ORIGINAL ARTICLE

Cardiopulmonary exercise testing for predicting postoperative morbidity in patients undergoing hepatic resection surgery

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Abstract

Objectives: Cardiopulmonary exercise testing (CPET) may predict which patients are at risk for adverse outcomes after major abdominal surgery. The primary aim of this study was to determine whether CPET variables are predicative of morbidity.

Methods: High-risk patients undergoing elective, one-stage, open hepatic resection were preoperatively assessed using CPET. Morbidity, as defined by the Postoperative Morbidity Survey (POMS), was assessed on postoperative day 3.

Results: A total of 104 patients underwent preoperative CPET and were included in the analysis. Of these, 73 patients (70.2%) experienced postoperative morbidity. Oxygen consumption at anaerobic threshold ($\dot{V}_{O_2}$ at AT, ml/kg/min) was the only CPET predictor of postoperative morbidity on multivariable analysis, with an area under the curve (AUC) of 0.66 [95% confidence interval (CI) 0.55–0.76]. In patients requiring a major hepatic resection (three or more segments), a $\dot{V}_{O_2}$ at AT of <10.2 ml/kg/min gave an AUC of 0.79 (95% CI 0.68–0.86) with 83.9% sensitivity and 52.0% specificity, 80.6% positive predictive value and 62.5% negative predictive value.

Conclusions: The application of a cut-off value for $\dot{V}_{O_2}$ at AT of <10.2 ml/kg/min in patients undergoing major hepatic resection may be useful for predicting which patients will experience morbidity.

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Introduction

Advances in hepatic resection surgery have enabled the safe resection of up to 60% of functional liver parenchyma[1] and improved in-hospital mortality rates to <2%.[2,3] However, the substantial physiological insult of this major procedure is associated with high rates of postoperative morbidity in the order of 50–60%.[4,5] The ability to identify patients at risk for postoperative morbidity can inform decision making and support the allocation of resources, including those of postoperative critical care.

Cardiopulmonary exercise testing (CPET) is a method of assessing preoperative cardiopulmonary fitness which has been used successfully to improve the accuracy of preoperative prediction of postoperative complications and mortality.[6–8] In major abdominal surgery, lower oxygen consumption at anaerobic threshold ($\dot{V}_{O_2}$ at AT, ml/kg/min) measured by CPET is associated with increased postoperative morbidity and poorer clinical outcomes.[9–11] However, the role of CPET in predicting morbidity in hepatic resection is unclear. The primary aim of this study was to determine whether CPET-derived variables were associated with short-term morbidity.

Materials and methods

This was a single-centre, prospective cohort study of consecutive patients aged over 18 years who underwent CPET as part of preoperative assessment for elective, one-stage, open hepatic resection at the Royal Marsden National Health Service Foundation Trust between May 2010 and April 2014. Patients considered to be at high risk were referred for CPET. These

included patients aged >70 years, patients aged <70 years with cardiorespiratory comorbidities and patients scheduled for hepatic resection involving synchronous bowel resection or vascular reconstruction or extensive biliary resection. The study was approved by the local institutional review board.

Cardiopulmonary exercise testing

Cardiopulmonary exercise testing was performed and reported by one of three consultant anaesthetists. Testing was conducted using the standardised approach recommended by the American Thoracic Society and American College of Physicians.[12]

Cardiopulmonary exercise testing was conducted on an electromagnetically braked cycle ergometer (Ultima CardiO$_2$®; Medical Graphics Corp., St Paul, MN, USA) following resting spirometry. Testing consisted of a 3-min rest period, 3 min of freewheeling and then pedalling against a ramped resistance/workload. The workload ramp gradient was determined using an accepted standard technique based on a calculation using predicted freewheel oxygen uptake ($\dot{V}_{O_2}$), predicted $\dot{V}_{O_2}$ at peak exercise, height and age.[12,13] Testing was terminated at the patient's volition, if the patient became symptomatic or if he or she was unable to maintain a cadence rate of 60 revolutions per minute (rpm). A 5-min recovery period was applied after the termination of testing.

Ventilation and gas exchange were measured using a metabolic cart (Geratherm Respiratory GmbH, Love Medical Ltd, Manchester, UK). Heart rate, full 12-lead electrocardiogram (ECG), blood pressure and pulse oximetry were monitored throughout CPET.

The CPET data were analysed using Cardioperfect 1.6.2.1105 [Welch Allyn (UK) Ltd, Aston Abbotts, UK] and MedGraphics BreezeSuite 7.2.0.64SP7 (Medical Graphics Corp.) to derive the following variables: $\dot{V}_{O_2}$ at AT (ml/kg/min); peak $\dot{V}_{O_2}$ (ml/kg/min); ventilatory equivalents for carbon dioxide (CO_2) at AT (VE_{CO_2}), and heart rate at AT (beats/min). The $\dot{V}_{O_2}$ peak was defined as the mean of the highest exertional oxygen uptake achieved over the last 30 s of maximal exercise. The AT was determined using the V-slope method outlined by Wasserman.[13] Values, where appropriate, were indexed to actual body weight. Table S1 (online) provides further explanation of the CPET variables. Results were routinely reviewed and reported by two of the consultant anaesthetists to ensure the validity of all CPET values derived.

Patient population

Baseline patient characteristics recorded for all patients included age, sex, body mass index (kg/m^2), American Society of Anesthesiologists (ASA) score, World Health Organization functional status score,[14] preoperative chemotherapy, history of smoking, type of liver resection determined according to the number of segments resected (minor for less than three segments and major for three or more segments),[15] reason for liver resection and presence of comorbidities.

Outcome measures

Outcomes were recorded by data collection officers blinded to CPET data and not directly involved in the study. Morbidity was measured using the Postoperative Morbidity Survey (POMS)[16] on postoperative day (PoD) 3. The POMS classifies morbidities according to whether they refer to cardiovascular, pulmonary, renal, gastrointestinal, neurological, infectious or haematological occurrences, wound complications or pain.

The primary outcome was the presence of postoperative morbidity defined as a POMS score of ≥1 on PoD 3. Complications were also classed according to the Clavien–Dindo system of classification,[17] but these data were not used in the primary outcome analysis because poor performance on CPET is associated with both postoperative medical and surgical complications and thus it was considered to be more appropriate to assess individual systems as per the POMS. Secondary outcomes measures were length of stay (LoS) in hospital, LoS in the critical care unit (CCU) and readmission to the CCU.

Perioperative management

All patients were admitted to hospital on the day of scheduled surgery. Anaesthesia was provided by one of three consultant anaesthetists and surgery performed by one of two consultant hepatobiliary surgeons. The hepatic resection was performed using the Cavitron Ultrasonic Surgical Aspirator (CUSA; Valleylab, Inc., Boulder, CO, USA) and argon beam coagulation. For patients with malignant tumours, the transection plane was first determined by intraoperative ultrasonography and the resection phase was performed under low central venous pressure conditions. There were no protocols for intraoperative management, but patients deemed to be at high risk were given additional cardiac output monitoring. The standard method of postoperative pain management referred to a thoracic epidural, from which the patient was weaned before PoD 3. Postoperative management included the routine admission of all patients to the CCU. A protocalized care package that included early mobilization and commencement of enteral nutrition was applied to all patients.

Statistical analysis

Continuous variables are reported as the mean ± standard deviation or median and interquartile range (IQR), depending on their distribution. Categorical variables are reported as frequencies with percentages. All statistical results are accompanied by 95% confidence intervals (CIs). Non-parametric receiver operating characteristic (ROC) curves were constructed for CPET variables associated with POMS-defined morbidity on PoD 3 to assess their independent ability to discriminate between patients with and without in-hospital postoperative morbidity. Optimal cut-off points were obtained by minimizing the distance between points on the ROC curve and the upper left corner.