



EFFECT OF PHYSIOTHERAPY ON VITAL CAPACITY BEFORE MAJOR ABDOMINAL SURGERY IN CANCER PATIENTS: A SYSTEMATIC REVIEW

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Summary

Introduction: Cancer is one of the leading causes of death worldwide. However, if diagnosed in an operable stage, it is treated as a chronic disease. As such, long-term results and quality of life requirements imposed a comprehensive approach. Prehabilitation programs encompassing nutritional, physical, and psychological components improved the recovery and minimized the complication rate after surgery. We will focus on physiotherapy as part of prehabilitation in this review.

Methods: For systematic search, we used the MEDLINE/PubMed (National Library of medicine), Cochrane Central Register of Controlled Trials (Wiley), Embase (Elsevier, Web of Science, and Cochrane database of systematic reviews. The last search update was on 15th December 2020. The search included randomized clinical trials or quasi-randomized clinical trials evaluating exercise or other non-pharmacological preoperative interventions in gastrointestinal cancers.

Results: The ten trials included 1058 patients, 535 (50,6%) patients were in the experimental group, and 523 (49,4%) patients were in the control group. Bicycle exercise training was the best-ranked intervention with the standard mean difference (SMD) of 1,4077 (95% C.I. is 0,7018 – 2,1135) to improve vital functional capacity ($\dot{V}O_2$ at $\dot{V}O_{2L}$). Short-term exercise affected inspiratory muscle strength, and SMD was 1,1819 (95% C.I., 2953 – 2,0684). Short-term intensity training program SMD was 0,8356 (95% C.I. 0,2042 – 1,4669), and short-term intensity program for muscle endurance 0,8156 (95% C.I. 0,2042 – 1,4669). Improves respiratory muscle endurance. Small effect was shown on quality of life in high-intensity cycling interval training SMD 0,7439 (95% C.I. 0,0856 – 1,4023), WHO performance status in bicycle exercise training SMD 0,7068 (95% C.I. 0,0547 – 1,3589), mean number of complication in high-intensity endurance training SMD 0,3606 (95% C.I. 0,0072 – 0,7141).

Conclusion: Although exercise therapy has been shown to improve vital capacity and respiratory muscle strength, there was a lack of comparison between different exercises. Evidence from these indirect-comparisons studies indicated that physical activity should be encouraged during the preoperative period before oncologic surgery.

KEYWORDS: exercise, rehabilitation, cancer, major abdominal surgery

INTRODUCTION

Cancer is a significant public health problem worldwide (1). Cancer is expected to rank as the

leading cause of death and the single most important barrier to increasing life expectancy in every country of the world in the 21st century. According to estimates from the World Health Organization (WHO) in 2015, cancer is the first or second leading cause of death under 70 years in 91 of 172 countries, and it ranks third or fourth in an additional 22 countries. Cancer incidence and mortality are rapidly growing worldwide (2).

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Surgery is the most common and still the most effective cancer treatment (3). About 300 million patients undergo surgery worldwide each year, with more procedures in high-income countries (4). Findings from epidemiological studies suggest that 4.8 billion people cannot access safe surgical treatments and that at least 143 million additional procedures are required each year, primarily in low and middle-income countries (4,5). However, as health care systems develop to improve access to surgical treatments, the number of patients who suffer postoperative complications will also increase. Postoperative complications increase treatment costs and reduce both life expectancy and quality of life (5).

Advances in diagnostic procedures, surgical technology, and perioperative care have improved safety and patient outcomes following cancer's surgical resection. The mortality and morbidity rates of primary surgical resection are between 4% and 10% (6) and 20% and 60%, respectively (7). Postoperative complications prolong hospital stay, readmissions, and costs, significantly impacting patient functioning and quality of life, and may have long-term implications on mortality. The impact of the stress of cancer and surgery is notable during the recovery period and is characterized by fatigue, decreased appetite, pain, reduced mobility and mental concentration. When the impact of abdominal surgery is evaluated using functional capacity measures, only 30% of older adults recover to preoperative levels at eight weeks after surgery and 50% after six months (8). Poor preoperative physical performance has been shown to increase the number of postoperative complications and mortality risk (9).

Prehabilitation is an intervention that capitalizes on the waiting period before surgery with preoperative strategies designed to optimize the patient's physical condition to promote an earlier postoperative recovery (10). Also, rehabilitation improves patient health in anticipation of a physiological stressor such as major surgery (11).

Cancer prehabilitation has been defined by Sliver and Baima as *a process on the cancer continuum of care that occurs between the time of cancer diagnosis and the beginning of acute treatment and includes physical and psychological assessments that establish a baseline functional level, identify impairments, and provide interventions that promote physical and men-*

tal health to reduce the incidence and severity of future impairments (12).

Preoperative physical status is often reduced in patients with cancer and is predictive of postoperative complications and poor prognosis. Therefore, preoperative status is an essential factor in improving postoperative outcomes in these patients (13). Over the last few years, several studies have evaluated the possibility of enhancing preoperative physical function by using prehabilitation to overcome surgical stress and improve postoperative recovery times (14).

Physical exercise is defined as an activity that is planned, structured, repetitive, and purposeful to improve or maintain one or more components of physical fitness, i.e., endurance, muscular strength, and body composition. Physical exercise has, in general, a positive impact on many biological processes such as energy expenditure, insulin resistance, inflammation, and most body organs and tissues. In cancer patients, there is evidence that physical exercise reduces fatigue, improves the quality of life, and relieves many of the adverse side effects experienced during and after treatment (15,16).

METHODS

Selection of studies

We systematically searched MEDLINE/PubMed (National Library of medicine), Cochrane Central Register of Controlled Trials (Wiley), Embase (Elsevier, Web of Science and Cochrane database of systematic reviews. The search strategy developed relevant keywords and controlled vocabulary that included: preoperative exercise, prehabilitation, oncologic surgery, gastrointestinal cancer, and randomized controlled trials. We last updated the search on 15th December 2020.

Data extraction

Individual reviewers screened titles and abstracts to identify potentially relevant articles. The senior author resolved discrepancies in judgment. In case of disagreement, we reached a consensus through discussion. At this stage, studies were excluded only if the available information in the title or the abstract made it clear that the article was not eligible. Full texts were retrieved for the other papers and read independently by these reviews.

Assessment of Risk of bias

We used the Cochrane risk-of-bias (RoB) tool published in the Cochrane handbook for systematic reviews of interventions, random sequence generation items, allocation concealment, baseline differences between groups, and blinding of participants, blinding of therapists, and blinding of assessors, incomplete outcome data, and intention-to-treat analysis. We provided RoB only to give a detailed overview of the characteristics of the included studies (i.e., we did not use RoB to exclude studies)

Inclusion and exclusion criteria

Inclusion criteria of study selection

We included published randomized clinical trials or quasi-randomized clinical trials evaluating all kinds of exercise or other non-pharmacological interventions such as relaxation intervention in cancer patients before surgery for gastrointestinal cancer, liver cancer, colon, and rectal cancer.

Exclusion criteria of study selection

We excluded trials comparing drugs or nutritional supplementations, acupuncture, electroacupuncture, acupressure, moxibustion, or healing without touching the patients.

Endpoints

The primary endpoint for this study included the measurement of functional vital capacity. The studies included had functional vital capacity quantification with a 6-minute walk test and/or inspiratory muscle strength. We used the percentage of patients with any complication as defined by the authors of the original study. We did not include readmissions, which were evaluated separately.

The secondary endpoint was the quality of life and health survey. Safety was defined as a report of any serious or nonserious adverse events (A.E.s) of any grade (17).

Data synthesis and analysis

Because functional vital capacity was assessed with various tests, we used standard mean difference (SMD). The SMD measure of effect is used when studies report efficacy in terms of a

continuous measurement, such as score on a pain-intensity rating scale. The SMD is also known Cohen's *d*. An SMD of zero means that the new treatment and the placebo have equivalent effect. If improved is associated with higher scores of the outcome measure, SMDs greater than zero indicate the degree to which treatment is less efficacious than placebo.

Cohen offered the following guidelines for interpreting the magnitude of the SMD, small, SMD = 0,2, medium SMD = 0,5, large, SMD = 0,8 (18).

We selected the SMD differences between the direct and indirect comparisons to evaluate the fundamental assumption of consistency: that direct and indirect evidence is compatible or that all studies are exchangeable. Heterogeneity was assessed using Higgins I2 for each pairwise comparison (19).

RESULTS

The database's systematic search yielded 84 articles, we screened 29 full texts, and finally included ten articles for further qualitative and quantitative analysis (20 - 29) - the dates of publication range from 2010 to 2019. Of the included articles, all included articles reported on the patients before major abdominal surgery exercise treatment. The duration of intervention ranged from 2 to 6 weeks. The ten trials included 1058 patients, 535 (50,6%) patients were in the experimental group, and 523 (49,4%) patients were in the control group.

The mean S.D. patient age in the experimental group was 67,8 years and in the control group was 67,8 years. In included studies, 35,92% of patients were women.

Most of the studies reported patients undergoing major abdominal surgery, various diagnosis (N=730, 69%), followed by studies reported colorectal surgery (N=248, 23,4%), rectal surgery (n=39, 3,7%) and liver surgery (n=57, 5,39%).

RoB 2 of included trials

The random sequence generation was adequate in all trials; allocation concealment was not problematic in all trials. One study did not balance the baseline characteristics (10%). Patients were not blinded in two trials (20%). Therapists were blinded in one trial (10%). More than 4,5% of

Table 1.

Standard mean difference of primary outcome measurement

Interventions	SMD	95% C.I.	P value
Bicycle exercise training	1,4077	0,7018 – 2,1135	0,129682
Short term exercise Inspiratory muscle strength	1,1819	0,2953 – 2,0684	0,204608
Short term intensity exercise program	0,8356	0,2042 - 1,4669	0,103766
Short-term intensity exercise program (muscle endurance)	0,8156	0,2042 – 1,4669	0,103766
High-intensity cycle interval training	0,7716	0,1116 – 1,4316	0,113389
Pre-operative inspiratory muscle training	0,7134	0,1725 – 1,2545	0,076145
Aerobic and resistance exercise	0,6275	0,2545 – 1,0002	0,036189
High intensity endurance training	0,6031	0,2446 – 0,9616	0,033457
Bike/strength / walk/breathing	0,3683	-0,0054 – 0,7421	0,036366
Breathing exercise training session	0,3152	0,1275 – 0,5028	0,009163

Table 2.

Standard mean difference of secondary outcome measurement

Interventions	SMD	95% C.I.	P value
Quality of life (high-intensity cycling interval training)	0,7439	0,0856 – 1,4023	0,112838
WHO performance status (bicycle exercise training)	0,7068	0,0547 – 1,3589	0,110683
Mean number of complication per patient (high-intensity endurance training)	0,3606	0,0072 – 0,7141	0,032522
Assessment of quality of life (inspiratory muscle strength training)	0,3195	-0,5061 – 1,1425	0,176457
Quality of life – functional status (short-term intensity exercise program)	0,3177	-0,2917 – 0,927	0,096656
Quality of life (short-term intensity exercise program)	0,0117	-0,5939 – 0,6172	0,095456
Anxiety (bike/strength vs. Walking/breathing)	0,0109	-0,3597 – 0,3846	0,03576
Length of hospital stay (breathing exercise training)	0,0089	-0,0975 – 0,2756	0,009059

drop-outs were present in 50% of the trials, and only 20% of the trials reported an intention-to-treat analysis.

Indirect-comparisons studies for primary outcome measurement

The network consisted of 10 studies. Studies were reporting on two various interventions: three studies reported on the effect of respiratory muscle strength and breathing exercise, and seven studies reported on the various exercise training program (bicycle exercise, aerobic and resistance exercise, high-intensity endurance training, two short-term intensity exercise program for muscle endurance, high-intensity cycle interval training and bike/strength training versus walking/breathing program).

The effect size for the difference between all interventions is presented in table 1(20 - 29). Bicycle exercise training was the best-ranked intervention with the SMD of 1,4077 (95% C.I. is 0,7018 – 2,1135) to improve functional vital capacity (s,

VO₂ at u^ˆ L). Short-term exercise affected inspiratory muscle strength, and SMD was 1,1819 (95% C.I.,2953 – 2,0684).

Short- term intensity training program SMD was 0,8356 (95% C.I. 0,2042 - 1,4669), and short-term intensity program for muscle endurance 0,8156 (95% C.I. 0,2042 – 1,4669). improves improve respiratory muscle endurance. High-intensity cycling interval training improve oxygen uptake SMD is 0,7716 (95% C.I. 0,1116 – 1,4316). —Inspiratory muscle strength training was been more effective than deep breathing SMD 0,7134 (95% C.I. 0,1725 – 1,2545).

Indirect-comparisons studies for secondary outcome measurement

The network consisted of studies that describe the quality of life status. The majority of trials included quality of life questionnaires. The most applied questionnaire was (EORTC QLQ-C30). The effect size for the difference between all interventions is depicted in table 2.

The result stresses that exercise training intervention has a small impact on the quality of life status, anxiety, and hospital stay. Small effect was shown on quality of life in high-intensity cycling interval training SMD 0,7439 (95% C.I. 0,0856 – 1,4023), WHO performance status in bicycle exercise training SMD 0,7068 (95% C.I. 0,0547 – 1,3589), mean number of complication in high-intensity endurance training SMD 0,3606 (95% C.I. 0,0072 – 0,7141).

There were no significant changes in the quality of life assessment between the experimental and control groups in other studies.

DISCUSSION

Summary of main results

This indirect-comparison of the randomized clinical trial includes studies evaluating the effect of physical exercise intervention before major abdominal oncologic surgery on vital capacity and quality of life.

We found evidence that bicycle interval training has moderate-to-high effect size during preoperative cancer treatment substantially more than usual care (95% C.I. is higher than 0,7), Similar results have Inspiratory muscle strength, aerobic and resistance exercise, high intensity endurance training short term intensity exercise program where is 95% C.I. higher of 0,2. Pre-operative inspiratory muscle training, breathing exercise training session for prevent PPC, High intensity cycle interval training and bike/strength vs walk/breathing have a small effect size, 95% C.I. is lower than 0,2.

Also, we found that Quality of life (high-intensity cycling interval training), WHO performance status (bicycle exercise training), mean number of complication per patient (high-intensity endurance training) have a small effect size of 95% C.I., lower than 0,2. Other results of quality of life 95% C.I. were less than zero.

The ranking of the different types of preoperative exercise's effectiveness may help health-care professionals (e.g., oncologists, surgeons, physiotherapists, nurses of family medicine specialists) and patients with cancer in their shared clinical decision-making process. For example, the patient's preferences, contraindications, availability, and the interventions' costs may influence

their decision. Our ranked interventions help patients and practitioners prioritize evidence-based interventions during and after treatment.

Quality of the evidence

The strength of indirect-comparison of randomized clinical trials was to include a set of various exercise interventions (without nutrition support or other prehabilitation procedure) for cancer patients before major abdominal surgery. This study's major limitation was a small number of studies and a small number of included participation. Another limitation of this study was difficulty in classifying the intervention described in the included studies. We have a different kind of intervention combination. Second, because specific information on training intensity or the extent of exercises lacked in most of the studies, it was not possible to analyze the effect of high versus low training intensity or high versus low exercise volume.

Comparison with other studies

It is well-known that exercise therapy has an impact on improving cardiorespiratory fitness and vital capacity. Also, physical exercise reduces tumor growth, and it has a significant benefit of the patient's quality of life (30- 46). This review used different exercises like aerobic exercise, anaerobic exercise, resistance exercise, high-intensity interval training, and moderate-intensity interval training.

There have been several systematic reviews and meta-analyses evaluating the effect of exercise therapy in oncologic patients during cancer of preoperative treatment, and most of them do favor exercise intervention compared with usual care (10,12-16,47-54). This study's conclusion is based on similar sets of published studies as used in another meta-analysis of systematic reviews. Also, the findings suggest that physical exercise before cancer surgery improves physical fitness and quality of life, reduces postoperative pulmonary complications, reduces hospital stay, decreases incidences of postoperative complications, and affects muscle strength and mass.

Different working mechanisms may explain the effectiveness of the interventions included in this study. Active exercises (e.g., resistance training, aerobic training, high-intensity interval train-

ing, etc.) with or without nutrition support may counteract the decreased level of activity before cancer surgery and improve physical capacity. Furthermore, higher physical activity levels may have a beneficial effect on physiological and psychological benefits, mental health performed in quality of life questionnaire.

Preoperative level of physical activity was associated with a faster self-assessment physical recovery after colorectal cancer surgery. Physical activity did not show any associations with the primary outcome measure length of hospital stay. Assessment of physical activity level preoperatively could be used for prognostic reasons (55). Prospective study on patients after radical resection of colorectal cancer found that the ERAS protocol attenuates the surgical stress response and accelerates postoperative recovery (56).

Implication for practice

These findings may have important clinical implications. They suggest that the effectiveness of various exercise interventions varies depending on the patient's cancer treatment status. During the preoperative cancer treatment cycle, a short-term high-intensity exercise program's exercise program seems to have the most significant effect. The health professionals consider physical activity, aerobic exercise, endurance training, resistance training of inspiratory muscle training as beneficial interventions. Unfortunately, this study's results do not allow for a more detailed specification of the exercise modalities such as training intensity or exercise volume. Health professionals might consult the ranking of the interventions presented in this study when planning an optimal, individually adapted exercise program to reduce postoperative complications. Because some of the interventions included in this analysis showed quite a similar effect, health professionals now have a choice between various interventions and can, for example, take into account the individual patient's preferences.

Implication for research

This review indicates what type of exercise might be better suited to improve patients' vital capacity, but it does not suggest clear-cut exercise modalities. The current knowledge of exercise modalities such as training intensity, exercise vol-

ume, resting intervals, and training frequency is not optimal.

CONCLUSION

Although, exercise therapy has been shown to be effective in improving vital capacity and respiratory muscle strength, there was a lack of concordance between different types of exercise. Evidence from these indirect-comparisons studies indicated that during the preoperative period before oncologic surgery, physical activity (such as aerobic training, anaerobic training, resistance training, high-intensity training, respiratory muscle training, or breathing exercise) showed similar moderate-to-large effect size.

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Sažetak

UTJECAJ FIZIOTERAPIJE NA VITALNI KAPACITET PRIJE VELIKIH ABDOMINALNIH OPERACIJA
KOD BOLESNIKA S KARCINOMOM, SUSTABNI PREGLED LITERATURE

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Uvod: Karcinom je jedan od vodećih uzroka smrti u svijetu. Međutim, ako se dijagnosticira u operabilnoj fazi, liječi se poput kroničnih bolesti. Kao takvi, dugoročni rezultati i zahtjevi za kvalitetom života nametnuli su sveobuhvatan pristup. Programi prehabilitacije koji uključuju nutritivne, fizičke i psihološke komponente, poboljšali su oporavak i minimizirali stopu komplikacija nakon operacije. U ovom ćemo se preglednom radu usredotočiti na fizioterapiju kao dio prehabilitacije.

Metode: Za sustavno pretraživanje koristili smo MEDLINE / PubMed (Nacionalna medicinska knjižnica), Cochraneov Centralni registar kontroliranih ispitivanja (Wiley), Embase (Elsevier, Web of Science i Cochrane baza podataka sustavnih pregleda). Posljednje ažuriranje pretraživanja bilo je 15. prosinca 2020. Pretraga je uključivala randomizirana klinička ispitivanja ili kvazi-randomizirana klinička ispitivanja koja ocjenjuju vježbanje ili druge nefarmakološke preoperativne intervencije kod karcinoma probavnog sustava.

Rezultati: Deset pokusa obuhvaćalo je 1058 bolesnika, 535 (50,6%) bolesnika bilo je u eksperimentalnoj skupini, a 523 (49,4%) bolesnika u kontrolnoj skupini. Trening s vježbama na biciklu bio je najbolje rangirana intervencija sa standardnom srednjom razlikom (SMD) od 1,4077 (95% C.I. je 0,7018 - 2,1135) za poboljšanje vitalne funkcionalne sposobnosti (s, VO² pri u[^]L). Kratkotrajno vježbanje utjecalo je na snagu inspiratornih mišića, a SMD je iznosio 1,1819 (95% C.I. 2953 - 2,6684). Program kratkotrajnog intenzivnog treninga SMD iznosio je 0,8356 (95% C.I. 0,2042 - 1,4669), a program kratkotrajnog intenzivnog treninga za izdržljivost mišića 0,8156 (95% C.I. 0,2042 - 1,4669). Pokazan je mali učinak na kvalitetu života u visokointenzivnom intervalnom treningu na biciklom SMD 0,7439 (95% C.I. 0,0856 - 1,4023), status izvedbe prema WHO-u u treningu na biciklu SMD 0,7068 (95% C.I. 0,0547 - 1,3589), srednji broj komplikacija u visokointenzivnom treningu izdržljivosti SMD 0,3606 (95% C.I. 0,0072 - 0,7141).

Zaključak: Iako se pokazalo da fizioterapija vježbanjem poboljšava vitalni kapacitet i snagu respiratornih mišića, nije bilo usporedbe između različitih vrsta vježbanja. Dokazi iz ovih studija neizravne usporedbe ukazuju na to da tjelesnu aktivnost treba poticati tijekom preoperativnog razdoblja prije velikih abdominalnih kirurških zahvata kod onkoloških pacijenata.

KLJUČNE RIJEČI: *vježbanje, prehabilitacija, karcinom, velike abdominalne operacije*