Ankle Brachial Index and Transcutaneous Partial Pressure of Oxygen as predictors of wound healing in diabetic foot ulcers

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Abstract:
Peripheral Occlusive Vascular Disease impairs the healing process in diabetic foot ulcers. Ankle Brachial Index is the conventional method of assessing POVD and Transcutaneous Partial Pressure of Oxygen. It is a relatively new measure of assessing microvascular circulation. Our aim was to compare and contrast the utility of ABI and TcPO₂ in predicting wound healing in diabetic foot ulcers. The study included 118 diabetic foot ulcer patients who had their ABI and TcPO₂ measured. A handheld doppler device measured the ABI, and an electrochemical transducer measured the TcPO₂. Wound outcome was classified as either healed or not healed. The mean ABI in the healed group was 0.96±0.24 and 0.61±0.27 (p<0.001) in the not healed group. The mean TcPO₂ in the healed group was 33.77±15.51 and 23.29±14.77 (p=0.002) in the not healed group. The agreement rate of ABI with TcPO₂ was 59.3%. More than 90% of ulcers with normal ABI and/or TcPO₂ healed. With aggressive management of POVD a good percent of wounds with abnormal ABI and/or TcPO₂ also healed. By plotting the ROC curve, in our population, an ABI value of 0.77 was found to have 80% sensitivity and 75% specificity, and a TcPO₂ value of 22.5 mm Hg was found to have 74.4% sensitivity and 53.6% specificity in predicting wound healing. Both ABI and TcPO₂ measured different aspects of POVD and were complementary in predicting wound healing in diabetic foot ulcers. The optimal cut-off values for both measures for our population were also defined.

Key words: Ankle Brachial Index, Diabetic Foot Ulcer, Peripheral Occlusive Vascular Disease, Transcutaneous Partial Pressure of Oxygen

INTRODUCTION
Having a diabetic foot ulcer is a major cause of morbidity for diabetic patients. Almost 50% of diabetic ulcers are ischemic in origin.¹ Peripheral Occlusive Vascular Disease (POVD) impairs the healing process in diabetic foot ulcers. Ankle Brachial Index (ABI) is the conventional method of assessing POVD and its influence on wound healing;²,³ however, it has certain limitations. Diabetic patients have microvascular and small vessel diseases which are not reliably measured by ABI. ABI can be unreliable in patients with calcification of the walls of arteries, which make vessels incompressible and can result in abnormally high values.⁴ TcPO₂ is a noninvasive measure of local arterial blood flow and skin oxygenation that predicts chances of wound healing. TcPO₂ values identify patients with subclinical microvascular impairment.⁵ Since wound healing depends on an adequate supply of oxygen to the tissues, measurement of TcPO₂, which is a direct measure of the tissue oxygen partial pressure, may be a more reliable method⁶,⁷,⁸ to predict wound healing. TcPO₂ measurements have also been used to determine the amputation risk in non-healing ulcers⁹ and the amputation levels.¹⁰ It also helps to heal surgical wounds.¹¹,¹²
Studies have shown that TcPO$_2$ is related to the degree of ischemia.$^{13}$ Some studies have shown that ABI has significant limitations for diagnosing and treating critical limb ischemia patients compared with TcPO$_2$.$^{14}$ Studies have defined different cut-off minimum values for ABI and TcPO$_2$ in predicting PVD and wound healing. The cut-off which best predict wound healing in our population is unknown.

The primary study objectives were to identify 1) the association of ABI and TcPO$_2$, with wound outcomes (healed and not healed) in diabetic foot ulcers and 2) the comparative utility of using ABI and TcPO$_2$ as a marker in predicting wound healing in diabetic ulcers. The secondary study objective was to attempt to define ABI and TcPO$_2$ cut-off values which predict wound healing in our population.

PATIENTS AND METHODS

This was a retrospective cross-sectional study. Based on the results of the association between ABI and TcPO$_2$ with wound healing$^{15}$ and with 99% confidence and 90% power, the minimum sample size computed was highest in the case of the ABI (40 patients). However, we also included 118 Type 2 diabetic patients with diabetic foot ulcers who visited the podiatry outpatient department of a tertiary referral university teaching hospital in South India.

Study participants’ ABI and TcPO$_2$ were measured. If patients were thought to have PVD, by either ABI or TcPO$_2$, an angiogram was performed. If possible, revascularization was also performed. In addition, all patients underwent routine treatment for diabetic foot ulcers including antibiotic treatment, surgical and chemical debridement, off-loading, and management of diabetes and co-morbid conditions.

A handheld doppler device measured the ABI. A blood pressure cuff was placed on the upper arm and inflated until the doppler device detected no brachial pulse. The cuff was then slowly deflated until a doppler-detected pulse, systolic pressure, returned. This maneuver was repeated on the leg, with the cuff wrapped around the distal calf and the doppler device placed over the dorsalis pedis or posterior tibia artery. The ankle systolic pressure divided by the brachial systolic pressure yielded the ABI. The highest arm pressure was used as the denominator. A normal ABI range was between 0.91 and 1.30. A resting ABI of ≤ 0.9 was noted as abnormal.$^2$ An ABI value greater than 1.3 suggested calcification of the walls of the arteries and incompressible vessels.$^{16}$ These patients were excluded from the study.

TcPO$_2$ is a test that uses oxygen sensing electrodes to measure the delivery of oxygen to the skin tissue. An electrochemical transducer was fixed to the skin of the dorsum of the foot with adhesive rings and contact liquid (Figure 1). The patient refrained from smoking and drinking coffee for at least two hours before the investigation. Readings were taken in the supine position. Values greater than 40 mm Hg were defined as normal and usually associated with good healing, while ≤ 40 mm Hg was defined as low with poor chances of healing.$^{17}$

Wound outcome was classified as healed or not healed. A wound was considered healed if it underwent complete epithelialization or skin grafting at the site of surgical debridement or local amputation. A wound was considered not healed if a major amputation was performed or if the patient died from an associated foot infection.$^{18}$

Figure 1. TcPO$_2$ being recorded with electrodes
STATISTICAL METHODS

We used the following three statistical methods to analyze the data.

1. T-test: To test the statistical significance of the difference in mean values of ABI and TcPO$_2$ between the healed and not healed groups.

2. Chi-Squared with Yates Continuity Correction: To test the statistical significance of the association of ABI and TcPO$_2$, categorized as normal and abnormal with wound healing.

3. Validity Parameters: Sensitivity and specificity tests were computed for ABI and TcPO$_2$ with respect to healing status. Based on the data collected using an ROC curve, an attempt was made to find appropriate cut-off points for ABI and TcPO$_2$ with respect to healing status.

RESULTS

The study included 118 patients who satisfied the inclusion criteria. Diabetic foot ulcers healed in 90 patients and did not heal in the remaining 28 patients. Baseline characteristics were similar in the healed and not healed groups and among the co-morbidities present; the presence of nephropathy and/or renal failure alone was significantly more prevalent in the not healed group. As Table 1 shows, the mean ABI in the healed population was 0.96±0.24 and 0.61±0.27 (p<0.001) in the not healed group. The mean TcPO$_2$ in the healed group was 33.77±15.51 and 23.29±14.77 (p=0.002) in the not healed group. ABI and TcPO$_2$, when cross tabulated, showed that 38.8% of people with a normal ABI had a normal TcPO$_2$, and the remaining 61.2% had an abnormal TcPO$_2$. 13.7% of patients with an abnormal ABI had a normal TcPO$_2$, and 86.3% with an abnormal ABI had an abnormal TcPO$_2$. 78.8% of patients with a normal TcPO$_2$ had a normal ABI, and the remaining 21.2% had abnormal ABIs. Among those with an abnormal TcPO$_2$, 48.2% had a normal ABI and 51.8% had abnormal ABIs. Overall, in the total population, 22% had both a normal ABI and TcPO$_2$; 37.3% had both an abnormal ABI and TcPO$_2$; 34.8% had an abnormal TcPO$_2$ with a normal ABI; and 5.9% had a normal TcPO$_2$ with an abnormal ABI. Thus, the percentage agreement rate of ABI and TcPO$_2$ was 59.3%, and the disagreement rate was 40.7%.

Table 1. Comparison of ABI and TcPO$_2$ between healed and not healed groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Healed (n=90)</th>
<th>Not Healed (n=28)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABI</td>
<td>0.96±0.24</td>
<td>0.61±0.27</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>TcPO$_2$</td>
<td>33.77±15.51</td>
<td>23.29±14.77</td>
<td>0.002*</td>
</tr>
</tbody>
</table>

*Statistically significant

Out of 90 patients whose ulcers healed, 61 (67.8%) showed normal ABIs, and 31 (34.4%) showed a normal TcPO$_2$. Of the 28 patients whose ulcers did not heal 22 (78.6%) showed an abnormal ABI, and 26 (92.9%) showed an abnormal TcPO$_2$. In this category, only 6 (21.4%) showed a normal ABI and 2 (7.1%) showed a normal TcPO$_2$. Table 2 shows the association of ABI, normal and abnormal, with wound outcomes categorized as healed and not healed. Table 3 shows the association of TcPO$_2$, normal and abnormal, with wound outcomes categorized as healed and not healed. Ninety-one percent of wounds with a normal ABI and 93.9% with a normal TcPO$_2$ healed, whereas 56.9% of those with an abnormal ABI and 69.4% with an abnormal TcPO$_2$ also healed (Figures 2 and 3).

Table 2. Association of ABI (normal and abnormal) with wound outcomes categorized as healed and not healed

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Normal (0.91 – 1.3) n=67</th>
<th>Abnormal (≤ 0.9) n=51</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healed</td>
<td>61 (91%)</td>
<td>29 (57%)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Not Healed</td>
<td>6 (9%)</td>
<td>22 (43%)</td>
<td></td>
</tr>
</tbody>
</table>

*Statistically significant
By plotting a ROC curve, in our population an ABI value of 0.77 was found to have 80% sensitivity and 75% specificity, and a TcPO$_2$ value of 22.5 was found to have 74.4% sensitivity and 53.6% specificity in predicting wound healing (Figure 4). Using a cut-off of 0.77 for ABI, 91% of wounds with an ABI > 0.77 healed while the rest did not heal, whereas 46% of those with ABI ≤ 0.77 also healed. Similarly with a TcPO$_2$ of >22.5, 84% healed and the remaining did not heal, whereas with a TcPO$_2$ ≤ 22.5, 61% healed and 39% did not heal.

Table 3. Association of TcPO$_2$ (normal and abnormal) with wound outcomes categorized as healed and not healed

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Normal (&gt; 40 mm Hg)</th>
<th>Abnormal (≤ 40 mm Hg)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healed</td>
<td>31 (94%)</td>
<td>59 (69%)</td>
<td>=0.001*</td>
</tr>
<tr>
<td>Not Healed</td>
<td>2 (6%)</td>
<td>26 (31%)</td>
<td></td>
</tr>
</tbody>
</table>

*Statistically significant

Table 4. Results of the multivariate logistic regression analysis (ABI and TcPO$_2$ against the outcome of nonhealing of ulcer)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio (95% confidence interval)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal ABI</td>
<td>6.21 (2.23, 17.35)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Abnormal TcPO$_2$</td>
<td>4.44 (0.93, 21.13)</td>
<td>0.061**</td>
</tr>
</tbody>
</table>

*Statistically significant

**Borderline significant
DISCUSSION

In this study of 118 patients with diabetic foot ulcers, the utility of ABI and TcPO$_2$ in predicting wound healing was assessed. The mean ABI and TcPO$_2$ in the healed and not healed group were significantly different ($p<0.001$ and $p=0.002$ respectively). The agreement rate between ABI and TcPO$_2$ was 59.3%. If either the ABI and/or TcPO$_2$ was normal, there was more than a 90% chance of wound healing. Though 0.9 is the conventionally used cut-off value for predicting POVD by ABI, the ROC curve in our study population showed an ABI of 0.77 to have the optimal sensitivity and specificity in predicting wound healing. For TcPO$_2$, the cut-off in our population with optimal sensitivity and specificity was 22.5 mm Hg. The study by Majid Kalani et al. showed that TcPO$_2$ was a better predictor for ulcer healing than toe blood pressure in diabetic patients with chronic foot ulcers. The cut-off level used for TcPO$_2$ in this study was 25 mm Hg. A study by Zimny et al. also emphasized TcPO$_2$ to be a useful tool in screening Type 2 diabetic patients for the foot at risk. A study done in the University Hospital of Tubingen, Germany evaluated whether TcPO$_2$ can be used to predict the risk of non-healing and amputation in diabetic foot ulcer patients with non-palpable pedal pulses. Of the 141 patients studied, wounds associated with a TcPO$_2$ of less than 20 mm Hg demonstrated a significantly decreased probability of healing compared with those associated with a TcPO$_2$ greater than 40 mm Hg ($p=0.008$). The Eurodiale study focused on outcome and determinants of outcome in diabetic foot disease. This study concluded that the predictors of healing differ between patients with and without peripheral arterial disease, and infections had a negative impact on healing.

Study results showed that if the ABI was abnormal there was a greater chance that the TcPO$_2$ was also abnormal, whereas if the ABI was normal the TcPO$_2$ 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. Even if ABI was normal there may have been microvascular disease in diabetes, which was evident from the higher percentage of abnormal TcPO$_2$ even if the ABI was normal. If ABI and/or TcPO$_2$ were normal there was more than 90% chance that wounds would heal. Good healing percentages in wounds where ABI and/or TcPO$_2$ was abnormal was a result of aggressive management of POVD and other aspects of the diabetic foot ulcer. This routinely occurred in a highly specialized podiatry unit where the limb salvage rate was very high. The revascularization rate, and its success, were not analyzed in this study.

Both ABI and TcPO$_2$ were complementary and measured different aspects of POVD; therefore, both were useful in predicting wound healing. All patients with abnormal ABI and TcPO$_2$ needed aggressive management of their POVD to improve the wound outcomes.

An angiogram, which is the gold standard for assessing POVD, was not able to be done on all patients because of its invasive nature and cost factors. Future studies on larger populations may yield more information regarding equal or better predictability of one test over the other.

CONCLUSION

Both ABI and TcPO$_2$ measure different aspects of POVD and are complementary in predicting wound healing in diabetic foot ulcers. In our study, the optimal cut-off values of these measures to predict wound healing was also defined.
References


