Transcutaneous monitoring of $pO_2$ in the assessment of peripheral vascular disease

December 1997

Arnost Fronek
Department of surgery
University of California
San Diego
California
USA

There are several diagnostic approaches to identify and quantify different types of vascular disease. However, these methods usually do not reflect the condition of the cutaneous circulation.

Because transcutaneous oxygen reveals the status of cutaneous circulation, it has been shown to be a powerful diagnostic tool in the evaluation of various aspects of arterial and venous diseases.

Introduction

There are several diagnostic approaches to identify and quantify different types of vascular disease, e.g. segmental pressure, doppler velocity, various types of plethysmography.

In most cases they fulfill this goal as long as the prime objective of examination is the circulatory state of the skeletal muscle system. These methods, however, usually do not reflect the condition of the cutaneous circulation because it represents only about 1/10 of the total limb circulation.

Transcutaneous $pO_2$ ($tcPO_2$), on the other hand, reveals the status of cutaneous circulation. $tcPO_2$ has been shown to be very useful in the evaluation of various aspects of arterial as well as venous disease.

Arterial Disease

Peripheral arterial occlusive disease (PAOD) is one of the most widely encountered impairments of the arterial system. It has been shown that the perfusion of the lower extremity has to be significantly compromised to affect a reduction of the skin circulation [1].

This explains why $tcPO_2$ values reflect the degree of skin viability. Reduction in skin perfusion lead to a spectrum of different degrees of skin viability ranging from mild trophic changes (e.g. absence of hair, nail changes) to more severe complications such as non-healing ulcers.
However, non-healing ulcers can also develop in the presence of an adequate arterial inflow (neuropathic ulcer) or due to a severe insufficiency of the venous system (venous ulcer).

**Venous Disease**

The efficiency of the venous circulation can be compromised by an insufficiency of the venous valvular system, an obstruction of the deep venous system (deep venous thrombosis), or both.

It has been documented that venous ulcers develop mainly if the site of venous pathology is below the knee [2, 3]. From a hemodynamic point of view, distal valvular insufficiency, including the perforating venous system, is the most frequent cause of trophic changes of the skin culminating with the extreme form: venous ulcers.

**Microvascular Disease**

The definition of microvascular disease is equivocal. There is no question about there being a primary impairment of microcirculation, but there is a dilemma: Is the microvasculature dysfunctional and the large arterial system (> 1 mm diameter) intact?

Or is the microcirculatory disturbance caused by a decreased arterial blood supply or increased venous pressure induced by venous disease? The ambiguity can be overcome by preceding any description of microvascular disease with an assurance that the large arterial or venous system functions within normal physiological limits.

**Physiology of the skin**

The skin consists of three different layers: epidermis, dermis, and subcutaneous tissue. Each one has specific functions:

**Epidermis** - is the outer layer which protects the body from the external environment. The cornified epidermis is a barrier to infection and a protection against water loss. It contains no vessels. Oxygen which diffuses from the capillaries has to traverse the epidermis to reach its surface.

**Dermis** - is the middle layer with a dense vascularization, mainly of arterioles, capillary loops and venules. In addition, it is the site of different types of glands, hair follicles and nerve fibers. The arterioles are very sensitive to temperature changes - an increase in temperature reduces the resistance, leading to an increased blood flow.

**Subcutaneous tissue** - sometimes defined as the hypodermis, contains different types of connective tissue cells especially fat cells - adipose tissue.

**Transcutaneous measurements**

Evans and Naylor [4] demonstrated, for the first time, that it is possible to monitor $pO_2$ of diffused oxygen from the surface of the skin by using a modified Clark-type electrode. The $pO_2$ varied under these conditions between 0 - 3.5 mmHg.

They proved, in addition, that with the removal of some superficial layers of epidermis (e.g. by stripping with tape) or with increasing skin blood flow (e.g. by using ultraviolet light), the recorded $pO_2$ reached up to 30 mmHg. Heat-induced vasodilation was utilized by Huch et al [5] and Eberhard et al [6], demonstrating good arterIALIZING by adding a heating element to the polarographic probe.

**Measurement Technique**

1. **Calibration** - following the calibration instructions recommended by manufacturer.

2. **Site selection** - an ideal site would be located over a homogenous capillary bed without large veins, skin defects, or hair. Placing it directly over bone may also give erroneous results, especially if a change in body position causes skin to be pulled against a protruding bone.

3. **Site preparation** - To improve oxygen diffusion and to standardize the measurement technique it is
recommended that excessive skin cells be removed by stripping the skin 10-15 times with an adhesive tape (e.g. 3M™ filament tape), using a fresh tape section each time.

4. **Probe placement** - Place the probe on the selected site immediately after calibration is completed. To prevent strain or tension on the probe, secure the cord against the skin by using standard medical tape.

5. **Measurement** - It takes about 15 minutes after the probe has been placed on the skin for the tcpO₂ to become stabilized.

**Factors Influencing tcpO₂ Values**

- Probe temperature (due to the affect on microvasculature and on the oxyhemoglobin dissociation curve).
- Arterial pO₂.
- Metabolic consumption of O₂ by the dermal tissue.
- Oxygen consumption by the electrodes.
- Skin thickness and skin resistance to O₂ diffusion (more pronounced to dynamics).
- Capillary density and rate of cutaneous blood flow.

**Transcutaneous pO₂ in arterial disease**

**Resting Values in Arterial Occlusive Disease**

Numerous studies have documented that tcpO₂ values are usually reduced in severe PAOD, especially in critical ischemia [1, 8, 9, 10, 11, 12, 13], but the separation between normal and ischemic skin is not reliable, except in critical ischemia.

Hauser *et al.* [14] introduced the “regional perfusion index (RPI)” which relates the limb tcpO₂ to that of the chest. It proved to be especially useful during exercise testing. In order to increase the sensitivity of the test, various sensitizing procedures, which are described below, have been proposed and tested.

In order to increase the sensitivity and specificity of tcpO₂ methodology, a number of “sensitizing” procedures have been applied. This applies not only to the improvement of diagnostic accuracy but also to better utilization of this methodology to prognosticate normal healing and optimal amputation level determination.

**Sensitizing Maneuvers**

**Leg position** - in normal lower extremities tcpO₂ values decrease with leg dependency if the skin temperature is maintained at 37 °C [15].

In patients with severe peripheral arterial occlusive disease (PAOD), an increase is usually observed. From a practical point of view the results with a 44 °C heated probe are more relevant. An average increase of 15.1 mmHg was observed in normal subjects when changing from a supine to sitting position, whereas in patients with PAOD the increase was significantly higher, 28.1 mmHg.

The effect of leg position was described by Becker *et al.* [16] as a useful test to classify the severity of PAOD. Only 5 % of PAOD patients required amputation if forefoot tcpO₂ (44 °C) was > 40 mmHg in the sitting position, while patients with <10 mmHg could expect a 85 % chance of amputation.

These findings were recently confirmed by Scheffler *et al.* [17], who could objectively identify critical ischemia if tcpO₂ in sitting position was found to be less than 40 mmHg.

**Transitional Occlusion (Post Occlusive Reactive Hyperemia PORH)**

The well described PORH response observed in flow studies, can be reproduced with tcpO₂ measurement with a probe temperature of only 37 °C [18] but, as described above, the results at this probe temperature, are not very reliable.

On the other hand, when the standard 43 °C or 44 °C probe temperature is used, the “overshoot” is not recorded (probably due to local vasodilatation) but the rate of circulatory recovery measured as tcpO₂, T/2 (the time it takes to reach 50 % of the initial tcpO₂ value) after a 4-minute occlusion can be easily measured: 87.1 seconds in control subjects and 136.1 seconds in patients with severe PAOD [19].
Similar results were reported by Kram et al [20] and Slagsvold et al [21].

**Effect of Exercise**

Exercise has been used to "sensitize" the investigative methods to separate claudicants from normal subjects. Standardized treadmill protocols were used by Hauser and Shoemaker [14] and Holdich et al [22], but the correlation of tcpO2 with pain-free walking distance was not satisfactory.

A more severe exercise protocol was probably the reason for a better correlation obtained by Schmidt et al [23]. Byrne et al [8] found 20 % of claudicants with normal tcpO2 values. However, they showed a significant decline after exercise (treadmill at a speed of 1.5 miles/hr and 20 degrees incline).

**Oxygen Inhalation**

Similar to leg dependency, oxygen inhalation helps to unmask hidden oxygen reserves by increasing O2 saturation in the arterial blood. Under normal conditions, following inhalation of 100 % oxygen, tcpO2 values from the foot increase by approximately 230 % [24].

This response is significantly reduced in patients with arterial disease [25, 26].

**Determination of Optimal Amputation Level**

There is a relatively wide range of critical tcpO2 values that separate successful from unsuccessful amputation stump healing. The majority of researchers consider 30 mmHg as the critical dividing line [27, 28, 29, 30, 31]. Kram and coworkers [20], using the calf/brachial tcpO2 ratio, concluded that a ratio >0.20 predicts successful stump healing.

Franzeck et al [19] originally considered 10 mmHg as a dividing line but in view of some primary stump healing occurring below 10 mmHg as well, they decided to apply oxygen inhalation as a “sensitizing” factor.

In subsequent studies from the same group, the 10 mmHg dividing line was reconfirmed, but the accuracy was increased if an increase of tcpO2 beyond the 10 mmHg with oxygen inhalation was considered to predict successful amputation stump healing [25, 32]. McCollum et al [24] prefer the determination of rate of change of tcpO2 during oxygen inhalation. A rate of increase of 9 mmHg/min is considered a dividing line.

Currently, it is difficult to explain the relatively wide range of tcpO2 “dividing lines” separating potential successful from unsuccessful stump healing. A number of factors have to be considered: the average experience of the surgical group, electrical specifications of the probes and especially oxygen consumption of the probe. It seems useful that each institution, together with the instrumentation used, establish its own exact criteria.

**Predicting Wound Healing**

Patients with severe arterial occlusive disease may develop a poorly healing wound even after a small trauma. In the most severe stage (Fontaine IV), spontaneously developing ulcers usually resist standard conservative treatment.

Under these conditions very low tcpO2 values are recorded; usually between 10-20 mmHg. A 10 mmHg level is generally considered to be incompatible with spontaneous or conservatively treated healing process. With leg dependency, a value of 40 mmHg can be considered as a discriminant value [17].

**Diabetic Neuropathy**

Gaylarde et al [33] have shown that at 37 oC, tcpO2 in the legs and feet of diabetic patients with peripheral neuropathy was significantly higher than in control subjects and diabetic patients without neuropathy.

After a probe temperature increase to 44 oC, tcpO2 increased in all three groups, but the increase was smallest in diabetics with neuropathy. These results are consistent with a loss of vasoconstrictor tone. Similar results were reported earlier by Weindorf et al [34] using heat or rubefacients.
Transcutaneous monitoring of $pO_2$ in the assessment of peripheral vascular disease

Therapeutic Control Using $tcpO_2$

Effect of Drugs
It is important to recognize that at probe temperature of 41 oC, local vasodilator administration does not increase $tcpO_2$ value [35]. It is therefore not surprising that studies using various vasodilator agents sometimes yielded confusing and even decreasing $tcpO_2$ values, especially in patients with arterial disease [36, 37, 38].

Positive results have been obtained, however, when probe temperature was kept at 37 oC [39, 40]. Under this condition it could be shown that there was a significant increase in $tcpO_2$ (at 37 oC) after an i.v. infusion of prostaglandin E in patients with critical ischemia.

Effect of Balneologic Treatment
Exposure to CO$_2$-containing water increased $tcpO_2$ (44 oC) from 63.8 mmHg to 71.3 mmHg (after 20 minutes) in patients with arterial occlusive disease. The effect of temperature was ruled out by a placebo study using standard water [41].

Transcutaneous $pO_2$ in venous disease
Most investigators have found $tcpO_2$ to be reduced in extreme cases of venous disease (e.g. in venous ulcers), while the results are normal in the unaffected skin. This is distinctly different in arterial disease, where reduced $tcpO_2$ can be detected in a significantly wider area.

An exception represents the liposclerotic skin where the overall $tcpO_2$ is reduced, but to a lesser degree than in the immediate proximity of the ulcer. It has to be pointed out that there is a pronounced overlap with normal values, except at the edge of ulcers where the $tcpO_2$ values are homogeneously lower.

An interesting explanation for the heterogeneity of $tcpO_2$ results was recently given by Roszinski and Smaller [42] who compared noninvasive $tcpO_2$ with invasive (needle electrodes) $pO_2$ determinations in the tissue.

While the results varied very little in normal patients when moving the needle in 1 mm intervals, the same movements of the needle in patients with venous trophic changes yielded alterations of 10-30 mmHg, depending on the severity of the condition.

The reduced $tcpO_2$ values in venous disease, reported by a number of investigators [43, 44, 45, 46, 47, 48, 49] can also be explained by the results obtained with a transparent $tcpO_2$ probe that permits simultaneous vital microscopy [11].

The correlation of $tcpO_2$ and morphologic characteristics also offers an explanation of the overlap reported by many authors. Franzeck et al [11] and, later, Hoffmann et al [50] demonstrated a direct correlation of $tcpO_2$ values with microvascular density.

At sites of white atrophy (atrophie blanche) there was also an unmeasurable $tcpO_2$ level which grew with the increasing numbers of capillaries. Moosa et al [51] confirmed the low $tcpO_2$ values close to venous ulcers, but could demonstrate a significant increase after oxygen inhalation.

Though the increase percentagewise was higher around the ulcers than in the healthy tissues, the final $tcpO_2$ values were still lower. This was interpreted by the authors as a confirmation of the "fibrin cuff" theory, which explains the trophic changes in venous disease by a layer of fibrin surrounding the capillaries thus compromising oxygen diffusion [52].

The lower post-oxygen inhalation $tcpO_2$ values can, however, also be explained by a decreased capillary density as discussed above. Partsch [53] argues that since oxygen inhalation leads to a higher $tcpO_2$ increase in the vicinity of venous ulcers than in the vicinity of arterial ulcers, the factor of diminished blood supply may be less of a contributing factor.

Effect of Drugs on $tcpO_2$ in Venous Disease

Neumann and van den Brock [54] observed a slight but statistically significant increase in $tcpO_2$ in patients with moderate degrees of venous insufficiency, after adminis-
tration of O-rutosides. Similar results were reported previously by Belcaro et al [55].

**Factors Affecting tcpO₂ in Venous Disease**

**Edema**
Edema reduction achieved for instance by external intermittent compression [56] did not influence the tcpO₂ reading which could be interpreted to mean that edema per se has no effect on tcpO₂. This question does not seem to be settled because Kolari et al [39] found an increase in tcpO₂ after edema reduction.

Similarly, Creutzig et al [38] recorded an increase in tcpO₂ (close to the ulcer) after compression (bandaging).

**Elastic Compression**
An interesting method to estimate a so-called venomotor index by comparing tcpO₂ values was obtained by Rooke et al [57] with two different temperatures (42 oC and 45 oC): the ratio of these two values represents the index.

They found in stasis dermatitis a decreased tcpO₂ and a decreased “venomotor” index which improved with elastic compression.
References


