Transcutaneous oxygen tension and capillary morphologic characteristics and density in patients with chronic venous incompetence

ULRICH K. FRANZECK, M.D., ALFRED BOLLINGER, M.D., RENATE HUCH, M.D., AND ALBERT HUCH, M.D.

ABSTRACT The transparent oxygen electrode, recently developed by Huch and his co-workers, permits monitoring of transcutaneous oxygen tension (tcPo2) at defined sites on the capillaroscopic image obtained by videomicroscopy. This combined system has been applied to study the nutritional skin capillaries of patients with chronic venous incompetence (CVI). The results of 44 studies in 17 patients with CVI demonstrated a direct correlation between tcPo2 and density and morphologic characteristics of the superficial capillaries. The mean tcPo2 was 47.7 ± 14.4 mm Hg at the site of incompetent perforating veins of the ankle without major trophic changes. There was no statistically significant difference between the mean values obtained in patients and control subjects (56.8 ± 9.9 mm Hg). Videomicroscopic examination revealed dilated and tortuous capillaries surrounded by halo formations. In areas of hyperpigmentation, induration, and hyperkeratosis, significantly decreased mean tcPo2 (22.5 ± 7.0 mm Hg; p < .001) corresponded to reduced capillary density (<10 capillaries/mm²). In avascular skin areas (scar tissue, white atrophy) tcPo2 was measured at 0 mm Hg. No capillaries, or a greatly reduced number, were visible at such sites, resulting in a distance between capillary and cathode tip of the oxygen sensor of greater than 100 μm. The combined system of tcPo2 measurement and simultaneous videomicroscopy gives new pathophysiologic information on the development of skin ulcers and may be useful for the objective comparison of different therapeutic modalities at the microcirculatory level.


IT HAS BEEN shown recently by intravital capillaroscopy that changes in blood capillaries are frequent in severe cases of venous incompetence.1,2 The fields of white atrophy common in patients with this disease may contain no capillaries at all.3 Moreover, lymphatic microangiopathy is a typical complication of chronic venous incompetence (CVI) and contributes to development of local edema.4

The present investigation focuses on the question of whether the known changes in skin microcirculation in patients with CVI result in a deficient local oxygen supply to the skin. To date, it has not been possible to study capillary morphology and density and flow dynamics while measuring Po2. The recently developed transparent transcutaneous oxygen electrode4 permits simultaneous measurement of the oxygen tension of the skin (tcPo2) and examination of the nutritional skin capillaries at the monitoring site by videomicroscopy.

This combined system was applied in the study of 17 patients with CVI and the results were compared with those obtained in a group of 24 healthy subjects.

Materials and methods

Patients. The CVI group consisted of 17 patients (six women, 11 men) with a mean age of 56 years (range 22 to 76). Forty-four measurements were obtained in this group. The method of selection of sites of measurement is described below.

In 12 patients CVI was caused by deep venous thrombosis (obstruction and/or incompetence of deep veins, incompetent perforating veins) and in five CVI resulted from primary varicose veins with incompetent perforating veins.

Nine patients had trophic skin changes without ulcers and eight had trophic skin changes with ulcers or healed ulcers. The diagnosis was based on patient history, clinical findings, and results of Doppler ultrasound examination. Venograms were obtained in seven patients.

No patient had clinical evidence of peripheral arterial occlusive disease. Palpation of pulses, auscultation, and photoplethysmography at the big toe were normal in all cases.

Control subjects. The group of 24 healthy subjects consisted of 17 men and seven women with a mean age of 48 years (range

From the Department of Internal Medicine, Policlinic, Angiology Division and Department of Obstetrics, Perinatal Physiology, University of Zurich.

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Address for correspondence: Prof. Dr. A. Bollinger, Department of Internal Medicine, Policlinic, Angiology Division, University Hospital, CH-8091 Zurich, Switzerland.

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19 to 75). They had no clinical signs of peripheral atherosclerosis or venous disease. In this group 35 measurements of tcPO₂ were obtained (11 bilateral measurements).

Protocol. The tcPO₂ measurement is basically a polarographic determination, by means of a modified Clark-type electrode, of molecular oxygen diffusing to the skin surface. Local hyperemia is necessary to measure PO₂ on the skin surface, which has a close relationship to changes in arterial PO₂. The hyperemic condition is achieved by heating the silver/silver chloride anode of the electrode (45°C). The PO₂ signal results from the reduction current at the platinum cathode, which is proportional to the amount of oxygen diffusing to the skin surface.

The combined technique of monitoring tcPO₂ and videomicroscopic examination of the skin has been described recently. Figure 1 shows a prototype of the new transparent oxygen electrode. In the transparent glass cylinder placed in the center of the electrode a single 100 µm platinum cathode with a tip diameter of 15 µm is sealed. The anode (silver/silver chloride) ring surrounds the transparent center part and can be heated by a built-in heating element. The temperature is controlled by a NTC thermometer. For all measurements the electrode was heated to 45°C, which resulted in a skin surface temperature of 43°C. The electrode was covered by a 25 µm Teflon membrane, which was not a significant optical barrier.

The calibration of the electrode is the same as that on commercially available tcPO₂ probes and is based on the actual barometric pressure (room PO₂) and against zero PO₂ achieved with a zero solution.

The reproducibility of tcPO₂ measurements has been studied, and accuracy was found to be within the 95% confidence limit.

The new transparent oxygen electrode was connected to the Servomed Oxymonitor SM 361 (Hellige GmbH, F.R.G.; Litton Medical Electronics, U.S.A.). The electrode is attached to the skin surface by means of double-sided adhesive ring tape.

The videomicroscopic system used was identical to that described in detail for use in intravital fluorescence videomicroscopic studies. Basically, it consists of an incident-light microscope (Wild + Leitz), a sensitive videocamera (Cadmium-Selenide-Vidicon, Siemens), a television monitor (Philips), and a videotape recorder (BK-204, Grundig). The light is provided by a mercury vapor lamp (HBO 100, Osram) connected to a direct-current power amplifier (EI-YH5P/L, Irem). The microscope is mounted on an especially solid stage (Wild + Leitz, Foba) that permits three-dimensional adjustment of the objectives to the glass part of the electrode and the skin area of interest, respectively.

For overview recordings a plane objective of 2.5/0.08 was used, which provided a final magnification of 180 times on the television monitor (screen diameter 60 cm). Details were examined with an iris-diaphragm objective of 10/22 (Leitz), resulting in a final magnification of 750 times (figure 2).

The skin of each subject was shaved at the selected measuring site, stripped with cellophane tape (10 times), and cleansed with the use of alcohol tabs. After attachment of the electrode as described above, initial focusing was performed on the 100 µm cathode lead. Continuously focusing along the platinum cathode down to the 15 µm tip allowed a well-focused image of the papillary capillaries to be obtained. The procedure was recorded on videotape, which provided accurate localization of the cathode tip in relation to the adjacent capillaries. Simultaneously recordings of tcPO₂ were made on the strip-chart recorder of the oxymonitor. The tcPO₂ readings were taken 10 to 15 min after attachment of the electrode. The total time needed for the measurements was about 30 min, including setting up and recording.

Simultaneous measurements of tcPO₂ and videomicroscopic examinations were performed at various skin sites at which capillary images characteristic of CVI were obtained, as follows: (1) skin areas without marked trophic lesions in the neighborhood of incompetent perforating veins at the medial ankle region, (2) hyperpigmented, indurated, and hyperkeratotic skin sites in the same area, (3) border zones of venous ulcers and spots of white atrophy, and (4) areas of scar tissue from healed venous ulcers and central areas of fields of white atrophy.

In the control group the measurements were also made in the medial ankle region. All patients and healthy subjects were supine for at least 20 min before measurements were obtained. The room temperature was between 22° and 24°C.

Statistical analysis. The unpaired Student’s test was performed by use of a Hewlett-Packard 41C calculator. All data are expressed as means, SDs, and ranges.

Results

Control group. In the 24 healthy subjects (n = 35 measurements) mean tcPO₂ of the medial ankle region was 56.8 ± 9.9 mm Hg (range 38 to 79). The superficial capillaries (medial ankle and lower leg region) were homogeneously distributed. The capillary density averaged 45 capillaries/mm². Depending on skin transparency, usually only the vertex of the hairpin-shaped capillary loops could be observed (figure 3). The arteriolar and venular limbs were seen only in a few loops running parallel to the skin surface.

Patients with CVI. In patients with CVI the mean tcPO₂ was 47.7 ± 14.5 mm Hg (range 21 to 83) when the measurements were obtained from the medial ankle area over incompetent perforating veins and without major trophic skin changes. This value did not differ significantly from that in control subjects (p > .05). The simultaneous videomicroscopic examination revealed dilated and tortuous capillaries in this area, which frequently appeared to be surrounded by a distinct halo structure. The number of capillaries was not

FIGURE 1. Prototype of the new transparent oxygen electrode (view from the skin side of the electrode). The diameter of the central glass cylinder is 4.5 mm. The 100 µm initial lead of the platinum cathode is visible, but the 15 µm tip of the oxygen sensor can only be seen through the microscope.
FIGURE 2. Experimental set-up, with the electrode attached at the medial ankle region. Above is the incident-light microscope with the television camera connected via television monitor to the videotape recorder in the background. The oxymonitor is in the right lower corner.

significantly reduced ($p > .05$) compared with that in healthy subjects and averaged $40/\text{mm}^2$.

Over skin areas with hyperpigmentation, induration, and hyperkeratosis $\text{tcPO}_2$ averaged $22.5 \pm 7.0$ mm Hg (range 13 to 26). This value is significantly decreased ($p < .001$) in comparison with that in the control group and in the group of patients without trophic skin changes. The capillary density was less

FIGURE 3. Videomicroscopic image of the medial ankle region of a healthy subject. The capillary density is 48 per $\text{mm}^2$ and $\text{tcPO}_2$ was measured at 73 mm Hg. The arrow indicates the tip of the platinum cathode (picture taken from single frame of the videotape on the television monitor).
than 10/mm² and the alterations in capillary morphology increased in proportion to the reduction in their numbers. The remaining capillaries that were observed were extremely dilated, with irregularly shaped arteriolar and venular limbs. Microvessels of the subpapillary venous plexus could sometimes be observed.

In the center of spots of white atrophy no capillaries were visible, whereas in the border zones they were enlarged and meandering. These capillaries sometimes had a glomerulus-like appearance, density was reduced (figure 4), and mean tcPo₂ reached 24.0 mm Hg (range 12 to 44) in these border zones.

The considerably large range of single Po₂ determinations is the result of the varying distance between oxygen sensor and adjacent capillaries in the border zones of white atrophy and in areas of decreased capillary density. This distance is of great importance for tcPo₂ measurement, since greater distance results in lower Po₂ values and vice versa. The same applies for the center areas of spots of white atrophy, where no capillaries were observed; tcPo₂ values were measured at 0 or close to 0 mm Hg at these sites. The distance between the cathode tip of the oxygen sensor and the capillary was more than 100 μm when the tcPo₂ was extremely reduced. An illustrative example is shown in figure 5.

Figure 6 is a plot of individual and mean tcPo₂ values according to clinical and microscopic findings at the site of measurement.

No harmful side effects (burns, blisters) of the heated electrode were noted in control subjects or patients. However, the time period of electrode attachment never exceeded 30 min.

**Discussion**

tcPo₂ reliably reflects levels and changes in arterial Po₂ under normal circulatory conditions. However, local oxygen availability can be quantitated transcutaneously if the measurements are obtained from areas of the skin in which there are pathologic changes in the microcirculation. Reduced tcPo₂ values have been noted in patients with peripheral arterial occlusive disease, skin transplants, and diabetic microangiopathy.9-13

The present study demonstrates that the known microangiopathy in patients with severe CVI1,2 leads to decreased tcPo₂ values in the medial ankle region. This confirms earlier results obtained by conventional tcPo₂ electrodes,14,15 which give no information on the microvascular involvement. The development of an electrode with a transparent center4 permits correlation of capillary morphology and density with tcPo₂ at the site of measurement. It appears that tcPo₂ levels depend on capillary density. In patients with CVI capillary mor-

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**FIGURE 4.** Composite photograph (several frames taken from the television monitor) showing part of the white atrophic center (right lower corner) and of the border zone in a patient with severe CVI. Note the coiled, glomerulus-like convolutes of the proliferated capillaries of the border zone.
Phenomenology and density are variable from site to site, even within a given patient. Characteristic extremes are white atrophy with a center completely devoid of perfused capillaries and capillary areas with more or less pronounced changes in morphology but normal density. In between are skin regions showing enlarged, meandering capillaries and decreased capillary density.

In contrast to these findings, Burnand et al.\textsuperscript{16} reported increased numbers of capillaries in histopathologic sections from patients with severe CVI. It is possible that the tortuous capillary convolutes that may even take a glomerulus-like aspect (figure 4) result in a falsely high capillary count in histologic sections. In this study the superficial capillary density determined by direct videomicroscopy was normal in areas with no or minor trophic changes and decreased in regions in which there were marked alterations.

The \( \text{tcPO}_2 \) measurements corresponded well to the four types of capillary morphology and density described (figure 6). Normal or subnormal values were found in areas without rarefaction of capillary loops, reduced values were obtained over coiled, enlarged, and rarefied capillaries, and values approached zero in avascular regions of white atrophy. In the latter lesion small tracer substances (Na fluorescein) needed extremely long times to diffuse into the center of the

\textbf{FIGURE 5.} A, View through the electrode of the almost avascular area (white on the photo) of scar tissue (healed venous ulcer) in a patient with severe CVI. On the right and left side capillaries of the revascularization zone are visible. The arrow indicates the tip of the sensing cathode. \textit{B, tcPO}_2 \textit{at such sites with extremely reduced capillary density and irregular distribution was in the proximity of 0 mm Hg.}
field. Both findings are in agreement with the clinical experience that spots of white atrophy are sites predisposed to venous ulcer formation.

A direct correlation between the number of capillaries per square unit and tcPO$_2$ was not possible. In the border areas of white atrophy in which there were meandering loops it was difficult to identify single capillaries. For this reason we preferred to describe capillary density by class (<10/mm$^2$, for example). In hyperkeratotic areas the thickness of the epidermis is increased, thus enlarging the diffusion distance to the skin surface and contributing to reduced tcPO$_2$ as well as to low capillary density. This effect was minimized by stripping the skin before the application of the tcPO$_2$ probe. Furthermore, it should be realized that the skin in areas of white atrophy may be atrophic.\footnote{17}

The very low tcPO$_2$ values in areas without capillaries and the reduced values in regions with decreased capillary density document that CVI may lead to marked local ischemia. The values are comparable to those measured in patients with severe peripheral arterial occlusive disease.\footnote{10, 11} However, CVI ischemia is a more localized phenomenon, affecting mostly the medial ankle region, because of the reduction in capillary density and morphologic alterations, whereas arterial occlusion affects larger areas of the lower extremity, especially of the foot, and decreased tcPO$_2$ results from the impairment of arterial blood flow.

The results obtained by the combination of videomicroscopic examination and tcPO$_2$ measurements show that the terminal vascular bed plays a crucial role in the development of the trophic skin lesions in patients with CVI. The described technique is well suited for the objective evaluation of various treatment modalities at the microcirculatory level.

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