Transcutaneous oxygen tension: a useful predictor of ulcer healing in critical limb ischaemia

• **Objective:** To investigate the threshold of transcutaneous oxygen tension ($TcPO_2$) values in predicting ulcer healing in patients with critical limb ischaemia in a prospective study.

• **Method:** 50 patients suffering from critical limb ischaemia with chronic ischemic ulcers or gangrenous toes were enrolled in this study between January and December 2008. Their demographic data and ankle brachial pressure index (ABPI) were collected. Baseline ulcers were measured with a wound measurement system (Visitrak, Smith & Nephew). $TcPO_2$ was measured at rest in the supine position and with 30° leg elevation. The patients with infective and ischemic ulcers underwent debridement and gangrenous toes were amputated. Ulcer outcome was classified as either: (1) A healing ulcer, showing good epithelialisation or granulation at both base and edges, or a decrease in ulcer area during the study; or (2) A non-healing ulcer, showing poor granulation tissue formation or a pale base and necrotic edges, or deterioration in an ischaemic ulcer.

• **Results:** The mean age of the patients was 67.6 ± 10.8 years. The most common risk factor was hypertension (90%). Mean ABPI was 0.75 ± 0.39. 13 patients (26%) had a $TcPO_2$ of less than 20mmHg, of which none showed any improvement in ulcer healing ($p<0.001$). 15 patients (30%) had a $TcPO_2$ of more than 40mmHg, of which all progressed to complete ulcer healing ($p<0.001$). In the borderline group (20–40mmHg, 22 patients, 44%), 10 patients (45%) had a $TcPO_2$ drop of ≤10mmHg with 30° leg elevation, of which 8 achieved complete ulcer healing ($p<0.001$). 12 patients (55%) had a $TcPO_2$ drop of >10mmHg with 30° leg elevation, of which 11 showed no ulcer healing ($p<0.001$).

• **Conclusion:** $TcPO_2$ measurement is an accurate, non-invasive, and good predictor of ischemic ulcer healing, for cut-off $TcPO_2$ values of less than 20mmHg and more than 40mmHg. In addition, the leg elevation method for $TcPO_2$ might provide an important adjunct in the assessment of patients with borderline values.

• **Declaration of interest:** None.

transcutaneous oxygen tension; critical limb ischaemia; ulcer healing

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Peripheral arterial occlusive disease (PAOD) is a common manifestation of systemic atherosclerosis. Most patients with PAOD develop chronic ischaemic ulcers, gangrene and rest pain, defined as critical limb ischaemia.[1] In 2007, the TransAtlantic Inter-Society Consensus (TASC II) defined objective criteria for the diagnosis of critical limb ischaemia as: ankle pressure <50mmHg, or toe pressure <30mmHg, or transcutaneous oxygen tension ($TcPO_2$) <30mmHg.[1]

Factors influencing ulcer healing include local skin macro- and microcirculation and tissue oxygenation surrounding the ulcer.[2] Peripheral pulse examination and ankle brachial pressure index (ABPI) measurement are commonly used in assessing limb macrocirculation, but they cannot predict whether or not the ulcer will heal.[3] Furthermore, ankle pressure measurement is not easily achieved in patients with poorly compressible tibial arteries, such as those with diabetes mellitus or chronic renal failure and medial arterial calcification.[1,4,5] In addition, both tibial arteries may be occluded, making ankle pressure assessment impractical.[6] While toe blood pressure measurement can be used with calcified tibial arteries, its use is limited in patients with gangrenous toes.

In contrast, it is much easier to measure the $TcPO_2$ at the dorsum of the foot in patients with critical limb ischaemia. This can be used to assess both local arterial blood flow and skin oxygenation.[7]

At present, there is no consensus on the $TcPO_2$ value that should be used to determine whether healing is likely to occur or whether revascularisation is indicated, with a range of 25–40mmHg being used.[1,5,8,9]

This prospective study aimed to investigate the diagnostic efficacy and threshold of transcutaneous oxygen tension values in predicting ulcer healing in patients with critical limb ischaemia.

Table 1. Inclusion and exclusion criteria

Inclusion criteria
Patients with PAOD diagnosis presenting with chronic ischaemic ulcer or gangrenous toe
Well-cooperating patients
Exclusion criteria
Patients with conditions that affect the $TcPO_2$ value
Anaemia (Hb <10g/dl)
Unstable vital signs or signs of poor tissue perfusion
Vasoactive drugs (vasoconstrictor or vasodilator)
Patient with asthma or COPD with pulse oximetry oxygen saturation <92% at room temperature
Drinking caffeine within 2 hours before testing
Smoking within 2 hours before testing
Infected ulcer
Oedema around an ulcer
Inability to lie supine for the period of testing
Poorly cooperating patients

Material and method

Patients

Between January 2008 and December 2008, 149 patients at Siriraj Hospital were diagnosed with critical limb ischaemia. Of these, 50 were enrolled in this study. The inclusion and exclusion criteria are presented in Table 1.

The Siriraj ethical committee for research in humans approved this study and written informed consent was received from all participants.

Study procedure

The patients' demographic data were collected and physical examinations were performed. ABPI was measured to determine the site and severity of arterial occlusion. Baseline ulcer characteristics were measured using Visitrak (Smith & Nephew) each week during admission and every 4–6 weeks during regular outpatient visits. Ulcer area was calculated through manual tracing, as described in previous studies.[10,11]

All patients underwent $TcPO_2$ measurement using a TCM400 (multi-channel $TcPO_2$ monitor, Radiometer America). Patients lay supine in a quiet room where the temperature was carefully controlled (21–23°C). During this procedure, the transcutaneous oxygen tension electrode was calibrated for 15 minutes. An estimated barometric pressure of 730mmHg was used for standard calibration at the geographic location.

The measuring site was carefully cleaned with saline. Transducers were fixed to the skin with double-sided adhesive rings and contact liquid supplied by the manufacturer. A reference electrode was applied to the chest wall in the left second intercostal space, in the mid-clavicular line. A second electrode was placed on the dorsum of the foot at the periwound site, avoiding any large veins, hair, skin defects, bone or tendons (Fig 1).[12]

Electrodes were then heated to 45°C — the heat from electrodes caused the underlying capillaries to dilate, increasing local perfusion and opening the skin pores. The diffusion of oxygen through the skin to electrodes and subsequent changes in partial pressure (pO_2) generated a current. This was measured and $TcPO_2$ values were generated on a monitor. Values were recorded at the 15th minute, resting supine, and at the 5th minute following 30° leg elevation.

In the present study, we have used the cut-off resting values of transcutaneous pressure measurement in amputated patients studied by Bacharach et al.[7] and five-minute 30° leg elevation values, that have previously been described as a useful measure in classifying the severity of PAOD.[12]

The patients were divided into three groups according to their resting, supine values:

- Group 1: patients with a $TcPO_2$ value <20mmHg
- Group 2: patients with a $TcPO_2$ of 20–40mmHg
- Group 3: patients with a $TcPO_2$ value >40mmHg.

Group 2 was further divided into two subgroups, based on leg elevation values: subgroup 1 comprised patients whose $TcPO_2$ decreased by ≤10mmg and subgroup 2 as patients whose $TcPO_2$ decreased by >10mmHg.

After $TcPO_2$ measurements, all ischaemic and infected ulcers were debrided, while a vascular surgery care team performed minor amputations on patients with gangrenous toes. Individualised topi-

Fig 1. An electrode was placed on the periwound area

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Fig 2. A 72-year-old female presented with a non-healing ulcer and second gangrenous toe. Her diagnosis was femoropopliteal arterial occlusive disease; ABPI was 0.70 but $TcPO_2$ was 32mmHg in the supine position and 26mmHg for leg elevation (a). A 70-year-old female presented with rest pain and fifth gangrenous toe. Her diagnosis was aorto-iliac arterial occlusive disease; ABPI was 0.20 but $TcPO_2$ was 50mmHg (b). Both ulcers were successfully complete healing after toe amputation and local wound dressing.

cal treatments and dressing changes were used, depending on the site and character of ulcers.

Ulcer outcomes were classified within two weeks of the initial assessment as:

- A healing ulcer, defined as having good epithelialisation or granulation at both base and edges,[13,14] or a decrease in ulcer area during the study (Fig 2)[11]
- A non-healing ulcer, defined as having poor granulation tissue formation or a pale base and necrotic edges, or deterioration in an ischaemic ulcer.[13,14]

In equivocal cases, ulcers were re-evaluated within two weeks using this same method. However, we decided to perform urgent revascularisation in patients who developed ischaemia or rest pain.

We analysed $TcPO_2$ values and outcomes in all patients to determine the statistical significance of ulcer-healing predictions.

Statistical analysis

Descriptive data analyses are given as mean ± standard deviation for continuous data or as percentages for discrete variables. The Chi-square test was used to compare $TcPO_2$ data between the two ulcer outcomes. A value of $p<0.05$ was considered to be statistically significant. Statistical analysis was conducted with SPSS software version 16 (SPSS Inc, Chicago, III).

Results

Fifty patients met the criteria for $TcPO_2$ measurement. Gender, age, presenting symptom, risk factor, ABPI and level of occlusion are summarised in Table 2, which shows that most patients presented with an ischaemic ulcer on the toes or a gangrenous toe. The most common risk factor was hypertension. Most patients (40%) were diagnosed with multilevel arterial occlusive disease.

$TcPO_2$ values are illustrated in Fig 3, which shows that most patients had values of 11–20mmHg. The outcomes for different groups are presented in Table 3. None of patients with a $TcPO_2$ of <20mmHg (group 1) showed signs of ulcer healing, whereas all of the patients with a $TcPO_2$ of >40mmHg (group 3) showed a progression towards healing during the study period ($p<0.001$). In the borderline group (20–40mmHg, group 2), 10 patients had a decrease in $TcPO_2$ of ≤10mmHg with leg elevation (subgroup 1), of whom eight (80%) healed ($p<0.001$). In contrast, 12 patients had a decrease in TcPO2 of >10mmHg with leg elevation (subgroup 2), and 11 of these (92%) failed to heal ($p<0.001$).

Discussion

Using peripheral pulses or ankle or toe pressure measurements alone to predict ischaemic ulcer healing has limitations.[3] This has led to numerous efforts to find a complementary technique that would allow for more accurate predictions. Our results suggest that $TcPO_2$ values of <20mmHg or >40mmHg when supine, and leg elevation $TcPO_2$ values of 20–40mmHg are clinically useful in predicting healing outcomes in patients with critical limb ischaemia.

ABPI measurement is a simple, non-invasive and reproducible test for evaluating the severity of PAOD.[15,16] However, its use is limited in patients with calcified or distally occluded tibial arteries.[1,5,6,8] Furthermore, it may fail to unmask the underlying

problem in a high-grade aorto-iliac stenosis, or where an occlusion has a rich collateral network.[17] Therefore, ABPI is not sufficient when making a decision regarding ulcer healing.[3]

At present, a variety of $TcPO_2$ values are used to predict whether or not an ulcer will heal.[1,2,5,8] In TASC II, it was stated that a $TcPO_2$ of <30mmHg was a clear sign of a non-healing ischaemic ulcer.[1] Kalani et al.[2] proposed that the probability of ulcer healing was low when $TcPO_2$ was <25mmHg. In addition, they found that all patients with a $TcPO_2$ of >38mmHg showed improved ulcer healing and none with a $TcPO_2$ of <13mmHg improved.[2] Another study concluded that a $TcPO_2$ of <34 mmHg indicated the need for revascularisation.[5] Fife et al.[8] demonstrated that a $TcPO_2$ of <40mmHg was associated with a reduced likelihood of amputation healing.

Based on our data, $TcPO_2$ values of <20mmHg and >40mmHg can accurately predict ulcer healing outcomes. Furthermore, we have been able to correctly predict more than 80% of outcomes for patients with $TcPO_2$ values of 20–40mmHg (group 2). Although these values have previously been used to assess amputated patients,[7] they may be applicable to outcomes in patients with critical limb ischaemia, chronic ischaemic ulcers and ulcers following gangrenous toe amputation, as examined here.

When assessing ulcers, we have regarded healthy granulation tissue at the base or edges to be an indication of healing.[13] In addition, we have evaluated outcomes within 2–4 weeks, which is consistent with Keast et al.,[11] who showed that the percentage decrease in ulcer area (measured with the Visitrak system) during that period was a predictor of healing at 12–24 weeks.

Most patients with critical limb ischaemia will be at increased operative risk because of diabetes mellitus, coronary heart disease or chronic renal failure. Nevertheless, some are suitable for revascularisation. This study demonstrates that surgical or endovascular revascularisation is not obligatory, especially in patients with a $TcPO_2$ >40mmHg. In fact, conservative treatment in this group is not only cost-effective, but also free of the risks of intra- or postoperative complications. However, patients with a $TcPO_2$ of <20mmHg should receive either surgical or endovascular treatment, depending on patient status and severity of PAOD. Treatment guidelines for different cut-off $TcPO_2$ values are shown in Table 4.

A significant limitation of $TcPO_2$ measurement is that it takes 45 minutes to do, compared with less than 10 minutes for ABPI. In addition, cellulitis or significant foot oedema may confound the accuracy of $TcPO_2$ measurement. In practice, if $TcPO_2$ values are <20mmHg in these patients, the test should be repeated following bed rest, leg elevation, intravenous antibiotics and resolution of any oedema.[3]

Table 2. Patient demographics and clinical characteristics

Gender	
Male/female	28/22 ((56%/44%)
Age	67.6 ± 10.8
Presenting symptom	
Ischaemic ulcer:	26
• Toes	14 (53.9%)
• Heel	3 (11.5%)
• Lateral or medial aspects	7 (26.9%)
• Other	2 (7.7%)
Gangrenous toe	24
Risk factor	
Hypertension	45 (90%)
Diabetes mellitus	35 (70%)
Dyslipidemia	34 (68%)
Cigarette smoking	23 (46%)
ABPI	0.75 ± 0.39
Level of occlusion	
Aortoiliac	2 (8%)
Iliofemoral	2 (8%)
Femoropopliteal	14 (28%)
Tibioperoneal	12 (24%)
Multilevel	20 (40%)

Results are presented as mean ± SD, unless otherwise stated

Fig 3. $TcPO_2$ values of all patients included in the study

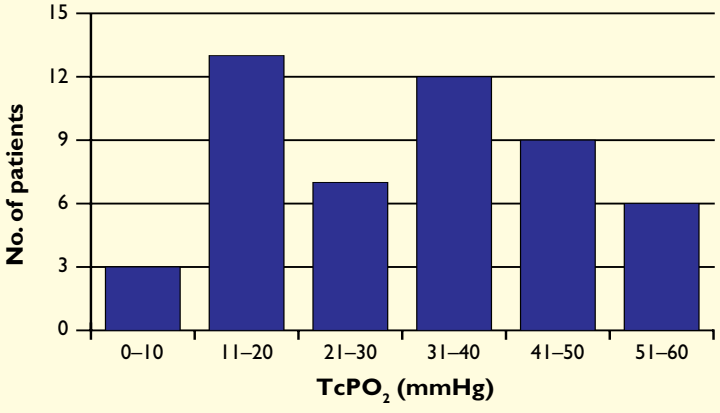

Table 3. Outcome of $TcPO_2$ measurement.

Outcome data	Healed	Non-healed	Total	p value
Group 1 (<20mmHg)	0	13	13	p<0.001
Group 2 (20–40mmHg)	9	13	22	
$TcPO_2$ decrease (30° leg elevation):				
• Subgroup 1 ≤10mmHg	8	2	10	p<0.001
• Subgroup 2 >10mmHg	1	11	12	p<0.001
Group 3 (>40mmHg)	15	0	15	p<0.001

Table 4. Guidelines for elective management of critical limb ischaemia in patients with ischaemic foot ulcers or gangrene of the toes

Group 1: $TcPO_2$ <20mmHg

Plan for revascularisation, either surgical or endovascular treatment, depending on the status of patient and severity of disease

Group 2: $TcPO_2$ 20–40mmHg (30° leg elevation)

- Subgroup 1 ($TcPO_2$ change ≤10mmHg): local wound care, wound debridement, or minor toe amputation
- Subgroup 2 ($TcPO_2$ change >10mmHg): plan for revascularisation, either surgical or endovascular treatment, depending on status of patient and severity of disease

Group 3: $TcPO_2$ >40mmHg

Local wound care, wound debridement or minor toe amputation

Two patients in group 2 had a reduction in $TcPO_2$ of ≤10mmHg during leg elevation (subgroup 1) but their ischemic ulcers did not heal. The first case was a 79-year-old female cigarette smoker with diabetes mellitus. She presented with aorto-iliac arterial occlusive disease and a gangrenous toe. The $TcPO_2$ value was 20mmHg supine and 17mmHg during leg elevation ($TcPO_2$ decrease = 3mmHg). The supine $TcPO_2$ value (20mmHg) was in the lower range of group 2. Therefore, this case may have involved inadequate microcirculation and tissue oxygenation for successful healing, following toe amputation. The second case was a 76-year-old male cigarette smoker with hypertension, diabetes mellitus and dyslipidemia, who presented with right femoropopliteal arterial occlusive disease and a non-healing ischaemic ulcer over the lateral aspect of the right foot. The $TcPO_2$ was 34mmHg supine and 24mmHg with leg elevation. The $TcPO_2$ drop (10mmHg) was borderline, and his ulcer did not heal.

Also of note, one of the 12 patients in group 2, subgroup 2, whose $TcPO_2$ fell by >10mmHg during leg elevation healed. This patient was a 56-year-old male smoker suffering from hypertension, diabetes mellitus and dyslipidemia, who presented with left femoropopliteal arterial occlusive disease and a non-healing ischaemic ulcer on the medial aspect of the left foot. The $TcPO_2$ value was 37mmHg supine and 14mmHg with leg elevation. The resting, supine $TcPO_2$ value of 37mmHg was near the upper range for group 2, hence, microcirculation and tissue oxygenation were probably adequate for ulcer healing. In future studies, it might be possible to use different, more accurate $TcPO_2$ values to evaluate ulcer healing outcomes.

The present study was limited by its small sample size, lack of randomisation with other investigations, and its relatively short-term nature. In future studies, larger sample sizes might be investigated, with randomisation, and patients should be monitored long term.

Conclusion

$TcPO_2$ measurement is an accurate, non-invasive, and good predictor of ischemic ulcer healing where $TcPO_2$ values are less than 20mmHg or more than 40mmHg. In addition, the leg elevation method might provide an important adjunct when assessing patients with borderline $TcPO_2$ values. This simple test can be used to select appropriate treatment for patients with critical limb ischaemia and help avoid intra- and postoperative complications in those with $TcPO_2$ values greater than 40mmHg, who can be managed without revascularisation. ■

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