Comparison of two devices for measuring exercise transcutaneous oxygen pressures in patients with claudication

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Summary: Background: We aimed at estimating the agreement between the Medicap® (photo-optical) and Radiometer® (electro-chemical) sensors during exercise transcutaneous oxygen pressure (tcpO2) tests. Our hypothesis was that although absolute starting values (tcpO2rest: mean over 2 minutes) might be different, tcpO2-changes over time and the minimal value of the decrease from rest of oxygen pressure (DROPmin) results at exercise shall be concordant between the two systems.

Patients and methods: Forty seven patients with arterial claudication (65 +/- 7 years) performed a treadmill test with 5 probes each of the electro-chemical and photo-optical devices simultaneously, one of each system on the chest, on each buttock and on each calf.

Results: Seventeen Medicap® probes disconnected during the tests. tcpO2rest and DROPmin values were higher with Medicap® than with Radiometer®, by 13.7 +/- 17.1 mm Hg and 3.4 +/- 11.7 mm Hg, respectively. Despite the differences in absolute starting values, changes over time were similar between the two systems. The concordance between the two systems was approximately 70% for classification of test results from DROPmin.

Conclusions: Photo-optical sensors are promising alternatives to electro-chemical sensors for exercise oximetry, provided that miniaturisation and weight reduction of the new sensors are possible.

Key words: Claudication, exercise, transcutaneous oxygen pressure, peripheral artery disease

Introduction:

Claudication is defined as pain or discomfort in the legs, thighs or buttocks that is worsened by exercise and relieved with rest. It is one of the symptoms of lower extremity peripheral artery disease, but can also occur in patients who have non-vascular problems. In addition to classical tools, the recording of transcutaneous oxygen pressure (tcpO2) during exercise is useful in selected patients with atypical claudication or claudication of questionable vascular origin [1 – 3]. Transcutaneous oximetry (tcpO2) is based on the measurement of the quantity of oxygen that diffuses through the tissue to the skin surface. Therefore, a transcutaneous gradient exists that results in the surface tcpO2 being lower than the arterial underlying oxygen pressure. This gradient is unpredictable and may vary from one probe position to another, resulting in a relatively wide variability of absolute values when two probes are positioned close to one another. An interesting point is that once the probe is in position, the absolute changes observed with transcutaneous oximetry mimic the changes of arterial pO2 provided that the latter changes are relatively slow [4, 5]. Therefore, transcutaneous oximetry at the chest level was proposed as a way of monitoring arterial pO2 in exercising subjects [4, 6]. Beyond the use of tcpO2 to evaluate critical limb ischaemia [7, 8], exercise tcpO2 can be used to monitor tcpO2 changes during exercise in patients with claudication. By replacing the previously proposed regional perfusion index [9], by an index that becomes independent from starting values (i.e.: DROP index), it was shown that exercise tcpO2 accuracy and reliability was increased [10 – 12]. It had previously been shown that exercise tcpO2 using the DROP was specifically useful to confirm the vascular origin of buttock claudication [10]. This DROP index is 85% accurate and reliable to detect arteriographic lesions toward the hypogastric and limb circulation [10 – 12] and allows additional diagnoses in patients with negative or non-contributive ultrasound imaging [1, 13]. Currently, the only tcpO2 available sensor is produced by the Radiometer® company and used on various commercially available devices. This sensor is based on an electrochemical analysis of oxygen. Recently, the Medicap® company has launched a device to measure tcpO2 at the skin level, with sensors using a photo-optical measuring principle, which has been extensively described elsewhere [14]. Both techniques claim to measure oxygen pressure. The potential advantages of the photochemical technique are that it is readily calibrated, the cleaning of the sensors is easy and does not require an expensive membrane change, and the fact that it is possible to connect up to 8 probes. Overall, the price of a 5-probe Medicap® system is much cheaper (30 – 40,000€) than most available 5-probe devices (Perimed®, Radiometer®) that use electrochemical sensors (55 – 65,000 €). The objective of this study was therefore to estimate the agreement between the Medicap® and Radiometer® devices for measuring tcpO2 at rest and during exercise. The DROP index was proposed for exercise tests as a way of removing the transcutaneous
unpredictable gradient. Therefore, our hypothesis was that although absolute values might be different, tcpO2 changes over time and DROP results shall be concordant between the two devices.

**Patients and methods**

This study was approved by the local Ethics Committee of Research. Over a two month period starting in June 2014, all new adult patients were proposed to participate if they were able to understand the study design, agreed to participate and signed a consent form. Written informed consent was obtained from all of the included patients.

**Study population**

Fifty three patients with symptoms of claudication were referred for exercise oximetry to the laboratory over the study period. Forty seven agreed to participate and signed a consent form. Before each test, information recorded in our database included patient’s history and characteristics (gender, age, body mass, stature, ongoing treatments, and ABI at rest on both legs). Usual walking speed was retrieved from a 10 m long walk in the laboratory corridor at the usual regular pace. The characteristics of the included patients are reported in Table I. As shown in Table I, patients were referred for claudication, not on the sole basis of a low ABI or abnormal ultrasound investigation, but also for proximal claudication or claudication of debatable vascular origin when ABI is likely not to be the optimal technique for diagnosis [1].

**Measurements**

**Treadmill test**

The treadmill speed and grade were increased from zero to 3.2 km·h⁻¹ and from zero to 10% within one minute. Then, the speed was stabilised to 3.2 km·h⁻¹ for a total of 15 minutes. At minute 16, if the patient was still able to walk, the speed and grade were progressively increased by steps of 1 minute up to exhaustion or to limitation by symptoms, as previously reported [15]. Roughly one minute increments of this second phase resulted in grade and speed that were comparable to the Bruce protocol values every three minutes [15]. Patients were encouraged orally to perform the highest possible test duration. In all cases, exercise was stopped at the patient’s request in case of claudication up to absolute walking distance (and not when pain first occurs) or in the case of persistent severe arrhythmia, dyspnoea or dizziness. Recovery was recorded for 10 minutes in the standing position. Following each test, we recorded the maximal walking time on treadmill.

**Methods for tcpO2 recordings**

As a routine, after a 20 minute period at rest, patients were installed in a 21 ± 2 °C air-conditioned room. TcpO2 measurements were performed using a 5-modules TC400 (Radiometer®, Copenhagen, DK) and a 5-modules Précise 8008 (Medicap®, Ulrichstein, Germany).

A one point calibration to air was performed before each experiment for both devices and repeated twice for the Radiometer® device. The calibration values were set according to actual barometric pressure. The temperature of all probes was 44.5 °C, to allow maximal local vasodilatation, thereby decreasing the arterial to skin pressure gradient. The tcpO2 measurements were automatically temperature-corrected to 37 °C by the transcutaneous devices. As a standard, one probe of each device

<table>
<thead>
<tr>
<th>Table I: Study population characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender: females/males:</strong></td>
</tr>
<tr>
<td><strong>Age (years):</strong></td>
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<tr>
<td><strong>Ankle to brachial index (ABI):</strong></td>
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<tr>
<td><strong>Ankle to brachial index &lt; 0.90 n (%):</strong></td>
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<tr>
<td><strong>Welch score (%):</strong></td>
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<tr>
<td><strong>Smoking habit:</strong></td>
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<tr>
<td><strong>Active n (%):</strong></td>
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<tr>
<td><strong>Former n (%):</strong></td>
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<tr>
<td><strong>Never n (%):</strong></td>
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<tr>
<td><strong>Body mass index (Kg / m²):</strong></td>
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<tr>
<td><strong>Diabetes mellitus n (%):</strong></td>
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<tr>
<td><strong>Chronic pulmonary bronchitis n (%):</strong></td>
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<tr>
<td><strong>Obstructive sleep apnoea n (%):</strong></td>
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<tr>
<td><strong>Arterial hypertension n (%):</strong></td>
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<tr>
<td><strong>Dyslipidemia n (%):</strong></td>
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<tr>
<td><strong>Ongoing treatments:</strong></td>
</tr>
<tr>
<td><strong>Anti platelet drug n (%):</strong></td>
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<tr>
<td><strong>Anti-diabetes medication n (%):</strong></td>
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<tr>
<td><strong>Beta blockers n (%):</strong></td>
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<tr>
<td><strong>Lipid lowering drug n (%):</strong></td>
</tr>
<tr>
<td><strong>Usual walking speed (km / h):</strong></td>
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<tr>
<td><strong>Blood glucose level (g / l):</strong></td>
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<tr>
<td><strong>Hemoglobin concentration (g / dL):</strong></td>
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<tr>
<td><strong>Systolic blood pressure (mm Hg):</strong></td>
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<tr>
<td><strong>Symptoms by history n (%):</strong></td>
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</tbody>
</table>
tcpO2 values observed on each probe
not calculated.

collection during the test, the CCC was
on one or both probes (almost flat
changes are observed during exercise
of cross-correlation will be low if few
this approach is that the coefficient
of the systems. The disadvantage of
slight differences in the time response
of each probe and may account for
independent from the starting value
in the recovery from exercise. A small
drift may occur during the recording
on tcpO2 probes resulting in the last
DROP value (DROPfinal) observed at
the time of the end of exercise (Tfinal)
being slightly different from zero.
This drift can be rectified to obtain
a drift-corrected DROP (DROP*)
by correcting each DROP value at
time “T” by the following formula:
DROP*D = DROP + T ∙ (DROPfinal/Tfinal).
The minimal DROP and DROP* values
(DROPmin) and DROP*min were
kept for the analysis. DROPmin or
DROP*min are expected to be zero (or
close to zero) in the absence of RBFI.
The lower DROPmin or DROP*min values
correspond to the more severe
RBFI. The previously validated
normal limit for DROP to detect arterio-
graphically proved lesions at the leg
and buttock level is minus 15 mm Hg.
The advantage of the DROP index is
that it is independent from the abso-
late starting value and only accounts
for absolute changes over time. In the
case of probe disconnection during
the test, the DROPmin or DROP*min
were not calculated.

Fourth, we compared the concor-
dance of result classification obtained
with the Medicap* device using dif-
ferent arbitrarily fixed thresholds to
the results observed with the Radi-
ometer* device using the previously
validated (−15 mm Hg) threshold
[10–12, 16].

Statistical analyses
Results are reported as mean +/− standard deviations (SDs) or
numbers and percentages (%). Two-
tailed paired t and MacNemar tests
were used to study the significance
of numerical and categorical data,
respectively. The CCC was calculated
from a cross-correlation over 16 itera-
tions. The agreement for tcpO2est (up
to 5 values per subject) and DROPmin
and DROP*min (up to 4 values per
subject) between Medicap* and Ra-
diometer* was studied by correlation
coefficients. The significance level for
all tests was set as 5 %. We used SPPS
V15.0.3 (SPSS* Inc.) for all tests.

Results
All but one patient were able to walk
at 3.2 km/h and 10 % slope for a
minimum of 30 seconds. The average
walking duration on treadmill was
402 ± 343 sec. In total, 41 (87 %) of
the patients reported lower limb pain
and 15 patients complained of non-
limb symptoms such as dyspnoea
(n = 13), fatigue (n = 2) or dizziness
(n = 1). Heart rate at the end of ex-
ercise was 119 ± /− 22 beats per min.
We observed no probe disconnection
with the radiometer device through-
out the recordings, whereas eleven
Medicap* probes disconnected during
the two minute rest period; of these,
two probes were at chest level.
Therefore, we had 224 tcpO2rest values
for the Medicap* and 235 tcpO2rest values
for the Radiometer*. In the case of
chest disconnection, the DROP index
of all peripheral probes could not be
calculated. As a result, since one chest
and five peripheral Medicap* probes
disconnected during the walking test
or the recovery period, 162 DROPmin
or DROP*min values were available for
the Medicap* vs. 188 values with the
Radiometer* system. A typical example of simultaneous
recording is shown in Figure 1. This
recording is observed in a patient suf-
ferring proximo-distal ischaemia as a
result of bilateral aorto-iliaic lesions.
The figure illustrates how absolute values clearly differed between the two systems but resulted in similar DROP changes over time. It also underlines the possibility of technical drifts occurring during the test with both systems and the interest of correcting this drift in the analysis to reach DROP*_{min} values that were almost similar with the two devices in this case.

Due to disconnections, we had 47 values for the Radiometer®, with average absolute results of 59.5 +/− 13.6, 67.9 +/− 12.7, 68.3 +/− 12.6, 64.6 +/− 10.5 and 68.8 +/− 11.0 mm Hg at the chest, left buttock, left leg, right buttock and right leg, respectively. As shown in Table II, when comparing only data for which both values were available, on average, the Medicap® tcpO₂_{rest} values were higher than the values observed with Radiometer® for the five different probe positions. Overall, Medicap® tcpO₂_{rest} was higher that Radiometer® tcpO₂_{rest} (n = 224) by 13.7 +/− 17.1 mm Hg (p < 0.001), as shown in Figure 2 (upper panel). The average of absolute differences of all available pairs of tcpO₂_{rest} recordings (n = 224) was 17.8 +/− 12.7 mm Hg. Despite the differences in absolute starting values, changes in tcpO₂ over time were generally similar in the different pairs (Radiometer® vs. Medicap®) of probes in close proximity. As a result, more than half of the CCC results were equal or superior to 0.80, as shown in Figure 3. Many of the CCC results that were close to zero or even negative (inverse relationship between the two probes in close proximity) relied on probes with very small changes over time (e.g.: stability over time with minimal changes around the starting value).

As for absolute values, we had 47 values for Radiometer® with average absolute results of –19.5 +/− 16.8, –23.5 +/− 16.1, –25.4 +/− 16.6, –18.6 +/− 15.9, –21.6 +/− 15.5, –18.1 +/− 12.9, and –23.4 +/− 15.7 mm Hg for left buttock.
Results for all probe positions are presented in Figure 2. It is of interest to note that, on average, the DROPmin or DROP*min were higher (smaller decrease during exercise) with Medicap® than with Radiometer® by 3.4+/−11.7 mm Hg and by 4.3+/−10.0 mm Hg, respectively (both p<0.01; n=162). The mean of absolute differences of all available pairs of recordings (n=162) was 9.4+/−9.2 mm Hg for DROPmin and 8.0+/−8.4 mm Hg for DROP*min. Overall, the correlation between the two devices was higher for DROPmin and DROP*min than for absolute values.

Finally, when interpretation of the DROPmin and DROP*min was performed using the −15 mm Hg standard value for Radiometer® and different cut-off values for Medicap®, we found a concordance of approximately 70% for DROPmin and 75 to 80% for DROP*min, as shown in Figure 4. It is interesting to note that the best concordance for DROP*min was observed for a cut-off value of minus 11 mm Hg for the Medicap®, which is consistent with the fact that DROP*min values observed on Medicap® probes were higher compared to those observed on the Radiometer® probes.

Discussion

This is the first report of the use of the Medicap® system in a clinical routine for exercise oximetry. Our results show a reasonable concordance of the tcpO2 changes observed with new photo-optical sensors with those found with the classical electrochemical sensors, at least during exercise. Nevertheless, there seems to be a trend for higher absolute values with the Medicap® than with the Radiometer® sensors.

Our results confirm that changes over time (as estimated through the CCC) are comparable with the two sensors.
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in most cases. Notably, the Medicap® sensors seem to provide smoother curves. This does not seem to result in a slower half time response of the Medicap® sensors, since we tested the two systems in a gas chamber with abrupt pO 2 changes and their half time response was comparable (data not shown). It is possible that this smoothed appearance explains the reduced changes observed with Medicap® compared to Radiometer® but whether electrochemical sensors on a Perimed® device would have provided comparable results was not studied in our experiment. This is one of the limits of the present study.

Additional data are needed to check whether higher absolute tcpO2 values would also be observed with Medicap® sensors than with Radiometer® ones, in patients with critical limb ischaemia (and resting limb values in a low range). This difference might rely on the consumption of oxygen by electrochemical but not photo-optical probes. If a difference was also observed, the use of the new technique would require that the limits proposed for the interpretation of tcpO2 at rest with electrochemical sensor for wound healing or critical limb ischaemia would be adapted for the new photo-optical sensors. It clearly seems necessary to define a specific normal limit at exercise with the Medicap® device, when the normal limit used is probably higher than -15 mm Hg, as suggested in Figure 4. Unfortunately, the number of available arterial images in our population did not allow a direct validation of the Medicap® DROP results versus imaging.

A significant issue that we faced with the Medicap® system was a high rate of probe disconnecting from the skin during the tests. This could result from our team being experienced with radiometer® devices and not with Medicap® ones, although the probe holders are the same. We think that this high rate of disconnection relies on the weight of the sensor head and stiffness of the optic fibre cable compared to the electric fibre of electrochemical probes. Nets around the limb might help to stabilise the probes, and we expect that the manufacturer might miniaturise this new system in the future.

Among others, one of the limits of this work is that we tested a relatively small number of patients in a single centre trial.

Finally, on the one hand, exercise tcpO2 remains a time-consuming technique and is unlikely to replace other non-invasive (ultrasound) approaches in the future. Nevertheless, it can help to diagnose patients with atypical claudication or claudication of doubtful vascular origins [1 – 3, 17] and is presently spreading in France [18] and abroad [19]. On the other hand, we do not report the data for invasive radiological investigations here since radio-vascular investigations were not systematically performed and overall because the exercise-tcpO2 technique itself has been largely validated in the past [10 – 12, 16, 20, 21].

### Table II: Absolute values observed at rest at the different probe positions. All results are in mmHg.

<table>
<thead>
<tr>
<th>Probe Position</th>
<th>Radiometer®</th>
<th>Medicap®</th>
<th>Number of available pairs</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest</td>
<td>59.9 +/− 13.5</td>
<td>66.9 +/− 18.2</td>
<td>45</td>
<td>0.036</td>
</tr>
<tr>
<td>Left buttock</td>
<td>68.5 +/− 12.9</td>
<td>81.3 +/− 17.5</td>
<td>44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Left leg</td>
<td>68.7 +/− 12.4</td>
<td>84.7 +/− 11.9</td>
<td>42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Right buttock</td>
<td>64.4 +/− 10.4</td>
<td>85.4 +/− 16.7</td>
<td>46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Right leg</td>
<td>68.8 +/− 11.0</td>
<td>81.1 +/− 16.0</td>
<td>47</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

http://econtent.hogrefe.com/doi/pdf/10.1024/0301-1526/a000454 - Damir Danic <ddanic@medicap.de> - Friday, September 25, 2015 1:40:36 AM - IP Address: 84.173.158.149
Table III: Results observed on peripheral probes for the minimal value of the decrease from rest of oxygen pressure before (DROP_{min}) or after (DROP^*_{min}) correction of the technical drift. All results are in mmHg.

<table>
<thead>
<tr>
<th></th>
<th>Radiometer*</th>
<th>Medicap*</th>
<th>Number of available pairs</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left buttock DROP_{min}</td>
<td>-19.0 +/- 16.5</td>
<td>-15.4 +/- 14.6</td>
<td>43</td>
<td><strong>0.020</strong></td>
</tr>
<tr>
<td>Left leg DROP_{min}</td>
<td>-24.7 +/- 17.1</td>
<td>-20.8 +/- 15.4</td>
<td>36</td>
<td>0.118</td>
</tr>
<tr>
<td>Right buttock DROP_{min}</td>
<td>-18.8 +/- 12.8</td>
<td>-16.3 +/- 13.2</td>
<td>41</td>
<td>0.189</td>
</tr>
<tr>
<td>Right leg DROP_{min}</td>
<td>-25.1 +/- 15.6</td>
<td>-23.7 +/- 17.8</td>
<td>42</td>
<td>0.559</td>
</tr>
<tr>
<td>Left buttock DROP^*_{min}</td>
<td>-18.1 +/- 15.7</td>
<td>-14.3 +/- 13.3</td>
<td>43</td>
<td><strong>0.007</strong></td>
</tr>
<tr>
<td>Left leg DROP^*_{min}</td>
<td>-22.7 +/- 16.6</td>
<td>-16.7 +/- 13.5</td>
<td>36</td>
<td><strong>0.002</strong></td>
</tr>
<tr>
<td>Right buttock DROP^*_{min}</td>
<td>-17.7 +/- 12.9</td>
<td>-14.8 +/- 11.7</td>
<td>41</td>
<td>0.097</td>
</tr>
<tr>
<td>Right leg DROP^*_{min}</td>
<td>-23.2 +/- 15.0</td>
<td>-20.1 +/- 15.6</td>
<td>42</td>
<td>0.133</td>
</tr>
</tbody>
</table>

Figure 4: Percentage of concordant results (n = 162) between DROP or DROP* obtained with Radiometer® using the usual – 15 mm Hg and with the Medicap® using different thresholds.

Conclusions

This study confirms that, at least for exercise tests, the photo-optical technology provides a promising alternative to the devices using electro-chemical sensors, provided that future validation studies confirm our results and that miniaturisation of the new sensors is possible. Additional studies are required in situations of critical limb ischaemia, specifically to confirm or not the trend observed here for higher absolute values with the photo-optical sensors than with electrochemical ones.

Acknowledgements

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Conflicts of interest

There are no conflicts of interest existing.

References

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