Reproducibility of proximal and distal transcutaneous oxygen pressure measurements during exercise in stage 2 arterial claudication

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Aim. Although transcutaneous oxygen pressure measurements (tcpO2) are largely used in the investigation of vascular patients, its reproducibility is still debated. Indeed an unpredictable gradient exists between arterial and transcutaneous oxygen pressure. We hypothesised that indices taking into account changes over time and independent of absolute starting values would be more reproducible than other indices.

Methods. Experimental design: comparative test-retest procedure (1 to 13 days between tests). Settings: institutional practice, ambulatory care. Patients and participants: 15 subjects with stage 2 claudication. Interventions: tcpO2 recordings at rest and at exercise during the 2 treadmill tests. Measures: calculation of the Delta-from-rest of oxygen pressure index (limb tcpO2 changes minus chest tcpO2 changes), of the resting — or minimal values attained during exercise — of absolute tcpO2 and of the regional perfusion index (regional perfusion index: ratio of limb to chest).

Results. Both absolute tcpO2 and regional perfusion index at rest showed low reproducibility. During exercise the best reproducibility was attained through Delta-from-rest of oxygen pressure index calculation. Equations from the linear regression analysis (test 2 versus test 1) were 0.88x-4.2 (r²=0.82) at the buttock level and 0.82x-3.8 (r²=0.80) at the calf level.

Conclusion. TcpO2 measurement on the calf or buttock during exercise, is a reproducible measurement in patients with vascular claudication, specifically when corrected for exercise-induced systemic pO2 changes through Delta-from-rest of oxygen pressure calculation.

Among the various non-invasive investigations that can be used in vascular patients is transcutaneous oxygen pressure measurement (tcpO2). The investigation has proved useful in patients with critical limb ischemia but is less frequently used in patients with stage 2 claudication. As compared to ankle pressure and Doppler recordings, tcpO2 appears as a sophisticated and time consuming technique although it has the theoretical advantage of being measurable on multiple sites during (and not only following) exercise. Thus, in stage 2 lower extremity arterial disease, tcpO2 is not recommended as a primary investigation. Nevertheless, it can provide interesting complementary information on patients suffering simultaneous disease of vascular and non-vascular origin or when arterial pressures cannot be performed. Indeed, we have recently shown that tcpO2 can be used at the buttock level to detect ischemia resulting from lesions located in the arterial tree towards the hypogastric circulation. The use of a chest reference electrode allows for the estimation of exercise-induced systemic hypoxemia as a possible cause of decreased tolerance of moderate arterial lesions. Multiple variables derived from tcpO2 recordings at rest and/or during exercise have been proposed among which some take into account the changes observed on the chest reference electrode (regional perfusion index) and some do not (absolute values). We recently proposed the use of the Delta-from-rest of oxygen pressure index rather than the usually proposed variables. The expected advantage of this index is the fact that it still takes into account the systemic changes at the
chest reference electrode, but contrary to the regional perfusion index it is independent of absolute starting values. We showed that the Delta-from-rest of oxygen pressure index provided the highest accuracy although test-retest reproducibility was not performed. We hypothesised

Figure 1.—Typical example of 2 consecutive tests performed on the same subjects with a 1-day interval. The walking period is presented as the rectangle. For simplification only one measurement every 30 s is shown. The chest values are presented as crosses. Squares are buttock and circles are leg values. Right is presented in white, left in black. RPI is regional perfusion index, DROP is decrease from rest of oxygen pressure.
that Delta-from-rest oxygen pressure would be more reliable than other indices derived from tcpO2 recordings and performed a study to test this hypothesis at both a proximal and distal site.

**Materials and methods**

**Populations**

A prospective study was undertaken on 15 patients referred for a walking test complaining of stage II claudication with an estimated maximal walking distance ranging 100-1 000 m. Patients were requested to perform 2 identical tests at an interval of 1 to 13 days.

Patients were 15 males, 60±11 years, 172±7 cm, height, 73±14 kg weight (mean±standard deviation). The protocol was conducted according to the declaration of Helsinki and the protocol was approved by the Institutional Review Board of Angers. All patients gave informed consent to the study.

**Exercise procedure**

After a 20 minutes resting period, patients were placed in a room at a constant temperature of 21±2°C. The treadmill test was performed using a 10% slope with a modified Strandness test procedure to progressively reaching 3.2 km.h⁻¹ in 4 minutes. The speed started at 1 km.h⁻¹ and increased by 0.5 km.h⁻¹ every minute up to 2.5 km.h⁻¹. After 1 min at this rate, the treadmill speed was stabilised at 3.2 km.h⁻¹ for an additional 16 minutes. Patients were encouraged to perform at the highest possible speed for the longest possible time. Exercise was discontinued on the patient’s request or, in the absence of claudication, after a total duration of 20 minutes.

**TcPO2 measurements**

Measurements were performed using 5 tcpO2 devices (TINA TCM3 Radiometer, Copenhagen DMK). A one-point calibration to air was performed before each experiment. The calibration value was set according to actual barometric pressure. The temperature of the probe was 44.5°C, to allow for maximal vasodilatation, thereby decreasing the arterial to skin surface oxygen pressure gradient. Afterwards tcpO2 measurements were automatically temperature corrected to 37°C by the transcutaneous device. A reference electrode was placed on the chest to measure eventual systemic changes. One electrode was positioned on each limb, 4 to 5 cm proximal to the lateral malleolus, and one on each buttoc, 4-5 cm posterior to the bony prominence of the trochanter. Before fixing the electrode, the skin was cleaned and dead cells from the epidermal surface were removed by gently rubbing the skin with gauze. Once the electrodes were in position, a pretest heating period of 15 to 20 minutes in the standing position was required to allow stable resting values to be achieved. Stable values were defined as tcpO2 changes <2 mmHg within 5 minutes. A 12 lead electrocardiogram was used to control the heart rate and to detect any arrhythmia or abnormal depolarisation events during the whole procedure. tcpO2 values were recorded for 2 minutes in the standing position before the treadmill was started, during the walking period and for 10 minutes in the standing position following the end of the exercise test. The data were recorded on a computer via an analogue to digital converter (Biopac System, Inc., California) with a sample rate of 2 Hz, on 16 bits. Moving averaging over 10 samples was performed on raw data to decrease the electronic artefacts on the signal. Then the values were averaged over 5 s intervals for further analysis. The tcpO2 values at rest were the mean of tcpO2 values over the 2 minutes of the resting period (24 intervals of 5 s) and either expressed in absolute values (pO2 at rest) or as a percentage of the chest reference (regional perfusion index at rest). The minimum absolute value and minimum of percent of the chest value (min-regional perfusion index) were the lowest values recorded on a 5-s interval during or in the 10 min following exercise. Lastly, at each 5-s interval, the absolute tcpO2-change from rest at each ankle

<table>
<thead>
<tr>
<th>Buttock</th>
<th>Limb</th>
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<tbody>
<tr>
<td>pO2 at rest (mmHg)</td>
<td>59+17 65+21</td>
</tr>
<tr>
<td>Minimal pO2 (mmHg)</td>
<td>77+13 81+14</td>
</tr>
<tr>
<td>Regional perfusion index at rest (%)</td>
<td>101+14 108+22</td>
</tr>
<tr>
<td>Minimal regional perfusion index (%)</td>
<td>70-25 75-27</td>
</tr>
<tr>
<td>Delta-from-rest of oxygen pressure (mmHg)</td>
<td>-22+15 -25+16</td>
</tr>
</tbody>
</table>
was corrected with the corresponding absolute value of the chest electrode tcpO2-change, chest-tcpO2 changes being subtracted from (if chest tcpO2 increased) or added to (if chest tcpO2 decreased) from the results of tcpO2 changes at the limb. As for the previous indices, the lowest negative value resulting from this calculation on a 5-s interval during exercise or in the 10 min following exercise was used. This maximal decrease of Delta-from-Rest of oxygen pressure value is expressed in mmHg. Determination of the characteristic point was automated through a home made computerised program.

Analysis of the results

We used the same descriptive approach for all variables with a Bland-Altman representation and equation for the regression line using the least-square method for test-retest scatterplot, \( r^2 \) Spearman’s coefficient of correlation and p value. According to the recommendation of Atkinson and Nevill,\(^4\) Bland-Altman representations have

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Figure 2.—Bland-Altman representations at the buttock level for the different parameters studied: resting (A) or minimal (C) pO2 in mmHg, resting (B) or minimal (D) regional perfusion index in arbitrary units, and decrease from rest of oxygen pressure (E) in mmHg.
been adapted in such a way that the scale used to study the test-retest differences (Y axis) is, in all cases, half of the one used on the X-axis to estimate the mean of test-retest values. Thus even in case of a heteroscedastic distribution (difference proportional to the mean) of the test-retest differences for one of the studied variables, the representation of the Bland-Altman plot for the data of this variable provides an estimation of the difference to mean ratio. For all statistical tests, a 2-tailed probability level of p less than 0.05 was used to indicate statistical significance.

**Results**

Satisfactory recordings were obtained in every subject. A typical example of 2 consecutive tests on the same subject is presented in Figure 1.
Subjects reported unilateral (n=2) or bilateral (n=4) proximo-distal claudication, unilateral (n=1) or bilateral (n=1) isolated proximal claudication, unilateral (n=4) or bilateral (n=3) isolated distal claudication during the treadmill test.

Table I shows the values for each parameter (mean±SD of the 15 subjects). Individual values being the average of test 1 and test 2. Although many subjects suffered claudication at the limb level due to lesions on distal arteries, values at the ankle level are constantly higher than those found at the buttock level as a result of increased hydrostatic pressure in the standing position.

Table II.—Slope, intercept and r² Spearman-coefficient of correlation resulting from the linear regression analysis for the different parameters studied between the 2 tests. * p<0.05; ** p<0.001, *** p<0.0001.

<table>
<thead>
<tr>
<th>Buttocks</th>
<th>Slope</th>
<th>Intercept</th>
<th>r²</th>
<th>p</th>
<th>Buttocks</th>
<th>Slope</th>
<th>Intercept</th>
<th>r²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>tcpO₂ at rest</td>
<td>0.40</td>
<td>48</td>
<td>0.20</td>
<td>*</td>
<td>0.61</td>
<td>31</td>
<td>0.51</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Minimal tcpO₂</td>
<td>-0.02</td>
<td>108</td>
<td>0.00</td>
<td>N.S.</td>
<td>0.87</td>
<td>19</td>
<td>0.40</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Resting regional perfusion index</td>
<td>0.25</td>
<td>45</td>
<td>0.05</td>
<td>N.S.</td>
<td>0.70</td>
<td>18</td>
<td>0.68</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Minimal regional perfusion index</td>
<td>0.28</td>
<td>55</td>
<td>0.10</td>
<td>N.S.</td>
<td>0.63</td>
<td>32</td>
<td>0.51</td>
<td>**</td>
<td></td>
</tr>
<tr>
<td>Decrease from rest of oxygen pressure</td>
<td>0.88</td>
<td>-4.2</td>
<td>0.82</td>
<td>***</td>
<td>0.82</td>
<td>-3.8</td>
<td>0.80</td>
<td>***</td>
<td></td>
</tr>
</tbody>
</table>

Discussion and conclusions

Transcutaneous oxygen pressure measurement, has been utilised for years to estimate arterial pO₂ in adults and in the assessment of lower extremity arterial disease. The transcutaneous analysis of partial oxygen pressure is based on a Clark polarographic electrode adapted for application to the skin surface. The skin is locally heated to produce local hyperemia and thus arterialisation of the local capillary circulation. Although local heating above the temperature of arterial blood displaces the oxyhemoglobin dissociation curve to the right producing an increase in pO₂ at a given hemoglobin saturation, tcpO₂ is generally inferior to arterial pO₂. Indeed, measured pO₂ at the surface of the skin is highly dependant on skin thickness and capillary density, and decreases with the presence of local edema, dead cells, local increased oxygen consumption (e.g. inflammation). Thus a transcutaneous gradient of up to 50 mmHg can be found. Changes from day to day of tcpO₂ at rest are reported to differ by 20-25% or less. Although satisfactory reproducibility has been reported in the literature, recent studies advocate against tcpO₂ as a non-reproducible technique. Indeed, due to the unpredictable and variable transcutaneous gradient, poor reproducibility of absolute resting values is the major pitfall of the technique. Nevertheless, whatever the resting value is, a close relationship exists between arterial oxygen pressure changes and the changes of tcpO₂ over time in healthy or diseased subjects.

During exercise, with the exception of Carter (that found increases in tcpO₂ values after brief repeated intermittent periods of walking in diseased subjects) all reports show a decrease in tcpO₂ in lower extremity arterial disease, whereas normal subjects show few if any changes. Thus, exercise tcpO₂ has been suggested to be more reliable than resting values in the diagnosis of arterial claudication. Among the variables derived from tcpO₂ recordings at rest and/or during exercise suggested in the literature, it is not surprising that those tacking into account changes overtime during exercise (% decrease from baseline, area under the curve, Delta-from-rest of oxygen pressure, % regional perfusion index) rather than resting absolute values (pO₂ at rest, regional perfusion index at rest) show a higher reproducibility.
In the vascular population, many patients being former smokers suffer from chronic bronchitis. Thus it is not an unusual finding to record significant systemic pO2 changes during walking tests. The use of a reference probe for regional perfusion index \(^3, 23\) or Delta-from-rest of oxygen pressure calculation, \(^1\) takes into account those systemic pO2 changes and should be recommended as compared to pO2min. Delta-from-rest of oxygen pressure has been shown to be more accurate at the buttock level \(^1\) and consistently shows good accuracy at the ankle level (unpublished data). It is also more reliable than regional perfusion index in test-retest procedures. This is not surprising since Delta-from-rest of oxygen pressure not only depends on tcpO2 changes but is independent of the absolute starting values whereas regional perfusion index calculation is influenced by absolute values. A theoretical example is shown in Table III.

Since the diagnostic approach of peripheral arterial disease with Doppler ultrasound recordings and arterial pressure measurements is largely used and validated, there seems to be no purpose in studying tcpO2 during exercise. Claudication is an exercise related symptom and adequate measurement of local ischemia during exercise is useful. Comparable situations occur for the use of exercise thallium-scintigraphy in exercise-related chest pain (as compared to electrocardiography) or oxygen consumption measurement during exercise in exercise induced dyspnea (as compared to resting spirometry). In addition, incapacity to sustain absolute horizontal lying position, cardiac arrhythmia, abnormal rigidity of the vessel wall (specifically in diabetic patients), as well as cutaneous lesions at the ankle, may limit the use of ankle pressures in many subjects. \(^24\) On the other hand, the ability to simultaneously record both systemic and local pO2 changes can be of major importance for patients with limb pain of questionable vascular origin. Indeed, other approaches, such as thallium scintigraphy \(^25, 26\) and near infrared spectroscopy \(^27\) have been recently proposed to estimate perfusion and saturation respectively in each muscle being exercised. Near infrared spectroscopy appears to be an easy and promising technique to estimate muscle pO2 saturation as compared with surface measurement in tcpO2. Nevertheless, the cost of the devices and the sigmoid shape of the relationship between oxygen pressure and haemoglobin saturation are serious pitfalls of the technique.

In conclusion, in stage 2 claudication resting absolute values of tcpO2 before exercise show low reproducibility, whereas exercise derived parameters show a higher reproducibility. Delta-from-rest of oxygen pressure, being independent of initial absolute values shows the highest reliability during exercise. It should be kept in mind that the patients studied in the present investigation have a healthy skin which is not comparable with that seen in advanced disease where, lesions and infections may be present. Thus, it is uncertain whether our results can be extended to more severe vascular patients. This would likely require further specific investigations.

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References
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**Table III.**—Example of the effect of a 20 mmHg decrease at the chest reference electrode due to exercise induced systemic hypoxia and a 50 mmHg decrease in arterial lesions at the level of the limb in a patient with various starting values resulting from different transcutaneous gradients (hypotheses 1-3).

<table>
<thead>
<tr>
<th>Hypothesis 1</th>
<th>Hypothesis 2</th>
<th>Hypothesis 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limb</td>
<td>Chest</td>
<td>Limb</td>
</tr>
<tr>
<td>pO2 at rest</td>
<td>75</td>
<td>65</td>
</tr>
<tr>
<td>Minimal pO2</td>
<td>25</td>
<td>45</td>
</tr>
<tr>
<td>Regional perfusion index at rest</td>
<td>115</td>
<td>—</td>
</tr>
<tr>
<td>Minimal regional perfusion index</td>
<td>55</td>
<td>—</td>
</tr>
<tr>
<td>Regional perfusion index decrease</td>
<td>60</td>
<td>—</td>
</tr>
<tr>
<td>Delta-from-rest of oxygen pressure</td>
<td>-30</td>
<td>—</td>
</tr>
</tbody>
</table>

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