text{Cr}\} * 0.85$ (if female)".

The participants were asked to avoid caffeine, smoking, and exercise about 2 h prior to the examination to prevent influencing pressure measurements [13]. Room temperature was monitored with a thermometer and was maintained between 23°C and 25°C to prevent vasoconstriction of digital arteries [3]. Next, while supine, each participant underwent ABI measurement, using both the automated plethysmographic device (Dopplex Ability (DA100PB), Huntleigh Healthcare, Cardiff, UK) and Doppler ultrasound (LifeDop 150; Summit Doppler, Wallach Surgical Devices, Turnbull, Conn) with hand-held sphygmomanometer [14], as well as bilateral TBI using Doppler ultrasound (LifeDop 150; Summit Doppler, Wallach Surgical Devices, Turnbull, Conn). The plethysmographic device was used according to the manufacturer's guideline and was undertaken first because there is no need for rest period before testing [15]. The device contains dual chamber cuffs. The upper chamber occludes the arterial blood flow and the lower chamber detects the returning pulsation while the pressure in the upper chamber is gradually reduced. The device measures the systolic pressure of all four limbs simultaneously and calculates an ABI for each leg automatically. It also provides a 5-s strip of PVWs for each leg. Like the phases of the cardiac cycle, PVW shows a sharp peak, occurring during the systole, and a gradual downslope, occurring in diastole, with a dicortic notch, representing the reflected blood flow. To qualitatively interpret the PVW, both the contour and amplitude of the waveform should be taken into account. Absence of the dicortic notch and reduction in the waveform amplitude represent arterial occlusion proximal to the point at which the recording is taken. Interpretation of PVWs can be undertaken by visually comparing them to a four-level grading system [16]. Then after 5 min ABI was measured using Doppler ultrasound in accordance with the American Heart Association's scientific statement for ABI measurement [14]. For this purpose, bilateral brachial systolic pressures and both dorsalis pedis and posterior tibial artery pressure in each limb were obtained using a hand-held sphygmomanometer. All measurements were undertaken by a trained nurse with an extensive experience in vascular assessment of the lower limbs. Not to influence the subjective Doppler measurements, the examiner was blinded to the results of the automated device. Afterward toe systolic pressure was measured by placing a 2-cm-wide pneumatic cuff around the proximal phalanx of the great toe. The cuff was inflated to 20 mmHg above the last signal. The cuff was then slowly deflated, the pressure was recorded when the onset of flow was detected with a Doppler

Table 1 – Grading of stenosis according to peak systolic velocity ratio [17].

PSV ratio	% Stenosis	PAD/no PAD
<2	Not hemodynamically significant	No PAD
≥2	≥50%	PAD
No color flow	Complete occlusion	PAD

PSV; peak systolic velocity, PAD; peripheral arterial disease.

ultrasound probe placed over the lateral side of toe. Subsequently PVWs obtained from automated plethysmographic device were graded by an experienced clinician, blinded to the results of ABI, in accordance with Rumwell and McPharlin's grading system [16]. ABI_{DOP} in each leg was calculated by dividing the higher of the posterior tibialis (PT) or dorsalis pedis (DP) pressure by the higher of the right or left arm systolic blood pressure (SBP) [14]. TBI in each leg was calculated by dividing the toe pressure by the higher of the right or left arm SBP. In the same session, DUS of both lower limbs' arteries were performed by a highly experienced sonographer (equipment utilized: E Zaote C-class) who was blinded to the results of ABI, TBI, and PVWs. UDS of both lower limbs' arteries were performed for all participants from the iliac and common femoral arteries (CFA) then continued distally assessing superficial femoral artery (SFA), popliteal, and tibial arteries in the longitudinal plane. The extent and severity of any arterial disease were assessed using triplex mode by measuring the peak systolic velocity (PSV) from the Doppler waveform just proximal to and through the stenosis. Disease severity was classified using standard criteria outlined in Table 1 [17].

2.1. Data analysis

For the purpose of this study the result of each test for each limb was included to determine the presence of PAD [14]. UDS was used as the reference standard because it has been illustrated to be a valid, non-invasive imaging technique for diagnosis of PAD due to the higher effectiveness at a lower cost [18]. PAD was defined as any arterial stenosis of ≥50% [17]. Sensitivity and specificity values of the ABI_{DOP}, ABI_{PLE}, and TBI for the detection of PAD were calculated using the standard cut-off score for an abnormal ABI (≤0.9) [3], as well as an abnormal TBI (<0.64). To determine the sensitivity and specificity of PVWs for the purpose of this study, they were considered as normal (grade A) and abnormal (grade B, C, D) (Fig. 1) [16].

2.2. Statistical analysis

The differences in baseline characteristics between the PAD and non-PAD patients were evaluated using the t-test or Mann Whitney test, depending on the data to be distributed normally or non-normally, respectively. Moreover, association between the categorical variables was assessed using the Chi-square test. To consider the prediction ability of ABI and TBI scores, logistic regression models were fitted, utilizing the PAD and non-PAD status as the response. This model fitting provided area under the ROC curve, cut-off values, sensitivity, and specificity of the studied clinical tools.

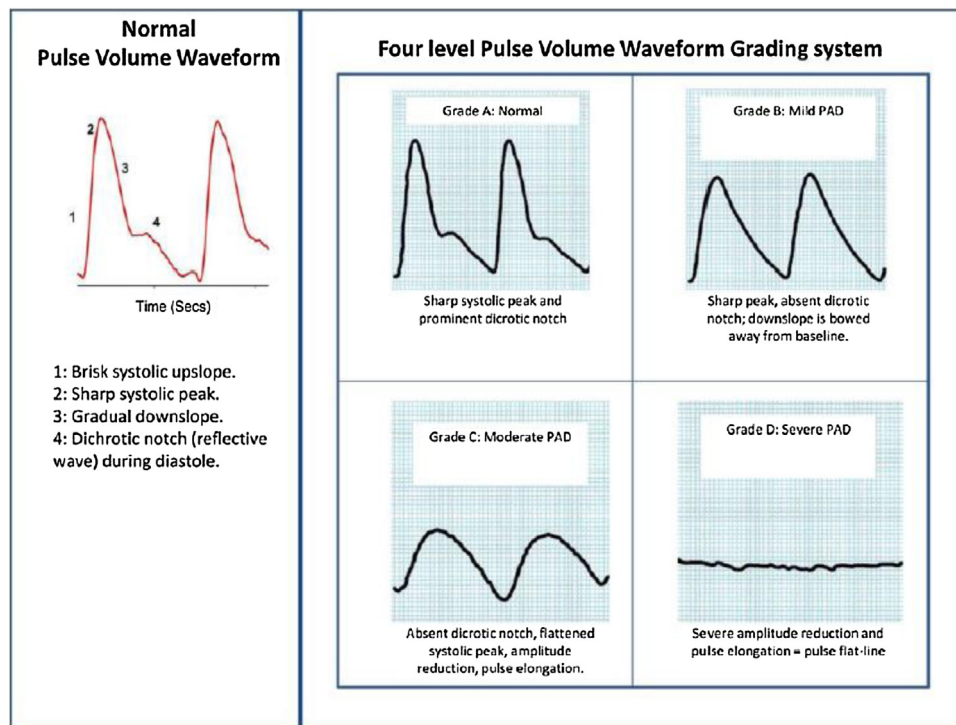


Fig. 1 – Pulse volume waveform interpretation (according to four-level grading system) [16].

3. Results

Considering the prevalence of PAD in patients with diabetes, a total sample of 303 patients with T2DM (606 limbs) were included in the final analysis. The mean age of the participants was 60.07 ± 0.34 years and 39.8% of them were male. Mean duration of diabetes was 13.29 ± 0.34 years. In total, 2.2% of the participants were found to have PAD defined by DUS as the reference standard. PAD was demonstrated to be positively associated with history of smoking ($p=0.000$), known CAD ($p=0.01$), presence of retinopathy ($p=0.02$) and neuropathy ($p=0.000$), history of claudication ($p=0.000$), rest pain ($p=0.01$), and foot ulcer ($p=0.000$). Moreover, PAD patients showed to have higher levels of total cholesterol ($p=0.04$), LDL ($p=0.02$), and a lower level of HDL ($p=0.000$). Furthermore, mean level of ABI_{DOP} (0.89 vs 1.10, $p=0.002$) as well as that of TBI (0.26 vs 0.76, $p=0.000$) were significantly lower in PAD patients. However, there was no significant difference between mean ABI_{PLE} of patients with and without PAD (1.12 vs 1.12) (Table 2).

The sensitivity and specificity of the ABI_{DOP} , ABI_{PLE} , PVW analysis, and TBI for detection of PAD, based on standard cut-off values, compared to the UDS as the reference standard, are presented in Table 3. PVW showed the highest sensitivity (81.8%) for detecting PAD, followed by ABI_{DOP} (72.7%), and ABI_{PLE} (20%). Moreover, all devices showed an excellent specificity for detecting PAD including 95.8% for ABI_{DOP} , 95.6% for ABI_{PLE} , and 93.2% for PVW. All methods show overall accuracy of more than 98%. However, we could not obtain the diagnostic accuracy of TBI, applying the cut-off value of 0.64, due to the small number of PAD events.

ROC curve analysis was performed to determine the best cut-off value for ABI_{DOP} , ABI_{PLE} , and TBI for detection of PAD in this population of patients with diabetes (Fig. 2). The results were as follow: the area under curve (AUC) was 0.99 (95% confidence interval (CI): 0.97–0.99, p -value=0.000) for TBI, 0.78 (95% CI: 0.74–0.81, p -value=0.02) for ABI_{DOP} , and 0.48 (95% CI: 0.44–0.52, p -value=0.8) for ABI_{PLE} . The optimal cut-off point for diagnosis of PAD was 0.90 for ABI_{DOP} , 1.2 for ABI_{PLE} , and 0.38 for TBI provided the sensitivity of 72.2%, 40% and 100%, as well as the specificity of 95.8%, 79.9%, and 95.8%, respectively (Supplementary Table 1).

The sensitivity, specificity, and overall accuracy of combined ABI_{PLE} and PVW analysis are presented in the Supplementary Table 2. The results show an increase in the sensitivity (75%), specificity (97.5%), and overall accuracy (96.7%) of ABI_{PLE} combined with PVW analysis.

4. Discussion

4.1. The ABI

Assessment of diagnostic performance of $ABI_{DOP} \leq 0.9$ to detect significant ($\geq 50\%$) arterial stenosis identified by UDS revealed sensitivity of 72.7%, and specificity of 95.8%, in this population of patients with T2DM. Moreover, ROC curve analysis of Doppler-derived ABI to determine the best cut-off value for detection of $\geq 50\%$ stenosis identified by UDS in this population of patients with diabetes showed the value of 0.9 as the best threshold provided sensitivity of 72.7% and specificity of 95.8%. These findings confirm the results of previous studies which recommend the $ABI_{DOP} \leq 0.9$ to be considered

Table 2 – Baseline characteristics of the participants.

Variable	Total (n = 606)	PAD (n = 13)	No PAD (n = 593)	P value
Age (year)	60.07 (0.34)	60.00 (1.92)	60.08 (0.34)	0.85*
Sex (%M)	39.8	61.5	39.3	0.10
Duration of diabetes (year)	13.29 (0.34)	16.38 (2.62)	13.19 (0.34)	0.17*
Smoking status (%)				
Never	93.1	53.8	93.9	0.000
Current	4.6	38.5	3.9	
Past	2.3	7.7	2.2	
Known CAD (%)	12.5	38.5	12.0	0.01
Known stroke (%)	1.6	7.7	1.5	0.19
Known HTN (%)	69.7	84.6	69.3	0.38
Retinopathy (%)	21.1	46.2	20.2	0.02
Neuropathy (%)	42.8	100.0	41.3	0.000
Claudication (%)	17.1	61.5	15.9	0.000
Rest pain (%)	20.1	46.2	19.3	0.01
Foot ulcer (%)	6.6	46.2	5.4	0.000
Vascular surgery (%)	17.4	38.5	17.0	0.04
Use of ASA (%)	81.3	100	80.8	0.14
Use of statin (%)	90.1	84.6	90.2	0.37
SBP (mmHg)	131.45 (0.84)	130 (5.46)	131.56 (0.85)	0.94*
DBP (mmHg)	77.79 (0.42)	80 (3.00)	77.75 (0.43)	0.62*
HbA1C (%)	7.76 (0.07)	7.23 (0.84)	7.77 (0.07)	0.69*
TG (mg/dl)	136.7(2.96)	152 (14.62)	136.50 (3.01)	0.14*
Total chol (mg/dl)	138.75 (1.25)	159.08 (11.03)	138.25 (1.26)	0.04*
LDL (mg/dl)	68.71 (1.28)	87.54 (9.07)	68.21 (1.29)	0.02*
HDL (mg/dl)	44.16 (0.50)	34.46 (2.54)	44.39 (0.51)	0.00*
eGFR (ml/min/m ²)	76.02 (1.01)	60.51 (7.95)	76.43 (1.01)	0.11*
Mean ABI _{DOP}	1.09 (0.01)	0.89 (0.08)	1.10 (0.01)	0.002*
Mean ABI _{PLE}	1.12 (0.001)	1.12 (0.10)	1.12 (0.01)	0.79*
Mean TBI	0.75 (0.01)	0.26 (0.04)	0.76 (0.01)	0.000*

PAD status according to Doppler ultrasound.

Mean (S.E.) for continuous variables.*Mann-Whitney test.

PAD; peripheral arterial disease, CAD; coronary arterial disease, HTN; hypertension, SBP; systolic blood pressure, DBP, diastolic blood pressure, TG; triglyceride, LDL; low density lipoprotein, HDL; high density lipoprotein, eGFR; estimated glomerular filtration rate, ABI_{DOP}; doppler-derived ankle brachial index, ABI_{PLE}; plethysmographic-derived ankle brachial index, TBI; toe brachial index.

Table 3 – Diagnostic performance of different methods in detecting PAD based on standard cut-off values.

	ABI _{DOP} ≤ 0.9 (603 limbs)	ABI _{PLE} ≤ 0.9 (n = 603 limbs)	PVW (grades B, C, D) (n = 603 limbs)
Sensitivity (%)	72.7	20	81.8
Specificity (%)	95.8	95.6	93.2
Overall accuracy	98.3	98.3	98.2

ABI_{DOP}; Doppler-derived ankle brachial index, ABI_{PLE}; Plethysmographic-derived ABI, PVW; pulse velocity wave.

as the optimal threshold for confirming the diagnosis of lower extremity PAD [3,4]. The diagnostic performance of ABI_{DOP} in this study is concordance with the results of previous studies which showed a high level of specificity but different levels of sensitivity [3,18] with lower sensitivity levels in patients with diabetes [3,7,19–21].

We also assessed diagnostic performance of Plethysmographic-based ABI ≤ 0.9 for detection of ≥50% stenosis identified by UDS. The results demonstrated sensitivity of 20% and specificity of 95.6%. ROC curve analysis of Plethysmographic-based ABI to discover the best cut-off value for detection of ≥50% stenosis identified by UDS in people with T2DM showed the value of 1.2 as the optimal threshold provided sensitivity of 40% and specificity of 79.9%. The fact that higher ABI_{PLE} cut-off value yielded higher level of sensitivity for detection of PAD has been frequently reported by previous studies [8,9]. However, our findings suggest higher

cut-off value with lower sensitivity and specificity compared to previous studies. This could be explained by the baseline characteristics of our studied population that only included patients with T2DM who were more likely to be affected by calcified arteries. Such incompressible arteries can artifactually raise ankle systolic pressures in patients with PAD, lead to higher levels of ABI within the normal range, and make the ABI less diagnostic in such a population. Moreover, the higher Plethysmographic-based ABI yet yielding the lower diagnostic performance compared to Doppler-derived ABI is a common finding associated with automated devices [22,23].

4.2. PVW analysis

Data suggest that analysis of PVW has good sensitivity (81.8%) and high specificity (93.2%) to detect PAD, providing better sensitivity compared to ABI. Although there are limited studies

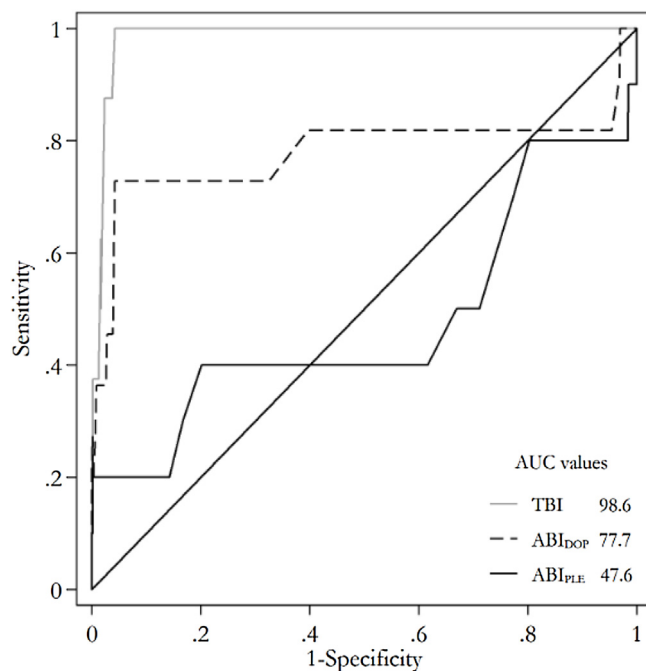


Fig. 2 – ROC analysis of TBI, ABI_{DOP}, and ABI_{PLE} for detecting PAD as defined by ultrasound Doppler scan. AUC for ABI_{DOP} = 0.78 (95% CI: 0.74–0.81, p-value = 0.02), AUC for ABI_{PLE} = 0.48 (95% CI: 0.44–0.52, p-value = 0.8), AUC for TBI = 0.99 (95% CI: 0.97–0.99, p-value = 0.000). ROC; receiver operating curve, TBI; toe brachial index, ABI_{DOP}; Doppler-derived ankle brachial index, ABI_{PLE}; plethysmographic-derived ABI.

investigating the diagnostic performance of PVW analysis for identification of PAD, the results are encouraging. A similar study demonstrated PVW analysis provides an excellent sensitivity for the detection of PAD while the ABI provided very good specificity [9]. Moreover, Lewis et al. showed pulse volume recording agrees well with color spectral waveforms, although the agreement with ABI was less than 50% [24]. That PVW analysis indicates better diagnostic performance than does ABI might be explained by the fact that the presence of calcified vessels or limb edema does not influence the pulse volume recording. This finding is well elucidated in a study by Davies et al. [25]. They showed in the presence of MAC, artefactually raising the ABI to normal or even high normal levels, analysis of PVW can be easily applied to identify patients who suffer from arterial insufficiency and may benefit from further vascular assessment and intervention [25]. Physiologically speaking, PVW represents the total blood flow through the examined area, not being able to provide accurate diagnostic information on where and to what extent a specific artery is diseased. In the other words, a normal waveform in patients with significant arterial stenosis indicates good collateral blood flow, making PVW analysis a useful tool in assessing whether a lower extremity wound has sufficient arterial blood supply to facilitate healing.

4.3. Combining ABI_{PLE} and PVW analysis

Combination of abnormal PVW results for each participant with normal or high normal ABI_{PLE} results showed an increase in the diagnostic accuracy of this method. This finding highlights the usefulness of a dual diagnostic device for diagnosis of PAD in patients with diabetes.

4.4. The TBI

Applying TBI cut-off of 0.64, we found the test is not able to correctly detect PAD. ROC curve analysis of TBI to discover the best cut-off value for detection of significant stenosis ($\geq 50\%$) identified by UDS demonstrated the value of 0.38 is the best cut point for detection of PAD in this population providing a sensitivity of 100% and specificity of 95.8%. On the contrary to the well-defined and evidence-based ABI cut-off value, the basis for diagnosis of PAD applying TBI cut-off value of 0.6 or 0.7 is not well referenced. There are some evidences that a proportion of people with TBI > 0.6 have been shown to have PAD according to the imaging studies [26]. To the best of our knowledge, the best cut-off value for TBI to detect PAD in a population of patients with T2DM has not been previously reported. Considering our results, TBI cut-off of less than 0.38 could be used as an accurate screening measure in high risk limbs.

4.5. Study strength and limitations

To the best of our knowledge, it is the first study assessed the diagnostic performance of all screening methods for detection of PAD in a population of patients with T2DM. Moreover, this study has utilized UDS, as the reference standard, which is recognized to be a non-invasive modality with excellent accuracy for diagnosis of PAD. Furthermore, most studies conducted to determine the diagnostic accuracy of these screening methods included severe cases of PAD, while we included a population of patients with diabetes who were eligible for vascular screening based on current ADA guidelines. Therefore, the results could be generalized to the majority of people with T2DM. However, this leaves a limitation in that despite an adequately large samples, only a small proportion (2.2%) of participants were found to have PAD. Moreover, lack of standardized pretest limb heating could partly explain the low average TBI found in this study and may compromise the reproducibility of the result.

5. Conclusion

Within this population of patients with T2DM, TBI less than 0.38 provided the best sensitivity for detection of PAD followed by PVW, ABI_{DOP} ≤ 0.9 , and ABI_{PLE} < 1.2 . With regard to the specificity, all diagnostic methods yield excellent results but for plethysmographic-derived ABI which provides a moderate specificity of 79.9%. The following conclusion may be drawn that TBI and qualitative waveform analysis are more effective screening methods than ABI for detection of PAD in patients with T2DM. Furthermore, the results indicate plethysmographic-derived ABI cannot provide sufficient diag-

nostic performance for diagnosis of PAD as a standalone test. However, applying the threshold of 1.2, this device can be used as a fast method to identify patients who require further arterial assessment using PVW analysis, Doppler-derived ABI, or TBI.

Conflict of interest

The authors state that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.pcd.2019.09.005>.

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