Northumbria Research Link

Exercise Prehabilitation in Elective Intra-cavity Surgery: a Role within the ERAS Pathway? A Narrative Review

Samuel T. Orange[1], Matthew J. Northgraves[1,2], Phil Marshall[1], Leigh A. Madden[3], and Rebecca V. Vince[1]*.

[1]Sport, Health and Exercise Science, School of Life Sciences, University of Hull, Hull, UK.

[2]Department of Health Sciences, University of York, York, UK.

[3]Centre of Biomedical Research, School of Life Sciences, University of Hull, Hull, UK.

Running heading: Exercise Prehabilitation: a Narrative Review

Corresponding author

*Rebecca Vince[1], PhD

[1]Sport, Health and Exercise Science, School of Life Sciences, University of Hull, Hull, UK, HU6 7RX.

Email: rebecca.vince@hull.ac.uk

Telephone: +44 (0)1482 463176

Abstract

The Enhanced Recovery after Surgery (ERAS) model integrates several elements of perioperative care into a standardised clinical pathway for surgical patients. ERAS programmes aim to reduce the rate of complications, improve surgical recovery, and limit postoperative length of hospital stay (LOHS). One area of growing interest that is not currently included within ERAS protocols is the use of exercise prehabilitation (PREHAB) interventions. PREHAB refers to the systematic process of improving functional capacity of the patient to withstand the upcoming physiological stress of surgery. A number of recent systematic reviews have examined the role of PREHAB prior to elective intra-cavity surgery. However, the results have been conflicting and a definitive conclusion has not been obtained. Furthermore, a summary of the research area focussing exclusively on the therapeutic potential of exercise prior to intra-cavity surgery is yet to be undertaken. Clarification is required to better inform perioperative care and advance the research field. Therefore, this "review of reviews" provides a critical overview of currently available evidence on the effect of exercise PREHAB in patients undergoing i) coronary artery bypass graft surgery (CABG), ii) lung resection surgery, and iii) gastrointestinal and colorectal surgery. We discuss the findings of systematic reviews and meta-analyses and supplement these with recently published clinical trials. This article summarises the research findings and identifies pertinent gaps in the research area that warrant further investigation. Finally, studies are conceptually synthesised to discuss the feasibility of PREHAB in clinical practice and its potential role within the ERAS pathway.

Keywords

Exercise training; Prehabilitation; Presurgical period; Intra-cavity surgery; Enhanced Recovery after Surgery

1. Introduction

Major surgery represents a considerable stressor for older adults. The majority of surgical patients are over 60 years old [1] and often present multiple comorbidities with a decreased ability to cope with trauma. These age-related impairments in physiological function, coupled with the raft of metabolic and hormonal perturbations that occur in response to surgery, often lead to a longer convalescence for elderly patients [2]. In particular, major intra-abdominal resections are associated with an in-hospital stay of up to 10-days [3] and complication rates of 15-20% [4, 5].

The Enhanced Recovery after Surgery (ERAS) pathway was initiated in the 1990s by a group of academic surgeons to improve perioperative care in these patients [6]. The ERAS model was originally developed for colorectal surgery but has now been applied to almost all major surgical specialities [7] and represents a paradigm shift towards a multimodal, patient-centred approach to surgical care. ERAS is designed to modify the physiological and psychological response to surgical trauma by integrating a range of evidence-based components into a standardised clinical pathway. Ultimately, ERAS programmes aim to reduce the rate of complications, improve surgical recovery, and limit postoperative length of hospital stay (LOHS). Indeed, a number of recent meta-analytic reviews have reported a 30% to 50% reduction in LOHS and complication rates in colorectal surgery patients receiving treatment through the ERAS pathway compared to traditional perioperative care [8-12]. Furthermore, this reduction has been achieved without compromising patient safety [10] and is associated with lower healthcare costs [9].

There are 24 core elements of ERAS that are distributed along the patient pathway, as outlined recently by Ljungqvist and colleagues [7]. One area that is not currently included within ERAS protocols, although it is a growing field of interest, is the use of preoperative exercise or prehabilitation (PREHAB) interventions. PREHAB refers to the systematic process of improving functional capacity of the patient to withstand the upcoming physiological stress of surgery [13]. The concept of PREHAB is contingent on the principle that patients with higher levels of fitness generally exhibit reduced postoperative complications and improved clinical outcomes [14]. The application of PREHAB prior to intra-abdominal and intra-thoracic surgery has received considerable attention in recent years [15-19]. However, the results of existing systematic reviews have been conflicting. Clarification is required to better inform perioperative care and to identify pertinent gaps in the research area that warrant further investigation.

To address this issue, a recent scoping review [20] has provided an extensive overview of the PREHAB literature. The review included all types of surgery and non-exercise pulmonary interventions, such as inspiratory muscle training (IMT) and incentive spirometry. Given that the effectiveness of PREHAB may differ between various types of surgery and different methods of preoperative therapy, a “review of reviews” that focuses exclusively on exercise interventions prior to intra-cavity resection is warranted. Therefore, this review aimed to evaluate the effect of exercise PREHAB on physical fitness, LOHS and postoperative complications in patients undergoing elective major intra-abdominal and intra-thoracic surgery.

2. Process of review

We conducted the literature search in PubMed (MEDLINE) and Google Scholar databases from 2006 to 2016 using a combination of keywords such as prehabilitation, preoperative, surgery, aerobic exercise, resistance training, physical function, abdominal, thoracic, cardiac, colorectal, and lung. Keywords were also combined with the following Medical Subject Headings (only relevant for search in PubMed): preoperative period, thoracic surgery, colorectal surgery, exercise, and exercise therapy. Focus was on systematic reviews and meta-analyses, although these were also supplemented with available individual studies. We defined *PREHAB* as a structured regimen of aerobic and/or resistance training, either home-based or in a supervised setting, prior to major elective intra-cavity surgery. *Intra-cavity surgery* was defined as elective intra-abdominal and intra-thoracic surgery [16]. In the cases of systematic reviews or meta-analyses that cited studies that included other types of surgery (e.g. orthopaedic) or the predominant use of pulmonary interventions (e.g. IMT), pertinent individual studies cited within the meta-analyses were reviewed independently. Finally, we discuss whether the current evidence-base supports the inclusion of PREHAB within ERAS pathways.

3. PREHAB in Intra-Thoracic Surgery

3.1. Coronary Artery Bypass Graft Surgery

Two well-designed meta-analyses [21, 22] have reviewed the effects of PREHAB in cardiac patients awaiting coronary artery bypass graft (CABG) surgery. The majority of studies cited within these reviews, however, exclusively involved educational interventions and/or IMT. For example, Hulzebos and colleagues [21] reviewed eight randomised controlled trials (RCTs), six of which only included the use of non-exercise pulmonary interventions. We identified just three studies, all of which were RCTs that involved the predominant use of exercise training as the PREHAB intervention [23-25]. In a small pilot RCT using the six minute walk test (6MWT) distance as the primary outcome [23], 17 patients engaged in eight weeks of aerobic exercise (walking and cycling at 85% maximal oxygen consumption [VO_{2max}]) and resistance exercises (body weight and resistance bands) twice per week. Compared with control, the PREHAB group improved 6MWT distance and 5-metre gait speed at the preoperative (6MWT: 136 metres; 5-metre gait speed: -1.6 sec) and 3-month postoperative (6MWT: 123 metres; 5-

metre gait speed: -1.2 sec) reassessments. No reduction in LOHS was found between groups (PREHAB = 5.3 ± 1.0 days; CON = 5.1 ± 1.4 days), suggesting that the improvement in functional capacity may not translate into favourable clinical outcomes. A lack of change in LOHS was also reported following 10 weeks of combined aerobic exercise training (40 minutes at 60% maximum heart rate [HR_{max}]) and mental stress reduction in 117 patients scheduled for CABG and/or valve surgery (PREHAB = 6 days [range: 5 to 8]; CON = 6 days [range: 5 to 8]) [24]. The absence of an objective measure of physical fitness means it is unknown whether PREHAB improved patients' fitness prior to surgery. Moreover, it is important to note that the sample sizes for both studies were calculated in order to provide power to detect changes in either objective [23] or subjective [24] measures of function, rather than clinical outcomes.

In the only RCT conducted with CABG patients that had LOHS as the primary outcome measure, 246 patients awaiting elective surgery for CABG were randomised to receive either a multi-dimensional preoperative intervention or usual care [25]. The intervention consisted of 30 minutes of supervised aerobic exercise (40 – 70% of VO_{2max}), in addition to a variety of mobility exercises, twice weekly for approximately eight weeks (mean duration: 8.3 weeks). Patients who received the PREHAB intervention spent one less day in hospital overall (95% CI: 0.0 to 1.0), and 2.1 hours less time in ICU (95% CI: -1.2 to 16.0) compared to the control group. The PREHAB group also displayed a greater quality of life during the waiting period (measured by the SF-36), which continued up to six months after surgery. Thus, engaging in PREHAB in the waiting period for CAGB surgery provided an imminent patient benefit that is likely to be meaningful. Furthermore, the authors calculated the cost of PREHAB would be C$342 per day, and that an exercise test before the intervention would cost C$240 [25]. Based on the rate of one day in a Canadian hospital (C$715), a one day reduction in LOHS would provide a net cost savings of approximately C$133 per patient per day.

3.2. PREHAB in Lung Resection Surgery

Overall, the quality of evidence for PREHAB in lung resection surgery is poor, with the research area being dominated by RCTs with small sample sizes and singe-group observational trials. In a recent systematic review [19] of 10 studies consisting of 277 participants (Table 1) , only four studies were RCTs, with one study being a case control study and the remaining five studies were prospective cohort trials. Furthermore, only four studies included in the review were considered as 'good quality' or above according to the Physiotherapy Evidence Database (PEDro) scale. Notwithstanding the lack of high quality studies, the findings indicated that PREHAB may have beneficial effects on physical fitness, which is consistent with another systematic review in patients undergoing elective intra-cavity surgery [16]. The authors also suggested that LOHS and complication rates may be reduced with PREHAB [19]. However, this conclusion was based on only two RCTs, both of which included less than 30 participants. In a meta-analysis of 21 studies (5 RCTs) that included 1189 patients from 2005 to 2013 [15], PREHAB reduced LOHS by -4.83 days (95% CI: -5.9 to -3.76) and decreased the relative risk for developing postoperative complications (RR 0.45; 95% CI: 0.28 to 0.74) based on pooled data from nine studies. While the meta-analysis did not quantify changes in exercise capacity, several included studies reported statistically significant improvements in 6MWT distance and VO_{2max}, ranging from 20 metres [26] to 170 metres [27] and from 2.3 $mL·kg^{-1}·min^{-1}$ [28] to 6.3 $mL·kg^{-1}·min^{-1}$ [27], respectively. Furthermore, two studies also demonstrated an increment in the maximal workload achieved during the cardiopulmonary exercise test [29, 30].

Interestingly, simple walking regimens have been shown to evoke discernible benefits to patients awaiting lung resection. In an RCT with LOHS as the primary outcome measurement [31], 60 patients with non-small cell lung cancer (NSCLC) received either usual care, or engaged in walking exercise on a treadmill three times per day for one week (intensity and duration not reported) in addition to chest physiotherapy (breathing exercises and incentive spirometry). The PREHAB group registered a significantly reduced LOHS in comparison to the control group (5.4 ± 2.7 vs. 9.7 ± 3.1 days, respectively). Compared with baseline values, the PREHAB group also significantly increased their pre-surgical walking duration (18.2 ± 7.4 vs. 39.7 ± 16.2 minutes), distance (614 ± 415 vs. 991 ± 535 metres), and speed (4.0 ± 1.0 vs. 5.0 ± 1.1 mph), although the testing involved non-standardised procedures and the change in walking capacity was measured within groups because the control group did not participate in exercise testing. Nevertheless, improvements in clinical and functional outcomes have also been reported following a similar four-week walking (10 – 30 minutes at 80% VO_{2max}, three times per week) and IMT (10 – 30 minutes daily) intervention prior to lung cancer resection [32]. Compared to patients receiving conventional chest physiotherapy (breathing exercises for lung expansion), the PREHAB group increased 6MWT distance (-4.6 ± 20.3 vs. 50 ± 16.2 metres), reduced LOHS (12.2 ± 3.6 vs. 7.8 ± 4.8 days), had fewer days with chest tubes (7.4 ± 2.6 vs. 4.5 ± 2.9 days) and exhibited less postoperative pulmonary complications (7 vs. 2), respectively. Though the inclusion of IMT is likely to have augmented the effects of exercise, these studies [31, 32] suggest that a short-term, simple PREHAB protocol may improve pre-surgical functional capacity and can have a substantial benefit on convalescence, at least in patients awaiting lung resection.

In the only home-based study, Coats et al. [33] investigated the effects of a 4 week PREHAB intervention in NSCLC patients. The intervention included 30 minutes of aerobic exercise at 60-80% of peak workload and free-weight resistance exercises (1-2 sets of 10-15 repetitions with 1-2 kg dumbbells) for 3-5 times per week. In contrast to several previous studies, no significant improvement was found in the VO_{2max} of the 13 patients to complete the intervention. The lack of supervision in Coats et al. [33] may have contributed to the difference between studies; supervised programmes tend to be more effective than unsupervised programmes for improving function in older adults [34]. Despite the lack of change in VO_{2max}, Coats et al. [33] reported significant and clinically meaningful improvements in the constant endurance test (from 264 ± 79 seconds to 421 ± 241 seconds) and 6MWT distance (540 ± 98 metres to 568 ± 101 metres). Small improvements were also noted in deltoid (Δ 1.8 ± 2.8 kg), triceps (Δ 1.3 ± 1.8 kg) and hamstring (Δ 3.4 ± 3.7 kg) muscle strength following PREHAB. While these changes were potentially trivial, an increase in muscle strength prior to surgery may play an important role in facilitating early mobilisation, which is a key component of the ERAS pathway. For this reason, measures of muscle strength should be considered important in future studies to assess the efficacy of PREHAB in context of ERAS.

In summary, there is some evidence that PREHAB can improve physical fitness prior to lung resection surgery. These improvements appear to be meaningful and may translate into favourable clinical outcomes. For example, studies measuring 6MWT distance reported an increase of between 20 and 170 metres following PREHAB, with the majority of improvements exceeding the minimal important difference previously reported in lung cancer patients (22 - 42 metres) [35]. In addition, Coats and colleagues [33] provided preliminary evidence that PREHAB can enhance the force-generating capacity of skeletal muscle. Even so, the research area is dominated by poor quality studies, mainly involving single-group observational trials with small sample sizes. It is also pertinent to note that the majority of studies consisted of at least five hospital-based supervised exercise sessions a week, therefore a considerable time and resource (money, facility and staffing availability) burden would be placed on both the exercise provider and patient in order to participate in the intervention. Older persons are more likely to engage in exercise interventions that are easily accessible, do not require transport, and involve no out-of-pocket costs [36].

4. PREHAB in Intra-Abdominal Surgery

4.1. Gastrointestinal and Colorectal Surgery

There are several published systematic reviews in the topic of PREHAB and surgery that have included gastrointestinal and colorectal patients, and a further four reviews that have focused solely on colorectal and/or abdominal surgery [16-18, 37]. In 2014, a meta-analysis [38] suggested that no recommendation can currently be made regarding exercise training as a routine intervention for colorectal cancer patients. However, this study [38] involved all stages of the perioperative pathway. In the only systematic review to date specifically evaluating PREHAB in patients awaiting surgery for colorectal cancer, Boereboom et al. [17] identified eight studies with a total of 518 patients from 2009 to 2015, including five RCTs, two prospective cohort trials and one non-randomised interventional study. Results indicated that exercise PREHAB improves functional capacity, and to a lesser extent cardiorespiratory fitness prior to colorectal cancer resection. 6MWT distance was the preferred primary outcome measure in five of the included studies (two studies analysed the same data [39, 40]), with reported improvements of between 4 metres [41] and 42 metres [42] compared with control. However, there was no evidence of reduced LOHS or complications rates, and thus the improvement in fitness may not translate into reduced perioperative risk or improved postoperative outcomes.

A similar finding was reported in a systematic review by O'Doherty and colleagues [16] including 10 studies from 1981 to 2011, containing 524 patients awaiting elective intra-cavity surgery. Four of the studies were RCTs and six were observational. It was concluded that PREHAB is effective in improving physical fitness, however, the evidence for augmented postoperative clinical outcome is limited. Seven of the studies reported VO_{2max} or predicted VO_{2max} as the primary outcome measure, with increases of up to 8 $mL\cdot kg^{-1}\cdot min^{-1}$ found in patients undergoing gastrointestinal surgery [43]. A beneficial effect of PREHAB on objective measures of cardiorespiratory performance has also been demonstrated recently by West and colleagues [44] in neoadjuvant chemoradiotherapy (NACRT) patients, although a non-randomised design was used and the intervention lasted six weeks, which may not be applicable for colorectal surgery patients not receiving NACRT because the duration exceeds the median wait time between surgical consultation and resection (~31 days) [45].

There appears to be a collective difficulty of converting promising results in a laboratory environment into meaningful improvements in the clinical setting. This may be related to the design and conduct of exercise interventions, or because all studies in this research area report measures of physical fitness as the primary outcome measure and are underpowered to detect differences in clinical outcomes. It has been suggested that 400 participants would be required to detect a 10% reduction in the incidence of absolute postoperative complications with an alpha of 0.05 and a power of 0.80 [17]; to date, these data do not currently exist.

In another systematic review [18] based on six RCTs (673 patients) from 1997 to 2010, the authors concluded that PREHAB may be effective in enhancing physical fitness in surgical patients awaiting abdominal resection. However, when considering the primary data from the individual studies included within the review, no study actually reported a PREHAB-induced increase in physical fitness. Of the three studies to measure physical fitness prior to surgery, Kim et al. [41] and Dronkers et al. [46] failed to show changes in VO_{2max} and predicted VO_{2max}, respectively. Furthermore, Carli et al. [39] showed that the proportion of patients with an improvement of ≥ 20 metres in the 6MWT was actually greater in a sham intervention group compared with the PREHAB group (47% vs. 22% preoperatively, and 41% vs. 11% postoperatively). Patients in the PREHAB group were instructed to cycle seven days per week (20-30 min at 50% of HR_{max}, progressing by 10% each week as tolerated) and perform resistance training three times per week (bodyweight and free-weight exercises until volitional failure), whereas the sham intervention consisted of a recommendation to walk for 30 minutes every day. While task specificity (e.g. walking intervention and walking-based outcome measure) and the multiple imputation of large amounts of data (i.e. due to the high attrition rates) may have contributed to the results, only 16% of the PREHAB group fully adhered to the protocol. Thus, patients with a low baseline fitness level may have found the intensive and time-consuming design of the bike/strengthening programme intimidating or too difficult. This highlights the necessity to find an appropriate balance between an exercise stimulus that is sufficient to improve physical fitness, but also to maximise patient engagement and safety.

In order to improve exercise compliance, the same research group have since conducted three trimodal home-based RCTs [42, 47, 48]. In all three studies the frequency of aerobic exercise was decreased from daily to three times per week, the training intensity did not exceed 50% HR_{max}, and patients were allowed to choose their preferred type of exercise. The exercise interventions lasted four weeks and were also appended with whey protein supplementation and psychological support. The PREHAB group displayed a greater improvement in 6MWT distance compared with controls in all three studies (from 29.1 metres [47] to 41.6 metres [48]), which was also associated with faster postoperative recovery of 6MWT performance 8 weeks following resection [from 45.2 metres [48] to 85.4 metres [42]]. Compliance in the preoperative period was above 75% in all three studies, suggesting that exercising at home may facilitate adherence to PREHAB programmes. Indeed, home-based cardiac rehabilitation programmes have tended to show greater adherence and maintenance rates than supervised hospital-based programmes [49]. However, consistent with other studies investigating PREHAB in abdominal surgery, no differences between PREHAB and control groups were found in LOHS, 30-day complication rate, or complication severity.

Generally, the literature shows that PREHAB prior to colorectal resection enhances walking capacity by approximately 25 to 40 metres, and can also induce small improvements cardiorespiratory fitness. The promotion of walking capacity prior to surgery has led to improved postoperative recovery of physical fitness, which is parallel with the objectives of the ERAS pathway. However, the magnitude of change in physical fitness appears insufficient or unable to translate into favourable clinical outcomes, such as reduced LOHS and complication rate. The lack of multi-centred adequately powered RCTs certainly underpin, at least in part, the negligible changes in perioperative outcomes. It is also conceivable that the current modalities of exercise PREHAB, rather than the theory of PREHAB *per se*, also contribute to the absence of improvement in outcome measures.

There is a distinct lack of standardised PREHAB guidelines for patients undergoing major intra-abdominal and intra-thoracic surgery, ostensibly due to the conflicting findings in the current literature. The majority of studies have involved generic prescriptions of moderate-intensity aerobic exercise, with resistance training less frequency included within PREHAB protocols. Likewise, the primary endpoint was usually a measurement of cardiorespiratory fitness such as VO_{2max} or 6MWT, presumably based on the well-established relationship between VO_{2max} and perioperative outcome [14]. When resistance training has been prescribed in PREHAB protocols, pertinent programme design variables have largely been ignored and/or not reported. Given that PREHAB is defined as the systematic process of improving functional capacity of the patient to withstand surgical stress [13], and strength training has consistently been shown to augment functional ability in older adults [50], further work is required to investigate the therapeutic benefits of individualised resistance training programmes prior to intra-cavity surgery.

5. A Role for PREHAB in the ERAS Pathway?

PREHAB appears to be effective for improving physical fitness prior to elective intra-cavity surgery. Some studies have also reported an accelerated recovery of postoperative functional capacity, which is a central tenet of ERAS pathways [7]. However, the rate of complications and LOHS are also important endpoints for ERAS care, and there is limited evidence suggesting that PREHAB can modify these clinical outcomes. Indeed, there appears to be a collective difficulty of translating favourable changes in functional capacity into a reduction in complication rates or LOHS. Furthermore, the majority of studies in the PREHAB literature are included in multiple systematic reviews, meaning there are a small number of primary studies and most of them are single-centred and inadequately powered to detect changes in any clinical endpoint.

The ERAS Society have published guidelines for evidence-based perioperative care in elective colonic surgery [51]. The preoperative components of the ERAS model are presented in Table 2. For PREHAB to be considered a worthwhile addition to the ERAS pathway, evidence is required demonstrating that the benefits of presurgical exercise exceed current practice in the preoperative period. Only two studies to date, both involving colorectal cancer patients, have administered PREHAB in the context of ERAS. Li et al. [42] compared PREHAB to a control group receiving standard ERAS care, whereas Gillis et al. [48] compared PREHAB to a group undergoing exercise rehabilitation within ERAS. In agreement with the totality of literature, both studies reported an increase in walking capacity following PREHAB, but there were no improvements in LOHS nor complication rates when compared to a standard ERAS programme [42, 48]. Further research is required directly comparing the effects of ERAS *with* PREHAB versus ERAS *without* PREHAB in patients undergoing intra-cavity surgery.

In addition to the well-established clinical benefits, studies have shown ERAS programmes to be cost-effective across a range of surgical specialities, including abdominal and thoracic surgery [52, 53]. This is thought to be a consequence of shorter convalescence and reductions in morbidity and complication rates [53]. In contrast, there is a paucity of data concerning the cost-effectiveness of PREHAB. However, the lack of benefit to clinical outcomes suggests that, currently, PREHAB may not be economically worthwhile for service providers. The adoption of any new intervention in the healthcare system requires rigorous justification because of major financial constraints. The absence of improvements in LOHS and complications, coupled with a lack of savings, impedes the potential uptake of PREHAB into existing ERAS pathways.

It is unknown whether PREHAB is simply unable to improve clinical outcomes, or that currently prescribed exercise interventions are insufficient to drive the necessary adaptations. The exercise programmes within this body of literature are largely heterogeneous, although the vast majority of studies have involved generic prescriptions of moderate-intensity aerobic exercise. While these protocols have generally induced changes in aerobic fitness, a more precise manipulation of training variables may improve the training stimulus and better prepare the patient for the upcoming physiological stress of surgery. Therefore, future work should compare the effectiveness of different training modalities and adhere to exercise trial reporting guidelines (e.g. [54]) to advance our understanding of the optimal exercise PREHAB characteristics and ultimately help develop consensus exercise guidelines for this patient population.

6. Conclusion

To conclude, the current evidence-base on PREHAB for patients undergoing elective intra-cavity surgery is limited by inadequately powered RCTs, single-group observational trials and a lack of evidence demonstrating favourable changes in clinical endpoints. Considering these drawbacks in the literature, and that only two studies have administered PREAB in the context of ERAS [42, 48], this review cannot recommend that PREHAB be introduced into existing ERAS pathways. Further randomised clinical trials should be powered to detect changes in clinical outcomes rather than changes in physical fitness. For example, prospective studies are needed to better characterise the impact of PREHAB on length of stay and complication rate. In addition, the quality of prescribed exercise PREHAB interventions must be examined in order to advance this research area.

Funding This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Greenlee RT, Hill-Harmon MB, Murray T, Thun M. Cancer statistics, 2001. CA: A Cancer Journal for Clinicians. 2001;51(1):15-36.

2. Baquero GA, Rich MW. Perioperative care in older adults. J Geriatr Cardiol. 2015;12(5):465-9.

3. Schoetz DJ, Jr., Bockler M, Rosenblatt MS, Malhotra S, Roberts PL, Murray JJ, et al. "Ideal" length of stay after colectomy: whose ideal? Dis Colon Rectum. 1997;40(7):806-10.

4. Basse L, Hjort Jakobsen D, Billesbolle P, Werner M, Kehlet H. A clinical pathway to accelerate recovery after colonic resection. Ann Surg. 2000;232(1):51-7.

5. Bokey EL, Chapuis PH, Fung C, Hughes WJ, Koorey SG, Brewer D, et al. Postoperative morbidity and mortality following resection of the colon and rectum for cancer. Dis Colon Rectum. 1995;38(5):480-6; discussion 6-7.

6. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. Br J Anaesth. 1997;78(5):606-17.

7. Ljungqvist O, Scott M, Fearon KC. Enhanced Recovery After Surgery: A Review. JAMA Surg. 2017;152(3):292-8.

8. Greco M, Capretti G, Beretta L, Gemma M, Pecorelli N, Braga M. Enhanced recovery program in colorectal surgery: a meta-analysis of randomized controlled trials. World Journal of Surgery. 2014;38(6):1531-41.

9. Roulin D, Donadini A, Gander S, Griesser AC, Blanc C, Hübner M, et al. Cost-effectiveness of the implementation of an enhanced recovery protocol for colorectal surgery. British Journal of Surgery. 2013;100(8):1108-14.

10. Varadhan KK, Neal KR, Dejong CH, Fearon KC, Ljungqvist O, Lobo DN. The enhanced recovery after surgery (ERAS) pathway for patients undergoing major elective

open colorectal surgery: a meta-analysis of randomized controlled trials. Clinical Nutrition. 2010;29(4):434-40.

11. Zhuang CL, Ye XZ, Zhang XD, Chen BC, Yu Z. Enhanced recovery after surgery programs versus traditional care for colorectal surgery: a meta-analysis of randomized controlled trials. Dis Colon Rectum. 2013;56(5):667-78.

12. Lv L, Shao YF, Zhou YB. The enhanced recovery after surgery (ERAS) pathway for patients undergoing colorectal surgery: an update of meta-analysis of randomized controlled trials. Int J Colorectal Dis. 2012;27(12):1549-54.

13. Topp R, Ditmyer M, King K, Doherty K, Hornyak J. The effect of bed rest and potential of prehabilitation on patients in the intensive care unit. AACN Advanced Critical Care. 2002;13(2):263-76.

14. Levett DZ, Grocott MP. Cardiopulmonary exercise testing for risk prediction in major abdominal surgery. Anesthesiology Clinics. 2015;33(1):1-16.

15. Garcia RS, Brage MI, Moolhuyzen EG, Granger CL, Denehy L. Functional and postoperative outcomes after preoperative exercise training in patients with lung cancer: a systematic review and meta-analysis. Interactive Cardiovascular and Thoracic Surgery. 2016;23(3):486-97.

16. O'Doherty AF, West M, Jack S, Grocott MP. Preoperative aerobic exercise training in elective intra-cavity surgery: a systematic review. British Journal of Anaesthesia. 2013;110(5):679-89.

17. Boereboom C, Doleman B, Lund JN, Williams JP. Systematic review of pre-operative exercise in colorectal cancer patients. Techniques in Coloproctology. 2016;2016(20):2.

18. Pouwels S, Stokmans RA, Willigendael EM, Nienhuijs SW, Rosman C, van Ramshorst B, et al. Preoperative exercise therapy for elective major abdominal surgery: a systematic review. International Journal of Surgery, . 2014;12(2):134-40.

19. Pouwels S, Fiddelaers J, Teijink JA, ter Woorst JF, Siebenga J, Smeenk FW. Preoperative exercise therapy in lung surgery patients: A systematic review. Respiratory Medicine. 2015;109(12):1495-504.

20. Pouwels S, Hageman D, Gommans LN, Willigendael EM, Nienhuijs SW, Scheltinga MR, et al. Preoperative exercise therapy in surgical care: a scoping review. J Clin Anesth. 2016;33:476-90.

21. Hulzebos EH, Smit Y, Helders PP, van Meeteren NL. Preoperative physical therapy for elective cardiac surgery patients. The Cochrane Library. 2012;11:CD010118.

22. Snowdon D, Haines TP, Skinner EH. Preoperative intervention reduces postoperative pulmonary complications but not length of stay in cardiac surgical patients: a systematic review. Journal of Physiotherapy. 2014;60(2):66-77.

23. Sawatzky JA, Kehler DS, Ready AE, Lerner N, Boreskie S, Lamont D, et al. Prehabilitation program for elective coronary artery bypass graft surgery patients: a pilot randomized controlled study. Clinical Rehabilitation. 2014;28(7):648-57.

24. Rosenfeldt F, Braun L, Spitzer O, Bradley S, Shepherd J, Bailey M, et al. Physical conditioning and mental stress reduction-a randomised trial in patients undergoing cardiac surgery. BMC Complementary and Alternative medicine. 2011;11:20.

25. Arthur HM, Daniels C, McKelvie R, Hirsh J, Rush B. Effect of a preoperative intervention on preoperative and postoperative outcomes in low-risk patients awaiting elective coronary artery bypass graft surgery: a randomized, controlled trial. Annals of Internal Medicine. 2000;133(4):253-62.

26. Bradley A, Marshall A, Stonehewer L, Reaper L, Parker K, Bevan-Smith E, et al. Pulmonary rehabilitation programme for patients undergoing curative lung cancer surgery. European Journal of Cardio-Thoracic Surgery, . 2013;44(4):e266-71.

27. Divisi D, Di Francesco C, Di Leonardo G, Crisci R. Preoperative pulmonary rehabilitation in patients with lung cancer and chronic obstructive pulmonary disease. European Journal of Cardio-Thoracic Surgery. 2013;43(2):293-6.

28. Jones LW, Peddle CJ, Eves ND, Haykowsky MJ, Courneya KS, Mackey JR, et al. Effects of presurgical exercise training on cardiorespiratory fitness among patients undergoing thoracic surgery for malignant lung lesions. Cancer. 2007;110(3):590-8.

29. Bobbio A, Chetta A, Ampollini L, Primomo GL, Internullo E, Carbognani P, et al. Preoperative pulmonary rehabilitation in patients undergoing lung resection for non-small cell lung cancer. . European Journal of Cardio-Thoracic Surgery. 2008;33(1):95-8.

30. Fang Y, Zhao Q, Huang D. The impact of exercise training on surgery tolerability in lung cancer patients with impaired pulmonary function. Chinese Journal of Rehabilitation Medicine. 2013;28:619-23.

31. Pehlivan E, Turna A, Gurses A, Gurses HN. The effects of preoperative short-term intense physical therapy in lung cancer patients: a randomized controlled trial. Annals of Thoracic and Cardiovascular Surgery. 2011;17(5):461-8.

32. Morano MT, Araújo AS, Nascimento FB, da Silva GF, Mesquita R, Pinto JS, et al. Preoperative pulmonary rehabilitation versus chest physical therapy in patients undergoing lung cancer resection: a pilot randomized controlled trial. Archives of Physical Medicine and Rehabilitation. 2013;94(1):53-8.

33. Coats V, Maltais F, Simard S, Frechette E, Tremblay L, Ribeiro F, et al. Feasibility and effectiveness of a home-based exercise training program before lung resection surgery. Canadian Respiratory Journal. 2013;20(2):e10-e6.

34. Lacroix A, Hortobagyi T, Beurskens R, Granacher U. Effects of Supervised vs. Unsupervised Training Programs on Balance and Muscle Strength in Older Adults: A Systematic Review and Meta-Analysis. Sports Med. 2017.

35. Granger CL, Holland AE, Gordon IR, Denehy L. Minimal important difference of the 6-minute walk distance in lung cancer. Chronic respiratory Disease. 2015;12(2):146-54.

36. Franco MR, Howard K, Sherrington C, Ferreira PH, Rose J, Gomes JL, et al. Eliciting older people's preferences for exercise programs: a best-worst scaling choice experiment. Journal of Physiotherapy. 2015;61(1):34-41.

37. Pouwels S, Willigendael EM, van Sambeek MR, Nienhuijs SW, Cuypers PW, Teijink JA. Beneficial Effects of Pre-operative Exercise Therapy in Patients with an Abdominal Aortic Aneurysm: A Systematic Review. European Journal of Vascular and Endovascular Surgery. 2015;49(1):66-76.

38. Cramer H, Lauche R, Klose P, Dobos G, Langhorst J. A systematic review and meta-analysis of exercise interventions for colorectal cancer patients. European Journal of Cancer Care 2014;23(1):3-14.

39. Carli F, Charlebois P, Stein B, Feldman L, Zavorsky G, Kim DJ, et al. Randomized clinical trial of prehabilitation in colorectal surgery. British Journal of Surgery. 2010;97(8):1187-97.

40. Mayo NE, Feldman L, Scott S, Zavorsky G, Kim DJ, Charlebois P, et al. Impact of preoperative change in physical function on postoperative recovery: argument supporting prehabilitation for colorectal surgery. Surgery. 2011;150(3):505-14.

41. Kim DJ, Mayo NE, Carli F, Montgomery DL, Zavorsky GS. Responsive measures to prehabilitation in patients undergoing bowel resection surgery. The Tohoku Journal of Experimental Medicine. 2009;217(2):109-15.

42. Li C, Carli F, Lee L, Charlebois P, Stein B, Liberman AS, et al. Impact of a trimodal prehabilitation program on functional recovery after colorectal cancer surgery: a pilot study. Surgical Endoscopy. 2013;27(4):1072-82.

43. Timmerman H, de Groot JF, Hulzebos HJ, de Knikker R, Kerkkamp HEM, Van Meeteren NLU. Feasibility and preliminary effectiveness of preoperative therapeutic exercise in patients with cancer: a pragmatic study. Physiotherapy Theory and Practice. 2011;27(2):117-24.

44. West MA, Loughney L, Lythgoe D, Barben CP, Sripadam R, Kemp GJ, et al. Effect of prehabilitation on objectively measured physical fitness after neoadjuvant treatment in preoperative rectal cancer patients: a blinded interventional pilot study. British Journal of Anaesthesia. 2015;114(2):244-51.

45. Gillis A, Dixon M, Smith A, Law C, Coburn NG. A patient-centred approach toward surgical wait times for colon cancer: a population-based analysis. Can J Surg. 2014;57(2):94-100.

46. Dronkers JJ, Lamberts H, Reutelingsperger IM, Naber RH, Dronkers-Landman CM, Veldman A, et al. Preoperative therapeutic programme for elderly patients scheduled for elective abdominal oncological surgery: a randomized controlled pilot study. Clinical Rehabilitation. 2010;24(7):614-22.

47. Chen BP, Awasthi R, Sweet SN, Minnella EM, Bergdahl A, Santa Mina D, et al. Four-week prehabilitation program is sufficient to modify exercise behaviors and improve preoperative functional walking capacity in patients with colorectal cancer. Supportive Care in Cancer. 2016;25(1):33-40.

48. Gillis C, Li C, Lee L, Awasthi R, Augustin B, Gamsa A, et al. Prehabilitation versus Rehabilitation: A Randomized Control Trial in Patients Undergoing Colorectal Resection for Cancer. The Journal of the American Society of Anesthesiologists. 2014;121(5):937-47.

49. Buckingham SA, Taylor RS, Jolly K, Zawada A, Dean SG, Cowie A, et al. Home-based versus centre-based cardiac rehabilitation: abridged Cochrane systematic review and meta-analysis. Open Heart. 2016;3(2):e000463.

50. Liu CJ, Latham NK. Progressive resistance strength training for improving physical function in older adults. Cochrane Database Syst Rev. 2009(3):Cd002759.

51. Gustafsson UO, Scott MJ, Schwenk W, Demartines N, Roulin D, Francis N, et al. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS((R))) Society recommendations. World J Surg. 2013;37(2):259-84.

52. Scarci M, Solli P, Bedetti B. Enhanced recovery pathway for thoracic surgery in the UK. J Thorac Dis. 2016;8(Suppl 1):S78-83.

53. Stowers MD, Lemanu DP, Hill AG. Health economics in Enhanced Recovery After Surgery programs. Can J Anaesth. 2015;62(2):219-30.

54. Slade SC, Dionne CE, Underwood M, Buchbinder R. Consensus on Exercise Reporting Template (CERT): Explanation and Elaboration Statement. Br J Sports Med. 2016.

Table Captions

Table 1. Overview of the included reviews

Table 2. Preoperative components of the Enhanced Recovery After Surgery (ERAS) Pathway

Table 1. Overview of the included reviews

Authors	Type of Review	Type of Surgery	Number of studies [RCTs]	Number of patients
Pouwels et al. [19]	SR	Lung	10 [4]	277
Garcia et al. [15]	SR and meta-analysis	Lung	21 [5]	1189
Boereboom et al. [17]	SR	Colorectal	8 [5]	518
O'Doherty et al. [16]	SR	Abdominal Cardiac	10 [4]	524
Pouwels et al. [18]	SR	Abdominal	6 [6]	673

RCT- randomised controlled trial, SR- systematic review

Table 2. Preoperative components of the Enhanced Recovery After Surgery (ERAS) Pathway

Component	Rationale
Cessation of smoking and excessive alcohol consumption	Reduce complications
Structured preoperative information, education and counselling	Reduce fear and anxiety
Preoperative carbohydrate treatment	Reduce insulin resistance and possibly improve recovery
Not routinely using preoperative bowel preparation	Reduce dehydration, prolonged ileus and risk of anastomotic leakage
Prophylaxis against thromboembolism	Reduce thromboembolic complications
Preoperative prophylaxis against infection	Reduce rate of infections