Validation of preoperative cardiopulmonary exercise testing-derived variables to predict in-hospital morbidity after major colorectal surgery –
A Multicenter Trial

MA West, R Asher, M Browning, G Minto, M Swart, K Richardson, L McGarrity, S Jack, MPW Grocott on behalf of the PeriOperative Exercise Testing and Training Society (POETTS)

Academic Unit of Cancer Sciences, Faculty of Medicine, University of Southampton, UK
Integrative Physiology and Critical Illness Group, Clinical and Experimental Sciences, University of Southampton, UK
Cancer Research UK Liverpool Cancer Trials Unit, Liverpool, UK
Department of Anaesthesia, Maidstone and Tunbridge Wells NHS Trust, UK
Directorate of Anaesthesia, 9th Floor Terence Lewis Building, Derriford Hospital Plymouth, UK
Department of Anaesthesia and Critical Care Medicine, Torbay Hospital, Torquay, UK
Anaesthesia and Intensive Care Medicine, Medway Maritime Hospital, Kent, UK
Department of Anaesthesia, University Hospital Crosshouse, Kilmarnock, East Ayrshire, Scotland, UK
Background - Fitness predicts morbidity

Cardiopulmonary exercise testing for the evaluation of perioperative risk in non-cardiopulmonary surgery

Philip J Hennis, Paula M Meale, Michael P W Grocott

Best Practice & Research Clinical Anaesthesiology 25 (2011) 427–437

Review

A Systematic Review of the Role of Cardiopulmonary Exercise Testing in Vascular Surgery


Best Practice & Research Clinical Anaesthesiology

Perioperative cardiopulmonary exercise testing in the elderly

M. West, Clinical Research Fellow, S. Jack, Consultant Clinician Scientist, M.P.W. Grocott, Professor of Anaesthesia and Critical Care Medicine


Role of cardiopulmonary exercise testing as a risk-assessment method in patients undergoing intra-abdominal surgery: a systematic review

J. Moran, F. Wilson, E. Guinan, P. McCormick, J. Hussey and J. Moriarty
Fitness predicts morbidity – Colonic Surgery

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

M. A. West¹,²,³*, D. Lythgoe⁴, C. P. Barben¹, L. Noble¹, G. J. Kemp³, S. Jack⁵,⁶ and M. P. W. Grocott²,⁵,⁶

Gender
VO₂ at AT
Operation Type

Area under ROC curve = 0.87
P<0.01 (CI - 0.75 to 0.95)
VO₂ at AT Cut off - 10.2ml/kg/min
Sensitivity - 85%
Specificity – 80%
Fitness predicts morbidity – Rectal Cancer Surgery

Cardiopulmonary exercise testing for the prediction of morbidity risk after rectal cancer surgery

M. A. West¹,²,⁴, M. G. Parry¹, D. Lythgoe³, C. P. Barben¹, G. J. Kemp², M. P. W. Grocott⁴,⁵,⁶ and S. Jack⁵,⁶

Area under ROC curve = 0.87
Cut off - 10.6ml/kg/min
p<0.0001 (CI - 0.78-0.95)
Sensitivity - 92%
Specificity - 76%

Area under ROC curve = 0.85
Cut off - 18.6ml/kg/min
p<0.0001 (CI - 0.77-0.93)
Sensitivity - 82%
Specificity - 80%
Primary Aim – The aim of this study was to confirm (or refute) the predictive value of selected CPET variables (identified in previous publications) and their association with in-hospital morbidity in patients scheduled to undergo major colorectal surgery in a multicenter setting.

Inclusion –
• Major elective colorectal surgery (defined as a bowel resection +/- anastomosis or stoma)

Exclusion-
• Mechanical inability to undergo CPET
• Inability to consent
• Undergoing neoadjuvant chemo/chemoradiotherapy
• Undergoing emergency surgery
• Distant metastasis
• Inflammatory bowel disease

Methods

**Recruiting Sites** – 6 tertiary referral centers in England and Scotland between February 2012 and July 2014

**CardioPulmonary Exercise Testing** – Undertaken using a similar protocol. VO$_2$ at AT derived by similar modified V-slope method.

**Post-Operative Outcome** - Post-Operative Morbidity Survey at day 5 and Clavien-Dindo complication score, 30-day and 1 year-mortality

**Statistical Analyses**

**Sample size** n=425 patients with complete VO$_2$ at AT and VO$_2$ at Peak data (AUROC >0.65; 5-day morbidity incidence of 48%, 90% power p<0.05)

Univivariate logistic regression with robust standard errors to investigate the association between baseline demographics and post-operative complications

ROC curves to discriminate patients with and without complications

Multivariable logistic regression model with the top 6 variables was used
## Results - Patient Demographics

<table>
<thead>
<tr>
<th></th>
<th>Overall (n = 703)</th>
<th>No (n = 445)</th>
<th>Yes (n = 258)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Centre</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aintree</td>
<td>192 (27.3)</td>
<td>111 (57.8)</td>
<td>81  (42.2)</td>
<td></td>
</tr>
<tr>
<td>Crosshouse</td>
<td>26 (3.7)</td>
<td>20 (77)</td>
<td>6   (23)</td>
<td></td>
</tr>
<tr>
<td>Medway</td>
<td>8 (1.1)</td>
<td>5 (63)</td>
<td>3   (37)</td>
<td></td>
</tr>
<tr>
<td>Torbay</td>
<td>180 (25.6)</td>
<td>101 (56.1)</td>
<td>79  (43.9)</td>
<td></td>
</tr>
<tr>
<td>Maidstone</td>
<td>58 (8.3)</td>
<td>51 (88)</td>
<td>7   (12)</td>
<td></td>
</tr>
<tr>
<td>Plymouth</td>
<td>239 (34.0)</td>
<td>157 (65.7)</td>
<td>82  (34.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>69 (61–76)</td>
<td>67 (60–74)</td>
<td>72  (64–78)</td>
<td></td>
</tr>
<tr>
<td><strong>Sex ratio (M:F)</strong></td>
<td>428:275</td>
<td>279:166</td>
<td>149:109</td>
<td>0.408</td>
</tr>
<tr>
<td><strong>Body mass index (kg/m²)</strong></td>
<td>27 (24–31)</td>
<td>27 (24–30)</td>
<td>29 (25–32)</td>
<td>0.007</td>
</tr>
<tr>
<td><strong>Method of surgery</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.026</td>
</tr>
<tr>
<td>Open</td>
<td>435 (61.9)</td>
<td>245 (55.1)</td>
<td>190 (73.6)</td>
<td></td>
</tr>
<tr>
<td>Laparoscopic</td>
<td>268 (38.1)</td>
<td>200 (44.9)</td>
<td>68  (26.4)</td>
<td></td>
</tr>
<tr>
<td><strong>Surgical procedure</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.426</td>
</tr>
<tr>
<td>Right hemicolecotomy</td>
<td>159 (22.6)</td>
<td>99 (22.2)</td>
<td>60  (23.3)</td>
<td></td>
</tr>
<tr>
<td>Transverse hemicolecotomy</td>
<td>4 (0.6)</td>
<td>2 (0.4)</td>
<td>2   (0.8)</td>
<td></td>
</tr>
<tr>
<td>Left hemicolecotomy</td>
<td>37 (5.3)</td>
<td>21 (4.7)</td>
<td>16  (6.2)</td>
<td></td>
</tr>
<tr>
<td>Subtotal colectomy</td>
<td>25 (3.6)</td>
<td>12 (2.7)</td>
<td>13  (5.0)</td>
<td></td>
</tr>
<tr>
<td>Anterior resection</td>
<td>374 (53.2)</td>
<td>247 (55.5)</td>
<td>127 (49.2)</td>
<td></td>
</tr>
<tr>
<td>Hartmann procedure</td>
<td>30 (4.3)</td>
<td>17 (3.8)</td>
<td>13  (5.0)</td>
<td></td>
</tr>
<tr>
<td>APR</td>
<td>47 (6.7)</td>
<td>29 (6.5)</td>
<td>18  (7.0)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>27 (3.8)</td>
<td>18 (4.0)</td>
<td>9   (3.5)</td>
<td></td>
</tr>
</tbody>
</table>
Results

CPET Safety –

No safety issues reported with CPET. 15 patients had undiagnosed significant coronary artery disease and required preoperative interventions

<table>
<thead>
<tr>
<th>CPET Data</th>
<th>Overall</th>
<th>Postoperative complications</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\dot{V}_{O_2}$ at $\theta_L$ (ml per kg per min)</td>
<td>11.9 (9.9–14.3)</td>
<td>No: 13 (11.3–15.5)</td>
<td>Yes: 9.9 (8.6–11.6)</td>
</tr>
<tr>
<td>$\dot{V}_{O_2peak}$ (ml per kg per min)</td>
<td>18.8 (15.4–22.9)</td>
<td>No: 20.4 (17.5–24.7)</td>
<td>Yes: 15.5 (12.8–18.6)</td>
</tr>
<tr>
<td>$O_2$ pulse at $\theta_L$ (ml per beat)</td>
<td>9.1 (7.1–11.2)</td>
<td>No: 9.9 (7.8–12.3)</td>
<td>Yes: 7.5 (5.7–9.2)</td>
</tr>
<tr>
<td>$\dot{V}<em>{E}/\dot{V}</em>{CO_2}$ at $\theta_L$</td>
<td>30.9 (27.5–34.2)</td>
<td>No: 30.2 (27.4–33.2)</td>
<td>Yes: 32.0 (27.9–36.0)</td>
</tr>
</tbody>
</table>

CPET data in relation to postoperative complications. Median (IQR) p-value derived by continuous univariable comparisons using logistical regression
Results - Post-Operative Outcome

<table>
<thead>
<tr>
<th>Grade*</th>
<th>( \dot{V_O}_2 ) at ( \dot{LO} ) (ml per kg per min)</th>
<th>( \leq 11.1 ) (n = 284)</th>
<th>&gt; 11.1 (n = 419)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100 (35.2)</td>
<td>344 (82.1)</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>20 (7.0)</td>
<td>9 (2.1)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>125 (44.0)</td>
<td>40 (9.5)</td>
<td></td>
</tr>
<tr>
<td>IIIa</td>
<td>10 (3.5)</td>
<td>11 (2.6)</td>
<td></td>
</tr>
<tr>
<td>IIIb</td>
<td>20 (7.0)</td>
<td>12 (2.9)</td>
<td></td>
</tr>
<tr>
<td>IVa</td>
<td>4 (1.4)</td>
<td>2 (0.5)</td>
<td></td>
</tr>
<tr>
<td>IVb</td>
<td>1 (0.4)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>4 (1.4)</td>
<td>1 (0.2)</td>
<td></td>
</tr>
</tbody>
</table>

Postoperative morbidity by Clavien-Dindo grade in patients grouped according to the optimal cut-off point for \( \dot{V_O}_2 \) at AT. \( P < 0.001 \) (Fisher’s Exact test)

Postoperative mortality at 30-days was 1.7% and 5.1% at 1 year. All patients who were dead at 1 year had a postoperative complication. The median \( \dot{V_O}_2 \) at AT in this group was 10.1ml.kg\(^{-1}\).min\(^{-1}\)
Results - CPET and Post-Operative Outcome Prediction

a) VO₂ at AT

Area under ROC curve = 0.79
Cut off = 11.1 ml/kg/min
\( p < 0.0001 \) (CI - 0.76-0.83)
Sensitivity - 78%
Specificity - 71%

b) VO₂ at Peak

Area under ROC curve = 0.77
Cut off = 18.2 ml/kg/min
\( p < 0.0001 \) (CI - 0.72-0.82)
Sensitivity - 70%
Specificity - 72%
Results -
CPET and Post-Operative Outcome Prediction

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds ratio</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\dot{V}_O_2$ at $\hat{\theta}_L$ ($\leq 11.1$ ml per kg per min)</td>
<td>7.56 (4.44, 12.86)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>$\dot{V}<em>O</em>{2peak}$ ($\leq 18.2$ ml per kg per min)</td>
<td>2.15 (1.01, 4.57)</td>
<td>0.047</td>
</tr>
<tr>
<td>$\dot{V}_E/\dot{V}co_2$ at $\hat{\theta}_L$ ($&gt; 30.9$)</td>
<td>1.38 (1.00, 1.89)</td>
<td>0.047</td>
</tr>
<tr>
<td>Age (per 5 years)</td>
<td>1.05 (0.92, 1.19)</td>
<td>0.451</td>
</tr>
<tr>
<td>BMI ($&gt; 27$ kg/m$^2$)</td>
<td>1.05 (1.03, 1.08)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Operation (laparoscopic)</td>
<td>0.30 (0.02, 0.44)</td>
<td>0.033</td>
</tr>
</tbody>
</table>

Model prediction between patients with and without complications was good with an **AUROC 0.83, sensitivity 86 % and specificity of 67%**
Strengths and Limitations

Strengths

1. Prospective multicenter study design
2. Homogenous study population
3. Wide-ranging socioeconomic and geographical location of recruited patients
4. Robust CPET and postoperative outcome reporting, with 1-year survival

Limitations

1. Lack of blinding of colorectal MDT’s and anesthetists from CPET data
2. Lack of CPET dual reporting (both undertaken in our previous publications)
Conclusions

This study gives definitive evidence that selected preoperative CPET variables can be used to reliably identify high-risk patients prior to major elective colorectal surgery.

Here we successfully validate the cut off points and multivariable models we published in colonic surgery in the Br J Anaesthesia and in rectal cancer surgery in the Br J Surgery in 2014.

Decisions regarding perioperative care or fitness for surgery should still be based on complete clinical and CPET assessment and not on individual CPET variables or predictive models in isolation.
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- **Maidstone and Tunbridge Wells:** Dr. Mike Browning
- **South Devon Healthcare:** Dr. Mike Swart
- **Medway Maritime Hospital:** Dr. Katherine Richardson
- **Plymouth Hospitals:** Dr. Gary Minto
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The patients and their families