Reference value of transcutaneous oxygen measurement in diabetic patients compared with nondiabetic patients

Vincent E. de Meijer, MD, MSc,a,b Hans P. van’t Sant, MD,a Sandra Spronk, PhD,c,d Freck J. Kusters, BSc,a and Pieter T. den Hoed, MD, PhD,a Rotterdam, The Netherlands; and Boston, Mass

Purpose: This study evaluated the values of transcutaneous oxygen tension (TcPO2) measurement in diabetic patients compared with nondiabetic patients and assessed its reproducibility.

Methods: In 60 diabetic patients (type 1 and type 2 diabetes mellitus) without signs of peripheral arterial disease or neuropathy, we measured TcPO2 at the chest and foot and compared these measurements with 60 age- and sex-matched nondiabetic patients in a cross-sectional fashion. The reproducibility of TcPO2 measurements in terms of interobserver variability was also assessed.

Results: Diabetic patients had a mean ± SD TcPO2 value at the foot of 50.02 ± 8.92 mm Hg, which was significantly lower compared with 56.04 ± 8.80 mm Hg in nondiabetic patients (P < .001). At the chest wall, values for TcPO2 were 51.77 ± 11.15 mm Hg, and 58.22 ± 12.47 mm Hg for diabetic patients and nondiabetic patients, respectively (P = .003). Regression analysis showed that TcPO2 was significantly associated with diabetes mellitus (coefficient = −0.258; P = .004), and with having a first-degree relative with diabetes mellitus (coefficient = −0.265; P = .003). Furthermore, the interobserver variability showed a substantial correlation for both measurements at the chest (P < .001; r = 0.654; intraclass correlation coefficient [ICC] = 0.79) and at the dorsum of the foot (P < .001; r = 0.426; ICC = 0.60).

Conclusion: Diabetic patients without signs of peripheral disease or neuropathy had significantly lower TcPO2 values compared with age- and sex-matched nondiabetic patients. The influence of the examiner on the variance in TcPO2 measurements was relatively small. We advocate the use of TcPO2 measurement in diabetic patients to detect subclinical microvascular impairment as an additional tool to assess peripheral vascular disease. (J Vasc Surg 2008;48:382–8.)

Transcutaneous oxygen tension (TcPO2) measurement is a noninvasive diagnostic study that provides information about the supply and delivery of oxygen to the underlying microvascular circulation by recording the partial pressure of oxygen at the skin surface. The amount of oxygen detected by the sensor is a balance of oxygen delivery and local physiologic demands and reflects the metabolic status of the skin. The TcPO2 measurement is used in determining amputation level, wound healing evaluation, hyperbaric therapy, and peripheral arterial disease assessment, including the status of spinal cord stimulation and revascularization procedures.

In the literature, a commonly accepted reference value with TcPO2 measurement for the diagnosis of peripheral arterial disease is approximately 60 mm Hg, regardless of electrode location. For wound healing to occur, studies found that the TcPO2 should be >40 mm Hg, and impaired wound healing is noted with values between 20 and 40 mm Hg. Failure of wound healing is demonstrated with TcPO2 values of <20 mm Hg.

The most appropriate clinical role for TcPO2 measurement is to assist in the assessment of severe ischemia. Because the measurements are not affected by arterial calcification, it is particularly useful in evaluating diabetic vascular disease. For diabetic patients, however, TcPO2 values might not be the same as for nondiabetic patients because potential subclinical microangiopathy may cause alterations in capillary flow. The use of the TcPO2 measurement in the diabetic population has been studied previously, but consistent reference values for diabetic patients without signs of peripheral arterial disease or neuropathy are lacking. With the increasing prevalence of obesity, the metabolic syndrome, and associated diabetes mellitus (diabetes), and previous studies reporting that tissue oxygenation measured by TcPO2 in patients with diabetes is impaired, determining a reference value for TcPO2 in the diabetic population could be of help in clinical daily practice.

This study evaluated the reference value for TcPO2 measurement in diabetic patients compared with nondiabetic patients and secondarily assessed the reproducibility of TcPO2 in terms of interobserver variability.

METHODS

Study design and patients. We performed a cross-sectional study at the Ikazia Hospital Rotterdam, The Netherlands, a large community hospital with a specialized...
surgical laboratory experienced in the field of vascular diseases. The study included 60 diabetic patients (types 1 or 2) from our outpatient clinic with diagnosed diabetes for at least 1 year and without signs of peripheral arterial disease and neuropathy. Selection criteria were on the basis of the medical history, a comprehensive interview, and levels of fasting blood glucose and glycosylated hemoglobin (HbA1C). Also invited to participate in the study were 60 nondiabetic patients to match for age and sex.

A physical examination including palpation of the pedal pulses, vibration thresholds, and standard fiber testing was used to exclude peripheral arterial disease, injury to the extremities, peripheral neuropathy and spinal conditions, cardiovascular disease, pulmonary disease, and psychiatric illness. Further evaluation of study participants considered age, sex, height, weight, body mass index (BMI), smoking habits, family history of diabetes, and if appropriate, type of diabetes, type of medication, and diabetes duration.

The study was approved by the local ethics committee, and was performed according to the declaration of Helsinki.18 In accordance with institutional guidelines, written informed consent to be part of this study and for their study data to be reported in the literature for the purpose of scientific articles was obtained from all patients before their participation.

**Measurement of TcPO2.** A Radiometer TCM400 (Copenhagen, Denmark) TcPO2 monitor was used to simultaneously measure the TcPO2 values at the chest and at the dorsum of the foot. The laboratory room temperature was maintained at approximately 25°C. All patients acclimatized for a minimum of 10 minutes before commencing the study, during which the device was calibrated at 159 mm Hg according to the manufacturer’s guidelines.20 The measurements were simultaneously performed on one randomly chosen lower extremity by two different vascular technologists with the patient resting in supine position during one session, each applying one electrode at the dorsum of the foot and one reference at the thorax. The reported values represent averages of the measurements assessed by both observers.

At the measured site, skin was shaved and cleaned with alcohol. A self-adhesive ring was filled with a buffered solution, both supplied by the manufacturer, and the electrode, heated to a temperature of 43°C, was attached. The electrode at the dorsum of the foot was placed between the first and second metatarsal heads just proximal to the first and second toe, not over a visible vein, bony, or tendon structure. The electrode at the chest was placed by the same observer on the ipsilateral anterior chest wall at the midaudicular line and infraclavicular fossa. The TcPO2 value was recorded for analysis after obtaining a stable reading after 20 minutes. Three registered vascular technologists were involved, all experienced in TcPO2 measurement.

**Statistical analysis.** All continuous variables were expressed as means ± standard deviation (SD). Significance of differences between the group means was assessed by using the Student t test, or if nonparametric, by using the Mann-Whitney U test. Significant differences between nominal and categoric variables were assessed by using Fisher’s exact test. A one-way sensitivity analysis was performed to test whether TcPO2 measurements >80 mm Hg had influenced the results. A subgroup analysis stratifying for type 1 and type 2 diabetes was performed within the group of diabetic patients. We then compared the subgroups of type 1 and type 2 diabetic patients separately with the group of nondiabetic patients. Backward multiple linear regression analysis was used to determine which factors were significantly associated with TcPO2.

Data from both observers were plotted using Bland-Altman graphs enabling an appreciation of the distribution of error.21 Typical error was calculated using the SD of the differences.22 The interobserver variability was assessed by using the Pearson correlation coefficient. However, because our data include more than one observation on each individual and outliers were present, the intraclass correlation coefficient (ICC) was calculated as well, using a two-way mixed-effects model with absolute agreement definition. The ICC is defined as the proportion of variance of an observation due to between-subject variability in the true scores and can be interpreted as poor (ICC < 0.20), fair (0.20 to 0.40), moderate (>0.40 to 0.60), substantial (>0.60 to 0.80), and almost perfect (>0.80 to 1.00).23,24

Significance was determined at a two-sided P < .05 and expressed with the 95% confidence interval (CI). All data were collected in an Excel database (Microsoft Inc, Bellingham, Wash). The analysis was performed using SPSS 12.1 software (SPSS Inc, Chicago, Ill).

**RESULTS**

The study included 60 diabetic patients and 60 nondiabetic patients matched for age and sex. Demographics and clinical characteristics of this study population are reported in Table I. Smoking habits, defined as current or never/ever (>1 year) were equally distributed among diabetic patients and nondiabetic patients (13 of 60 vs 10 of 60; P = .643; Table I). Significantly more diabetic patients had a first-degree relative who was diagnosed with diabetes (36 vs 21; P = .010) but had a lower BMI (27.20 ± 5.73 vs 30.21 ± 6.25 kg/m²; t = 2.74118, P = .007) compared with the nondiabetic patients (Table I). Within the diabetic patients, however, positive family history of diabetes (13 of 25 vs 23 of 35; P = .293) and BMI (t = 2.1458, P = .047) were equally distributed between type 1 and type 2 diabetic patients (26.59 ± 3.77 and 27.64 ± 6.81 kg/m², respectively).

**Fig 1** illustrates the mean values and corresponding 95% CI for TcPO2 for diabetic and nondiabetic patients: The averaged mean values for TcPO2 measurements (mm Hg) were, respectively, 50.02 ± 8.92 and 56.04 ± 8.80 at the dorsum of the foot and 51.77 ± 11.15 and 58.22 ± 12.47 at the chest wall. When diabetic and nondiabetic patients were compared, the absolute difference of TcPO2 values measured at the foot and chest were 6.02 mm Hg (95% CI, 2.81-9.22; P < .001) and 6.45 mm Hg (95% CI, 2.17-10.73; P = .003), respectively. The absolute differences for TcPO2 values between type 1 and type 2 diabetics measured at
foot and chest were 3.35 mm Hg (95% CI, –1.28 to 7.99; \( P = .153 \)), and 2.18 mm Hg (95% CI, –3.68 to 8.05; \( P = .459 \)) and showed no significant difference.

After comparing nondiabetic patients with type 2 diabetic patients, however, both the values for TcPO2 measured at the dorsum of the foot and chest wall were significantly different, with absolute differences of 7.41 mm Hg (95% CI, 3.68–11.15; \( P < .001 \)), and 7.36 mm Hg (95% CI, 2.41–12.31; \( P = .004 \)), respectively. The absolute differences for TcPO2 between nondiabetic patients and those with type 1 diabetes were 5.18 mm Hg (95% CI, –0.72 to 11.07; \( P = .084 \)) for TcPO2 values measured at the chest and 4.06 mm Hg (95% CI, –0.10 to 8.22; \( P = .056 \)) at the foot, not reaching statistical significance.

Backward stepwise multiple linear regression analysis showed that TcPO2 was significantly associated with diabetes (coefficient = –0.258; \( P = .004 \)) and with having a first-degree relative with diabetes (coefficient = –0.265;
Cigarette smoking, BMI, type of diabetes, and duration of diabetes showed no significant associations with TcPO2.

Interobserver variability. Table II reports the mean values and corresponding 95% CI for TcPO2 for diabetic and nondiabetic patients as recorded by the different observers. The absolute differences for TcPO2 between observers measured at the chest wall were 1.067 mm Hg (95% CI, –2.20 to 4.33; \( P = .516 \)) for diabetic patients and –0.733 mm Hg (95% CI, –3.29 to 1.83; \( P = .568 \)) for nondiabetic patients. At the dorsum of the foot, the absolute differences for the TcPO2 measurement between observers were –0.117 (95% CI, –2.59 to 2.35; \( P = .925 \)) for diabetic patients and –0.283 (95% CI, –3.86 to 3.29; \( P = .875 \)) for nondiabetic patients (Table II).

The results related to the Bland-Altman analyses show that the distribution of the error was low and, although outliers were present, randomly distributed across the range of values for TcPO2 measured at the dorsum of the foot and chest wall (Fig 2). After a one-way sensitivity analysis by censoring the outlying TcPO2 values >80 mm Hg (7 of 480 individual measurements), the results did not change substantially. Fig 3 presents the correlation of TcPO2 values measured by the different observers at the chest wall and dorsum of the foot (Fig 3, A) and dorsum of the foot (Fig 3, B). The values for TcPO2 measured by the different observers at the chest wall and dorsum of the foot were both positively correlated \( r = 0.654; P < .001, \) and \( r = 0.426; P < .001, \) respectively. The ICC describing the interobserver variation was 0.79 (95% CI, 0.69-0.89; \( P < .001 \)) for all TcPO2 measurements at the chest wall and 0.60 (95% CI, 0.42-0.72; \( P < .001 \)) for all TcPO2 measurements at the dorsum of the foot.

### Table II. Mean values for transcutaneous oxygen tension in diabetic patients and nondiabetic patients measured by two different observers

<table>
<thead>
<tr>
<th>Location</th>
<th>Patient</th>
<th>Observer</th>
<th>No.</th>
<th>Mean</th>
<th>95% CI</th>
<th>Difference</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest</td>
<td>Nondiabetic</td>
<td>Observer 1</td>
<td>60</td>
<td>57.85</td>
<td>54.16-61.54</td>
<td>–0.733</td>
<td>.568</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Observer 2</td>
<td>60</td>
<td>58.58</td>
<td>55.51-61.65</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetic</td>
<td>Observer 1</td>
<td>60</td>
<td>52.30</td>
<td>48.76-55.84</td>
<td>1.067</td>
<td>.516</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Observer 2</td>
<td>60</td>
<td>51.23</td>
<td>48.31-54.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foot</td>
<td>Nondiabetic</td>
<td>Observer 1</td>
<td>60</td>
<td>55.90</td>
<td>52.76-59.04</td>
<td>–0.283</td>
<td>.875</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Observer 2</td>
<td>60</td>
<td>56.18</td>
<td>53.69-58.67</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetic</td>
<td>Observer 1</td>
<td>60</td>
<td>49.97</td>
<td>47.64-52.30</td>
<td>–0.117</td>
<td>.925</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Observer 2</td>
<td>60</td>
<td>50.08</td>
<td>47.31-52.85</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CI, confidence interval.

*Student’s \( t \) test.
DISCUSSION

This study assessed mean values for TcPO2 measurements in diabetic patients without signs of peripheral arterial disease compared with age- and sex-matched nondiabetic patients without signs of peripheral arterial disease. The main finding of our study was a significantly lower TcPO2 value measured at both the foot and chest for diabetic patients compared with nondiabetic patients.

Many studies about TcPO2 and diabetes have been published since the 1970s. To our knowledge, however, no studies have been reported in which the study design was to assess a reference value for TcPO2 in diabetic patients. What we do know is that impaired tissue oxygenation is an independent risk factor for diabetic foot ulceration.25,26 Therefore, consistent reference values for TcPO2 in the diabetic population are crucial to identify patients with a foot at risk. A previous study showed that TcPO2 measurement is also a useful diagnostic modality to prevent peripheral vascular disease in diabetic patients because it detects early changes in skin oxygenation before the development of clinically overt microangiopathy.27

In our study we found that when the nondiabetic patients were compared with patients with type 2 diabetes, the values for TcPO2 measured at both the dorsum of the foot and chest wall were significantly lower. However, the absolute differences of TcPO2 values at both the dorsum of the foot and chest wall between nondiabetic patients and patients with type 1 diabetes did not reach statistical significance. An explanation could be the difference in number: 25 type 1 diabetic patients were compared with 35 type 2 diabetic patients.

Next, because we found conflicting studies in the literature on the effects of age and sex on TcPO2 results,17,28,29 we matched our patient groups for age and sex. Furthermore, in our study cigarette smoking and BMI showed no association with lower TcPO2 values, which is consistent with the findings by Rooke et al17 but contrasts with a study by Strauss et al,30 who identified that cigarette smoking cessation improved the TcPO2 value measured at the foot. Despite our results, however, the controversy about the effect of cigarette smoking and BMI on TcPO2 remains.

Further, we also investigated the interobserver variability in TcPO2 measurement. No significant absolute differences were noted between observers. For measurements at foot and chest level, TcPO2 values obtained by both observers simultaneously showed a highly significant correlation. Although variation in the measurements was present, distribution of error was low and randomly assigned across the range of values for TcPO2, meaning that the biologic variance was relatively small. Presented as an ICC value, the interobserver variability showed a substantial correlation for measurements at the chest and at the dorsum of the foot. The ICC value in our study was somewhat smaller compared with the reported ICC value of 0.77 by De Graaff et al,31 but was identically classified.

The lower ICC value for the TcPO2 measurements obtained at the dorsum of the foot compared with the chest may be explained by the position of the electrodes. Although the electrodes were attached to the first intermetatarsal space as instructed, skin oxygenation could have been influenced by skin thickness and partially positioning the electrode on the metatarsal bony or tendon structures, which may have introduced some variation in our measurements. Overall, the influence of the examiner on the variance in TcPO2 measurements appeared to be relatively small.

![Fig 3. The correlation of transcutaneous oxygen tension (TcPO2) values is shown between observer 1 and 2 for values measured at the (A) chest wall and the (B) dorsum of the foot.](jvascaur08155fig03a.png)
Several possible limitations of this study warrant consideration. First, by using a cross-sectional design, we are unable to infer causality because the study was done at one time point without follow-up.

Second, because we only provided a snapshot of the situation at one specific point in time, results might be different if another timeframe were chosen. We did not perform repeated measurements, which have previously been shown to introduce greater variability. Our data from the interobserver variability analysis, however, showed a substantial correlation between the measurements taken by both observers at the same time.

Third, because the toe pressure measurements in our first 20 diabetic patients were in the normal range (unpublished data), neither in the subsequently included diabetic patients nor in the nondiabetic patients has the diagnosis of peripheral arterial disease been excluded by additional testing. All patients had bilateral palpable pedal pulses, and all passed standard neurosensory testing. One may rather favor to have baseline values of toe blood pressures or ankle-brachial pressure indexes, or both, to objectively exclude any evidence of peripheral arterial disease; however, these modalities may often lack discriminative accuracy and do not reflect local microvascular perfusion status.

This study was designed in such a way that we relied on the patient’s medical history in addition to a comprehensive interview and a routine physical examination to provide a representative sample of patients which physicians daily encounter in clinical practice.

CONCLUSION

Our results demonstrate that diabetic patients without signs of peripheral arterial disease and neuropathy have significantly lower TcPO2 values at both the dorsum of the foot and the chest wall compared with matched nondiabetic patients. The reduced supply of oxygen to the skin in diabetic patients reflects an early subclinical impairment in their microcirculation, thus providing the TcPO2 measurement as an additional tool in the diagnostic armamentarium of vascular surgeons to assess peripheral vascular disease in diabetic patients.

We thank Karin Goederaad and Willeke Dolman, vascular technologists, for performing TcPO2 measurements, and the patients for their voluntary participation in the study.

AUTHOR CONTRIBUTIONS

Conception and design: VM, HS, SS, PH
Analysis and interpretation: VM, SS, PH
Data collection: VM, HS, SS, FK
Writing the article: VM
Critical revision of the article: VM, HS, SS, FK, PH
Final approval of the article: VM, HS, SS, FK, PH
Statistical analysis: VM, SS
Obtained funding: Not applicable
Overall responsibility: PH

REFERENCES


Submitted Feb 8, 2008; accepted Mar 5, 2008.