

Pulse Oximetry as a Potential Screening Tool for Lower Extremity Arterial Disease in Asymptomatic Patients With Diabetes Mellitus

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Background: Lower extremity arterial disease (LEAD) is common and underdiagnosed in patients with diabetes mellitus and is associated with higher total mortality.

Methods: We compared the accuracy of pulse oximetry, the ankle-brachial index (ABI), and the combination of the two to diagnose LEAD in consecutive outpatients with type 2 diabetes who had no symptoms of LEAD, in a primary care setting. Exclusions were age younger than 40 years, known LEAD, or typical symptoms of LEAD. Fifty-seven patients were enrolled. All patients had (1) ABI measurement; (2) pulse oximetry to measure SaO₂ of their index fingers and big toes in the supine position and at 12-in elevation; and (3) Doppler waveform analysis of the lower extremity arteries. The ABI was considered abnormal if it was less than 0.9. Pulse oximetry of the toes was considered abnormal if the SaO₂ was more than 2% lower from the finger or on 12-in elevation of the foot. The combination was considered positive if either the ABI or pulse oximetry was positive for

LEAD and negative if both were negative. We defined LEAD as monophasic waveforms on waveform analysis.

Results: Of our patients, 31% had LEAD. Pulse oximetry had a sensitivity of 77% (95% confidence interval [CI], 61%-88%) and a specificity of 97% (95% CI, 91%-99%); ABI had a sensitivity of 63% (95% CI, 46%-77%) and a specificity of 97% (95% CI, 91%-99%). Positive likelihood ratios were 30 (95% CI, 7.6-121) for pulse oximetry and 24.8 (95% CI, 6.2-99.8) for ABI; negative likelihood ratios were 0.23 (95% CI, 0.12-0.43) for pulse oximetry and 0.38 (95% CI, 0.25-0.59) for ABI. For the combination, sensitivity was 86% (95% CI, 71%-94%) and specificity was 92% (95% CI, 84%-96%).

Conclusions: Pulse oximetry of the toes seems as accurate as ABI to screen for LEAD in patients with type 2 diabetes. Combination of the two tests increases sensitivity.

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A TOTAL OF 86 000 AMPUTATIONS are performed annually in the United States on patients with diabetes mellitus for complications of peripheral arterial disease.¹ Early detection of lower extremity arterial disease (LEAD), before the onset of symptoms in patients with diabetes mellitus, is desirable and can lead to tighter, better control of risk factors for arterial disease.² The ideal screening test would be inexpensive, noninvasive, accurate, and easily administered in the physician's office.

Doppler ultrasound methods, such as waveform analysis and duplex color mapping, are accurate but expensive and are not appropriate for screening purposes. Palpation of foot pulses, by itself, is not sensitive and has poor interobserver variability.³ The ankle-brachial index (ABI), currently the recommended screening test

for LEAD,⁴ was shown to be a sensitive marker for LEAD.⁵ It has been reported to have a sensitivity and specificity in excess of 90% in patients with LEAD.⁶ Yao et al⁵ reported that in patients with angiographically proven stenosis of lower limb arteries, the ABI was less than 1 in 93% of patients. Stoffers et al⁷ reported a sensitivity of 87% at an ABI cutoff value of less than 0.92. However, these authors have studied patients with symptoms and signs of LEAD, not asymptomatic patients. Feigelson et al⁸ found that when they excluded patients with symptoms and signs of LEAD, ABI values of less than 0.9 had a sensitivity of only 28.4%. Therefore, the ABI seems less accurate as a screening test in patients without symptoms or signs of LEAD. Moreover, doubts have been cast about the accuracy of the ABI in screening for diabetes,⁹ probably due to increased incidence of arterial calcification in diabetes mellitus,¹⁰ which can spuri-

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ously elevate the ABI. The performance characteristics of the ABI as a screening test in patients with diabetes have not been well studied, because most studies of the ABI have included patients with and without diabetes.

Measurement of the tissue oxygen level at the toe by transcutaneous oximetry⁹ and toe pulse pressure measurement¹¹ are more sensitive than the ABI in detecting LEAD in patients with diabetes but need special equipment and training. Pulse oximetry measures the oxygen saturation of peripheral blood (SaO₂). The instrument is commonly available in physicians' offices. Mixed results have been reported with its use in detecting arterial disease in a general group of patients.^{12,13} Joyce et al¹² reported that patients with LEAD had significantly lower SaO₂ in the ischemic limbs. The SaO₂ improved after revascularization. Jawahar et al¹³ found that pulse oximetry had low sensitivity to detect LEAD when compared with the ABI used as the reference test. The patients in these studies were suspected of having arterial disease on clinical grounds, so pulse oximetry was not used as a screening test.

The aim of this study was to assess the efficacy of pulse oximetry as a screening tool to detect significant LEAD in patients with diabetes mellitus and to compare it with the ABI for the same purpose. We also wanted to know if the combination of pulse oximetry and ABI would yield better results than either one by itself. Our hypothesis was that pulse oximetry is as accurate as the ABI in screening for peripheral arterial disease in diabetes mellitus and that the combination of the ABI and pulse oximetry would improve accuracy.

METHODS

PATIENTS AND SETTING

We conducted a cross-sectional study of patients with type 2 diabetes mellitus to compare the ability of pulse oximetry and ABI to screen for significant LEAD. During a 4-month period, December 2002 to March 2003, we approached successive patients who presented for scheduled office visits. All patients had to have an established diagnosis of type 2 diabetes mellitus for enrollment in the study. All were patients at Unity Faculty Partners (Rochester, NY), a 7-physician academic primary care group that provides outpatient care. Exclusion criteria were age younger than 40 years, known LEAD or symptoms of LEAD (typical intermittent claudication or rest pain), and inability to lie supine for the period of testing. Informed consent was obtained. The study protocol was approved by the institutional review board at Unity Health System. We obtained informed consent for the tests and medical record review.

INSTRUMENTS

We gathered information on patient demographics and comorbidities (Table 1) with a questionnaire and medical record analysis. A handheld pulse oximeter (NPB-40; Nellcor Puritan Bennett Inc, Pleasanton, Calif) was used to measure SaO₂. Systolic blood pressures of the arms and legs were measured with a sphygmomanometer cuff and a handheld 8-MHz Doppler probe (Huntleigh Mini-Dopplex; HNE Healthcare Inc, Manalapan, NJ). We used a standard sphygmomanometer and cuff sizes of 14 and 16 cm, according to the size of the arm. We did not use a random-zero sphygmomanometer, because we were interested in the ratio of the blood pressures rather than abso-

Table 1. Demographics and Selected Comorbidities in Patients With Type 2 Diabetes Mellitus Screened for Lower Extremity Arterial Disease*

Variable	Value
Total patients/total legs	57/114
Age, mean (range), y	63 (41-84)
Female	30 (53)
Known duration of diabetes, mean (range), y	9 (1-39)
Known coronary artery disease†	10 (18)
Known carotid artery disease‡	2 (4)
Current tobacco use§	17 (30)
Hyperlipidemia	29 (42)
Hypertension¶	37 (66)

*Data are given as number (percentage) of patients unless otherwise indicated.

†Coronary artery disease diagnosed by cardiac stress testing or angiography and documented in patient's medical record.

‡Carotid artery disease diagnosed by ultrasound examination or angiography and documented in patient's medical record.

§Tobacco use within the month before testing for lower extremity arterial disease.

||Diagnosis of hyperlipidemia documented in patient's medical record and treated by dietary therapy or medicines.

¶Hypertension documented in patient's medical record and treated with medicines.

lute values. Moreover, most physicians' offices use a standard sphygmomanometer. Doppler waveform analyses of lower extremity arteries were performed using the Philips HDI 5000 (Phillips Medical Systems, NA, Bothell, Wash).

PROCEDURES

One of the investigators (G.I.P.) obtained the following measurements during the office visit: SaO₂ of both index fingers; SaO₂ of both big toes with the patients in the supine position and at 12-in elevation of the foot, using a pulse oximeter at room air; and systolic blood pressure of both arms at the elbow and both legs at the ankles in the supine position, using a sphygmomanometer cuff and a handheld Doppler probe (Huntleigh Mini-Dopplex). The ABI measurements were performed after the pulse oximetry measurements. The ABIs were derived for each leg by dividing the ankle pressure by the higher of the elbow pressures. The ankle pressures were measured using the posterior tibial artery. If the Doppler signal was not obtainable, the dorsalis pedis artery was used. All patients also underwent Doppler waveform analysis examination of their lower extremity arteries (femoral, popliteal, tibial, posterior tibial, and dorsalis pedis arteries) by 1 investigator (K.B.), who was not aware of the ABI and pulse oximetry results, at a later date in the radiology department.

DEFINITIONS

Abnormal pulse oximetry of the toes was defined as an SaO₂ value of more than 2% lower than the finger value or a decrease of more than 2% on elevation of the leg (decrease from the value at the supine position). An abnormal ABI was defined as less than 0.9. For the combination of ABI and pulse oximetry, we defined a positive test result as either an ABI of less than 0.9 or a decrease in SaO₂ of more than 2%, as described herein; a negative test result for the combination was an ABI of 0.9 or more and an SaO₂ decrease of 2% or less. Significant LEAD was defined as the presence of monophasic waveforms at any one of the lower extremity arteries during Dop-

Table 2. Results for Pulse Oximetry Test, Ankle-Brachial Index, and Combination

Test Results	LEAD Present No. (%) [*]	LEAD Absent No. (%) [*]	Sensitivity (95% CI), %	Specificity (95% CI), %	Positive LR (95% CI)	Negative LR (95% CI)
Pulse oximetry test			77 (61-88)	97 (91-99)	30 (7.6-121)	0.23 (0.12-0.43)
Positive [†]	27 (24)	2 (2)				
Negative [†]	8 (7)	77 (68)				
Ankle-brachial index			63 (46-77)	97 (91-99)	24.8 (6.2-99.8)	0.38 (0.25-0.59)
<0.9	22 (19)	2 (2)				
≥0.9	13 (11)	77 (68)				
Combination			86 (71-94)	92 (84-96)	11.29 (5.17-24.64)	0.15 (0.07- 0.35)
Positive [‡]	30 (26)	6 (5)				
Negative [§]	5 (4)	73 (64)				

Abbreviations: CI, confidence interval; LEAD, lower extremity arterial disease; LR, likelihood ratio.

^{*}LEAD as diagnosed by presence of monophasic waveforms in Doppler waveform analysis.

[†]Positive pulse oximetry test result indicates oxygen saturation at big toe is more than 2% lower than finger saturation or decreases by more than 2% on foot elevation.

[‡]Combination positive indicates either positive pulse oximetry test result or ankle-brachial index of less than 0.9.

[§]Combination negative indicates negative pulse oximetry test result and ankle-brachial index of 0.9 or higher.

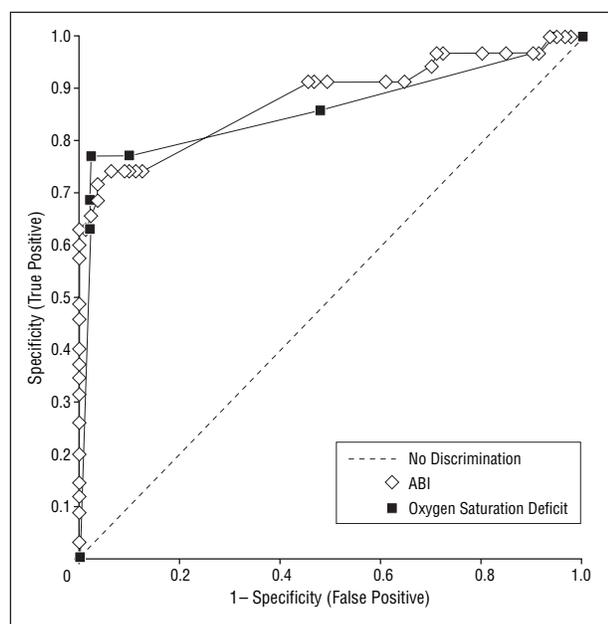


Figure. Receiver operating characteristic curves for the ankle-brachial index (ABI) and pulse oximetry tests.

pler waveform analysis. We used Doppler waveform analysis as the standard for comparison. This test has been shown to have a specificity of 97% in the diagnosis of LEAD¹⁴ when compared with arteriography and has been used as the standard in previous studies of ABI.⁷

STATISTICAL ANALYSIS

We calculated that we needed a sample size of 109 legs, assuming 20% prevalence of LEAD in our study population. We analyzed the data using the Doppler waveform analysis as the gold standard. Sensitivity, specificity, and likelihood ratios were derived for abnormal pulse oximetry and ABI results to detect LEAD and for the combination of the two with Microsoft Excel (Microsoft Inc, Redmond, Wash) and Analyze-it (Analyze-it Software Ltd, Leeds, England). We calculated 95% confidence intervals (CIs) for these values. The likelihood ratios were calculated using a statistical calculator, which used a sen-

sitivity and specificity calculated to the fourth decimal point. We plotted receiver operating characteristic (ROC) curves to compare pulse oximetry and ABI results at different cutoff points. The cutoff points used for the pulse oximetry test in the ROC curve were SaO₂ deficits of 1%, 2%, 3%, 4%, and more than 4%.

RESULTS

We approached 84 patients with known type 2 diabetes mellitus for enrollment. We excluded 5 patients with known LEAD not recorded in the medical records, and 13 patients refused to participate. The remaining 66 patients (132 legs) had pulse oximetry and ABI testing. Nine of these patients did not have Doppler waveform analyses performed. One patient died suddenly, 6 patients did not keep appointments (despite 3 rescheduling attempts), and 2 patients decided to withdraw before the Doppler waveform analysis test was complete. The final study sample consists of 57 patients and 114 extremities that were examined with all 3 tests (pulse oximetry, ABI, and Doppler waveform analysis). Patient characteristics are given in Table 1. We found significant LEAD, by Doppler waveform analysis, in 35 (31%) of 114 legs examined. This incidence is similar to previous reports of LEAD in patients with diabetes mellitus.²

The results are summarized in **Table 2** and the **Figure**. As indicated in the tables, the pulse oximetry test had better test characteristics but with 95% CIs that overlapped with the ABI test results. The areas under the ROC curves were 0.86 (95% CI, 0.77- 0.95) for pulse oximetry and 0.88 (95% CI, 0.80- 0.96) for the ABI. The sensitivity for the combination (positive indicating that either of the 2 test results were positive for LEAD) was 86%. Specificity (negative indicating that both of the 2 test results were negative for LEAD) was 92%.

COMMENT

We found that pulse oximetry of the big toes, at the supine and 12-in elevation positions, is at least as accurate

as the ABI in detecting LEAD in patients with type 2 diabetes mellitus. Although the total area under the ROC curves is slightly larger for ABI, the difference is negligible in the clinically useful parts of the curve. The likelihood ratios are also similar to those for the ABI. The area under the ROC curve for the ABI in this study closely approximates previously reported results for the value of the ABI in primary care settings.⁷ The combination of the 2 tests had a higher sensitivity than the ABI but reduced specificity. The 95% CIs were narrower for the combination. The higher sensitivity is desirable in a screening test.

LEAD is a risk factor for increased total mortality and cardiovascular events.^{15,16} This risk seems to persist even when LEAD is subclinical.¹⁷ Early detection of LEAD can lead to better control of risk factors for cardiovascular events and better outcomes.² The prevalence of LEAD in patients with diabetes mellitus is higher than in the general population, and both the American Heart Association and American Diabetes Association recommend annual screening for LEAD in patients with type 2 diabetes and those older than 40 years.⁴ To be most effective, this screening should be performed in primary care settings. However, awareness of LEAD, its significance, and screening for LEAD is low among physicians.^{2,18}

Currently recommended screening tests include pulse palpation and the ABI.⁴ Pulse palpation is easy to perform but has interobserver variability. The negative predictive value of a posterior tibial pulse is 96%, but the positive predictive value is only 49%.¹⁹ The dorsalis pedis is congenitally absent in 4% to 12% of the population.²⁰ The ABI has been reported to be very sensitive and specific in patients suspected of having arterial disease,⁷ but others report that the ABI is not a sensitive test in patients with diabetes mellitus.⁹ Previous reports^{5,6} of sensitivity and specificity in excess of 90% for the ABI have involved patients with symptoms and signs of LEAD and have not used ABI strictly as a screening test. When used in patients with no symptoms of LEAD, the ABI has been reported to have a sensitivity of less than 30%.⁸ The ABI is more sensitive in more severe LEAD. Carter²¹ reported that in patients with severe arterial stenosis on arteriography, the ABI was abnormal in 80%. However, when only mild arterial stenosis was present, the ABI was low in only 50%. This finding suggests that for early detection of LEAD before the onset of symptoms, the ABI may not be as sensitive as reported.

Pulse oximeters measure peripheral blood hemoglobin SaO₂. Low blood flow in an extremity produces lower SaO₂ in the blood, a fact that vascular surgeons use to assess patency of arterial reconstructions.²² Previous investigations of pulse oximetry to diagnose LEAD have produced mixed results. Joyce et al¹² compared the ABI, pulse oximetry measurement of the toes, and transcutaneous oxygen tension measurement with the arteriographic appearance in patients suspected of having limb ischemia. They found that pulse oximetry correlated best with the arteriographic appearance. Jawahar et al¹³ studied patients referred to a vascular laboratory with suspected LEAD and a control group not suspected of having LEAD. When an ABI less than 0.9 was considered as LEAD, pulse oximetry had a sensitivity of only 16%. Pulse oximetry results were defined as abnormal if there was a decrease of more than 2% in saturation at the toe from the finger or a de-

crease of more than 2% on elevation of the foot by 12 in. However, this study included patients with and without diabetes and involved patients with symptoms suggestive of LEAD. Moreover, those suspected of having LEAD had further evaluation with Duplex ultrasound scanning of leg arteries, but the control group did not. The authors do not report the comparison of the ABI, pulse oximetry, and duplex scanning results.

Our study differs from the ones cited herein by comparing pulse oximetry and ABI results against a reference test in patients with no symptoms of LEAD. We used the cutoff value of more than 2% to define a positive pulse oximetry test result. This value and the technique we used have been previously used.¹³ On studying the ROC curves in our results, this value gives the best combination of sensitivity and specificity for the pulse oximetry test. We used extremities rather than patients as units because we were assessing test characteristics rather than measuring patient outcomes. All of the tests were performed on each extremity for comparison.

Our results suggest that pulse oximetry is at least as accurate as ABI and is an effective additional method for screening patients with type 2 diabetes mellitus for LEAD. Pulse oximeters are widely available in patient care areas and easy to use. The technique of measuring SaO₂ in the blood of a finger, using a pulse oximeter, is well described and well known.²³ The technique is noninvasive. It is commonly used in emergency departments, hospitals, and physician offices during assessment of respiratory and cardiac problems. The application of the pulse oximeter probe to the big toe does not differ from that with a finger. We found the pulse oximetry test, as described herein, simple to perform and easy to teach to our nurses. On average, it took 5 minutes to complete the test. We have not tested interobserver variability of the test but plan to do this in the future. We believe that the pulse oximetry test can be easily incorporated into a regular outpatient visit.

The limitations of this study are as follows: (1) the small number of patients, leading to the wide CIs; (2) performance of the tests by 1 investigator, so interobserver variability was not assessed; and (3) the sequence of measurements, pulse oximetry followed by ABI performed by 1 investigator, which might have influenced the measurements and results.

In conclusion, these results suggest that pulse oximetry may be a useful additional tool to screen for LEAD in patients with diabetes mellitus. It has a sensitivity and specificity similar to the ABI. Larger studies are needed to confirm how it compares with the ABI. When combined with the ABI, the results for the combination of the 2 tests are superior to those reported for the ABI alone in detecting LEAD in these patients. Assessment of change in clinical outcomes owing to modification of risk factors for atherosclerosis in asymptomatic patients identified by screening as having LEAD is an area that needs further research.

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