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REVIEW ARTICLE

Effect of inspiratory muscle training associated or not to physical rehabilitation in preoperative anatomic pulmonary resection: a systematic review and meta-analysis

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Abstract

Objective The aim of this study is to systematically review the effect of inspiratory muscle training (IMT) associated or not with physical rehabilitation in the preoperative period of anatomical pulmonary resection.

Methods Search in the databases: MEDLINE, Cochrane CENTRAL, EMBASE, LILACS and PEDro up to November 2019. Randomized clinical trials (RCTs) were included in adults in the preoperative period of pulmonary resection. The selection of studies and data extraction was performed by two independent reviewers. The risk of bias assessed with RoB 2.0 and the quality of evidence with GRADE. PROSPERO: CRD42018105859.

Results Six RCTs were included; patients who underwent IMT in the preoperative period showed a significant improvement in functional capacity assessed by the 6-min walk test (6WT) (MD 28,93 [IC 95% 0,28; 57,58], $p = 0{,}04$, $I^2 = 0\%$) and significantly reduced the length of hospital stay (MD –3,63 [IC 95% −4,96; −2,29], $p = 0{,}00$, $I^2 = 0\%$). There was no significant difference between groups regarding pulmonary function, in postoperative complications such as pneumonia (RR 0,56 [IC 95% 0,29; 1,10], $p = 0{,}09$, $I^2 = 0\%$), atelectasis (RR 0,81 [IC 95% 0,24; 2,69], $p = 0{,}72$, $I^2 = 0\%$), mechanical ventilation > 48 h (RR 0,43 [IC 95% 0,12; 1,58], $p = 0{,}20$, $I^2 = 0\%$), in mortality (RR 0,33 [IC 95% 0,04; 3,12], $p = 0{,}33$, $I^2 = 0\%$), and quality of life.

Conclusion IMT associated with physical exercise in the preoperative period of pulmonary resection improves functional capacity and reduces the length of hospital stay in the postoperative period.

Keywords Lung neoplasms · Breathing exercises · Respiratory muscles · Randomized controlled trial

Introduction

Lung cancer is the most common cancer in the world, being the leading cause of cancer death in men. About 1.8 million new cases of lung cancer were diagnosed worldwide in 2012, which represented 12.9% the incidence of cancer in the world [1–4]. Surgical treatment is the first choice for neoplasia at initial stages. Among the options for anatomic pulmonary resection, there is traditional open thoracotomy, which tends to cause more trauma, and the video-assisted thoracic surgery (VATS) which is less invasive and has less systemic repercussions [5–9].

A pulmonary rehabilitation program in the preoperative period intervenes broadly in physical training, education and change of behavior [10]. This component plays an essential role in the global management strategy of high-risk surgical patients, since it improves physical conditioning, speeds up the return to autonomy, helps reduce the length of hospital stay, diminishes postoperative complications, and improves the cost-benefit ratio of healthcare [11–14].

Studies that performed pulmonary rehabilitation with inspiratory muscle training (IMT) associated with physical exercise in the preoperative period showed a significant improvement in functional capacity and shorter hospital stay [15, 16]. In a systematic review, Garcia et al. (2016) [17] concluded that a program based on exercises in the preoperative period improves lung function before surgery and reduces the length of stay in hospital and postoperative complications. Thus, a

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well-structured training program in the preoperative period can improve the cardiorespiratory aptitude, aiming to prepare patients with resectable lung cancer for surgery and, thus, optimize postoperative recovery [13].

However, no systematic review analyzed rehabilitation programs in the preoperative period before anatomic pulmonary resection with IMT associated or not with physical exercise. Therefore, the main objective of this study was to systematically revise in the literature the effect of IMT associated or not with physical rehabilitation on functional capacity and pulmonary capacity in the preoperative period of anatomic pulmonary resection. As a secondary objective, its possible effects on quality of life, postoperative complications, length of stay in hospital and mortality.

Methods

Protocol and register

This systematic review was conducted according to the Cochrane Handbook for Systematic Reviews of Interventions and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) [18, 19]. The protocol was recorded in the Prospective Register of Systematic Reviews (PROSPERO), under identification number CRD42018105859.

Search strategy

The search was performed in the following databases: MEDLINE (via PubMed), Cochrane CENTRAL, EMBASE, LILACS, and Physiotherapy Evidence Database (PEDro) up to November 2019. In addition, a manual search was performed in the references of the articles published. The search terms used were "lung cancer," "respiratory exercises," "respiratory muscles," and "randomized controlled clinical trial". We did not include words related to the outcomes of interest to enhance search sensitivity. There was no restriction regarding study language or date of publication. The search terms were adapted to meet the requirements of each database. The complete search strategy used in the different databases is described as a Supplementary Table (S1).

Eligibility criteria and outcomes of interest

Randomized clinical trials in adults (> 18 years) who performed IMT associated or not with physical exercise in the preoperative period of anatomic pulmonary resection were included. The studies that did not use IMT as the main intervention, and that occurred only in the postoperative phase were not included. Also excluded were studies that did not approach at least one of the following outcomes: functional capacity, pulmonary function, quality of life, complications during the postoperative period, length of hospital stay, and mortality.

Selection of studies and data extraction

First, the duplicates were excluded, and the titles and abstracts of the search results were selected. The studies that clearly did not meet the inclusion criteria were excluded. Later, the complete text of the selected references was assessed, and the studies that met the already specified eligibility criteria were included in the review.

Then, relevant data were extracted from the selected studies using pre-established tables. The data extracted included methodological characteristics of the studies and outcomes of interest. The authors of the selected studies were contacted by e-mail if the complete data were not available in the study.

All the stages of study selection and data extraction were performed by two independent reviewers (C.V. and B.M.). Disagreements about the selection of the study and data extraction were solved by consensus or by a third reviewer (F.E.M.).

Risk of bias and evaluation of quality

Two independent reviewers (C.V. and B.M.) critically assessed the studies using the RoB 2.0 tool [20]. The general quality of the evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) [21]. The discrepancies in the assessment of study quality were resolved by consensus or by a third reviewer (F.E.M.).

Data analysis

Whenever possible, the data were grouped using a meta-analytic approach. The random effects model was used with the DerSimonian and Laird estimator of variance, and the data were presented as a mean difference for the continuous outcomes or relative risk for the categorical outcomes. We assessed the heterogeneity using statistic I^2. The results were presented as forest plots with point estimates and confidence intervals of 95% (CI 95%). The meta-analyses were performed using statistical software R version 3.4.0 with the meta version of package 4. 9-1 [22]. In addition, we performed a descriptive synthesis for the outcome of quality of life that was not transformed into a common numerical scale.

Results

Description of the studies

We identified 583 studies after duplicates and non-relevant registers were removed. Four hundred and sixty-seven (467) articles were assessed by title and abstract, and nine were selected for analysis of the full text, six of which met the inclusion criteria, supplying data from 219 participants [15, 16, 23–26]. Figure 1 shows the flow diagram of the study selection.

The characteristics of the studies included in the review were described in Table 1, in which the data were separated into intervention group (IG) and control group (CG). The exercise sessions were predominantly supervised or partially supervised. Five [15, 16, 23–25] studies assessed the associated effect of IMT using a rehabilitation program based on physical exercise. There were variations among the studies with regard to duration, frequency of sessions, and modality of overload used in the training, but the sessions were performed daily, varying between one and two times a day, while the intervention period varied between 1 and 4 weeks before the resection.

Risk of bias assessment

For the functional capacity outcome, two studies presented a high risk of bias [15, 25], and two studies presented some concerns [16, 24]. For pulmonary function, two studies presented a high risk of bias [15, 26], and two studies presented some concerns [16, 24]. As to quality of life, two studies presented a high risk of bias [15, 25], and one study presented some concerns [16]. Regarding complications during the postoperative period, three studies presented a high risk of bias [15, 23, 26], and two presented some concerns [16, 24]. During the days of the hospital stay, two studies presented a high risk of bias [15, 23], and two presented some concerns [16, 24]. For mortality, all the studies that assessed this outcome presented some concerns [15, 16, 26]. Generally, the studies did not report the randomization process, the concealment of allocation, and the blinding. Moreover, the lack of published or recorded protocols was a problem for the results that could be evaluated in several ways. The complete assessment of the risk of bias of the studies included is found in Table 2.

The assessment of the quality of the evidence using GRADE is fully described in Table 3.

Fig. 1 Flow diagram of studies included in the review

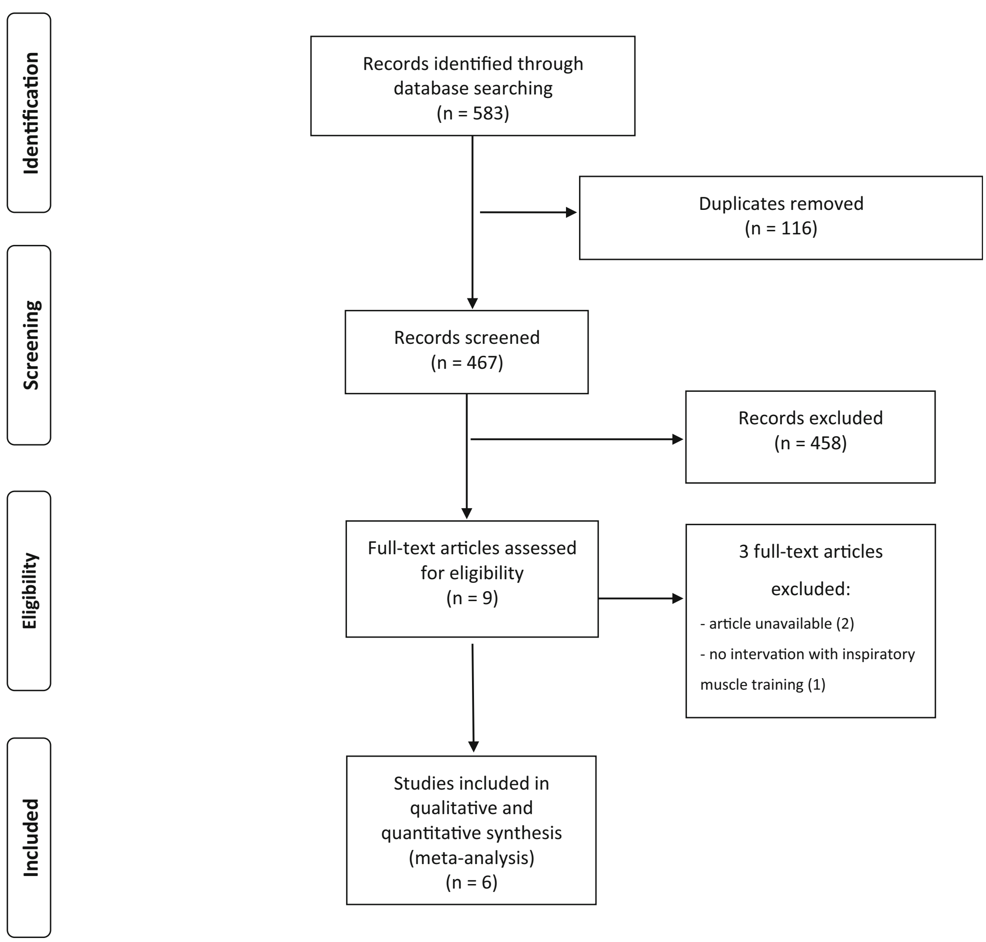

Table. 1 Characteristics of the studies included in the systematic review

Author, year	N (IG/CG)	Mean age±SD (IG/CG)	Men (IG/CG)	IG protocol	CG protocol
Benzo et al. (2011), EUA [23]	10/9	70.2±8.61/72.0±6.69	5/4	IMT: slow a rhythmic breathing pattern, with a daily goal for the use of the inspiratory resistor of 15–20 min. Load increased according to report on patient's difficulties while using the technique Endurance exercises: UE on ergometer and LE on the treadmill, both for 20 min Strength exercises: elastic band, alternating days for UE and LE, 10–12 repetitions Ventilatory exercises: prolonging the expiratory time, 10 min per session 10 sessions, 2x day, 1 week	Usual care—no description in the study
Huang et al. (2017), China [15]	30/30	63.0±8.7/63.6±6.5	20/21	IMT: patients advised regarding the use of the resistor and performed the training at least 4x a day, 20 min per session Endurance exercises: high intensity, performed on the NuStep. Velocity and power adjusted by the patient himself, according to their tolerance, 2x a day, 20 min per session One week, duration and frequency of sessions not informed	They were submitted to routine preoperative preparation, including preoperative education and psychological care for surgery
Lai et al. (2016), China [16]	30/30	72.5±3.4/71.6± 1.9	16/18	IMT: patients advised regarding the use of the resistor did it 3x a day, 20 min per session Endurance exercises: high intensity, performed on the NuStep. Velocity and power adjusted by the patient himself according to their tolerance, 2x a day, 20 min per session One week, duration and frequency of sessions not informed	Routine care—not described
Morano et al. (2013), Brazil [24]	12/12	64.8±8/68.8±7,3	4/5	IMT: resistor begun with 20% of the MIP in the 1st week, with a load increase of 5% to 10% at each session, maximum load of 60%. Daily sessions with 10 to 30-min duration Endurance exercises: 10-min use of treadmill in the 1st week, with a 10-min increment every week, maximum time of 30 min. The training was based on 80% maximum load obtained during an incremental test on the treadmill Four weeks, 5x a week, duration of session not informed	Instructions regarding techniques for pulmonary expansion, sustained maximum breathing. Fractionated inspiration with or without a pause during the inspiration, ventilatory (diaphragmatic) patterns, labial frenulum, and incentive inspirometer
Morano et al. (2014), Brazil [25]	12/12	65±8/69±7	4/5	IMT: no description of the training Endurance exercises: warm-up, aerobic conditioning on the treadmill with 80% of the maximum load Strength exercises: strengthening the UE Four weeks, 5x a week, duration of session not informed	Instructions about techniques for pulmonary expansion: sustained maximum inspiration, ventilatory patterns, labial frenulum, and use of an incentive inspirometer
	17/15	Not informed	13/10		Not described

Table. 1 (continued)

Author, year	N (IG/CG)	Mean age±SD (IG/CG)	Men (IG/CG)	IG protocol	CG protocol
Weiner et al. (1997), Israel [26]				IMT: 15% endurance of MIP in the 1st week and 20% in the second week Incentive inspirometer: guided for slow maximum and sustained inspiration. Performed at least 30x during the 30 min period Two weeks, 6x a week, 1 duration 1-h	

Effect of the interventions

Functional capacity

Four randomized clinical trials (RCTs) ($n = 168$) assessed functional capacity through 6-min walk test (6WT) and were included in the meta-analysis [15, 16, 24, 25]. On the average, there was an increase of 28.93 m in the patients who carried out a rehabilitation program with IMT during the preoperative period (MD 28.93 [CI 95% 0.28; 57,58], $p = 0.04$, $I^2 = 0\%$, low quality of evidence) (Fig. 2a).

Pulmonary function

Four RCTs ($n = 176$) assessed pulmonary functions using variables forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) obtained in spirometry [15, 16, 24, 26]. In the meta-analysis, there was no significant difference among the groups as regards FEV1 (DM 0.0 [CI 95% −0.16; 0.16], $p = 0.99$, $I^2 = 0\%$, moderate quality of evidence) and FVC (MD -0.07 [CI 95% −0.27; 0.14], $p = 0.51$, $I^2 = 0\%$, moderate quality of evidence) (Fig. 2b and c respectively).

Quality of life

Three RCTs ($n = 144$) [15, 16, 25] assessed quality of life with different scales. Two studies utilized the health-related quality of life *(*HRQOL*)*. Huang et al. (2017) [15] found a significant difference among groups after the rehabilitation program in the Global QoL item (IG, 71.9 ± 13.8/74.2 ± 12, and CG, 68.9 ± 11.8/67.5 ± 11.9, $p = 0.03$), but without a significant difference in the other items. Lai et al. (2016) [16] did not observe a significant difference among groups in any item of the scale. The two studies mentioned presented a low quality of evidence. Morano et al. (2014) [25] utilized the SF-36 physical component summary (PCS) and mental component summary (MCS) scales, but did not find a significant difference between groups. The methodological assessment indicates low quality of evidence.

Complications during the postoperative period

Five RCTs ($n = 195$) assessed the postoperative incidence of pneumonia and were included in the meta-analysis [15, 16, 23, 24, 26]. The intervention group did not show a significant reduction in the incidence of pneumonia compared to the control group (RR 0.56 [CI 95% 0.29; 1,10], $p = 0.09$, $I^2 = 0\%$, low quality of evidence) (Fig. 3a).

Four RCTs ($n = 163$) assessed the incidence of atelectasis postoperatively and were included in the meta-analysis [15, 16, 23, 24]. There was no significant difference between groups in the incidence of atelectasis (RR 0.81 [CI 95% 0.24; 2.69], $p = 0.72$, $I^2 = 0\%$, low quality of evidence) (Fig. 3b).

Table 2 Bias risk assessment RoB 2.0

Author, year	Outcome	Randomization process	Deviations from intendent intervention	Missing outcome data	Measurement of the outcome	Selection of the reported outcome	Overall bias
Benzo et al. (2011) [23]	Pneumonia Atelectasis Mechanical ventilation Hospital stays	Some concerns	High	High	High	Some concerns	High
Huang et al. (2017) [15]	Functional capacity FEV1 FVC Pneumonia Atelectasis Mechanical ventilation Hospital stays Quality of life	Some concerns	Low	Low	High	Some concerns	High
	Mortality	Some concerns	Low	Low	Low	Some concerns	Some concerns
Lai et al. (2016) [16]	Functional capacity FEV1 FVC Pneumonia Atelectasis Mechanical ventilation Hospital stays Quality of life	Some concerns	Low	Low	Low	Some concerns	Some concerns
	Mortality	Some concerns	Low	Low	Low	Some concerns	Some concerns
Morano et al. (2013) [24]	Functional capacity FEV1 FVC Pneumonia Atelectasis Mechanical ventilation Hospital stays	Low	Low	Low	Low	Some concerns	Some concerns
Morano et al. (2014) [25]	Functional capacity Quality of life	Low	Some concerns	Low	High	Some concerns	High
Weiner et al. (1997) [26]	FEV1 FVC Pneumonia	Some concerns	Some concerns	Low	High	Some concerns	High
	Mortality	Some concerns	Some concerns	Low	Low	Some concerns	Some concerns

Table 3 Quality of evidence using GRADE

No. of participant's (studies) follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With exercise	With inspiratory muscle training + exercise		Risk with exercise	Risk difference with inspiratory muscle training + exercise
Functional capacity (assessed with: 6-MWD)											
168 (4 RCTs)	Serious[a]	Not serious	Not serious	Serious[b]	None	⊕⊕○○ Low	84	84	–	MD 28.93 higher (0.28 higher to 57.58 higher)	
Pulmonary function test—FEV1 (assessed with: spirometry)											
176 (4 RCTs)	Serious[c]	Not serious	Not serious	Not serious	None	⊕⊕⊕○ Moderate	87	89	–	MD 0 (0.16 lower to 0.16 higher)	
Pulmonary function test—FCV (assessed with: spirometry)											
176 (4 RCTs)	Serious[c]	Not serious	Not serious	Not serious	None	⊕⊕⊕○ Moderate	87	89	–	MD 0.07 lower (0.27 lower to 0.14 higher)	
Quality of life											
144 (3 RCTs)	Serious[a]	Not serious	Not serious	Serious[d]	None	⊕⊕○○ Low	Three studies (n=144) evaluated the quality of life with different scales. Two studies used health-related quality of life (HRQOL) and the third used SF-36 physical component summary and SF-36 mental component summary. The studies do not find significant difference between groups in quality of life				
Length of hospital stay											
161 (4 RCTs)	Serious[e]	Not serious	Not serious	Not serious	None	⊕⊕⊕○ Moderate	80	81	–	The mean length of hospital stay was 0	MD 3.63 lower (4.96 lower to 2.29 lower)
Pneumonia											
195 (5 RCTs)	Serious[f]	Not serious	Not serious	Serious[b]	None	⊕⊕○○ Low	20/96 (20.8%)	11/99 (11.1%)	RR 0.56 (0.29 to 1.10)	208 per 1.000	92 fewer per 1.000 (from 148 fewer to 21 more)
Atelectasis											
163 (4 RCTs)	Serious[g]	Not serious	Not serious	Serious[b]	None	⊕⊕○○ Low	7/81 (8.6%)	5/82 (6.1%)	RR 0.81 (0.24 to 2.69)	86 per 1.000	16 fewer per 1.000 (from 66 fewer to 146 more)
Mechanical ventilation											
144 (3 RCTs)	Serious[h]	Not serious	Not serious	Serious[b]	None	⊕⊕○○ Low	7/72 (9.7%)	3/72 (4.2%)	RR 0.43 (0.12 to 1.58)	97 per 1.000	55 fewer per 1.000 (from 86 fewer to 56 more)
Mortality											
152 (3 RCTs)	Serious[i]	Not serious	Not serious	Very serious[b]	None	⊕○○○ Very low	2/75 (2.7%)	0/77 (0.0%)	RR 0.33 (0.04 to 3.12)	27 per 1.000	18 fewer per 1.000 (from 26 fewer to 57 more)

CI confidence interval, *MD* mean difference, *RR* risk ratio

Explanations

[a] Two studies did not report outcome measurement (Huang et al., 2017 and Morano et al., 2014)

[b] The studies present a large confidence interval (CI)

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[c] Two studies did not report outcome measurement (Huang et al., 2017 and Weiner et al., 1997), three studies had some concerns in the randomization process (Huang et al., 2017; Lai et al., 2016 and Weiner et al., 1997), and all studies had some concerns in selecting the outcome reported

[d] Small sample size

[e] Two studies did not report outcome measurement (Benzo et al., 2011 and Huang et al., 2017), and all studies had some concerns in the randomization process and in the selection of the reported outcome

[f] Three studies did not report outcome measurement (Benzo et al., 2011; Huang et al., 2017 and Weine r et al., 1997), four studies had some concerns in the randomization process (Benzo et al., 2011; Huang et al., 2017; Lai et al., 2016 and Weiner, 1997), and all studies had some concerns in selecting the outcome reported

[g] Two studies did not report outcome measurement (Benzo et al., 2011 and Huang et al., 2017), three studies had some concerns in the randomization process (Be nzo et al., 2011; Huang et al., 2017 and Lai et al., 2016), and all studies had some concerns in selecting the outcome reported

[h] Two studies had some concerns in the randomization process (Huang et al., 2017 and Lai et al., 2016), and all studies had some concerns in selecting the reported outcome

[i] All studies had some concerns in the randomization process and in the selection of the reported outcome

Three RCTs ($n = 144$) assessed the incidence of mechanical ventilation longer than 48 h postoperatively and were included in the meta-analysis [15, 16, 24]. In the meta-analysis, there was no significant difference in the incidence of mechanical ventilation longer than 48 h between the intervention group and the control (RR 0.43 [CI 95% 0.12; 1.58], $p = 0.20$, $I^2 = 0\%$, low quality of evidence) (Fig. 3c).

Days of hospital stay

Four RCTs ($n = 161$) quantified the days of hospital stay, enabling the meta-analysis [15, 16, 23, 24]. The patients who underwent a rehabilitation program with IMT in the preoperative period had their time in hospital significantly reduced an average of 3.63 days (MD –3.63 [CI 95% −4.96; −2.29], $p = 0.00$, $I^2 = 0\%$, moderate quality of evidence) (Fig. 4a).

Mortality

Three RCTs ($n = 152$) assessed postoperative mortality enabling the meta-analysis [15, 16, 26]. There was no significant difference between groups as to mortality (RR 0.33 [CI 95% 0.04; 3.12], $p = 0.33$, $I^2 = 0\%$, very low quality of evidence) (Fig. 4b).

Discussion

After a systematic review of the literature searching for studies that have used inspiratory muscle training associated or not with a rehabilitation program based on physical exercise during the preoperative period of anatomic pulmonary resection, we observed that only one RCT [26] did not associate physical exercise with IMT. The other studies [15, 16, 23–25] in many different manners associated IMT with sessions of peripheral muscle overload, predominantly of the lower limbs, both to gain strength and for endurance. There was a clear discrepancy between the studies as regards the structure of the physical rehabilitation sessions, but the most relevant fact observed in the meta-analyses was the mean increase of the distance traveled in the 6WT (MD = 28.93 m) and the reduction of the time of hospital stay (MD = −3.63 days) of the patients inserted in the different preoperative programs.

As far as we know, this is the first systematic review with meta-analysis based on data from 219 participants that assessed the benefits of IMT associated or not with physical exercise on the functional capacity, pulmonary function, quality of life, length of hospital stays, mortality, and complications in the postoperative period of pulmonary resection. Recently, a systematic review showed evidence that the preconditioning based exclusively on physical exercise may improve pulmonary function and reduce the length of hospital

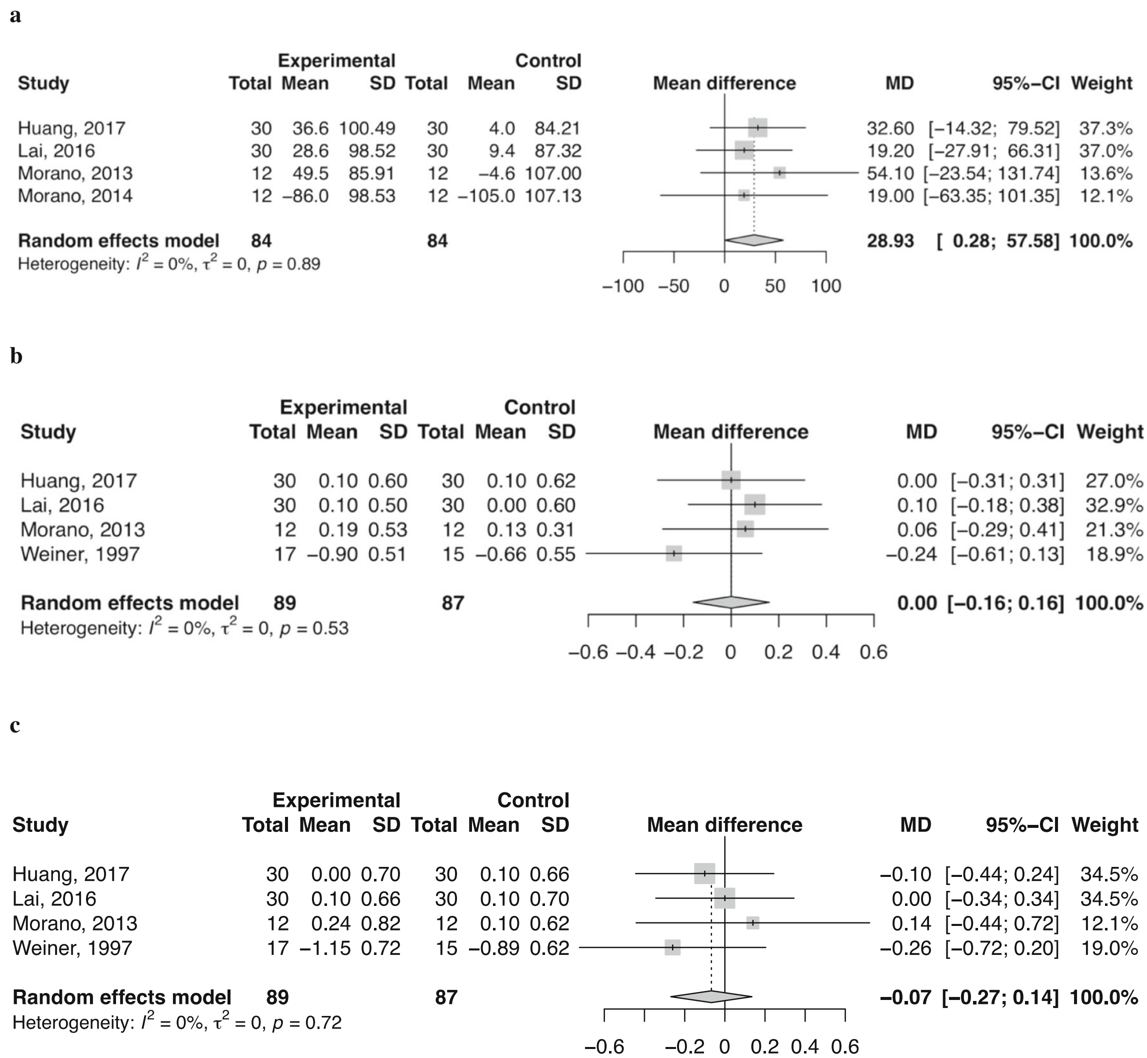

Fig. 2 Effect of IMT in the preoperative period of anatomical pulmonary resection on functional capacity and lung function, showing the weighted difference of means and 95% confidence interval in **a** 6-minute walk test (6WT), **b** forced expiratory volume in one second (FEV1), and **c** forced vital capacity (FVC)

stay and postoperative complications in patients with lung cancer before the pulmonary resection surgery, corroborating some of our findings [17].

Apparently, the isolated use of IMT in the preoperative period of anatomic pulmonary lung resection does not promote significant benefits in the outcomes studied, but because of the scarcity of studies that assessed the exclusive use of this training, this finding cannot be conclusively stated. Huang et al. (2017) [15] performed an RCT with three groups, one of them being the isolated effect of IMT. This group, compared to the control group, did not present a significant difference in the outcomes evaluated. However, in the same study, the comparison between the group that associated IMT to the physical exercise with the control group showed a significant improvement in the functional capacity, in the peak expiratory flow, in quality of life, and in the reduction of the number of days in hospital.

Another important aspect is the discrepancy in the structure of the rehabilitation programs. The duration, frequency, and intensity of the overload were broadly distinct and render it impossible to establish a protocol that can be considered in future studies. As to the IMT, five studies [15, 16, 23, 24, 26] performed daily sessions, where the duration of each session varied between 10 and 30 min, and the frequency varied from two to four times a day. A study [24] described the IMT with an initial load of 20% of the maximum inspiratory pressure (MIP) in the 1st week, with a load increment of 5% to 10% at each session, determining 60% as the maximum load. In another study [26], the IMT began with a resistance of 15% of the MIP in the 1st week and 20% in the 2nd week. Morano et al. (2014) [25] cite the IMT but do not describe how they advised the patients, nor the frequency and load used in the session.

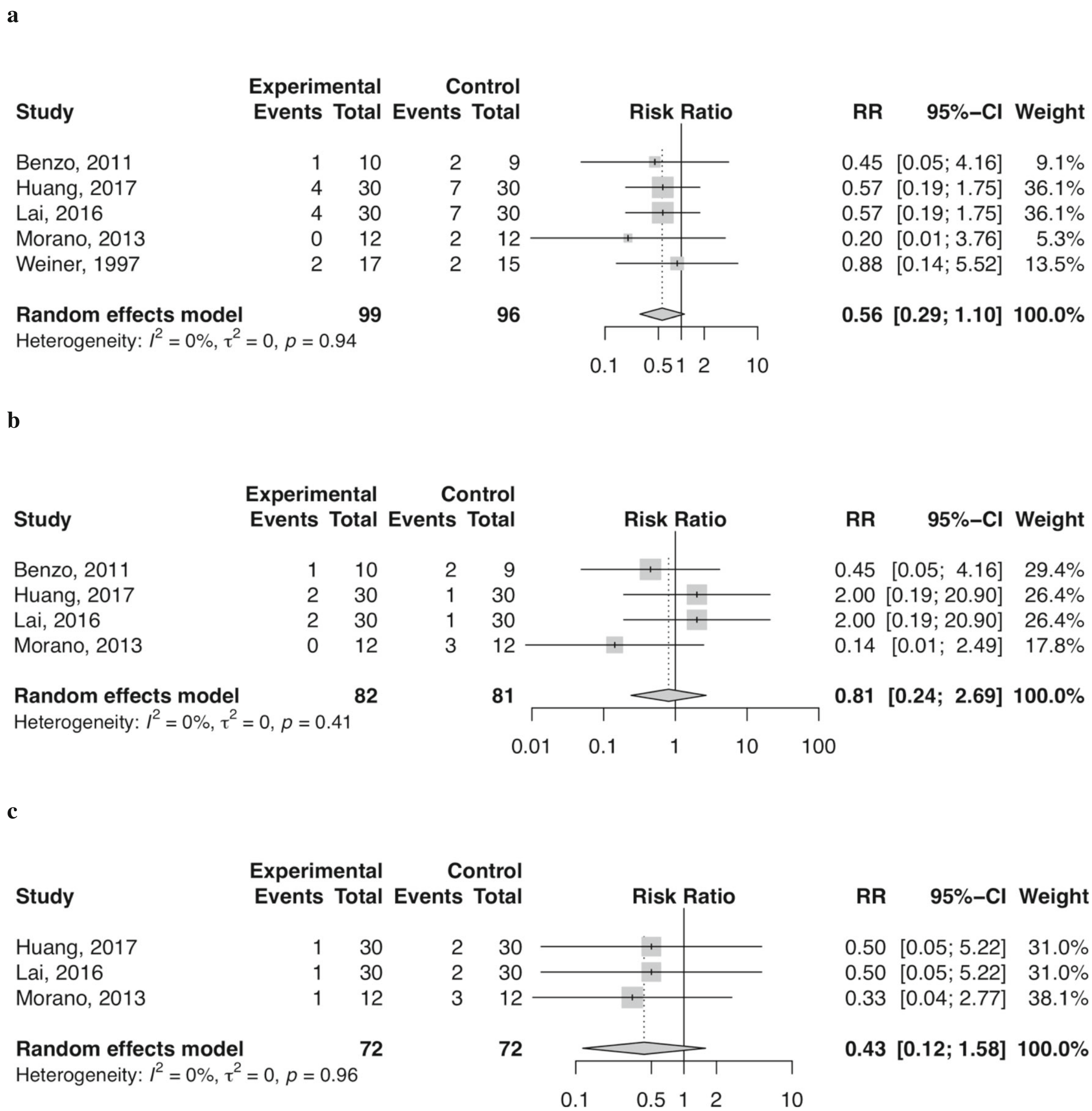

Fig. 3 Effect of IMT in the preoperative period of anatomical pulmonary resection on postoperative complications, showing the relative risk and 95% confidence interval for **a** pneumonia, **b** atelectasis, and **c** mechanical ventilation > 48 h

The way the physical exercises were structured also varied widely, mostly on the peripheral overload of large muscle groups. Special attention must be given to oncological patients since various factors must be considered at the time of establishing a rehabilitation program. Brunelli et al. (2012) [27] suggest that regular exercise with a moderate intensity may be associated with a 30% to 50% reduction in mortality after cancer has been diagnosed. Recently, a systematic review with a meta-analysis revealed a reduction in the mortality of survivors of breast cancer [28]. When exercise is regularly performed, it may alter the main prognostic markers of oncological mortality, besides significantly reducing the comorbidities associated both with the paraneoplastic effects and with the side effects induced by the antineoplastic treatment [29–31].

In their RCT, Edvardsen et al. (2014) [32] suggest that in recently operated patients with non-small cell lung carcinoma (NSCLC), the high intensity endurance and strength training induce clinically significant improvement in the peak oxygen consumption, functional capacity, and quality of life. Among the studies included in our meta-analysis, two studies [23, 25] included strength and endurance training in the same session, and three [15, 16, 24] only performed endurance training. There was a variation in the form of load increment, as well as in the duration and frequency of the sessions. The lack of details in the descriptions of the method utilized in rehabilitation limits the possibility of analysis and recommendations for preoperative physical training for elective anatomic pulmonary resection surgery.

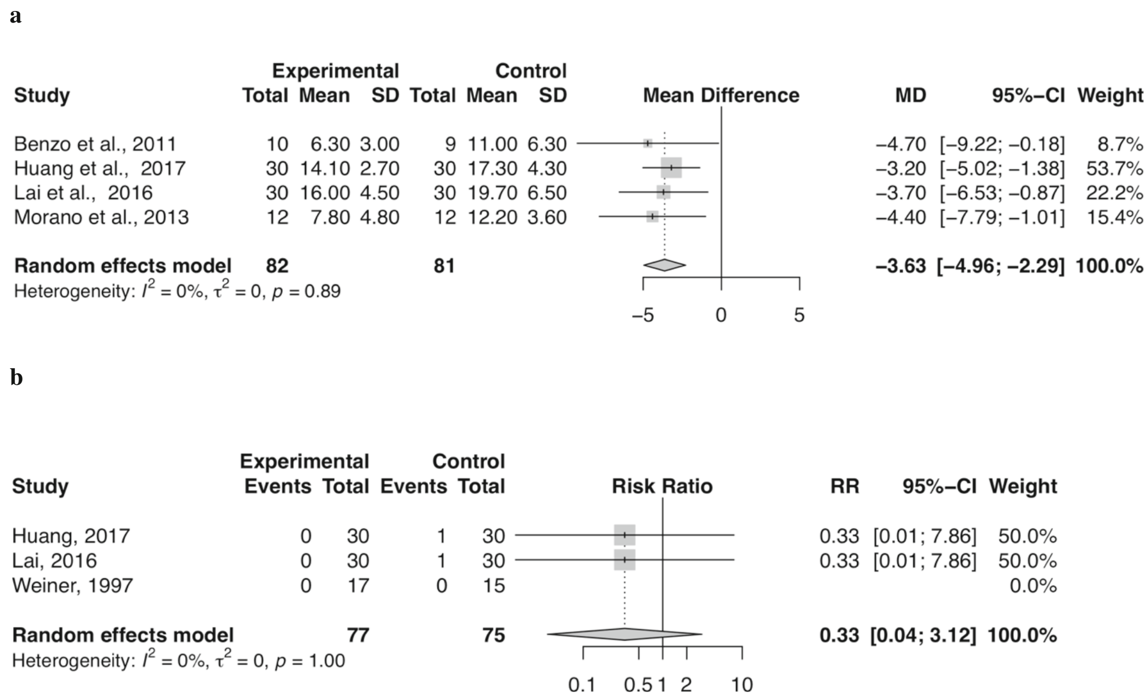

Fig. 4 Effect of IMT in the preoperative period of anatomical pulmonary resection on **a** hospitalization days, showing the weighted difference of means and 95% confidence interval, and **b** mortality, showing the relative risk and interval of 95% confidence

The functional capacity in the studies of this review was assessed by 6WT [15, 16, 24, 25]. According to Kasymjanova et al. (2009) [33], the patients with inoperable NSCLC who traveled a distance equal to or greater than 400 m in the 6WT presented a significantly longer survival. On the other hand, the benefits attributed to improved functional capacity in the patients with lung cancer are expressed, according to Granger et al. (2015) [34], once there is a 22-m increase in the maximum distance traveled in the 6WT. This means that the objective of the rehabilitation programs must be to ensure a minimum of functional gain for the patient to experience the benefits attributed to physical capacity. In two studies [24, 25], the 6WT performance of the patients in the control group, at reassessment, was less than 400 m. There is not a clear cause and effect relationship, but the functional limitation in these patients may be a factor indicating shorter survival, as previously observed by Kasymjanova et al. (2009) [33]. The result of the meta-analysis of the studies included in this review shows an addition, on average of 28.93 m, in the distance traveled in 6WT. These results supply positive evidence that it is possible to improve the functional capacity by intervening before the surgical procedure. However, it is not clear how much impact the physical improvement can have on postoperative recovery from pulmonary resection.

One of the relevant data of this study refers to the days of hospital stay. In the systematic review, four homogeneous studies [15, 16, 23, 24] point out that the rehabilitation of the patients with lung cancer, before the surgical resection, diminishes the hospital stay by an average of 3.63 days. This is an interesting fact, since our results show that the entire effort made to improve pulmonary function and the patients' functionality resulted in a small, but significant, increase in the distance traveled in the 6WT, but that there were no improvements in the pulmonary function tests, and little effect on the quality of life postoperatively. This left a gap when an attempt was made to identify which physical-functional adaptations effectively contributed to reducing the length of hospital stay, since the performance in the pulmonary function tests was similar in the patients exposed and not exposed to preoperative rehabilitation.

In the immediately postoperative period of anatomic pulmonary resection, factors such as pain and mechanical trauma imposed by surgery on the ribcage have a direct effect on the capacity and efficiency of the pulmonary ventilation mechanisms. Among the main changes are the limitation of chest movement, the reduction of the cough reflex, and the difficulty in eliminating secretion. Often, the repercussion of these problems delays recovery and can contribute negatively to the occurrence of postoperative complications such as atelectasis, pneumonia, acute respiratory failure, need to reintubate, pulmonary edema, bronchospasm, and pneumothorax [12–14]. Among the postoperative complications assessed in this review, there was no significant difference in the results, but there was a tendency to reduce the incidence of pneumonia in the patients exposed to preoperative rehabilitation. It is likely that this effect promoted the greater impact on the reduction in the length of hospital stay; however, from the mathematical standpoint, the data available do not allow extrapolating this observation. Mans et al. (2015) [35] told that preoperative IMT significantly improves the function of the respiratory muscles during the immediately postoperative period of cardiothoracic and abdominal surgery, thus halving the risk of pulmonary complications. Li et al. (2019) [36] also observed a reduction in the pulmonary complications after preoperative training.

Pulmonary function was assessed using FEV1 and FVC. Initially, we believed that preoperative IMT would improve pulmonary function, but the studies [15, 16, 24, 26] included in the meta-analyses showed that most of the parameters investigated in spirometry were mainly equal to or slightly higher after the rehabilitation program, except for Morano et al. (2013) [24] who found a significant improvement of FVC after training. Similar findings were described in a recent systematic review, where 404 patients submitted to a preoperative exercise program for pulmonary resection, with or without chronic obstructive pulmonary disease (COPD), did not show a significant improvement in pulmonary function after training [36]. On the other hand, Mujovic et al. (2015) [37] found an improvement in the pulmonary function in the patients submitted to preoperative training, but the analysis of the results identified a dependency between the degree of pulmonary function and the extent of pulmonary resection, and the significant improvement was recorded only in patients submitted to lobectomy. So far, the results are still conflicting, but, everything points to the fact that the pre-surgical training of ventilatory muscles can significantly improve pulmonary function, depending rather on the extent of the mechanical trauma induced by surgery than on the training protocol used.

The studies [15, 16, 26] in this review that assessed patient mortality in the preoperative period did not present a significant difference between groups, with a very low quality of evidence. Finally, the assessment of the impact of pre-surgical rehabilitation on quality of life was limited to three studies that utilized different instruments which made it impossible to perform a meta-analysis. Even so, between the two studies [15, 16] that used HRQOL, Huang et al. (2017) [15] reported a benefit only regarding the Global QoL of the scale. Morano et al. (2014) [25] utilized the SF-36 PCS and SF-36 MCS scales and did not find a significant difference between groups. Pompili et al. (2011) [38] performed a study to identify the clinically relevant predictors of decline of the physical and emotional component of quality of life after pulmonary resection and observed that a proportion consisting of patients submitted to surgery presents a major postoperative reduction in their quality of life.

In this meta-analysis, the strong points were establishing broad, explicit eligibility criteria, a meticulous search in different databases and the absence of language restrictions. We assessed the risk of bias and applied the GRADE criterion to determine the certainty in the body of evidence. The analysis was restricted to the highest standard of evidence, considering that only RCTs were included. However, the evidence must be carefully analyzed due to the restricted number of samples, the lack of blinding of therapists and patients, and the diversity of the structure of physical rehabilitation programs used in the protocols of the studies selected.

Our systematic review suggests that IMT in the preoperative period of anatomic pulmonary resection, combined with a physical rehabilitation program, is effective to improve functional capacity and diminish the length of stay in hospital. The effects on quality of life, pulmonary function, postoperative complications, and mortality remain uncertain.

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Data availability All authors ensure that the data produced and the materials and the code number (PROSPERO CRD42018105859) are their own and materials used by other authors are properly identified. The manuscript and all its data support the authors' statements and comply with the journal's standards.

Declarations

Ethics approval Not applicable.

Consent to participate Not applicable.

Consent for publication Not applicable.

Conflict of interest The authors declare no competing interests.

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