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Is preoperative physical activity level of patients undergoing cancer surgery associated with postoperative outcomes? A systematic review and meta-analysis

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ABSTRACT

Background: There is uncertainty about the role of preoperative physical activity (PA) level and its influence on postoperative outcomes, especially for patients undergoing cancer surgery.
Aim: To investigate if the level of preoperative PA in patients undergoing cancer surgery is associated with postoperative complication rates, length of hospital stay (LOS) and quality of life (QOL).
Methods: An electronic search was performed from inception to 26th November 2017 in MEDLINE, Embase, AMED and CINAHL. Studies investigating the association between objective or subjective level of PA and postoperative complication rates, LOS and QOL were included. Risk of bias was assessed using the Quality in Prognosis Studies (QUIPS) tool. When possible, summary odds ratios (OR) and 95% confidence intervals (CI) were calculated using random-effect models.
Results: 13 studies (5523 unique patients) were included. Overall, most studies were rated as having low or moderate risk of bias. Higher preoperative level of PA was not significantly associated with absence of postoperative complications (OR = 2.60; 95%CI = 0.59 to 11.37) but was significantly associated with shorter LOS (OR = 3.66; 95%CI = 1.38 to 9.6) and postoperative QOL (OR = 1.29; 95%CI = 1.11 to 1.49).
Conclusions: The available literature suggests higher levels of preoperative PA in patients undergoing cancer surgery may be associated with better postoperative outcomes, particularly shorter LOS and better QOL. There is a need for high-quality studies investigating the association between preoperative PA and postoperative outcomes.
Systematic review registration: PROSPERO 2017 CRD42017082334. Available from:http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017082334.

Introduction

There is good evidence that participation in regular physical activity (PA) has important cardiovascular and other health related benefits, including reduced risk of cancer, especially bowel, endometrial and breast cancer [1,2]. However, the literature shows that the majority of cancer patients undergoing curative resection do not meet exercise recommendations preoperatively [3,4]. More recently, the Clinical Oncology Society of Australia (COSA) released a position statement recommending cancer patients to avoid inactivity and progress towards reaching at least 2.5 h of moderate intensity aerobic exercise and 2 to 3 moderate intensity resistance exercise sessions each week [4]. Emerging evidence suggests that physical inactivity reduces the ability of a person to cope mentally and physically with hospitalisation and surgery, compromising postoperative recovery, leading to an increase in postoperative

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complication rates and length of hospital stay (LOS), and a decrease in quality of life (QOL) [5]. However, these findings are not specific to patients undergoing cancer surgery and increased knowledge about the role of level of PA participation preoperatively in this population is of great interest.

A recent systematic review found evidence that the implementation of a preoperative exercise program was effective in reducing the number of postoperative complications and LOS in patients undergoing lung cancer surgery [6]. Likewise, a previous review reported the benefits of physical activity interventions on cardiorespiratory fitness, symptoms and physiological effects during and/or after cancer treatment [7]. However, there is no synthesis of the literature investigating whether preoperative PA level is associated with postoperative recovery. This information is important for healthcare providers to better predict the likely postoperative course and guide patient selection; to determine if thresholds of preoperative PA levels are associated with increased risk; and to identify groups of patients more likely to benefit from a preoperative exercise program.

Recently, a number of individual studies have suggested that higher levels of PA participation during the preoperative period are associated with positive postoperative outcomes. A study conducted in 169 patients undergoing major oncological abdominal surgery [8], found that higher preoperative PA level was associated with reduced short-term mortality (Odds ratio [OR] = 5.2; 95% confidence interval [CI] = 1.4 to 19.1) and shorter LOS (Hazard ratio [HR] = 0.6; 95%CI = 0.4 to 0.8). Similarly, patients who had elective colorectal cancer surgery and engaged in regular PA preoperatively had a faster postoperative recovery (OR = 3.3; 95%CI = 1.07 to 10.1) [9]. Thus, a better understanding of the association between preoperative PA level and postoperative outcomes in patients undergoing cancer surgery, through evaluating the evidence in a systematic manner, would be valuable and of great interest. We are unware of any previous systematic review investigating the association between preoperative level of PA and postoperative outcomes. Therefore, the aim of this review was to investigate if preoperative PA level in patients undergoing cancer surgery is associated with postoperative complication rates, LOS and QOL outcomes.

Material and methods

Protocol and registration

The protocol of this systematic review was written in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) [10] and registered a priori in the International Prospective Register of Systematic Reviews (PROSPERO 2017 CRD42017082334), available from www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD420170.82334.

Eligibility criteria

Eligible studies included adult patients aged ≥18 years old, undergoing any cancer-related surgical procedure that reported: (I) objective (e.g. accelerometer) or subjective (e.g. self-reported questionnaire) measures of PA level preoperatively; (II) at least one postoperative outcome measure including complication rate, LOS or QOL; (III) data on the association between preoperative PA level and one of the aforementioned postoperative outcomes; and (IV) studies with a longitudinal design (cohort studies, clinical trials, case series, and case-control studies). Cross-sectional studies, case reports and abstracts published in conference proceedings were excluded.

Search strategy

A sensitive electronic search was performed from the earliest records to 26th November 2017 in MEDLINE via Ovid, Embase via Ovid, AMED via Ovid and CINAHL via EBSCO using a combination of Medical Subject Headings (MeSH) terms and key words for “preoperative”, “physical activity” and “cancer” (Supplementary Table 1). In addition, citation tracking of the included studies was conducted. No date or language restriction was applied.

Study selection

Initially, one review author (DS) removed only clearly irrelevant studies. Screening of titles, abstracts and full-text of potentially eligible studies was performed by two independent review authors (DS and TMS). Disagreements over the eligibility of particular studies were resolved through discussion with a third reviewer (MJH or PRB). The inter-rater agreement for the full-text screening was 92% (Cohen's kappa coefficient = 0.83).

Data collection

A standardised form was used to extract data from eligible studies for assessment of the study quality and evidence synthesis. Two independent review authors (DS and TMS) extracted all data. Disagreements over data extraction were resolved through discussion and consensus with a third review author (MJH or PRB). The following information was extracted: participant characteristics, study characteristics, description of PA measure, outcome measures, and measures of association. The inter-rater agreement for data collection was 95% (Cohen's kappa coefficient = 0.92).

Risk of bias assessment

Two independent review authors (DS and PRB) assessed risk of bias using the Quality in Prognostic Studies (QUIPS) tool [11]. Risk of bias was rated as “high”, “moderate” or “low” risk across the following domains: (i) Study participation; (ii) Study attrition; (iii) Prognostic factor measurement; (iv) Outcome measurement; (v) Study confounding; and (vi) Statistical analysis and reporting. The inter-rater agreement for the risk of bias assessment was 91% (Cohen's kappa coefficient = 0.81).

Syntheses of results

Measures of association (e.g., odds ratio) between preoperative PA level and postoperative complication rates, LOS and/or QOL were extracted from individual studies.

For studies that were heterogenous in terms of PA measures and postoperative outcomes, it was not possible or appropriate to pool findings, and these results are, therefore, presented descriptively. For homogeneous studies (e.g., presenting comparable measures of PA level and postoperative outcomes) reporting on the association between preoperative PA level and postoperative outcomes, a meta-analysis was conducted. If the study reported enough information on the preoperative PA level and the postoperative outcomes of interest that allowed for calculation of a measure of association [9,12–16], the calculation was performed by the review authors and this measure was used in this review.

Results

Selection of studies

The search identified 666 citations after removing all duplicates.

After review of titles and abstracts, 608 records were excluded. Hence, a total of 58 full-text articles were assessed for eligibility. Of these, 45 were excluded due to the following reasons: not a cancer population (n = 3); conference proceedings (n = 5); no measure of association (n = 15); no measure of PA (n = 7); no outcome of interest (n = 14); and study protocol (n = 1). Therefore, a total of 13 studies [8,9,12–22] (5523 unique patients) met the inclusion criteria and were included in the systematic review (Fig. 1).

Risk of bias

The risk of bias assessment for each included study is presented in Table 1. Overall, most studies were rated as having low or moderate risk of bias. Most studies had high risk of bias for study attrition; while they were rated low risk of bias for study participation and outcome measurement.

Study characteristics

Four studies reported on a sample of patients undergoing surgery for colorectal cancer [8,9,19,22], four on prostate cancer [13,16,17,20], two on oesophageal cancer [15,18], one on cervical cancer [21], one on colon cancer [14] and one on breast cancer [12]. Most studies included older male and female patients (mean age ranged from 52 to 80 years). The sample size of the included studies ranged from 33 to 3706 participants (Table 2).

PA was assessed using self-reported questionnaires in 11 studies, while two studies used an objective measure (one used the NL100 Activity monitor [14] and one used SenseWear Pro3 Armband [20]). The most common self-reported measure used was the Longitudinal Ageing Study Amsterdam (LASA) Physical Activity Questionnaire (LAPAQ), reported in 3 studies [8,18,22], followed by the Saltin-Grimby Physical Activity Level Scale (SGPALS), reported in two studies [9,12]. Three studies used a single question to measure preoperative PA level [13,17,19]. A comprehensive description of the characteristics of each included study is provided in Table 2.

The design of the included studies were mostly prospective cohorts (n = 9) [8,9,12,15,16,18–20,22], followed by randomised controlled trial (n = 1) [14] and retrospective cohort (n = 1) [21]. Two included studies used data from the same non-randomised controlled trial – LAParoscopic Prostatectomy Robot Open

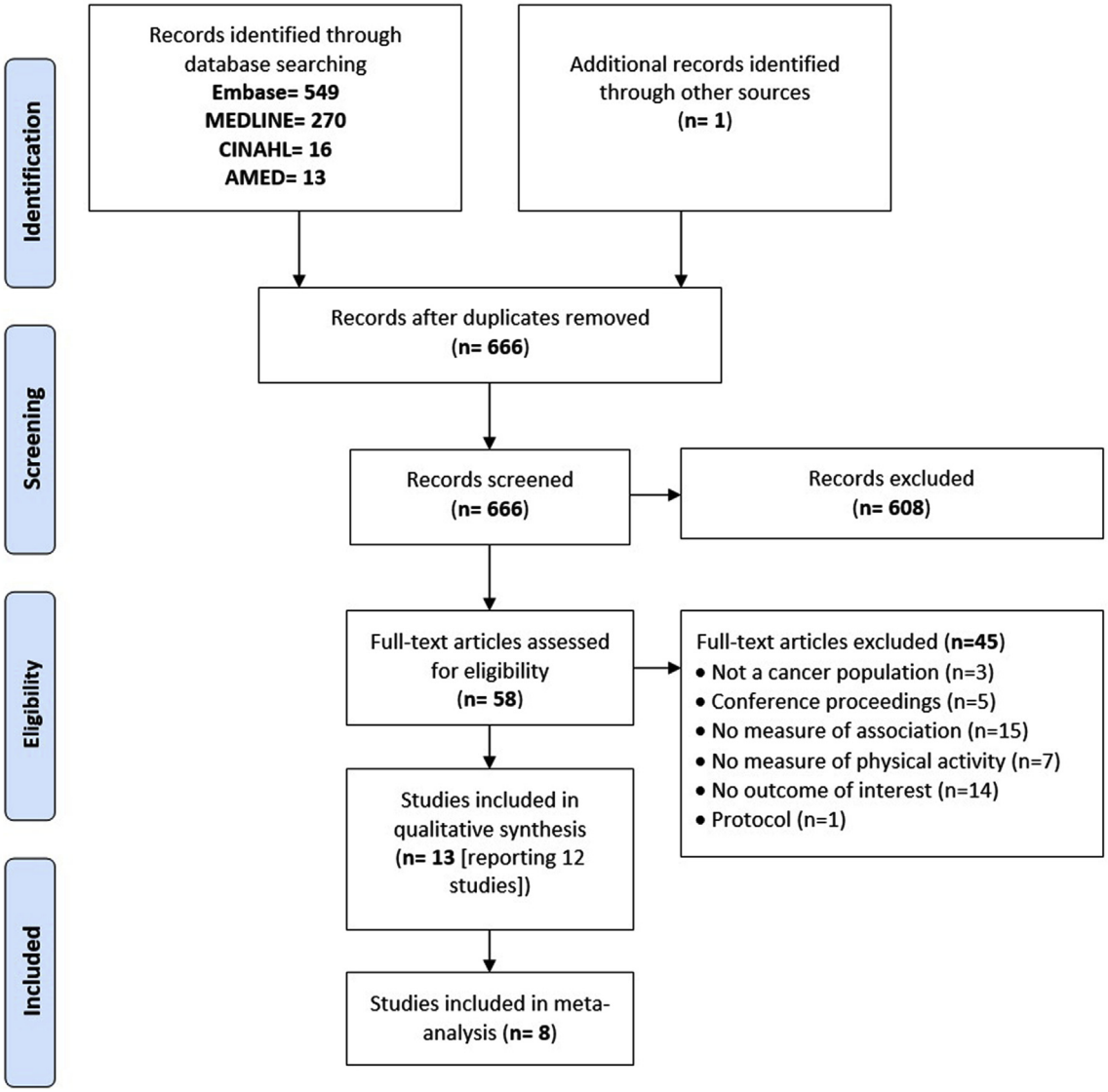

Fig. 1. Flow chart.

Table 1
Risk of bias assessment using the Quality in Prognosis Studies (QUIPS) tool.

Study, year	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting
Axelsen, 2006	Moderate	High	High	Low	Moderate	Moderate
Dronkers, 2010	Moderate	Low	Low	Low	Not Applicable	Not Applicable
Kristjansson, 2012	Low	Low	High	Low	Low	Moderate
Dronkers, 2013	Low	Low	Low	Low	Low	Low
Mungovan, 2013	Moderate	High	Moderate	Low	High	High
Tatematsu, 2013	Low	Low	Low	Low	Not Applicable	Not Applicable
Santa Mina, 2014	Moderate	High	Moderate	Moderate	Not Applicable	Not Applicable
Angenete, 2016	Low	High	Moderate	Moderate	Not applicable	Not Applicable
Nilsson, 2016	Low	Moderate	Low	Low	Not Applicable	Not Applicable
Onerup, 2016	Low	high	Moderate	Low*	Not Applicable	Not Applicable
Bock, 2017	Low	High	Moderate	Moderate	Not Applicable	Not Applicable
Heldens, 2017	Low	High	Moderate	Low	Not Applicable	Not Applicable
van Egmond, 2017	Low	High	Moderate	Low	Not Applicable	Not Applicable

*Length of hospital stay outcome was rated as 'low' risk of bias, while the quality of life outcome was rated as 'moderate' risk of bias. For studies that reported enough information that allowed for calculation of measures of association, the items 'study confounding' and 'statistical analysis and reporting' were deemed not applicable. Studies are ordered chronologically.

(LAPPRO TRIAL), however, investigated different outcomes [13,17].

Complication rates

Nine studies investigated the association between preoperative PA levels and number of postoperative complications (Table 3) [13–16,18–22]. Four studies (n = 257 participants) investigated the association of preoperative PA level and presence of overall postoperative complication rate (i.e. presence of any postoperative complication) [14,15,18,22]. These studies were included in the random-effects meta-analysis. There was a trend towards patients presenting with higher levels of preoperative PA more commonly having an absence of postoperative complications (OR = 2.60; 95% CI = 0.59 to 11.37), although this association was not statistically significant (Fig. 2).

The association between higher preoperative PA and the severity of postoperative complications (i.e. Clavien-Dindo ≤Grade I versus ≥Grade II) in 176 patients undergoing surgery for colorectal cancer was investigated in one study [19]. Higher preoperative PA level was not associated (p = 0.10; measure of association not reported) with less severe postoperative complications (classified as Clavien-Dindo grade ≤I).

Two studies investigated the association of preoperative PA level and postoperative surgical complication in 1476 patients undergoing colorectal (n = 75) [22] and prostate cancer (n = 1401) [13] surgery. The meta-analysis revealed that higher preoperative PA level was not associated with absence of postoperative surgical complications (OR = 0.76; 95%CI = 0.34 to 1.68) (Fig. 2).

Angenete et al. [13] investigated the association of preoperative PA and postoperative complications, such as infection, cardiovascular and gastrointestinal, in a sample of 1408 patients undergoing radical prostatectomy for prostate cancer. Preoperative level of PA was not associated with any of the postoperative complications investigated (OR ranging from 0.92 to 1.17).

Postoperative urinary continence was investigated in two studies [16,20]. Santa Mina et al. [16] reported a significant association between higher preoperative PA level and postoperative continence (assessed using a single item of the Patient Oriented Prostate Utility Scale - PORPUS questionnaire) at 6 weeks (n = 366 participants) postoperative (OR = 1.60; 95%CI = 1.05 to 2.44), but not at 26 weeks (n = 346 participants) postoperative (OR = 1.46; 95%CI = 0.90 to 2.37) after prostate cancer surgery. Mungovan et al. [20] reported the association in 33 patients. Preoperative PA was not correlated with continence at 3 (p = 0.805) and 6 weeks (p = 0.691) postoperative.

Axelsen et al., 2006, investigated the association of preoperative PA level and the occurrence of postoperative cystitis/dysuria in 333 cervical cancer patients undergoing radical hysterectomy [21]. Higher level of preoperative PA was a significant predictor of the absence of postoperative cystitis/dysuria (OR = 1.82; 95%CI = not reported).

Length of hospital stay

Four studies described the association between preoperative PA level and LOS (Table 3) [8,9,12,22]. One study included a sample of 194 patients undergoing breast cancer surgery [12], while three studies included a combined sample of 361 patients undergoing colorectal cancer surgery [8,9,22].

A random-effects meta-analysis showed a non-significant association between higher level of preoperative PA and shorter LOS when comparing high/moderate/low PA vs inactive (OR = 1.15; 95% CI = 0.34 to 3.89) and high/moderate PA vs low PA/inactive (OR = 2.01; 95%CI = 0.67 to 6.07) (Fig. 2). When we performed a sensitivity analysis including only studies that dichotomised PA level in high/moderate PA vs low PA/inactive (n = 305), our meta-analysis showed a significant association between higher PA level and reduced LOS (OR = 3.66; 95%CI = 1.38 to 9.69) (Supplementary Figure 1) [9,12].

Dronkers et al. [8] investigated the association between preoperative PA level (higher LAPAQ score ≥530 kcal versus lower LAPAQ score <530 kcal) and postoperative LOS in 175 elderly patients undergoing oncological colorectal surgery. Higher preoperative PA level (LAPAQ score ≥530 kcal) was significantly associated with decreased LOS (Hazard ratio = 0.60; 95% CI = 0.40 to 0.80).

Quality of life

Only two studies investigated the association between preoperative PA level and postoperative QOL outcomes [9,17]. Both studies assessed QOL using a single question, "how would you describe your QOL last week/during the past month?". Scores ranged from 0 to 6, with 0 representing worst QOL outcomes.

Onerup et al. [9] investigated 89 patients undergoing colorectal cancer surgery and Bock et al. [17] reported on a sample of 3239 patients undergoing prostate cancer surgery. In the short-term (6–12 weeks postoperative), higher level of preoperative PA was associated with better postoperative QOL scores (QOL ≤4, scale range from 0 to 6; OR = 1.29; 95%CI = 1.11 to 1.49) (Fig. 2); Bock et al. (n = 3037 participants) reported similar results at long-term

Table 2
Characteristics of the included studies.

Author, year	Study Population	Preoperative PA assessment	PA definition	Postoperative Outcomes	Outcome definition
Axelsen, 2006	Study design: Retrospective cohort Sample: 333 (0% male) Cancer type: Cervical Mean age (SD): 52.5 (12.2)	Not reported	Not reported	Complications	**Cystitis and/or dysuria**: self-reported questionnaire.
Dronkers, 2010	Study design: RCT Sample: 42 (74% male) Cancer type: Colon Mean age (SD): 70.0 (6.4)	Activity monitor (NL100 Activity monitor)	**Low PA**: <4000 steps p/day **High PA**: >4000 steps p/day	Complications	**Atelectasis**: diagnosed by a radiologist. **Hypoxia**: need for additional oxygen. **Pneumonia**: defined according to Arozullah et al., 2001.
Kristjansson, 2012	Study design: Prospective cohort Sample: 176 (43% male) Cancer type: Colorectal Mean age (range): 80.0 (70–94)	Single question: "Do you need to stay in bed or a chair during the day?"	**Low PA**: 'quite a bit' or 'very much' **High PA**: 'not at all' or 'a little'	Complications	**No/mild:** Clavien-Dindo grade I **Severe:** Clavien-Dindo ≥ grade II
Dronkers, 2013	Study design: Prospective cohort Sample: 169 (59% male) Cancer type: Colorectal Mean age (SD): NR (NR)	LASA Physical Activity Questionnaire (LAPAQ)	**Low PA:** LAPAQ <530 Kcal **High PA:** LAPAQ ≥530 Kcal	LOS	Number of days spent in hospital from the day of operation until the day the patient left the hospital.
Mungovan, 2013	Study design: Prospective cohort Sample: 33 (100% male) Cancer type: Prostate Mean (SD): 62.0 (6.0)	Activity monitor (SenseWear Pro3 Armband)	**PA level**: MET.min/wk (continuous outcome)	Complications	**Urinary incontinence**: measured using a 24 h pad test at 3 and 6 weeks postoperative.
Tatematsu, 2013	Study design: Prospective cohort Sample: 51 (86% male) Cancer type: Oesophageal Mean age (SD): 65.0 (7.3)	International Physical Activity Questionnaire (IPAQ)	**Low PA:** <9METs-h/wk **High PA:** ≥9METs-h/wk	Complications	**Pulmonary**: pneumonia, atelectasis, and respiratory failure. **Cardiovascular**: myocardial infarction, severe arrhythmia, heart failure, cardiogenic pulmonary edema and pulmonary embolism. **Anastomotic leakage**, **Chylothorax**, and **recurrent laryngeal nerve palsy**: assessed with the National Cancer Institute Common Terminology Criteria for Adverse Events.
Santa Mina, 2014	Study design: Prospective cohort Sample: 509 (100% male) Cancer type: Prostate Mean age (SD): 59.5 (8.3)	Godin Leisure-Time Exercise Questionnaire (GLTEQ)	**Low PA:** <150min of moderate PA or <150min of vigorous PA p/wk **High PA**: ≥150min of moderate PA or ≥150min of vigorous PA p/wk	Complications	**Urinary incontinence**: Occasionally leak urine or lose bladder control interferes with a few activities or worse (single item from PORPUS questionnaire). Measured at 6 and 26 weeks postoperative.
Angenete, 2016	Study design: Non-RCT Sample: 1569 Cancer type: Prostate Median age (range): 59.0 (39–64)	Single question: "*How often have you been physically active for 30 min or more with for example bicycling, walking, gymnastics, or similar, in the past month?*"	**Low PA**: sometimes (1–2 times/wk) **Moderate PA:** often (3–4 times/wk) **High PA**: daily or almost daily (5–7 times/wk)	Complications	**Infection**: wound infection, pneumonia or urinary tract infection. **Cardiovascular:** pulmonary embolism, hypertension, acute myocardial infarction, arrhythmia or other heart diseases, deep venous thrombosis, stroke. **Surgical:** wound and lower/upper abdomen pain, wound and urinary tract bleeding, inguinal hernia. **Gastrointestinal:** nausea, impaired appetite, loose or frequent stools, constipation.
Nilsson, 2016	Study design: Prospective cohort Sample: 220 (0.5% male) Cancer type: Breast Mean age (SD): 60.5 (11.9)	Saltin-Grimby Physical Activity Level Scale (SGPALS)	**Inactive**: almost completely inactive **Low PA**: active (≥4 h/wk) **Moderate/High PA**: spending time on heavy activities (2–3 h/wk)	LOS	Number of days spent in hospital from the day of operation until the day the patient left the hospital (Dichotomised into ≤1 day or ≥2 days).
Onerup, 2016	Study design: Prospective cohort Sample: 115 (56% male) Cancer type: Colorectal Median age (IQR): 71.0 (NR)	Saltin-Grimby Physical Activity Level Scale (SGPALS)	**Inactive**: almost completely inactive **Low PA**: active (≥4 h/wk) **Moderate/High PA**: Spending time on heavy activities (2–3 h/wk)	LOS QOL	Number of days spent in hospital from the day of operation until the day the patient left the hospital (Dichotomised into <7 day or ≥7 days). "How would you describe your QOL last week?" (Score range 0–6; <4 worst QOL and ≥4 better QOL). Collected at 3 and 6 weeks postoperative.
Bock, 2017	Study design: Non-RCT Sample: 3706 (100% male) Cancer type: Prostate	Single question: "*How often have you been physically active for 30 min or more with for*	**Inactive/low PA**: never or sometimes (1–2 times/wk) **Moderate/high PA**: often (3–4	QOL	"How would you describe your QOL during the past month?" (Score range 0–6; ≤4 low/moderate QOL and ≥5

Table 2 (*continued*)

Author, year	Study Population	Preoperative PA assessment	PA definition	Postoperative Outcomes	Outcome definition
	Median age (range): 63.0 (37–79)	*example bicycling, walking, gymnastics, or similar, in the past month?*"	times/wk) or daily or almost daily (5–7 times/wk)		good/very good QOL). Collected at 12 and 52 weeks postoperative.
Heldens, 2017	Study design: Prospective cohort Sample: 75 (57% male) Cancer type: Colorectal Median age (IQR): 69.2 (11.7)	LASA Physical Activity Questionnaire (LAPAQ)	**Low PA**: 50% lowest physically active (LAPAQ) **High PA**: 50% most physically active (LAPAQ)	Complications LOS	**Overall postoperative complications** and **surgical complication**: absent or present. Number of days spent in hospital from the day of operation until the day the patient left the hospital (Dichotomised into <7 days or ≥7 days).
van Egmond, 2017	Study design: Prospective cohort Sample: 94 (79% male) Cancer type: Oesophageal Mean age (SD): 63.8 (9.4)	LASA Physical Activity Questionnaire (LAPAQ)	**Low PA**: <856 kcal/day **High PA**: ≥856 kcal/day	Complications	Presence or absence of complications within 30 days of surgery defined according to the Esophagectomy Complications Consensus Group (ECCG).

PA=Physical activity; RCT = Randomised controlled trial; N-RCT=Non-randomised controlled trial; LOS = Length of stay; SD=Standard deviation; IQR= Interquartile; QOL = Quality of life. Studies are ordered chronologically.

(52 weeks postoperative) follow-up (OR = 1.40; 95%CI = 1.20 to 1.63) (Table 3) [17].

Discussion

Statement of principal findings

A total of 13 studies were included in this systematic review and, despite the heterogeneity on PA measures and postoperative outcomes across the included studies, we were able to conduct a number of meta-analyses including data from 8 studies. Our meta-analyses indicated that higher preoperative PA level was associated with shorter LOS (OR = 3.66; 95%CI = 1.38 to 9.69) and better postoperative QOL (OR = 1.29; 95%CI = 1.11 to 1.49), but not with reduced postoperative complications (OR = 2.60; 95%CI = 0.59 to 11.7). Interestingly, we identified 10 significant associations reported in single studies; with all demonstrating that higher preoperative PA level was associated with better postoperative outcomes.

Strengths and weaknesses of the study

The strengths of this review include the use of a pre-specified protocol registered on PROSPERO, the use a comprehensive and sensitive search strategy that was developed by a senior librarian, and inclusion of all available literature irrespective of language. In addition, we assessed risk of bias using a valid and reliable tool recommended by the Cochrane Prognosis Review Group.

One limitation of our review is that we did not attempt to include studies that were not published, such as abstracts published in conference proceedings, increasing the possibility of publication bias.

Comparison with other studies

To our knowledge, this is the first systematic review investigating the association between preoperative PA level and postoperative outcomes in patients undergoing oncological surgery. A previous systematic review investigated the association of preoperative PA level and postoperative outcomes on adult cardiac surgical patients [23]. The heterogeneity between included studies in PA measurements, definition of outcomes, and poor statistical analysis (i.e., not adjusting for potential confounders) prevented the authors from drawing any definite conclusions. Therefore, it seems that similar limitations in the literature exist across disciplines.

Meaning of the study

To achieve health benefits, the World Health Organisation Guidelines on PA recommends that adults should exercise at a moderate level for at least 150 min, or at least 75 min of higher intensity exercises per week [24]. In cancer patients undergoing surgery, our review found positive trends, with our meta-analyses and the single studies demonstrating that patients engaged in higher level of preoperative PA were more likely to experience better postoperative outcomes. Recent reviews have demonstrated some positive effects of exercise on attenuating chemotherapy induced symptoms [25] and reducing postoperative complication rates and LOS [6]. Therefore, while the evidence on the association between preoperative PA level and postoperative outcomes is somewhat limited, clinicians should still advise patients to maintain good health by keeping active, as there is strong evidence that PA has health related benefits, such as cardiovascular and mental disorders.

Recommendations for future research

There is a clear lack of high-quality evidence on the association of preoperative PA level and postoperative outcomes in cancer patients undergoing surgery; urging the development of high-quality and appropriately powered studies to confidently answer this important question. This review identified some important limitations in the current literature that should be amended in future studies. Objective measures of PA (i.e., wearable devices) taken preoperatively (within days or weeks of the surgery) should be preferred over self-reported questionnaires, taking into account neoadjuvant treatments, comorbidities and other factors that could influence preoperative PA levels. Previous studies have demonstrated that cancer patients overestimate their self-reported PA level by 366% when compared to objective measures [26]; the authors also acknowledge the difficulty of collecting objective measures of PA due to insufficient wearing time, malfunction and financial costs (non funded research) [27]; and, therefore, suggest the use of validated and reliable instruments that have been tested in the population of interest. Similarly, future studies should use previously accepted and validated patient reported outcome measures that are specific to the disease of interest in addition to tools

Table 3
Association between level of preoperative physical activity and postoperative outcome measures.

Outcome	Author, year	Cancer type (N)	Preoperative physical activity threshold	Postoperative outcomes threshold	OR (95%CI), unless indicated*
Postoperative outcome (Complication)					
Any complication	Dronkers, 2010	Colon (n = 41)	High *vs* low	No complication *vs* complication	**25.88 (2.82 to 237.55)**
Any complication	Tatematsu, 2013	Oesophageal (n = 51)	High *vs* low	No complication *vs* complication	**8.00 (2.24 to 28.61)**
Any complication	van Egmond, 2017	Oesophageal (n = 90)	High *vs* low	No complication *vs* complication	1.00 (0.42–2.38)
Any complication	Heldens, 2017	Colorectal (n = 75)	High *vs* low	No complication *vs* complication	0.53 (0.21–1.39)
Any complication - severity	Kristjansson, 2012	Colorectal (n = 176)	High *vs* low	≤Grade I *vs* ≥grade II	High PA not associated with ≤grade I (p = 0.10)
Surgical complication	Heldens, 2017	Colorectal (n = 75)	High *vs* low	No surgical complication *vs* surgical complication	0.42 (0.14–1.21)
Surgical complication	Angenete, 2016	Prostate (n = 1401)	High/moderate *vs* low	No surgical complication *vs* surgical complication	1.00 (0.76–1.32)
Surgical complication	Angenete, 2016	Prostate (n = 1401)	High *vs* moderate/low	No surgical complication *vs* surgical complication	1.17 (0.86–1.60)
Urinary complication (6 weeks)	Santa Mina, 2014	Prostate (n = 366)	High *vs* low	Continent *vs* incontinent	**1.60 (1.05 to 2.44)**
Urinary complication (26 weeks)	Santa Mina, 2014	Prostate (n = 346)	High *vs* low	Continent *vs* incontinent	1.46 (0.90–2.37)
Urinary complication (3 weeks)	Mungovan, 2013	Prostate (n = 33)	Not reported	Not reported	PA not correlated with 24 h pad test (r = 0.046; p = 0.805)
Urinary complication (6 weeks)	Mungovan, 2013	Prostate (n = 33)	Not reported	Not reported	PA not correlated with 24 h pad test (r = −0.073; p = 0.691)
Urinary complication	Axelsen, 2006	Cervical (n = 333)	Not reported	No cystitis/dysuria vs cystitis/dysuria	**1.82 (95%CI not reported)**
Infection	Angenete, 2016	Prostate (n = 1408)	High/moderate *vs* low	No infection *vs* infection	1.04 (0.80–1.36)
Infection	Angenete, 2016	Prostate (n = 1408)	High *vs* moderate/low	No infection *vs* infection	1.14 (0.85–1.54)
Cardiovascular complication	Angenete, 2016	Prostate (n = 1389)	High/moderate *vs* low	No cardiovascular vs cardiovascular	0.96 (0.59–1.56)
Cardiovascular complication	Angenete, 2016	Prostate (n = 1389)	High *vs* moderate/low	No cardiovascular vs cardiovascular	0.92 (0.54–1.55)
Gastrointestinal complication	Angenete, 2016	Prostate (n = 1400)	High/moderate *vs* low	No gastrointestinal vs gastrointestinal	1.03 (0.74–1.42)
Gastrointestinal complication	Angenete, 2016	Prostate (n = 1400)	High *vs* moderate/low	No gastrointestinal vs gastrointestinal	1.06 (0.74–1.52)
Postoperative outcome (Length of hospital stay)					
Length of stay	Nilsson, 2016	Breast (n = 194)	High/moderate/low *vs* inactive	≤1 day *vs* ≥2 days	2.17 (0.65–7.24)
Length of stay	Nilsson, 2016	Breast (n = 194)	High/moderate *vs* low/inactive	≤1 day *vs* ≥2 days	4.67 (0.60–36.32)
Length of stay	Onerup, 2016	Colorectal (n = 111)	High/moderate/low *vs* inactive	<7 days *vs* ≥7 days	0.62 (0.20–1.98)
Length of stay	Onerup, 2016	Colorectal (n = 111)	High/moderate *vs* low/inactive	<7 days *vs* ≥7 days	**3.41 (1.13 to 10.31)**
Length of stay	Heldens, 2017	Colorectal (n = 75)	High *vs* low	<7 days *vs* ≥7 days	0.86 (0.34–2.17)
Length of stay	Dronkers, 2013	Colorectal (n = 175)	High *vs* low	Length of stay (days)	**HR = 0.60 (0.40 to 0.80)**
Postoperative outcome (Quality of life)					
QOL (3 weeks)	Onerup, 2016	Colorectal (n = 89)	High/moderate/low *vs* inactive	QOL ≥4 (0–6) *vs* QOL <4 (0–6)	**10.12 (2.03 to 50.44)**
QOL (6 weeks)	Onerup, 2016	Colorectal (n = 82)	High/moderate/low *vs* inactive	QOL ≥4 (0–6) *vs* QOL <4 (0–6)	**4.83 (1.32 to 17.57)**
QOL (3 weeks)	Onerup, 2016	Colorectal (n = 89)	High/moderate *vs* low/inactive	QOL ≥4 (0–6) *vs* QOL <4 (0–6)	1.21 (0.37–3.92)
QOL (6 weeks)	Onerup, 2016	Colorectal (n = 82)	High/moderate *vs* low/inactive	QOL ≥4 (0–6) *vs* QOL <4 (0–6)	1.04 (0.26–4.21)
QOL (12 weeks)	Bock, 2017	Prostate (n = 3129)	High/moderate *vs* low/inactive	QOL ≥5 (0–6) *vs* QOL ≤4 (0–6)	**1.29 (1.12 to 1.50)**
QOL (52 weeks)	Bock, 2017	Prostate (n = 3037)	High/moderate *vs* low/inactive	QOL ≥5 (0–6) *vs* QOL ≤4 (0–6)	**1.40 (1.20 to 1.63)**

PA=Physical activity; OR=Odds ratio; HR=Hazard ratio; LAPAQ = LASA physical activity questionnaire; QOL = Quality of life; r = Pearson correlation coefficient *Effect size not reported. Odds ratio >1 means the more favourable outcome was more common in those with higher physical activity level preoperatively. Significant associations are highlighted in bold.

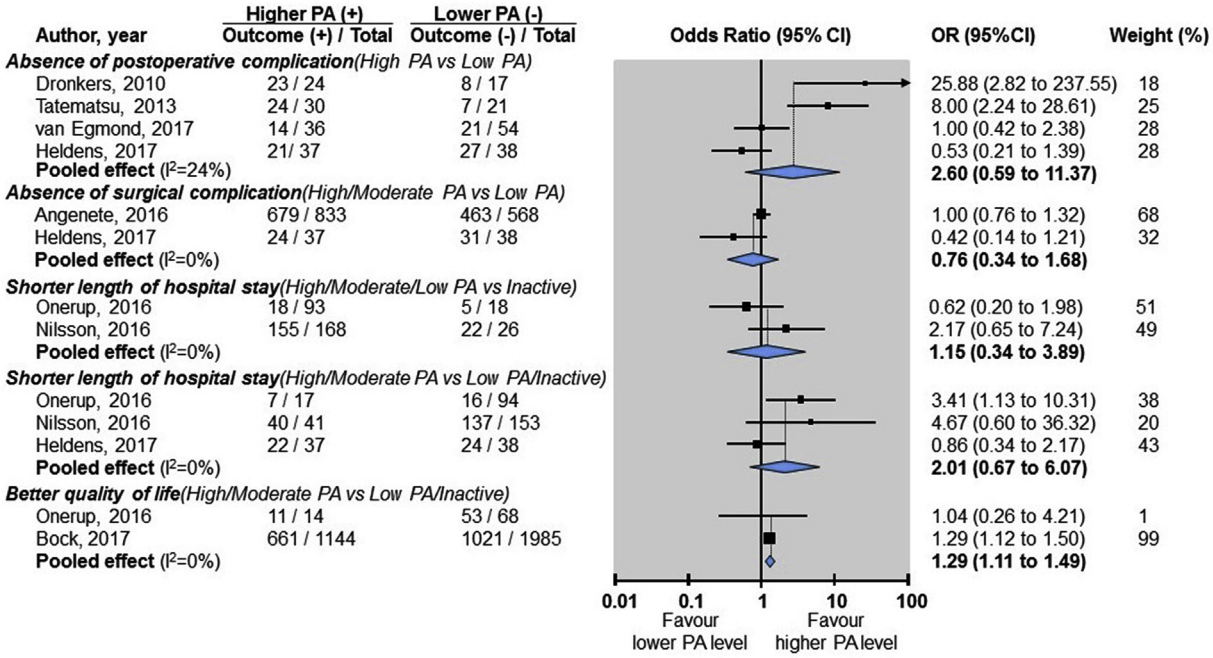

Fig. 2. Meta-analysis of the association between preoperative physical activity level and postoperative complication rates, length of hospital stay and quality of life. Studies are ordered chronologically within outcomes measures. Odds ratio >1 favours higher physical activity level at the preoperative. CI=Confidence Interval; PA=Physical activity.

suitable for the general population to allow comparability with other populations. Lastly, the statistical analysis of the included studies should take into account potential confounders for the condition of interest, such as preoperative neoadjuvant therapy and comorbidities.

Future studies should focus on better understanding the relationship between different thresholds of preoperative PA levels (e.g. inactive, low, moderate and high PA levels) and postoperative outcomes; investigating if there is a critical threshold of preoperative PA that is associated with better postoperative outcome, or if the relationship is linear and progressively higher PA levels provide even better postoperative outcomes. The relationship between preoperative PA and postoperative outcomes may be influenced by other factors such as age and gender. This could be investigated in future studies. In addition, future RCTs investigating the effectiveness of preoperative exercise program should clearly define the preoperative PA level of their population, as intervention effects might be different depending on the preoperative PA level of the included participants. Therefore, trials could investigate if the effect of preoperative exercise programs varies according to participants' preoperative PA level.

Conclusions

Our systematic review and meta-analyses show that higher preoperative PA level is associated with shorter LOS and better postoperative QOL outcomes. Furthermore, individual studies reported significant association between higher level of preoperative PA and lower postoperative complication rates, LOS and better QOL outcomes. In addition, our review highlights the shortcomings of the current evidence on the association of preoperative level of PA and postoperative complication, LOS and QOL on cancer patients and made recommendation for future studies. Nevertheless, this review provides preliminary evidence that higher preoperative PA level is associated with improved outcomes postoperatively in patients undergoing cancer surgery.

Author contributions

Contributors: Conception and design: DS, PRB, MJH, TMS, MS and JY. Analysis and interpretation of the data: DS, PRB, MJH, TMS, MS and JY. Drafting of the article: DS, PRB, MJH, TMS, MS and JY. All authors participated in the revision and final approval of the manuscript. Statistical expertise: DS, MJH, MS and JY. Collection and assembly of data: DS, TMS and PRB. DS is the guarantor.

Conflict of interest

None declared.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ejso.2018.10.063.

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