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Intra-test and test-retest reliability of exercise oximetry in arterial claudication

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ABSTRACT

Background: Transcutaneous oxygen pressure (tcpO2) reliability is blunted by an unpredictable transcutaneous gradient through the skin. We hypothesized that the "Decrease from Rest of Oxygen pressure (DROP: subtraction of limb-changes from chest-changes from the respective starting values) would show a good to excellent reliability during Exercise -tcpO2 investigations.

Methods: In three different experiments we tested: The intra-test variability at the peripheral level (Experiment A: 32 patients, 16 at each location), at the chest level (Experiment B: 45 patients) and the test-retest reproducibility within 3 months (Experiment C: 67 patients). We calculated the intra-class coefficient of correlation (ICC) with 95% confidence interval [Lower/upper limit]. ICC between 0.60 and 0.749 indicate a good agreement. ICC above 0.750 indicates an excellent agreement.

Results: ICC values for DROP-min were 0.848 [0.723/0.935] at the buttock and 0.920 [0.846/0.967] at the calf levels, in experiment A; ICC were 0.873 [0.799/0.923] at the buttock and 0.898 [0.790/0.953] at the calf levels, in experiment B; 0.806 [0.716/0.871] at then buttock level (n = 67) and 0.807 [0.722/0.868] at the calf in experiment C.

Conclusions: Intra-test and test-retest reliability is excellent using the DROP calculation for exercise-tcpO2 investigations.

1. Introduction

Transcutaneous oxygen pressure (tc*p*O2) sensors have been initially used in neonates to estimate absolute arterial pO2 with satisfactory results. In adults, due to extra thickness of the skin and sub-cutaneous fat, the correlation of transcutaneous to arterial pO2 is less satisfactory. Careful removal of epidermal dead cells before each test, local heating of the skin by the tc*p*O2 probe (that allows for an increase of skin perfusion and facilitates the diffusion of gas through the tissue) may improve the results. Nevertheless, an unpredictable surface-to-tissue-pO2 gradient exists and the surface pO2 value is lower than the underlying tissue-pO2 to be measured, at least in adults (Matsen 3rd et al., 1980). Transcutaneous oxygen pressure is largely used in vascular medicine for patients with severe or critical limb ischemia (Rosfors et al., 2016). Recording tc*p*O2 during exercise (Ex-tc*p*O2) has proved accuracy to estimate the presence of arteriographic lesions at the buttock and distal level (Abraham et al., 2005; Abraham et al., 2003) with recent external validations with computed tomography angiography (Koch et al., 2016; Audonnet et al., 2017). Ex-tc*p*O2 is not a primary approach to vascular claudication because, as compared to usual routine non-invasive investigations (i.e.: Doppler and arterial pressures), it is technically demanding and time consuming. Nevertheless, it provides useful information for patients suffering atypical claudication (e.g.: proximal-without-distal) or claudication of questionable vascular origin (e.g.: exercise-induced systemic hypoxemia) (Mouren et al., 1998; Modesti et al., 1990; Picquet et al., 2005).

Published studies have shown that the reproducibility of tcpO2 measurements at exercise (Ex- tc*p*O2) as absolute values or "Regional Perfusion Index" (RPI) was fair on test–retest experiments (Mouren et al., 1996; Larsen et al., 1988). This is mainly due, to the unpredictable tissue to skin oxygen pressure gradient. Indeed, it is well known that distribution of cutaneous microcirculation is inhomogeneous even in areas of close proximity. Further, probe position differences may result in differences in the regional vascular supply to the skin. Specifically, blood flow supply to the skin at the buttock level during exercise may rely on both perforating arteries from the pelvic

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circulation (terminal branches of the gluteal arteries) or from branches of the lumbar arteries.(Jaquinandi et al., 2007) Thus, spatial heterogeneity could be high specifically at the buttock rather than at the calf level.

In 2003, we have proposed the "Decrease from Rest of Oxygen pressure", so-called "DROP" (calculated as the subtraction of limb-changes from chest-changes) (Abraham et al., 2003) for the interpretation of Ex-tc*p*O2 investigations. The DROP is by construction independent of absolute starting values. It was shown to increase the diagnostic accuracy of the technique as compared to RPI and absolute values (Abraham et al., 2005; Abraham et al., 2003). To date, intra-test and test–retest results for the reliability of Ex-tc*p*O2 are missing. In a small group of eleven patients we also showed that it provided the best correlation (Bouye et al., 2004) analysis in term of Intra-class correlation (ICC) was not reported.

Our hypothesis was that the DROP would show a good to excellent reliability during Ex-tc*p*O2 investigations. Then we performed three different experiments to evaluate: 1) the intra-test variability at the peripheral level (Experiment A: variability related to different probe positions at the limb level), and at the chest level (Experiment B: variability related to the effect of changing the positions of the reference chest probe on peripheral DROP values), 2) The test–retest reproducibility (Experiment C).

2. Methods

Since 2003, all patients referred for exercise oximetry are recorded to a computer database for research purpose. Data recorded in the database include: age, height, weight, sex, maximal walking distance performed on treadmill (MWD) and ankle brachial index (ABI). This database contains approximately 6000 tests performed in approximately 4000 patients to date. The database is recorded according to French law and patients are aware that they may refuse that their medical record can be used for research analysis. Then written informed consent for the retrospective statistical use of these recordings is not required. All procedures were performed according to the recommendations of the conference of Helsinki.

Due to technical requirements, we performed a series of three different investigations in different patients.

- For experiment A: A prospective study was performed among patients reporting stage 2 peripheral arterial disease and referred for exercise tests with simultaneous tc*p*O2 measurement at the chest and limb level as a part of the EOIP study (Clinicaltrial.gov register number: NCT00152737). Two groups were studied: one at the proximal (buttock) level, the other at the distal (calf) level. We studied 16 patients at the buttock level and 16 other patients at the calf level
- For experiment B: We performed a retrospective analysis of the 45 consecutive patients referred to the laboratory since July 1st 2017 that had a standard test with two chest probes. Indeed, we presently record simultaneously chest tcpO2 on both sides while recording buttock and calf tcpo2 simultaneously.
- For experiment C: We performed a retrospective screening of our database to analyze the patients that, since 2003 have had 2 tests within a maximal interval of three months with no significant treatment or methodological change between the two tests. In the database, we found 67 patients that had two tests with a maximal interval of 3 months.

2.1. Exercise procedure

The exercise procedure for all the three experiments have been performed according to our standard procedure that has been extensively described elsewhere (Abraham et al., 2003). In brief, for all exercise tests, the treadmill procedure used a 10% slope, and speed of 3.2 km·h^{-1}. Exercise was stopped on patient request at maximal pain and not at pain occurrence. A 12 lead ECG was used to measure the heart rate and to detect abnormal events during the whole exercise test.

Table 1
Characteristics of the patients at inclusion in each experiment. MWD is maximal walking distance on treadmill; ABI is Ankle to brachial systolic pressure index.

	Experiment A buttock	Experiment A calf	Experiment B	Experiment C
Number of subjects	16	16	45	67
Age (years)	63 ± 10	67 ± 10	66 ± 11	61 ± 9
Height (cm)	172 ± 7	166 ± 7	169 ± 8	170 ± 8
Weight (kg)	78 ± 11	75 ± 9	75 ± 13	75 ± 14
Males/ females (n =)	16/0	14/2	22/3	58/19
MWD (m)	383 ± 324	501 ± 395	449 ± 411	364 ± 313
ABI	0.81 ± 0.27	0.81 ± 0.20	0.80 ± 0.25	0.81 ± 0.21

2.2. Tcpo2 recording

For all experiments, we used tcpO2 electrodes of a single type (E5250; Radiometer Brønshøj, Sweden) connected to various devices (PF6000® Perimed, TCM3®/TCM400® Radiometer, Fr). Each probe has been carefully membraned according to the manufacturer recommendations and contains a thermostatic system that allows heating of the skin locally in order to improve local perfusion and oxygen transcutaneous diffusion. A one-point calibration to air was performed for each device before each experiment. Then probes were fixed to the skin through specific probe holders that isolates the probe from ambient air and sticks to the skin by double-sided adhesive. In all tests, as a standard, one probe on the left scapular area of the chest was used as a reference electrode for the RPI and DROP calculation.

- In experiment A, in addition to the chest probe, we recorded limb tc*p*O2 with 5 probes simultaneously: one was used as a centre probe and 4 other probes were positioned 3 cm apart above, below, internal or external from the centre probe. The test was performed on upper external quarter of the buttock in sixteen patients and on one the mid external part of the calf in another 16 patients.
- In experiment B, in addition to the standard chest probe, a second chest probe was positioned on the right sub-scapular area (contralateral to the standard chest position). Last, we used one probe on the upper external quarter of each buttock and on probe on each calf (lower third of the posterior and external part of the calf).
- In Experiment C, in addition to the chest probe, we recorded limb tc*p*O2 on 4 probes simultaneously: one on each buttock (upper external quarter) and one on each calf (lower third of the posterior and external part of the calf) in experiment B.

No specific marks were drawn on the skin to position the probes. Attention was only paid to avoid scars of area of concavity in order to attain good probe stability. Probes are fixed to the skin with a probe and were secured with a net at the calf level. A minimum of 15 min was required before the start of tc*p*O2 recording to allow tc*p*O2 probes to heat the skin locally to 44.5 °C. The devices express tc*p*O2 in millimeters of mercury (mmHg) after automatic correction of oxygen pressure to 37 °C.

2.3. Data recording

Tc*p*02 values were recorded for 2 min in the standing position before the treadmill was started, during the walking period and for 10 min in the standing position following the end of the exercise test. For TCM-3 devices (experiment A) the data were recorded real time through the