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Cardiopulmonary exercise testing and survival after elective abdominal aortic aneurysm repair†

S. W. Grant[1,3], G. L. Hickey[3,4], N. A. Wisely[2], E. D. Carlson[1], R. A. Hartley[2], A. C. Pichel[5], D. Atkinson[5] and C. N. McCollum[1]*

[1] Academic Surgery Unit, Education and Research Centre and [2] Department of Anaesthesia, University of Manchester, Manchester Academic Health Science Centre, University Hospital of South Manchester, Southmoor Road, Manchester M23 9LT, UK
[3] National Institute for Cardiovascular Outcomes Research, Institute of Cardiovascular Science, University College London, London, UK
[4] Centre for Health Informatics, Manchester Academic Health Science Centre, University of Manchester, Oxford Road, Manchester, UK
[5] Manchester Royal Infirmary, Department of Anaesthesia, Central Manchester University Hospitals, Manchester Academic Health Science Centre, Manchester, UK

* Corresponding author. E-mail: cnmcc@manchester.ac.uk

Editor's key points

- There are few data on cardiopulmonary exercise testing (CPET) before aortic surgery and subsequent outcome.
- In this study, some CPET variables were associated with reduced survival after aortic repair.
- However, CPET may be performed differently in different centres and confidence intervals in this study were wide.
- This study adds to the body of evidence on CPET as part of preoperative assessment, but its contribution remains uncertain and further data are required.

Background. Cardiopulmonary exercise testing (CPET) is increasingly used in the preoperative assessment of patients undergoing major surgery. The objective of this study was to investigate whether CPET can identify patients at risk of reduced survival after abdominal aortic aneurysm (AAA) repair.

Methods. Prospectively collected data from consecutive patients who underwent CPET before elective open or endovascularAAA repair (EVAR) at two tertiary vascular centres between January 2007 and October 2012 were analysed. A symptom-limited maximal CPET was performed on each patient. Multivariable Cox proportional hazards regression modelling was used to identify risk factors associated with reduced survival.

Results. The study included 506 patients with a mean age of 73.4 (range 44–90). The majority (82.6%) were men and most (64.6%) underwent EVAR. The in-hospital mortality was 2.6%. The median follow-up was 26 months. The 3-year survival for patients with zero or one sub-threshold CPET value ($\dot{V}O_2$ at AT$<$10.2 ml kg^{-1} min^{-1}, peak $\dot{V}O_2<15$ ml kg^{-1} min^{-1} or $\dot{V}E/\dot{V}CO_2$ at AT$>$42) was 86.4% compared with 59.9% for patients with three sub-threshold CPET values. Risk factors independently associated with survival were female sex [hazard ratio (HR)=0.44, 95% confidence interval (CI) 0.22–0.85, P=0.015], diabetes (HR=1.95, 95% CI 1.04–3.69, P=0.039), preoperative statins (HR=0.58, 95% CI 0.38–0.90, P=0.016), haemoglobin g dl^{-1} (HR=0.84, 95% CI 0.74–0.95, P=0.006), peak $\dot{V}O_2<15$ ml kg^{-1} min^{-1} (HR=1.63, 95% CI 1.01–2.63, P=0.046), and $\dot{V}E/\dot{V}CO_2$ at AT$>$42 (HR=1.68, 95% CI 1.00–2.80, P=0.049).

Conclusions. CPET variables are independent predictors of reduced survival after elective AAA repair and can identify a cohort of patients with reduced survival at 3 years post-procedure. CPET is a potentially useful adjunct for clinical decision-making in patients with AAA.

Keywords: abdominal aortic aneurysm; cardiopulmonary exercise test; cardiovascular surgical procedure; endovascular procedures

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Accurate assessment of perioperative risk and prediction of long-term clinical outcomes are essential in elective abdominal aortic aneurysm (AAA) repair as for most patients it is a prophylactic procedure. Several methods of assessing perioperative risk have been proposed in patients undergoing AAA repair, including risk prediction models,[1] biomarkers,[2] assessment of functional capacity,[3] and genetic testing.[4] Recent guidelines have emphasized that when indicated, a preoperative assessment of a patient's functional capacity should be performed for patients undergoing major vascular surgery.[5–8]

Cardiopulmonary exercise testing (CPET) provides a 'gold standard' assessment of functional capacity. It has been used in elite sport performance and research for some time and is now increasingly utilized in the preoperative assessment of patients before major non-cardiac surgery. CPET has been

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used to identify patients at increased risk of adverse perioperative outcomes in a variety of settings.[9 10] The evidence for its role in risk stratifying patients undergoing AAA repair has so far been limited to a number of small single-centre studies.[3 11–13] As a result of this there is uncertainty about its usefulness in the preoperative assessment of patients with AAA. A recent systematic review called for more research into its role in the preoperative assessment of patients undergoing vascular surgery.[14]

A previous study by our group demonstrated that variables derived from CPET were independent predictors of 30- and 90-day mortality after elective AAA repair.[15] While short-term outcomes are clearly important for both patients and clinicians, better understanding of the risks of mid-term adverse outcomes is important for clinical decision-making. The objective of this study was therefore to investigate whether preoperative CPET-derived variables are predictors of survival after elective open and endovascular AAA repair (EVAR).

Methods

Data were collected prospectively as part of the standard multi-disciplinary assessment on all patients who underwent a symptom-limited maximal exercise CPET before elective AAA repair at Central Manchester Foundation Trust and University Hospital of South Manchester between January 24, 2007 and October 1, 2012. The cohort significantly overlaps with a previous study by our group on CPET and perioperative mortality after elective AAA repair.[15] Both contributing hospitals are part of Vascular Governance North West which has both NRES Committee North West (09/H1010/2+5) and Section 251 approval. As stated in the terms of the VGNW ethical approval, because this project involved the analysis of pseudonymous, non-identifiable patient data, specific ethical approval was not required.

CPET was performed using a cycle ergometer and a ramped test (Wasserman) protocol,[16] with the Ultima™ CardiO$_2^{®}$ MedGraphics equipment (Medical Graphics, St Paul, MN, USA) linked into the BreezeSuite™ software package (Medical Graphics, St Paul, MN, USA). CPET equipment was maintained under manufacturer maintenance contracts and calibrated before testing, in keeping with manufacturer recommendations. All CPET tests were performed and interpreted by appropriately trained consultant anaesthetists to a set of standardized clinical criteria across the two participating centres.

Baseline data were recorded and the patient then cycled for 3 min with no resistance at a rate of ~60 rpm. After these 3 min increasing resistance was applied at between 5 and 20 W min^{-1}. Each CPET was performed to achieve maximal patient effort. Criteria used to determine whether maximal effort was achieved were (i) heart rate >80% of predicted peak heart rate, (ii) respiratory exchange ratio >1.15, (iii) criteria for ventilatory limitation to exercise reached (breathing reserve <15%). The CPET was terminated if ST depression of >2 mm on the exercise ECG was observed, a cadence of >40 rpm could not be maintained, the patient experienced distressing cardiorespiratory or musculoskeletal symptoms or at the request of the patient. After the test patients were monitored until cardiorespiratory parameters returned to baseline levels. Data for the following CPET variables were collected: $\dot{V}O_2$ at anaerobic threshold (AT) in millilitre per kilogram per minute, peak $\dot{V}O_2$ in millilitre per kilogram per minute, and $\dot{V}E/\dot{V}CO_2$. The following discriminatory thresholds for these CPET variables were selected a priori based on published studies shown to identify those at increased risk of morbidity and death among patients undergoing major non-cardiac surgery; $\dot{V}O_2$ at AT<10.2 ml kg^{-1} min^{-1},[17] peak $\dot{V}O_2$<15 ml kg^{-1} min^{-1},[18] and $\dot{V}E/\dot{V}CO_2$ at AT>42.[3] Absolute patient weight in kilograms was used to calculate all variables. AT was determined using a combination of V-slope and ventilatory equivalent methods and recorded in millilitre per kilogram per minute.[19] $\dot{V}E/\dot{V}CO_2$ was recorded at AT, or when AT was unclear, taken to be the lowest recorded value during the incremental part of the exercise test.[20]

Inducible cardiac ischaemia (ICI) was recorded when ≥1 mm of ST-segment depression in two or more adjacent ECG leads on the CPET exercise ECG, gas analysis changes, or both consistent with ischaemia were present.[21] Reversible ischaemia present on either stress myoview or dobutamine stress echocardiogram within 5 years of surgery was also classified as ICI. Patients continued their usual medication up until CPET testing and heart rate limiting medications were not stopped. Patient co-morbidity data were collected either by the clinician responsible for the patient or by a clinical audit team. Preoperative laboratory investigations included haemoglobin (anaemia defined as <13.0 g dl^{-1} for men and <11.0 g dl^{-1} for women), urea (abnormal defined as >7.5 mmol l^{-1}), creatinine (abnormal defined as >120 μmol l^{-1}), and diagnosis of a juxta/supra renal AAA as defined by the operating surgeon. The primary outcome measure was survival after elective AAA repair. The follow-up data were collected using the NHS Demographic Batch Service on August 1, 2013.

Statistical analysis

All variables missing for more than 15% of subjects were excluded from analysis. For remaining variables, missing data were imputed with the median value for continuous or categorical variables and the baseline value for dichotomous variables. If AT could not be determined from the CPET, it was assumed to be <10.2 ml kg^{-1} min^{-1}. Continuous variables are reported as mean (SD), and dichotomous variables reported as number (percentage). Patient characteristics were compared between open AAA repair and EVAR groups using an independent samples Student *t*-test for continuous variables and the χ^2 test for dichotomous variables. Categorical and dichotomous variables were examined graphically using Kaplan–Meier graphs, and compared using the log-rank test. Continuous variables were assessed by fitting univariable Cox proportional hazards (PHs) regression models. The functional form of continuous variables other than CPET measurements was assessed by fitting smoothing curves to Martingale residual plots.