BJA

British Journal of Anaesthesia, 118 (5): 747–54 (2017)

doi: 10.1093/bja/aew445
Clinical Practice

Total haemoglobin mass, but not haemoglobin concentration, is associated with preoperative cardiopulmonary exercise testing-derived oxygen-consumption variables

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Abstract

Background. Cardiopulmonary exercise testing (CPET) measures peak exertional oxygen consumption ($\dot{V}O_2$peak) and that at the anaerobic threshold ($\dot{V}O_2$ at AT, i.e. the point at which anaerobic metabolism contributes substantially to overall metabolism). Lower values are associated with excess postoperative morbidity and mortality. A reduced haemoglobin concentration ([Hb]) results from a reduction in total haemoglobin mass (tHb-mass) or an increase in plasma volume. Thus, tHb-mass might be a more useful measure of oxygen-carrying capacity and might correlate better with CPET-derived fitness measures in preoperative patients than does circulating [Hb].

Methods. Before major elective surgery, CPET was performed, and both tHb-mass (optimized carbon monoxide rebreathing method) and circulating [Hb] were determined.

Results. In 42 patients (83% male), [Hb] was unrelated to $\dot{V}O_2$ at AT and $\dot{V}O_2$peak (r=0.02, P=0.89 and r=0.04, P=0.80, respectively) and explained none of the variance in either measure. In contrast, tHb-mass was related to both (r=0.661, P<0.0001 and r=0.483, P=0.001 for $\dot{V}O_2$ at AT and $\dot{V}O_2$peak, respectively). The tHb-mass explained 44% of variance in $\dot{V}O_2$ at AT (P<0.0001) and 23% in $\dot{V}O_2$peak (P=0.001).

Conclusions. In contrast to [Hb], tHb-mass is an important determinant of physical fitness before major elective surgery. Further studies should determine whether low tHb-mass is predictive of poor outcome and whether targeted increases in tHb-mass might thus improve outcome.

Editorial decision: November 28, 2016; **Accepted:** December 13, 2016

Key words: anaemia; anaerobic threshold; cardiopulmonary exercise test; oxygen consumption; physical fitness; surgery

Editor's key points

- Reduced exertional oxygen consumption quantified by cardiopulmonary exercise testing is associated with increased postoperative morbididy and mortality, as is preoperative anaemia.
- In a study of 42 preoperative elective surgery patients, total haemoglobin mass correlated with exertional oxygen consumption, but circulating haemoglobin concentration did not.
- Preoperative total haemoglobin mass is a determinant of physical fitness and might be useful in predicting postoperative outcome.

Cardiopulmonary exercise testing (CPET) is routinely used to quantify exertional oxygen consumption ($\dot{V}O_2$), both the peak attained ($\dot{V}O_2$peak) and that at the anaerobic threshold ($\dot{V}O_2$ at AT, i.e. the point during incremental exercise when anaerobic metabolism makes a significant contribution to overall metabolism). Both measures are used as indices of physical fitness before major surgery,[1–3] given that reduced values are associated with increased postoperative morbidity and mortality.[4 5]

Haemoglobin (Hb), carried in circulating red blood cells, is the blood's oxygen-carrying protein. Its circulating concentration ([Hb]) reflects both its total circulating mass (tHb-mass) and the volume of plasma in which the red blood cells are suspended. Anaemia, defined as [Hb] <130 g litre^{-1} in men and <120 g litre^{-1} in women,[6] is associated with decreased aerobic exercise capacity.[7–9] Preoperative anaemia is common (affecting one-third of surgical patients) and is associated with an increased risk of postoperative morbidity and mortality.[10 11]

As the proportion of oxygen carried in plasma is minimal, the relationship of aerobic fitness with tHb-mass might be stronger than that with [Hb]. Indeed, in healthy individuals, [Hb] is not significantly correlated with either $\dot{V}O_2$peak or maximal $\dot{V}O_2$,[12 13] unlike tHb-mass.[14 15] However, whether this applies to patient populations, and to perioperative patients in particular, is less certain. We thus sought to explore the relationship of [Hb] and tHb-mass with CPET-derived measures of physical fitness in preoperative patients.

Methods

Ethical approval was granted by the London, Camden, and Kings Cross Research Ethics Committee (REC reference: 13/LO/1901). We fully adhered to Caldicott guidelines and followed the standards established by the Declaration of Helsinki. All participants provided written informed consent before taking part.

Patients

Adult (>18 yr old) elective (non-cardiac) surgical patients at University College Hospital [University College London Hospitals (UCLH) National Health Service (NHS) Foundation Trust] and Southampton General Hospital (University Hospital Southampton NHS Foundation Trust) were prospectively studied between February and August 2015. Patients were either receiving CPET as part of their routine preoperative assessment or were (approved) co-recruits to the 'METS' study of the relationship between CPET-derived physiological variables and surgical outcome.[16] Age, sex, height, weight, diagnosis, planned surgical procedure, co-morbidities (such as diagnosis of diabetes, respiratory, or cardiovascular disease), and current medications were documented.

Cardiopulmonary exercise testing

Cardiopulmonary exercise testing was supervised by a clinical exercise physiologist (and clinician where appropriate) and performed in accordance with international guidelines.[17]

Patients cycled on an electromagnetically braked ergometer (at UCLH, Lode BV, Groningen, The Netherlands; and at Southampton, Ergoline 2000, Ergoline GmbH, Bitz, Baden-Württemberg, Germany), with respiratory gas analysis made by calibrated metabolic carts [at UCLH, Cortex Biophysik, Leipzig, Saxony Germany; and at Southampton, Geratherm Respiratory GmbH (Love Medical Ltd, Manchester, Lancashire, UK)]. Breath-by-breath $\dot{V}O_2$ and carbon dioxide output were recorded, concurrently with minute ventilation, tidal volume, respiratory rate, and end-tidal gas tensions for O_2 and CO_2.

Patients were connected to appropriate monitoring equipment and rested for an initial 3 min period, after which 3 min of unloaded cycling was completed. Subsequently, patients performed a symptom-limited incremental ramp test set to 10–20 W min^{-1} (based on patient height, weight, and age) such as to deliver an intended test duration of 8–12 min.[18] Test cessation occurred at patient exhaustion or when the cadence reduced below 40 r.p.m. for more than 30 s in spite of verbal encouragement. The CPET was terminated by testing staff on safety grounds if the patient developed a sign or symptom listed in the American Thoracic Society/American College of Chest Physicians (ATS/ACCP) CPET guidelines.[17] After stopping CPET, patients completed a 3–5 min period of unloaded cycling to 'cool down'.

The anaerobic threshold (in millilitres per kilogram per minute) was determined by a clinical exercise physiologist, consultant physician, or both, skilled in CPET analysis, using the modified V-slope method with corroboration by ventilatory equivalents and end-tidal gas tensions for O_2 and CO_2.[19] The highest average $\dot{V}O_2$ throughout the final 30s of exercise was recorded as the $\dot{V}O_2$peak (in millilitres per kilogram per minute).[20]

Optimized carbon monoxide rebreathing method

The tHb-mass was determined using the optimized carbon monoxide (CO) rebreathing (oCOR) method described in detail by Schmidt and Prommer[21] and was calculated based on the equation in Fig. 1. In brief, CO binds avidly to Hb. The carboxyhaemoglobin (COHb) concentration is measured in blood before and after 2 min of rebreathing a known CO volume. In this study, the CO volume was 0.5–0.9 ml kg^{-1}, depending on gender in the first instance, with fine-tuning by [Hb], BMI, and the general condition of the patient. Each participant was seated for 15 min to allow stabilization of plasma volume, after which a mouthpiece containing ~10 g 'soda lime' (calcium oxide–sodium hydroxide mixture as a carbon dioxide scrubber) connected