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REVIEW ARTICLE – GASTROINTESTINAL ONCOLOGY

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, including peak oxygen uptake (peak VO_2), anaerobic threshold (AT), or ventilatory equivalent for carbon dioxide (V_E/V_{CO2}), and postoperative outcomes (complications, length of stay, and quality of life) 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 VO_2 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 V_E/V_{CO2} 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 VO_2, 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

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perioperative management, particularly in high-risk patients undergoing high-risk surgery.[4,5] 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.[6] This is extremely important for clinicians to inform decision-making, to better understand the post-operative 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,[5,7,8] others have reported nonsignificant association.[9–11] The prospective, multinational cohort (METS) study, for example, demonstrated an association between peak oxygen uptake (peak VO_2) and noncardiac complications in a cohort of relatively well patients having noncardiac surgery and not limited to cancer surgery.[12] 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.[5,7–11] 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 VO_2, anaerobic threshold (AT), and ventilatory equivalent for carbon dioxide (VE/VCO_2), 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.[13] 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 $\geq$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 VO_2): defined as the highest VO_2 attained on a rapid incremental test. (b) Anaerobic threshold (AT): a submaximal index of exercise capacity defined as the oxygen uptake (VO_2) 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 (V_E/V_{CO2}): 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 noncancer 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 VO_2 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.

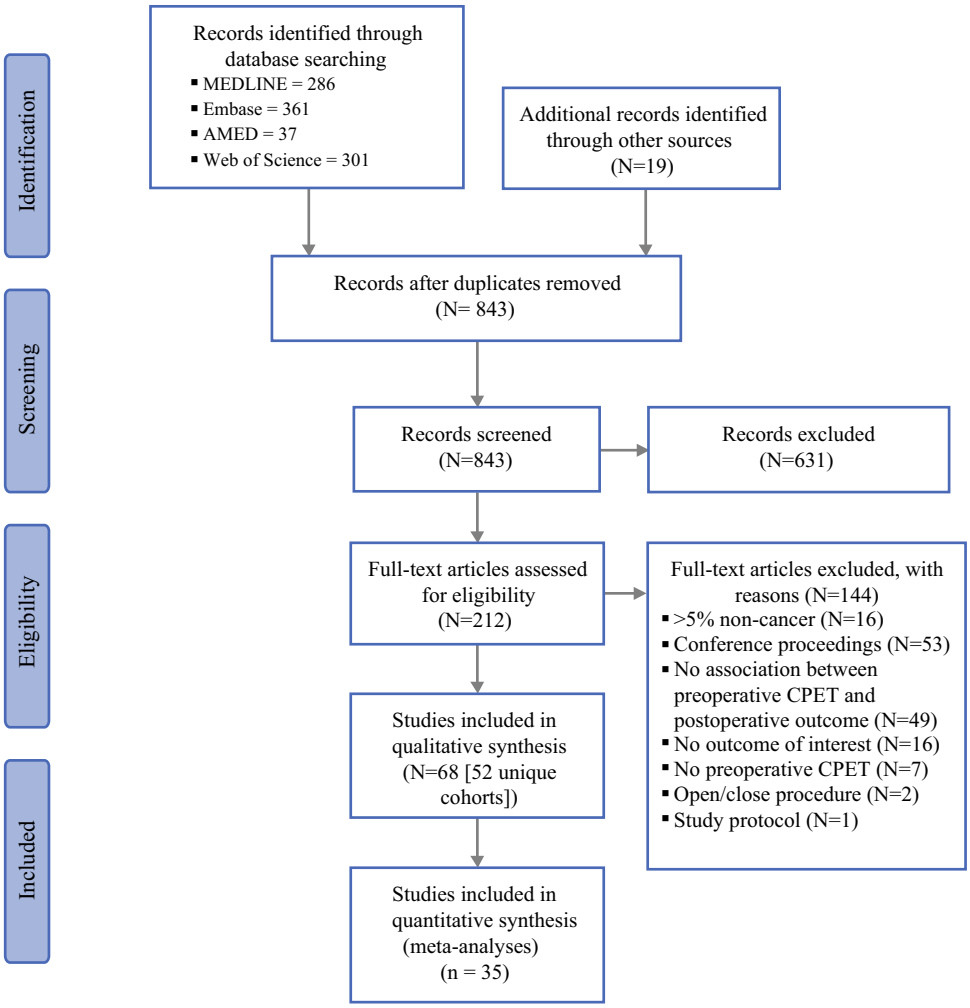
Risk of Bias

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 VO_2 The association between preoperative Peak VO_2 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 VO_2 (MD: 2.28; 95% CI: 1.26–3.29; $I^2 = 9\%$)

FIG. 1 Included studies



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; I^2 = 0%), minor complications (MD: 2.01; 95% CI: 0.90–3.13; I^2 = 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 VO_2 (Fig. 2). No difference in Peak VO_2 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; I^2 = 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; I^2 = 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).

V_E/V_{CO2} The association between preoperative V_E/V_{CO2} and postoperative complications are presented in Fig. 4 and Tables 3 and 4. Our pooled analysis demonstrated that preoperative V_E/V_{CO2} 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; I^2 = 0%). No significant differences in

TABLE 1 Characteristics of the included studies

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) Sample size: 111 Female (%): 30 (27%)	Cycloergometer	Peak VO_2 (ml/kg/min) AT (ml/kg/min) V_E/V_{CO2}	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) Sample size: 69 Female (%): 21 (30%)	Cycloergometer	Peak VO_2 (ml/kg/min) AT (ml/kg/min) V_E/V_{CO2}	Any complication	Clavien-Dindo classification
Tolchard 2015	Bladder	Mean age (SD): 70.2 (10.3) Sample size: 105 Female (%): 17 (16%)	Cycloergometer	Peak VO_2 (ml/kg/min) AT (ml/kg/min) V_E/V_{CO2}	Minor/major complication	Clavien-Dindo classification (≥2 major complication)
Bowles 2008	Colorectal	Mean age (SD): NR Sample size: 121 Female (%): 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) Sample size: 48 Female (%): 18 (38%)	Cycloergometer	Peak VO_2 (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) Sample size: 1214 Female (%): 501 (41.3%)	NR	AT (ml/kg/min) V_E/V_{CO2}	Unplanned critical care Mortality LOS	Unplanned critical care use was defined as any unexpected admission or re-admission 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 Sample size: 38 Female (%): 8 (21%)	Cycloergometer	Peak VO_2 (ml/kg/min)	Any complication Minor/major complication LOS	Not specified Not specified Not specified
Nikolopoulos 2015	Colorectal	Mean age (SD): 59.3 (12.7) Sample size: 69 Female (%): 34 (49%)	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) Sample size: 78 Female (%): 14 (18%)	Cycloergometer	Peak VO_2 (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

TABLE 1 continued

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) Sample size: 206 Female (%): 48 (23%)	Cycloergometer	Peak VO_2 (ml/kg/min) AT (ml/kg/min)	Any complication Cardiopulmonary complication	Esophageal Complications Consensus Group definitions Esophageal Complications Consensus Group definitions
Nagamatsu 2001/1994	Esophageal	Mean age (SD): 59.0 (9.0) Sample size: 91 Female (%): 3 (3.3%)	Cycloergometer	Peak VO2 (ml/min/m^2) AT (ml/min/m^2)	Cardiopulmonary complication	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
Patel 2019	Esophageal	Mean age (SD): 64.6 (9.0) Sample size: 120 Female (%): 20 (17%)	Cycloergometer	Peak VO_2 (ml/kg/min) AT (ml/kg/min) V_E/V_{CO2}	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
Sinclair 2017	Esophageal	Mean age (SD): 66.0 (8.9) Sample size: 240 Female (%): 59 (25%)	Cycloergometer	Peak VO_2 (ml/kg/min) AT (ml/kg/min) V_E/V_{CO2}	Any complication Cardiopulmonary complications LOS	Cardiovascular (acute coronary syndrome, heart failure, problematic atrial fibrillation); Respiratory (pneumonia, pulmonary embolism, acute respiratory distress syndrome); Gastro-intestinal (anastomotic leak); and other complications Not specified No. of days spent in hospital from the day of operation until the day the patient left the hospital
Dunne 2014	Liver	Mean age (SD): 69.6 (8.2) Sample size: 197 Female (%): 59 (30%)	Cycloergometer	Peak VO_2 (ml/kg/min) V_E/V_{CO2}	Any complication Minor/major complication LOS	Clavien-Dindo classification. 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
Kasivisvanathan 2015	Liver	Mean age (SD): 63.2 (11.3) Sample size: 104 Female (%): 44 (42%)	Cycloergometer	Peak VO_2 (ml/kg/min)	Any complication LOS	POMS score ≥1 on postoperative Day 3 No. of days spent in hospital from the day of operation until the day the patient left the hospital
Ulyett 2017	Liver	Mean age (SD): 68.0 (12.7) Sample size: 172 Female (%): 53 (31%)	Cycloergometer	Peak VO_2 (ml/kg/min) V_E/V_{CO2}	Minor/major complication	Clavien-Dindo classification (≥3 major complication)
Bayram 2007	Lung	Mean age (SD): 59.0 (14.8) Sample size: 55 Female (%): 6 (11%)	Cycloergometer	Peak VO_2 (ml/kg/min)	Postoperative complications LOS	Cardiopulmonary Pulmonary Respiratory Mortality (30 days) Pneumonia Actelectasis Bronchopleural fistula Prolonged air leak Arrhytmia No. of days spent in hospital from the day of operation until the day the patient left the hospital

TABLE 1 continued

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 VO_2 (ml/kg/min) AT (L/min)	Any complication	Cardiopulmonary complications were defined as acute CO_2 retention (partial pressure of CO_2 >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 VO_2 (ml/kg/min) V_E/V_{CO2}	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 VO_2 (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 VO_2 (ml/kg/min) V_E/V_{CO2}	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 O_2/fraction of inspired O_2 <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

TABLE 1 continued

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_2 (ml/kg/min) AT (ml/kg/min)	Any complication	Any of the below defined complications
					Pulmonary complication	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
					Mortality	In-hospital death
Brunelli 2012	Lung	Mean age (SD): 67.2 (9.8) Sample size: 225 Female (%): 42 (19%)	Cycloergometer	Peak VO_2 (ml/kg/min) V_E/V_{CO2}	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)
Brutsche 2000	Lung	Mean age (SD): 63.0 (11.0) Sample size: 125 Female (%): 24 (19%)	Cycloergometer	Peak VO_2 (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 angiogram); Lobar atelectasis (necessitating bronchoscopy); Death
Dales 1993	Lung	Mean age (SD): NR Sample size: 46 Female (%): NR	Treadmill	Peak VO_2 (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; hemothoras 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,

TABLE 1 continued

Author, year	Type of cancer	Characteristics	CPET assessment	CPET variables	Postoperative outcomes	Definition postoperative outcomes
						radiographic changes, or elevated pulmonary artery wedge pressure and requiting therapy). Other complications were renal failure requiring dialysis, cerebrovascular accident, gastrointestinal bleeding, and wound infection
Epstein 1993	Lung	Mean age (SD): 62.6 (4.8) Sample size: 42 Female (%): 1 (2%)	Cycloergometer	Peak VO_2 (ml/kg/min) Peak VO_2 (mL/m^2) Peak VO_2 (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 [PaCO.sub.2] (≥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
Fang 2014	Lung	Mean age (SD): 67.3 (7.0) Sample size: 107 Female (%): 3 (2.8%)	Cycloergometer	Peak VO_2 (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 VO_2 (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 VO_2 (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 VO_2 (ml/kg/min)	Any complication Cardiovascular complication Pulmonary complications	Any of the below defined complications Myocardial infarction, arrhythmias, congestive heart failure, stroke, thromboembolism, or renal dysfunction Atelectasis, pneumonia, or acute lung injury

TABLE 1 continued

Author, year	Type of cancer	Characteristics	CPET assessment	CPET variables	Postoperative outcomes	Definition postoperative outcomes
Loewen 2007	Lung	Mean age (SD): NR Sample size: 403 Female (%): 158 (39%)	Cycloergometer	Peak VO_2 (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) Sample size: 198 Female (%): 35 (18%)	Cycloergometer	Peak VO_2 (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) Sample size: 47 Female (%): 17 (36%)	Cycloergometer	Peak VO_2 (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) Sample size: 209 Female (%): 87 (42%)	Cycloergometer	Peak VO_2 (ml/kg/min) V_E/V_{CO2}	Cardiopulmonary complication	Adult respiratory distress syndrome, pneumonia, pulmonary embolism, pulmonary edema, atelectasis requiring bronchoscopy, respiratory failure (>24-h mechanical ventilation or needing re-intubation 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) Sample size: 8 Female (%): 1 (13%)	NR	Peak VO_2 (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) Sample size: 211 Female (%): 55 (26%)	Cycloergometer	Peak VO_2 (ml/kg/m^2) AT (ml/kg/m^2)	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) Sample size: 12 Female (%): 2 (17%)	Cycloergometer	Peak VO_2 (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; Arrhythmias, myocardial infarction, pulmonary embolism, hypotension, atelectasis, and death
Rodrigues 2016	Lung	Mean age (SD): 64.7 (7.9) Sample size: 50 Female (%): 4 (8%)	Cycloergometer	Peak VO_2 (ml/kg/min)	Pulmonary complication	Not specified
Torchio 2017	Lung	Mean age (SD): 65 (8) Sample size: 263 Female (%): 51 (19%)	Treadmill	Peak VO_2 (ml/kg/min) V_E/V_{CO2}	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-

TABLE 1 continued

Author, year	Type of cancer	Characteristics	CPET assessment	CPET variables	Postoperative outcomes	Definition postoperative outcomes
						probability perfusion scan or helical computed tomographic scan; adult respiratory distress syndrome; respiratory failure (partial arterial oxygen pressure (PaO_2) <65 mm Hg and/or partial arterial carbon dioxide pressure ($PaCO_2$) >45 mm Hg) requiring noninvasive or invasive mechanical ventilation; pneumonia defined by typical clinical, laboratory, and radiographic features; atelectasis requiring bronchoscopy and/or noninvasive assisted ventilation
Villani & Busia 2004	Lung	Mean age (SE): 57.1 (0.7) Sample size: 150 Female (%): 9 (6%)	Cycloergometer	Peak VO_2 (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 VO_2 (ml/kg/min)	Any complication	Postoperative death, myocardial infarction, heart failure, renal failure, respiratory failure, pulmonary embolism, septicemia, or pneumonia
Yakal 2018	Lung	Mean age (SD): 63.0 (8.0) Sample size: 125 Female (%): 19 (15%)	Treadmill	Peak VO_2 (ml/kg/min) AT (ml/kg/min) V_E/V_{CO2}	Any complication	Not specified
Begum 2016	Lung	Mean age (SD): NR Sample size: 1684 Female (%): NR	NR	Peak VO_2 (ml/kg/min)	Cardiopulmonary	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
					Mortality	Death within 30 days from surgery
Huang 2016	Mixed	Mean age (SD): 67.7 (9.6) Sample size: 26 Female (%): 4 (15%)	Cycloergometer	Peak VO_2 (ml/kg/min)	Minor/major complication	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 VO_2 (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 VO_2 (ml/kg/min) AT (ml/kg/min) V_E/V_{CO2}	Mortality	In-hospital death
Whibley 2018	Mixed	Mean age (SD): 64.9 (9.5) Sample size: 81 Female (%): NR	NR	Peak VO_2 (ml/kg/min) AT (ml/kg/min)	Respiratory complication	Not specified

TABLE 1 continued

Author, year	Type of cancer	Characteristics	CPET assessment	CPET variables	Postoperative outcomes	Definition postoperative outcomes
Wilson 2010	Mixed	Mean age (SD): 72.2 (12.8) Sample size: 847 Female (%): 341 (40%)	Cycloergometer	AT (ml/kg/min) V_E/V_{CO2}	Mortality LOS	In-hospital death No. of days spent in hospital from the day of operation until the day the patient left the hospital
Ausania 2012	Pancreas	Mean age (SD): 65.4 (8.7) Sample size: 124 Female (%): 57 (46%)	Cycloergometer	AT (ml/kg/min)	Any complication Mortality LOS	Postoperative morbidity survey In-hospital mortality No. of days spent in hospital from the day of operation until the day the patient left the hospital
Chandrabalan 2013	Pancreas	Median age: 66.0 Sample size: 100 Female (%): 40 (40%)	Cycloergometer	AT (ml/kg/min)	Postoperative complication LOS	The International Study Group for Pancreatic Surgery (ISGPS) definitions were used to classify pancreatic fistulae and post-operative haemorrhage. The Clavien-Dindo classification was used to grade other complications (≥3 major complication) No. of days spent in hospital from the day of operation until the day the patient left the hospital
Junejo 2014	Pancreas	Mean age (SD): 63.8 (7.5) Sample size: 64 Female (%): 26 (41%)	Cycloergometer	Peak VO_2 (ml/kg/min) AT (ml/kg/min) V_E/V_{CO2}	Any complication Cardiopulmonary complication Mortality	International Study Group for Pancreatic Surgery Acute myocardial infarction (detection of a rise in serum troponin) and electrocardiographic changes indicative of new ischemia; congestive cardiac failure; and serious dysrhythmia resulting in compromised tissue perfusion and primary cardiac arrest. Pneumonia, pleural effusion, and respiratory failure requiring ventilatory support In-hospital death and death within 30 days from surgery
West 2014	Rectal	Mean age (SD): 66 (10) Sample size: 95 Female (%): 23 (24%)	Cycloergometer	Peak VO2 (ml/kg/min) V_E/V_{CO2}	Postoperative complication	Postoperative Morbidity Survey (POMS) on Day 5, the Dindo–Demartines–Clavien classification (highest grade for the most serious sustained in-hospital morbidity) and in-hospital mortality were recorded

preoperative V_E/V_{CO2} 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_E/V_{CVO2} (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

TABLE 2 continued

Author, year	Study participation	Study attrition	Outcome measurement	Statistical analysis and reporting
Ausania 2012	Low	Low	Low	Moderate
Chandrabalan 2013	High	Low	Low	Low
Junejo 2014	Low	Moderate	Low	Low
West 2014	Low	Moderate	Low	Low

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_2, AT, and lower V_E/V_{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 stablished 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_2 and VO_2 max were used in this review interchangeably.[6] Because these patients are older and debilitated by their conditions, it is difficult to demonstrate that the plateau criterion for VO_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.[5,7,8,10,11] 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

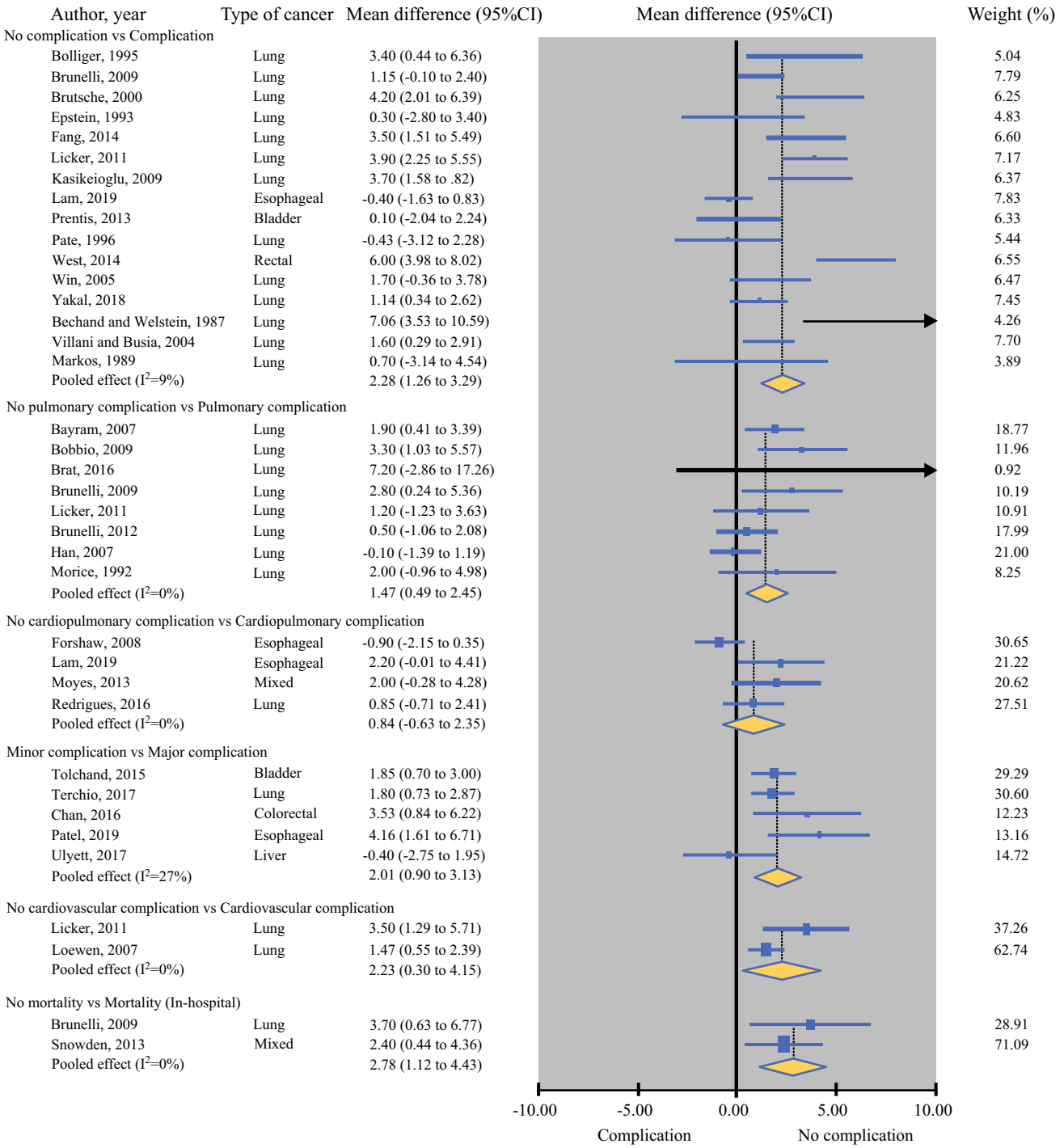


FIG. 2 Forest plot of the association between preoperative peak oxygen uptake (peak VO_2) in ml/kg/min and postoperative complication. Mean difference > 0 indicate higher preoperative peak VO_2 in patients with no postoperative complications. CI=Confidence level

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

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		Peak VO_2 >10 (mL/Kg/min)	Peak VO_2 ≤10 (mL/Kg/min)	No complication	Complication	0.19 (0.09–0.42)	⊕
West 2014	Rectal (95)	Peak VO_2 ≥10.6 (mL/Kg/min)	Peak VO_2 <10.6 (mL/Kg/min)	No complication	Complication	0.02 (0.01–0.10)	⊕
Bayram 2007	Lung (55)	Peak VO_2 >15 (mL/Kg/min)	Peak VO_2 <15 (mL/Kg/min)	No complication	Complication	0.47 (0.15–1.46)	〓
Epstein 1993	Lung (42)	Peak VO_2 >15 (mL/Kg/min)	Peak VO_2 <15 (mL/Kg/min)	No complication	Complication	0.42 (0.11–1.55)	〓
Licker 2011	Lung (215)	Peak VO_2 ≥17 (mL/Kg/min)	Peak VO_2 <17 (mL/Kg/min)	No complication	Complication	0.35 (0.17–0.73)	⊕
McSorley 2018	Colorectal (38)	Peak VO_2 >19 (mL/Kg/min)	Peak VO_2 <19 (mL/Kg/min)	No complication	Complication	0.94 (0.24–3.71)	〓
Dales 1993	Lung (46)	Peak VO_2 ≥1250 (ml)	Peak VO_2 <1250 (ml)	No complication	Complication	0.27 (0.08–0.93)	⊕
Epstein 1993	Lung (42)	Peak VO_2 >1 (L)	Peak VO_2 ≤1 (L)	No complication	Complication	0.33 (0.09–1.29)	〓
Epstein 1993	Lung (42)	Peak VO_2 >500 (ml/m^2)	Peak VO_2 ≤500 (ml/m^2)	No complication	Complication	0.17 (0.04–0.74)	⊕
Chan 2016	Colorectal (48)	Peak VO_2 (mL/Kg/min)		No complication	Complication	NR	〓
Dunne 2014	Liver (197)	Peak VO_2 (mL/Kg/min)		No complication	Complication	1.02 (0.96–1.09)	〓
Junejo 2014	Pancreas (64)	Peak VO_2 (mL/Kg/min)		No complication	Complication	1.00 (0.86–1.18)	〓
Sinclair 2017	Esophagus (240)	Peak VO_2 (ml)		No complication	Complication	1.00 (1.00–1.00)	⊕
Kasivisvanathan 2015	Liver (104)	Peak VO_2 (mL/Kg/min)		No complication	Complication	1.03 (1.01–1.06)	⊕
Nagamatsu 2001/Nagamatsu 1994	Esophagus (91)	Peak VO_2 ≥1000 ($ml/min/m^2$)	Peak VO_2 <1000 ($ml/min/m^2$)	No cardiopulmonary complication	Cardiopulmonary complication	0.22 (0.05–1.03)	〓
Miyazaki 2018	Lung (209)	Peak VO_2 ≥12 (mL/Kg/min)	Peak VO_2 <12 (mL/Kg/min)	No cardiopulmonary complication	Cardiopulmonary complication	0.62 (0.24–1.59)	〓
Bayram 2007	Lung (55)	Peak VO_2 >15 (mL/Kg/min)	Peak VO_2 <15 (mL/Kg/min)	No cardiopulmonary complication	Cardiopulmonary complication	0.07 (0.01–0.35)	⊕

TABLE 3 continued

Author, year	Cancer type (N)	Preoperative CPET threshold		Postoperative complication		Estimates, odds ratio (95% confidence intervals)	Summary
		Favorable	Unfavorable	Favorable outcome	Unfavorable outcome		
Mao 2010	Lung (198)	Peak VO_2 >15 (mL/Kg/min)	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)	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 >15 (mL/Kg/min)	Peak VO_2 <15 (mL/Kg/min)	No cardiopulmonary complication	Cardiopulmonary complication	0.82 (0.65–1.03)	=
Mao 2010	Lung (198)	Peak VO_2 ≥20 (mL/Kg/min)	Peak VO_2 <20 (mL/Kg/min)	No cardiopulmonary complication	Cardiopulmonary complication	0.56 (0.29–1.09)	=
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)	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)	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)	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)	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)	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)	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)	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)	Peak VO_2 <14 (mL/Kg/min)	No respiratory complication	Respiratory complication	NR	=
Bayram 2007	Lung (55)	Peak VO_2 >15 (mL/Kg/min)	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)	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)	Peak VO_2 <15 (mL/Kg/min)	No mortality (30 days)	Mortality (30 days)	0.20 (0.01–5.7)	=

TABLE 3 continued

Author, year	Cancer type (N)	Preoperative CPET threshold		Postoperative complication		Estimates, odds ratio (95% confidence intervals)	Summary
		Favorable	Unfavorable	Favorable outcome	Unfavorable outcome		
Begum 2016	Lung (1684)	Peak VO_2 >15 (mL/Kg/min)	Peak VO_2 <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 VO_2 (mL/Kg/min)		No mortality (in–hospital)	Mortality (in–hospital)	1.32 (0.91–1.93)	
West 2014	Rectal (46)	Peak VO_2 ≥10.6 (mL/Kg/min)	Peak VO_2 <10.6 (mL/Kg/min)	Minor complication	Major complication	0.60 (0.13–2.49)	
McSorley 2018	Colorectal (38)	Peak VO_2 >19 (mL/Kg/min)	Peak VO_2 <19 (mL/Kg/min)	Minor complication	Major complication	1.00 (0.08–11.67)	
Dunne 2014	Liver (194)	Peak VO_2 (mL/Kg/min)		Minor complication	Major complication	1.04 (0.97–1.11)	
Huang 2016	Mixed (26)	Peak VO_2 (mL/Kg/min)		Minor complication	Major complication	0.72 (0.17–2.21)	
West 2014	Rectal (95)	Peak VO_2 ≥10.6 (mL/Kg/min)	Peak VO_2 <10.6 (mL/Kg/min)	No infection	Infection	0.10 (0.03–0.26)	
West 2014	Rectal (95)	Peak VO_2 ≥10.6 (mL/Kg/min)	Peak VO_2 <10.6 (mL/Kg/min)	No wound dehiscence	Wound dehiscence	0.10 (0.00–1.16)	
West 2014	Rectal (95)	Peak VO_2 ≥10.6 (mL/Kg/min)	Peak VO_2 <10.6 (mL/Kg/min)	No renal complication	Renal complication	0.20 (0.04–1.07)	
West 2014	Rectal (95)	Peak VO_2 ≥10.6 (mL/Kg/min)	Peak VO_2 <10.6 (mL/Kg/min)	No gastrointestinal complication	Gastrointestinal complication	0.30 (0.09–0.80)	
West 2014	Rectal (95)	Peak VO_2 ≥10.6 (mL/Kg/min)	Peak VO_2 <10.6 (mL/Kg/min)	No neurological complication	Neurological complication	0.70 (0.01–35.72)	
West 2014	Rectal (95)	Peak VO_2 ≥10.6 (mL/Kg/min)	Peak VO_2 <10.6 (mL/Kg/min)	No hematological complication	Hematological complication	0.70 (0.13–3.56)	
West 2014	Rectal (95)	Peak VO_2 ≥10.6 (mL/Kg/min)	Peak VO_2 <10.6 (mL/Kg/min)	No pain	Pain	2.9 (0.31–27.21)	
Bayram 2007	Lung (55)	Peak VO_2 >15 (mL/Kg/min)	Peak VO_2 <15 (mL/Kg/min)	No Pneumonia	Pneumonia	0.20 (0.01–3.30)	
Bayram 2007	Lung (55)	Peak VO_2 >15 (mL/Kg/min)	Peak VO_2 <15 (mL/Kg/min)	No atelectasis	Atelectasis	0.10 (0.0–1.31)	
Bayram 2007	Lung (55)	Peak VO_2 >15 (mL/Kg/min)	Peak VO_2 <15 (mL/Kg/min)	No bronchopleural fistula	Bronchopleural fistula	0.20 (0.01–5.70)	

TABLE 3 continued

Author, year	Cancer type (N)	Preoperative CPET threshold		Postoperative complication		Estimates, odds ratio (95% confidence intervals)	Summary
		Favorable	Unfavorable	Favorable outcome	Unfavorable outcome		
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	Arrhytmia	2.2 (0.18–25.32)	=
Ausania 2012	Pancreas (124)	AT ≥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 ≥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 ≤10.9 (ml/kg/min)	No mortality (90 days)	Mortality (90 days)	0.14 (0.03–0.62)	=
Bowles 2008	Colorectal (121)	AT >11 (ml/kg/min)	AT ≤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 ≥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 ≥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 ≥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 ≥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 >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)	+

TABLE 3 continued

Author, year	Cancer type (N)	Preoperative CPET threshold		Postoperative complication		Estimates, odds ratio (95% confidence intervals)	Summary
		Favorable	Unfavorable	Favorable outcome	Unfavorable outcome		
Junejo 2014	Pancreas (64)	AT (mL/Kg/min)		No cardiopulmonary complication	Cardiopulmonary complication	1.05 (0.82–1.34)	=
Forshaw 2008	Esophagus (75)	AT >11 (mL/Kg/min)	AT <11 (mL/Kg/min)	No Noncardiopulmonary complication	Noncardiopulmonary complication	1.60 (0.31–7.94)	=
Lamb 2016	Bladder (82)	AT ≥11 (NR)	AT <11 (NR)	Minor complication (CD <3)	Major complication (CD 3–5)	1.10 (0.30–3.85)	=
Bowles 2008	Colorectal (121)	AT ≥11 (NR)	AT <11 (NR)	Minor complication (CD <3)	Major complication (CD 3–5)	1.45 (0.55–3.79)	=
Lamb 2016	Bladder (82)	AT ≥11 (NR)	AT <11 (NR)	Minor complication (CD <3)	Major complication (CD 3–5)	0.30 (0.04–2.46)	=
Chandrabalan 2013	Pancreas (100)	AT ≥10 (mL/Kg/min)	AT <10 (mL/Kg/min)	Minor cardiac complications (CD <3)	Major cardiac complications (CD 3–5)	0.50 (0.02–14.5)	=
Chandrabalan 2013	Pancreas (100)	AT ≥10 (mL/Kg/min)	AT <10 (mL/Kg/min)	Minor respiratory complications (CD <3)	Major respiratory complications (CD 3–5)	0.70 (0.15–3.32)	=
Chandrabalan 2013	Pancreas (100)	AT ≥10 (mL/Kg/min)	AT <10 (mL/Kg/min)	Minor intra–abdominal abscess (CD <3)	Major intra–abdominal abscess (CD 3–5)	0.30 (0.09–1.00)	=
Chandrabalan 2013	Pancreas (98)	AT ≥10 (mL/Kg/min)	AT <10 (mL/Kg/min)	No pancreatic fistula	Pancreatic fistula	0.30 (0.13–0.91)	+
Chandrabalan 2013	Pancreas (100)	AT ≥10 (mL/Kg/min)	AT <10 (mL/Kg/min)	No hemorrhage	Hemorrhage	1.70 (0.58–5.25)	=
Ausania 2012	Pancreas (124)	AT ≥10.1 (mL/Kg/min)	AT <10.1 (mL/Kg/min)	No cardiorespiratory complications	Cardiorespiratory complications	0.30 (0.08–1.52)	=
Whibley 2018	Mixed (81)	AT ≥11 (NR)	AT <11 (NR)	No respiratory complications	Respiratory complications	NR	=
Forshaw 2008	Esophagus (75)	AT >11 (mL/Kg/min)	AT <11 (mL/Kg/min)	No unplanned ITU admission	Unplanned ITU admission	0.60 (0.13–2.46)	=
Junejo 2014	Pancreas (64)	V_E/V_{CO2}		No complication	Complication	0.97 (0.89–1.07)	=
Dunne 2014	Liver (194)	V_E/V_{CO2}		No complication	Complication	0.98 (0.93–1.04)	=
Sinclair 2017	Esophagus (240)	V_E/V_{CO2}		No complication	Complication	0.90 (0.84–0.96)	+
Junejo 2014	Pancreas (64)	V_E/V_{CO2}		No mortality (in–hospital)	Mortality (in–hospital)	0.79 (0.66–0.95)	+
Wilson 2010	Mixed (847)	V_E/V_{CO2} <34	V_E/V_{CO2} ≥34	No mortality (in–hospital)	Mortality (in–hospital)	0.20 (0.06–0.74)	+

TABLE 3 continued

Author, year	Cancer type (N)	Preoperative CPET threshold		Postoperative complication		Estimates, odds ratio (95% confidence intervals)	Summary
		Favorable	Unfavorable	Favorable outcome	Unfavorable outcome		
Junejo 2014	Pancreas (64)	V_E/V_{CO2}		No mortality (30 days)	Mortality (30 days)	0.74 (0.56–0.97)	⊕
Mann 2020	Colorectal (1193)	V_E/V_{CO2} ≤34	V_E/V_{CO2} >34	No mortality (30 days)	Mortality (30 days)	0.30 (0.12–0.68)	⊕
Miyazaki 2018	Lung (172)	V_E/V_{CO2} <40	V_E/V_{CO2} >40	No mortality (90 days)	Mortality (90 days)	0.30 (0.09–0.86)	⊕
Miyazaki 2018	Lung (172)	V_E/V_{CO2} <40	V_E/V_{CO2} >40	No cardiopulmonary complication	Cardiopulmonary complication	0.60 (0.32–1.26)	=
Junejo 2014	Pancreas (64)	V_E/V_{CO2}		No cardiopulmonary complication	Cardiopulmonary complication	0.98 (0.90–1.07)	=
Sinclair 2017	Esophagus (240)	V_E/V_{CO2}		No cardiopulmonary complication	Cardiopulmonary complication	0.91 (0.85–0.96)	⊕
Mann 2020	Colorectal (1193)	V_E/V_{CO2} ≤34	V_E/V_{CO2} >34	No unplanned critical care	Unplanned critical care	0.80 (0.53–1.30)	=
Dunne 2014	Liver (194)	V_E/V_{CO2}		Minor complication (CD <3)	Major Complication (CD >3)	0.99 (0.93–1.05)	=

⊕ Significant association between favorable preoperative cardiopulmonary exercise test (CPET) variables and absence of postoperative complications
= No significant association between preoperative CPET variables and postoperative compilations
⊖ Significant association between unfavourable preoperative CPET variables and absence of postoperative complications
Peak VO_2 = peak oxygen uptake; AT = anaerobic threshold; V_E/V_{CO2} = ventilatory equivalent for carbon dioxide

in most of the previous systematic reviews. This has prevented the pooling of a larger number of studies and a stronger conclusion across the identified reviews.

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

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_2 (ml/kg/min)	Major complication (CD 3–5)	Median: 17.00	Median: 15.00	NR	=
Forshaw 2008	Esophageal (78)	Peak VO_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_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_E/V_{CO2}	Major complication (CD 3–5)	Median: 34.00	Median: 33.70	NR	=
Snowden 2013	Mixed (389)	V_E/V_{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)	=

+ Significant association between favorable preoperative cardiopulmonary exercise test (CPET) variables and absence of postoperative complications

= No significant association between preoperative CPET variables and postoperative compilations

– Significant association between unfavorable preoperative CPET variables and absence of postoperative complications

Peak VO_2 = peak oxygen uptake; AT = anaerobic threshold; V_E/V_{CO2} = ventilatory equivalent for carbon dioxide

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.[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_2 and AT before and after the preoperative exercise regime would facilitate the investigation of this effect.

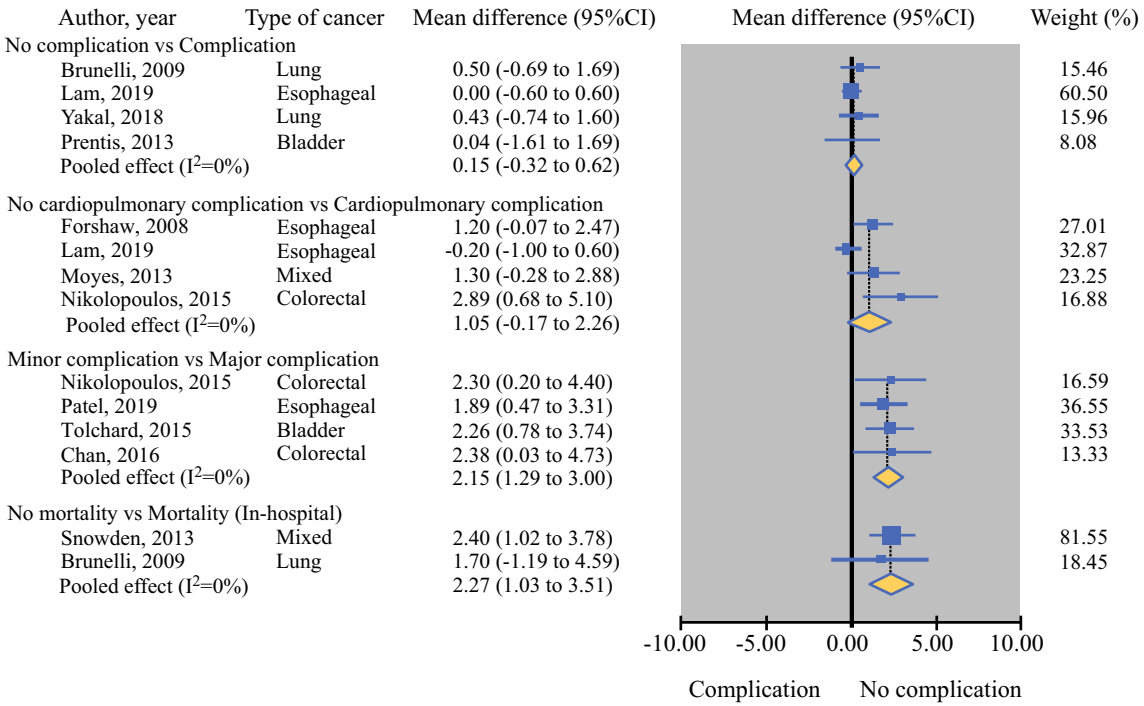


FIG. 3 Forest plot of the association between preoperative anaerobic threshold (AT) in ml\kg\min and postoperative complication. Mean difference>0 indicate higher preoperative AT in Patients with no postoperative complications. CI = Confidence level

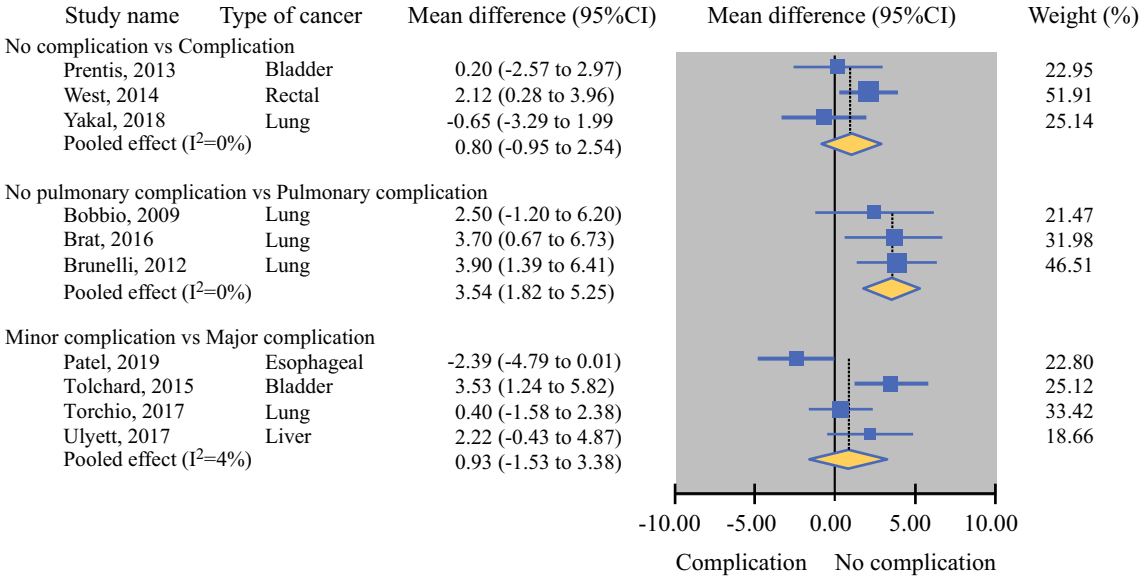


FIG. 4 Forest plot of the association between preoperative ventilatory equivalent for carbon dioxide (V_E/VCO_2) and postoperative complications. Mean difference >0 indicate lower preoperative V_E/VCO_2 in patients with no postoperative complications. CI=Confidence level

CONCLUSIONS

This systematic review and meta-analysis has demonstrated that superior preoperative CPET values, especially peak VO_2, 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

TABLE 5 Association between preoperative cardiopulmonary exercise test variables and length of hospital stay

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 VO_2 >15 (mL/Kg/min)	Peak VO_2 <15 (mL/Kg/min)	Mean: 6	Mean: 7	Not reported	=
Patel 2019	Esophageal (120)	Peak VO_2 >17 (mL/Kg/min)	Peak VO_2 <17 (mL/Kg/min)	Median (range): 15 (9–153)	Median (range): 16 (6–106)	Not reported	+
McSorley 2018	Colorectal (38)	Peak VO_2 >19 (mL/Kg/min)	Peak VO_2 <19 (mL/Kg/min)	Median (range): 9 (5–19)	Median (range): 8 (3–15)	Not reported	=
Kasivisvanathan 2015	Liver (104)	Peak VO_2 (mL/Kg/min)		Not reported	Not reported	Hazard ratio (95% CI): 1.15 (0.99–1.40)	=
Dunne 2014	Liver (197)	Peak VO_2 (mL/Kg/min)		Not reported	Not reported	Hazard ratio (95% CI): 1.10 (0.98–1.04)	=
Sinclair 2017	Esophageal (240)	Peak VO_2 (mL/Kg/min)		Not reported	Not reported	Odds ratio (95% CI): 1.00 (1.0–1.1)	+
Chan 2016	Colorectal (48)	Peak VO_2 (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	=

TABLE 5 continued

Author year	Cancer type (N)	Preoperative CPET threshold		Length of hospital stay (days)		Pooled estimates	Summary
		Favorable	Unfavorable	Favorable CPET	Unfavorable CPET		
Sinclair 2017	Esophageal (240)	AT (mL/Kg/min)		Not reported	Not reported	Odds ratio (95% CI): 1.00 (1.00–1.10)	⊕
Mann 2020	Colorectal (1193)	$V_E/V_{CO2} \leq 34$	$V_E/V_{CO2} > 34$	Not reported	Not reported	Odds ratio (95% CI): 1.70 (1.30-2.20)	⊕
Sinclair 2017	Esophageal (240)	V_E/V_{CO2}		Not reported	Not reported	Odds ratio (95% CI): 0.90 (0.90–0.90)	⊕
Dunne 2014	Liver (197)	V_E/V_{CO2}		Not reported	Not reported	Hazard ratio (95% CI): 0.90 (0.90–1.00)	=

⊕ Significant association between favorable preoperative cardiopulmonary exercise test (CPET) variables and length of hospital stay

= No significant association between preoperative CPET variables and length of hospital stay

⊖ Significant association between unfavorable preoperative CPET variables and length of hospital stay

Peak VO_2 = peak oxygen uptake; AT = anaerobic threshold; V_E/V_{CO2} = ventilatory equivalent for carbon dioxide

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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