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CLINICAL PRACTICE

Cardiopulmonary exercise variables are associated with postoperative morbidity after major colonic surgery: a prospective blinded observational study

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Editor's key points

- Clinical acumen and subjective assessment of a patient's fitness for surgery have modest predictive utility.
- Cardiopulmonary exercise testing (CPET) evaluates the overall capacity of the cardiovascular and respiratory systems to work maximally.
- This study provides good evidence that CPET enhances risk stratification for patients undergoing major surgery.

Background. Postoperative complications are associated with reduced fitness. Cardiopulmonary exercise testing (CPET) has been used in risk stratification. We investigated the relationship between preoperative CPET and in-hospital morbidity in major colonic surgery.

Methods. We prospectively studied 198 patients undergoing major colonic surgery (excluding neoadjuvant cancer therapy), performing preoperative CPET (reported blind to clinical state), and recording morbidity (assessed blind to CPET), postoperative outcome, and length of stay.

Results. Of 198 patients, 62 were excluded: 11 had emergency surgery, 25 had no surgery, 23 had incomplete data, and three were unable to perform CPET. One hundred and thirty-six (89 males, 47 females) were available for analysis. The median age was 71 [inter-quartile range (IQR) 62–77] yr. Sixty-five patients (48%) had a complication at day 5 after operation. Measurements significantly lower in patients with complications than those without were O_2 uptake ($\dot{V}O_2$) at estimated lactate threshold ($\hat{\theta}_L$) [median 9.9 (IQR 8.3–12.7) *vs* 11.2 (9.5–14.2) ml kg^{-1} min^{-1}, $P<0.01$], $\dot{V}O_2$ at peak [15.2 (12.6–18.1) *vs* 17.2 (13.7–22.5) ml kg^{-1} min^{-1}, $P=0.01$], and ventilatory equivalent for CO_2 ($\dot{V}_E/\dot{V}CO_2$) at $\hat{\theta}_L$ [31.3 (28.0–34.8) *vs* 33.9 (30.0–39.1), $P<0.01$]. A final multivariable logistic regression model contained $\dot{V}O_2$ at $\hat{\theta}_L$ {one-point change odds ratio (OR) 0.77 [95% confidence interval (CI) 0.66–0.89], $P<0.0005$; two-point change OR 0.61 (0.46–0.81) and gender [OR 4.42 (1.78–9.88), $P=0.001$]}, and was reasonably able to discriminate those with and without complications (AUC 0.71, CI 0.62–0.80, 68% sensitivity, 65% specificity).

Conclusions. CPET variables are associated with postoperative morbidity. A multivariable model with $\dot{V}O_2$ at $\hat{\theta}_L$ and gender discriminates those with complications after colonic surgery.

Keywords: anaerobic threshold; cardiopulmonary exercise test; colorectal surgery; morbidity; postoperative complications

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Major colorectal surgery carries substantial morbidity (15–20%)[1 2] and mortality, particularly in elderly patients and those with co-morbidities.[3] Recent UK cancer audits show 30 day mortality of 2.3% for elective and 11.4% for emergency surgery.[4] Outcome after major surgery depends both on modifiable factors such as perioperative medical care and physiological tolerance of surgical trauma. Accurate risk stratification permits modification of preoperative status and optimization of intra- and postoperative management, and thus facilitates efficient use of resources (e.g. intensive care beds),

and enhances shared decision-making.[5] Approaches to risk evaluation include clinical acumen, clinical prediction scores [e.g. ASA physical status (ASA-PS), Duke's Activity Scores, POSSUM, CR-POSSUM],[6–8] plasma biomarkers,[9] measures of cardiac function,[10 11] and shuttle walk tests,[12–14] but their effectiveness in predicting complications is not well established.[15–17]

Cardiopulmonary exercise testing (CPET), which has been used for risk stratification before thoracic and abdominal surgery,[17–21] tests cardiorespiratory reserve (physical fitness) at rest and under the stress of maximal exercise (mimicking that of major surgery), and is the most objective and precise means of evaluating pre-surgical fitness.[22–24]

This prospective, blinded, observational study tests the hypothesis that CPET variables are related to short-term in-hospital morbidity in patients undergoing major colonic surgery.

Methods

Patients

We included all patients aged >18 yr considered for major colonic surgery (benign or malignant), except those with inflammatory bowel disease, patients undergoing neoadjuvant cancer therapy, or patients who were unable to perform CPET as part of their preoperative evaluation between February 2009 and December 2010. Patients were excluded on the basis of having no surgery performed or interim emergency surgery, lacking complete in-hospital morbidity data, or their inability to attain a definable lactate or anaerobic threshold ($\dot{V}O_2$ at $\hat{\theta}_L$). Discussions with Aintree University Hospitals NHS Foundation Trust and the North West Research Ethics Committee established that formal ethical approval was unnecessary, since CPET had been recently introduced as routine assessment in the hospital for major colorectal surgical patients, and results were not used by the multidisciplinary team (MDT) to alter clinical management as yet. We however adhered fully to Caldicott guidelines. All patients received an information sheet regarding CPET and written consent was obtained. No patient was refused surgery on the basis of gas-exchange measurements, although any ECG abnormalities were raised at the colorectal MDT meeting and referred appropriately.

Cardiopulmonary exercise testing

CPET followed American Thoracic Society/American College of Chest Physicians recommendations.[25] After resting spirometry (flow-volume loops), CPET on an electromagnetically braked cycle ergometer (Ergoline 2000) comprised 2 min rest, 2 min freewheel pedalling, ramped incremental pedalling until volitional termination, and 5 min recovery. Ventilation and gas exchange was measured using a metabolic cart [Geratherm Respiratory GmbH (Love Medical Ltd, Manchester, UK)]. Pulse, 12-lead ECG, arterial pressure, and pulse oximetry were monitored throughout. Ramp gradient was set to 10–25 W min^{-1} based on a calculation[26] using predicted freewheel oxygen uptake ($\dot{V}O_2$), predicted $\dot{V}O_2$ at peak exercise, height, and age. No major adverse clinical events occurred during CPET.

Measurements

Patient characteristics recorded at CPET included age, gender, height, weight, diagnosis, staging (if malignancy), surgical procedure planned, WHO classification, and ASA-PS, and also diagnosis of diabetes, ischaemic heart disease, cerebrovascular disease, or heart failure. Resting flow-volume loops were used to derive forced expiratory volume over 1 s (FEV1) and forced vital capacity (FVC). Ventilation and gas exchange variables derived from CPET included $\dot{V}O_2$, ventilatory equivalents for oxygen and carbon dioxide ($\dot{V}_E/\dot{V}O_2$; $\dot{V}_E/\dot{V}CO_2$), and oxygen pulse ($\dot{V}O_2$/heart rate), all measured at $\hat{\theta}_L$ and at peak exercise.[26] $\hat{\theta}_L$ was estimated conventionally [breakpoint in the $\dot{V}CO_2 - \dot{V}O_2$ relationship,[27] with increases in $\dot{V}_E/\dot{V}O_2$ and end-tidal ($P_{E'}$) O_2 but no increase in $\dot{V}_E/\dot{V}CO_2$ or decrease in $P_{E'_{CO_2}}$].[28] Peak $\dot{V}O_2$ was averaged over the last 30 s of exercise. CPETs were reported by two experienced assessors both blind to patient characteristics and outcome data.

Short-term surgical outcome was assessed as morbidity (by medical and nursing staff blind to any CPET data) using the nine domains listed in the Post-Operative Morbidity Survey[29] on day 5, Clavien–Dindo Classification[30] (highest grade for the most serious sustained in-hospital complication), and in-hospital mortality. Length of hospital stay (days) was recorded prospectively, and patients were followed for 30 days post-discharge for re-admission and mortality. The patients and the colorectal MDT (including anaesthetists) were blind to all CPET data. No perioperative management or decisions were influenced by CPET data.

The primary aim was to establish the relationship between postoperative complications (POMS present or absent on day 5) and $\dot{V}O_2$ at $\hat{\theta}_L$; a secondary aim was to explore the multivariable relationship between CPET variables and other important prognostic variables with complications at day 5 after operation.

Statistical methods

Non-parametric receiver operator characteristic (ROC) curves were constructed for $\dot{V}O_2$ at $\hat{\theta}_L$, $\dot{V}O_2$ at peak, O_2 pulse at $\hat{\theta}_L$, and $\dot{V}_E/\dot{V}CO_2$ at $\hat{\theta}_L$ in order to assess their independent ability to discriminate between patients with and without day 5 morbidity. Optimal cut-points were obtained by minimizing the distance between points on the ROC curve and the upper left corner. Six variables (to satisfy the 10 events per variable rule)[31] were identified as candidates for a multivariable logistic regression model: $\dot{V}O_2$ at $\hat{\theta}_L$ and at peak, gender, operation type (laparoscopic/open), and O_2 pulse at $\hat{\theta}_L$ and $\dot{V}_E/\dot{V}CO_2$ at $\hat{\theta}_L$. A final multivariable model was obtained using forward stepwise selection [minimizing Akaike information criteria (AIC)]. Its sensitivity to variable exclusion and re-inclusion was also assessed using AIC. Model fit was assessed using the Hosmer–Lemeshow goodness-of-fit test. In order to explore the univariate relationship between CPET variables and length of stay, continuous CPET variables were dichotomized at the optimal cut-point for the ROC curve and the Kaplan–Meier curves were constructed. The log-rank test was used to compare survival curves; patients who died before discharge ($n=2$) were treated as right-censored.