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Validity of the 6 min walk test in prediction of the anaerobic threshold before major non-cardiac surgery

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Editor's key points

- The 6 min walk test was compared with cardiopulmonary exercise testing (CPET) in predicting anaerobic threshold.
- The authors conclude that those walking >563 m do not require CPET, and those walking <427 m do.
- Patients who walk a distance between the two cut-off points need careful further evaluation.
- The findings of this study provide important validation of simple walk test in risk stratification and prognosis.

Background. For perioperative risk stratification, a robust, practical test could be used where cardiopulmonary exercise testing (CPET) is unavailable. The aim of this study was to assess the utility of the 6 min walk test (6MWT) distance to discriminate between low and high anaerobic threshold (AT) in patients awaiting major non-cardiac surgery.

Methods. In 110 participants, we obtained oxygen consumption at the AT from CPET and recorded the distance walked (in m) during a 6MWT. Receiver operating characteristic (ROC) curve analysis was used to derive two different cut-points for 6MWT distance in predicting an AT of <11 ml O_2 kg^{-1} min^{-1}; one using the highest sum of sensitivity and specificity (conventional method) and the other adopting a 2:1 weighting in favour of sensitivity. In addition, using a novel linear regression-based technique, we obtained lower and upper cut-points for 6MWT distance that are predictive of an AT that is likely to be ($P \geq 0.75$) <11 or >11 ml O_2 kg^{-1} min^{-1}.

Results. The ROC curve analysis revealed an area under the curve of 0.85 (95% confidence interval, 0.77–0.91). The optimum cut-points were <440 m (conventional method) and <502 m (sensitivity-weighted approach). The regression-based lower and upper 6MWT distance cut-points were <427 and >563 m, respectively.

Conclusions. Patients walking >563 m in the 6MWT do not routinely require CPET; those walking <427 m should be referred for further evaluation. In situations of 'clinical uncertainty' (≥427 but ≤563 m), the number of clinical risk factors and magnitude of surgery should be incorporated into the decision-making process. The 6MWT is a useful clinical tool to screen and risk stratify patients in departments where CPET is unavailable.

Keywords: anaerobic threshold; exercise test; oxygen consumption; preoperative care

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The assessment of exercise capacity before major non-cardiac surgery is recommended to help improve risk prediction perioperatively at the individual patient level.[1 2] There are two principal methods utilized in clinical practice in the UK: a cardiopulmonary exercise test (CPET) and patient-reported metabolic equivalent (MET) scores. A CPET is generally regarded as the 'gold standard' assessment, providing objective rather than subjective analysis of exercise capacity. Specific measurements obtained during testing have been validated in the prediction of perioperative risk for major non-cardiac surgery.[3–6] The anaerobic threshold (AT) currently has the largest evidence base with cut-off thresholds of <11 and <8 ml O_2 kg^{-1} min^{-1} generally regarded as representing high and very high perioperative risk, respectively.[4–7] A high-risk cut-off threshold of slope >34 for the ventilatory equivalent for carbon dioxide ($\dot{V}E/\dot{V}CO_2$) has a more limited evidence base.[6] In thoracic surgery, a cut-off of <15 ml O_2 kg^{-1} min^{-1} for maximum oxygen consumption achieved ($\dot{V}O_2$ max) identifies high-risk cases.[8 9]

Service infrastructure costs may prohibit setting up a CPET service. Subjective functional assessment of METs, although a simpler alternative, has been shown to have user and physiological limitations.[10–12] An alternative, simple, objective measure of exercise capacity may therefore more robustly aid risk stratification, where CPET is unavailable. Ideally, such a test should be validated against measured CPET parameters.

A review of the validity data supporting functional exercise tests revealed the 6 min walk test (6MWT) to be the most extensively researched and established test for use in clinical or research contexts in the cardiorespiratory domain.[13] Previous studies have demonstrated a positive correlation between CPET measurements and distance walked in patients with cardiorespiratory disease.[14–17] Although the 6MWT has been shown to predict outcome after pulmonary resection[18] and lung volume reduction surgery,[19] there is no literature pertaining to major non-cardiac surgery. We believe that based on this evidence and pilot data from

our institution, the 6MWT might be suitable to provide the simple, objective assessment of exercise capacity outlined above.

The aim of this study was to assess the validity of the distance walked during the 6MWT in predicting the AT (and other parameters) derived from CPET.

Methods

The protocol for this concurrent validity study was approved by the National Research and Ethics Service in August 2008 (08/H1305/62). Trial registration: ISRCT 12656789.

Participants were recruited from the preoperative assessment clinics at the James Cook University Hospital between October 2008 and January 2010. After verbal explanation and a patient information sheet, written informed consent was obtained.

Participants included in the study were aged 50–85 yr and awaiting scheduled major non-cardiac surgery (Grade 3 or 4 surgery as defined by NICE guidance).[20] Exclusion criteria comprised: medical contraindication to CPET[21] or failure to complete a baseline CPET, lower limb claudication and inability to maintain a steady walking pace on level ground. After a medical screening examination, patients were invited to participate.

For a desired precision of estimation of ± 0.10 (95% confidence interval width) around a postulated validity correlation coefficient of $r=0.70$ (for 6MWT distance in the prediction of AT) derived from pilot work, a sample size of 100 patients was estimated. Allowing for an attrition rate of 25%, a final sample size of 125 participants was required. A total of 186 individuals were screened for inclusion. Of these, 129 participants were enrolled. Characteristics, co-morbid diseases, surgical procedures undertaken, and medications prescribed for participants completing both CPET and 6MWT (119 participants) are shown in Supplementary Table S1.

Participants were asked to complete two exercise tests: CPET (on a cycle ergometer) and a 6MWT. The CPET was performed first, in order to screen for significant cardiovascular pathology, thus ensuring the safe conduct of the 6MWT. To minimize participant inconvenience, both tests were undertaken on the same day. After CPET, patients were provided with refreshments and allowed an appropriate rest interval between tests. The 6MWT was only undertaken once the participants had reported that they had no residual fatigue from CPET. To avoid study bias, the 6MWT was administered by an investigator blinded to the results of the CPET.

Cardiopulmonary exercise test

The CPET was performed using the Medgraphics Ultima system (Tewkesbury, Gloucestershire, UK) and a Lode Corival V2 cycle ergometer (BV Medical Technology, Groningen, The Netherlands). Flow and gas calibrations were performed before each test session, which was subsequently conducted to our standard protocol (available in Supplementary material). All usual patient medication was continued. The test was terminated when the participant reached volitional exhaustion ($\dot{V}O_2$ peak) or earlier if another termination criterion was fulfilled. The *V*-slope comparison plot was compiled using Breeze software (Medgraphics) and interpreted by two trained observers on completion of all study testing (G.R.D. and R.C.F.S.).

Six min walk test

After successful completion of CPET, participants performed the 6MWT as outlined in the guidance published by the American Thoracic Society (ATS).[22] Individuals walked to their own maximum pace along a flat corridor, marked with a 30 m track, aiming to cover as much distance as possible in the timed 6 min. Participants wore a MIROxi pulse oximeter (Medical International Research, Roma, Italy) to record heart rate response and oxygen saturations.

The ATS suggest that a practice test is not needed in most settings.[22] Furthermore, data from our pilot study (unpublished observation) confirmed that the test was highly reproducible, with an intraclass correlation coefficient (ICC 3.1) of 0.94, and a non-substantial mean bias of 18 m greater on a second walk. Thus, a single 6MWT was performed in the current study.

Test outcome measures recorded

- CPET—oxygen consumption at the AT (using the *V*-slope technique),[23] oxygen consumption at volitional exhaustion ($\dot{V}O_2$ peak), the $\dot{V}E/\dot{V}CO_2$ recorded at AT, and maximum heart rate achieved (HR_{max})
- 6MWT—maximal distance walked and HR_{max}

Statistical analysis

Ordinary least-squares linear regression models were applied to obtain the validity coefficient (*r*) and the standard error of the estimate (SEE)—the typical error associated with the prediction of AT (or $\dot{V}O_2$ peak or $\dot{V}E/\dot{V}CO_2$ slope) from 6MWT distance in an individual patient. Receiver operating characteristic (ROC) curve analysis was used to derive cut-points for 6MWT distance for the prediction of AT <11 ml O_2 kg^{-1} min^{-1}, AT <8 ml O_2 kg^{-1} min^{-1}, $\dot{V}O_2$ peak <15 ml O_2 kg^{-1} min^{-1}, and a combination of AT <11 ml O_2 kg^{-1} min^{-1} and $\dot{V}E/\dot{V}CO_2$ slope >34. The optimum cut-point was determined as the value corresponding with the greatest accuracy (highest sum of sensitivity plus specificity; i.e. with sensitivity and specificity weighted equally). When a test is to be used for screening purposes and risk stratification, however, a cut-off value with greater sensitivity (fewer false-negatives) may be desirable. Therefore, we derived an alternative cut-point by adopting a 2:1 weighting for sensitivity:specificity.

To refine the ROC-derived cut-offs, we used the obtained regression equation and SEE, to derive lower and upper cut-points for 6MWT distance that are predictive of an AT that is *likely to be* less than or greater than these prognostic AT thresholds. (A 6MWT distance falling between these two cut-points is assumed to be in an area of 'clinical uncertainty'.)