



Ankle Brachial Index vs Transcutaneous Partial Pressure of Oxygen for Predicting Healing of Diabetic Foot Ulcers with Peripheral Arterial Disease: a Comparative Study

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Abstract

Foot ulcer is a common complication of diabetes mellitus. The co-existence of peripheral arterial disease (PAD) increases the risk of non-healing of the ulcer. Ankle brachial index (ABI) and transcutaneous partial pressure of oxygen (TcPO₂) are two tests used to assess the vascularity of the foot, using two different parameters. This study was done to compare the sensitivity, specificity and diagnostic accuracy of ABI and TcPO₂ and to find out which of these is a better predictor of healing in diabetic foot ulcers in patients without palpable foot pulses. The hospital-based longitudinal study was done from March 2016 to March 2018 among 121 adult patients diagnosed with diabetic foot ulcer without palpable peripheral pulses who fit the inclusion and exclusion criteria. Vascularity of the foot in these patients was assessed using ABI and TcPO₂. The participants were followed up for 3 months, and the healing status was recorded. The mean (SD) age of patients was 64.99 (10.03) years. Out of 121 patients, 89 were men and 32 were women. The mean ABI in healed and non-healed group were significantly different (P value < 0.001). TcPO₂ also showed significant difference in healed and non-healed groups (P value < 0.001). The values of 0.65 in receiver operating characteristic (ROC) curve showed optimal sensitivity (86.1%) and specificity (75.5%) for ABI. ROC curve with a TcPO₂ cut-off value of 27.5 mmHg had optimal sensitivity (84.7%) and specificity (81.6%). Although sensitivity of TcPO₂ and ABI is comparable (84.7% v 86.1%), specificity and diagnostic accuracy are better for TcPO₂.

Keywords Diabetic foot ulcer · Ankle brachial index · Peripheral arterial disease · Transcutaneous partial pressure of oxygen

Introduction

Diabetes mellitus (DM) is the commonest metabolic disorder affecting about 20% of the population in various parts of the world [1]. Prevalence of DM is increasing worldwide. In 2011, 366 million adults had DM worldwide, and by 2030, it is proposed to be 552 million [2, 3]. This exponential increase in DM causes an increase in diabetes-related complications like coronary artery disease (CAD), chronic kidney disease (CKD), cardiovascular accidents (CVA), diabetic foot and peripheral arterial disease (PAD). The incidence of DM is increasing worldwide because of increased life expectancy and changing dietary habits [4]. Diabetic foot ulcer is a

devastating long-term complication of DM [5]. It has been estimated that 15% of all people with diabetes will develop foot ulcer at some stage of their life and the annual incidence rate is 2% [6, 7]. Diabetic foot ulcers have significant health and socioeconomic implications, affecting the quality of life of the patient and imposing a heavy economic burden on the patient's family [8].

Diabetic foot ulcers and PAD often coexist. The term PAD indicates narrowing or occlusion of the arteries other than those that supply the heart or the brain. It most commonly affects the legs, but other arteries may also be involved. Peripheral artery disease (PAD) is present in about 50% of patients with diabetic foot ulcer [9]. It affects the outcome of the ulcer, in that it prolongs the healing or may lead to amputation and a poor quality of life [10–12]. Ulcers secondary to arterial insufficiency are the second most common lower extremity ulcers [13, 14]. About 85% of non-traumatic major amputations are associated with diabetic foot ulcers [15].

Assessment of the vascularity is a key step for the management of diabetic foot ulcer as PAD is an independent risk

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factor for the development and non-healing of diabetic foot ulcer. It is often missed, leading to increased morbidity to the patient. There are several methods to assess the vascularity of foot. Absence of pulse is the most important sign of PAD which can be easily assessed [16, 17]. Methods to assess severity of PAD include ankle brachial index (ABI), toe pressure assessment, transcutaneous partial pressure of oxygen (TcPO₂) and angiography. ABI is a simple method to assess vascularity of foot. It is the ratio of the systolic pressure at the ankle to that at the arm in a person at rest. TcPO₂ is a relatively newer technique which quantifies cutaneous tissue oxygenation.

Understanding how well these methods predict ulcer healing can influence management modalities and help plan treatment. Studies comparing the accuracy of these tests in such prediction are scarce in literature. Hence, this study was done with the objective of comparing ABI and TcPO₂ with regard to sensitivity, specificity and diagnostic accuracy in predicting diabetic foot ulcer healing.

Methodology

It was a longitudinal observational study conducted in a tertiary care centre in Kerala, South India. The study population was all adult patients (above 18 years of age) admitted in the surgical wards with diabetic foot ulcer. The inclusion criteria were that the ulcer should be below the level of the ankle joint and belong to Wagner's grades 1–4 and the patient should not have palpable pulsations in both dorsalis pedis and posterior tibial arteries on the affected limb on clinical examination. Wagner's grade 5 ulcers and ulcers extending above ankle joint were excluded from this study as difficulties were expected to arise in feeling foot pulses and in the accurate measurement of ABI and TcPO₂. Patients with varicose vein of grade C2 or above and those with grade 2 or 3 of lymphedema also were excluded because the co-occurrence of these conditions was expected to interfere with wound healing. As some of the patients are under revascularisation procedures like angioplasty or bypass surgeries, those patients with palpable peripheral pulsations after successful revascularisation procedures also were excluded from this study. Diabetes mellitus was defined as per the diagnostic criteria of the World Health Organization (WHO), as someone with a fasting blood glucose level of ≥ 126 mg/dl, 2-h post-prandial glucose of ≥ 200 mg/dl and HbA_{1c} value of ≥ 6.5 DCCT%.

Sample Size and Sampling

Sample size was calculated based on the results of a previous study [18]. Assuming the specificity of ABI and TcPO₂ in predicting wound healing to be 75% and 53.6%, respectively, and the ulcer healing rate to be 76%, at 80% power and at 5%

alpha error, minimum sample size required was 103 cases of diabetic foot ulcer. Consecutive sampling of all eligible cases that were admitted during the study period was done, and a total of 121 patients were recruited to account for possible attrition.

Study Procedure

The study was approved by the Institute Ethical Committee (IEC) of Malabar Institute of Medical Sciences Limited, Kozhikode. Recruitment of participants was done between March 2016 and March 2018. Eligible patients admitted in the wards who fit the inclusion and exclusion criteria were approached, and all those who gave informed consent were enrolled into the study. Socio-demographic details like age and gender were collected, and history of comorbidities was collected from the case notes. The sites of ulcer, ABI and TcPO₂ were assessed by the investigator.

Using a blood pressure cuff and a handheld Doppler, systolic pressure of dorsalis pedis and tibialis posterior were recorded. In a similar technique, brachial artery systolic pressures on both sides were also recorded. ABI was calculated by dividing the higher ankle pressures (dorsalis pedis or posterior tibial artery) in the affected foot by the higher of the two brachial artery systolic pressures. The ABI values were categorised as false elevation (> 1.3), normal/borderline (0.91–1.29), mild PAD (0.7–0.9), moderate PAD (0.4–0.69) and severe PAD (< 0.4).

TcPO₂ was recorded by keeping an adhesive sensor (fixation ring with contact liquid) containing a platinum electrode on the affected foot near the ulcer on a relatively flat surface (Fig. 1). The value of partial pressure of oxygen in the tissue was recorded after 15 min as seen on a monitor. Once the test was completed, the sensors were removed, the testing sites were cleaned, and any dressings were reapplied on the ulcers.



Fig. 1 Recording of TcPO₂ by keeping an adhesive sensor to the foot and monitor displaying value of TcPO₂

Follow-up review was done after 3 months, when the condition of the ulcer was recorded again. Those patients with ulcers that had healed or had healing changes like granulation tissue were grouped into one group, and those ulcers without any healing changes or those that led to amputation at a level above the ankle were grouped into another. Values of ABI and TCPO₂ in each group were compared.

Data Entry and Analysis

Data was collected on paper-based forms and entered into Microsoft Excel 2013. Data analysis was done using Statistical Package for the Social Sciences (SPSS) v22. Continuous variables like age, ABI and TcPO₂ were expressed in mean (SD) when normally distributed and median (IQR) when non-normal. These values were also categorised based on standard definitions and expressed as proportions. Categorical variables were expressed as frequency and proportion. Healing status was considered primary outcome variable. ABI on the affected foot and TcPO₂ on the affected foot were considered primary explanatory variables. The association between explanatory variables and categorical outcomes was assessed by cross tabulation and comparison of percentages. Chi-square test was used to test statistical significance. ROC analysis: The utility of ABI on the affected foot and TcPO₂ on the affected foot in predicting healing status was assessed by receiver operative curve (ROC) analysis. Area under the ROC curve along with its 95% CI and *P* value are presented. The test results were categorised into high and low based on the cut-off obtained from receiver operating characteristic (ROC) analysis. The sensitivity, specificity, predictive values and diagnostic accuracy of the screening along with their 95% CI were presented. Chi-square test was also employed to look at association of healing status with the test categories. A *P* value < 0.05 was considered statistically significant.

Results

A total of 382 patients were admitted for the treatment of diabetic foot ulcer during the study period. After applying the inclusion and exclusion criteria, 121 patients were included in the study. The socio-demographic details of the patients are given in Table 1. The age of the patients ranged between 40 and 85 years with a mean (SD) age of 64.9 (10.03) years. Men constituted 73.6% of the study sample. Coronary artery disease and hypertension were the most common comorbidities, found in 38.8% and 30.6% subjects, respectively.

The ABI and TcPO₂ values recorded on the affected foot are given in Table 2. ABI values were found to be normal/ borderline in 24 (19.8%) and high (above 1.3) indicator of calcified vessel wall in 20 (16.5%) participants. Mild,

Table 1 Socio-demographic characteristics and comorbidities of persons enrolled in the study (*N* = 121)

| Variable | Frequency | Percentage (%) |
|-------------------------|-----------|----------------|
| Age | | |
| 40–50 | 10 | 8.26 |
| 51–60 | 33 | 27.27 |
| 61–70 | 39 | 32.23 |
| 71–80 | 30 | 24.79 |
| 80–85 | 9 | 7.43 |
| Gender | | |
| Male | 89 | 73.60 |
| Female | 32 | 26.40 |
| Comorbidities | | |
| Coronary artery disease | 47 | 38.80 |
| Hypertension | 37 | 30.60 |
| Chronic kidney disease | 25 | 20.70 |
| Dyslipidaemia | 16 | 13.20 |

moderate and severe PAD were found in 24 (19.8%), 31 (25.6%) and 22 (18.2%), respectively.

After 3 months of follow-up, 72 (59.5%) participants had a positive outcome, and the remaining had a negative outcome. Out of the 72 participants with positive outcome, 43 (59.7%) had ulcers that were partially healed and 29 (40.3%) had complete healing. Out of the 49 participants with a negative outcome, 35 (71.4%) presented with an unhealthy wound, 13 (26.5%) had undergone a below knee amputation, and 1 (2.1%) had undergone an above knee amputation.

Analysis based on receiver operator characteristic curve (ROC) revealed that both ABI and TcPO₂ can be used as a tool to predict healing of diabetic ulcer, and this result was statistically significant for both the variables. The ROC curve is shown in Fig. 2. Areas under the curve for ABI and TcPO₂ were 0.817 (95% CI 0.732–0.900; *P* value < 0.001) and 0.896 (95% CI 0.836–0.960; *P* value < 0.001), respectively. The optimum cut-off point identified for ABI was 0.65 and that for TcPO₂ 27.5. Higher values of ABI and TcPO₂ were associated with higher recovery, and this was found to be statistically significant, as seen in Table 3.

An ABI value of 0.65 or more on the affected foot had a sensitivity of 86.1% (95% CI 78.11% to 94.1%) and specificity of 75.5% (95% CI 63.46 to 87.5) in predicting healing status. Positive and negative predictive values were 83.8% (95% CI 75.41 to 92.2) and 78.7% (95% CI 66.99–90.4), and the total diagnostic accuracy was 81.8% (95% CI 74.95 to 88.7). TcPO₂ value of 27.5 and above on the affected foot had a sensitivity of 84.7% (95% CI 76.38 to 93.0) and specificity of 81.6% (95% CI 70.75 to 92.4). Positive predictive value was 87.1% (95% CI 79.25% to 95.0%), negative predictive value was 78.4% (95% CI 67.11% to 89.7%), and the

Table 2 Values of ankle brachial index (ABI) and transcutaneous partial pressure of oxygen (TcPO₂) of patients enrolled in the study (N = 121)

| Variable | Range | Mean (standard deviation) | Median (interquartile range) | 95% confidence Interval |
|-------------------|--------|---------------------------|------------------------------|-------------------------|
| ABI | 0–2.30 | 0.83 (0.48) | 0.72 (0.50–1.07) | 0.74–0.92 |
| TcPO ₂ | 10–74 | 35.39 (17.93) | 29 (23–48) | 32.17–38.63 |

total diagnostic accuracy was 83.5% (95% CI 76.85% to 90.1%). These are summarised in Table 4.

Discussion

The study was conducted among 121 participants, majority of whom were men and above 50 years of age. The older age group is explained as diabetes mellitus has skewed prevalence that progresses with the aged demographic. The definitive male predominance in diabetic foot ulcers may be due to higher exposure of males to smoking. A similar observation was made by Veves et al. [19].

According to ROC analysis, both ABI and TcPO₂ can be good predictors in diabetic foot ulcer healing, with area under the curve being slightly higher for TcPO₂. ABI showed better sensitivity, but TcPO₂ had better specificity, positive predictive value and overall diagnostic accuracy. The cut-off obtained by the ROC analysis was 0.65, which is close to the conventionally used cut-off of 0.7 for the presence of PAD. A study conducted in South India documented the optimal cut-off to be 0.77. The cut-off identified for TcPO₂ in the same study was 25 mmHg, which is two points lower than the present study [18]. Another study in China has also recorded that ulcer healing was better in those with higher TcPO₂, and everyone with a value at or above 40 mmHg achieved wound closure, and 25 mmHg was identified as the best threshold for predicting wound healing [20]. These differences may be attributed to instrumental errors, or sampling error, and are nevertheless coherent with the results generated.

Similar to our study, Majid Kalani et al. concluded that TcPO₂ was a better predictor than ABI in diabetic patients

Table 3 Association of healing status with tests of vascularity (N = 121)

| Variable | Healing status | | P value |
|-------------------|-------------------------|-----------------------------|---------|
| | Healed, n (%) N = 72 | Not healed, n (%) N = 49 | |
| ABI | | | |
| ≥ 0.65 | 62 (86.1) | 12 (24.5) | < 0.001 |
| < 0.65 | 10 (13.9) | 37 (75.5) | |
| TcPO ₂ | | | |
| ≥ 27.5 | 61 (84.7) | 9 (18.4) | < 0.001 |
| < 27.5 | 11 (15.3) | 40 (81.6) | |

with chronic foot ulcers [21]. This might be due to several factors. ABI estimates the average blood flow at the level of ankle joint but does not consider the microvascular changes that occur in diabetic foot [22]. However, TcPO₂ indicates average oxygen level in the tissue near the ulcer; hence, the microvascular changes at the foot will affect the value. Another drawback of ABI is that it may read falsely high values in calcified vessel wall [23, 24]. The Eurodiale study noted that if ABI was abnormal, there was a greater chance that TcPO₂ would also be abnormal, whereas if the ABI was normal, the TcPO₂ may have been normal or abnormal. This was well explained by the fact that ABI measures circulation in medium-sized vessels which, if low, will mostly lead to a lower capillary blood flow and low transcutaneous pressure of oxygen [25]. Hence, TcPO₂ is a more reliable predictor of tissue perfusion and wound healing.

However, keeping in mind the higher sensitivity and ease of measuring, ABI may be employed as a screening test to aid identification of individuals at a higher risk for delayed healing and amputation. In such a scenario, a larger sensitivity would help in ensuring lesser false negativity rates.

Our study has several strengths. It is one of the few studies done in India to look at the predictive validity of ABI and TcPO₂ in diabetic ulcer healing. As it was a prospective study, temporality could be clearly established. There was no attrition or loss to follow-up. All the measurements and assessments were done by a single investigator with a calibrated

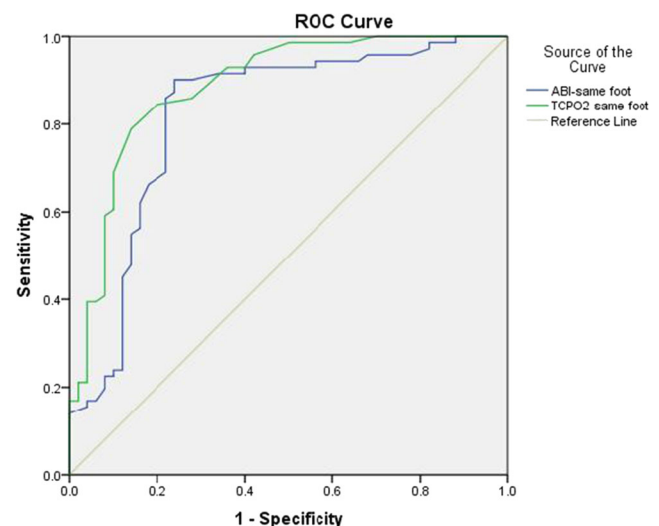
**Fig. 2** Comparison of ability of ankle brachial index and transcutaneous partial pressure of oxygen in the prediction of healing status of diabetic ulcer (N = 121)

Table 4 Diagnostic validity of ankle brachial index and transcutaneous partial pressure of oxygen in predicting healing status of diabetic ulcer (N = 121)

| Parameter | Value (%) | | 95% confidence Interval | |
|---------------------------|-----------|-------------------|-------------------------|-------------------|
| | ABI | TcPO ₂ | ABI | TcPO ₂ |
| Sensitivity | 86.1 | 84.7 | 78.1–94.1 | 76.3–93.0 |
| Specificity | 75.5 | 81.6 | 63.4–87.5 | 70.7–92.4 |
| False positive rate | 24.5 | 18.4 | 12.4–36.5 | 7.5–29.2 |
| False negative rate | 13.9 | 15.3 | 5.9–21.9 | 6.9–23.6 |
| Positive predictive value | 83.8 | 87.1 | 75.4–92.2 | 79.2–95.0 |
| Negative predictive value | 78.7 | 78.4 | 66.9–90.4 | 67.1–89.7 |
| Diagnostic accuracy | 81.8 | 83.5 | 74.9–88.7 | 76.8–90.1 |

instrument; hence, interobserver bias was eliminated. The required sample size was achieved. The main limitation of the study is that it was done at a single centre catering to patients of a limited demographic area. Confounding factors like adherence to treatment and history of smoking was not assessed.

Conclusion

ABI and TcPO₂ are both good predictors of ulcer healing among patients with diabetes with area under the curve being slightly higher for TcPO₂ in ROC analysis. ABI had better sensitivity, while TcPO₂ had better specificity, positive predictive value and diagnostic accuracy.

Authors' Contributions All authors were involved in the clinical care of the patient. All authors have read and approved the manuscript.

Compliance with Ethical Standards

The study was approved by the Institute Ethical Committee (IEC) of Malabar Institute of Medical Sciences Limited, Kozhikode.

Conflict of Interest The authors declare no potential conflicts of interest.

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