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Preoperative physical performance as predictor of postoperative outcomes in patients aged 65 and older scheduled for major abdominal cancer surgery: A systematic review

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Background: Abdominal cancer surgery is associated with considerable morbidity in older patients. Assessment of preoperative physical status is therefore essential. The aim of this review was to describe and compare the objective physical tests that are currently used in abdominal cancer surgery in the older patient population with regard to postoperative outcomes.
Methods: Medline, Embase, CINAHL and Web of Science were searched until 31 December 2020. Non-interventional cohort studies were eligible if they included patients ≥65 years undergoing abdominal cancer surgery, reported results on objective preoperative physical assessment such as Cardiopulmonary Exercise Testing (CPET), field walk tests or muscle strength, and on postoperative outcomes.
Results: 23 publications were included (10 CPET, 13 non-CPET including Timed Up & Go, grip strength, 6-minute walking test (6MWT) and incremental shuttle walk test (ISWT)). Meta-analysis was precluded due to heterogeneity between study cohorts, different cut-off points, and inconsistent reporting of outcomes. In CPET studies, ventilatory anaerobic threshold and minute ventilation/carbon dioxide production gradient were associated with adverse outcomes. ISWT and 6MWT predicted outcomes in two studies. Tests addressing muscle strength and function were of limited value. No study compared different physical tests.
Discussion: CPET has the ability to predict adverse postoperative outcomes, but it is time-consuming and requires expert assessment. ISWT or 6MWT might be a feasible alternative to estimate aerobic capacity. Muscle strength and function tests currently have limited value in risk prediction. Future research should compare the predictive value of different physical instruments with regard to postoperative outcomes in older surgical patients.

1. Introduction

More than half of the newly diagnosed cancer cases are in patients 65 years and older [1]. Consequently, the population undergoing treatment for cancer is aging rapidly. For abdominal cancers, surgical resection is often the only curative treatment option. As a result of advances in surgical techniques and improved perioperative care, surgery has become an increasingly feasible treatment option for cancer also for the older, more vulnerable patients. However, major abdominal surgery is still associated with considerable morbidity and mortality. Especially older patients have more cardiopulmonary complications [2]. It remains essential to select

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the right patient for the right procedure.

There is great variation in the degree of frailty and physical resilience among older patients, implying that age alone cannot be used as a selection criterion for surgery. The patient's physical condition (a determinant of biological age) is a more important predictor of treatment outcomes than chronological age [3]. Poor physical performance has been previously linked to worse survival and treatment-related complications in older adults with cancer [4,5]. In oncological surgery, an assessment of the older patient's physical status can potentially guide the preoperative decision-making process regarding the further care trajectory. For example, high-risk patients may be referred for preoperative physical enhancement (prehabilitation) or a broader evaluation (such as the Comprehensive Geriatric Assessment (CGA [6])).

At the moment, several different objective physical screening instruments can be used to determine the physical condition of presurgical patients. Such instruments may (indirectly) measure the patient's cardiopulmonary capacity, muscle strength, physical endurance or consist of a combination of different variables. Ideally, a preoperative physical screening instrument has adequate predictive power without being too cumbersome for the patient or the physician. One of the most comprehensive physical assessments is cardiopulmonary exercise testing (CPET) during which the patient's metabolic response to exercise and maximal aerobic capacity are measured. CPET is performed on a cycle ergometer or a treadmill with a progressive increase in workload and results in several different variables with which reduced functional capacity can be identified. The most commonly used CPET-derived variables include oxygen consumption at maximal exercise (peak VO_2), oxygen consumption at anaerobic threshold (VO_2 at AT), and ventilatory (in) efficiency which can be determined by calculating the minute ventilation to carbon dioxide (CO_2) production (V_E/VCO_2 gradient). Field walk tests such as the 6-minute walking test (6MWT) and incremental shuttle walk test (ISWT) test have been suggested as potential surrogates to CPET to estimate cardiopulmonary capacity [7]. Compared to CPET, field walk tests can be performed without special equipment and are more straightforward to interpret. Skeletal muscle strength and function can be assessed with physical tests such as hand grip strength, Timed Up-and-Go (TUG) or Short Physical Performance Battery (SPPB) which are quick to administer and relatively easy to perform for older patients. It is currently not clear which physical tests should preferentially be used to preoperatively assess older patients' physical status in the setting of abdominal cancer surgery. The aims of this systematic review are twofold: first, to identify the instruments that are being used to objectively measure physical functioning in older patients (≥65 years) undergoing major abdominal cancer surgery, and second, to describe the available evidence on the prognostic value of these instruments regarding postoperative outcomes.

2. Methods

The study protocol has been made available online in Prospero (ID 126147). This systematic review was conducted in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [8].

2.1. Eligibility criteria

The inclusion and exclusion criteria are described in detail in Appendix A. Prospective or retrospective cohort studies were eligible for inclusion if they reported on preoperatively measured objective physical test (e.g., CPET, hand grip strength, walk test or a combination of different tests as long as they all measured some physical attribute), at least 80% of the participants were 65 years or older or the median age was at least 70 years, at least 80% of the participants underwent major abdominal surgery for primary or metastatic malignancy (e.g., colorectal cancer surgery or liver metastasectomy), and the study reported on at least one of the following postoperative outcomes: complications including post-operative delirium, short-term mortality (e.g., in-hospital or 90-day mortality), long-term mortality (e.g., 1-year mortality), length of stay (LOS), discharge destination, functional decline, or quality of life (QoL). Studies were ineligible for inclusion if they reported on other types of preoperative assessment (e.g., CGA [6] or Fried's frailty phenotype [9] without reporting on the individual physical components or imaging-based assessment such as muscle mass measured on a CT-scan) or if the participants were subjected to a systematic physical intervention before surgery (e.g., prehabilitation).

2.2. Database search

The databases search was conducted in MEDLINE, Embase, CINAHL and Web of Science on 20 February 2019 and updated on 31 December 2020. A search strategy was constructed in collaboration with a medical librarian and the search terms were defined in three categories using the following terms and related terms: older patients, abdominal (cancer) surgery, and physical performance tests. The search is included in detail in Appendix B. There were no restrictions regarding the publication date or language.

2.3. Study selection

All citations found during database search were imported into Rayyan, a web-based program designed for screening of studies (https://rayyan.qcri.org) [10]. After removing duplicates, two review authors (TA and TH) independently screened the titles and abstracts according to the prespecified inclusion criteria. If an article fit the eligibility criteria set for the screening phase, two review authors independently assessed the full text to reach a final decision on study eligibility. Finally, the reference lists of included studies were hand-searched by one review author for additional potentially eligible studies.

2.4. Data extraction and analysis

Data extraction for each study was performed by one review author (TA) and checked by a second author (TH). The data extracted included study details (e.g., design, setting, number of participants), patient and treatment characteristics (e.g., age, sex, comorbidity level, type of surgery), physical performance assessment (e.g., method, timing, cut-off values), and postoperative outcomes including covariates that were adjusted for in multivariable analyses. If studies reported on more than one follow-up moment (for example, 30- and 90-day complications), the longest follow-up was considered. For dichotomous outcomes, we extracted number and percentage, odds ratios (OR) or hazard ratios (HR) with 95% confidence intervals (CI) as reported in the studies. For continuous outcomes, we extracted mean and standard deviation (SD) or median and (interquartile) range (IQR). For all outcomes, estimates from multivariable analyses were presented when available. A two-tailed p-value <0.05 was considered statistically significant.

2.5. Risk of bias assessment

The risk of bias (ROB) in each study was independently assessed by two review authors (TA and TH) using the QUIPS tool [11]. Disagreements were resolved through discussion and consensus with a third author if necessary.

3. Results

3.1. Selected studies

A flow chart of study inclusion is depicted in Fig. 1. The database search resulted in 9077 records of which 6743 remained after removal of duplicates. After title and abstract screening, 215 records were selected for full text assessment. Hand searching of the full texts did not yield any new publications. Twenty-three publications reporting on 22 individual studies were included in the qualitative synthesis [12–34]. The results of one study were reported in two publications [17,18]. Three studies reported on partially overlapping patient populations with different predictors and outcome assessments [21,25,26].

3.2. Study characteristics

The characteristics of the 23 publications are shown in Table 1. Three studies partly included patients who had abdominal surgery for other indications than cancer (12% inflammatory/diverticular colorectal disease in one study [19], 11% benign colorectal disease in one study, and 11% benign colorectal/esophagogastric/biliopancreatic or liver disease in one study [30]).

Preoperative physical assessment methods varied widely between the studies. An overview of the different tests reported in the review is given in Appendix C. Ten studies focused on the prognostic value of preoperative CPET variables [12,13,20–22,24–26,28,29]. In all ten studies, the testing was performed on a stationary cycle with a ramped exercise protocol. In eight studies, patients were excluded from the study if they were not able to perform CPET or reach the AT [12,13,21,22,24,25,28,29]. The percentage of excluded patients ranged from 1.5% to 6.8%. In six studies [12,20–22,25,26], CPET outcomes were available for clinicians to guide perioperative management. Changes included not proceeding with surgery in case of suboptimal CPET results [12], more invasive intraoperative monitoring [21,22], or elective postoperative admission to higher level care [20–22,25,26].

Twelve studies analyzed preoperative physical assessment methods other than CPET [14–19,23,27,30–34]. The TUG test was the sole focus of six studies [27,30–34], one study considered ISWT [19], three studies focused on two different physical tests (TUG and hand grip strength [15], TUG and gait speed [16] or gait speed and hand grip strength [23]), one study assessed TUG, hand grip strength and chair rise time over 10 repetitions [14], and one study reported on four physical assessment methods (hand grip strength, gait speed, number of chair stands over 30 s (chair stand test), and the 6MWT) [17,18]. Physical tests were not directly compared with each other within the individual studies. Schmidt et al. [32] mentioned explicitly that the physical tests were not used to change the perioperative course of the patients. Dronkers et al. [14] stated that the results of the assessment were not blinded to health care workers. Other studies made no mention of whether the physical test results were available in the clinic.

3.3. Risk of bias assessment

The results of the ROB assessment are shown in Table 2. The two publications of Karlsson et al. [17,18] were rated separately for ROB due to differences regarding study attrition and method of outcome measurement. The overall study quality was moderate to good. Most studies performed well with prognostic factor and outcome measurement. Regarding bias due to study participation, eight studies had a high ROB in this domain due to limited description of the source population and/or unclear or low participation rates [13,17–20,28,29,34]. In seven studies, ROB in study confounding was high mostly due to CPET results being available to guide clinical decision-making [20–22,24–26,28].

3.4. Associations between preoperative physical performance and postoperative outcomes

Associations between physical tests and most often reported outcomes are summarized in Table 3 (for CPET-studies) and Table 4 (for non-CPET studies).

3.4.1. Short-term mortality

The in-hospital mortality reported in nine studies ranged from 0% to 8% [12–14,21,22,24,29,30,32]. 30-day ranged from 0% to 5% in seven studies [17,19,20,23,31–33] and 90-day mortality ranged from 4% to 6% in four studies [21,25,26,28].

Six studies predicted mortality using a preoperative physical performance test [12,14,21,24–26]. Five studies reported on CPET results and mortality [12,21,24–26]. In the study by Junejo et al. [12], AT>9.9 ml/kg/min was associated with lower in-hospital mortality (OR 0.48, 95%CI 0.25–0.94) whereas other CPET variables were not. Snowden et al. [24] showed that patients with

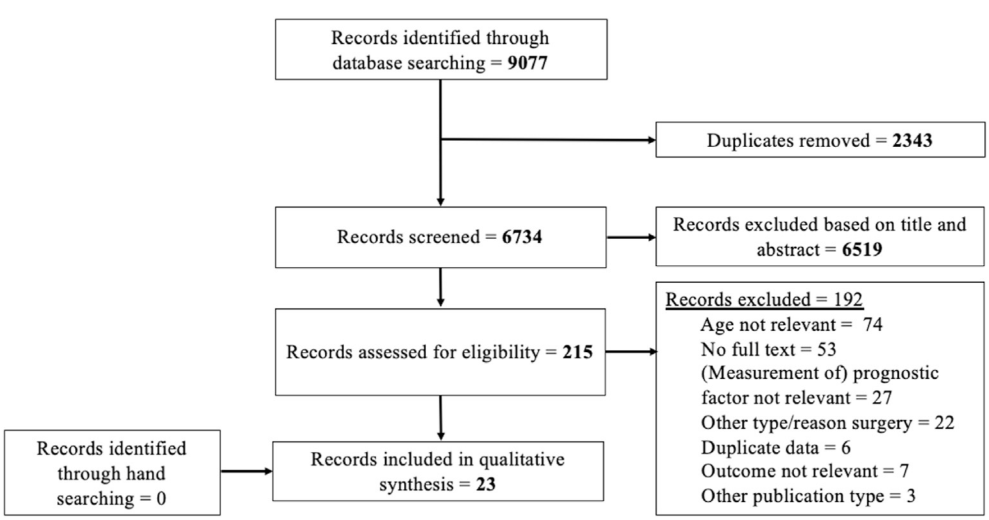

Fig. 1. PRISMA flow chart of study inclusion.

Table 1
Characteristics of included studies.

Reference	Study country & inclusion period	Study design & number of participants	Study bias	Sex, % (M/F)	Age of participants	Type of surgery	Physical assessment	Outcomes	Length of follow-up
Chan 2016 [20]	United Kingdom 2011–2013	Retrospective cohort 48	CPET more often in frail patients; critical care partly based on CPET results	63/37	Median 85	Colorectal cancer surgery	CPET	Overall complications (CDC I–V) Severe complications (CDC III-V) LOS	30 days
Dunne 2014 [22]	United Kingdom 2009–2012	Retrospective cohort 197	High-risk CPET patients admitted to critical care	70/30	Median 70	Hepatic resection for malignancy	CPET	Overall complications (CDC I–V) Severe complications (CDC III-IV) LOS	30 days
Junejo 2012 [12]	United Kingdom 2007–2009	Prospective cohort 94	CPET results may have been used to decline surgery	64/36	Median 71	Hepatic resection for malignancy	CPET	Overall complications (postoperative morbidity survey) In-hospital mortality LOS	Duration of admission
Mann 2020 [26]	United Kingdom 2004–2016	Retrospective cohort 1214	CPET results used to guide clinical management	59/41	Mean 72	Colorectal cancer surgery	CPET	Postoperative mortality Prolonged LOS (top quartile in the cohort) Overall survival	90 days 2 years
Prentis 2013 [13]	United Kingdom Not reported	Prospective cohort 69	Patients excluded if AT was not attained (7%)	70/30	Mean 70	Radical cystectomy for bladder cancer	CPET	Severe complications (CDC III-V) LOS	Duration of admission
Snowden 2013 [24]	United Kingdom Not reported	Prospective cohort 389, subgroup >75 years 57	Patients excluded if AT was not attained (4%)	14/86	Mean 66, subgroup >75 years	Hepatectomy, pancreaticoduodenectomy or sarcoma resection	CPET	In-hospital mortality LOS	Duration of admission
Tolchard 2015 [28]	United Kingdom Not reported	Prospective cohort 105	Patients excluded if AT was not attained (2%)	84/16	Median 71	Radical cystectomy for bladder cancer	CPET	Overall complications (CDC II-V) Postoperative mortality LOS	90 days
West 2014 [29]	United Kingdom 2009–2010	Prospective cohort 136	Patients excluded if AT was not attained (2%)	65/35	Median 71	Major colonic surgery (89% oncological surgery)	CPET	Overall complications within 5 days of surgery (postoperative morbidity survey, CDC I–V) Postoperative mortality LOS	30 days
Wilson 2010 [21]	United Kingdom 2004–2009	Retrospective cohort 847	CPET results used to guide clinical management	60/40	Mean ~70	Colorectal, bladder or kidney cancer resection	CPET	Postoperative mortality	90 days
Wilson 2019 [25]	United Kingdom 2004–2016	Retrospective cohort 1375	CPET results used to guide clinical management	59/41	Mean 72	Colorectal cancer surgery	CPET	Postoperative mortality Overall survival	90 days 5 years
Brouquet 2010 [30]	France 2006–2008	Prospective cohort 118	No mention whether physical test results available in the clinic	47/53	Mean 81	Major abdominal surgery (87% oncological surgery)	TUG	Postoperative delirium	30 days
Giannotti 2020 [27]	Italy 2015–2017	Prospective cohort 99	No mention whether physical test results available in the clinic	63/37	Mean 80	Colorectal and gastric cancer surgery	TUG	Overall complications Mortality	NR 1 year
Monacelli 2018 [31]	Italy Jan–Dec 2016	Prospective cohort 107	No mention whether physical test results available in the clinic	32/67	Mean 80	Colorectal cancer surgery	TUG	Postoperative delirium	Duration of admission
Schmidt 2018 [32]	Germany 2008–2010	Prospective cohort 131	–	44/56	Median 71	Surgery for thoracoabdominal, gynecological or urogenital cancer	TUG	Overall survival	12 months
Scholtz 2018 [33]	Germany 2011–2014	Prospective cohort 517	No mention whether physical test results available in the clinic	68/32	Median 71	Surgery for upper gastrointestinal, urological, gynecological, colorectal or prostate cancer	TUG	Overall complications (ordinal variable CDC 0-V) Severe complications (CDC III-V)	30 days
Ugolini 2015 [34]	Italy 2009–2012	Prospective cohort 46	No mention whether physical test results available in the clinic	52/48	Median 80	Colorectal cancer surgery	TUG	Overall survival	Median 4.6 years
Dronkers 2013 [14]	The Netherlands 2006–2009	Prospective cohort 169	No mention whether physical test results available in the clinic	59/41	Median >70	Colorectal cancer surgery	TUG HGS CRT (10 repetitions)	In-hospital mortality Discharge destination (other than home) LOS	Duration of admission
					Median 82	Colorectal cancer surgery			

(continued on next page)

Table 1 (*continued*)

Reference	Study country & inclusion period	Study design & number of participants	Study bias	Sex, % (M/F)	Age of participants	Type of surgery	Physical assessment	Outcomes	Length of follow-up
Rønning 2014 [15]	Norway 2006–2009	Prospective cohort 84	No mention whether physical test results available in the clinic	41/59			TUG HGS	Functional decline (decrease in Barthel Index or NEADL index)	Median 22 months
Burg 2019 [16]	United States 2014–2017	Prospective cohort 123	No mention whether physical test results available in the clinic	83/17	Median 74	Radical cystectomy for bladder cancer	GS over 15 feet (4.5 m) HGS	Overall complications Severe complications (CDC ≥ IIIa)	90 days
Chandoo 2018 [23]	China 2014–2016	Prospective cohort 357	Patients using walking aid were excluded; No mention whether physical test results available in the clinic	72/28	Mean 73	Gastric cancer surgery	GS over 6 m HGS	Overall complications (CDC ≥ II) Medical complications Surgical complications LOS	30 days
Karlsson 2018 [17]	Sweden 2015–2017	Prospective cohort 191	No mention whether assessment results available in the clinic	60/40	Mean 76	Abdominal cancer surgery	GS over 10 m (habitual speed and maximal speed) HGS CST (number of repetitions in 30 s) 6MWT	Overall complications (CDC I–V) Discharge destination (other than rehab/home)	30 days
Karlsson 2019 [18]	Sweden 2015–2017	Prospective cohort 191	No mention whether assessment results available in the clinic	60/40	Mean 76	Abdominal cancer surgery	GS over 10 m (habitual speed and maximal speed) HGS CST (number of repetitions in 30 s) 6MWT	Functional decline (inability to perform CST)	Duration of admission
Nutt 2012 [19]	United Kingdom Not reported	Prospective cohort 120	Patients unable to walk unaided were excluded; no mention whether physical test results available in the clinic	50/50	Mean 72	Colorectal surgery (88% oncological surgery)	ISWT (distance covered)	Overall complications (postoperative morbidity survey, CDC I–V) Severe complications (CDC ≥ III) LOS	30 days

Abbreviations: 6MWT *6-min walk test*; AT *anaerobic threshold*; BMI *body mass index*; CDC *Clavien-Dindo classification*; CRT *chair rise time*; CST *chair stand test*; CPET *cardio-pulmonary exercise testing*; GS *gait speed*; HGS *hand grip strength*; IQR *interquartile range*; ISWT *incremental shuttle walk test;* LOS *length of stay*; NEADL *Nottingham Extended Activities of Daily Living*; NR *not reported;* TUG *Timed Up&Go.*

AT<10 ml/kg/min had a higher in-hospital mortality (22% vs 4%, p = 0.01). In their 2010 study, Wilson et al. [21] showed that both AT≤10.9 ml/kg/min and V_E/VCO_2>34 were associated with 90-day mortality (5% vs 2%, p = 0.034, and 6% vs 2%, p = 0.021, respectively). In their 2019 study, Wilson et al. [25] used another cut-off for ventilatory inefficiency (V_E/VCO_2>39). High V_E/VCO_2 was associated with increased 90-day mortality in multivariable analysis (OR 4.04, 95% CI 2.09–7.84). Mann et al. [26] reported on 90-day mortality. The study was mainly focused on oxygen pulse response (surrogate for cardiac stroke volume), but standard CPET variables were also reported. AT<11 ml/kg/min was not associated with mortality. V_E/VCO_2>34 was associated with the outcome in univariable analysis (p = 0.016), but not in multivariable analysis. Abnormal oxygen pulse response was associated with increased mortality in multivariable analysis (OR 2.76, 95% CI 1.36–5.60).

Regarding non-CPET tests, Dronkers et al. [14] reported results on several physical assessment tests (TUG, hand grip strength and chair rise time), but none of them predicted in-hospital mortality.

3.4.2. Long-term mortality

Two studies [27,32] reported on 1-year survival (19%–28% mortality rate), one study reported on 2-year survival [26] (mortality rate not reported), and one study [34] reported survival over a median follow-up of 4.6 years (39% mortality rate).

Three studies reported on the association between a physical test and long-term survival.[32,3426] In the only CPET study reporting on long-term survival, Mann et al. [26] showed that V_E/VCO_2>34 and abnormal oxygen pulse response were associated with increased mortality in multivariable analyses (OR 1.57, 95% CI 1.12–2.20 and OR 1.56, 95% CI 1.10–2.23, respectively).

Regarding non-CPET studies, impaired TUG (>20s) predicted mortality in the study by Ugolini et al. [34] (HR 3.507, 95%CI 1.35–9.11). In contrast, Schmidt et al. [32] did not find an association between impaired TUG (≥10s) and mortality.

3.4.3. Overall complications

Twelve studies reported on postoperative overall complications during hospital admission (incidence 51–56%) [12,13] or within 5 days (incidence 48%) [29], 30 days (incidence 18–74%) [17,19,20,22,23,33] or 90 days of surgery (incidence 31–59%) [16,28]. One study only reported the OR without specifying the number of patients with complications or follow-up duration [27]. Most studies treated complications as a dichotomous variable. Karlsson et al. [17] analyzed complications as an ordinal variable (increasing severity on the Clavien-Dindo Classification (CDC) score 1–5).

Six CPET-studies reported on at least two CPET variables and postoperative complications. West et al. [29] found significant

Table 2
Risk of bias in included studies.

Reference	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting
Chan 2016[20]	High	Low	Low	Low	High	Moderate
Dunne 2014[22]	Moderate	Low	Low	Low	High	Moderate
Junejo 2012[12]	Moderate	Low	Low	Low	Low	Low
Mann 2020[26]	Low	Low	Moderate	Low	High	Moderate
Prentis 2013[13]	High	Low	Moderate	Moderate	Moderate	High
Snowden 2013[24]	Moderate	Low	Low	Low	High	Low
Tolchard 2015[28]	High	Low	Low	Low	High	High
West 2014[29]	High	Moderate	Low	Low	Moderate	Low
Wilson 2010[21]	Low	Low	Low	Low	High	Low
Wilson 2019[25]	Low	Low	Moderate	Low	High	Moderate
Brouquet 2010[30]	Low	Low	Moderate	Moderate	Moderate	Low
Monacelli 2018[31]	Moderate	Moderate	High	Low	Moderate	Moderate
Schmidt 2018[32]	Moderate	Low	Low	Low	Low	Low
Scholtz 2018[33]	Moderate	Moderate	Moderate	Low	Low	Low
Ugolini 2015[34]	High	Low	Moderate	Moderate	Moderate	Moderate
Burg 2019[16]	Moderate	Moderate	Moderate	Low	Low	Low
Chandoo 2018[23]	Moderate	Low	Low	Low	Low	Moderate
Dronkers 2013[14]	Moderate	Low	Moderate	Low	Moderate	Moderate
Giannotti 2020[27]	Moderate	High	Moderate	Moderate	Moderate	High
Karlsson 2018[17]	High	Low	Low	Low	Low	Low
Karlsson 2019[18]	High	Moderate	Low	Low	Low	Low
Rønning 2014[15]	Moderate	High	Low	Moderate	Moderate	Moderate
Nutt 2012[19]	High	Low	Low	Low	Low	Moderate

relationships between AT, peak VO_2, V_E/VCO_2 and 5-day complications in univariable analyses. In multivariable analysis, higher AT was independently associated with a lower risk of complications when adjusted for the other CPET variables and sex (OR 0.77, 95% CI 0.66–0.89, $p < 0.0005$). They also mentioned that all three patients who were unable to attain AT (and who were excluded from formal analyses) had complications. Tolchard et al. [28] analyzed the same three variables. In multivariable analyses, AT and V_E/VCO_2, but not peak VO_2, remained predictors of complications in multivariable analyses. A unit decrease in AT (OR 1.38, 95% CI 1.11–1.73) and in V_E/VCO_2 (OR 1.38, 95% CI 1.11–1.73) were associated with a higher risk of complications. Junejo et al. [12] considered AT and V_E/VCO_2. Only $V_E/VCO_2 \geq 34.5$ was found to be predictive of complications in multivariable analysis adjusted for age (OR 3.97, 95%CI 1.44–10.96). Prentis et al. [13] analyzed AT, peak VO_2 and V_E/VCO_2 but found no association between any of the variables and complications. Likewise, Chan et al. [20] found no association between AT, peak VO_2 and complications. Finally, Dunne et al. [22] analyzed seven different CPET variables including AT, peak VO_2 and V_E/VCO_2 in relation to postoperative complications. Heart rate (HR) at AT was the only variable that was associated with complications remained associated in multivariable analysis.

In the non-CPET studies, gait speed and hand grip strength were the most frequently reported tests [16,17,23]. In the study by Karlsson et al. [17], a unit increase in maximal gait speed was associated with less overall complications in multivariable analysis (OR 0.29, 95% CI 0.13–0.63) whereas habitual gait speed was not. Burg et al. [16] found that although slower gait speed was associated with 90-day complications in univariable analysis ($p = 0.042$), it did not remain a predictor in multivariable analysis. Chandoo et al. [23] found no association between slow gait speed (<0.8 m/s) and overall or surgical complications. However, compared to patients with normal gait speed, patients with slow gait speed were more likely to develop medical complications in a model adjusted for age ($p = 0.027$). Regarding hand grip strength, Karlsson et al. [17] showed that higher hand grip strength was associated with less complications in a multivariable model (OR 0.94, 95% CI 0.90–0.97) whereas Burg et al. [16] and Chandoo et al. [23] found no association. Karlsson et al. [17] also considered chair stand test and 6MWT. Each extra repetition on chair stand test (OR 0.91, 95% CI 0.85–0.98) and each extra 20-m increment on 6MWT (OR 0.92, 95% CI 0.87–0.98) were associated with a lower risk of complications in multivariable analyses. In the study by Nutt et al. [19], patients were preoperatively assessed with ISWT. Patients with complications performed worse on ISWT compared to patients without complications (mean 276.6 m vs 389.6 m, $p < 0.001$). When the ISWT results were dichotomized to <250 m vs > 250 m, it was shown that patients who were not able to attain 250 m had a higher risk of complications (79.5% vs 27.2%, $p < 0.0001$). Finally, two studies reported on TUG [27,33]. Giannotti et al. [27] found a correlation between increasing TUG and complications (OR 1.15, 95% CI 1.00–1.33). Scholtz et al. [33], compared impaired TUG (>20s) and normal TUG (<11s) and showed that patients with impaired TUG had a higher risk of complications in multivariable analysis (OR 2.59, 95% CI 1.05–6.39).

3.4.4. Severe complications

Six studies reported on severe postoperative complications (CDC score ≥3) during hospital admission (incidence 16%) [13], within 30 days (incidence 13–30%) [19,20,22], or within 90 days of surgery (incidence 19–26%) [16,33].

Prentis et al. [13] found AT to be associated with severe complications after adjusting for other CPET variables, sex, age and BMI (OR 0.74, 95% CI 0.57–0.97). Peak VO_2 or V_E/VCO_2 did not predict

Table 3
Associations between preoperative physical fitness as assessed with cardiopulmonary exercise testing and study outcomes.

Ref	CPET variable	Cut-off	CPET results	Short-term mortality	Long-term mortality	Complications	Severe complications	LOS
Chan 2016 [20]	VO_2 at AT	Continuous (ml/kg/min)	NR	–	– –	Univariable: ns	Multivariable: ns	Univariable: ns
	Peak VO_2	Continuous (ml/kg/min)	NR	–		Univariable: ns	Univariable: ns	Univariable: ns
Dunne 2014 [22]	VO_2 at AT	Continuous (ml/kg/min)	Mean 11.5 (SD 2.4)	–	–	Univariable: ns	Univariable: ns	Univariable: ns
	Peak VO_2	Continuous (ml/kg/min)	Mean 17.8 (SD 4.5)	–	–	Univariable: ns	Univariable: ns	Univariable: ns
	V_E/VCO_2 at AT	Continuous	Mean 31.6 (IQR 28.5–35.0)	–	–	Univariable: ns	Univariable: ns	Univariable: ns
Junejo 2012 [12]	VO_2 at AT	Continuous (ml/kg/min)	Median 11.2 (range 7.4–21.0)	–	–	Univariable: ns	–	–
		<9.9 ml/kg/min	NR	**Univariable: OR 0.48, p = 0.032**	–	–	–	Univariable: ns
	V_E/VCO_2 at AT	≥34.5	Median 32.0 (range 23.0–45.0)	Univariable: ns	–	**Multivariable: OR 3.97 p = 0.008**	–	–
Mann 2020 [26]	VO_2 at AT	<11 ml/kg/min	High risk: 540 Low risk: 665	Univariable: ns	Univariable: ns	–	–	–
	V_E/VCO_2 at AT	>34	High risk: 464 Low risk: 729	Multivariable: ns	**Multivariable: OR 1.57, p = 0.009**	–	–	**Univariable: OR 1.66, p<0.001**
Prentis 2013 [13]	VO_2 at AT	Continuous (ml/kg/min)	NR	–	–	Univariable: ns	**Multivariable: OR 0.74, p = 0.03**	–
		<12 ml/kg/min	NR	–	–	Univariable: ns	–	**22 vs 16 days, p = 0.006**
	Peak VO_2	Continuous (ml/kg/min)	NR	–	–	Univariable: ns	Univariable: ns	–
	V_E/VCO_2 at AT	Continuous	NR	–	–	Univariable: ns	Univariable: ns	–
Snowden 2013 [24]	VO_2 at AT	<10 ml/kg/min	Mean 11.3 (SD 2.7)	–	–	–	–	**23 vs 12 days, p<0.001**
Tolchard 2015 [28]	VO_2 at AT	Continuous (ml/kg/min)	Median 11.2 (range 5.8–22.0)	–	–	**Multivariable: OR 1.38, p = 0.005**	–	**p = 0.035**
	Peak VO_2	Continuous (ml/kg/min)	Median 15.2 (range 9.0–27.6)	–	–	Multivariable: ns	–	Univariable: ns
	V_E/VCO_2 at AT	Continuous	Median 31 (range 21–47.2)	–	–	**Multivariable: OR 1.16, p = 0.008**	–	**p = 0.001**
		≥33	NR	–	–	–	–	**13 vs 9 days, p = 0.008**
West 2014 [29]	VO_2 at AT	Continuous (ml/kg/min)	Mean 11.5 (SD 2.4)	–	–	**Multivariable: OR 0.77, p<0.0005**	–	–
		<10.1 ml/kg/min	NR	–	–	–	–	**p = 0.003**
	Peak VO_2	Continuous (ml/kg/min)	Mean 17.8 (SD 4.5)	–	–	Multivariable: ns	–	–
		<16.7 ml/kg/min	NR	–	–	–	–	**p = 0.004**
	V_E/VCO_2 at AT	Continuous	Mean 28.6 (SD 5.0)	–	–	Multivariable: ns	–	–
		>32.9	NR	–	–	–	–	**p<0.001**
Wilson 2010 [21]	VO_2 at AT	≤10.9 ml/kg/min	High risk: 457 Low risk: 390	**5% vs 2%, p = 0.034**	–	–	–	**9 vs 8 days, p = 0.001**
	V_E/VCO_2 at AT	≥34	High risk: 442 Low risk: 405	**6.2% vs 2%, p = 0.021**	–	–	–	–
Wilson 2019 [25]	VO_2 at AT	Continuous	Median 11.2 (range 9.6–13.0)	Univariable: ns	–	–	–	–
	V_E/VCO_2 at AT	>39	High risk: 245 Low risk: 1127	**Multivariable: OR 4.04, p<0.001**	**Multivariable: OR 2.67, p<0.001**	–	–	–

Abbreviations: AT *anaerobic threshold*; CPET *cardiopulmonary exercise testing*; IQR *interquartile range;* LOS *length of stay*; OR *odds ratio;* SD *standard deviation;* NR *not reported;* ns *not significant;* VE/VCO_2 *minute ventilation/carbon dioxide production*; VO_2 *oxygen uptake*.

severe complications in their study. Chan et al. [20] found no significant relationship between AT, peak VO_2 and V_E/VCO_2 and severe complications. Dunne et al. [22] performed multivariable analyses with several CPET variables and found that only HR at AT (beats/min) was associated with severe complications.

Regarding non-CPET tests, four different tests were analyzed in three separate studies [16,19,33]. In the study by Burg et al. [16], lower gait speed was associated with an increased risk of 90-day severe complications when adjusted for age (OR 1.70, 95% CI 1.05–2.89). In the same study, lower hand grip strength was not associated with severe complications. In the study by Nutt et al. [19], preoperative ISWT distance was lower in patients who experienced severe complications compared to patients with no or minor complications (mean 256.8 m vs 382.7 m, $p < 0.001$). In the study by Scholtz et al. [33], TUG was not associated with severe complications in univariable analysis.

3.4.5. *Length of stay*

Twelve studies reported on LOS [12–14,19–24,26,28,29]. Regarding CPET-results, AT below a cut-off value (11–12 ml/kg/

Table 4
Associations between preoperative physical fitness as assessed with short physical tests other than cardiopulmonary exercise testing and study outcomes.

Reference	Physical assessment	Cut-off	Physical assessment results	Short-term mortality	Long-term mortality	Complications	Severe complications	LOS	Functional decline
Brouquet 2010 [30]	TUG	>20 s	Impaired: 21 Not impaired: 97	–	–	Delirium **Multivariable: OR 4.8, p = 0.009**	–	–	–
Giannotti 2019 [27]	TUG	Continuous (s)	NR	–	Univariable: ns	**Univariable: OR 1.15, p = 0.048**	–	–	–
Monacelli 2018 [31]	TUG	Continuous (s)	Mean 10.84 (SD 0.59)	–	–	Delirium **Multivariable: OR 1.18, p = 0.005**	–	–	–
Schmidt 2018 [32]	TUG	≥20 s	Impaired: 43 Not impaired: 88	–	Univariable: ns	–	–	–	–
Scholtz 2018 [33]	TUG	>20 s	Impaired: 20 Not impaired: 388	–		**Multivariable: OR 2.59, p = 0.039**	Multivariable: ns	–	–
Ugolini 2015 [34]	TUG	>20 s	Impaired: 11 Not impaired: 35	–	**Univariable: HR 3.507, p = 0.01**	–	–	–	–
Dronkers 2013 [14]	TUG	>8 s	Impaired: 66 Not impaired: 109	–	–	–	–	Univariable: ns	–
		>11 s	Impaired: 24 Not impaired: 151	Multivariable: ns	–	–	–	–	–
	HGS	<233 N	Impaired: 37 Not impaired: 183	Multivariable: ns	–	–	–	–	–
		<240 N	Impaired: 40 Not impaired: 135	–	–	–	–	Univariable: ns	–
	CRT	>25 s	Impaired: 81 Not impaired: 94	–	–	–	–	Univariable: ns	–
		>27 s	Impaired: 62 Not impaired: 113	Univariable: ns	–	–	–	–	–
Rønning 2014 [15]	TUG	≥19 s	Median 12 IQR 8-17	–	–	–	–	–	Univariable: ns
	HGS	Gender- and BMI-specific cut-off (kg)	Median 29.4 (IQR 9.9)	–	–	–	–	–	Univariable: ns
Burg 2019 [16]	HGS	Continuous (kg)	Median 28 (IQR 21–35)	–	–	Univariable: ns	Univariable: ns	–	–
	HGS	Gender- and BMI-specific cut-off (kg)	Impaired: 60 Not impaired: 62	–	–	Univariable: ns	Univariable: ns	–	–
	GS	Continuous (m/s)	Median 5.08 (IQR 4.15 –5.69)	–	–	Univariable: ns	**Multivariable: OR 1.70, p = 0.038**	–	–
	GS	Gender- and height- specific cut-off (m/s)	Impaired: 16 Not impaired: 96	–	–	Univariable: ns	Univariable: ns	–	–
Chandoo 2018 [23]	HGS	Males <26 kg, females <18 kg	Impaired: 145 Not impaired: 212	–	–	Univariable: ns	–	–	–
	GS	<0.8 m/s	Impaired: 95 Not impaired: 262	–	–	Univariable: ns	–	**19.88 vs 16.42 days, p = 0.003**	–
Karlsson 2018 & 2019 [17,18]	HGS	Continuous (k/g)	Mean 31.5 (SD 11.7)	–	–	**Multivariable: OR 0.94, p = 0.001**	–	–	**Multivariable: OR 0.91, p = 0.012**
	GS (habitual)	Continuous (m/s)	Mean 1.23 (SD 0.25)	–	–	Multivariable: ns	–	–	**Multivariable: OR 0.00, p = 0.001**

(*continued on next page*)

Table 4 (*continued*)

Reference	Physical assessment	Cut-off	Physical assessment results	Short-term mortality	Long-term mortality	Complications	Severe complications	LOS	Functional decline
	GS (maximal)	Continuous (m/s)	Mean 1.85 (SD 0.41)	–	–	**Multivariable: OR 0.29, p = 0.002**	–	–	**Multivariable: OR 0.05, p = 0.002**
	CST	Continuous (N repetitions)	Mean 13 (SD 4)	–	–	**Multivariable: OR 0.91, p = 0.01**	–	–	**Multivariable: OR 0.74, p = 0.004**
	6MWT	Continuous (m)	Mean 462 (SD 108)	–	–	**Multivariable: OR 0.92, p = 0.006**	–	–	**Multivariable: OR 0.82, p = 0.003**
Nutt 2012 [19]	ISWT	Continuous (m)	Mean 340 (SD 148)	–	–	**Univariable: p<0.001**	**Univariable: p<0.001**	–	–
	ISWT	<250 m	NR	–	–	**Impaired: 79.5% vs not impaired: 27.2%, p<0.0001**	**Univariable: p<0.001**	**14 vs 8 days, p<0.0001**	–

Abbreviations: 6MWT *6-min walk test*; BMI *body mass index*; CRT *chair rise time*; CST *chair stand test*; GS *gait speed*; HGS *hand grip strength*; HR *hazard ratio;* IQR *interquartile range*; ISWT *incremental shuttle walk test;* LOS *length of stay*; NR *not reported;* ns *not significant;* SD *standard deviation;* TUG *Timed Up&Go.*

min) was associated with longer LOS in the studies by Wilson et al. [21] (median 9 vs 8 days, p = 0.001), Prentis et al. [13] (median 22 vs 16 days, p = 0.006) and Snowden et al. [24] (median 23 vs 12 days, p < 0.0001). Junejo et al. [12] found no correlation between AT and LOS. In the study by West et al. [29], lower AT was correlated with longer LOS (p = 0.003) and patients with peak VO_2 < 16.7 ml/kg/min and $V_E/VCO_2>33$ also had longer LOS (p = 0.004 and p < 0.001, respectively). Tolchard et al. [28] also reported on three CPET variables. In their study, AT was inversely correlated with LOS (p = 0.035). $V_E/VCO_2>33$ was also associated with longer LOS (median 13 vs 9 days, p = 0.008) whereas peak VO_2 was not [28]. Chan et al. [20] did not find a correlation between AT or peak VO_2 and LOS. In the study by Mann et al. [26], patients with $V_E/VCO_2>34$ had a higher risk of prolonged LOS (OR 1.66, 95% CI 1.27–2.17). Dunne et al. [22] performed multivariable analyses with several CPET variables; in their study absolute AT (L/min) was the only variable that was independently associated with LOS.

Three non-CPET studies reported on LOS; only univariable analyses were performed. Chandoo et al. [23] analyzed gait speed as predictor of LOS; patients with gait speed <0.8 m/s had a longer LOS (19.88 vs 16.42 days, p = 0.003). Nutt et al. [19] showed that patients who were not able to reach 250 m on ISWT had a longer LOS (14.0 vs 8.0 days, p < 0.0001). Dronkers et al. [14] analyzed several physical tests (TUG, hand grip strength, chair rise time), but none of them were associated with LOS.

3.4.6. Postoperative delirium

Two studies reported on the association between TUG and postoperative delirium (incidence 12–24%) [30,31]. Postoperative delirium was diagnosed by a geriatrician according to the Confusion Assessment Method [30] or the 4AT test [31]. Brouquet et al. [30] showed that a TUG>20s was an independent risk factor for postoperative delirium in a multivariable model adjusted for ASA-status and tramadol administration (OR 4.8, 95% CI 1.5–15.6). Similarly, Monacelli et al. [31] showed that each extra second on TUG was associated with an increased risk of postoperative delirium when adjusted for age and sex (OR 1.18, 95% CI 1.05–1.31).

3.4.7. Discharge destination

Discharge destination was reported in two studies [14,17]. Karlsson et al. [17] showed that each 20-m increment on 6MWT (OR 0.89, 95% CI 0.79–0.99), higher hand grip strength (OR 0.90, 95% CI 0.82–0.98) and higher maximal gait speed (OR 0.14, 95% CI 0.02–0.93) were associated with lower odds of being discharged to a nursing home in multivariable models adjusted for age, sex and duration of surgery or surgical approach. Chair stand test and habitual gait speed did not remain predictors in multivariable analysis. Dronkers et al. [14] found no association between TUG and discharge destination other than home.

3.4.8. Functional decline

Two studies reported on the association between physical tests and functional decline [15,18]. Karlsson et al. [18] reported on short-term functional impairment (the inability to rise from a chair without assistance at hospital discharge) (incidence 15%). They showed that each 20-m increment on 6MWT (OR 0.82, 95% CI 0.73–0.94), each extra repetition on chair stand test (OR 0.74, 95% CI 0.60–0.91), higher hand grip strength (OR 0.91, 95% CI 0.84–0.98, p = 0.012) and higher habitual (OR 0.00, 95% CI 0.00–0.06) and maximal gait speed (OR 0.05, 95% CI 0.01–0.35) were all associated with lower odds of functional decline in models adjusted for age, sex and duration of surgery. Rønning et al. [15] reported on long-term functional decline (1-point decrease in Barthel Index (incidence 31%) or 4-point decrease in Nottingham Extended Activities of Daily Living (NEADL) Scale (incidence 69%) after a median of 22 months). They found no association between TUG or hand grip strength and the outcomes.

4. Discussion

Improvements in perioperative care have led to less morbidity and mortality also in older patients, but the patient's physical condition remains an important determinant of a successful postoperative recovery. As physical fitness is a sum of many factors, different approaches have been introduced to measure the patients' physical reserve preoperatively. In this systematic review, we included 23 publications that evaluated a wide variety of different physical assessment instruments with regard to their ability to predict postoperative outcomes in the older population undergoing oncological abdominal surgery.

Major surgery leads to higher metabolic demands of the body which in healthy individuals are matched by concomitant increases in cardiac output and ventilation. Patients with insufficient cardiopulmonary reserves are therefore at risk for postoperative complications. Previous studies on CPET have demonstrated its utility as a risk stratification tool in abdominal surgery [35,36]. This is the first review with a specific focus on older patients undergoing intra-abdominal cancer surgery.

There were differences in the predictive potential among the CPET variables. Compared to peak VO_2 which was not an independent predictor of any outcomes in any of the included studies, VO_2 at AT and V_E/VCO_2 performed relatively well. VO_2 at AT was an independent predictor of complications in three studies and V_E/VCO_2 was independently associated with complications (two studies) and mortality (two studies). In the included studies, VO_2 at AT between 9 and 11 ml/kg/min was consistently used to define at-risk groups which was in accordance with studies on other cohorts undergoing intra-abdominal surgery [36]. A cut-off value for V_E/VCO_2 of $\geq$33 was also consistently used in the present studies. However, almost half of the CPET studies reported on continuous predictor variables instead of defining at-risk groups which is an area for improvement.

Most CPET studies excluded patients who were unable to perform CPET or attain AT and, with the exception of one study [29], no outcome data were reported for these patients. As shown in a previous study, not achieving AT likely reflects low physical fitness and thus predicts an increased risk of postoperative complications [37]. In addition, in half of the studies, CPET results were used to influence the clinical course of the patients. It is possible that this resulted in underestimation of the predictive potential of CPET. For example, standard CPET variables did not predict complications in the two studies that had made the results available in the clinic [20,22], whereas all four studies in which CPET results were not available did find an association between at least one variable and complications [12,13,28,29]. On the other hand, more intensive postoperative monitoring or admission to higher level care of high-risk patients could have led to more diligent reporting of complications.

The main drawbacks of CPET are that it is time-consuming and requires expert assessment. Having to make an extra appointment in the hospital to perform the test might be too cumbersome for the more vulnerable older patients. It can also be difficult for older patients to reach maximal exercise which may also explain the fact that peak VO_2 was not a useful prognostic variable in the older patient population. Therefore, CPET may not be the most feasible initial risk assessment tool when considering the older patient population. Submaximal exercise tests (field walk tests) have been proposed as a potential surrogate to assess older patients' cardiopulmonary capacity. The 6MWT and ISWT have been developed for this purpose. A previous study in patients with colorectal cancer showed a positive correlation between 6MWT and CPET-derived VO_2 max; both were associated with increased postoperative morbidity [38]. In another study in patients with lung cancer, ISWT correlated with CPET-derived VO_2 max whereas 6MWT did not [39]. However, we identified only two studies that addressed these tests as risk prediction tools and although they were associated with negative outcomes in both studies, more research is required to validate these results.

Next to measuring cardiopulmonary capacity, a preoperative assessment of skeletal muscle strength and function may help to detect at-risk patients. Postoperative immobility (even in the absence of complications) can lead to a significant loss of muscle mass and strength [40,41]. In patients with low baseline muscle mass and function (sarcopenia), this can potentially lead to permanent functional decline. We identified several tests that measured some aspect of muscle strength or function in the older patient population (TUG, gait speed, chair rise time, chair stand test, and hand grip strength). TUG was the most often reported test, and although it was independently associated with delirium and complications in three studies [30,31,33], it failed to predict negative outcomes in the remaining studies or only univariable analyses were performed [14,15,27,32,34]. Hand grip strength had the least predictive potential, as it was only associated with postoperative outcomes in one of the five studies. For practical uses, consistent cut-off points need to be defined for what constitutes an impaired result. The four different cut-off values for TUG in this review clearly demonstrate the need for further standardization. Therefore, despite the positive findings in some of the studies, none of the instruments assessing muscle strength or function can currently be recommended as risk prediction tools in older patients undergoing oncological-abdominal surgery.

None of the studies included in this review chose to aggregate the results of different physical tests in order to arrive at a more robust definition of physical frailty. A combination of physical instruments measuring different elements (for instance, aerobic fitness and muscle strength) might provide a more comprehensive view on the patient's physical condition than a single preoperative test. For example, the SPPB consists of three elements assessing muscle function (balance, walking speed and lower extremity strength) and has been shown to predict complications and mortality in lung and cardiac surgery patients [42,43]. It should also be mentioned that, although not in the scope of this review, malnutrition is also a determinant of physical frailty and contributes to sarcopenia [44] and measuring nutritional status next to other objective physical parameters may improve risk prediction.

Next to their potential value in risk prediction, poor physical performance indices can serve as targets to improve the patient's physical status in the preoperative phase. CPET and 6MWT have been previously successfully used to measure changes in physical fitness levels after prehabilitation in (colo)rectal cancer patients, and for both, minimally clinically important differences have been determined [45–49]. A recent RCT in patients with poor cardiopulmonary fitness based on low anaerobic threshold (<11 ml/kg/min) undergoing colorectal cancer surgery showed that patients who received a moderate-to-high intensity exercise intervention experienced significant preoperative improvements in CPET parameters and had less complications than the control group [49]. Another recent RCT showed that frail older patients with colorectal cancer who had received moderate intensity exercise prehabilitation but were afterwards unable to attain 400 m on the 6MWT suffered more postoperative complications, implying that 400 m could be set as the minimum threshold to indicate successful prehabilitation [50]. It may also be possible to mitigate low muscle mass and strength through exercise and nutritional interventions, although data on the effectiveness of interventions to combat sarcopenia in older patients undergoing cancer surgery are still scarce [51].

5. Conclusion

There is a wide variety of objective physical performance tests available for older patients undergoing major abdominal cancer surgery ranging from aerobic fitness to muscle strength and function tests. CPET is a comprehensive assessment of the patient's cardiopulmonary capacity with the ability to predict adverse postoperative outcomes, but it is time-consuming and requires expert assessment. It may not be the most suitable initial test to screen all older preoperative patients. The field walk tests (6MWT and ISWT) might be a feasible alternative to estimate aerobic capacity, but studies comparing these instruments to CPET and as risk predictors in older patients undergoing abdominal cancer surgery are still scarce. Physical tests addressing muscle strength or function currently appear to have limited value as risk prediction instruments. Future studies should compare the predictive value of different objective physical tests using standardized outcome measures, determine appropriate cut-off points for impaired physical performance, and demonstrate that the test improves traditional preoperative risk prediction with acceptable positive and negative predictive values.

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Appendix A. Supplementary data

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