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Original Article

Exercise transcutaneous oximetry significantly modifies the diagnostic hypotheses and impacts scheduled investigations or treatments of patients with exertional limb pain

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ABSTRACT

Introduction: In lower extremity peripheral artery disease (PAD), transcutaneous oximetry at exercise (Ex-TcpO2) has been largely validated in research practice, but evidence of routine practice in various vascular laboratories is missing. We hypothesized that Ex-TcPO2 would change the diagnosis hypotheses, investigations and treatments for patients referred for exertional limb pain.

Material & methods: A multicenter prospective trial was conducted in nine different referral centers. Investigators performed Ex-TcpO2 and recorded investigations and treatments already scheduled for the patient. We encoded referral physician's diagnostic hypothesis. Before Ex-TcpO2, vascular physicians were asked to give their diagnosis hypotheses. A minimal decrease from rest of oxygen pressure (DROP) < minus 15 mm Hg defined the presence of exercise-induced ischemia on the area of interest. After Ex-TcPO2, we recorded post-test diagnostic hypothesis and investigations and treatments to be cancelled or performed. We compared the diagnosis hypotheses, scheduled investigations and treatments, before and after the Ex-TcpO2.

Results: We included 603 patients (485 males: 80.4%), aged 64.7 ± 9.8 years. The post-test diagnosis hypothesis differed in 266 patients (44.1%; $p < 0.0001$) and in 96 patients (15.9%) from the pre-test hypothesis of referring and vascular physician, respectively. This led to the recommendation to cancel 27 scheduled investigations or treatments of a total cost of ~130,000 euros.

Discussion: Ex-TcPO2 in patients with exertional limb pain is applicable in various vascular institutions, and significantly modifies the diagnostic hypotheses and impacts scheduled investigations or treatments of patients with exertional limb pain.

1. Introduction

In 2010, approximately 202 million subjects suffered from lower extremity peripheral artery disease (PAD) [1]. When symptomatic, most patients complain claudication that limits their walking capacity and results in altered quality of life [2]. Recent definitions have

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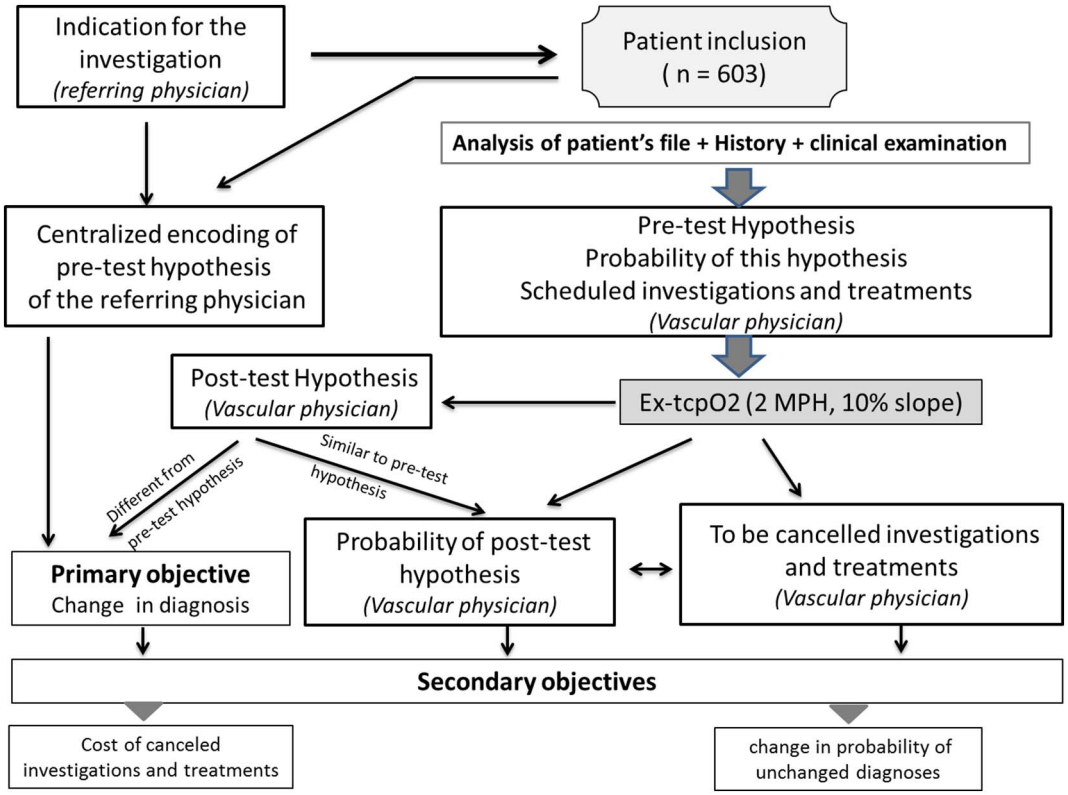

Fig. 1. Schematic representation of the study.

extended the original definition of the typical (calf) claudication [3] to a limb pain (including thigh or buttock or lower back), that is absent at rest, forces to slow down or stop walking, disappears with 10 min after walking is stopped [4]. Atypical claudication or exertional limb pain of doubtful arterial origin, are frequent clinical issues in clinical practice [5]. Last, even if typical vascular symptoms are observed, the presence of co-morbid conditions may question the responsibility of PAD as the sole cause, of walking impairment and exertional limb pain [6].

Transcutaneous oximetry (TcpO2) can be used to estimate underlying tissue oxygen pressure. It has been largely used at rest in situation of critical limb ischemia [7–9]. In patients with exertional limb pain, TcpO2 at exercise (Ex-TcpO2) consists in continuously measuring skin oxygen at the limb and chest level before, during and after exercise to provide objective arguments for the presence of regional oxygen use/delivery mismatch during walking tests. Ex-TcpO2 has been used in the early eighties with the use of the regional perfusion index (RPI: ratio of limb to chest values [10]. Since 2003, we use the DROP (Decrease from Rest of Oxygen Pressure, calculated as limb changes from rest minus chest changes from rest) [11,12]. Because it accounts for absolute changes and is independent from starting absolute values, the DROP allows to get rid of the unpredictable transcutaneous gradient. Thereby, the DROP solves the problem of absolute value and RPI reliability and has led to a renewed interest towards Ex-TcpO2 [12–15], specifically since multi-probe devices were made available.

DROP results from Ex-TcpO2 have been compared to gold standard arteriography [12,16] or computer tomography angiography [17,18], and has shown accuracy for the diagnosis of exercise–induced Regional Blood Flow Impairment (RBFI). It has also been shown to be sensitive to changes after surgical or medical treatment [19–22]. We have used Ex-TcpO2 over the last 15 years in Angers to document the presence of exercise-induced ischemia in the limb during exertional limb pain of suspected of doubtful arterial origin and in research protocols [12,15,16]. This single institution experience with Ex-TcPO2 in patients with PAD may question the applicability of the technique to other institutions, its clinical interest and the potential limitations of this practice. Few referral international centers have started the technique with our custom-made program such as the Mayo clinic (Minnesota USA) or the university hospital in Rennes, but evidence of routine practice and potential benefits of implementing the practice in various vascular laboratories is missing [17,23].

We hypothesized that Ex-TcpO2 would result in a significant amount of diagnostic hypotheses changes, or at least would reinforce, or argue against, the diagnostic hypothesis in patients with exertional limb pain. For this purpose, we assessed in a prospective multicenter trial, whether Ex-TcPO2 changed the diagnosis hypotheses, investigations and treatments for patients referred for exertional limb pain.

2. Methods

The National CINEY-SOFT trial (Clinicaltrial NCT01808989) granted by the French Society of Vascular Medicine (SFMV) has allowed making the custom-made program (developed by the ESEO (Ecole Supérieure d'Electronique de l'Ouest) engineer school in Angers) available to eight other referral centers in France. Between April 2013 and December 2016, nine different university hospitals (by alphabetic order: Angers, Caen, Lille, Lomme, Lyon, Marseille, Rennes, Toulouse, Tours), participated to the study. Six centers had never performed the technique locally before the start of the CINEY-Soft study. The program automatically retrieved the data from the TcpO2 devices and automatically calculated the DROP. A four-hour learning and training meeting was organized to: Learn or recall the details of how the investigation had to be performed; How Ex-tcpO2 had to be interpreted for the protocol; How to fill the electronic report form (e-CRF) for the trial. It should be noted here, that the participation of Angers (coordinating center of the study) was limited to the first 65 patients performed in 2013 by local investigators novice to the technique, after which the coordinating institution stopped the inclusion in this trial, while still performing > 500 Ex-TcpO2 investigations per year.

Eligible patients were all patients aged 18 years old or above, referred for Ex-TcpO2, with no gender restriction. Inclusion criteria