Transcutaneous oxymetry as predictive test of peripheral vascular revascularization in haemodialysis population

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Abstract
Background. Peripheral arterial disease (PAD) occurs frequently among haemodialysis patients but it is underestimated. Vascular treatment and amputations are more frequent in end stage renal disease (ESRD) population compared to the general population possibly because of a diagnosis of PAD delayed. Transcutaneous oxymetry (TcPO2) is commonly used in vascular medicine to reflect local arterial blood flow and skin oxygenation. The aim of this study was to assess the accuracy of the TcPO2 measurements to screen PAD and to predict vascular outcomes in haemodialysis population.

Methods. In a 1-year prospective study, the value of TcPO2 was assessed in a cohort of 48 patients when starting haemodialysis.

Results. Twenty one patients had at least one vascular stenosis (42%) on Doppler examination and were considered as affected by PAD. At inclusion a pathologic resting TcPO2 (<40mmHg) was found in 13 patients (29%). A severe ischemia (TcPO2 <30mmHg) was noted in 8 patients (16.7%) and a critical limb ischemia (TcPO2 <10mmHg) in 3 patients (6%). Eleven (25.5%) and 6 patients (15%) had a TcPO2 <40mmHg at 6 and 12 months respectively. During the follow-up, death was seven times more frequent in patients with abnormal TcPO2 at T0 compared to patients with normal TcPO2 (38% vs 5.7%; p = 0.04). Revascularization (n = 6) or amputation (n = 5) were required for 5 patients. TcPO2 was pathologic in all patients and legs requiring a vascular treatment. The sensitivity, specificity, positive predictive value and negative predictive value were 100%, 85.2%, 38% and 100% respectively.

Conclusions. This study confirms the underestimated PAD diagnosis and the severity of PAD in haemodialysis population. A TcPO2 less than 40mmHg at the onset of the haemodialysis could identify patients at high risk of death and patients requiring vascular treatment. Moreover, since haemodialysis seems to be an accelerating factor of atherosclerosis, TcPO2 might be perform as a complement to traditional vascular explorations to assess the distal vascular conditions of limbs of haemodialysis patients.

Keywords: amputation; haemodialysis; microcirculation; revascularization; transcutaneous oxymetry

Introduction
Peripheral arterial disease (PAD) frequently occurs among patients with end-stage renal disease (ESRD) and, when present, is considered as a marker of poor prognosis. [1–3]. In the general population, the ankle–brachial index is the most sensitive and specific non-invasive test performed to screen an asymptomatic PAD [4, 5]. However, the high prevalence of mediacicosis in the ESRD population could be limited to this use [6]. Transcutaneous oxymetry (TcPO2) is another vascular tool commonly used in vascular medicine to reflect local arterial blood flow and skin oxygenation [7, 8]. TcPO2 is influenced by both central arterial oxygen content and local factors, such as tissue perfusion. The use of TcPO2 to quantify the degree of ischaemia is well known and a <30mmHg value of TcPO2 in a decubitus position is considered as a severe ischaemia [9]. In addition, TcPO2 is accurate to predict a primary healing after an amputation [10–12]. Vascular treatment and amputations are more frequent in the ESRD population compared to the general population, [13] possibly because of a delayed PAD diagnosis. Moreover, recent studies have shown that outcomes of lower extremity revascularization in patients with ESRD are inferior to those in non-ESRD controls with a high amputation rate [14]. Therefore, a detection of early-stage PAD is important to improve the prognosis of these patients, who are mostly asymptomatic. However, TcPO2 has been poorly studied in ESRD and no data on its performances has been published to establish a diagnosis of severe ischaemia in haemodialysis patients. In the present study we attempted to assess the accuracy of the TcPO2 to detect severe ischaemia and to predict vascular treatment in an incident haemodialysis cohort.
Value of TcPO2 in haemodialysis patients

Materials and methods

The study was approved by the Rouen University Hospital Ethics Committee, and all patients gave their informed consent before inclusion in the study.

Patients

The study population consisted of incident patients with ESRD undergoing maintenance haemodialysis. All patients were treated with maintenance haemodialysis during the 1-year follow-up. On the other hand, all patients have undergone haemodialysis for no more than 1 month before inclusion. Patients were recruited from two haemodialysis centres, between November 2007 and June 2008, and followed-up prospectively for 1 year. The diagnosis of PAD was exclusively established based on vascular stenosis on ultrasonographic examinations.

Methods

Transcutaneous oxymetry. All the TcPo2 measurements were performed the day after the haemodialysis session to minimize the impact of leg oedema. Thus, TcPO2 measurements were taken at the dorsum of both feet in the first intermetatarsal space with the patient resting in supine position, in an air-conditioned room maintained at 22°C. A double-sided adhesive rings and contact liquid supplied by the manufacturer were used to obtain a hermetic area measurements. TcPO2 was measured as previously described [7, 15] by an electrochemical transducer (TCM™3; Radiometer GMBH, Copenhagen, Denmark). To increase the permeability of the skin in order to oxygen molecules at the measuring site, the transducer was heated to 44°C. The calibration period was, at average, 10 min and the TcPo2 signal was continuously recorded on a computer software for 10 min. A value <40 mmHg is considered as pathological. Severe ischaemia and critical limb ischaemia were retained when TcPO2 measurements were <30 and 10 mmHg, respectively [4, 16, 17].

TcPo2 was measured by an electrochemical transducer, which was placed at the dorsum of both feet in the first intermetatarsal space. A double-sided adhesive ring and contact liquid supplied by the manufacturer were used to obtain a hermetic area measurements. Measurements at this location have shown values similar to more proximal measurements over the dorsal pedal artery, and the reproductibility was good. The skin oxygen partial pressure was determined by measuring the oxygen reduction current by means of measuring cells. To increase the permeability of the skin to oxygen molecules at the measuring site, the transducer was heated to 44°C. The calibration period was, at average, 10 min and the TcPo2 signal was continuously recorded on computer software for 10 min.

Ultrasoundography. Examination of the inferior limbs arteries was performed with an ultrasound device equipped with a 3–11 MHz linear array high-resolution transducer using a dedicated software for B-mode analysis. In the beginning of each ultrasonographic examination, the ankle blood index (ABI) was systematically calculated as previously described [18]. Afterwards, the following parameters were measured: the presence of atherosomatous plaques in the vessel, Doppler blood flow parameters and vascular calcifications.

Follow-up

Follow-up visits were scheduled at 6 and 12 months from study inclusion. During the follow-up visits, TcPO2 measurements were calculated and patients were asked about the occurrence of vascular treatment (revascularization or amputation). Death from any cause was noted.

Statistical analysis

Demographic data and clinical features were analysed using descriptive methods. Quantitative variables were expressed as mean ± SD and compared using the Student-t-test or Mann–Whitney U-test as appropriate. A comparison between groups was performed using chi-square test and in the 2 × 2 tables, Fisher’s exact test as appropriate. Qualitative variables were compared using the Mac Nemar test. Statistical analyses were performed using STATVIEW (Version 5.0 de SAS Institute Inc.) programme. P-value <0.05 was considered statistically significant.

Results

Baseline patients characteristics

A total of 48 patients (mean age 66 years old) were included in the study. The patient population was 26 males (55%) and 22 females (45%). Demographic characteristics and ultrasonographic results are listed in Table 1. Twenty-one patients had at least one vascular stenosis (42%) and were considered as affected by PAD. At inclusion (T0), an abnormal ABI <0.9 was found in 15 patients (33%). The concordance with the ultrasonography examination was perfect except for one patient who had an ABI <0.9, whereas no vascular stenosis was found.

We distinguished four groups of renal diseases responsible for ESRD: diabetic nephropathy (27%), vascular nephropathy (37.5%), chronic glomerulonephritis (16.6%) and others (18.9%) such as chronic interstitial nephritis, polycystic kidney disease or nephrectomy.

Table 1. Baseline characteristics of the patients

<table>
<thead>
<tr>
<th>Co-morbid conditions</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female</td>
<td>26/22</td>
<td>55/45</td>
</tr>
<tr>
<td>Diabetes</td>
<td>15</td>
<td>30.6</td>
</tr>
<tr>
<td>Hypertension</td>
<td>42</td>
<td>87.7</td>
</tr>
<tr>
<td>Smokers</td>
<td>16</td>
<td>34.7</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>35</td>
<td>73.5</td>
</tr>
<tr>
<td>Ischaemic cardiopathy</td>
<td>10</td>
<td>20.4</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>8</td>
<td>16.3</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>11</td>
<td>24.5</td>
</tr>
<tr>
<td>Vascular stenosis</td>
<td>21</td>
<td>42.8</td>
</tr>
<tr>
<td>Echographic calcifications</td>
<td>39</td>
<td>81</td>
</tr>
</tbody>
</table>

Fig. 1. Evolution in percentage of pathologic TcPo2 during the follow-up.

TcPO2 results

At T0, a pathologic TcPO2 (<40 mmHg) was found in 13 patients (29%). Eleven (25.5%) and 6 (15%) patients have a TcPO2 <40 mmHg at 6 and 12 months, respectively. When the pathologic TcPO2 was analysed for each leg of patients, the proportion of TcPO2 <40 mmHg was 21.8% (n = 21). At 6 and 12 months, these proportions of abnormal TcPO2 values were, respectively, 22.9% (n = 19) and 6.5% (n = 5). No statistical difference was observed between the values at each follow-up visit (Figure 1).

Equally, no difference was noted at inclusion and during the follow-up for frequency of TcPO2 <40 or 30 mmHg.
between diabetics and non-diabetic patients. The mean level of TcPO2 at inclusion was similar in both groups (46 mmHg in the diabetic group and 53 in the non-diabetic group; P = 0.20).

At inclusion, a severe ischaemia (TcPO2 <30 mmHg) was noted in eight patients (16.7%) and critical limb ischaemia (TcPO2 <10 mmHg) in three patients (6%). All these patients were asymptomatic. During the follow-up, at 6 and 12 months, seven and three patients had a severe ischaemia. No patient could be considered as having critical limb ischaemia at 6 and 12 months.

When PAD was diagnosed, nine patients had a pathologic TcPO2 value (43%) and seven patients had a TcPO2 measurement <30 mmHg.

TcPO2 and clinical outcomes

The different outcomes are listed in Table 2. We did not observed ulceration in patients at inclusion, however, during the follow-up, five ulcerations occurred which did not compromised the TcPO2 measurements. Seven patients (14.5%) died before the end of the follow-up. Five of the seven patients who died had an abnormal TcPO2 (71.5%). On opposite, patients alive had normal TcPO2 in 80.4%. Death was seven times more frequent in patients with abnormal TcPO2 at T0 compared to patients with normal TcPO2 (38 versus 5.7%; P = 0.04). Revascularization (n = 6) or amputation (n = 5) was required for five patients. For five of the six revascularizations, vascular surgeons have performed an angioplasty with a stenting. In one case, the patient underwent to a peripheral vascular bypass. TcPO2 was pathologic in all patients and legs requiring a vascular treatment. The sensitivity, specificity, positive predictive value and negative predictive value were 100, 85.2, 38 and 100%, respectively.

Discussion

The TcPO2 is a non-invasive method reflecting local arterial skin blood flow and oxygenation and can be used as a means of determining severity and clinical progression of PAD [7]. TcPo2 is also a complement to macrocirculatory investigations in the prediction of the outcome of chronic foot ulcers [19, 20]. Correlations between values of TcPO2 and clinical stage of PAD have been previously established [9]. In our study, TcPO2 values were <40 mmHg in 13 patients (29%) revealing a frequent and unknown PAD. In addition, eight patients at inclusion had a TcPO2 <30 mmHg reflecting a permanent ischaemia, whereas three of them had a critical limb ischaemia (TcPO2 <10 mmHg) without any vascular symptoms. Thus, in our cohort, PAD was not only frequent but also severe with poor local and general outcomes for patients. Indeed, the rate of amputation in our cohort was greater than usually (9/100 patients per year versus 5% at 5-year follow-up) [17, 21]. TcPO2 was pathologic in all patients (n = 5) and in all legs (n = 11) requiring a vascular treatment. The mean value of TcPO2 was 26.6 mmHg in patients requiring vascular treatment. In others studies, the value of TcPO2 to predict limb loss or revascularization has been already established in the general population and a different cut-off of TcPO2 has been suggested. Usually, a value of TcPO2 <20 mmHg is retained to be predictive of amputation [22]. However, data available in the haemodialysis population are poor and TcPO2 has been exclusively evaluated as a marker of haemodynamic changes occurring during a course of haemodialysis but never as a test competent to assess the vascular state of patients. Thus, Weiss et al. [23] in 1998 have shown that TcPO2 dropped significantly during haemodialysis. These changes were more pronounced in patients with PAD and persisted after dialysis, but in this study the resting TcPO2 values were in the normal range. Equally, Santesson et al. have shown that the peripheral microcirculation by measurement of TcPO2 was impaired during haemodialysis. This effect of haemodialysis on peripheral blood perfusion was seen in diabetic and non-diabetic patients but patients with peripheral arterial occlusive disease seemed more susceptible to TcPO2 reduction during haemodialysis. Authors concluded that a dialysis-associated lower limb hypoxia may be a factor leading to the increased incidence of critical limb and gangrene in ESRD population [24].

Our study confirms the underestimated PAD diagnosis in the haemodialysis population and, for the first time, the predictive value of TcPO2 for vascular treatment in this population. According to us, the TcPO2 should be performed at least once, as a complement to traditional vascular explorations in every incident patients with ESRD undergoing maintenance haemodialysis, in order to assess their distal vascular conditions. In this way, an appropriate haemodialysis strategy could be then established.

Conflict of interest statement. None declared.

References

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