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Effects of physical exercise on the functional capacity and muscle strength of patients with gastric and esophageal cancer: a systematic review

Efeitos do exercício físico na capacidade funcional e força muscular de pacientes com câncer gástrico e esofágico: uma revisão sistemática

Efectos del ejercicio físico sobre la capacidad funcional y la fuerza muscular de pacientes con cáncer gástrico y de esófago: una revisión sistemática

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Abstract
Esophageal and gastric cancers have a significant prevalence. These patients often face a decline in functional capacity (FC) and muscle strength (MS), as consequence of neoadjuvant treatments and surgical resection; however, this decline can be minimized through appropriate exercise protocols. To assess evidence of the effects of physical exercise on HR and MS in patients with esophageal and stomach cancer. Systematic review of Randomized clinical trials with intervention based on exercises for patients with esophagogastric cancer (EGC). FC and MS were the outcomes. Searches in Medline via Pubmed, PEDro, Cochrane Library, Embase and CINAHL databases were performed. Cochrane Collaboration tool and GRADE system for risk of bias assessment. From 117 articles identified, eight studies were included, involving a total of 673 patients. In general, the approach during neoadjuvant therapy had a positive effect on the 6-minute walk test (6MWT) and on FM. Exercise performed in the preoperative period showed divergent results for inspiratory muscle strength, but improved HR assessed by the 6-minute walk test (6MWT). The postoperative exercise protocol increased the FC in 6MWT, and maximal oxygen consumption (VO2max). However, it does not improve MS. Studies also showed a moderate-to-high risk of bias. Although some studies point to positive results in favor of physical exercise in improving FC and MS in patients being treated for esophagogastric cancer, the degree of clinical recommendation is low.
Keywords: Exercise; Physical functional performance; Stomach neoplasms; Esophageal neoplasms.

Resumo
Os cânceres de esôfago e gástrico têm prevalência significativa. Esses pacientes frequentemente apresentam declínio da capacidade funcional (CF) e da força muscular (FM), como consequência de tratamentos neoadjuvantes e ressecções cirúrgicas; no entanto, esse declínio pode ser minimizado por meio de protocolos de exercícios apropriados. Avaliar evidências dos efeitos do exercício físico na FC e SM em pacientes com câncer de esôfago e estômago. Revisão sistemática de ensaios clínicos randomizados com intervenção baseada em exercícios para pacientes com câncer esofagogástrico (CEG). CF e MS foram os desfechos. Foram realizadas buscas no Medline via Pubmed, PEDro, Cochrane Library, Embase e CINAHL. Ferramenta Cochrane Collaboration e sistema GRADE para avaliação de risco de viés. Dos 117 artigos identificados, oito estudos foram incluídos, envolvendo um total de 673 pacientes. Em geral, a abordagem durante a terapia neoadjuvante teve efeito positivo no teste de caminhada de 6 minutos (TC6) e na FM. O exercício realizado no pré-operatório apresentou resultados divergentes para a força muscular inspiratória, mas melhorou a CF avaliada pelo teste de caminhada de 6 minutos (TC6). O protocolo de exercício pós-operatório aumentou a FC no TC6 e o consumo máximo de oxigênio (VO2max). No entanto, não melhora a FM. Os estudos também mostraram um risco moderado a alto de viés. Embora alguns estudos apontem

resultados positivos a favor do exercício físico na melhora da CF e FM em pacientes em tratamento para câncer esofagogástrico, o grau de recomendação clínica é baixo.
Palavras-chave: Exercício físico; Desempenho físico functional; Neoplasias gástricas; Neoplasias de esôfago.

Resumen
Los cánceres de esófago y gástrico tienen una prevalencia significativa. Estos pacientes a menudo se enfrentan a una disminución de la capacidad funcional (CF) y la fuerza muscular (FM), como consecuencia de los tratamientos neoadyuvantes y la resección quirúrgica; sin embargo, esta disminución se puede minimizar a través de protocolos de ejercicio apropiados. Evaluar la evidencia de los efectos del ejercicio físico sobre la CF y la FM en pacientes con cáncer de esófago y estómago. Revisión sistemática de Ensayos clínicos aleatorizados con intervención basada en ejercicios para pacientes con cáncer esofagogástrico (CEG). CF y FM fueron los resultados. Se realizaron búsquedas en Medline a través de las bases de datos Pubmed, PEDro, Cochrane Library, Embase y CINAHL. Herramienta de la Colaboración Cochrane y sistema GRADE para la evaluación del riesgo de sesgo. De 117 artículos identificados, se incluyeron ocho estudios, involucrando un total de 673 pacientes. En general, el abordaje durante la terapia neoadyuvante tuvo un efecto positivo en la prueba de caminata de 6 minutos (PC6M) y en la FM. El ejercicio realizado en el período preoperatorio mostró resultados divergentes para la fuerza de los músculos inspiratorios, pero mejoró la CF evaluada por la prueba de caminata de 6 minutos (PC6M). El protocolo de ejercicio postoperatorio aumentó la FC en PC6M y el consumo máximo de oxígeno (VO2max). Sin embargo, no mejora la EM. Los estudios también mostraron un riesgo de sesgo de moderado a alto. Aunque algunos estudios apuntan resultados positivos a favor del ejercicio físico en la mejora de la CF y la FM en pacientes en tratamiento por cáncer esofagogástrico, el grado de recomendación clínica es bajo.
Palabras clave: Ejercicio físico; Rendimiento físico funcional; Neoplasias gástricas; Neoplasias esofágicas.

1. Introduction

Cancer is the leading cause of death and a barrier to increasing life expectancy worldwide. World statistics revealed about 19.3 million new cancer cases and nearly 10.0 million cancer deaths for the biennium 2020-2021(Sung et al., 2021). In addition, stomach and esophagus cancer accounts for 5.6% and 3.1% of expected new cases, respectively, as well as 7.7% and 5.5% of estimated deaths, respectively(Sung et al., 2021).

The clinical approach to esophageal or gastric cancer involves a combination of treatments, including chemotherapy and/or neoadjuvant radiotherapy followed by surgical resection. Neoadjuvant therapy in esophagogastric cancer (EC) is associated with short- and long-term adverse effects, in addition to nutritional compromise(Tully et al., 2020).

Surgery, in turn, is planned for up to 80% of esophagogastric cancer patients, and is considered primordial for curative or palliative treatment(Carcas, 2014). Open resection, however, is associated with greater trauma, numerous complications, slow recovery, prolonged hospitalization, and many other problems(Sato et al., 2015). The act itself represents a stressful event that can lead to adverse effects unrelated to the objective of treatment, impairing postoperative recovery(Gonçalves & Groth, 2019). Therefore, the current best surgical practice involves the Enhanced Recovery After Surgery (ERAS) program, which aims to optimize preoperative status, reduce surgical stress and postoperative complications, and accelerate recovery through an integrated multidisciplinary approach(Guinan et al., 2017).

Despite these advances, esophagogastric surgery is still associated with undesirable outcomes, including high rates of postoperative complications and mortality(Van Adrichem et al., 2014), which add to the difficulty of these cancer patients to achieve a positive energy balance, leading to weight loss, decreased muscle mass and strength, respiratory complications, physical inactivity, reduced functional capacity, fatigue, depression, emotional stress, anxiety, and poor quality of life(Bolger et al., 2019; Lidoriki et al., 2019; Minnella et al., 2018; Van Adrichem et al., 2014). The risk of postoperative pulmonary complications after esophagectomy is generally high (27%–57%)(Feeney et al., 2010). Respiratory complications are commonly reported after esophagectomy and contribute to prolonged hospital stay and intensive care unit (ICU) stay, with increased health care costs(Ferguson et al., 2011).

The vast majority of exercise-based interventions for oncology patients have been evaluated in patients with breast cancer, prostate cancer, and hematologic neoplasms, which precludes generalizing the results to cancer types with more

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complex multimodal treatment, such as EC(van Vulpen et al., 2021). However, recent studies with exercise-based interventions before and after surgery associated with nutritional support seem to be important elements for patients to withstand surgical stress and minimize postoperative morbidities(Minnella et al., 2018) for important benefits in functional capacity, muscle function and quality of life of patients with EC(Minnella et al., 2018; Van Adrichem et al., 2014). However, the effect needs to be measured together with other publications and the risk of bias of the studies evaluated.

In order that rehabilitation professionals and those involved in oncologic care can safely transpose the evidence to clinical practice, contributing to the improvement of the physical performance of gastric cancer patients(Cho et al., 2014). In addition, how much the types of exercise and the standardization of training protocols influence this outcome is not yet well defined in the literature(Bolger et al., 2019). Thus, this review aimed to evaluate the quality of evidence on the effects of physical exercise on functional capacity (FC) and muscle strength (MS) of with esophagogastric cancer patients.

2. Methodology

This systematic review was developed following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher et al., 2009; Page et al., 2021) and the protocol was registered at PROSPERO under number CRD42021225201.

2.1 Data source and search strategy

The data search was performed on 06 October 2021 using the databases Medline via Pubmed, PEDro, Cochrane Library, Embase and CINAHL. The search strategy involved combining MESH descriptors in combination with Boolean operators as follows: Population: (Oesophago cancer OR esophagus cancer OR esophagus neoplasm OR oesophageal cancer OR Gastric cancer OR stomach cancer); Intervention: (Muscle Strength Exercise OR Exercise Therapy OR Resistance Training OR Strength Training OR aerobic training OR exercise training); Outcomes: (Functional Capacity OR Functional Status OR Physical function OR exercise performance OR exercise capacity OR exercise tolerance OR Respiratory muscle strength OR Peripheral muscle strength); Type of study: clinical trial. No language or year of publication restriction were applied. Then, we included any review published until September 2021.

2.2 Study selection and eligibility criteria

The eligibility criteria were as follows: (i) randomized clinical trials (RCT), with adult patients (≥18 years) of both sexes, with histologically diagnosed esophageal cancer, esophagogastric or gastric junction, treated with surgery (esophagectomy / gastrectomy, total or partial) and/or neoadjuvant treatment (chemotherapy and/or radiotherapy); (ii) interventions applied at different clinical times, parallel with neoadjuvant treatment, during the pre- and/or postoperative period; and (iii) studies that evaluated the effect of exercise protocols, which may be combined with other therapies or nutritional support, on functional capacity and muscle strength of these patients. Studies that evaluated the effect of exercise-based intervention through another type of methodological design (systematic review articles, meta-analysis, cohort, case-control, case studies, or protocols), or that did not present data on the outcomes of interest were excluded. No publication year or language restrictions were applied.

After excluding duplicate entries, the titles and abstracts were identified by two independent and geographically separate researchers and were considered for inclusion based on study design and relevance to the proposed research question. Relevant articles were read in full to apply the eligibility criteria and studies meeting the criteria were included. Disagreements were resolved by a third researcher.

The articles included were independently reviewed by the reviewers and the data extracted using an electronic form. The following data were extracted: publication year, authors, country, patient characteristics, intervention protocol (type of exercise, frequency, intensity, and progression), moment of intervention (during neoadjuvant treatment, pre- or post-surgical), outcome measures, results, and risk of bias.

2.3 Outcomes

The primary outcome was the functional capacity measured by peak oxygen consumption (VO2 peak), by maximal oxygen consumption (VO2max), by the 6-minute walk test (6MWT) or other validated physical evaluation. Respiratory and peripheral muscle strength were the secondary outcomes.

2.4 Risk of bias assessment

The methodological quality of the included studies was assessed using the Cochrane Collaboration tool for risk of bias(Higgins et al., 2019) using RevMan (version 5.3), which analyzes the risk of bias in seven domains: random sequence generation, allocation confidentiality, blinding of participants and professionals, blinding in outcome assessment, incomplete outcome data, selective outcome reporting and other sources of bias. The risk of bias of the selected studies was classified as low, uncertain, or high based on the tool-established criteria(Higgins et al., 2019). The degree of recommendation of the evidence was assessed by the GRADE system as very low, low, moderate, or strong (Guyatt et al., 2011),(Brugnolli et al., 2014).

2.5 Data analysis

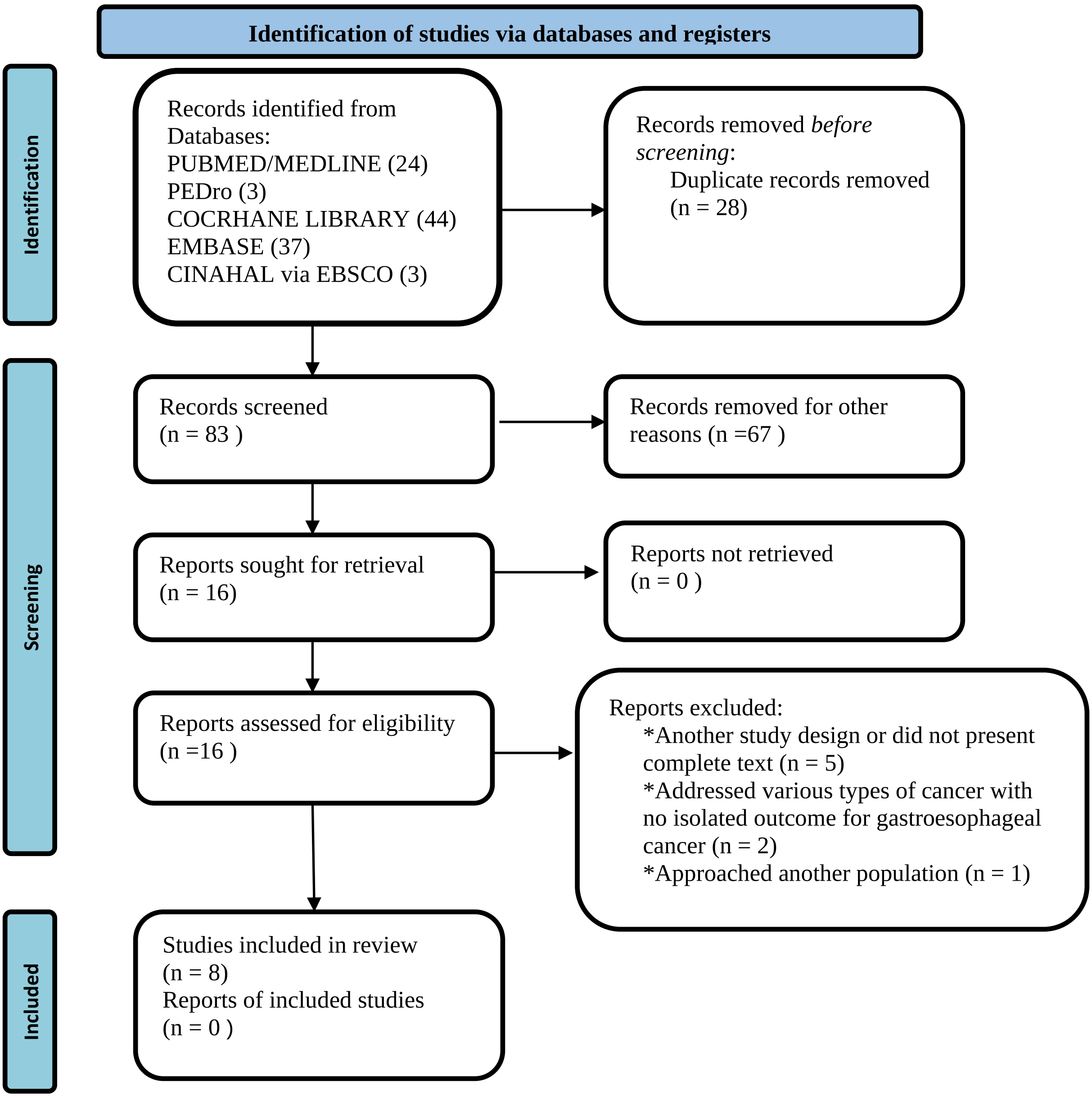
Inter-reviewer agreement during study selection was measured using the kappa coefficient (k), with values of 0.61–0.80 and 0.81–0.100 considered as substantial and almost perfect, respectively.(McHugh, 2012). The main characteristics of the samples and interventions, and main outcomes and results obtained in each selected study were qualitatively described and summarized in tables.

3. Results

3.1 Study Selection

The article selection and inclusion processes are summarized in Figure 1. Of the 117 articles identified, 89 were screened by title and abstract, and eight articles were included at the end. The agreement between reviewers was substantial (k = 0.700).

Figure 1. Flowchart of systematic review selection.



Source: Authors (2022).

3.2 Characteristics of the Studies

Table 1 describes the characteristics of the selected studies. A total of 673 patients were included. Of the eight studies, four applied postoperative intervention protocols, three started the intervention preoperatively, and one started the intervention during neoadjuvant therapy. The studies varied in terms of outcome measures and exercise protocols. The intervention protocols and results are shown in Tables 2 and 3, respectively.

Table 1. Characteristics of the included studies.

Author	**Country**	**Year**	**Sample (n)**	**Males n(%)**	**Females n(%)**	**Age mean (SD)**	**Type of cancer**	**Oncological treatment**
Xu et al.	China	2015	56	52 (92,85)	4 (7,15)	IG: 58.1(9.6) CG:61.1(9.0)	Esophagus	Neoadjuvant QT or RXT
Van Adrichen et al.	Netherlands	2014	39	29 (74,4)	10 (25,6)	IMT-HI: 62.7 (7.1) IMT-E: 61.3 (7.3)	Esophagus	Esophagectomy
Valkenet et al.	Netherlands, Belgium, Iceland and Finland	2018	241	186 (77.17)	55 (22.82)	IG: 63.7 (7.5) CG: 62.7 (8.9)	Esophagus	Esophagectomy
Minnella et al.	Canada	2018	51	38 (74,5)	13 (25,5)	IG: 67.3 (7.4) CG: 68 (11.6)	Esophagogastric	Preoperative surgery
Ólsen et al.	Sweden	2017	43	35 (81,4)	8 (18,6)	IG:62.7(10.7) CG: 62.3 (8.4)	Esophagus	Ivor-Lewis surgery
O'Neill et al.	Ireland	2018	43	35 (81.40)	8 (18.60)	IG:67.19 (7.49) CG:64.14(10.46)	Esophagogastric	Esophagectomy or Gastrectomy. Neoadjuvant therapy with QT/RXT with curative intent
Chang et al.	China	2020	88	80 (90.9)	8 (9.1)	IG: 56 (8.9) CG: 56 (10.0)	Esophagus	Esophagectomy
Van Vulpen et al.	Netherlands	2021	120	104 (86,7)	16 (13,3)	IG: 64.3 (7.8) CG: 63.1 (8.5)	Esophagus	Esophagectomy

QT: chemotherapy; RXT: radiation therapy; SD: standard deviation; IMT-HI: high-intensity inspiratory muscle training; IMT-E: inspiratory endurance training; IG: intervention group; CG: control group.
Source: Authors.

Table 2. Composition of the interventions.

Author	Control	Intervention	Duration	Exercise protocol	Professional responsible for the intervention
Xu et al.	CMC + NA	Walking + NA	4–5 weeks 1x/week	5-minutes water break + 20-minutes walk	Nurse
Van Adrichen et al.	SPP	IMT-HI IMT-E	3 weeks	IMT-HI: 6 cycles of 6 MIns, Start: 60% Pimax in 1st week and 80% in the following; IMT-E: 20-minutes of MIns,. Start: 60% Pimax, progresses 5% of the load if Borg <5.	Physiotherapist
Valkenet et al.	NS	IMT	2 weeks or more, until the surgery date	30 inspirations, 2x/day, 7 days/week	Physiotherapist
Minnella et al.	PBP	ARE + NA	4x/week	**AE:** 5-minutes WE + 30-minutes AEMI + 5-minutes cooling - 3 days/week. **ER:** 30 minutes: 5-minutes Fl + 5-minutes St - 3 sets of 8 to 12 rep for 8 MG, 1 day/week.	Medical
Ólsen et al.	NPPA	RE + EM .	3 months	The IG received leaflet with 3 training programs and guidance on how to perform the exercises and progression.	Physiotherapist
O'Neill et al.	PBP	ARE + NA + PE	12 weeks	Supervised ARE- 4 weeks. HE without supervision - other weeks **AE:** start with LI (30-40% HRres), progressed weekly to MI (40-60% HRres). **RE:** start 2 sets 12 RPM and progress to 6 sets of 17 RPM	NI
Chang et al.	PBP + RPA	Walk + EP	12 weeks	Walking (MI) - 3–5 days/week, for 30 minutes, or 150 minutes/week.	Nurses and Physiotherapist
Van Vulpen et al.	RPA	ARE	12 weeks	2x/week - 5-minutes WE + 50-minutes ARE + 5-minutes cooling Other days: 30 minutes RPA	Physiotherapist

CMC: conventional medical ca.re; NA: nutritional advice; SPP: standardized postoperative physiotherapy; IMT-HI: high-intensity inspiratory muscle training; IMT-E: inspiratory endurance training; MIns, inspiratory maneuvers; Pimax: maximum inspiratory pressure; NS, not standardized; IMT: inspiratory muscle training; PBP, standardized according to best practices; ARE: aerobic and resistance exercise; AE: aerobic exercise; WE: warm-up exercise RE, resistance exercise; AEMI: aerobic exercise moderate intensity; Fl: flexibility; St: stretching; MG: muscle groups; NPPA: guidance not to perform physical activity; RE: respiratory exercise; EM: early mobilization; EP, education program; HE, home exercises; LI: low intensity; HRres, heart rate reserve; MI: moderate intensity; RPM, maximum repetitions; NI: not informed; RPA: regular physical activity; EP: educational program.
Source: Authors.

Table 3. Results of the included studies.

Author	Intervention period	Moment of evaluation	Outcome	Outcome measures	Results
Xu et al.	During NT	Before and after intervention	FC	6MWT (m) PGS (Kg)	There was a significant difference between the groups: 6MWT: 100.0 m (95% CI, 29.9–170.2) , p = 0.012 PGS: 3.0 Kg (95% CI, 1.3–4.9), p = 0.002
Van Adrichen et al.	Pre-op	Before and after intervention	IMS	Pimax(cmH2O)	There was no intergroup difference (p = 0.316) 9.00 (CI95% = -9.97 to 27.97)
Valkenet et al.	Pre-op	T0: baseline, T1: before surgery, T2: 3rd POD, T3: 6th POD; T4:9° POD	IMS	Pimax(cmH2O)	There was no significant difference between the groups (p>0.05) in all measures post intervention.
Minnella et al.	Pre-op	T0: base line T1: before surgery T2: 4-8 weeks after surgery	CF	6MWT (m)	Significant difference between the groups: perioperative: 36,9 (51,4) m *vs* -22,8 (52,5) m, p<0,001 postoperative: 15,4 (65,6) m *vs* -81,8 (87,0) m, p<0,001
Ólsen et al.	Post-op	Pre-op and 3 months after hospital discharge.	PMS	PGS(N)	There was no significant difference between the groups (p= 0.758), but there a clinical effect (d = 0,28)
O'Neill et al.	Post-op	T0: base line T1: immediately after intervention T2: at 3-month follow-up	CRC	VO_2 peak (ml.min^{-1}.Kg $^{-1}$)	There was an improvement in cardiorespiratory fitness in intervention group compared to controls at T1 ($p<0.001$; $\eta_p^2 = 0.35$) and T2 ($p=0.001$; $\eta_p^2 = 0.28$).
Chang et al.	Post-op	Before and 3 months after discharge	CRC	VO_2 max (ml.min^{-1}.Kg $^{-1}$) 6MWT (m)	There was a significant difference between the groups for VO2max (d= 0.97) Favour to intervention: 2.61 (ml.min^{-1}.Kg $^{-1}$) (CI 95%: 1.54 to 3.69), p<.001 There was a significant difference between the groups for 6MWT (d= 0.36) Favour to intervention: 83.30m (CI 95%: 52.60 to 113.99) p<.001
Van Vulpen et al.	Post-op	Before and after intervention	CRC	VO_2 peak (ml.min-1.Kg-1)	There was a significant difference between the groups (d: 0,33) Favour to intervention: 1,80 ml/min/Kg (CI 95%: 0,62 to 2,99), p<0,05

NT: neoadjuvant therapy; Pre-op: pre-operative; Post-op: post-operative; POD: postoperative day; PMS: peripheral muscle strength; IMS: inspiratory muscle strength; FC: functional capacity; CRC: cardiorespiratory capacity; Pimax: maximal inspiratory pressure; VO2max: maximal oxygen consumption; VO2peak: peak oxygen consumption; PGS: palmar grip strength; 6MWT: 6-minute walk test; CG, control group; IG, intervention group; CI, confidence interval; d = Cohen`s d; η_p^2, partial eta square.
Source: Authors.

3.3 Effect of exercise during neoadjuvant therapy

A study evaluated the impact of exercise on functional capacity and muscle strength during neoadjuvant therapy(Xu et al., 2015). In this study, the intervention group (IG) was submitted to a supervised walking exercise protocol thrice a week and nutritional counseling once a week. The exercise consisted of 5 minutes of warm-up and 20 minutes of walking at the patient's pace, before and after neoadjuvant therapy (chemotherapy and radiotherapy). Functional capacity was assessed by 6MWT and peripheral muscle strength by handgrip strength (HGS). Analysis of pre-treatment and post-treatment changes indicated that the intervention group had a significantly lower decline in the 6MWT walking distance when compared to the usual care - control group (CG) (18 vs. 118 m; group difference: 100, adjusted p = 0.012). Similarly, the IG had significantly lower decline in FPP when compared to the CG (1.1 vs. 4.1 kg, respectively, mean difference between groups (CI: 95%): 3.0 (1.3–4.9); adjusted p = 0.002).

3.4 Effect of exercise performed preoperatively

Three studies evaluated the impact of exercise performed preoperatively(Minnella et al., 2018; Valkenet et al., 2018; Van Adrichem et al., 2014) .

One of the studies evaluated inspiratory muscle strength through maximal inspiratory pressure (Pimax), when comparing two inspiratory muscle training protocols: high-intensity inspiratory muscle training (IMT-HI) and endurance inspiratory muscle training (IMT-E)(Van Adrichem et al., 2014). The median Pimax in cmH2O for the TMI-HI group showed a significant increase of 12% from T0 to T1 (z = -3.24; p = 0.001; r = -0.76). The TMI-E group showed a significant increase of 35% (z = -3.82; p = ³ 0.001; r = -0.88). No significant difference in change from T0 to T1 was found between groups (U = 138.00; p = 0.316; r = -0.17).

Another study also evaluated inspiratory muscle strength through Pi max(Valkenet et al., 2018). Inspiratory muscle training was performed daily, a series of 30 breaths, 2x/day, for 2 weeks or more until the date of surgery. An initial inspiratory load of 60% of the initial Pimax was used. When the perceived effort rate was below 7, the inspiratory load was increased by 5%; this evaluation was done at the end of each session. Inspiratory muscle strength was assessed at 5 moments: baseline (T0), before surgery (T1) and during hospitalization in the postoperative period on day 3 (T2), day 6 (T3) and day 9 (T4). Mean (SD) maximal inspiratory muscle strength increased from 76.2 (26.4) to 89.0 (29.4) cmH2O (p <0.001) in GI and from 74.0 (30.2) to 80.0 (30.1) cmH 2 O in CG (p <0.01). The increases were greater in GI when compared to CG (p <0.050), however there was no significant difference between the groups in all measures post intervention.

The third study selected evaluated the impact of a pre-habilitation program (Minnella et al., 2018). The functional capacity was evaluated by the 6MWT after the intervention group went through the following exercise program: moderate intensity aerobic exercise, performed for 30 minutes, 3x/week, with intensity selected by the Borg Scale of Perceived Effort (12 to 13). Strengthening activity: 30 minutes, 3 sets of 8 to 12 repetitions for 8 muscle groups, using elastic band with resistance. A statistically significant difference in the change in walking distance was observed between the groups both in the preoperative evaluation [mean (SD), 36.9 m (51.4) in the pre-rehabilitation group vs -22.8 m (52.5) in the CG; p <0.001] and after surgery [mean (SD), 15.4 m (65.6) in the pre-rehabilitation group vs -81.8 m (87.0) in the CG; p <0.001].

3.5 Effect of exercise performed postoperatively

Of the included studies, four evaluated the impact of exercise in the postoperative period(Chang et al., 2020; Fagevik Olsen et al., 2017; O'Neill et al., 2018; van Vulpen et al., 2021).

In one study, the IG was submitted to an exercise program to restore lung function, range of motion in the thoracic spine and shoulder and strength exercises for the extensors of the back, shoulders and legs, performed daily(Fagevik Olsen et al., 2017). The intervention started one week after surgery and lasted until the third month. The program was gradually increased in intensity during the rehabilitation period. Preoperative and postoperative grip strength (of the dominant hand) was assessed in IG and CG. Both groups had significantly lower grip strength postoperatively ($p < 0.05$), but there were no significant differences between the groups.

Another selected study evaluated the impact of exercise on functional capacity performed postoperatively. The exercise program consisted of aerobic and resistance exercise. Aerobic exercise was initiated at low intensity (30%–40% HR reserve) and progressed weekly to moderate intensity (45%–60% HR reserve). Resistance exercise was started with 6 sets of 12 repetitions and progressed to 6 sets of 17 repetitions, aligned with standard repetitions. Nutritional counseling and group education was associated. Functional capacity was assessed by VO2 peak. At the beginning of the study (T0), the CG had a significantly higher mean VO2peak [21.75 ml/min·kg (4.49)] compared to the IG (18.73 ml/min·kg (4.07); (CI: 95%, 0.38-5.67, p = 0.026). Correcting for baseline VO2peak, GI had significantly higher mean VO2peak in both T1, 22.20 ml/min·kg (4.35) versus 21.41 ml/min·kg (4.49), p <0.001, and T2, 21.75 ml/min·kg (4.27) versus 20.74 ml/min·kg ($4.^{-1}65$), p = 0.001, compared to CG.

Another study that was selected used the 6MWT and VO2 max to evaluate the physical capacity of patients in the postoperative period of esophagectomy(Chang et al., 2020). The IG was submitted to a home walking exercise program for 12 weeks, with moderate intensity walking, 3 to 5 days a week, for 30 minutes, totaling 150 minutes of walking per week. Exercise capacity was significantly different for IG compared to CG for VO2max (β = 2.61, 95% CI 1.54, 3.69, p <0.001) and for 6MWT (β = 83.30, 95% CI 52.60, 113.99, p <001). The effect size for exercise capacity measures at 3 months for VO2max was large (0.97) and for the 6MWT was small (0.36).

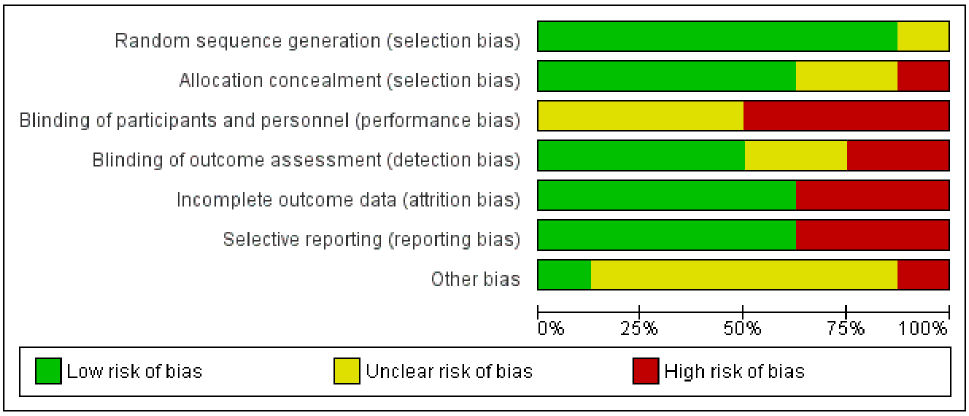
The last study in question evaluated the effect of exercise, performed postoperatively, on cardiorespiratory fitness through VO2peak (van Vulpen et al., 2021). In this study it was evidenced that there was significant difference in cardiorespiratory fitness by VO2peak (0.13 l / minutes, 95% CI (0.04 to 0.22), P < 0.05, however, the effect size (ES) was small (0.26).

3.6 Risk of Bias and Quality of Evidence Analysis

The risk of bias analysis was performed by the Cochrane Collaboration tool and are summarized in Figures 2 and 3. The studies showed moderate-to-high risk of bias, especially in the items of blinding of assessors and participants. In addition, the studies provided a poor description of the intervention, limiting the assessment of other risks of bias.

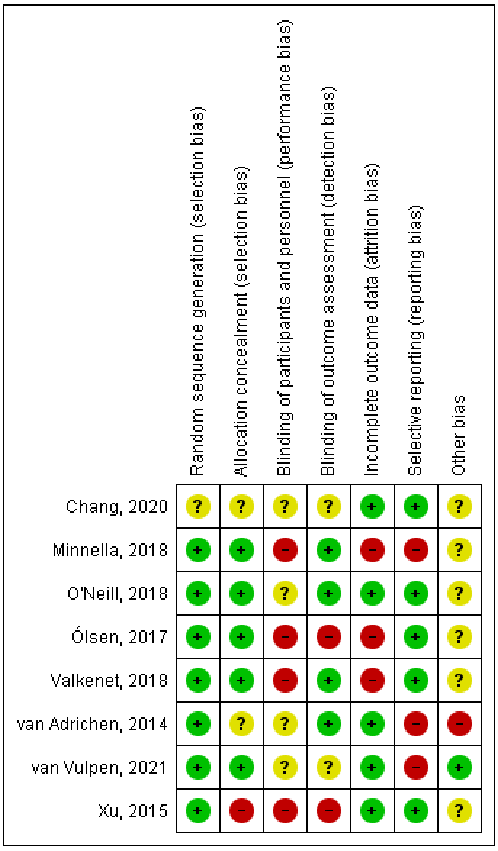
The quality of the evidence was evaluated by the GRADE system. Exercise has a low recommendation for changes in the functional capacity of patients, when evaluated by the 6MWT and VO2peak, and moderate when evaluated by VO2max. Regarding muscle strength, the degree of evidence is low that physical exercise promotes improvements in respiratory and peripheral muscle strength.

Figure 2. Gráfico do Risco de Viés.



Source: Authors (2022).

Figure 3. Sumário do Risco de Viés.



Source: Authors (2022).

4. Discussion

According to the evidence, physical exercise seems to be a tool to allow patients to support oncological treatment with less damage to their functional capacity. However, the heterogeneity of intervention protocols and clinical moments applied stands out. Moreover, the studies have important methodological issues that impose moderate-to-high risk of bias to the results found. Such limitations corroborate a previous study that found high heterogeneity between preoperative and postoperative exercises in cancer patients(Bolger et al., 2019).

Esophagogastric neoplasms offer very specific challenges in dealing with poor nutritional status and declining functional capacity, combined with an advanced age population. In addition, toxicities associated with neoadjuvant therapy can be challenging in the preoperative and postoperative periods (Christensen et al., 2019; Horowitz et al., 2015). Therefore, strategies that aim to enhance the patient's physical condition are necessary to allow better recovery to treatment.(Adamsen et al., 2009).

In this review, one study evaluated the impact of exercise on functional capacity by 6MWT and muscle strength by PGS during chemo- and radiotherapy (Xu et al., 2015). The most notable finding of this pilot randomized controlled trial is that the intervention effectively preserved functional walking ability between the initiation and completion of neoadjuvant therapy for patients with newly diagnosed, locally advanced esophageal cancer. The benefits were clinically significant. Patients who walked had 100 m less decline in walking distance. In this study, the patients received weekly nutritional orientation. Regarding the PGS, there was a significant effect in favor of exercise. It was clear that the control group had a significant decline, both in walking distance and in handgrip strength, indicating a strong need for intervention. The benefits of this intervention seem evident for patients with esophageal cancer, but our results cannot be compared with those of other studies, as this population is poorly studied. A randomized clinical trial that evaluated the effect of walking during chemotherapy in cancer patients (breast, intestinal, hematological, and other malignant neoplasms) showed significant results, corroborating with the study included in our review(Katrin Stuecher et al., 2019).

Despite advances in surgical techniques, most patients do not recover satisfactorily. Patients submitted to major abdominal surgeries for neoplasms, for example, can benefit from pre-habilitation(Ryan et al., 2016). This is defined as the process of increasing functional and nutritional capacity to reduce the potential deleterious effects of a significant stressor, which is the surgical procedure itself(Carli & Zavorsky, 2005).

In this review, three studies evaluated the effect of exercise performed preoperatively. Two studies focused on inspiratory muscle training (IMT) as an intervention and aimed to improve inspiratory muscle strength (Van Adrichem et al, 2014; Valkenet et al, 2018). However, the included studies provided divergent results, making them inconclusive for this outcome. The effect of preoperative IMT on inspiratory muscle strength is not comparable to the results reported in another study of IMT in preoperative esophagectomy(Dettling et al., 2013).

The other study selected investigated the effect of exercise in the context of pre-habilitation, with a positive impact on the functional capacity of patients submitted to the walking program performed before surgery, when compared to the group that received usual care (Minnella et al., 2018). In this study, functional capacity was evaluated by the 6MWT, with a positive impact for the intervention group and a significant difference between the groups. Reduced functional capacity is a potential limitation for patients to resist cancer treatment interventions. Studies have shown that receiving full cancer treatment is related to good physical and nutritional status(Argudo et al., 2021; Katrin Stuecher et al., 2019), and 60%–70% of esophageal cancer patients do not receive the planned treatment(Dunphy & Schöder, 2014). By mitigating functional impairment, pre-habilitation in cancer treatment pathways can be of considerable value.

A good functional capacity is directly related to the postoperative evolution(Dronkers et al., 2013). Rehabilitation exercises performed postoperatively have shown beneficial effects on cardiorespiratory performance, physical performance, and muscle strength in oncologic patients (K Stuecher et al., 2019).

In this review, one study with postoperative intervention protocols evaluated the effect of exercise on muscle strength in patients in the postoperative period of esophageal resection of Ivor-Lewis (Fagevik Olsen et al., 2017). Although some rehabilitation treatments exist, few patients receive rehabilitation and there is little scientific evidence about its possible value in this group of patients. This trial is the first to evaluate 3 months of long-term training intervention aimed at improving chest motion, lung function and physical activity for this category of patients. Grip strength was assessed in patients who had undergone a postoperative training program; however, there was no significant difference between the groups(Fagevik Olsen et al., 2017).

Another study selected in this review showed that the exercise intervention had benefits on maximal and submaximal cardiorespiratory fitness, suggesting the importance of supervised exercise after esophageal cancer treatment regarding physical recovery, since multimodal treatment of esophageal cancer causes short- and long-term decline in VO2peak (van Vulpen et al., 2021). The significant results observed at the submaximal level are relevant, since most activities of daily living are performed at a submaximal level (von Döbeln et al., 2016). Another included study evaluated cardiorespiratory fitness by VO2peak using the RESTORE intervention protocol(O'Neill et al., 2018). This clinical trial was the first to demonstrate that exercise rehabilitation significantly improves cardiorespiratory fitness levels in esophagogastric cancer survivors. Cardiorespiratory fitness in cancer survivors is invariably 30% lower than sedentary survivors of the same age and sex in control groups(Jones et al., 2011).

Another selected study evaluated the effect of exercise performed postoperatively showed that exercise showed improvement in exercise capacity for participants in the computer-based exercise program (Chang et al., 2020). VO2max and the 6MWT significantly improved 3 months after hospital discharge for the intervention group. This results is similar to other study demonstrating improvements in exercise capacity resulting from exercise programs beginning after surgical treatment(Minnella et al., 2018).

A limitation of this review was that in some studies, the exercise program was combined with other interventions, such as nutritional counseling and educational guidelines. Thus, the effect of exercise alone cannot be isolated. However, esophagogastric cancer patients suffer nutritional deterioration and nutritional counseling is part of the surgical guidelines(Guinan et al., 2017). Another limitation was the variation in intervention protocols and their form of application. Some protocols were unsupervised, only using computerized programs or guided through telephone calls. There was variation in the professionals who applied the intervention protocols. This variety may have impacted the adherence and results of the exercises on the outcomes measured. Due to the different outcome measures evaluated, it was not possible to group the studies and meta-analysis for a better estimate of the size of the effects found.

5. Conclusion

Given the above, exercise seems to bring benefits to patients with esophagogastric cancer, regardless of the therapeutic moment in which the patient is. Physical exercise should be a modality of clinical intervention for these patients, in order to provide a better physical condition to patients within their line of treatment. The available evidence the effect of physical capacity improvement on exercise patients in esophagogastric fitness cancer treatment has moderate-to-high risk of bias. Therefore, there is a low degree of recommendation for physical exercise in improving the functional capacity and muscle strength of these patients.

Thus, we highlight the importance of further studies on the implementation of exercises in patients with esophagogastric cancer. These studies must follow good practice guidelines and improve the description of intervention protocol for more reliability and incorporation in clinical practice. Then, better evidence about exercise in this context may help professionals and recovery of patients with esophageal and gastric cancer.

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