Preoperative Cardiopulmonary Exercise Test Associated with Postoperative Outcomes in Patients Undergoing Cancer Surgery: A Systematic Review and Meta-Analyses

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ABSTRACT

Backgrounds. There is mixed evidence on the value of preoperative cardiorespiratory exercise test (CPET) to predict postoperative outcomes in patients undergoing a cancer surgical procedure. The purpose of this review was to investigate the association between preoperative CPET variables and postoperative complications, length of hospital stay, and quality of life in patients undergoing cancer surgery.

Methods. A search was conducted on MEDLINE, Embase, AMED, and Web of science from inception to April 2020. Cohort studies investigating the association between preoperative CPET variables and postoperative complications, length of hospital stay, and quality of life in patients undergoing cancer surgery were included. Risk of bias was assessed using the QUIPS tool. A random-effect model meta-analysis was performed whenever possible.

Results. Fifty-two unique studies, including 10,030 patients were included. Overall, most studies were rated as having low risk of bias. Higher preoperative peak VO2 was associated with absence of postoperative complications (mean difference [MD]: 2.28; 95% confidence interval [CI]: 1.26–3.29) and no pulmonary complication (MD: 1.47; 95% CI: 0.49–2.45). Preoperative AT and VE/VCO2 also demonstrated some positive trends. None of the included studies reported a negative trend.

Conclusions. This systematic review and meta-analysis demonstrated a significant association between superior preoperative CPET values, especially peak VO2, and better postoperative outcomes. The assessment of preoperative functional capacity in patients undergoing cancer surgery has the potential to facilitate treatment decision making.

The incidence of cancers in the global population is increasing.1 For selected patients, surgery with or without radiochemotherapy is the main treatment option. The goal of surgery is to obtain a clear resection margin and ultimately cure or prolong survival with an acceptable quality of life.2,3 However, despite the significant improvements in long-term survival over the recent years, the rate of postoperative morbidity remains high—increasing the length of hospital stay, reducing quality of life and contributing to a high treatment burden.

During the past 20 years, cardiopulmonary exercise test (CPET) was introduced during the preoperative period as an objective measure of functional capacity to evaluate the risk of adverse perioperative events and inform the
perioperative management, particularly in high-risk patients undergoing high-risk surgery. Recently, CPET has gained popularity and is commonly used in high-risk patients undergoing cancer surgery in some surgical units. It is hypothesised that fitter patients, who were identified by using CPET, have greater physiological reserve to undergo surgery and recover sooner with fewer postoperative complications. This is extremely important for clinicians to inform decision-making, to better understand the postoperative course, and to guide postoperative management.

Several systematic reviews have explored the potential association between preoperative CPET variables and postoperative outcomes, demonstrating mixed results. While some systematic reviews have reported a significant positive association between preoperative CPET variables and postoperative complications, length of hospital stay, unplanned ICU admission, and 12-months survival, others have reported nonsignificant association. The prospective, multinational cohort (METS) study, for example, demonstrated an association between peak oxygen uptake (peak VO₂) and noncardiac complications in a cohort of relatively well patients having noncardiac surgery and not limited to cancer surgery. Some limitations encountered within the previous systematic reviews include the absence of meta-analysis, inclusion of a mixed population (i.e., cancer and noncancer patients), outdated, or focused on a narrow cohort of patients. Better understanding of the potential association between preoperative CPET variables and postoperative outcomes in cancer patients is extremely important; this can guide preoperative interventions designed to improve patients preoperative physical status. This, in turn, has the potential to reduce postoperative morbidity.

As the number of publications are rapidly growing further analysis, taking into consideration the limitations of the previous systematic reviews, is warranted. This systematic review aims to determine whether the preoperative CPET variables peak VO₂, anaerobic threshold (AT), and ventilatory equivalent for carbon dioxide (VE/VCO₂), are associated with postoperative complication rates, length of hospital stay, and quality of life in patients undergoing cancer surgery.

METHODS

Protocol and Registration

This systematic review was reported in accordance with the meta-analyses of Observational Studies in Epidemiology (MOOSE) checklist. The protocol for this systematic review was registered on the Open Science Framework website (https://osf.io/8ntvc/).

Information Sources and Search

A sensitive electronic search was performed via Ovid in MEDLINE, Embase, AMED, and Web of science via www.webofknowledge.com from inception to April 2020. An amalgamation of Medical Subject Headings (MeSH) terms and key words for “preoperative,” “cardiopulmonary exercise test,” and “neoplasm” was used in the search strategy (Supplementary Table 1). In addition, citation tracking of the included studies and relevant systematic reviews were conducted. The search was limited to humans with no date or language restrictions applied.

Study Selection

The screening process was conducted using Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org). The initial screening was completed by one review author removing clearly irrelevant studies (DS). Screening of titles and abstracts of potentially eligible studies was be performed by two independent review authors (DS and PRB) with full-text article assessed against the inclusion and exclusion criteria. Any disagreements over the eligibility of particular studies were resolved through discussion with a third review author (NP).

Data Collection Process

A standardized data form was used to extract data from eligible studies for assessment of the study quality and evidence synthesis. Two independent review authors extract the data independently (DS and PRB). Disagreements over the data extraction were resolved through discussion with a third reviewer (NP). The following information were extracted from each individual study: participant characteristics, study characteristics, CPET description and measures, postoperative outcome measures, and measures of association.

Eligibility Criteria

Longitudinal studies reporting on the association between preoperative CPET values and postoperative outcomes in adult patients aged ≥18 years old undergoing a cancer-related surgical procedure were included if they reported the following: (i) at least one of the CPET measures of interest: (a) Peak Oxygen uptake (peak VO₂): defined as the highest VO₂ attained on a rapid incremental test. (b) Anaerobic threshold (AT): a submaximal index of exercise capacity defined as the oxygen uptake (VO₂) above which there is a metabolic transition to increased glycolysis and lactate begins to rise with an associated
metabolic acidosis. (c) Ventilatory equivalent for carbon dioxide (VE/VCO2): defined as the ratio of minute ventilation to carbon dioxide production usually reported at the AT; (ii) reported at least one postoperative outcome measure, including complication rate, length of hospital stay, and/or quality of life; (iii) Reported data on the association between preoperative CPET and postoperative outcome or provide enough data for the association to be calculated by the review authors.

Studies were excluded if they presented the following: (i) reported on mixed populations (e.g., cancer and non-cancer patients, where the noncancer population ≥5% of the investigated sample); (ii) the population of interest underwent open and close procedure (e.g., not completed as planned); (iii) abstracts of studies published on conference proceedings.

Risk of Bias Assessment

Risk of bias was assessed by using the Quality in Prognosis Studies (QUIPS) tool and was rated by two review authors (DS and PRB).14 Risk of bias was rated as “high”, “moderate”, or “low” risk according to the following domains: (i) Study participation; (ii) Study attrition; (iii) Outcome measurement; (vi) Statistical analysis and reporting. Due to the nature of this systematic review, the prognostic factor and study confounding domains were not judged as they were deemed not applicable. Disagreements over the risk of bias were resolved through discussion with a third review author (NP).

Strategy for Data Synthesis

For studies reporting on the association between preoperative CPET values and postoperative outcomes using continuous data, measures of central tendency (i.e., mean, median) and dispersion (i.e., standard deviation, 95% confidence intervals [CI]) were extracted. However, for the studies reporting on dichotomous data, the number of patients presenting high/low CPET values and presence or absence of postoperative outcomes were extracted. Whenever possible, mean values and standard deviation were estimated using previously published formulas in order to pool data.15 When raw data were available, mean difference and 95% CI (continuous) or odds ratios and 95% CI (dichotomous) were calculated. For homogeneous studies (e.g., presenting comparable measures of CPET and postoperative outcomes) reporting on the association between preoperative CPET and postoperative outcomes a meta-analysis using a random-effect model was conducted. Studies presenting high variability of data types and format were presented descriptively. A post-hoc subgroup analysis was performed to investigate the association between preoperative CPET variables and postoperative outcomes according to cancer type. Pooled estimates were obtained with Comprehensive Meta-Analysis Software V.3 (Biostat, Englewood, NJ).

RESULTS

Study Selection

The electronic search yielded 843 potential studies after duplicates were removed. Of these, 212 full-text articles were considered for inclusion. A total of 58 published articles (including 52 unique cohorts) were included in this systematic review. The flow diagram of the inclusion process is presented in Fig. 1.

Study Characteristics

Of the 52 unique cohorts included, three included patients presenting with bladder cancer,16–18 5 colorectal,19–23 5 esophageal,24–29 3 liver,30–32 27 lung,33–60 3 pancreatic,61–63 1 rectal,64 and 5 included mixed cancer populations.65–70 The sample size of the included studies ranged from 8 to 1684.51,60 Most of the preoperative CPETs were performed by using a cycle ergometer. Peak VO2 was assessed in most studies (88%), followed by AT (44%). All included studies reported postoperative complication as an outcome, whereas quality of life was not reported in any of the included studies. The characteristics of the individual studies are presented in Table 1.

Risk of Bias

Overall, most studies were rated as having low risk of bias. Study participation was the domain with higher risk of bias (46% rated as moderate/high risk of bias), whereas study attrition (10% rated as moderate risk of bias), outcome measurement (10% rated as moderate risk of bias), and statistical analysis and reporting (13% rated as moderate risk of bias) were rated with lower risk of bias. The risk of bias assessment for each of the included study can be found in Table 2.

Association between Preoperative CPET Values and Postoperative Complications

Peak VO2 The association between preoperative Peak VO2 and postoperative complications are presented in Fig. 2, Supplementary Fig. 1, and Tables 3 and 4. Our pooled analysis demonstrated that patients with no postoperative complication presented for surgery with a higher Peak VO2 (MD: 2.28; 95% CI: 1.26–3.29; I2 = 9%)
compared with patients who had postoperative complications (Fig. 2). A subgroup analysis in lung cancer patients demonstrated similar association (MD: 2.40; 95% CI: 1.50-3.30) (Supplementary Fig. 2).

In addition, patients with no postoperative pulmonary complications (MD: 1.47; 95% CI: 0.49–2.45; I² = 0%), minor complications (MD: 2.01; 95% CI: 0.90–3.13; I² = 27%), no cardiovascular complication (MD: 2.23; 95% CI: 0.30–4.15), or no in-hospital mortality (MD: 2.78; 95% CI: 1.12–4.43) compared with patients who presented with postoperative complications, presented for surgery with a significantly higher Peak VO₂ (Fig. 2). No difference in Peak VO₂ was found for patients with or without postoperative cardiopulmonary complications (Fig. 2). Other studies were not pooled in the meta-analysis due to high heterogeneity and reported mixed results (Tables 3 and 4).

AT The association between preoperative AT and postoperative complications are presented in Fig. 3, Supplementary Fig. 1, and Tables 3 and 4. Our pooled analysis demonstrated no significant difference in preoperative AT values for patients with or without postoperative complications (MD: 0.15; 95% CI: −0.32 to 0.62) and cardiopulmonary complication (MD: 1.05; 95% CI: −0.17 to 2.26; I² = 0%). Preoperative AT values were significantly higher in patients who presented minor complications compared with major complications (MD: 2.15; 95% CI: 1.29–3.00; I² = 0%) and for no in-hospital mortality compared with in-hospital mortality (MD: 2.27; 95% CI: 1.03–3.51) (Fig. 3). Other studies were not pooled in the meta-analysis due to heterogeneity and reported mixed results (Tables 3 and 4). Similar results were found on our subgroup analysis according to cancer type (Supplementary Fig. 3).

Vₑ/Vₖₑ The association between preoperative Vₑ/Vₖₑ and postoperative complications are presented in Fig. 4 and Tables 3 and 4. Our pooled analysis demonstrated that preoperative Vₑ/Vₖₑ values were significant lower in patients with no pulmonary complication compared with patients with pulmonary complication (MD: 3.54; 95% CI: 1.82–5.25; I² = 0%). No significant differences in
| Author, year | Type of cancer | Characteristics | CPET assessment | CPET variables | Postoperative outcomes | Definition postoperative outcomes |
|-------------|----------------|----------------|----------------|----------------|-----------------------|----------------------------------|
| Lamb 2016   | Bladder        | Mean age (SD): 65.0 (9.4) | Cycloergometer | Peak VO₂ (ml/kg/min) AT (ml/kg/min) VE/VCO₂ | Minor/major complication LOS | Clavien-Dindo classification (≥3 major complication) No. of days spent in hospital from the day of operation until the day the patient left the hospital |
| Prentis 2013| Bladder        | Mean age (SD): 69.6 (6.5) | Cycloergometer | Peak VO₂ (ml/kg/min) AT (ml/kg/min) VE/VCO₂ | Any complication | Clavien-Dindo classification |
| Tolchard 2015| Bladder       | Mean age (SD): 70.2 (10.3) | Cycloergometer | Peak VO₂ (ml/kg/min) AT (ml/kg/min) VE/VCO₂ | Minor/major complication | Clavien-Dindo classification (≥2 major complication) |
| Bowles 2008 | Colorectal     | Mean age (SD): NR | NR | AT (ml/kg/min) | Minor/major complication Mortality | Clavien-Dindo classification (≥3 major complication) Not specified |
| Chan 2016   | Colorectal     | Mean age (SD): 85.0 (10.4) | Cycloergometer | Peak VO₂ (ml/kg/min) AT (ml/kg/min) | Any complication Minor/major complication | Clavien-Dindo classification Clavien-Dindo classification (≥3 major complication) |
| Mann 2020   | Colorectal     | Mean age (SD): 71.7 (8.8) | NR | AT (ml/kg/min) VE/VCO₂ | Unplanned critical care Mortality LOS | Unplanned critical care was defined as any unexpected admission or readmission to high dependency unit (HDU) or ICU from the general surgical ward Death within 30 days from surgery No. of days spent in hospital from the day of operation until the day the patient left the hospital |
| McSorley 2018| Colorectal   | Mean age (SD): NR | Cycloergometer | Peak VO₂ (ml/kg/min) | Any complication Minor/major complication LOS | Not specified |
| Nikolopoulos 2015| Colorectal      | Mean age (SD): 59.3 (12.7) | Cycloergometer | AT (ml/kg/min) | Minor/major complication | Major complications included respiratory failure, pneumonia with radiological evidence, pulmonary embolism, myocardial infarction verified by rise in cardiac enzymes and ECG changes, cardiac arrhythmias and congestive heart failure requiring treatment, renal failure, and sepsis |
| Forshaw 2008 | Esophageal     | Mean age (SD): 64.4 (8.5) | Cycloergometer | Peak VO₂ (ml/kg/min) AT (ml/kg/min) | Cardiopulmonary complication Unplanned ITU admission LOS | Common Terminology Criteria for Adverse events Unplanned reintubation and mechanical ventilation No. of days spent in hospital from the day of operation until the day the patient left the hospital |
| Author, year | Type of cancer | Characteristics | CPET assessment | CPET variables | Postoperative outcomes | Definition postoperative outcomes |
|--------------|----------------|----------------|----------------|----------------|------------------------|----------------------------------|
| Lam 2019     | Esophageal     | Mean age (SD): 66.9 (9.2) | Cycloergometer | Peak VO₂ (ml/kg/min) | Any complication | Esophageal Complications Consensus Group definitions |
|              |                | Sample size: 206 |                | AT (ml/kg/min) | Cardiopulmonary complication | Esophageal Complications Consensus Group definitions |
|              |                | Female (%): 48 (23%) |                |                |                        | More than 10 days of mechanical ventilatory support, more than 3 days of continuous therapy for a pulmonary complication, or more than 3 days of therapy for cardiac arrhythmias |
| Nagamatsu 2001/1994 | Esophageal | Mean age (SD): 59.0 (9.0) | Cycloergometer | Peak VO₂ (ml/min/m²) | Cardiopulmonary complication | Cardiopulmonary complication |
|              |                | Sample size: 91 |                | AT (ml/min/m²) |                        | |
|              |                | Female (%): 3 (3.3%) |                |                |                        | |
| Patel 2019   | Esophageal     | Mean age (SD): 64.6 (9.0) | Cycloergometer | Peak VO₂ (ml/kg/min) | Minor/major complication | Clavien-Dindo classification (≥3 major complication) |
|              |                | Sample size: 120 |                | AT (ml/kg/min) |                        | No. of days spent in hospital from the day of operation until the day the patient left the hospital |
|              |                | Female (%): 20 (17%) |                |                |                        | |
| Sinclair 2017 | Esophageal    | Mean age (SD): 66.0 (8.9) | Cycloergometer | Peak VO₂ (ml/kg/min) | Any complication | Cardiovascular (acute coronary syndrome, heart failure, problematic atrial fibrillation); Respiratory (pneumonia, pulmonary embolism, acute respiratory distress syndrome); Gastro-intestinal (anastomotic leak); and other complications |
|              |                | Sample size: 240 |                | AT (ml/kg/min) |                         | Not specified |
|              |                | Female (%): 59 (25%) |                |                |                        | |
| Dunne 2014   | Liver          | Mean age (SD): 69.6 (8.2) | Cycloergometer | Peak VO₂ (ml/kg/min) | Any complication | Clavien-Dindo classification. |
|              |                | Sample size: 197 |                | AT (ml/kg/min) | Minor/major complication | Clavien-Dindo classification (≥3 major complication) |
|              |                | Female (%): 59 (30%) |                |                | Clavien-Dindo classification | No. of days spent in hospital from the day of operation until the day the patient left the hospital |
| Kasivisvanathan 2015 | Liver | Mean age (SD): 63.2 (11.3) | Cycloergometer | Peak VO₂ (ml/kg/min) | Any complication | POMS score ≥1 on postoperative Day 3 |
|              |                | Sample size: 104 |                | AT (ml/kg/min) | LOS | No. of days spent in hospital from the day of operation until the day the patient left the hospital |
|              |                | Female (%): 44 (42%) |                |                |                        | |
| Ulyett 2017  | Liver          | Mean age (SD): 68.0 (12.7) | Cycloergometer | Peak VO₂ (ml/kg/min) | Minor/major complication | Clavien-Dindo classification (≥3 major complication) |
|              |                | Sample size: 172 |                | AT (ml/kg/min) |                        | |
|              |                | Female (%): 53 (31%) |                |                |                        | |
| Bayram 2007  | Lung           | Mean age (SD): 59.0 (14.8) | Cycloergometer | Peak VO₂ (ml/kg/min) | Postoperative complications | Cardiopulmonary Pulmonary Respiratory Mortality (30 days) Pneumonia Acteletasis Bronchopleural fistula Prolonged air leak Arrhythmia |
|              |                | Sample size: 55 |                |                | LOS | No. of days spent in hospital from the day of operation until the day the patient left the hospital |
|              |                | Female (%): 6 (11%) |                |                |                        | |
| Author, year | Type of cancer | Characteristics | CPET assessment | CPET variables | Postoperative outcomes | Definition postoperative outcomes |
|--------------|----------------|----------------|----------------|----------------|-----------------------|----------------------------------|
| Bechard & Wetstein 1987 | Lung | Mean age (SD): 63.8 (6.5) Sample size: 50 Female (%): 50 (100%) | Cycloergometer | Peak VO₂ (ml/kg/min) AT (L/min) | Any complication | Cardiopulmonary complications were defined as acute CO₂ retention (partial pressure of CO₂ >45 mm Hg), prolonged mechanical ventilation (>48 hours), myocardial infarction, cardiac arrhythmias necessitating therapy, pneumonia (temperature >38 °C, purulent sputa, and infiltrate on chest roentgenogram), pulmonary embolism (high-probability ventilation/perfusion scan or diagnostic pulmonary angiogram), lobar atelectasis, and death |
| Bobbio 2009 | Lung | Mean age (SD): 66.7 (8.7) Sample size: 73 Female (%): 12 (16%) | Cycloergometer | Peak VO₂ (ml/kg/min) VE/VCO₂ | Pulmonary complication | Presence of pulmonary atelectasis requiring bronchoscopy, in the case of pneumonia (defined as a progressive radiological infiltrate with fever and/or leukocytosis) and in the case of respiratory failure |
| Bolliger 1995 | Lung | Mean age (SD): 62.8 (8.1) Sample size: 25 Female (%): 8 (32%) | Cycloergometer | Peak VO₂ (ml/kg/min) | Any complication | Acute retention (partial pressure of arterial >45 mm Hg); Prolonged mechanical ventilation (>48 h); Symptomatic cardiac arrhythmias necessitating treatment; Myocardial infarction; Pneumonia (temperature >38 °C, purulent sputum, and infiltrate on chest radiograph; Pulmonary embolism (high-probability ventilation/perfusion scan or diagnostic pulmonary angiogram); Lobar atelectasis (necessitating bronchoscopy); and Death |
| Brat 2016 | Lung | Mean age (SD): 65.0 (6.0) Sample size: 76 Female (%): 27 (35%) | Cycloergometer | Peak VO₂ (ml/kg/min) VE/VCO₂ | Pulmonary complications | Pneumonia (chest roentgenogram infiltrates and at least two other markers including fever or leukocytosis or leukopenia or purulent sputum production); Atelectasis (chest roentgenogram signs and bronchoscopy with plug removal); Respiratory failure requiring mechanical ventilation (noninvasive ventilation or tracheal intubation and invasive pulmonary ventilation); Adult respiratory distress syndrome (arterial partial pressure of O₂/fraction of inspired O₂ <300); Pneumothorax present on the third postoperative day, as confirmed by chest roentgenogram (changes or a new air-fluid level in case of pneumonectomy), thoracic ultrasound, or drain leak; tracheostomy. Long-lasting pleural effusions present on the third postoperative day, as confirmed by chest roentgenogram (rapid filling of the postpneumonectomy cavity with a shift toward the opposite side in case of pneumonectomy), thoracic ultrasound, or drainage of more than 200 mL/day |
| Author, year | Type of cancer | Characteristics | CPET assessment | CPET variables | Postoperative outcomes | Definition postoperative outcomes |
|-------------|----------------|-----------------|----------------|----------------|-----------------------|---------------------------------|
| Brunelli 2009 | Lung | Mean age (SD): 66.5 (9.6) Sample size: 204 Female (%): 35 (17%) | Cycloergometer | Peak VO<sub>2</sub> (ml/kg/min) AT (ml/kg/min) | Any complication Pulmonary complication | Any of the below defined complications Respiratory failure: Assisted mechanical ventilation for 48 h. Pneumonia: Infiltrates seen on chest. ARDS: Radiologic bilateral infiltrates. Pulmonary edema: Radiologic and clinical findings. Pulmonary embolism: Confirmed by perfusion scan/CT scan Cardiac complication Myocardial infarction: Suggestive ECG findings and increased myocardial enzymes; Arrhythmia: Hemodynamically unstable and requiring new treatment; Cardiac failure: Suggestive radiograph findings, physical examination findings, and symptoms; Acute renal insufficiency: Change in serum creatinine level 2 mg/dL compared with preoperative values; Stroke: Clinical findings/CT scan or MRI |
| Brunelli 2012 | Lung | Mean age (SD): 67.2 (9.8) Sample size: 225 Female (%): 42 (19%) | Cycloergometer | Peak VO<sub>2</sub> (ml/kg/min) V<sub>E</sub>/V<sub>CO<sub>2</sub></sub> | Mortality Pulmonary complication | Pneumonia (chest roentgenogram infiltrates/consolidation, leukocytosis, fever), atelectasis requiring bronchoscopy, respiratory failure needing mechanical ventilation for >48 hours, adult respiratory distress syndrome (defined according to the American-European consensus conference), pulmonary edema, or pulmonary embolism (confirmed by V/Q scan or computed tomography scan) In-hospital death |
| Brutsche 2000 | Lung | Mean age (SD): 63.0 (11.0) Sample size: 125 Female (%): 24 (19%) | Cycloergometer | Peak VO<sub>2</sub> (ml/kg/min) | Any complication | Acute carbon dioxide retention; Prolonged mechanical ventilation (>48 h); Treated symptomatic cardiac arrhythmia; Myocardial infarction; Pneumonia (temperature >38 °C and purulent sputum and infiltrate on radiography); Pulmonary embolism (high probability on ventilation perfusion scan or angio gram); Lobar atelectasis (necessitating bronchoscopy); Death |
| Dales 1993 | Lung | Mean age (SD): NR Sample size: 46 Female (%): NR | Treadmill | Peak VO<sub>2</sub> (mL) | Respiratory complications | Atelectasis prompting bronchoscopy; Pneumonia defined by a radiographic infiltrate plus at least two of the following: temperature >37.7 °C, white blood cell count > 10,500, initiation of antibiotics therapy, and demonstration of pathogenic organisms; air leak or effusion requiring intercostal tube drainage >7 days; bronchopleural fistula; empyema; chylothorax; hemothorax requiring drainage or reoperation; tension pneumothorax; pulmonary embolism; lobar gangrene; mechanical ventilation ≥72 h for any reason; intercostal tube drainage ≥14 days for any reason; and alveolar-arterial oxygen gradient ≥300 mm Hg 24 h postoperatively Any complication Included respiratory complication and cardiac complications (myocardial infarct defined by new-onset “Q” waves or elevated CK-MB fraction, arrhythmia requiring treatment, and congestive heart failure defined by bilateral crackles. |
| Author, year | Type of cancer | Characteristics | CPET assessment | CPET variables | Postoperative outcomes | Definition postoperative outcomes |
|-------------|----------------|----------------|----------------|----------------|-----------------------|----------------------------------|
| Epstein 1993 Lung | Mean age (SD): 62.6 (4.8) Sample size: 42 Female (%): 1 (2%) | Cycloergometer | Peak VO₂ (ml/kg/min) Peak VO₂ (mL/m²) Peak VO₂ (L) | Any complication | Myocardial infarction (positive ECG changes with elevated cardiac isoenzymes), unstable angina (appropriate clinical presentation with new ischemic ECG changes but normal isoenzyme levels), congestive heart failure (rales on physical examination with chest x-ray film showing pulmonary edema with pulmonary capillary wedge pressure, ≥18 mm Hg or clinical response to diuretics), arrhythmia requiring therapy, reintubation, or prolonged mechanical ventilation (≥48 h after surgery), pneumonia (temperature ≥38 °C for ≥48 h without an identifiable nonpulmonary source, plus purulent sputum and an infiltrate on the chest radiograph), lobar atelectasis requiring medical or bronchoscopic intervention, elevated [PaCO₂] (≥50 mm Hg or ≥10-mm Hg increase from baseline lasting for ≥48 h after surgery), pulmonary embolism (high probability perfusion scan or abnormal pulmonary arteriogram), and death. | radiographic changes, or elevated pulmonary artery wedge pressure and requiring therapy). Other complications were renal failure requiring dialysis, cerebrovascular accident, gastrointestinal bleeding, and wound infection. |
| Fang 2014 Lung | Mean age (SD): 67.3 (7.0) Sample size: 107 Female (%): 3 (2.8%) | Cycloergometer | Peak VO₂ (ml/kg/min) | Any complication | Not specified |
| Han 2007 Lung | Mean age (SD): 65.0 (11.0) Sample size: 467 Female (%): 184 (39%) | NR | Peak VO₂ (ml/kg/min) | Pulmonary complication | Atelectasis diagnosed by chest x-ray, pneumonia with sputum test, mechanical ventilation ≥24 h, reintubation, pulmonary embolism, ARDS, and pulmonary edema |
| Kasikcioglu 2009 Lung | Mean age (SD): 61.0 (9.0) Sample size: 49 Female (%): 5 (10%) | Treadmill | Peak VO₂ (ml/kg/min) | Any complication | Cardiopulmonary: prolonged mechanical ventilation (≥48 h); respiratory insufficiency; lobar atelectasis on radiography; myocardial infarction verified by rise in enzymes; cardiac arrhythmias requiring therapy; pneumonia; heart failure requiring therapy; death caused by respiratory insufficiency or heart failure. Furthermore, technical related complications were defined as empyema; wound infections; leak of the bronchus stump; bronchopleural fistula; blood loss requiring transfusion. |
| Licker 2011 Lung | Mean age (SD): 62.9 (10.7) Sample size: 210 Female (%): 65 (31%) | Cycloergometer | Peak VO₂ (ml/kg/min) | Any complication | Any of the below defined complications |

| Cardiovascular complication | Pulmonary complications |
|-----------------------------|-------------------------|
| Myocardial infarction, arrhythmias, congestive heart failure, stroke, thromboembolism, or renal dysfunction | Atelectasis, pneumonia, or acute lung injury |
| Author, year | Type of cancer | Characteristics | CPET assessment | CPET variables | Postoperative outcomes | Definition postoperative outcomes |
|-------------|---------------|----------------|----------------|----------------|------------------------|---------------------------------|
| Loewen 2007 | Lung          | Mean age (SD): NR | Cycloergometer | Peak VO2 (ml/kg/min) | Cardiovascular complication | Red blood cell transfusion; Postoperative fever; Wound infection; Empyema; Prolonged air leak; Atelectasis Pneumonia; Respiratory failure Dysrhythmia; Myocardial infarction; Deep vein thrombosis; Pulmonary embolism; Postoperative death |
| Mao 2010    | Lung          | Mean age (SD): 64.7 (11.5) | Cycloergometer | Peak VO2 (ml/kg/min) | Cardiopulmonary complication | Respiratory failure, pneumonitis/atelectasis, arrhythmia, supraventricular, ventricular, myocardial infarction, heart failure, severe shortness of breath, other complications including pulmonary artery embolism and gastrointestinal tract bleeding |
| Markos 1989 | Lung          | Mean age (SD): 64.0 (10.7) | Cycloergometer | Peak VO2 (ml/kg/min) | Any complication | Death, respiratory failure, pneumonia, lobar atelectasis, pulmonary embolism, myocardial infarction or ischemia, symptomatic arrhythmias requiring therapy, or admission to the intensive care unit, or coronary care unit |
| Miyazki 2018 | Lung          | Mean age (SD): 72.4 (8.3) | Cycloergometer | Peak VO2 (ml/kg/min) | Cardiopulmonary complication | Adult respiratory distress syndrome, pneumonia, pulmonary embolism, pulmonary edema, atelectasis requiring bronchoscopy, respiratory failure (>24 h mechanical ventilation or needing reintubation after surgery), arrhythmia requiring electrical or medical cardioversion, myocardial ischemia, cardiac failure, stroke, and acute renal failure |
| Morice 1992 | Lung          | Mean age (SD): 68 (3.8) | NR | Peak VO2 (ml/kg/min) | Cardiopulmonary complication | Mechanical ventilation(>48 h); myocardial infarction, as evidenced by EGG and elevation of cardiac enzyme levels; cardiac arrhythmias requiring short-term therapy; pneumonia, defined as fever for 48 h and an infiltrate evident on chest roentgenograms; roentgenographic evidence of atelectasis; angiographically documented pulmonary embolism; and death within 30 days after surgery |
| Nagamatsu 2004 / 2005 | Lung | Mean age (SD): 65.9 (8.4) | Cycloergometer | Peak VO2 (ml/kg/m²) AT (ml/kg/m²) | Cardiopulmonary complication | Need for tracheostomy; mechanical ventilation for at least 2 days; daily bronchoscopic lavage for at least 7 days; and the presence of arrhythmias requiring treatment for at least 3 days |
| Pate 1996 | Lung          | Mean age (SD): 63.6 (4.9) | Cycloergometer | Peak VO2 (ml/kg/min) | Any complication | Prolonged mechanical ventilation (>48 h), respiratory insufficiency (defined as ventilator dependence or incapacitating dyspnea as determined by survey), persistent air leak (>10 days), and pneumonia; Arhythmias, myocardial infarction, pulmonary embolism, hypotension, atelectasis, and death |
| Rodrigues 2016 | Lung | Mean age (SD): 64.7 (7.9) | Cycloergometer | Peak VO2 (ml/kg/min) | Pulmonary complication | Not specified |
| Torchio 2017 | Lung          | Mean age (SD): 65 (8) | Treadmill | Peak VO2 (ml/kg/min) | Minor/major complication | Major complication defined if >1 of the following were present: cardiac failure requiring inotropic support other than renal dose dopamine; hemodynamically unstable arrhythmia requiring treatment; pulmonary embolism diagnosed by high-
| Author, year | Type of cancer | Characteristics | CPET assessment | CPET variables | Postoperative outcomes | Definition postoperative outcomes |
|-------------|---------------|----------------|----------------|---------------|------------------------|----------------------------------|
| Villani & Busia 2004 | Lung | Mean age (SE): 57.1 (0.7) Sample size: 150 Female (%): 9 (6%) | Cycloergometer | Peak VO₂ (ml/ kg/min) | Any complication | Respiratory failure requiring oxygen supplementation, lobar atelectasis, cardiac arrhythmia requiring therapy, pneumonia, acute respiratory distress syndrome (ARDS), and pulmonary embolism |
| Win 2005 | Lung | Mean age (SD): 68.4 (8.0) Sample size: 99 Female (%): 38 (38%) | Treadmill | Peak VO₂ (ml/ kg/min) | Any complication | Postoperative death, myocardial infarction, heart failure, renal failure, respiratory failure, pulmonary embolism, sepsis, or pneumonia |
| Yakal 2018 | Lung | Mean age (SD): 63.0 (8.0) Sample size: 125 Female (%): 19 (15%) | Treadmill | Peak VO₂ (ml/ kg/min) AT (ml/kg/ min) Vₖ/V₇ₐ₅ | Any complication | Not specified |
| Begum 2016 | Lung | Mean age (SD): NR Sample size: 1684 Female (%): NR | NR | Peak VO₂ (ml/ kg/min) | Cardiopulmonary complication | Adult respiratory distress syndrome, pneumonia, pulmonary embolism, pulmonary edema, atelectasis requiring bronchoscopy, respiratory failure, arrhythmia requiring electrical or medical cardioversion, myocardial ischemia, cardiac failure, stroke, and acute renal failure |
| Huang 2016 | Mixed | Mean age (SD): 67.7 (9.6) Sample size: 26 Female (%): 4 (15%) | Cycloergometer | Peak VO₂ (ml/ kg/min) | Mortality Minor/major complication | Death within 30 days from surgery Clavien-Dindo classification (>3 major complication) |
| Moyes 2013 Drummond 2018 | Mixed | Mean age (SD): 66.0 (9.0) Sample size: 108 Female (%): 25 (23%) | Cycloergometer | Peak VO₂ (ml/ kg/min) AT (ml/kg/ min) | Cardiopulmonary complication | Common terminology criteria for adverse events |
| Snowden 2013 | Mixed | Mean age (SD): 65.8 (10.3) Sample size: 389 Female (%): 171 (44%) | Cycloergometer | Peak VO₂ (ml/ kg/min) AT (ml/kg/ min) Vₖ/V₇ₐ₅ | Mortality | In-hospital death |
| Whibley 2018 | Mixed | Mean age (SD): 64.9 (9.5) Sample size: 81 Female (%): NR | NR | Peak VO₂ (ml/ kg/min) AT (ml/kg/ min) | Respiratory complication | Not specified |
preoperative $V_\text{E}/V_{\text{CO}_2}$ values were observed for patients with or without postoperative complication (MD: 0.80; 95% CI: −0.95 to 2.54) and minor or major postoperative complication (MD: 0.93; 95% CI: −1.53 to 3.38) (Fig. 4). Other studies were not pooled in the meta-analysis due to heterogeneity and reported mixed results (Tables 3 and 4).

**Association between Preoperative CPET Values and Length of Hospital Stay**

The association between preoperative Peak VO$_2$ (7 studies), AT (8 studies), and $V_\text{E}/V_{\text{CO}_2}$ (3 studies) and length of hospital stay is presented in Table 5. Results of individual studies provided mixed results. Some studies reported a positive association between CPET variables and length of hospital stay (i.e., patients presenting higher CPET values stayed shorter in hospital), and others reported no statistical differences. However, none of the
### TABLE 2
Risk of bias assessment using the Quality in Prognosis Studies (QUIPS) tool

| Author, year                     | Study participation | Study attrition | Outcome measurement | Statistical analysis and reporting |
|----------------------------------|---------------------|-----------------|---------------------|-----------------------------------|
| Lamb 2016                        | Low                 | Low             | Low                 | Moderate                          |
| Prentis 2013                     | Moderate            | Low             | Low                 | Low                               |
| Tolchard 2015                    | Moderate            | Low             | Low                 | Low                               |
| Bowles 2008                      | Moderate            | Low             | Low                 | Low                               |
| Chan 2016                        | Low                 | Low             | Low                 | Moderate                          |
| Mann 2020                        | Low                 | Low             | Low                 | Low                               |
| McSorley 2018/Stephen 2018       | Moderate            | Low             | Moderate            | Moderate                          |
| Nikolopoulos 2015                | Moderate            | Low             | Low                 | Low                               |
| Forshaw 2008                     | Low                 | Low             | Low                 | Low                               |
| Lam 2019                         | Low                 | Low             | Low                 | Low                               |
| Nagamatsu 2001/Nagamatsu 1994    | Low                 | Low             | Low                 | Low                               |
| Patel 2019                       | Low                 | Low             | Low                 | Moderate                          |
| Sinclair 2017                    | Low                 | Low             | Low                 | Low                               |
| Dunne 2014                       | Moderate            | High            | Low                 | Low                               |
| Kasivisvanathan 2015             | Low                 | Moderate        | Low                 | Low                               |
| Ulyett 2017                      | Low                 | Moderate        | Low                 | Low                               |
| Bayram 2007                      | Low                 | Low             | Low                 | Low                               |
| Bechard & Wetstein 1987          | Moderate            | Low             | Low                 | Low                               |
| Bobbio 2009                      | Moderate            | Low             | Low                 | Low                               |
| Bolliger 1995/ Bolliger 1996     | Low                 | Low             | Low                 | Low                               |
| Brat 2016                        | Low                 | Low             | Low                 | Low                               |
| Brunelli 2009                    | Moderate            | Low             | Low                 | Low                               |
| Brunelli 2012                    | Low                 | Low             | Low                 | Low                               |
| Brutsche 2000                    | Low                 | Low             | Low                 | Low                               |
| Dales 1993                       | Moderate            | Low             | Low                 | Low                               |
| Epstein 1993                     | Low                 | Low             | Low                 | Low                               |
| Fang 2014                        | Moderate            | Low             | Moderate            | Low                               |
| Han 2007                         | Low                 | Low             | Low                 | Low                               |
| Kasikcioglu 2009                 | Moderate            | Low             | Low                 | Low                               |
| Licker 2011                      | Moderate            | Low             | Low                 | Low                               |
| Loewen 2007                      | Low                 | Low             | Low                 | Low                               |
| Mao 2010                         | Moderate            | Low             | Low                 | Low                               |
| Markos 1989                      | Low                 | Low             | Low                 | Low                               |
| Miyazki 2018                     | Moderate            | Moderate        | Low                 | Low                               |
| Morice 1992                      | Moderate            | Low             | Low                 | Low                               |
| Nagamatsu 2004/Nagamatsu 2005    | Moderate            | Low             | Low                 | Low                               |
| Pate 1996                        | Low                 | Low             | Low                 | Low                               |
| Rodrigues 2016                   | Moderate            | Low             | Moderate            | Low                               |
| Torchio 2010/Torchio 2017        | Low                 | Low             | Low                 | Low                               |
| Villani & Busia 2004             | Low                 | Low             | Low                 | Low                               |
| Win 2005                         | Low                 | Low             | Low                 | Low                               |
| Yakal 2018                       | Moderate            | Low             | Moderate            | Low                               |
| Begum 2016                       | Low                 | Low             | Low                 | Low                               |
| Huang 2016                       | Low                 | Low             | Low                 | Low                               |
| Moyes 2013 Drummond 2018         | Moderate            | Low             | Low                 | Low                               |
| Snowden 2013                     | Moderate            | Low             | Low                 | Low                               |
| Whibley 2018                     | Moderate            | Low             | Moderate            | Moderate                          |
| Wilson 2010                      | Moderate            | Low             | Low                 | Moderate                          |
studies reported a significant negative association (i.e., patients presenting lower CPET values stayed for shorter periods in hospital) (Table 5).

**Association between Preoperative CPET Values and Postoperative Quality of Life**

Currently, no study has investigated the association between preoperative CPET values and postoperative quality of life outcomes in patients undergoing cancer surgery.

**DISCUSSION**

**Statement of Principal Findings**

This systematic review identified many studies investigating the potential association between preoperative CPET values and postoperative complications and length of hospital stay. Our meta-analysis demonstrated that higher preoperative Peak VO\textsubscript{2}, AT, and lower V\textsubscript{E}/V\textsubscript{CO2} values were predominately significantly associated with absence of postoperative complications. Several individual studies were not included in the meta-analysis due to heterogeneity in the CPET values and outcomes or did not report appropriate values to be pooled. While the results of individual studies provided mixed results, it is important to note that none reported a negative association (i.e., superior preoperative CPET values associated with worst postoperative outcome). Similarly, the association between preoperative CPET values and length of hospital stay reported in individual studies provided mixed results; none reported a negative association. Interestingly, this review was not able to identify any study investigating the association between preoperative CPET values and postoperative quality of life outcomes.

**Strengths and Weaknesses of the Study**

The strengths of this systematic review and meta-analyses were the methodology employed, following recommendation from the Cochrane Prognosis Review Group, and were reported according to the MOOSE framework. In addition, we conducted a sensitive search on major medical databases, that was supported by a senior librarian. Our search was only limited by human subjects and included all the literature irrespective of language and publication year. Furthermore, we assessed risk of bias using a well established tool (QUIPS).

The limitation of our systematic review included the heterogeneity between the included studies. For many included studies, meta-analysis was not possible as the CPET variables and outcome measures were not standardised and prevented pooling of the data. Also, due to the population of interest (patients undergoing cancer surgery), peak VO\textsubscript{2} and VO\textsubscript{2} max were used in this review interchangeably. Because these patients are older and debilitated by their conditions, it is difficult to demonstrate that the plateau criterion for VO\textsubscript{2} max has been met in response to exercise. Furthermore, none of the included studies investigated the association between preoperative CPET and postoperative quality of life, underpinning the lack of evidence for this important patient reported outcome. Lastly, while we included a large number of full-text manuscripts published in scientific journals, we excluded studies that were published as abstracts of conference proceedings.

**Comparison with Other Studies**

The association between preoperative CPET variables and postoperative complications and/or length of hospital stay has been investigated in previous systematic reviews, reporting mixed results. While there are few systematic reviews indicating a positive association between superior preoperative CPET values and absence of postoperative complications, others reported no significant association. This is somewhat in line with the results of the current review. Our meta-analysis showed that superior preoperative CPET values are significantly associated with the absence of most postoperative complications. However, results from studies that were not included in our meta-analysis are somewhat less favorable.

Despite this, there are some differences between the current and previous systematic reviews that are important to note. Previous systematic reviews included a smaller
number of studies (ranging from 7–37), investigated postoperative complications as the main outcome measure, and included either a specific cancer population undergoing surgery (e.g., lung, esophageal), or mixed populations undergoing surgery for cancer and/or noncancer related conditions.5,7–11 Meta-analysis was attempted in only half of the previous published systematic reviews. Therefore, the mixed results encountered between the current review and previous reviews may be because the inclusion and exclusion criterion were different. The heterogeneity of the included cohorts, including the lack of consistency in reporting or standardisation of outcomes were highlighted.

| Author, year | Type of cancer | Mean difference (95% CI) | Mean difference (95% CI) | Weight (%) |
|--------------|----------------|--------------------------|--------------------------|------------|
| No complication vs Complication | | | | |
| Bolliger, 1995 | Lung | 3.40 (0.44 to 6.36) | 5.04 |
| Brunelli, 2009 | Lung | 1.15 (-0.10 to 2.40) | 7.79 |
| Brutsche, 2000 | Lung | 4.20 (2.01 to 6.39) | 6.25 |
| Epstein, 1993 | Lung | 0.30 (-2.80 to 3.40) | 4.83 |
| Fang, 2014 | Lung | 3.50 (1.51 to 5.49) | 6.60 |
| Licker, 2011 | Lung | 3.90 (2.25 to 5.55) | 7.17 |
| Kasikieoglou, 2009 | Lung | 3.70 (1.58 to 5.82) | 6.37 |
| Lam, 2019 | Bladder | -0.40 (-1.63 to 0.83) | 7.83 |
| Prentis, 2013 | Rectal | 0.10 (-2.04 to 2.24) | 6.33 |
| Pat, 1996 | Lung | -0.43 (-3.12 to 2.28) | 5.44 |
| West, 2014 | Rectal | 6.00 (3.98 to 8.02) | 6.55 |
| Win, 2005 | Lung | 1.70 (-0.36 to 3.78) | 6.47 |
| Yakal, 2018 | Lung | 1.14 (0.34 to 2.62) | 7.45 |
| Bechand and Welstein, 1987 | Lung | 7.06 (3.53 to 10.59) | 4.26 |
| Villani and Bussia, 2004 | Lung | 1.60 (0.29 to 2.91) | 7.70 |
| Markos, 1989 | Lung | 0.70 (-3.14 to 4.54) | 3.89 |
| Pooled effect (I²=9%) | | 2.28 (1.26 to 3.29) |  |

| No pulmonary complication vs Pulmonary complication | | | | |
| Bayram, 2007 | Lung | 1.90 (0.41 to 3.39) | 18.77 |
| Bobbio, 2009 | Lung | 3.30 (1.03 to 5.57) | 11.96 |
| Brat, 2016 | Lung | 7.20 (-2.86 to 17.26) | 0.92 |
| Brunelli, 2009 | Lung | 2.80 (0.24 to 5.36) | 10.19 |
| Licker, 2011 | Lung | 1.20 (-1.23 to 3.63) | 10.91 |
| Brunelli, 2012 | Lung | 0.50 (-1.06 to 2.08) | 17.99 |
| Han, 2007 | Lung | -0.10 (-1.39 to 1.19) | 21.00 |
| Morice, 1992 | Lung | 2.00 (-0.96 to 4.98) | 8.25 |
| Pooled effect (I²=0%) | | 1.47 (0.49 to 2.45) |  |

| No cardiopulmonary complication vs Cardiopulmonary complication | | | | |
| Forshaw, 2008 | Esophageal | -0.90 (-2.15 to 0.35) | 30.65 |
| Lam, 2019 | Esophageal | 2.20 (-0.01 to 4.41) | 21.22 |
| Moyes, 2013 | Mixed | 2.00 (-0.28 to 4.28) | 20.62 |
| Rodrigues, 2016 | Lung | 0.85 (-0.71 to 2.41) | 27.51 |
| Pooled effect (I²=0%) | | 0.84 (-0.63 to 2.35) |  |

| Minor complication vs Major complication | | | | |
| Tolchand, 2015 | Bladder | 1.85 (0.70 to 3.00) | 29.29 |
| Terchio, 2017 | Lung | 1.80 (0.73 to 2.87) | 30.60 |
| Chan, 2016 | Colorectal | 3.53 (0.84 to 6.22) | 12.23 |
| Patel, 2019 | Esophageal | 4.16 (1.61 to 6.71) | 13.16 |
| Ulyett, 2017 | Liver | -0.40 (-2.75 to 1.95) | 14.72 |
| Pooled effect (I²=27%) | | 2.01 (0.90 to 3.13) |  |

| No cardiovascular complication vs Cardiovascular complication | | | | |
| Licker, 2011 | Lung | 3.50 (1.29 to 5.71) | 37.26 |
| Loewen, 2007 | Lung | 1.47 (0.55 to 2.39) | 62.74 |
| Pooled effect (I²=0%) | | 2.23 (0.30 to 4.15) |  |

| No mortality vs Mortality (In-hospital) | | | | |
| Brunelli, 2009 | Lung | 3.70 (0.63 to 6.77) | 28.91 |
| Snowden, 2013 | Mixed | 2.40 (0.44 to 4.36) | 71.09 |
| Pooled effect (I²=0%) | | 2.78 (1.12 to 4.43) |  |

**FIG. 2** Forest plot of the association between preoperative peak oxygen uptake (peak VO₂) in ml/kg/min and postoperative complication. Mean difference > 0 indicate higher preoperative peak VO₂ in patients with no postoperative complications. CI=Confidence level.
TABLE 3 Association between preoperative cardiopulmonary exercise test variables and postoperative complication

| Author, year | Cancer type (N) | Preoperative CPET threshold | Postoperative complication | Estimates, odds ratio (95% confidence intervals) | Summary |
|--------------|----------------|-----------------------------|---------------------------|--------------------------------------------------|---------|
|              |                | Favorable                   | Unfavorable               | Favorable outcome | Unfavorable outcome |               |
| Licker 2011  | Lung (215)     | Peak VO₂ ≥17 (mL/Kg/min)    | Peak VO₂ <17 (mL/Kg/min)  | No complication | Complication        | 0.35 (0.17–0.73) |
| West 2014    | Rectal (95)    | Peak VO₂ ≥10.6 (mL/Kg/min)  | Peak VO₂ <10.6 (mL/Kg/min)| No complication | Complication        | 0.02 (0.01–0.10) |
| Bayram 2007  | Lung (55)      | Peak VO₂ >15 (mL/Kg/min)    | Peak VO₂ <15 (mL/Kg/min)  | No complication | Complication        | 0.47 (0.15–1.46) |
| Epstein 1993 | Lung (42)      | Peak VO₂ >15 (mL/Kg/min)    | Peak VO₂ <15 (mL/Kg/min)  | No complication | Complication        | 0.42 (0.11–1.55) |
| Licker 2011  | Lung (215)     | Peak VO₂ ≥17 (mL/Kg/min)    | Peak VO₂ <17 (mL/Kg/min)  | No complication | Complication        | 0.35 (0.17–0.73) |
| McSorley 2018| Colorectal (38)| Peak VO₂ ≥19 (mL/Kg/min)    | Peak VO₂ <19 (mL/Kg/min)  | No complication | Complication        | 0.94 (0.24–3.71) |
| Dales 1993   | Lung (46)      | Peak VO₂ ≥1250 (ml)         | Peak VO₂ <1250 (ml)       | No complication | Complication        | 0.27 (0.08–0.93) |
| Epstein 1993 | Lung (42)      | Peak VO₂ <1 (L)             | Peak VO₂ ≥1 (L)           | No complication | Complication        | 0.33 (0.09–1.29) |
| Epstein 1993 | Lung (42)      | Peak VO₂ ≥500 (ml/m²)       | Peak VO₂ ≤500 (ml/m²)     | No complication | Complication        | 0.17 (0.04–0.74) |
| Chan 2016    | Colorectal (48)| Peak VO₂ (mL/Kg/min)        |                           | No complication | Complication        | NR            |
| Dunne 2014   | Liver (197)    | Peak VO₂ (mL/Kg/min)        |                           | No complication | Complication        | 1.02 (0.96–1.09) |
| Junejo 2014  | Pancreas (64)  | Peak VO₂ (mL/Kg/min)        |                           | No complication | Complication        | 1.00 (0.86–1.18) |
| Sinclair 2017| Esophagus (240)| Peak VO₂ (ml)               |                           | No complication | Complication        | 1.00 (1.00–1.00) |
| Kasivisvanathan 2015 | Liver (104) | Peak VO₂ (mL/Kg/min) | No complication | Complication | 1.03 (1.01–1.06) |
| Nagamatsu 2001/Nagamatsu 1994 | Esophagus (91) | Peak VO₂ ≥1000 (ml/min/m²) | Peak VO₂ <1000 (ml/min/m²) | No cardiopulmonary complication | Cardiopulmonary complication | 0.22 (0.05–1.03) |
| Miyazaki 2018| Lung (209)     | Peak VO₂ ≥12 (mL/Kg/min)    | Peak VO₂ <12 (mL/Kg/min)  | No cardiopulmonary complication | Cardiopulmonary complication | 0.62 (0.24–1.59) |
| Bayram 2007  | Lung (55)      | Peak VO₂ ≥15 (mL/Kg/min)    | Peak VO₂ <15 (mL/Kg/min)  | No cardiopulmonary complication | Cardiopulmonary complication | 0.07 (0.01–0.35) |
| Author, year | Cancer type (N) | Preoperative CPET threshold | Postoperative complication | Estimates, odds ratio (95% confidence intervals) | Summary |
|-------------|----------------|----------------------------|---------------------------|-----------------------------------------------|---------|
| Mao 2010    | Lung (198)     | Peak VO$_2$ >15 (mL/Kg/min) | No cardiopulmonary complication | Cardiopulmonary complication | 0.23 (0.08–0.62) | ✔️ |
| Miyazaki 2018 | Lung (209)     | Peak VO$_2$ >15 (mL/Kg/min) | No cardiopulmonary complication | Cardiopulmonary complication | 0.88 (0.49–1.60) | ❌ |
| Begum 2016  | Lung (1684)    | Peak VO$_2$ >20 (mL/Kg/min) | No cardiopulmonary complication | Cardiopulmonary complication | 0.56 (0.29–1.09) | ✔️ |
| Mao 2010    | Lung (198)     | Peak VO$_2$ >15 (mL/Kg/min) | No cardiopulmonary complication | Cardiopulmonary complication | 0.23 (0.08–0.62) | ✔️ |
| Junejo 2014 | Pancreas (64)  | Peak VO$_2$ (mL/Kg/min)     | No cardiopulmonary complication | Cardiopulmonary complication | 1.00 (0.86–1.17) | ✔️ |
| Sinclair 2017 | Esophagus (240) | Peak VO$_2$ (mL)           | No cardiopulmonary complication | Cardiopulmonary complication | 0.99 (0.99–1.00) | ✔️ |
| West 2014   | Rectal (95)    | Peak VO$_2$ >10.6 (mL/Kg/min) | No pulmonary complication | Pulmonary complication | 0.09 (0.02–0.46) | ✔️ |
| Bayram 2007 | Lung (55)      | Peak VO$_2$ >15 (mL/Kg/min) | No pulmonary complication | Pulmonary complication | 0.03 (0.00–0.53) | ✔️ |
| Licker 2011 | Lung (215)     | Peak VO$_2$ >10 (mL/Kg/min) | No cardiovascular complication | Cardiovascular complication | 0.25 (0.10–0.63) | ✔️ |
| West 2014   | Rectal (95)    | Peak VO$_2$ >10.6 (mL/Kg/min) | No cardiovascular complication | Cardiovascular complication | 0.17 (0.03–0.87) | ✔️ |
| Licker 2011 | Lung (215)     | Peak VO$_2$ >17 (mL/Kg/min) | No cardiovascular complication | Cardiovascular complication | 0.42 (0.16–1.09) | ✔️ |
| Dales 1993  | Lung (46)      | Peak VO$_2$ >1250 (mL/Kg/min) | No respiratory complication | Respiratory complication | 0.24 (0.06–0.88) | ✔️ |
| Licker 2011 | Lung (215)     | Peak VO$_2$ >10 (mL/Kg/min) | No respiratory complication | Respiratory complication | 0.28 (0.12–0.68) | ✔️ |
| Whibley 2018 | Mixed (81)     | Peak VO$_2$ >14 (mL/Kg/min) | No respiratory complication | Respiratory complication | NR | ✔️ |
| Bayram 2007 | Lung (55)      | Peak VO$_2$ >15 (mL/Kg/min) | No respiratory complication | Respiratory complication | 0.51 (0.02–15.84) | ✔️ |
| Licker 2011 | Lung (215)     | Peak VO$_2$ >17 (mL/Kg/min) | No respiratory complication | Respiratory complication | 0.40 (0.16–0.95) | ✔️ |
| Bayram 2007 | Lung (55)      | Peak VO$_2$ >15 (mL/Kg/min) | No mortality (30 days) | Mortality (30 days) | 0.20 (0.01–5.7) | ✔️ |
| Author, year | Cancer type (N) | Preoperative CPET threshold | Postoperative complication | Estimates, odds ratio (95% confidence intervals) | Summary |
|--------------|----------------|----------------------------|---------------------------|-----------------------------------------------|---------|
| Begum 2016   | Lung (1684)    | Peak VO2 >15 (mL/Kg/min)    | No mortality (30 days)    | Mortality (30 days) 0.60 (0.35–0.93)           |         |
| Junejo 2014  | Pancreatic (64) | Peak VO2 (mL/Kg/min)        | No mortality (30 days)    | Mortality (30 days) 1.03 (0.77–1.37)           |         |
| Junejo 2014  | Pancreatic (64) | Peak VO2 (mL/Kg/min)        | No mortality (in-hospital)| Mortality (in-hospital) 1.32 (0.91–1.93)       |         |
| West 2014    | Rectal (46)    | Peak VO2 ≥10.6 (mL/Kg/min)  | Minor complication        | Major complication 0.60 (0.13–2.49)            |         |
| McSorley 2018| Colorectal (38)| Peak VO2 >19 (mL/Kg/min)    | Minor complication        | Major complication 1.00 (0.08–11.67)           |         |
| Dunne 2014   | Liver (194)    | Peak VO2 (mL/Kg/min)        | Minor complication        | Major complication 1.04 (0.97–1.11)            |         |
| Huang 2016   | Mixed (26)     | Peak VO2 (mL/Kg/min)        | Minor complication        | Major complication 0.72 (0.17–2.21)            |         |
| West 2014    | Rectal (95)    | Peak VO2 ≥10.6 (mL/Kg/min)  | No infection              | Infection 0.10 (0.03–0.26)                     |         |
| West 2014    | Rectal (95)    | Peak VO2 ≥10.6 (mL/Kg/min)  | No wound dehiscence       | Wound dehiscence 0.10 (0.00–1.16)              |         |
| West 2014    | Rectal (95)    | Peak VO2 ≥10.6 (mL/Kg/min)  | No renal complication     | Renal complication 0.20 (0.04–1.07)            |         |
| West 2014    | Rectal (95)    | Peak VO2 ≥10.6 (mL/Kg/min)  | No gastrointestinal       | Gastrointestinal complication 0.30 (0.09–0.80)|         |
| West 2014    | Rectal (95)    | Peak VO2 ≥10.6 (mL/Kg/min)  | No neurological            | Neurological complication 0.70 (0.01–35.72)    |         |
| West 2014    | Rectal (95)    | Peak VO2 ≥10.6 (mL/Kg/min)  | No hematological           | Hematological complication 0.70 (0.13–3.56)   |         |
| West 2014    | Rectal (95)    | Peak VO2 ≥10.6 (mL/Kg/min)  | No pain                   | Pain 2.9 (0.31–27.21)                         |         |
| Bayram 2007  | Lung (55)      | Peak VO2 >15 (mL/Kg/min)    | No Pneumonia              | Pneumonia 0.20 (0.01–3.30)                     |         |
| Bayram 2007  | Lung (55)      | Peak VO2 >15 (mL/Kg/min)    | No atelectasis             | Atelectasis 0.10 (0.0–1.31)                    |         |
| Bayram 2007  | Lung (55)      | Peak VO2 >15 (mL/Kg/min)    | No bronchopleural fistula | Bronchopleural fistula 0.20 (0.01–5.70)       |         |
| Author, year (N) | Cancer type | Preoperative CPET threshold | Postoperative complication | Estimates, odds ratio (95% confidence intervals) | Summary |
|-----------------|-------------|-----------------------------|---------------------------|------------------------------------------------|---------|
| Bayram 2007 Lung (55) | Peak VO$_2$ >15 (mL/Kg/min) | Peak VO$_2$ <15 (mL/Kg/min) | No prolonged air leak | Prolonged air leak | 0.50 (0.15–1.46) |
| Bayram 2007 Lung (55) | Peak VO$_2$ >15 (mL/Kg/min) | Peak VO$_2$ <15 (mL/Kg/min) | No arrhythmia | Arrhythmia | 2.2 (0.18–25.32) |
| Ausania 2012 Pancreas (124) | AT $\geq$10.1 (mL/Kg/min) | AT $<10.1$ (mL/Kg/min) | No complication | Complication | 0.27 (0.10–0.75) |
| Chan 2016 Colorectal (48) | AT (mL/Kg/min) | No complication | Complication | NR |
| Junejo 2014 Pancreas (64) | AT (mL/Kg/min) | No complication | Complication | 1.07 (0.83–1.39) |
| Sinclair 2017 Esophagus (240) | AT (mL/Kg/min) | No complication | Complication | 0.95 (0.90–1.01) |
| Chandrabalan 2013 Pancreatic (100) | AT $\geq$10 (mL/Kg/min) | AT $<10$ (mL/Kg/min) | No mortality (30 days) | Mortality (30 days) | 1.30 (0.28–6.16) |
| Wilson 2010 Mixed (847) | AT $>$10.9 (mL/kg/min) | AT $\leq$10.9 (mL/kg/min) | No mortality (90 days) | Mortality (90 days) | 0.14 (0.03–0.62) |
| Bowles 2008 Colorectal (121) | AT $\geq$11 (mL/kg/min) | AT $\leq$11 (mL/kg/min) | No mortality (NR) | Mortality (NR) | 2.56 (0.29–22.73) |
| Junejo 2014 Pancreas (64) | AT (mL/Kg/min) | No mortality (in–hospital) | Mortality (in–hospital) | 0.90 (0.52–1.53) |
| Ausania 2012 Pancreas (124) | AT $\geq$10.1 (mL/Kg/min) | AT $<10.1$ (mL/Kg/min) | No mortality (in–hospital) | Mortality (in–hospital) | 0.76 (0.08–7.18) |
| Junejo 2014 Pancreas (64) | AT (mL/Kg/min) | No mortality (30 days) | Mortality (30 days) | 1.23 (0.72–2.11) |
| Mann 2020 Colorectal (1205) | AT $\geq$11 (mL/Kg/min) | AT $<$11 (mL/Kg/min) | No mortality (30 days) | Mortality (30 days) | 0.70 (0.32–1.51) |
| Moyes 2013 Mixed (103) | AT $\geq$9 (mL/Kg/min) | AT $<9$ (mL/Kg/min) | No cardiopulmonary complication | Cardiopulmonary complication | 0.40 (0.16–1.07) |
| Moyes 2013 Mixed (103) | AT $\geq$11 (mL/Kg/min) | AT $<$11 (mL/Kg/min) | No cardiopulmonary complication | Cardiopulmonary complication | 0.50 (0.18–1.12) |
| Forshaw 2008 Esophagus (75) | AT $\geq$11 (mL/Kg/min) | AT $<$11 (mL/Kg/min) | No cardiopulmonary complication | Cardiopulmonary complication | 0.40 (0.12–1.44) |
| Sinclair 2017 Esophagus (240) | AT (mL/Kg/min) | No cardiopulmonary complication | Cardiopulmonary complication | 0.89 (0.84–0.95) |
| Author, year | Cancer type (N) | Preoperative CPET threshold | Postoperative complication | Estimates, odds ratio (95% confidence intervals) | Summary |
|--------------|----------------|-----------------------------|---------------------------|------------------------------------------------|---------|
| Junejo 2014  | Pancreas (64)  | AT (mL/Kg/min)              | No cardiopulmonary        | 1.05 (0.82–1.34)                                |         |
|              |                | AT >11 (mL/Kg/min)          | Noncardiopulmonary        | 1.60 (0.31–7.94)                                |         |
| Lamb 2016    | Bladder (82)   | AT ≥11 (NR)                 | Minor complication (CD <3) | 1.10 (0.30–3.85)                                |         |
| Bowles 2008  | Colorectal (121)| AT ≥11 (NR)               | Minor complication (CD <3) | 1.45 (0.55–3.79)                                |         |
| Lamb 2016    | Bladder (82)   | AT ≥11 (NR)                 | Minor complication (CD <3) | 0.30 (0.04–2.46)                                |         |
| Chandrabalan | Pancreas (100)| AT ≥10 (mL/Kg/min)         | Minor cardiac complications (CD <3) | 0.50 (0.02–14.5)                                |         |
| Chandrabalan | Pancreas (100)| AT >10 (mL/Kg/min)         | Major cardiac complications (CD 3–5) | 0.70 (0.15–3.32)                                |         |
| Chandrabalan | Pancreas (100)| AT ≥10 (mL/Kg/min)         | Minor respiratory         | 0.30 (0.09–1.00)                                |         |
| Chandrabalan | Pancreas (98)  | AT ≥10 (mL/Kg/min)         | Major intra-abdominal      | 0.30 (0.13–0.91)                                |         |
| Chandrabalan | Pancreas (100)| AT ≥10 (mL/Kg/min)         | No hemorrhage             | 1.70 (0.58–5.25)                                |         |
| Ausania 2012 | Pancreas (124)| AT ≥10.1 (mL/Kg/min)       | No cardiorespiratory       | 0.30 (0.08–1.52)                                |         |
| Whibley 2018 | Mixed (81)     | AT ≥11 (NR)                | No respiratory            | Respiratory complications NR                    |         |
| Forshaw 2008 | Esophagus (75)| AT >11 (mL/Kg/min)         | Unplanned ITU admission   | 0.60 (0.13–2.46)                                |         |
| Junejo 2014  | Pancreas (64)  | Ve/VCO2                    | No complication            | 0.97 (0.89–1.07)                                |         |
| Dunne 2014   | Liver (194)    | Ve/VCO2                    | No complication            | 0.98 (0.93–1.04)                                |         |
| Sinclair 2017| Esophagus (240)| Ve/VCO2                   | No complication            | 0.90 (0.84–0.96)                                |         |
| Junejo 2014  | Pancreas (64)  | Ve/VCO2                    | No mortality (in-hospital) | 0.79 (0.66–0.95)                                |         |
| Wilson 2010  | Mixed (847)    | Ve/VCO2 <34                | No mortality (in-hospital) | 0.20 (0.06–0.74)                                |         |
Meaning of the Study

Despite the advances in the medical field and surgical approaches, postoperative complications following cancer surgery remain high, increasing the length of hospital stay and subsequently hospital costs. Therefore, identifying preoperative factors that accurately predict adverse postoperative outcomes would be of great benefit to inform potential optimization strategies, improve the processes of shared decision making, and informed consent in patients presenting for major cancer surgery. In a mixed group of cancer patients undergoing surgery, our systematic review and meta-analysis found that superior CPET values were associated with improved postoperative outcomes. Furthermore, results for individual studies, not included in the meta-analysis, also provided some positive trends. These also trends have been reported in other systematic reviews.5,7,8 Therefore, the assessment of functional capacity in the preoperative period should be used in conjunction with other clinical assessments to support clinicians, patients, and payers on optimization strategies and treatment decision making. This has the potential to provide the best possible outcome for patients and reduce the economic burden.

Unanswered Questions and Future Research

One of the goals of this study was to explore the association between preoperative CPET values and postoperative quality of life outcomes. Unfortunately, none of the included literature assessed this potential association. Future prospective cohort studies should include quality of life as one of the postoperative outcomes of interest. Our review not only focused on continuous measures of preoperative CPET, but also extracted dichotomous outcomes, or potential CPET cutoff points. This information was...
presented descriptively as the included studies presented a wide range of heterogeneity, especially using different cutoff points. Larger, prospective, cohort studies or perhaps a systematic review of individual patient data, should explore this further. Whenever possible, a subgroup analysis, involving specific groups of patients should be explored, to test whether different cutoff points for different patient cohorts provide more accurate predictive models. Future studies should attempt to use standardized CPET protocols and standardized definitions for postoperative outcomes.\textsuperscript{71} This would allow future systematic reviewers to pool data from a larger number of studies. Finally, future clinical trials should investigate the most effective exercise regime to increase preoperative physical fitness. The measurement of peak VO\textsubscript{2} and AT before and after the preoperative exercise regime would facilitate the investigation of this effect.

### TABLE 4 Association between preoperative cardiopulmonary exercise test variables and postoperative complications

| Author year | Cancer type (N) | CPET variable | Outcome | Postoperative complication | Estimates | Summary |
|-------------|----------------|---------------|---------|----------------------------|-----------|---------|
|             |                |               |         | Absent | Present |                   |
| Lamb 2016   | Bladder (82)   | Peak VO\textsubscript{2} (ml/kg/min) | Major complication (CD 3–5) | Median: 17.00  | Median: 15.00  | NR      |
| Forshaw 2008| Esophageal (78) | Peak VO\textsubscript{2} (ml/kg/min) | Unplanned ICU admission | Mean (SD): 20.80 (5.00) | Mean (SD): 18.90 (5.10) | Mean difference (95%CI): 1.90 (–1.10 to 4.90) |
| Brunelli 2009| Lung (204)      | Peak VO\textsubscript{2} (ml/kg/min) | Cardiac complication | Mean (SD): 16.00 (3.80) | Mean (SD): 15.00 (3.70) | Mean difference (95%CI): 1.00 (–0.50 to 2.50) |
| Bechard and Wetstein 1987 | Lung (29) | AT (L/Min) | Any complication | Mean (SD): 0.93 (0.20) | Mean (SD): 0.61 (0.10) | Mean difference (95%CI): 0.32 (0.10 to 0.60) |
| Lamb 2016   | Bladder (82)   | AT (ml/kg/min) | Major complication (CD 3–5) | Median: 10.00  | Median: 11.00  | NR      |
| Brunelli 2009| Lung (204)      | AT (ml/kg/min) | Pulmonary complication | Mean (SD): 10.10 (3.80) | Mean (SD): 9.20 (1.90) | Mean difference (95%CI): 0.90 (–0.50 to 2.30) |
| Brunelli 2009| Lung (204)      | AT (ml/kg/min) | Cardiac complication | Mean (SD): 10.00 (3.80) | Mean (SD): 9.90 (1.60) | Mean difference (95%CI): 0.10 (–1.40 to 1.60) |
| Forshaw 2008| Esophageal (78) | AT (ml/kg/min) | Unplanned ICU admission | Mean (SD): 14.20 (2.80) | Mean (SD): 12.60 (3.20) | Mean difference (95%CI): 1.60 (–0.10 to 3.30) |
| Lamb 2016   | Bladder (45)    | V\textsubscript{E}/V\textsubscript{CO2} | Major complication (CD 3–5) | Median: 34.00  | Median: 33.70  | NR      |
| Snowden 2013| Mixed (389)     | V\textsubscript{E}/V\textsubscript{CO2} | Mortality (in–hospital) | Mean (SD): 35.40 (6.20) | Mean (SD): 36.30 (4.70) | Mean difference (95%CI): 0.90 (–2.00 to 3.80) |

\begin{itemize}
  \item Significant association between favorable preoperative cardiopulmonary exercise test (CPET) variables and absence of postoperative complications
  \item No significant association between preoperative CPET variables and postoperative compilations
  \item Significant association between unfavorable preoperative CPET variables and absence of postoperative complications
\end{itemize}

Peak VO\textsubscript{2} = peak oxygen uptake; AT = anaerobic threshold; V\textsubscript{E}/V\textsubscript{CO2} = ventilatory equivalent for carbon dioxide
CONCLUSIONS

This systematic review and meta-analysis has demonstrated that superior preoperative CPET values, especially peak VO2, were significantly associated with improved postoperative outcomes in patients undergoing cancer surgery. The predictive value of preoperative CPET on length of hospital stay or quality of life outcomes was not able to be determined, due to the high heterogeneity or lack of studies, respectively. Results from individual studies not included in the meta-analysis also reported positive trends. Most importantly, none of the identified studies reported a negative association between preoperative CPET values

| Study name | Type of cancer | Mean difference (95%CI) | Weight (%) |
|------------|----------------|------------------------|------------|
| Prentis, 2013 | Bladder | 0.20 (-2.57 to 2.97) | 22.95 |
| West, 2014 | Rectal | 2.12 (0.28 to 3.96) | 51.91 |
| Yakal, 2018 | Lung | -0.65 (-3.29 to 1.99) | 25.14 |
| Pooled effect (I²=0%) | | 0.80 (-0.95 to 2.54) | |
| Bobbio, 2009 | Lung | 2.50 (-1.20 to 6.20) | 21.47 |
| Brat, 2016 | Lung | 3.70 (0.67 to 6.73) | 31.98 |
| Brunelli, 2012 | Lung | 3.90 (1.39 to 6.41) | 46.51 |
| Pooled effect (I²=0%) | | 3.54 (1.82 to 5.25) | |
| Patel, 2019 | Esophageal | -2.39 (-4.79 to 0.01) | 22.80 |
| Tolchard, 2015 | Bladder | 3.53 (1.24 to 5.82) | 25.12 |
| Torchio, 2017 | Lung | 0.40 (-1.58 to 2.38) | 33.42 |
| Ulyett, 2017 | Liver | 2.22 (-0.43 to 4.87) | 18.66 |
| Pooled effect (I²=4%) | | 0.93 (-1.53 to 3.38) | |

FIG. 3 Forest plot of the association between preoperative anaerobic threshold (AT) in ml/kg/min and postoperative complication. Mean difference >0 indicate higher preoperative AT in Patients with no postoperative complications. CI = Confidence level

FIG. 4 Forest plot of the association between preoperative ventilatory equivalent for carbon dioxide (VE/VCO2) and postoperative complications. Mean difference >0 indicate lower preoperative VE/VCO2 in patients with no postoperative complications. CI=Confidence level
| Author year | Cancer type (N) | Preoperative CPET threshold | Length of hospital stay (days) | Pooled estimates | Summary |
|-------------|----------------|-----------------------------|-------------------------------|-----------------|---------|
|             |                | Favorable                    | Unfavorable                   | Favorable CPET  | Unfavorable CPET |         |
| Bayram 2007 | Lung (55)      | Peak VO₂ >15 (mL/Kg/min)     | Peak VO₂ <15 (mL/Kg/min)      | Mean: 6         | Mean: 7         | Not reported |
| Patel 2019  | Esophageal (120)| Peak VO₂ >17 (mL/Kg/min)    | Peak VO₂ <17 (mL/Kg/min)      | Median (range): 15 (9–153) | Median (range): 16 (6–106) | Not reported |
| McSorley 2018 | Colorectal (38)| Peak VO₂ >19 (mL/Kg/min)    | Peak VO₂ <19 (mL/Kg/min)      | Median (range): 9 (5–19) | Median (range): 8 (3–15) | Not reported |
| Kasivisvanathan 2015 | Liver (104) | Peak VO₂ (mL/Kg/min) | Not reported | Not reported | Hazard ratio (95% CI): 1.15 (0.99–1.40) |
| Dunne 2014  | Liver (197)    | Peak VO₂ (mL/Kg/min)        | Not reported                  | Not reported    | Hazard ratio (95% CI): 1.10 (0.98–1.04) |
| Sinclair 2017 | Esophageal (240) | Peak VO₂ (mL/Kg/min) | Not reported | Not reported | Odds ratio (95% CI): 1.00 (1.0–1.1) |
| Chan 2016   | Colorectal (48) | Peak VO₂ (mL/Kg/min) | Not reported | Not reported | Not reported |
| Chandrabalan 2013 | Pancreas (93) | AT ≥10 (mL/Kg/min) | AT <10 (mL/Kg/min) | Not reported | Not reported | Hazard ratio (95% CI): 1.70 (1.1–2.6) |
| Ausania 2012 | Pancreas (124) | AT ≥10.1 (mL/Kg/min) | AT <10.1 (mL/Kg/min) | Median (range): 17.5 (8–99) | Median (range): 29.4 (12–54) | Not reported |
| Patel 2019  | Esophageal (120) | AT ≥10.5 (mL/Kg/min) | AT <10.5 (mL/Kg/min) | Median: 16 | Median: 16 | Not reported |
| Wilson 2010 | Mixed (847)    | AT ≥10.9 (mL/Kg/min)        | AT <10.9 (mL/Kg/min)          | Median: 8       | Median: 9     | Not reported |
| Lamb 2016   | Bladder (111)  | AT ≥11 (mL/Kg/min)          | AT <11 (mL/Kg/min)            | Median (IQR): 10 (7–13) | Median (IQR): 11 (7.5–14.5) | Not reported |
| Chandrabalan 2013 | Pancreas (93) | AT ≥11 (mL/Kg/min) | AT <11 (mL/Kg/min) | Not reported | Not reported | Hazard ratio (95% CI): 1.40 (0.90-2.20) |
| Forshaw 2008 | Esophageal (75) | AT ≥11 (mL/Kg/min) | AT <11 (mL/Kg/min) | Mean (SD): 19 (23) | Mean (SD): 19 (9) | Mean difference (95% CI): 0.00 (–13.30 to 13.30) |
| Lamb 2016   | Bladder (111)  | AT ≥12 (mL/Kg/min)          | AT <12 (mL/Kg/min)            | Median (IQR): 9 (8–12) | Median (IQR): 11 (8–15) | Not reported |
| Chan 2016   | Colorectal (48) | AT (mL/Kg/min)              | Not reported                  | Not reported    | Not reported | Not reported |
and postoperative outcomes. The authors of this review recommend the use of preoperative CPET before cancer surgery to predict postoperative outcomes.

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