

ORIGINAL ARTICLE

Pre-operative cardiopulmonary exercise testing predicts adverse post-operative events and non-progression to adjuvant therapy after major pancreatic surgery

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Abstract

Background: Surgery followed by chemotherapy is the primary modality of cure for patients with resectable pancreatic cancer but is associated with significant morbidity. The aim of the present study was to evaluate the role of cardiopulmonary exercise testing (CPET) in predicting post-operative adverse events and fitness for chemotherapy after major pancreatic surgery.

Methods: Patients who underwent a pancreaticoduodenectomy or total pancreatectomy for pancreatic head lesions and had undergone pre-operative CPET were included in this retrospective study. Data on patient demographics, comorbidity and results of pre-operative evaluation were collected. Post-operative adverse events, hospital stay and receipt of adjuvant therapy were outcome measures.

Results: One hundred patients were included. Patients with an anaerobic threshold less than 10 ml/kg/min had a significantly greater incidence of a post-operative pancreatic fistula [International Study Group for Pancreatic Surgery (ISGPS) Grades A–C, 35.4% versus 16%, $P = 0.028$] and major intra-abdominal abscesses [Clavien–Dindo (CD) Grades III–V, 22.4% versus 7.8%, $P = 0.042$] and were less likely to receive adjuvant therapy [hazard ratio (HR) 6.30, 95% confidence interval (CI) 1.25–31.75, $P = 0.026$]. A low anaerobic threshold was also associated with a prolonged hospital stay (median 20 versus 14 days, $P = 0.005$) but not with other adverse events.

Discussion: CPET predicts a post-operative pancreatic fistula, major intra-abdominal abscesses as well as length of hospital stay after major pancreatic surgery. Patients with a low anaerobic threshold are less likely to receive adjuvant therapy.

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Introduction

Pancreatic cancer is the 10th most common cancer in the UK but the fifth most common cause of cancer death with only 16–17% surviving beyond the first year and 3% surviving beyond 5 years.¹ The majority of patients (80–85%) with pancreatic cancer present with inoperable disease.^{1,2} In patients with resectable disease, surgery^{2–4} followed by adjuvant chemotherapy^{5,6} remains the primary modality of cure.

The decision to operate on these patients depends not only on the pre-operative tumour stage but also on patient factors.^{7,8}

Patient factors, in particular those that affect fitness, are also important in determining the short-term outcome in those that do undergo potentially curative surgery.^{9,10} However, major pancreatic surgery is associated with significant morbidity and mortality and patients who have post-operative complications are less likely to get adjuvant therapy.¹¹

There have been a number of attempts to objectively define patient fitness and its relationship with post-operative outcome. Copeland *et al.* (1991) reported that the Physiological and Operative Severity Score for the enumeration of Mortality and Morbidity (POSSUM) criteria, in particular the POSSUM physiology

score (PPS) could be used to quantify the risk of post-operative morbidity and mortality.¹² However, the role of POSSUM in predicting post-operative outcome after surgery for pancreatic cancer is not entirely clear.^{13–17} The physiological component of POSSUM as well as other similar risk scoring systems such as E-PASS (Estimation of Physiologic Ability and Surgical Stress)¹⁸ are calculated based on known comorbidities, clinically evident abnormalities in patient physiology or blood tests.

More recently, there has been some evidence that the presence of an ongoing systemic inflammatory response before surgery is associated with the development of post-operative complications in patients undergoing surgery for colorectal cancer,¹⁹ oesophageal cancer²⁰ as well as pancreatic cancer.²¹

Older *et al.* (1993) reported that cardiopulmonary exercise testing (CPET) was an objective evaluation of the response of the cardiovascular and respiratory systems to an increase in oxygen demand during exercise and was useful in predicting peri-operative morbidity and mortality in patients undergoing major abdominal surgery.²²

The aim of the present study was to evaluate the role of various measures of patient physiological fitness including cardiopulmonary exercise testing in predicting post-operative adverse events as well as fitness for adjuvant therapy in patients undergoing major pancreatic surgery.

Methods

Patients who underwent a pancreaticoduodenectomy or total pancreatectomy for pancreatic head lesions between August 2008, when cardiopulmonary exercise testing was first used for fitness assessment at our hospital, and January 2012 were considered for this retrospective study. Patients who had not undergone cardiopulmonary exercise testing as part of their preoperative assessment and patients who underwent cardiopulmonary exercise testing but did not undergo surgery were excluded.

Data on patient demographics, comorbidity including cardiovascular and respiratory disease, pre-operative blood tests, chest X-ray and cardiopulmonary exercise tests were collected from prospectively maintained databases (March 2009–January 2012) and case note review (August 2008–March 2009). Data were also collected for patients who did not undergo cardiopulmonary exercise testing to allow comparison with the study group. The POSSUM Physiology Score was calculated based on 11 physiological parameters [cardiac disease including hypertension, ischaemic heart disease and heart failure, respiratory disease causing breathlessness on exertion and chronic obstructive pulmonary disease (COPD), electrocardiography (ECG) changes, pulse rate, blood pressure, haemoglobin, white cell count, serum sodium, serum potassium, serum urea and Glasgow Coma Scale] as described previously.

Cardiopulmonary exercise tests were performed in the Department of Respiratory Medicine at the Glasgow Royal Infirmary using the ZAN-600 CPET suite (nSpire Health, Longmont, CO,

USA). An electrically-braked cycle ergometer was used to perform a symptom-limited, incremental work-load test preceded by a 3-min rest period. The test was stopped at maximum exercise tolerance, significant ischaemic changes on ECG or for other safety reasons. The anaerobic threshold was calculated using the V-slope^{23,24} and ventilatory equivalents²³ methods. A low anaerobic threshold was defined as oxygen consumption less than 10 ml/kg/min based on previous work by Snowden *et al.*²⁵ who reported that an anaerobic threshold less than 10.1 ml/kg/min was associated with an increase in post-operative complications after major abdominal surgery.

The decision to operate was based on overall pre-operative evaluation of the patient's comorbid conditions and performance status and not exclusively on the result of cardiopulmonary exercise testing. While the results of cardiopulmonary exercise tests were available to the clinicians before surgery, no specific changes were made to peri-operative management based exclusively on these results. These results were used in conjunction with other established forms of pre-operative evaluation for risk assessment and peri-operative care. All patients were routinely admitted to the surgical high-dependency unit unless intra-operative events or post-operative complications required admission to the intensive care unit. Patients were discharged after resolution of organ dysfunction and/or sepsis and when nutrition, analgesia and mobilization were adequately established to the clinician's and patient's satisfaction.

Post-operative adverse events were recorded using internationally recognized definitions. The International Study Group for Pancreatic Surgery (ISGPS) definitions were used to classify pancreatic fistulae²⁶ and post-operative haemorrhage.²⁷ The Clavien–Dindo (CD) classification^{28,29} was used to grade other complications and CD grades III–V were considered major. Multiple admissions to critical care as well as re-operations were recorded. Operative mortality was defined as post-operative death in-hospital regardless of duration of stay or occurring within 30 days of the surgery. All complications were discussed at a weekly multidisciplinary meeting attended by three pancreatic surgeons and a radiologist with a specialist interest in pancreatic diseases and recorded in a prospective database.

Primary outcome measures were length of stay in hospital, major post-operative adverse events including operative mortality and fitness to undergo adjuvant therapy when indicated. Secondary outcome measures included cumulative length of stay in critical care and the number of critical care admissions.

Statistical analysis

Grouping of the variables was carried out using standard or previously published thresholds. In the absence of such thresholds, the variables were treated as continuous variables and analysed using non-parametric statistical methods. Cox proportional hazards regression analysis was used to study the relationship between pre-operative risk factors and length of hospital stay. The chi-square test

Table 1 Clinico-pathological characteristics of patients undergoing major pancreatic surgery during the study period

	All patients <i>n</i> = 129	Excluded <i>n</i> = 29	Included <i>n</i> = 100	<i>P</i>
Age (years)				
≤65	71 (55%)	24	47	0.001
>65	58 (45%)	5	53	
Gender				
Male	77 (60%)	17	60	0.894
Female	52 (40%)	12	40	
BMI (kg/m ²)				
≤25	53 (44%)	8	45	0.817
>25	66 (56%)	11	55	
Pre-operative biliary drainage				
No	68 (59%)	12	56	0.154
Yes	48 (41%)	4	44	
mGPS				
0	76 (59%)	13	63	0.279
1	11 (9%)	5	6	
2	41 (32.0%)	10	31	
Haemoglobin (g/dl)				
≥12	80 (64%)	18	62	0.353
<12	45 (36%)	7	38	
POSSUM Physiology Score				
11–14	61 (51%)	12	50	0.701
>14	59 (49%)	10	50	
Serum bilirubin (micromol/l)				
≤35	70 (55%)	12	58	0.156
>35	58 (45%)	16	42	
Operation type				
Pancreatico-duodenectomy	127 (98%)	29	98	0.045
(Sub-)Total Pancreatectomy	2 (2%)	0	2	
Operative mortality	7 (5%)	0	7	0.144
Postoperative stay (days)	17 (13–27)	20 (13–30)	17 (13–26)	0.518
Critical care stay (days)	7 (6–12)	7 (6–14)	7 (6–12)	0.448

Values are either median (inter-quartile range) with *P* statistic using the Mann–Whitney test or number of patients (percentage) with *P* statistic using the chi-square test.

was used to examine the relationship between complications and anaerobic threshold as a categorical variable. Univariate binary logistic regression analysis with a calculation of hazard ratios (HR) and 95% confidence intervals (CIs) was used to explore the association between peri-operative clinico-pathological factors and receipt of adjuvant therapy. Multivariate binary logistic regression analysis was performed on all variables showing a significant association on univariate analysis. Backward stepwise regression was used starting with a saturated model and variables with *P*-value > 0.1 were excluded at each step until no more variables could be excluded. SPSS software (Version 17.0; SPSS Inc., Chicago, IL, USA) was used to perform statistical analysis.

Results

One hundred and twenty-nine patients had undergone a pancreaticoduodenectomy (*n* = 127), sub-total pancreatectomy (*n* = 1) or total pancreatectomy (*n* = 1) during the study period. Sub-total and total pancreatectomies were performed in patients scheduled for a pancreaticoduodenectomy but were found to have pancreatic remnants either too friable or too atrophic during the operation to perform an anastomosis. Of these, 100 patients (pancreaticoduodenectomy, 98 and sub-total/total pancreatectomy, 2) had undergone cardiopulmonary exercise testing as part of their pre-operative assessment and were included in the study. Pathological

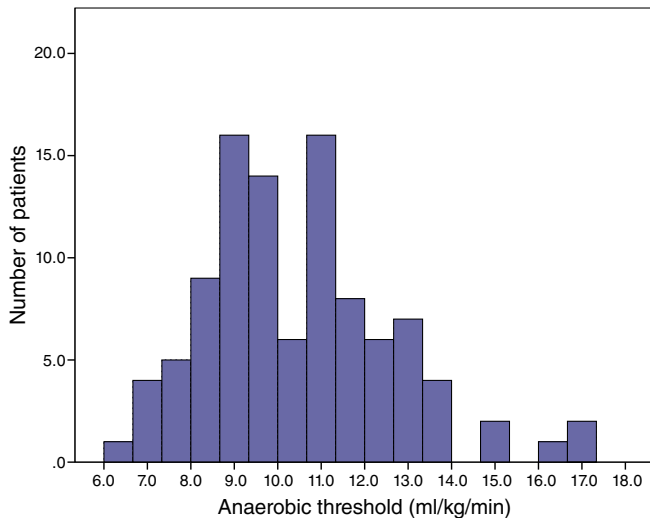


Figure 1 Distribution of anaerobic threshold across the study population

examination of the resected specimen showed pancreatic ductal adenocarcinoma ($n = 37$), ampullary adenocarcinoma ($n = 18$), cholangiocarcinoma ($n = 17$), duodenal adenocarcinoma ($n = 6$), intraductal papillary mucinous neoplasia ($n = 4$), neuroendocrine tumours ($n = 7$), other neoplasia ($n = 4$) or chronic pancreatitis ($n = 2$).

Twenty-nine patients did not undergo cardiopulmonary exercise testing owing to reasons including subjective assessment of fitness, resource constraints and logistics. Table 1 shows the clinico-pathological characteristics of patients included in the study compared with the excluded patients. The median age in the study cohort was higher than in the excluded cohort (66 versus 54 years, $P = 0.001$). However, there was no difference in gender, body mass index, pre-operative biliary drainage, jaundice at the time of surgery, modified Glasgow Prognostic Score, POSSUM physiology score, pre-operative blood tests including haemoglobin and liver function tests and length of critical care/hospital stay. The overall post-operative mortality during the study period was 5.4% (7/129) with all deaths occurring in the study cohort ($P = 0.144$).

The median anaerobic threshold was 10.3 ml/kg/min (interquartile range, IQR 8.8–11.6). The anaerobic threshold was less than 10 ml/kg/min in 49 patients. The distribution of anaerobic threshold across the study cohort is shown in Fig. 1.

The relationship between anaerobic threshold and major post-operative adverse events including mortality is shown in Table 2. Patients with an anaerobic threshold less than 10 ml/kg/min had a significantly greater incidence of post-operative pancreatic fistula (35.4% versus 16%, $P = 0.028$) as well as major intra-abdominal abscesses (CD Grade III–V, 22.4% versus 7.8%, $P = 0.042$). While there was an association between low anaerobic threshold and grade of pancreatic fistula, this was not statistically significant ($P = 0.091$).

There was no association between low anaerobic threshold and cardiopulmonary complications or post-operative mortality.

Major cardiopulmonary complications occurred more often in patients with major intra-abdominal adverse events including major intra-abdominal abscesses or Grade B and C pancreatic fistulae or haemorrhage than in patients who did not have these complications (5/31, 16.1% versus 2/69, 2.9%, $P = 0.017$). Post-operative mortality was not associated with anaerobic threshold (HR 0.77, 95% CI 0.16–3.61, $p = 0.737$) or the POSSUM Physiology Score (HR 0.39, 95% CI 0.07–2.12, $P = 0.277$). Post-operative mortality was associated with post-operative pancreatic fistula ($n = 5$), post-pancreatectomy haemorrhage ($n = 3$), major intra-abdominal sepsis ($n = 6$) and major cardiorespiratory complications ($n = 4$) with six patients requiring radiological or operative intervention.

The median length of post-operative stay was 17 days (IQR 13–26). The median cumulative length of stay in critical care was 7 days (IQR 6–12). Twenty-six patients were admitted to critical care more than once. The relationship between pre-operative clinico-pathological characteristics and length of post-operative stay in patients who were discharged from hospital ($n = 93$) is shown in Table 3. On univariate analysis, age over 65 years ($P = 0.072$) and low anaerobic threshold ($P = 0.010$) were associated with prolonged post-operative stay. On multivariate Cox proportional hazards regression analysis, an anaerobic threshold less than 10 ml/kg/min (hazard ratio 1.74, 95% CIs 1.14–2.65, $P = 0.010$) was the only significant factor associated with prolonged post-operative stay. A Kaplan–Meier plot for the probability of remaining in hospital over time for patients with low and normal anaerobic thresholds is shown in Fig. 2. Patients with a low anaerobic threshold stayed a median 6 days longer in hospital (14 versus 20 days, Mann–Whitney U -test $P = 0.001$). There was no significant association between any of the pre-operative factors including anaerobic threshold and length of critical care stay or number of critical care admissions.

The relationship between clinico-pathological patient factors and receipt of adjuvant therapy is shown in Table 4. Fifty-five patients were included in the analysis. Patients were excluded if chemotherapy was not indicated ($n = 28$), in the event of operative mortality ($n = 7$), if chemotherapy was offered but declined by the patient ($n = 4$), or where they had not been seen by an oncologist yet ($n = 6$). On binary logistic regression analysis, an anaerobic threshold less than 10 ml/kg/min was the only pre-operative factor that was associated with non-receipt of adjuvant therapy (HR 6.30, 95% CI 1.25–31.75, $P = 0.026$).

Discussion

The results of the present study show that a low anaerobic threshold is associated with prolonged post-operative stay in hospital, post-operative pancreatic fistula and intra-abdominal abscesses in patients undergoing major resections for pancreatic head lesions. The results of this study also show that patients with a low anaerobic threshold are less likely to receive adjuvant therapy.

Table 2 The relationship between the anaerobic threshold and complications in patients undergoing major pancreatic surgery

Complications	Anaerobic threshold (ml/kg/min)			P	
		≥10 n	<10 n		
Cardiac complications					
	Grade 0–II	99	51	48	0.308
	Grade III–V	1	0	1	
Respiratory complications					
	Grade 0–II	93	48	45	0.657
	Grade III–V	7	3	4	
Intra-abdominal abscess					
	Grade 0–II	85	47	38	0.042
	Grade III–V	15	4	11	
Pancreatic fistula (total/sub-total pancreatectomies excluded)					
	No	73	42	31	0.028
	Yes	25	8	17	
Pancreatic fistula (ISGPS Classification)					
	No	73	42	31	0.091
	Grade A	9	3	6	
	Grade B	8	1	7	
	Grade C	8	4	4	
Post-pancreatectomy haemorrhage (ISGPS Classification)					
	No	84	41	43	0.207
	Grade A	4	2	2	
	Grade B	4	2	2	
	Grade C	8	6	2	
Admissions to critical care					
	1	74	38	36	0.906
	>1	26	13	13	
Re-operation					
	No	89	47	42	0.306
	Yes	11	4	7	
Operative mortality					
	No	93	47	46	0.737
	Yes	7	4	3	

Therefore, it would appear that objective measurement of patient physiological fitness using cardiopulmonary exercise testing is superior to conventional measures of patient fitness including the POSSUM Physiology Score or the modified Glasgow Prognostic Score and may have a role in predicting short-term outcome which in turn affects the overall management of these patients including receipt of adjuvant therapy.

Patients with a low anaerobic threshold stayed longer in hospital after their operation. While length of stay in hospital is influenced by multiple factors including post-operative complications, it would appear that patients with a low anaerobic threshold take longer to recover from the physiological stress placed by major pancreatic surgery and its sequelae.

The incidence of a pancreatic fistula was greater in patients with a low anaerobic threshold. This association needs further evaluation taking into consideration other well-recognised risk factors for pancreatic fistula such as pancreatic texture, pancreatic duct size and intra-operative blood loss.^{30–32} It is possible that local or operative factors may be compounded by poor oxygen delivery and organ perfusion as measured by cardiopulmonary exercise testing. There was a non-significant trend towards clinically relevant pancreatic fistulae (ISGPS Grades B and C) as well as a significant association with major intra-abdominal abscesses (CD Grades 3–5, i.e. requiring intervention, associated with organ dysfunction requiring intensive care or resulting in mortality). This would suggest that complications in

Table 3 The relationship between clinico-pathological characteristics and post-operative stay in patients (excluding operative mortality) undergoing major pancreatic surgery ($n = 93$): Cox's regression analysis

Variable	n	Univariate			Multivariate		
		HR	95% CI	P	HR	95% CI	P
Age (years)							
≤65	44						
>65	49	1.47	0.97–2.24	0.072	1.48	0.97–2.25	0.068
Gender							
Male	56						
Female	37	1.32	0.86–2.03	0.199			
BMI (kg/m ²)							
≤25	42						
>25	51	0.87	0.58–1.32	0.512			
Smoking							
No	56						
Yes	37	1.26	0.82–1.94	0.294			
POSSUM Physiology Score							
≤14	45						
>14	48	1.28	0.85–1.95	0.240			
Pre-operative biliary drainage							
No	53						
Yes	40	1.08	0.71–1.65	0.724			
Serum bilirubin (micromol/l)							
≤35	54						
>35	39	1.26	0.83–1.92	0.277			
mGPS							
0	59						
1	5	1.22	0.78–1.92	0.387			
2	29	1.87	0.71–4.88	0.204			
Haemoglobin (g/dl)							
≥12	57						
<12	36	1.19	0.78–1.81	0.422			
Anaerobic threshold (ml/kg/min)							
≥10	47						
<10	46	1.74	1.14–2.64	0.010	1.74	1.14–2.65	0.010
Anaerobic threshold (ml/kg/min)							
≥11	33						
<11	60	1.44	0.94–2.22	0.097			0.395

patients with a low anaerobic threshold are more likely to be severe than in patients with normal anaerobic threshold. However, there was no difference in mortality between patients with a normal or low anaerobic threshold, indicating that multiple factors including pre-operative patient fitness, local and operative factors, systemic inflammatory response, number of complications as well as peri-operative critical care all play a role.

The results of this study also show that patients with a low anaerobic threshold were less likely to receive adjuvant therapy.

Adjuvant therapy in patients undergoing pancreatic resections for cancer has been shown in multiple randomized trials to improve survival significantly.^{5,6} While post-operative mortality after pancreatic surgery has steadily improved over the years with major improvements in the quality of surgical and critical care over the past decade³¹ even in elderly patients,³³ post-operative morbidity remains high.¹⁰ The results of this study show that poor pre-operative fitness is not only associated with a protracted post-operative course with complications but also with non-receipt of adjuvant therapy.

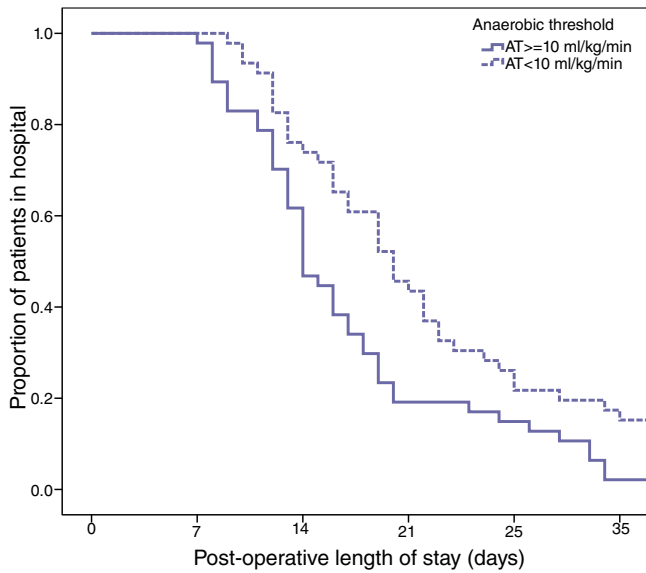


Figure 2 Kaplan–Meier Plot of post-operative length of stay in patients with an anaerobic threshold ≥ 10 ml/kg/min compared with < 10 ml/kg/min

In the present study, the anaerobic threshold was less than 10 ml/kg/min in 49% of patients and less than 11 ml/kg/min in 64% of patients. The proportion of patients with an anaerobic threshold less than 11 ml/kg/min in this study was much greater than reported in studies involving patients undergoing oesophageal surgery (16%),³⁴ liver transplantation (39%)³⁵ or other major abdominal surgery (29%)²² and may indicate the poor pre-operative fitness levels of patients undergoing major pancreatic surgery at our unit. While several previous studies have shown that low anaerobic threshold and/or low VO_2 peak are associated with post-operative complications or prolonged hospital stay after major abdominal surgery as well as non-abdominal surgery,^{22,35–39} others have disputed this.^{34,40,41} Older *et al.* reported in 1993 that a low anaerobic threshold less than 11 ml/kg/min was associated with a significantly higher risk of postoperative mortality from cardiovascular causes in a series of 187 elderly patients undergoing major abdominal surgery.²² However, Snowden *et al.*²⁵ reported that patients with an anaerobic threshold less than 10.1 ml/kg/min had significantly greater cardiopulmonary complications as well as non-cardiopulmonary and infectious complications whereas Forshaw *et al.*³⁴ reported that using a cut-off of 11 ml/kg/min for the anaerobic threshold did not predict post-operative adverse events less after an oesophagectomy. The lack of an association between a low anaerobic threshold and cardiopulmonary complications in this study may have been due to two reasons. Major cardiopulmonary complications occurred more often in association with major intra-abdominal adverse events which are determined largely by pancreatic morphology and local anatomy.³⁰ Moreover, the stringent fitness criteria for undergoing a pancreaticoduodenectomy may have excluded patients with

Table 4 The relationship between clinico-pathological characteristics and receipt of adjuvant therapy in patients undergoing major pancreatic surgery ($n = 55$): binary logistic regression

Variable	n = 55	Univariate		
		HR	95% CI	P
Age (years)				
≤65	25			
>65	30	2.63	0.71–9.74	0.149
Gender				
Male	31			
Female	24	2.08	0.61–7.13	0.242
BMI (kg/m ²)				
≤25	25			
>25	30	0.78	0.23–2.64	0.693
Smoking				
No	35			
Yes	20	0.96	0.27–3.41	0.953
POSSUM physiology score				
≤14	25			
>14	30	1.63	0.46–5.73	0.447
Pre-operative biliary drainage				
No	27			
Yes	28	0.95	0.28–3.21	0.937
Serum bilirubin (micromol/l)				
≤35	27			
>35	28	2.08	0.60–7.30	0.251
mGPS				
0	32			
1	2	0.0	0.0	
2	21	1.20	0.35–4.15	0.773
Haemoglobin (g/dl)				
≥12	31			
<12	24	0.96	0.28–3.26	0.946
Anaerobic threshold (ml/kg/min)				
≥10	23			
<10	32	6.30	1.25–31.75	0.026
Anaerobic threshold (ml/kg/min)				
≥11	16			
<11	39	3.11	0.61–15.88	0.172

known co-morbid cardiorespiratory diseases such as severe chronic obstructive pulmonary disease or cardiac failure.

The results of this study are consistent with the results of the previous study by Ausania *et al.*⁴² who reported an increased incidence of pancreatic fistula and prolonged post-operative stay in patients with an anaerobic threshold less than 10.1 ml/kg/min. However, this study did not report the association between anaerobic threshold and receipt of adjuvant therapy.

The physiological demands placed on a patient undergoing major pancreatic surgery are significant, both during and after the

operation. It is not entirely surprising therefore, that conventional parameters of patient fitness such as the POSSUM Physiology Score or the modified Glasgow Prognostic Score are limited in their ability to distinguish patients based on their performance under physiological stress. Cardiopulmonary exercise testing overcomes this disadvantage by replicating some of the physiological burden major pancreatic surgery places on the functional capacity of the patient's cardiovascular and respiratory systems.

This functional capacity of patients to withstand the physiological burden of major surgery can be improved by the process of 'prehabilitation'.⁴³ It has been suggested that prehabilitation not only improves aerobic capacity⁴⁴ but may also improve post-operative recovery.^{45,46} The results of this study show that impaired aerobic capacity is associated with post-operative adverse events. Therefore, it would appear that prehabilitation using interventions such as exercise and nutrition, by improving physiological fitness, may have a role in improving post-operative outcomes after major pancreatic surgery and may improve the proportion of patients receiving adjuvant therapy.

Further work needs to be carried out to study the value of cardiopulmonary exercise testing in predicting post-operative complications in conjunction with previously established factors such as pancreatic morphology and operative factors before it can be used on its own to select or exclude patients for a pancreaticoduodenectomy. Cardiopulmonary exercise testing would play an important role not only in identifying patients who will benefit from prehabilitation, but also in the objective measurement of the effects of such interventions on aerobic capacity as well as in identifying high-risk patients who may not be able to complete oncological treatment. Prehabilitation and optimized perioperative care may allow a greater proportion of high-risk patients to progress to oncological treatment after surgery.

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Conflicts of interest

None declared.

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