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Review Article

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

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Abstract

Background: Cardiopulmonary exercise testing (CPET) is used as a preoperative risk-stratification tool for patients undergoing non-cardiopulmonary intra-abdominal surgery. Previous studies indicate that CPET may be beneficial, but research is needed to quantify CPET values protective against poor postoperative outcome [mortality, morbidity, and length of stay (LOS)].

Methods: This systematic review aimed to assess the ability of CPET to predict postoperative outcome. The following databases were searched: PubMed, EMBASE, PEDro, The Cochrane Library, Cinahl, and AMED. Thirty-seven full-text articles were included. Data extraction included the following: author, patient characteristics, setting, surgery type, postoperative outcome measure, and CPET outcomes.

Results: Surgeries reviewed were hepatic transplant and resection (n=7), abdominal aortic aneurysm (AAA) repair (n=5), colorectal (n=6), pancreatic (n=4), renal transplant (n=2), upper gastrointestinal (n=4), bariatric (n=2), and general intra-abdominal surgery (n=12). Cardiopulmonary exercise testing-derived cut-points, peak oxygen consumption ($\dot{V}O_2$ peak), and anaerobic threshold (AT) predicted the following postoperative outcomes: 90 day–3 yr survival (AT 9–11 ml kg^{-1} min^{-1}) and intensive care unit admission (AT <9.9–11 ml kg^{-1} min^{-1}) after hepatic transplant and resection, 90 day survival after AAA repair ($\dot{V}O_2$ peak 15 ml kg^{-1} min^{-1}), LOS and morbidity after pancreatic surgery (AT <10–10.1 ml kg^{-1} min^{-1}), and mortality and morbidity after intra-abdominal surgery (AT 10.9 and <10.1 ml kg^{-1} min^{-1}, respectively).

Conclusions: Cardiopulmonary exercise testing is a useful preoperative risk-stratification tool that can predict postoperative outcome. Further research is needed to justify the ability of CPET to predict postoperative outcome in renal transplant, colorectal, upper gastrointestinal, and bariatric surgery.

Key words: exercise test/methods; general surgery; health status indicators; postoperative complications; preoperative care/methods; preoperative period; prognosis; risk; risk assessment/methods

Cardiopulmonary exercise testing (CPET) is a dynamic, non-invasive assessment of the cardiorespiratory system at rest and under stress. Cardiopulmonary exercise testing is the gold-standard method of measuring an individual's aerobic capacity. Cardiopulmonary exercise testing measures several physiological variables, including ventilatory parameters, heart rate (HR), and inspiratory and expiratory gases (the definitions for CPET variables are provided in Supplementary material, Table S1).

Cardiopulmonary exercise testing can be implemented to aid clinical decision-making. These uses include assessing patients

with significant complaints of exercise intolerance and dyspnoea[1] and determining the severity impairment related to heart failure and chronic obstructive pulmonary disease.[2] Cardiopulmonary exercise testing is used as a preoperative risk-stratification tool to predict postoperative mortality, length of stay (LOS), and morbidity; however, its role requires validation.

Numerous studies have reported that CPET is a valid prognostic measure of postoperative outcome in cardiopulmonary surgery.[3–5] There have been four previous reviews of CPET in non-cardiopulmonary surgery.[6–9] All reviews concluded that CPET may be a strong predictor of postoperative outcome. These reviews also concluded that: (i) CPET-derived cut-points need to be refined and optimized for different surgical procedures and (ii) the validity of CPET variables, such as O_2 pulse and the ventilatory equivalent for carbon dioxide ($\dot{V}_E/\dot{V}_{CO_2}$), needs to be analysed; and (iii) further studies need to be performed to obtain a greater understanding of the role of CPET as a preoperative risk-stratification method. Since the publication of these reviews, the number of studies analysing CPET has grown.

The aim of the present review is to assess the prognostic ability of CPET in predicting postoperative outcome associated with non-cardiopulmonary intra-abdominal surgery. The objectives are as follows: (i) to quantify the optimal CPET variable to predict postoperative outcome; and (ii) to analyse and compare cardiopulmonary measurements such as anaerobic threshold (AT), maximal oxygen uptake ($\dot{V}_{O_2}$ max) and $\dot{V}_E/\dot{V}_{CO_2}$ to find the most accurate CPET variable in determining postoperative outcome within each subgroup of surgery.

Postoperative outcome includes all-cause mortality, morbidity, and LOS. Morbidity after surgical intervention includes all complications; pulmonary, infectious, renal, gastrointestinal (GI), cardiovascular, neurological, and haematological. The outcome LOS covers the overall length of stay in hospital, intensive care unit (ICU), high-dependency unit (HDU), and critical care unit (CCU) admission and length of stay.

Methods

Literature search

The preferred reporting items for systematic reviews (PRISMA) standardized reporting guidelines were used to standardize the methods of conducting and reporting this review.[10] The databases CINAHL, AMED, PEDro, EMBASE, The Cochrane Library, and PubMed were searched up to May 2015. A search strategy was defined with all keywords and subject headings included (Supplementary data, Appendix S1). In addition, the abstracts from the annual European Anaesthisiology Congress (2004–2014), the Anaesthetic Research Society (2007–2015), the Society of Academic & Research Surgery 2012–2015, the Vascular Society (2005–2012), the International Anaesthesia Research Society (2003–2015), the World Federation of Society of Anaesthesiologists (2008–2012), and the American Society of Anaesthesiologists (2000–2014) were reviewed for eligibility. A hand search of reference lists of the studies of interest was conducted to identify extra articles.

The inclusion criteria consisted of the following: (i) prognostic studies of intra-abdominal surgery among adult populations; (ii) the use of a preoperative CPET; (iii) measurement of postoperative outcome (mortality, morbidity, or length of stay); and (iv) comparison of preoperative CPET variables (anaerobic threshold etc.) with postoperative outcome.

Studies were excluded if they contained the following: (i) a cardiopulmonary surgical procedure; (ii) paediatric surgery; (iii) head and neck surgery; (iv) orthopaedic surgery; (v) spinal surgery; (vi) transfusion procedures, (e.g. blood or stem cells); (vii) preoperative interventions (e.g. preoperative exercise programmes); or (viii) were systematic reviews, meta-analyses, case studies, letters to the editor, or abstracts with no full text available.

If studies had split the analysis of intra-abdominal and cardiopulmonary surgery then the subgroup containing intra-abdominal surgery was taken and the cardiopulmonary surgery group was excluded. Procedures involving multiple incisions which included major intra-abdominal surgery were included (e.g. oesophagectomy).

Data extraction

Data extraction was performed independently by the lead investigator (J. Moran). All data were reviewed blind by another author (F.W.). The data extracted included author, patient characteristics, study setting, surgery type, postoperative outcome measure, method of CPET, and CPET variables assessed (Table 1).

A total of 1086 titles were identified using the search strategy on the above-mentioned databases. Of these, 1049 studies were excluded (Fig. 1). The authors (J. Moran and F.W.) excluded articles based on titles and abstracts. If any disagreements could not be resolved through discussion, an independent third author was asked to intervene (J.H.). Thirty-seven full-text articles were included in the data extraction and synthesis (Fig. 1). The authors of abstracts and conference posters were contacted to gain the full text. If full-text articles were not acquired then abstracts were excluded because of the potential high risk of bias and lack of a detailed methodology.

Assessment of the risk of bias

The methodological quality of the studies was assessed using the Quality in Prognosis Studies (QUIPS) tool[11] (Supplementary material, Appendix S2). The QUIPS tool analyses the risk of bias in observational prognostic studies in six key areas, as follows: study participation, attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis and reporting. Each area contained several criteria. If a study failed to address one or fewer criteria within an area, it was deemed to have a low risk of bias. Two authors (J. Moran and F.W.) independently assessed the risk of bias in each study. An independent third author (J.H.) was asked to intervene if any disagreements could not be resolved through discussion. The overall risk of bias is presented in Table 2.

Results

The papers included in this review were categorized by surgical procedures, as follows: hepatic transplant and resection (n=7), abdominal aortic aneurysm (AAA) repair (n=5), colorectal surgery (n=4), pancreatic surgery (n=4), renal transplant (n=2), upper gastrointestinal surgery (n=3), bariatric surgery (n=2), and intra-abdominal surgery (studies that did not differentiate between surgical procedures; n=10). A total of 7852 patients were included.

A meta-analysis was deemed inappropriate because of the large heterogeneity of the data. The studies included varied in the type of surgery, CPET variable analysed, outcome, time to outcome, and the use of hazard ratios and odds ratios, resulting in an inability to pool data effectively. A quantitative synthesis of the results was deemed most appropriate.

Tables 3–5 show the outcomes and CPET variables deemed significant that predict poor postoperative outcome. Supplementary material, Tables S2–S4 provide a more detailed Results section.

Table 1: Demographic details of included studies

Author	Surgery	Sample Size (n=)	Age	Gender:	Location	Outcome	CPET Type	Variables Reported
Ausania et al. (2012)	Pancreaticoduodenectomy	124	66 (Range: 37–82)	67 M, 57 F	Newcastle Upon Tyne, UK	Mortality, Morbidity, LOS	Cycle Ergometer	Vo_2 Peak, AT, V_E/Vco_2
Ausania, Vallance et al. (2012)	Pancreatic (Palliative Double Bypass) Surgery	50	64 (Range: 39–79)	33 M, 17 F	Newcastle Upon Tyne, UK	Mortality, Morbidity	N/R	AT
Bernal et al. (2014)	Liver Transplant	223	56 (Range: 42–61)	151 M, 72 F	London, UK	Mortality, LOS	Cycle Ergometer	Vo_2 Peak, AT
Carlisle and Swart (2007)	Abdominal Aortic Aneurysm Repair	130	N/R	N/R	Torquay, UK	Mortality	Cycle Ergometer	Vo_2 Peak, AT, V_E/Vco_2, V_E/Vo_2
Chandrabalan et al. (2013)	Pancreatic Surgery	100	≤65=47, >65=53	60 M, 40 F	Glasgow, UK	Mortality, Morbidity, LOS	Cycle Ergometer	AT
Colson et al. (2012)	Major Thoraco-Abdominal Surgery	1,725	71 (Range: 36–93)	1,121 M, 604 F	Geelong, Australia	Mortality	Cycle Ergometer	AT
Dunne et al. (2014)	Liver Surgery	197	70 (IQR: 64–75)	138 M, 59 F	Liverpool, UK	Morbidity, LOS	Cycle Ergometer	Vo_2 Peak AT, V_E/Vco_2, HR
Epstein et al. (2004)	Liver Transplant	59	46	35 M, 24 F	Boston, USA	Mortality	Cycle Ergometer	Vo_2 Peak, AT, o_2 Pulse
Forshaw et al. (2008)	Oesophagectomy	78	65 (SD: 9) (Range: 40–81)	64 M, 14 F	London, UK	Mortality, Morbidity, LOS	Cycle Ergometer	Vo_2 Peak, AT
Grant et al. (2015)	Abdominal Aortic Aneurysm Repair	506	73.4 (Range: 44–90)	418 M, 88 F	Manchester, UK	Mortality	Cycle Ergometer	Vo_2 Peak, AT, V_E/Vco_2
Hartley et al. (2012)	Abdominal Aortic Aneurysm Repair	415	N/R	349 M, 66 F	Manchester, UK	Mortality	Cycle Ergometer	Vo_2 Peak, AT, V_E/Vco_2
Hennis et al. (2012)	Gastric Bypass Surgery	106	43 (IQR: 41–44.9)	18 M, 88 F	London, UK	Morbidity, LOS	Cycle Ergometer	Vo_2 Peak, AT
Hightower et al. (2010)	Major Abdominal Surgery	32	63 (Range: 22–80)	21 M, 11 F	Texas, USA	Morbidity	Cycle Ergometer	Vo_2 Peak, AT
James et al. (2013)	Intra-Abdominal	83	68 (IQR: 63–75)	60 M, 23 F	London, UK	Morbidity	Cycle Ergometer	Vo_2 Peak, AT
Junejo et al. (2012)	Hepatic Resection	94	71 (Range: 24–85)	N/R	Manchester, UK	Mortality, Morbidity, LOS	Cycle Ergometer	Vo_2 Peak, AT, V_E/Vco_2, Peak Vo_2 Pulse
Junejo et al. (2014)	Pancreaticoduodenectomy	64	64 (Range: 45–80)	38 M, 26 F	Manchester, UK	Mortality, Morbidity	Cycle Ergometer	Vo_2 Peak, AT, V_E/Vco_2, V_E/Vo_2
Kaibori et al. (2013)	Hepatectomy	61	70 (SD: 9)	45 M, 16 F	Osaka, Japan	Mortality	Cycle Ergometer	Vo_2 Peak, AT
Lai et al. (2013)	Colorectal Surgery	269	N/R	N/R	Plymouth, UK	Mortality, LOS	Cycle Ergometer	Vo_2 Peak, AT
Lee et al. (2013)	Colorectal Surgery	112	59.9 (SD: 15.5)	65 M, 47 F	Montreal, Canada	Morbidity	Cycle Ergometer	Vo_2 Peak, Distance
McCullough et al. (2006)	Bariatric Surgery	109	46 (SD: 10.4)	27 M, 82 F	Michigan, USA	Mortality, Morbidity, LOS	Treadmill	Vo_2 Peak, AT, V_E/Vco_2, RER
Moyes et al. (2013)	Oesophagogastric Cancer Surgery	108	66 (SD: 9, IQR: 38–84)	83 M, 25 F	Glasgow, UK	Morbidity	Cycle Ergometer	Vo_2 Peak, AT

Continued

Table 1: *Continued*

Author	Surgery	Sample Size (n=)	Age	Gender:	Location	Outcome	CPET Type	Variables Reported
Nagamatsu et al. (2001)	Oesophagectomy and Lymphadenectomy	91	59 (Range: 38–74)	88 M, 3 F	Fukuoka, Japan	Morbidity	Cycle Ergometer	Vo_2 Peak, AT
Neviere et al. (2014)	Liver Transplant	263	58.8 (SD: 8.5)	198 M, 65 F	Lille, France	Mortality	Cycle Ergometer	Vo_2 Peak, AT, V_E/Vco_2, V_E/Vo_2, o_2 Pulse
Nugent et al. (1998)	Abdominal Aortic Aneurysm Repair	30	71.3 (Range: 57–85)	24 M, 6 F	Belfast, UK	Mortality, Morbidity	Treadmill	Vo_2 Peak, AT, o_2 Pulse
Older et al. (1993)	Major Abdominal	187	70 (SD: 7)	102 M, 85 F	Victoria, Australia	Mortality	Cycle Ergometer	AT
Older et al. (1999)	Major Abdominal Surgery	548	69	N/R	Victoria, Australia	Mortality, Morbidity, LOS	Cycle Ergometer	AT
Prentis et al. (2012)	Liver Transplant	60	N/R	N/R	Newcastle Upon Tyne, UK	Mortality, LOS	Cycle Ergometer	Vo_2 Peak, AT, V_E/Vco_2
Prentis et al. (2012)	Abdominal Aortic Aneurysm Repair	185	73.4 (SD: 8.2)	161 M, 24 F	Newcastle Upon Tyne, UK	Morbidity, LOS	Cycle Ergometer	Vo_2 Peak, AT, V_E/Vco_2
Prentis et al. (2013)	Radical Cystectomy	69	N/R	48 M, 21 F	Newcastle Upon Tyne, UK	Mortality, LOS	Cycle Ergometer	Vo_2 Peak, AT, V_E/Vco_2, Peak Vo_2 Pulse
Snowden et al. (2010)	Major Surgery	123 (7 excluded from analysis)	69.2 (SD: 9.3)	78 M, 45 F	Newcastle Upon Tyne, UK	Morbidity, LOS	Cycle Ergometer	Vo_2 Peak, AT
Snowden et al. (2013)	Non-Laproscopic Hepatobiliary Surgery	389	65.8 (SD: 10.3)	218 M, 171 F	Newcastle Upon Tyne, UK	Mortality, LOS	Cycle Ergometer	Vo_2 Peak, AT, V_E/Vco_2
Ting et al. (2013)	Kidney Transplant	70	41.7 (SD: 14.5)	42 M, 28 F	Coventry, UK	LOS	Cycle Ergometer	Vo_2 Peak, AT, V_E/Vco_2, Vo_2/HR
Tolchard et al. (2015)	Radical Cystectomy	105	71 (Range: 38–90)	88 M, 17 F	Bristol, UK	Mortality, Morbidity, LOS	Cycle Ergometer	Vo_2 Peak, AT, V_E/Vco_2
Ulubay et al. (2010)	Renal Transplant	16	30.3 (SD: 6.5)	10 M, 6 F	Ankara, Turkey	Mortality	Cycle Ergometer	Vo_2 Peak, AT, V_E/Vco_2
West et al. (2013)	Rectal Cancer Surgery	95	66 (SD: 10)	72 M, 23 F	Liverpool, UK	Mortality, Morbidity	Cycle Ergometer	Vo_2 Peak, AT, V_E/Vco_2, V_E/Vo_2
West et al. (2014)	Major Colonic Surgery	136	71 (IQR: 62–77)	89 M, 47 F	Liverpool, UK	Mortality, Morbidity, LOS	Cycle Ergometer	Vo_2 Peak, AT, V_E/Vco_2, o_2 Pulse Peak
Wilson et al. (2010)	Colorectal Resection, Radical Nephrectomy or Cystectomy	847	N/R	506 M, 341 F	York, UK	Mortality, LOS	Cycle Ergometer	AT, V_E/Vco_2

AT = Anaerobic Threshold, V_E = Minute Ventilation, N/R = Not Reported

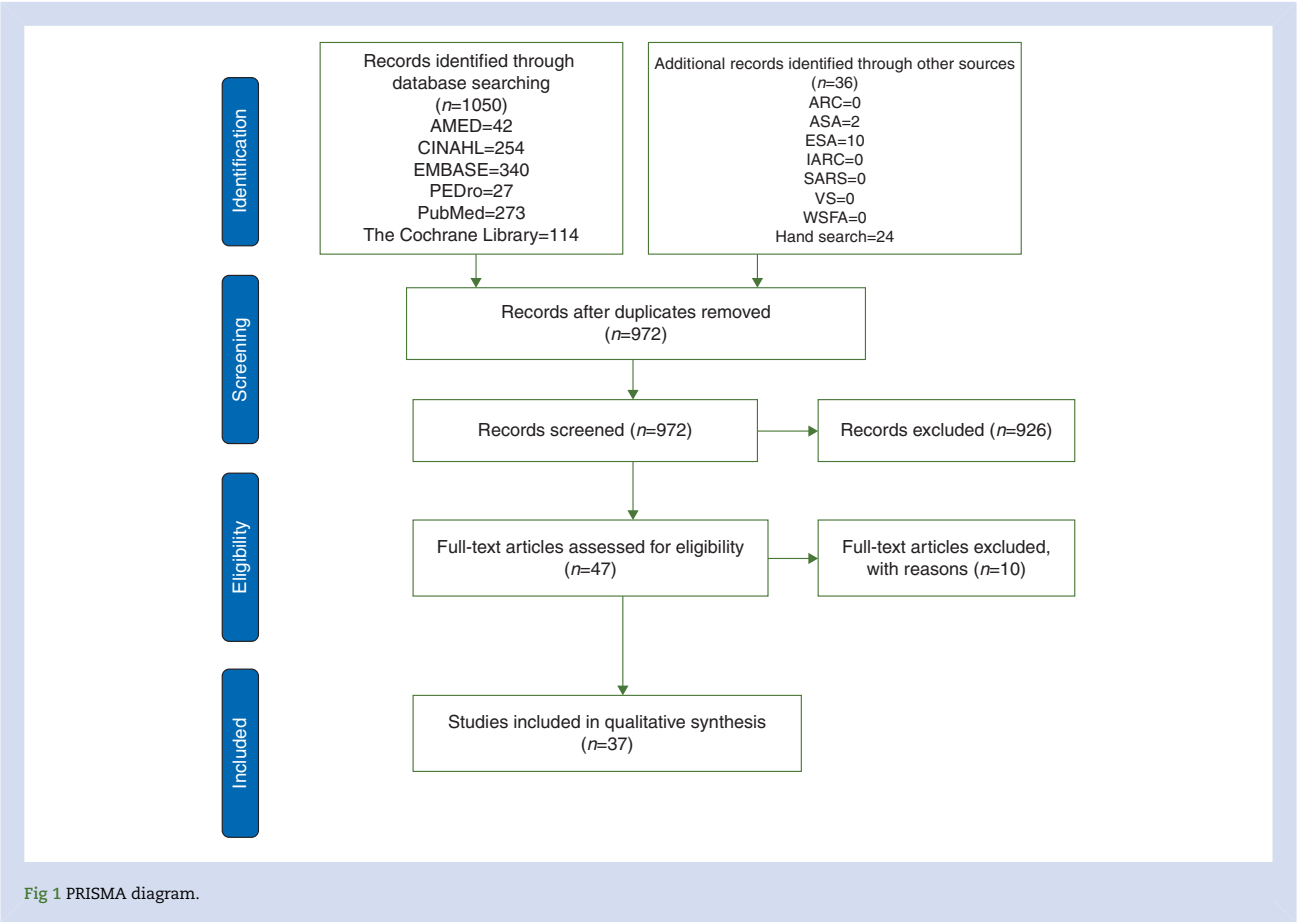

Fig 1 PRISMA diagram.

Hepatic transplant and resection

Mortality

Six studies reported CPET as a significant predictor of mortality after hepatic surgery[12–17] (Table 3). Junejo and colleagues[12] reported an AT of 9.9 ml kg^{-1} min^{-1} to be predictive of survival 30 days after surgery, whereas at 90 days after surgery an AT cut-off point of 9.0 ml kg^{-1} min^{-1} was shown to be significant (P<0.05) and had a 90.7% sensitivity and 83.3% specificity rate.[13] Bernal and colleagues[14] reported that survivors had a median AT of 11.7 ml kg^{-1} min^{-1} compared with non-survivors (median, 9.8 ml kg^{-1} min^{-1}) at 1 yr post-transplant (P=0.04). Kaibori and colleagues[15] followed patients for 2 (range 1–3) yr and found an AT ≥11.5 ml kg^{-1} min^{-1} to be predictive of survival (P<0.05). From the results of these four studies, a minimal AT of 9 ml kg^{-1} min^{-1} can predict short-term mortality (up to 90 days), but an AT of at least 11.5 ml kg^{-1} min^{-1} may predict long-term mortality (≥1 yr).

Peak oxygen uptake ($\dot{V}O_2$ peak) has also been shown to be beneficial at predicting mortality after liver surgery. Neviere and colleagues[16] reported that survivors of liver transplant at 1 yr had a $\dot{V}O_2$ peak of 18.6 (SD 2.8) ml kg^{-1} min^{-1} when compared with non-survivors 17.1 (SD 3.3) ml kg^{-1} min^{-1} (P=0.04). Kaibori and colleagues[15] presented a cut-off of ≥16.5 ml kg^{-1} min^{-1} as predictive of survival at 24 months after surgery (P<0.05). Epstein and colleagues[17] stated that both predicted $\dot{V}O_2$ peak and AT were effective at predicting mortality at 100 days. Peak oxygen uptake appears to be beneficial at predicting mortality, but the evidence for its use is weaker than than that for AT.

Length of stay

The relationship between AT and LOS is unclear. Junejo and colleagues[12] and Prentis and colleagues[13] found no relationship between AT and LOS. In contrast, Dunne and colleagues[18] reported that patients with higher AT (in litres per minute) were more likely to be discharged early; however, this AT cut-off was not quantified [hazard ratio 2.16; 95% confidence interval (CI) 1.18–3.96; P<0.05]. An AT <9.2 ml kg^{-1} min^{-1} was associated with a LOS of 21 days (inter-quartile range 14–30) compared with patients with an AT ≥9.2 ml kg^{-1} min^{-1} [LOS of 15 days (inter-quartile range 13–23); P<0.03].[14]

Junejo and colleagues[12] reported that an AT of <9.9 ml kg^{-1} min^{-1} was associated with increased unplanned ICU stay (1.2 *vs* 0.3 days, P<0.05). In agreement, Prentis and colleagues[13] demonstrated that an AT of 11 ml kg^{-1} min^{-1} was significantly correlated with CCU LOS (P<0.05).

The evidence for $\dot{V}O_2$ peak as a predictive factor of LOS and ICU admission is weaker than that for AT. Dunne and colleagues[18] reported that $\dot{V}O_2$ peak was associated with LOS (P<0.05). Peak oxygen consumption may also be predictive of ICU LOS stay in liver transplant surgery (P<0.05).[14] Anaerobic threshold appears to be predictive of ICU or CCU admission after liver surgery.[12 13] Further studies are required to draw a definite conclusion about the ability of CPET to predict postoperative LOS after liver surgery.

Morbidity

Many studies did not examine postoperative morbidity. Kaibori and colleagues[15] grouped morbidity with mortality and analysed

Table 2: Risk of Bias Assessment

Authors	The QUIPS Tool					
	Study Participation	Study Attrition	Prognostic Factor Measurement	Outcome Measurement	Study Confounding	Statistical Analysis and Reporting
Ausania et al. (2012)	Low Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Ausania, Vallance et al. (2012)	Low Bias	Low Bias	High Bias	High Bias	High Bias	Low Bias
Bernal et al. (2014)	Low Bias	Low Bias	Low Bias	Low Bias	High Bias	Low Bias
Carlisle and Swart (2007)	High Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Chandrabalan et al. (2014)	High Bias	Low Bias	Low Bias	Low Bias	High Bias	Low Bias
Colson et al. (2012)	Moderate Bias	High Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Dunne et al. (2014)	Moderate Bias	High Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Epstein et al. (2004)	Low Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Forshaw et al. (2008)	Low Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Grant et al. (2015)	Low Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Hartley et al. (2012)	Low Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Hennis et al. (2012)	Low Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Hightower et al. (2010)	Low Bias	Low Bias	Low Bias	Low Bias	Low Bias	Low Bias
James et al. (2013)	Low Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Junejo et al. (2012)	Low Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Junejo et al. (2014)	Low Bias	Moderate Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Kaibori et al. (2013)	Low Bias	Low Bias	Low Bias	Low Bias	Low Bias	Low Bias
Lai et al. (2013)	Low Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Lee et al. (2013)	Low Bias	Low Bias	Low Bias	Moderate Bias	Moderate Bias	Low Bias
McCullough et al. (2006)	Low Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Moyes et al. (2008)	Low Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Nagamatsu et al. (2001)	Low Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Neviere et al. (2014)	Low Bias	Low Bias	Low Bias	Low Bias	Low Bias	Low Bias
Nugent et al. (1998)	Moderate Bias	Low Bias	Low Bias	High Bias	Moderate Bias	Low Bias
Older et al. (1993)	Moderate Bias	Moderate Bias	Low Bias	Low Bias	High Bias	Low Bias
Older et al. (1999)	Moderate Bias	Low Bias	Low Bias	Moderate Bias	Moderate Bias	High Bias
Prentis et al. (2012)	Low Bias	Moderate Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Prentis et al. (2012)	Low Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Prentis et al. (2013)	Moderate Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Snowden et al. (2010)	Low Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Snowden et al. (2013)	Moderate Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Ting et al. (2013)	Moderate Bias	Low Bias	Low Bias	Low Bias	Low Bias	Low Bias
Tolchard et al. (2015)	Moderate Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Ulubay et al. (2010)	Moderate Bias	Low Bias	Low Bias	Moderate Bias	Moderate Bias	Low Bias
West et al. (2013)	Low Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
West et al. (2014)	Low Bias	Moderate Bias	Low Bias	Low Bias	Moderate Bias	Low Bias
Wilson et al. (2010)	Moderate Bias	Low Bias	Low Bias	Low Bias	Moderate Bias	Low Bias

outcome as event-free survival. This latter parameter will not be included in the analysis of this section. Both Junejo and colleagues[12] and Dunne and colleagues[18] analysed the possible relationship between CPET and postoperative complications. In a multivariable predictive regression model, a $\dot{V}_E/\dot{V}_{CO_2}$ threshold of 34.5 at AT was predictive of postoperative cardiopulmonary complications.[12] Dunne and colleagues[18] reported that heart rate at AT ($P<0.05$) and HR at $\dot{V}_{O_2}$ peak ($P<0.05$) were associated with all postoperative complications.

Preoperative CPET shows possible benefit for predicting postoperative complications after liver surgery, but further studies are required to validate the prognostic ability of CPET.

Abdominal aortic aneurysm repair

Mortality

Four full-text articles analysing the potential predictive ability of CPET in AAA repair were reviewed.[19–22] In a small cohort ($n=30$), with only two documented deaths, Nugent and colleagues[19] reported no difference in preoperative $\dot{V}_{O_2}$ peak between patients who did and did not experience postoperative morbidity and mortality.

Grant and colleagues[20] found in the multivariable analysis that $\dot{V}_E/\dot{V}_{CO_2}$ >42 at AT was predictive of mortality ($P<0.05$) as was $\dot{V}_{O_2}$ peak <15 ml kg^{-1} min^{-1} ($P<0.05$). Anaerobic threshold was not included because of missing values. An AT of <10.2 ml kg^{-1} min^{-1} was reported to be predictive of 30 day mortality ($P<0.05$), and $\dot{V}_{O_2}$ peak <15 ml kg^{-1} min^{-1} was predictive of 90 day mortality ($P<0.05$).[21] The $\dot{V}_E/\dot{V}_{CO_2}$ was predictive of 30 ($P<0.05$) and 90 day mortality ($P<0.05$) after AAA repair.[21] In a univariable analysis, Carlisle and Swart[22] reported that $\dot{V}_E/\dot{V}_{CO_2}$ ($P<0.01$), ventilatory equivalent for oxygen ($\dot{V}_E/\dot{V}_{O_2}$; $P<0.01$), AT ($P<0.01$), and $\dot{V}_{O_2}$ peak ($P<0.01$) were predictive of mortality. In the multivariable analysis, $\dot{V}_E/\dot{V}_{CO_2}$ and AT were predictive of postoperative survival ($P<0.01$ and $P=0.03$, respectively).

The prognostic ability of CPET in determining postoperative mortality after AAA repair appears useful but requires further

Table 3: Preoperative Cardiopulmonary Exercise Testing and Mortality

Cardiopulmonary Exercise Testing and Mortality

Author	Sample Size	In-hospital	30 days	90 days	1 year	≥ 2 years	Duration of follow-up not reported
Hepatic Resection and Transplant							
Bernal and colleagues[14]	223	–	–	–	AT 9.8 (non-survivors) vs. 11.7 (survivors) ml/kg/min	–	–
Dunne and colleagues[18]	197	–	–	–	–	–	–
Epstein and colleagues[17]	59	–	–	(100 days) Predicted Vo_2 Peak <60% Predicted AT <50%	–	–	–
Junejo and colleagues[12]	94	–	AT <9.9 ml/kg/min	–	–	–	–
Kaibori and colleagues[15]	61	–	–	–	–	AT <11.5 ml/kg/min	–
Neviere and colleagues[16]	263	–	–	–	Vo_2 Peak; 18.6 vs. 17.1 ml/kg/min	–	–
Prentis and colleagues[13]	60	–	–	AT of 9.0 ml/kg/min	–	–	–
Abdominal Aortic Aneurysm							
Carlisle and Swart[22]	130	–	–	–	–	V_E/ Vco_2 and AT	–
Grant and colleagues[20]	506	–	–	–	–	Vo_2 Peak <15 ml/kg/min and V_E/ Vco_2 >42 at AT	–
Hartley and colleagues[21]	415	–	AT <10.2 ml/kg/min and V_E/ Vco_2	Vo_2 Peak <15 ml/kg/min and V_E/ Vco_2	–	–	–
Nugent and colleagues[19]	30	–	–	–	Vo_2 Peak - Not Significant	–	
Colorectal							
Lai and colleagues[24]	269	–	AT <11.0 ml/kg/min	AT <11.0 ml/kg/min	–	AT <11.0 ml/kg/min	–
West and colleagues[25]	95	–	–	–	Vo_2 Peak of <10.6 ml/kg/min	–	–
West and colleagues[26]	136	–	–	–	–	–	–
Pancreatic							
Ausania and colleagues[28]	124	–	AT <10.1 ml/kg/min - Not Significant	–	–	–	–
Ausania and colleagues[30]	50	–	–	–	–	–	AT - Not Significant
Chandrabalan *and colleagues*[29]	100	AT – Not Significant	–	–	–	–	–
Junejo and colleagues[31]	64	V_E/Vco_2^*	V_E/Vco_2 > 41	–	–	–	–
Renal Transplant							
Ulubay and colleagues[32]	16	–	–	–	–	–	–
Upper Gastrointestinal							
Forshaw and colleagues[34]	78	–	–	–	–	–	–

Continued

Table 3: Continued

Cardiopulmonary Exercise Testing and Mortality							
Author	**Sample Size**	**In-hospital**	**30 days**	**90 days**	**1 year**	**≥ 2 years**	**Duration of follow-up not reported**
Bariatric							
McCullough and colleagues[37]	109	–	Vo_2 Peak†	–	–	–	–
Intra-Abdominal							
Colson and colleagues[43]	1,725	–	AT – Not Significant	–	AT – Not Significant	AT – Not Significant	–
Older and colleagues[42]	187	–	–	–	–	–	AT <11 ml/kg/min
Older and colleagues[41]	548	–	–	–	–	–	AT <11 ml/kg/min
Snowden and colleagues[48]	389	AT <10 ml/kg/min	–	–	–	–	–
Wilson and colleagues[40]	847	–	–	AT of 10.9 ml/kg/min and V_E/ Vco_2 of 34	–	–	–

AT = Anaerobic Threshold, * = No value was given for V_E/VCO_2, † = Only one death

validation. Only one study did not find $\dot{V}O_2$ peak to be predictive.[19] The variables and cut-off points used between studies vary or are not reported.[19 22] The length of postoperative follow-up also differs; therefore, further studies will need to examine the prognostic ability of CPET and mortality at specific time points to allow for suitable comparison (e.g. 30 and 90 days and 5 yr). A $\dot{V}O_2$ peak cut-off point of 15 ml kg^{-1} min^{-1} is a good starting point because it is predictive of 90 day mortality[21] and at (median) 26 months.[20]

Length of stay

Anaerobic threshold was reported to be predictive of CCU and overall hospital LOS in open AAA repair, but not endovascular aneurysm repair.[23]

Morbidity

Nugent and colleagues[19] reported no statistically significant relationship between $\dot{V}O_2$ peak and postoperative complications. An AT of 10 ml kg^{-1} min^{-1} has been reported to be predictive of postoperative morbidity[13] (Table 5).

Colorectal surgery

Mortality

Lai and colleagues[24] stratified patients into the following three categories: fit (AT ≥11 ml kg^{-1} min^{-1}), unfit (AT <11 ml kg^{-1} min^{-1}), and unable (unable to generate an AT). This study compared mortality at 30 and 90 days and 2 yrs between fit and unfit and between unfit and unable and reported that mortality was significantly different between groups ($P<0.01$).

West and colleagues[25] reported that seven patients (total $n=95$) died within 1 yr after surgery, all of whom had a $\dot{V}O_2$ peak of <10.6 ml kg^{-1} min^{-1}. West and colleagues[26] were unable to conclude whether CPET was predictive of mortality after major colonic surgery because there were only two deaths (1.5%; Table 3). Anaerobic threshold and $\dot{V}O_2$ peak appear to be beneficial in predicting postoperative mortality, but owing to the low rate of mortality it is difficult to draw conclusions.

Length of stay

Patients with higher AT values (≥11 ml kg^{-1} min^{-1}) had a significantly shorter LOS in hospital compared with unfit (AT <11 ml kg^{-1} min^{-1}) and unable groups (unable to generate an AT; $P<0.01$).[24] West and colleagues[26] reported that patients with low AT ($P<0.01$) or $\dot{V}O_2$ peak ($P<0.01$) or with high $\dot{V}E/\dot{V}CO_2$ ($P<0.01$) were susceptible to an increased hospital stay. The prognostic ability of CPET appears viable; however, more research is needed to validate the ability of AT to determine postoperative LOS.

Morbidity

Peak oxygen uptake and AT have been reported to be associated with postoperative complications using the Postoperative Morbidity Survey (POMS) on day 5 after rectal cancer surgery and major colonic surgery.[25 26] After major colonic surgery, West and colleagues[26] reported that $\dot{V}O_2$ peak, AT, and $\dot{V}E/\dot{V}CO_2$ were independently predictive of morbidity in rectal cancer surgery and major colonic surgery. Lee and colleagues[27] reported that $\dot{V}O_2$ peak was associated with occurrence of medical complications ($P<0.01$) but not surgical and all complications (Table 5).

The data regarding preoperative CPET as a predictor of postoperative morbidity are strong, but further research is needed to quantify a level of aerobic fitness that is protective against complications.

Table 4: Preoperative Cardiopulmonary Exercise Testing and Length of Stay

Cardiopulmonary Exercise Testing and Length of Stay				
Author	**Sample Size**	**Hospital LOS**	**ICU/CCU Admission**	**ICU/CCU LOS**
Hepatic Transplant and Resection				
Bernal and colleagues[14]	223	AT <9.2 ml/kg/min,	–	Vo_2 Peak <13.4 ml/kg/min
Dunne and colleagues[18]	197	AT, Vo_2 Peak (L/min)	–	–
Junejo and colleagues[12]	94	–	–	AT <9.9 ml/kg/min
Prentis and colleagues[13]	60	–	–	AT <11 ml/kg/min
Abdominal Aortic Aneurysm				
Prentis and colleagues[23]	185	AT <10 ml/kg/min (Open Repair and EVAR)	–	AT <10 ml/kg/min (Open Repair)
Colorectal				
Lai and colleagues[24]	269	AT <11 ml/kg/min	–	–
West and colleagues[26]	136	AT, Vo_2 Peak, V_E/Vco_2	–	–
Pancreatic				
Ausania and colleagues[28]	124	AT ≤10.1 ml/kg/min	–	–
Chandrabalan and colleagues[29]	100	AT (<10 ml/kg/min	–	–
Renal Transplant				
Ting and colleagues[33]	70	–	AT	–
Upper Gastrointestinal				
Forshaw and colleagues[34]	78	AT <11 ml/kg/min – Not Significant	–	–
Bariatric				
McCullough and colleagues[37]	109	Vo_2 Peak*	–	–
Hennis and colleagues[38]	106	AT <11.4 ml/kg/min	–	–
Intra-Abdominal				
Snowden and colleagues[39]	389	AT <10 ml/kg/min	–	AT <10 ml/kg/min
Tolchard and colleagues[45]	105	AT, V_E/Vco_2	Vo_2 Peak*	–
Wilson and colleagues[40]	847	AT <11 ml/kg/min	–	–

AT = Anaerobic Threshold, CCU = Critical Care Unit, EVAR = Endovascular Aneurysm Repair, ICU = Intensive Care Unit, LOS = Length of Stay
*= No value given for Vo_2 Peak

Pancreatic surgery

Mortality

Three studies exclusively reported on the ability of AT to predict postoperative mortality and concluded that there was no significant relationship. Ausania and colleagues[28] reported similar mortality rates between groups, AT ≤10.1 and >10.1 ml kg^{-1} min^{-1} (P=1.00). Anaerobic threshold was not associated with postoperative mortality (P=0.74).[29] Ausania and colleagues[30] performed Cox regression analysis and reported that AT was not correlated with long-term survival (P=0.5). Their study failed to quantify the length of long-term survival. Junejo and colleagues[31] reported $\dot{V}_E/\dot{V}_{CO_2}$ to be a significant predictor of both 30 day (P=0.03) and in-hospital mortality (P=0.02; Table 3).

Preoperative AT is not predictive of postoperative mortality after pancreatic surgery; however, $\dot{V}_E/\dot{V}_{CO_2}$ may be able to predict postoperative survival. Further studies are required to determine the validity of $\dot{V}_E/\dot{V}_{CO_2}$.

Length of stay

Only two studies examined LOS and CPET variables. Chandrabalan and colleagues[29] reported that an AT <10 ml kg^{-1} min^{-1} was predictive of a median of 6 days longer LOS than those of AT ≥10 ml kg^{-1} min^{-1} (P<0.01). Likewise, Ausania and colleagues[28] reported that an AT value of ≤10.1 ml kg^{-1} min^{-1} resulted in a median LOS of 29.4 days, whereas patients with an AT >10.1 ml kg^{-1} min^{-1} had a median LOS of 17.5 days (P<0.01; Table 4).

An AT of 10–10.1 ml kg^{-1} min^{-1} appears to be predictive of LOS after pancreatic surgery. This may be used in current practice to guide postoperative care. Future studies will be required to validate this CPET result.

Morbidity

Junejo and colleagues[31] reported that no CPET variable was related to postoperative morbidity (P<0.05). Ausania and colleagues[30] reported that patients with a mean AT of 14.1 (range 10.3–16.9) ml kg^{-1} min^{-1} experienced no complications, whereas patients who did develop complications had a mean AT of 11.3 (range 6.2–15.4) ml kg^{-1} min^{-1} (P=0.02). In contrast, Chandrabalan and colleagues[29] reported that an AT <10 ml kg^{-1} min^{-1} was significantly related to postoperative pancreatic fistula (P=0.03) and major intra-abdominal abscesses (P=0.04), but not cardiac (P=0.31) or pulmonary complications (P=0.66). Ausania and colleagues[28] reported that the postoperative complication rate was significantly lower in the group with AT >10.1 ml kg^{-1} min^{-1} (P=0.01).

Renal transplant

Mortality

Ulubay and colleagues[32] were unable to determine whether CPET was predictive of postoperative mortality after renal transplant surgery because there were no deaths in the relatively small sample size (n=16; Table 3).

Length of stay

No single study examined whether there was a relationship between CPET variables and LOS after renal transplant. Ting and colleagues[33] reported that mean AT was significantly lower in the CCU admission group *vs* the non-CCU admission group (P<0.01; Table 4).

Morbidity

There was no study that examined the prognostic ability of CPET for postoperative morbidity after renal transplant.

Table 5: Preoperative Cardiopulmonary Exercise Testing and Morbidity

Cardiopulmonary Exercise Testing and Morbidity								
Author	**Sample Size**	**Morbidity Measure**	**In-hospital**	**7 days**	**30 days**	**90 days**	**>90 Days**	**Not Reported**
Hepatic Resection and Transplant								
Dunne and colleagues[18]	197	Clavien-Dindo	–	–	Heart Rate at AT and Heart Rate at Vo_2 Peak	–	–	–
Junejo and colleagues[12]	94	POMS, Clavien-Dindo	–	–	V_E/Vco_2 at AT	–	–	–
Kaibori and colleagues[15]	61	Clavien-Dindo	–	–	–	–	AT <11.5 ml/kg/min	–
Abdominal Aortic Aneurysm								
Nugent and colleagues[19]	30	Self-Defined		–	–	–	Vo_2 Peak – Not Significant	–
Prentis and colleagues[23]	185	Self-Defined	AT ≤10 ml/kg/min, Vo_2 Peak* and V_E/Vco_2	–	–	–	–	–
Colorectal								
Lee and colleagues[27]	112	Clavien-Dindo	–	–	Vo_2 Peak*	–	–	–
West and colleagues[25]	95	POMS, Clavien-Dindo	–	–	AT <10.1 ml/kg/min and Vo_2 Peak 16.7 ml/kg/min	–	–	–
West and colleagues[26]	136	POMS, Clavien-Dindo	–	–	–	–	Vo_2 Peak <18.6 ml/kg/min and AT <10.6 ml/kg/min	–
Pancreatic								
Ausania and colleagues[28]	124	POMS, ISGPF	–	–	AT ≤10.1 ml/kg/min	–	–	–
Ausania and colleagues[30]	50	POMS	–	–	–	–	–	AT ≥14.1 ml/kg/min
Chandrabalan and colleagues[29]	100	Clavien-Dindo and ISGPF	AT <10 ml/kg/min					
Junejo and colleagues[31]	64	ISGPS for pancreatic complications. Non pancreatic complications were self-defined.	–	–	–	–	No CPET variable was significant	–
Upper Gastrointestinal								
Moyes and colleagues[36]	108	Cardiopulmonary complications defined according to the Common Terminology Criteria for Adverse Events. Non-cardiopulmonary complications were self-defined.	–	–	–	–	–	AT 9.9 (complications) vs. 11.2 (no complications) ml/kg/min

Nagamatsu and colleagues[35]	91	Self-Defined	–	–	–	–	–	Vo_2 Max/m^2 *
Bariatric								
Hennis and colleagues[38]	106	POMS	AT <11 ml/kg/min	–	–	–	–	–
McCullough and colleagues[37]	109	Self-Defined	–	–	Vo_2 Peak <18.5 ml/kg/min	–	–	–
Intra-Abdominal								
Hightower and colleagues[46]	32		–	Heart Rate at AT, Difference between Heart Rate from rest to AT and Percentage of predicted AT achieved (<75% vs. ≥75%)	–	–	–	–
James and colleagues[47]	83	Major adverse cardiac events and self-defined	–	–	AT <10.6 ml/kg/min and Vo_2 Peak <14.0 ml/min/kg	–	–	–
Prentis and colleagues[44]	69	Clavien-Dindo	AT <12 ml/kg/min	–	–	–	–	–
Snowden and colleagues[48]	116	POMS	AT (POMS ≤1) 11.9 vs. 9.1 ml/kg/min (POMS >1)	–	–	–	–	–
Tolchard and colleagues[45]	105	Clavien-Dindo	–	–	–	AT (complications) 10.6 vs. 11.8 ml/kg/min (no complications), Vo_2 Peak (complications) 14.3 vs. 15.4 ml/kg/min (no complications), V_E/Vco_2 complications 33.3 (complications) vs. 30.3 (no complications)	–	–

AT = Anaerobic Threshold, ISGPF = International Study Group on Pancreatic Fistula, POMS = Postoperative Morbidity Survey
*= No value was given

Upper gastrointestinal surgery

Mortality

Forshaw and colleagues[34] could not conclude whether CPET was predictive of postoperative mortality because there was only one death after oesophagectomy (Table 3).

Length of stay

Forshaw and colleagues[34] reported that there was no apparent correlation with AT and LOS (P=0.89). Cardiopulmonary exercise testing appears unable to determine LOS after upper GI surgery, but there have been few studies in this area. The present review expresses the need for more high-quality CPET prognostic studies in the area of upper GI surgery.

Morbidity

Nagamatsu and colleagues[35] reported that $\dot{V}_{O_2}$ max m^{-2} was lower in patients with cardiopulmonary complications *vs* patients without complications (P<0.01) after oesophagectomy with lymphadenectomy. In contrast, Moyes and colleagues[36] reported that $\dot{V}_{O_2}$ peak was not associated with cardiopulmonary complications (14 *vs* 16 ml min^{-1} kg^{-1}, P=0.07) but that AT was associated with morbidity (P=0.05).

There have been too few studies to conclude whether CPET is predictive of postoperative morbidity after upper GI surgery, but the results are optimistic. The present review expresses the need for more high-quality CPET prognostic studies in the area of upper GI surgery.

Bariatric surgery

Mortality

McCullough and colleagues[37] (total n=99) reported that $\dot{V}_{O_2}$ peak was predictive of morbidity and mortality (grouped together); however, there was only one death, and the results of this study cannot solely predict postoperative mortality (Table 3).

Length of stay

McCullough and colleagues[37] reported that $\dot{V}_{O_2}$ peak was predictive of LOS (P<0.01). The AT of patients with LOS >3 days was lower than that of patients with LOS ≤3 days after gastric bypass surgery (P=0.02).[38] The literature suggests that CPET is able to identify patients subject to increased LOS, but a consensus on the optimal CPET variable and cut-point is required.

Morbidity

Hennis and colleagues[38] reported that AT was significantly lower in patients with complications compared with those without complications (P<0.05). McCullough and colleagues[37] presented a multivariable model using $\dot{V}_{O_2}$ peak as a continuous variable and included smoking status that was a significant predictor of complications (odd ratio 1.61, 95% CI 1.19–2.18, P<0.01; Table 5).

Cardiopulmonary exercise testing shows potential for determining patients at risk of postoperative complications in the preoperative period, but further studies are required to quantify the optimal CPET variable and cut-off point.

Intra-abdominal surgery

Mortality

Anaerobic threshold has been reported in four of the above-mentioned studies to be a significant predictor of mortality.[39–42] Snowden and colleagues[39] reported an AT of 10.9 ml kg^{-1} min^{-1} to be predictive of postoperative survival; however, their follow-up was limited to in-hospital stay. An AT of 10.9 ml kg^{-1} min^{-1} was reported to be predictive of survival up to 90 days (P=0.03).[40] Two studies presented an AT <11 ml kg^{-1} min^{-1} to be predictive of postoperative mortality.[41 42]

Colson and colleagues[43] concluded that AT was not a statistically significant predictor of mortality. Prentis and colleagues[44] reported only two postoperative deaths, and no statistical analysis was performed. Tolchard and colleagues[45] reported an insufficient sample size (Table 3).

The present review suggests that an AT of 10.9 ml kg^{-1} min^{-1} may have good clinical utility. It may also be beneficial to explore the prognostic ability of other CPET variables. A $\dot{V}_E/\dot{V}_{CO_2}$ of 34 has been reported to be associated with postoperative mortality at 90 days (P=0.02).[40]

Length of stay

Tolchard and colleagues[45] reported that a lower mean oxygen uptake was correlated with ICU admission (14.9 *vs* 16.5 ml kg^{-1} min^{-1}, P<0.05) and $\dot{V}_E/\dot{V}_{CO_2}$ ≥33 correlated with LOS (P<0.01). Wilson and colleagues[40] reported that the overall median LOS was lower in the group with AT ≥11 ml kg^{-1} min^{-1} (8 *vs* 9 days, P<0.01). Snowden and colleagues[39] reported that cardiovascular fitness was a significant independent predictor of hospital and critical care LOS. The prognostic ability of CPET in predicting LOS after intra-abdominal surgery is strong; however, a consensus needs to be reached on the optimal CPET variable.

Morbidity

Hightower and colleagues[46] reported that HR at AT (P<0.01), the difference between HR at rest and at AT (P=0.01), and the percentage AT achieved (P=0.02) to be predictive of postoperative morbidity. Tolchard and colleagues,[45] using Mann–Whitney U-tests, compared patients who experienced complications with those who did not and showed $\dot{V}_{O_2}$ peak (P=0.02) and $\dot{V}_E/\dot{V}_{CO_2}$ (P<0.01) to be predictive of complications. The following AT cut-off values have been reported: 12,[44] 11,[45] 10.6,[46] and 10.1 ml kg^{-1} min^{-1}.[48]

Anaerobic threshold is the strongest predictor of postoperative morbidity in intra-abdominal surgery. Patients with an AT of <10.1 ml kg^{-1} min^{-1} should have appropriate measures adopted to ensure a smooth postoperative outcome. Any patients with an AT between 10.1 and 12 ml kg^{-1} min^{-1} should be considered with caution.

Discussion

There are two main theories on how CPET can predict postoperative outcome. One theory suggests that patients with a higher level of fitness function better with the prolonged increase in oxygen delivery induced by surgery without outpacing their anaerobic physiological parameters. The alternative theory suggests that regular exercise can create a systemic effect similar to ischaemic preconditioning. By increasing a person's ability to extract oxygen and tolerate ischaemic conditions, this lessens the impact of any deficit in oxygen delivery and demand associated with surgery.[8]

Previous reviews concluded that CPET is valuable, but more research is needed to determine its validity in non-cardiopulmonary surgery.[6 8] The area has since grown, and the present review has analysed considerably more studies and is the largest systematic review of preoperative CPET to date. Given that a quantitative synthesis approach was undertaken, definite conclusions cannot be drawn from the present review regarding the ability of CPET to predict postoperative outcome after surgery, but certain areas can be highlighted and suggestions can be made.

Main findings

This review recommends that CPET is included in the preoperative assessment of liver, pancreatic, and intra-abdominal surgery and AAA repair and that the following cut-points are used.

- Hepatic transplant and resection: 90 day survival, AT 9 ml kg^{-1} min^{-1}; 3 yr survival, AT 11.5 ml kg^{-1} min^{-1}; and ICU/CCU admission, AT <9.9–11 ml kg^{-1} min^{-1}.
- Abdominal aortic aneurysm repair: 90 day survival, $\dot{V}O_2$ peak 15 ml kg^{-1} min^{-1}.
- Pancreatic surgery: LOS and morbidity, AT 10–10.1 ml kg^{-1} min^{-1}.
- Intra-abdominal surgery: mortality, AT of 10.9 ml kg^{-1} min^{-1}; morbidity, AT <10.1 ml kg^{-1} min^{-1}; and patients with an AT 0f 10.1–12 ml kg^{-1} min^{-1} should be treated with caution.

Anaerobic threshold is the optimal predictor of outcome in liver, pancreatic, and intra-abdominal surgery. The reason for the variation in the type and strength of the relationship between CPET variable and outcome in various surgical interventions has been underexplored, but a possible explanation may be that there is variation in the relative importance of different CPET variables predisposing to adverse outcome.[6] Despite this, the results suggest AT to be the superior indicator within certain surgical interventions.

Studies were divided based on surgery type, similar to previous reviews.[6 8 9] The variation in cut-points between surgeries may be because of the possibility that certain surgical procedures require a greater physiological demand, or the pre- and postoperative management varies between surgical procedures.[7] This topic has been underexplored and requires further validation.

There are four main reasons for associations in observational studies between cardiopulmonary fitness and postoperative outcome: bias, confounding, chance, and cause.[49] The level of bias and confounding was assessed using the QUIPS tool.[11] The level of chance of association is summed up by the 95% CIs and *P*-value (Supplementary material, Tables S2–S4). The CPET-derived cut-points are similar between studies; as the level of bias, chance, and confounding have been accounted for, it is possible that a cause of poor postoperative outcome is cardiorespiratory fitness below these cut-points.

Morbidity after pancreatic surgery has produced some conflicting results. One study reported no relationship between AT and morbidity,[31] and two studies produced similar findings,[28 29] whereas one study produced different results. The present review suggests using an AT of 10–10.1 ml kg^{-1} min^{-1} as a cut-point for morbidity after pancreatic surgery[28 29] instead of 14.1 ml kg^{-1} min^{-1} as reported by Ausania and colleagues[30] because we found this study, using the QUIPS tool, to have a relatively high bias in a number of areas.

There is large heterogeneity between studies; therefore, results could not be pooled to produce a meta-analysis. All surgeries were grouped together by surgical intervention (or grouped into the intra-abdominal cohort when no distinctions were made) to improve homogeneity. Despite this, there is considerable variation in areas such as surgical procedure (e.g. laparoscopic *vs* open), the outcome measures used (e.g. postoperative morbidity survey *vs* self-defined morbidity), and accounting for co-morbidities. A number of important variables, such as type of anaesthesia, were not reported in most studies (n=34). The choice of statistical approaches also varied between studies.

The present review included studies that did not have *a priori* power calculation. The sample sizes of the included studies may be underpowered and could potentially influence results. In order for future studies to have sufficient power to determine the ability of an AT <11 ml kg^{-1} min^{-1} to predict mortality at 90 days, we estimate that a sample size of 406 patients above and below AT <11 ml kg min is required, and for 2 yr mortality a sample size of 253 above and below AT <11 ml kg min is required (α=0.05, β=0.80). The calculations were based on data reported by Lai and colleagues.[24]

A robust methodology should also be used[50] consisting of the following: (i) reporting all measured CPET variables (e.g. $\dot{V}O_2$ peak, AT, $\dot{V}E/\dot{V}CO_2$, and HR); (ii) predetermined outcome time points should be used, including 30 day, 90 day, 1, 3, and 5 yr time points for mortality and morbidity, and LOS should include overall hospital stay, ICU/HDU/CCU admission, and length of stay along with readmission; (iii) morbidity should be measured using a combination of the Clavien–Dindo classification scoring system[51] and the Postoperative Morbidity Survey;[52] and (iv) odds ratios should be determined for mortality and morbidity outcomes to allow results to be pooled in a future meta-analysis. Length of stay should be recorded with medians, standard deviations, and CIs.

Many studies conclude separate CPET-defined cut-points that predict postoperative outcome. Perhaps a single cut-point cannot be recommended; instead, subgroups based on fitness could be created to stratify patients before surgery based on the risk of poor surgical outcome.[37] It is also possible that the variation between CPET variables and strength of relationship with outcome between studies is subject to the inconsistent methodology coupled with data analysis and presentation.

Future research

The areas of colorectal, renal transplant, upper GI, and bariatric surgery require further research to draw conclusions concerning the ability of CPET to predict postoperative outcome. In hepatic surgical intervention, the postoperative morbidity has not been well analysed; currently, there is no consensus on the CPET variable and cut-point to use. To predict LOS after hepatic surgery, the ability of AT produces a divided opinion. The $\dot{V}O_2$ peak shows potential, but evidence in its support is weak. It is recommended that future studies examine the possible link between preoperative aerobic fitness and morbidity and LOS.

A number of studies have examined CPET and survival after AAA repair, but time points to survival vary and so future studies will need to use specific time points, such as 1 and 5 yr survival. The present review suggests future research should examine the possible relationship between CPET and LOS and morbidity after AAA repair because research in this area is lacking.

Increased physical fitness is correlated with improved postoperative outcome. Patients with cardiopulmonary fitness below the recommended cut-points are susceptible to postoperative complications and mortality. Preoperative exercise programmes can improve fitness before surgery.[53] The ability of preoperative exercise interventions to improve postoperative outcome requires further validation.

Conclusion

Cardiopulmonary exercise testing provides a good objective measure of a patient's preoperative fitness, which in turn is a strong predictor of postoperative outcome. Cardiopulmonary exercise testing has been well documented in certain surgical interventions (liver, AAA, pancreatic, and intra-abdominal), but it is less well defined in other areas (colorectal, renal transplant,

upper GI, and bariatric). The CPET variables AT and $\dot{V}_{O_2}$ peak are the most analysed. Anaerobic threshold is a stronger predictor of outcome in hepatic, pancreatic, and intra-abdominal surgery, whereas $\dot{V}_{O_2}$ peak is superior in AAA repair. Variables such as $\dot{V}_E/\dot{V}_{CO_2}$ show emerging significance but continue to be underused. Future studies should use a robust methodology to clarify further the role of CPET in preoperative risk prediction.

Authors' contributions

Conception: J. Moran, F.W., J.H., J. Moriarty
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Supplementary material

Supplementary material is available at *British Journal of Anaesthesia* online.

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Declaration of interest

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References

1. Stringer WW. Cardiopulmonary exercise testing: current applications. *Exp Rev Respir Med* 2010; **4**: 179–88
2. Weisman IM, Zeballos RJ. Clinical exercise testing. *Clin Chest Med* 2001; **22**: 679–701, viii
3. Mancini DM, Eisen H, Kussmaul W, Mull R, Edmunds LH Jr, Wilson JR. Value of peak exercise oxygen consumption for optimal timing of cardiac transplantation in ambulatory patients with heart failure. *Circulation* 1991; **83**: 778–86
4. Beckles MA, Spiro SG, Colice GL, Rudd RM. The physiologic evaluation of patients with lung cancer being considered for resectional surgery. *Chest* 2003; **123**: 105S–14S
5. Brunelli A, Belardinelli R, Refai M, *et al*. Peak oxygen consumption during cardiopulmonary exercise test improves risk stratification in candidates to major lung resection. *Chest* 2009; **135**: 1260–7
6. Hennis PJ, Meale PM, Grocott MP. Cardiopulmonary exercise testing for the evaluation of perioperative risk in non-cardiopulmonary surgery. *Postgrad Med J* 2011; **87**: 550–7
7. Levett DZ, Grocott MP. Cardiopulmonary exercise testing for risk prediction in major abdominal surgery. *Anesthesiol Clin* 2015; **33**: 1–16
8. Smith TB, Stonell C, Purkayastha S, Paraskevas P. Cardiopulmonary exercise testing as a risk assessment method in non cardio-pulmonary surgery: a systematic review. *Anaesthesia* 2009; **64**: 883–93
9. West M, Jack S, Grocott MP. Perioperative cardiopulmonary exercise testing in the elderly. *Best Pract Res Clin Anaesthesiol* 2011; **25**: 427–37
10. Antes G, von Elm E. [The PRISMA Statement – what should be reported about systematic reviews?]. *Dtsch Med Wochenschr* 2009; **134**: 1619
11. Hayden JA, van der Windt DA, Cartwright JL, Cote P, Bombardier C. Assessing bias in studies of prognostic factors. *Ann Intern Med* 2013; **158**: 280–6
12. Junejo MA, Mason JM, Sheen AJ, *et al*.Cardiopulmonary exercise testing for preoperative risk assessment before hepatic resection. *Br J Surg* 2012; **99**: 1097–104
13. Prentis JM, Manas DM, Trenell MI, Hudson M, Jones DJ, Snowden CP. Submaximal cardiopulmonary exercise testing predicts 90-day survival after liver transplantation. *Liver Transpl* 2012; **18**: 152–9
14. Bernal W, Martin-Mateos R, Lipcsey M, *et al*. Aerobic capacity during cardiopulmonary exercise testing and survival with and without liver transplantation for patients with chronic liver disease. *Liver Transpl* 2014; **20**: 54–62
15. Kaibori M, Ishizaki M, Matsui K, *et al*. Assessment of preoperative exercise capacity in hepatocellular carcinoma patients with chronic liver injury undergoing hepatectomy. *BMC Gastroenterol* 2013; **13**: 119
16. Neviere R, Edme JL, Montaigne D, Boleslawski E, Pruvot FR, Dharancy S. Prognostic implications of preoperative aerobic capacity and exercise oscillatory ventilation after liver transplantation. *Am J Transplant* 2014; **14**: 88–95
17. Epstein SK, Freeman RB, Khayat A, Unterborn JN, Pratt DS, Kaplan MM. Aerobic capacity is associated with 100-day outcome after hepatic transplantation. *Liver Transpl* 2004; **10**: 418–24
18. Dunne DF, Jones RP, Lythgoe DT, *et al*. Cardiopulmonary exercise testing before liver surgery. *J Surg Oncol* 2014; **110**: 439–44
19. Nugent AM, Riley M, Megarry J, O'Reilly MJG, MacMahon J, Lowry R. Cardiopulmonary exercise testing in the preoperative assessment of patients for repair of abdominal aortic aneurysm. *Irish J Med Sci* 1998; **167**: 238–41
20. Grant SW, Hickey GL, Wisely NA, *et al*. Cardiopulmonary exercise testing and survival after elective abdominal aortic aneurysm repair. *Br J Anaesth* 2015; **114**: 430–6
21. Hartley RA, Pichel AC, Grant SW, *et al*. Preoperative cardiopulmonary exercise testing and risk of early mortality following abdominal aortic aneurysm repair. *Br J Surg* 2012; **99**: 1539–46
22. Carlisle J, Swart M. Mid-term survival after abdominal aortic aneurysm surgery predicted by cardiopulmonary exercise testing. *Br J Surg* 2007; **94**: 966–9
23. Prentis JM, Trenell MI, Jones DJ, Lees T, Clarke M, Snowden CP. Submaximal exercise testing predicts perioperative hospitalization after aortic aneurysm repair. *J Vasc Surg* 2012; **56**: 1564–70
24. Lai CW, Minto G, Challand CP, *et al*. Patients' inability to perform a preoperative cardiopulmonary exercise test or demonstrate an anaerobic threshold is associated with inferior outcomes after major colorectal surgery. *Br J Anaesth* 2013; **111**: 607–11
25. West MA, Parry MG, Lythgoe D, *et al*. Cardiopulmonary exercise testing for the prediction of morbidity risk after rectal cancer surgery. *Br J Surg* 2014; **101**: 1166–72

26. West MA, Lythgoe D, Barben CP, *et al*. Cardiopulmonary exercise variables are associated with postoperative morbidity after major colonic surgery: a prospective blinded observational study. *Br J Anaesth* 2014; **112**: 665–71
27. Lee L, Schwartzman K, Carli F, *et al*. The association of the distance walked in 6 min with pre-operative peak oxygen consumption and complications 1 month after colorectal resection. *Anaesthesia* 2013; **68**: 811–6
28. Ausania F, Snowden CP, Prentis JM, *et al*. Effects of low cardiopulmonary reserve on pancreatic leak following pancreaticoduodenectomy. *Br J Surg* 2012; **99**: 1290–4
29. Chandrabalan VV, McMillan DC, Carter R, *et al*. Pre-operative cardiopulmonary exercise testing predicts adverse postoperative events and non-progression to adjuvant therapy after major pancreatic surgery. *HPB (Oxford)* 2013; **15**: 899–907
30. Ausania F, Vallance AE, Manas DM, *et al*. Double bypass for inoperable pancreatic malignancy at laparotomy: postoperative complications and long-term outcome. *Ann R Coll Surg Eng* 2012; **94**: 563–8
31. Junejo MA, Mason JM, Sheen AJ, *et al*. Cardiopulmonary exercise testing for preoperative risk assessment before pancreaticoduodenectomy for cancer. *Ann Surg Oncol* 2014; **21**: 1929–36
32. Ulubay G, Ulasli SS, Kupeli E, Yilmaz EB, Sezgin A, Haberal M. Value of exercise testing to estimate post-operative complications and mortality in solid organ recipients: a preliminary study. *Ann Transplant* 2010; **15**: 11–20
33. Ting SM, Iqbal H, Hamborg T, *et al*. Reduced functional measure of cardiovascular reserve predicts admission to critical care unit following kidney transplantation. *PLoS ONE* 2013; **8**: e64335
34. Forshaw MJ, Strauss DC, Davies AR, *et al*. Is cardiopulmonary exercise testing a useful test before esophagectomy? *Ann Thorac Surg* 2008; **85**: 294–9
35. Nagamatsu Y, Shima I, Yamana H, Fujita H, Shirouzu K, Ishitake T. Preoperative evaluation of cardiopulmonary reserve with the use of expired gas analysis during exercise testing in patients with squamous cell carcinoma of the thoracic esophagus. *J Thorac Cardiovasc Surg* 2001; **121**: 1064–8
36. Moyes LH, McCaffer CJ, Carter RC, Fullarton GM, Mackay CK, Forshaw MJ. Cardiopulmonary exercise testing as a predictor of complications in oesophagogastric cancer surgery. *Ann R Coll Surg Engl* 2013; **95**: 125–30
37. McCullough PA, Gallagher MJ, Dejong AT, *et al*. Cardiorespiratory fitness and short-term complications after bariatric surgery. *Chest* 2006; **130**: 517–25
38. Hennis PJ, Meale PM, Hurst RA, *et al*. Cardiopulmonary exercise testing predicts postoperative outcome in patients undergoing gastric bypass surgery. *Br J Anaesth* 2012; **109**: 566–71
39. Snowden CP, Prentis J, Jacques B, *et al*. Cardiorespiratory fitness predicts mortality and hospital length of stay after major elective surgery in older people. *Ann Surg* 2013; **257**: 999–1004
40. Wilson RJT, Davies S, Yates D, Redman J, Stone M. Impaired functional capacity is associated with all-cause mortality after major elective intra-abdominal surgery. *Br J Anaesth* 2010; **105**: 297–303
41. Older P, Hall A, Hader R. Cardiopulmonary exercise testing as a screening test for perioperative management of major surgery in the elderly. *Chest* 1999; **116**: 355–62
42. Older P, Smith R, Courtney P, Hone R. Preoperative evaluation of cardiac failure and ischemia in elderly patients by cardiopulmonary exercise testing. *Chest* 1993; **104**: 701–4
43. Colson M, Baglin J, Bolsin S, Grocott MPW. Cardiopulmonary exercise testing predicts 5 yr survival after major surgery. *Br J Anaesth* 2012; **109**: 735–41
44. Prentis JM, Trenell MI, Vasdev N, *et al*. Impaired cardiopulmonary reserve in an elderly population is related to postoperative morbidity and length of hospital stay after radical cystectomy. *BJU Int* 2013; **112**: E13–9
45. Tolchard S, Angell J, Pyke M, *et al*. Cardiopulmonary reserve as determined by cardiopulmonary exercise testing correlates with length of stay and predicts complications after radical cystectomy. *BJU Int* 2015; **115**: 554–61
46. Hightower CE, Riedel BJ, Feig BW, *et al*. A pilot study evaluating predictors of postoperative outcomes after major abdominal surgery: physiological capacity compared with the ASA physical status classification system. *Br J Anaesth* 2010; **104**: 465–71
47. James S, Jhanji S, Smith A, O'Brien G, Fitzgibbon M, Pearse RM. Comparison of the prognostic accuracy of scoring systems, cardiopulmonary exercise testing, and plasma biomarkers: a single-centre observational pilot study. *Br J Anaesth* 2014; **112**: 491–7
48. Snowden CP, Prentis JM, Anderson HL, *et al*. Submaximal cardiopulmonary exercise testing predicts complications and hospital length of stay in patients undergoing major elective surgery. *Ann Surg* 2010; **251**: 535–41
49. Jepsen P, Johnsen SP, Gillman MW, Sørensen HT. Interpretation of observational studies. *Heart* 2004; **90**: 956–60
50. Grocott MPW, Pearse RM. Prognostic studies of perioperative risk: robust methodology is needed. *Br J Anaesth* 2010; **105**: 243–5
51. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004; **240**: 205–13
52. Bennett-Guerrero E, Welsby I, Dunn TJ, *et al*. The use of a postoperative morbidity survey to evaluate patients with prolonged hospitalization after routine, moderate-risk, elective surgery. *Anesth Analg* 1999; **89**: 514–9
53. Dronkers JJ, Lamberts H, Reutelingsperger IM, *et al*. Preoperative therapeutic programme for elderly patients scheduled for elective abdominal oncological surgery: a randomized controlled pilot study. *Clin Rehab* 2010; **24**: 614–22

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