Effect of peripheral arterial disease on the onset of lactate threshold during cardiopulmonary exercise test: study protocol

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ABSTRACT

**Introduction:** Cardiopulmonary exercise test (CPET) is widely used in preoperative assessment and cardiopulmonary rehabilitation. The effect of peripheral arterial disease (PAD) on oxygen delivery (VO2) measured by CPET is not known. The aim of this study was to investigate the effect of PAD on VO2 measurements during CPET.

**Methods and analysis:** We designed a prospective cohort study, which will recruit 30 patients with PAD, who will undergo CPET before and after treatment of iliofemoral occlusive arterial disease. The main outcome measure is the difference in VO2 at the lactate threshold (LT) between the 2 CPETs. The secondary outcome measure is the relationship between change in VO2 at the LT and peak exercise pretreatment and post-treatment and haemodynamic measures of PAD improvement (ankle–brachial index differential). For VO2 changes, only simple paired bivariate comparisons, not multivariate analyses, are planned, due to the small sample size. The correlation between ABI and VO2 rise will be tested by linear regression.

**Ethics and dissemination:** The study was approved by the North West-Lancaster Research and Ethics committee (reference 15/NW/0801). Results will be disseminated through scientific journal and scientific conference presentation. Completion of recruitment is expected by the end of 2016, and submission for publication by March 2017.

**Trial registration number:** NCT02657278.

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**Strengths and limitations of this study**

- First study to address the influence of peripheral arterial disease (PAD) on cardiopulmonary exercise test (CPET) results.
- Prospective design, established CPET protocol.
- Small sample size.
- Inclusion of patients with proximal PAD only, treated with multiple interventional modalities.

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**INTRODUCTION**

Cardiopulmonary exercise testing (CPET) is frequently used in the preoperative assessment of elderly patients, 1 as well as in the evaluation and follow-up of patients with cardiorespiratory disease. 2,3 Peripheral arterial disease (PAD) is highly prevalent in this population, due to its age and the presence of cardiovascular risk factors. 3 CPET documents cardiorespiratory fitness by various means, including the measurement of systemic oxygen delivery (VO2) at the lactate threshold (LT)—the moment, during exercise, when muscles start working anaerobically—and at peak exercise. Low values suggest poor fitness and may indicate that surgery is of inappropriately high risk. Patients with PAD may develop ischaemia during leg exercise not because of poor cardiorespiratory reserve, but, independent of cardiorespiratory performance, because the blood supply to the muscles is impaired, resulting in early lactate release. On this basis, the LT may not reflect cardiorespiratory status, risk and prognosis in this group of patients. In addition, screening for PAD prior to CPET is not currently advocated or practiced.

To the best of our knowledge, there is no literature documenting or quantifying the effect of PAD on the results of CPET. Our hypothesis is that correction of PAD may cause improvement in VO2 proportional to the degree of improvement in the peripheral circulation. The aim of this study is to determine whether VO2 during CPET is influenced by the presence of haemodynamically significant PAD. More specifically, our research question was: in patients with PAD, does improvement in blood flow to the leg muscles result in a rise in VO2 at LT and peak exercise, as measured by CPET?
METHODS
Design
In order to answer our research question, we designed a prospective cohort study recruiting patients scheduled to undergo percutaneous or surgical correction of proximal (iliofemoral) occlusive PAD. We chose patients with iliofemoral (rather than infrainguinal) disease because of the greater muscle mass experiencing ischaemia during CPET in this population (quadriceps, glutei). Inclusion and exclusion criteria are summarised in table 1. We excluded patients with critical ischaemia because this condition (severe pain at rest with/without tissue loss) might affect their ability to perform a CPET.

Recruitment
Patients are recruited among those referred to the Liverpool Vascular and Endovascular Service for treatment of their PAD. Potential candidates are approached at the time of clinic attendance to determine interest in the study and offered a patient information leaflet as well as verbal information. Alternatively, they receive a study letter containing the patient information leaflet by post. In either case, patients are then approached by the study team by telephone >48 hours later to confirm participation. All participants are asked to provide written informed consent, which is obtained by either the first or the senior author.

Intervention
Patients undergo symptom limited CPET before and 4 weeks after surgical or endovascular correction of their PAD. The CPET protocol is described in detail in previous publications from our group.45 The test is performed according to the American Thoracic Society/
measurements. The study was conceived because of lack of information, in the literature, on the effect of PAD on systemic VO2 measured by CPET by cycle ergometry, a commonly performed test, in different settings, to evaluate cardiorespiratory fitness. The study was not designed to provide conclusive results, rather as an exploratory investigation. Any evidence of a positive effect of (correction of) PAD on the outcome measures may stimulate further research and inform future sample size estimates. Furthermore, assuming a positive finding, the study may suggest caution in interpreting the results of CPET in patients with PAD, pending further evidence. It may also induce clinicians to screen for PAD prior to CPET. Although one of the secondary outcome measures is the correlation between changes in VO2 and ABI, the study is not specifically powered for this, nor could it be, due to the lack of evidence in the literature. Furthermore, ABI is only a crude measurement of the effect of treatment of PAD, and not solely dependent on the presence of PAD, and it is influenced by infragenual disease, whose presence is not addressed by the treatment of the patients included in this study.

In conclusion, this study will provide further insight on the use and interpretation of CPET in the elderly, and evaluate PAD as a potential limiting factor of cardiorespiratory performance in this group of patients.

REFERENCES
