## **CLINICAL PRACTICE**

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

M. A. West<sup>1,2,3\*</sup>, D. Lythgoe<sup>4</sup>, C. P. Barben<sup>1</sup>, L. Noble<sup>1</sup>, G. J. Kemp<sup>3</sup>, S. Jack<sup>5,6</sup> and M. P. W. Grocott<sup>2,5,6</sup>

<sup>1</sup> Colorectal Surgery Research Group, 3rd Floor Clinical Sciences Building, Aintree University Hospitals NHS Foundation Trust, Lower Lane, Liverpool L9 7AL, UK

<sup>2</sup> Critical Care Research Area, NIHR Respiratory Biomedical Research Unit, University Hospital Southampton NHS Foundation Trust, Southampton, UK

<sup>3</sup> Department of Musculoskeletal Biology, Faculty of Health and Life Sciences and <sup>4</sup> Cancer Research UK Liverpool Cancer Trials Unit, Waterhouse Building, University of Liverpool, Liverpool, UK

<sup>5</sup> Integrative Physiology and Critical Illness Group, Clinical and Experimental Sciences, Mailpoint 810, Sir Henry Wellcome Laboratories, Faculty of Medicine, University of Southampton, University Hospital Southampton NHS Foundation Trust, Tremona Road, Southampton SO16 6YD, UK <sup>6</sup> Anaesthesia and Critical Care Research Unit, University Hospital Southampton NHS Foundation Trust, Mailpoint 27, D Level, Centre Block, Tremona Road, Southampton SO16 6YD, UK

\* Corresponding author. E-mail: mwest@liverpool.ac.uk

## **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<sub>2</sub> uptake (VO<sub>2</sub>) at estimated lactate threshold ( $\hat{\theta}_L$ ) [median 9.9 (IQR 8.3–12.7) vs 11.2 (9.5–14.2) ml kg<sup>-1</sup> min<sup>-1</sup>, *P*<0.01], VO<sub>2</sub> at peak [15.2 (12.6–18.1) vs 17.2 (13.7–22.5) ml kg<sup>-1</sup> min<sup>-1</sup>, *P*=0.01], and ventilatory equivalent for CO<sub>2</sub> (V<sub>E</sub>/VCO<sub>2</sub>) 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 VO<sub>2</sub> 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  $(15-20\%)^{1}$ <sup>2</sup> and mortality, particularly in elderly patients and those with co-morbidities.<sup>3</sup> Recent UK cancer audits show 30 day mortality of 2.3% for elective and 11.4% for emergency surgery.<sup>4</sup> 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.<sup>5</sup> Approaches to risk evaluation include clinical acumen, clinical prediction scores [e.g. ASA physical status (ASA-PS), Duke's Activity Scores, POSSUM, CR-POSSUM],<sup>6-8</sup> plasma biomarkers,<sup>9</sup> measures of cardiac function,<sup>10 11</sup> and shuttle walk tests,<sup>12-14</sup> but their effectiveness in predicting complications is not well established.<sup>15-17</sup>

Cardiopulmonary exercise testing (CPET), which has been used for risk stratification before thoracic and abdominal surgery,<sup>17–21</sup> 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.<sup>22–24</sup>

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 (VO<sub>2</sub> at  $\hat{\theta}_1$ ). 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.<sup>25</sup> 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<sup>-1</sup> based on a calculation<sup>26</sup> using predicted freewheel oxygen uptake ( $\dot{VO}_2$ ), predicted  $\dot{VO}_2$  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 (VO<sub>2</sub>/heart rate), all measured at  $\hat{\theta}_{\rm L}$  and at peak exercise.<sup>26</sup>  $\hat{\theta}_{L}$  was estimated conventionally [breakpoint in the  $\dot{V}CO_2 - \dot{V}O_2$  relationship,<sup>27</sup> with increases in  $\dot{V}_E/\dot{V}O_2$  and endtidal (PE') O<sub>2</sub> but no increase in  $\dot{V}_E/\dot{V}CO_2$  or decrease in  $Pe'_{CO_2}$ ].<sup>28</sup> 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<sup>29</sup> on day 5, Clavien–Dindo Classification<sup>30</sup> (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  $\dot{VO}_2$  at  $\hat{\theta}_L$ ,  $\dot{VO}_2$  at peak,  $O_2$  pulse at  $\hat{\theta}_{\rm L}$ , and  $\hat{V}_{\rm E}/\rm{VCO}_2$  at  $\hat{\theta}_{\rm L}$  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)<sup>31</sup> were identified as candidates for a multivariable logistic regression model:  $\dot{VO}_2$  at  $\hat{\theta}_L$  and at peak, gender, operation type (laparoscopic/open), and  $O_2$  pulse at  $\hat{\theta}_{L}$  and  $\hat{V}_{E}/VCO_{2}$  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.

**Table 1** Patient characteristics. Data presented as median (25th – 75th percentile), mean (sp), or frequency (%). *P*-values obtained using univariate logistic regression,  $\chi^2$  tests, or Fisher's exact tests where cell counts were insufficient. All percentages represent proportions within complications (yes/no classifications), except 'n' which refers to the proportion of patients with and without complications

Variable	No complications	Complications	Overall	P-value
n	71 (52%)	65 (48%)	136	_
Gender				
Male	41 (58%)	48 (74%)	89 (65%)	
Female	30 (42%)	17 (26%)	47 (35%)	0.05
Age (yr)	67 (59–75)	72 (65–77)	71 (62–77)	0.03
ASA	2 (2-3)	2 (2-3)	2 (2-3)	0.13
BMI (kg m $^{-2}$ )	27 (6)	27 (7)	27 (7)	0.78
Laparoscopic	31 (44%)	21 (32%)	52 (38%)	
Open	40 (56%)	44 (68%)	84 (62%)	0.18
Operation type				
Right hemicolectomy	22	19	41	
Left hemicolectomy	3	5	8	
Subtotal colectomy	0	1	1	
Anterior resection	28	18	46	
Abdominoperineal resection	7	6	13	
Hartmann's procedure	3	5	8	
Other colonic resection	8	11	19	
Anastomosis				
Yes	61 (86%)	54 (83%)	115 (85%)	0.65
No	10 (14%)	11 (17%)	21 (15%)	
Surgery type				
Oncological surgery	63 (89%)	58 (89%)	121 (89%)	
Benign surgery	8 (11%)	7 (11%)	15 (11%)	0.56
Ischaemic heart disease	9 (13%)	5 (8%)	14 (10%)	0.34
Diabetes	6 (8%)	10 (15%)	16 (12%)	0.21
Cerebrovascular disease	1 (1%)	3 (5%)	4 (3%)	0.27
Heart failure	0 (0%)	5 (8%)	5 (4%)	0.01
ASA physical status				
I	10 (14%)	6 (9%)	16 (12%)	
II	41 (59%)	28 (44%)	69 (51%)	
III	18 (26%)	28 (44%)	46 (34%)	
IV	1 (1%)	2 (3%)	3 (2%)	

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Patients who left the study before day 5 (n=14) were excluded from the analysis of length of stay. All analyses were conducted using Stata (StataCorp., 2011, *Stata Statistical Software: Release 12*. College Station, TX: StataCorp LP). Continuous variables are reported as mean and standard deviation (sD) or median and inter-quartile range (IQR) depending on the distribution. Categorical variables are presented as frequency (%). *P*-values in Tables 1 and 2 were obtained using univariate logistic regression (continuous) and  $\chi^2$  or Fisher's exact tests (categorical). Statistical significance was taken at 5%.

## Results

One hundred and ninety-eight patients consented; of whom, 25 had no surgery (15 due to patient choice, 10 due to irresectable metastasis), 11 needed an emergency procedure, and three were unable to perform a CPET. Of the 159 who had adequate CPET and underwent major elective surgery, 23 lacked complete data. Of the remaining 136 (89 males, 46 females), 41 had right and nine left hemicolectomy, 46 anterior resection, one subtotal colectomy, 13 abdominoperineal resections, eight Hartman's procedure, and 19 other major colonic resections. One patient developed a supraventricular tachycardia at peak exercise. The patient's ECG was discussed at MDT and was subsequently referred to a cardiologist. Surgery on this patient proceeded as normal. Table 1 shows patients grouped by occurrence or not of in-hospital postoperative complications: these groups differed significantly in gender, age, and preoperative heart failure, but not in operation type, surgery, or presence of anastomosis/stoma. Table 2 shows grouped CPET data: patients with a complication had significantly lower VO<sub>2</sub> at  $\hat{\theta}_{L}$ , VO<sub>2</sub> at peak, and higher  $\hat{V}_{E}$ /VCO<sub>2</sub> at  $\hat{\theta}_{L}$ . Three patients unable to attain  $\hat{\theta}_{L}$  sustained a complication and their discharge was delayed; these were excluded from analysis.

 Table 2
 CPET variables. Data presented as median (25th – 75th percentile) and as frequency (%)\*. P-values obtained using univariate logistic regression or Fisher's exact tests where cell counts were insufficient

Variable	No complications	Complications	Overall	P-value
$\dot{VO}_2$ at LT (ml kg <sup>-1</sup> min <sup>-1</sup> )	11.2 (9.5–14.2)	9.9 (8.3–11.8)	10.6 (8.9–12.7)	< 0.01
$\dot{V}O_2$ at peak (ml kg $^{-1}$ min $^{-1}$ )	17.2 (13.7–22.5)	15.2 (12.6-18.1)	15.8 (12.9–20.2)	0.01
$O_2$ pulse at LT (ml beat <sup>-1</sup> )	7.7 (6.2–10.2)	7.5 (5.9–9.2)	7.5 (6.1–9.7)	0.22
$\dot{V}_{E}/\dot{V}CO_{2}$ at LT	31.3 (28.0-34.8)	33.9 (30.0-39.1)	32.3 (29.4–37.4)	< 0.01
Attained LT?*				
Yes	71 (100%)	62 (89%)	133 (98%)	
No	0 (0%)	3 (11%)	3 (2%)	0.05

**Table 3** Total postoperative morbidity assessed by the Clavien – Dindo classification (highest grade of morbidity attained in-hospital) and postoperative morbidity assessed by POMS at day 5 after operation (nine domains of morbidity assessed at day 5 after operation) dichotomized at the optimal cut-off for  $\dot{VO}_2$  at  $\hat{\theta}_L$  (10.1 ml kg<sup>-1</sup> min<sup>-1\*</sup>). *P*-values obtained using the  $\chi^2$  tests or Fisher's exact tests where cell counts were insufficient

Complication type	Clavien-Dindo classification	POMS defined morbidity at day 5		P-value
		LT≤10.1* (n=64)	LT>10.1* (n=72)	
Pulmonary				
Pneumonia	II	10 (16%)	2 (3%)	< 0.001
Infection				
Febrile and requiring antibiotics	II	15 (23%)	6 (8%)	0.02
Anastomotic leak or collection requiring re-operation	IIIb	4 (6%)	4 (6%)	1.00
Renal				
Acute kidney injury	Ι	8 (13%)	4 (6%)	0.15
Gastrointestinal				
Ileus	Ι	14 (22%)	10 (14%)	0.22
Total parenteral nutrition	II	5 (8%)	2 (3%)	0.25
Cardiovascular				
Arrhythmias	II	8 (13%)	4 (6%)	0.15
Myocardial infarction	II	3 (5%)	2 (3%)	0.67
Neurological	IV	2 (3%)	0 (0%)	0.22
Haematological	II	2 (3%)	2 (3%)	1.00
Pain	Ι	5 (8%)	3 (4%)	0.48
Wound				
Abdominal	II	4 (6%)	2 (3%)	0.42
Perineal	Ι	3 (5%)	2 (3%)	0.67

Sixty-five patients (48%) sustained a complication at day 5; of whom, two died in hospital (1.5% mortality) from myocardial infarction (at days 3 and 5) and eight (6.5%) suffered anastomotic leak at a median of 6 days (four anterior resection, three right, and one left hemicolectomy): of these, five were re-operated, three treated conservatively with radiologicalinserted drains and i.v. antibiotics. A further two patients were re-operated at median 5 days (one patient suffered intestinal obstruction and another a necrotic stoma). All these suffered further complications and delayed hospital discharge. Table 3 shows POMS-defined complication at day 5 after operation and Clavien-Dindo classification. POMS episodes were dichotomized around the ROC curve cut-point for  $VO_2$  at  $\hat{\theta}_L$ . Pulmonary and infective complications (patients requiring antibiotics for a febrile episode) differed between the groups (P<0.001 and 0.02, respectively).

Independently,  $\dot{VO}_2$  at  $\hat{\theta}_L$ ,  $\dot{VO}_2$  at peak, and  $\dot{V}_E/\dot{VCO}_2$  were associated with day 5 morbidity (P < 0.05), whereas  $O_2$  pulse at  $\hat{\theta}_L$  and ASA were not (P = 0.22 and 0.11, respectively). For  $\dot{VO}_2$  at  $\hat{\theta}_L$  [area under the curve (AUC) 0.63, confidence interval (CI) 0.54–0.73], the optimal cut-point was 10.1 ml kg<sup>-1</sup> min<sup>-1</sup>, giving 68% sensitivity and 58% specificity (Fig. 1), while for  $\dot{VO}_2$  at peak (AUC 0.63, CI 0.53–0.73), the cut-point was 16.7 ml kg<sup>-1</sup> min<sup>-1</sup>, giving 55% sensitivity and 69% specificity. For  $\dot{V}_E/\dot{VCO}_2$  at  $\hat{\theta}_L$  (AUC 0.64, CI 0.55–0.74), the cut-point was 32.9, giving 60% sensitivity and 66% specificity.

Only VO<sub>2</sub> at  $\hat{\theta}_{\rm L}$  and gender were retained in the final multivariable logistic regression model. In this model, the odds of complications are higher for a male than a female with the same VO<sub>2</sub> at  $\hat{\theta}_{\rm L}$  [odds ratio (OR) 4.19, CI 1.78–9.88, P<0.001]; a 1.0 ml kg<sup>-1</sup> min<sup>-1</sup> increase in VO<sub>2</sub> at  $\hat{\theta}_{\rm L}$  is associated with ~20% reduction in the odds of complications (OR 0.77, CI



Fig 1 ROC curve for oxygen uptake at estimated lactate threshold (VO\_2 at  $\hat{\theta}_L).$ 



**Fig 2** ROC curve for multivariable logistic regression.

0.66–0.89, P<0.0005) and a 2.0 ml kg<sup>-1</sup> min<sup>-1</sup> increase with ~40% reduction (OR 0.60, CI 0.45–0.80, P<0.001), after adjustment for sex. The ability of this model to discriminate between patients with and without a complication was reasonable (AUC 0.71, CI 0.62–0.80, 68% sensitivity and 65% specificity at the optimal cut-point; positive predictive value=62%, negative predictive value=69%) (Fig. 2).

There is evidence to suggest that, independent of other predictive variables, patients with  $\dot{VO}_2$  at  $\hat{\theta}_L$  (P=0.003) (Fig. 3) or  $\dot{VO}_2$  at peak (P=0.004) above the cut-point and  $\dot{V}_E/\dot{VCO}_2$  at  $\hat{\theta}_L$ (P<0.0001) below the cut-point have a significantly reduced length of hospital stay.

## Discussion

#### Main findings and comparison with other studies

This prospective, blinded, observational study provides novel evidence supporting CPET as an objective risk assessment



**Fig 3** Kaplan-Meier curve relating oxygen uptake at estimated lactate threshold ( $\dot{V}O_2$  at  $\hat{\theta}_L$ ) to length of hospital stay (LOS). Blue line  $\dot{V}O_2$  at  $\hat{\theta}_L \leq 10.1$  ml kg<sup>-1</sup> min<sup>-1</sup> and green line  $\dot{V}O_2$  at  $\hat{\theta}_L > 10.1$  ml kg<sup>-1</sup> min<sup>-1</sup>.

tool before major colonic surgery. In this cohort,  $\dot{V}O_2$  at  $\hat{\theta}_{L}$ and peak were significantly lower and  $\dot{V}_{\rm E}/\dot{\rm V}{\rm CO}_2$  at  $\hat{\theta}_{\rm L}$  significantly higher, in patients encountering POMS-defined complication at day 5 after operation, and single-variable analysis confirms these associations, albeit with only moderate sensitivity and specificity. The poor predictive performance of CPET variables in our study when assessed independently is consistent with the literature<sup>23 24</sup> and reflects the complex interactions between baseline physiology and elective surgical trauma on postoperative outcomes. However, multivariable analysis showed that  $\dot{V}O_2$  at  $\hat{\theta}_L$  and gender were independent predictors of complications after surgery with moderate discrimination between patients with, and without, complications. ASA was not independently related to outcome and inclusion of this variable in the multivariable model had a negligible effect.

This study adds to the literature supporting objective measures of physical fitness for risk assessment in major abdominal surgery. The findings by Older and colleagues<sup>32</sup> in 187 elderly patients undergoing major intra-abdominal surgery that preoperative  $\hat{\theta}_{\rm L}$  <11.0 ml kg<sup>-1</sup> min<sup>-1</sup> was associated with increased cardiovascular mortality established CPET as a tool for preoperative risk assessment and stratification. In a later study and a review, <sup>20 33</sup> Older investigated triaging: if a patient had  $\hat{\theta}_{\rm L} < 11$ ml  $kg^{-1}$  min<sup>-1</sup>, they were assigned to ICU before operation. Assessing 843 patients >55 yr undergoing major colorectal surgery, radical nephrectomies, and cystectomies, Wilson and colleagues<sup>18</sup> concluded that  $\hat{\theta}_{\rm L} < 10.9$  ml kg<sup>-1</sup> min<sup>-1</sup> and  $\dot{V}_{\rm E}/\dot{\rm V}{\rm CO}_2$  at  $\hat{\theta}_{\rm L} \ge 34$  had 88% sensitivity and 47% specificity for hospital mortality. Snowden and colleagues<sup>17</sup> evaluated CPET in preoperative risk assessment in elderly (mean age 70 yr) patients undergoing major intra-abdominal surgery, finding that the  $\hat{\theta}_{\rm L}$  optimal cut-point of 10.1 ml kg<sup>-1</sup> min<sup>-1</sup> gave 88% sensitivity and 79% specificity for discriminating postoperative complications (AUC 0.85; CI 0.78-0.91; P<0.001). In 32 patients

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undergoing major intra-abdominal surgery, Hightower and colleagues<sup>6</sup> found that  $\hat{\theta}_L < 75\%$  of predicted value predicted complications [AUC 0.72 (CI 0.57–0.87); sensitivity 88%; specificity 56%, *P*=0.016]. A particular strength of our study, and those of Snowden and Hightower, is that clinicians were blinded to CPET results, which eliminates 'confounding by indication'.<sup>34</sup>

Junejo and colleagues<sup>35</sup> evaluated preoperative CPET in predicting outcome after major hepatic resection in 108 patients:  $\hat{\theta}_L < 9.9 \text{ ml kg}^{-1} \text{ min}^{-1}$  was 100% sensitive and 76% specific for in-hospital mortality, age and  $\dot{V}_E/\dot{V}CO_2$  at  $\hat{\theta}_L$  (84% specificity and 47% sensitivity) were related to post-operative complications, and long-term survival with  $\hat{\theta}_L < 9.9 \text{ ml kg}^{-1} \text{ min}^{-1}$  was significantly worse (hazard ratio 1.81, CI 1.04–3.17); however, only eight deaths out of 94 patients were recorded. Otto and colleagues<sup>36</sup> retrospectively studied aerobic exercise capacity in inflammatory bowel disease patients, finding that adjusted  $\hat{\theta}_L$  in Crohn's disease was lower than in colorectal cancer [mean (sd): 11.4 (3.4) vs 13.2 (3.5) ml kg<sup>-1</sup> min<sup>-1</sup>]. This justifies our exclusion of inflammatory bowel disease patients as pathophysiologically distinct.

Our data further support CPET in perioperative risk assessment.<sup>22-24</sup> Our best prognostic markers of postoperative complications were  $\dot{V}_{\rm F}/\dot{\rm V}{\rm CO}_2$  at  $\hat{\theta}_1$  with a cut-off at 32.9,  $\dot{\rm V}{\rm O}_2$  at  $\hat{\theta}_1$ with a cut-off at 10.1 ml kg<sup>-1</sup> min<sup>-1</sup>, and  $\dot{V}O_2$  at peak with a cut-off at 16.7 ml kg<sup>-1</sup> min<sup>-1</sup>. These are similar to cut-off points found by Older and colleagues,<sup>20</sup> Snowden and colleagues,<sup>17</sup> and Junejo and colleagues,<sup>35</sup> although the sensitivity and specificity of individual variables were moderate when compared with other studies. However, our multivariable logistic regression model identifies gender and  $\hat{\theta}_{L}$  as important predictors of day 5 complications, albeit with moderate AUC, specificity, and sensitivity. Interestingly, in upper gastrointestinal cancer surgery,<sup>37</sup> bariatric surgery,<sup>38</sup> and liver transplantation<sup>39</sup> surgery, the association with outcome and the cut-off point for  $\dot{V}O_2$  at  $\hat{\theta}_L$  is different. However, a recently published series by Colson and colleagues<sup>40</sup> concludes that singlevariable primary endpoints commonly derived from CPET (such as  $\hat{\theta}_{l}$ ) were not associated with 5 yr survival, although in a multivariable analysis, many CPET variables were important predictors.

#### Strengths and weaknesses

Strengths of this study include the homogeneous nature of the study population (only colonic surgical patients were included, rectal cancer patients who were undergoing cancer therapies were excluded), the blinded reporting of objectively measured CPET variables, the prospective nature of the study, the blinding to CPET results of caring clinicians and outcome data collectors, and the use of POMS<sup>29</sup> (which has been validated in the UK) as a primary outcome measure and is currently used in National Institute for Health Research and Medical Research Council funded studies.

Potential weaknesses include the single-centre design which limits generalizability to other centres, as the ROC curve cut-off points are optimized for this local cohort and future validation work in similar cohorts should be performed.

#### **Conclusion and further research**

Our results indicate that when using CPET in patients awaiting colonic surgery, clinicians should consider using VO<sub>2</sub> at  $\hat{\theta}_L$  (ROC cut-off 10.1 ml kg<sup>-1</sup> min<sup>-1</sup>) and gender as a simple risk prediction tool. Of course, decisions regarding patient care or fitness for surgery should be made using the overall clinical and CPET picture. The identification of  $\hat{\theta}_L$  and gender as a predictor for short-term outcome in colonic surgery is novel; however, confirmation of these results in a larger colonic surgical cohort is encouraged to establish whether several preoperative risk assessment tools can be combined to predict risk more effectively. Furthermore, we suggest that improving physical fitness, for example, VO<sub>2</sub> at  $\hat{\theta}_L$  and peak might improve surgical outcome in this population; to test this, we are currently investigating the role of a structured preoperative exercise training programme (prehabilitation) in this patient group (NCT01325909).

## Authors' contributions

M.A.W.: conception, study design, data acquisition, analysis, drafting article, revision, and final approval. D.L.: analysis and interpretation of data, drafting article, revising for intellectual content, and final approval. C.P.B.: study design, data acquisition, analysis, drafting article, revision, and final approval. L.N.: study design, data acquisition, analysis, drafting article, revision, and final approval. S.J.: conception, study design, revision, and final approval. G.J.K.: analysis and interpretation of data; critical revision of manuscript, and final approval. M.P.W.G.: conception, study design, revision, and final approval.

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## **Declaration of interest**

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