



## REVIEW

# The role of physiotherapy in patients undergoing pulmonary surgery for lung cancer. A literature review



F. Kendall<sup>a,b,c,\*</sup>, P. Abreu<sup>d</sup>, P. Pinho<sup>a</sup>, J. Oliveira<sup>c</sup>, P. Bastos<sup>a</sup>

<sup>a</sup> Department of Cardio-Thoracic Surgery, Centro Hospitalar de São João, Porto, Portugal

<sup>b</sup> CESPU, Polytechnic Health Institute of the North, Gandra, Portugal

<sup>c</sup> CIAFEL, Faculty of Sports, University of Porto, Porto, Portugal

<sup>d</sup> Department of Physiotherapy, Escola Superior Saúde Dr. Lopes Dias, Polytechnic Institute of Castelo Branco, Castelo Branco, Portugal

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**Abstract** This review aims to appraise the role of physiotherapy care in patients submitted to pulmonary surgery, in preoperative, perioperative, and postoperative phases.

Pulmonary surgery is the *gold standard* treatment for patients with lung cancer if it is completely resectable. However, the major impairments and complications induced by surgery are well known. Physiotherapy has been regularly used both in the preparation of the surgical candidates; in their functional recovery in the immediate postoperative period, and in the medium/long term but there is a lack of concise evidence-based recommendations. Therefore, the aim of this review is to appraise the literature about the role of physiotherapy interventions in patients undergoing lung surgery for lung cancer, in preoperative, perioperative, postoperative and maintenance stages, to the recovery and well-being, regardless of the extent of surgical approach.

In conclusion, physiotherapy programs should be individually designed, and the goals established according to surgery timings, and according to each subject's needs. It can also be concluded that in the preoperative phase, the main goals are to avoid postoperative pulmonary

**Abbreviations:** NSCLC, non-small cell lung cancer; PPC, postoperative pulmonary complications; COPD, chronic obstructive pulmonary disease; PO, postoperative predictive; FVC, forced vital capacity; FEV<sub>1</sub>, forced expiratory volume in first second; ERS/ESTS, European Respiratory Society and the European Society of Thoracic Surgery; DLCO, diffusion capacity for carbon monoxide; CPET, cardiopulmonary exercise test; O<sub>2</sub>, oxygen; VATS, video-assisted thoracic surgery; RVATS, robotic video-assisted thoracic surgery; MIP, maximal inspiratory pressure; IMT, inspiratory muscle training; LOS, length of stay; RCT, randomized controlled trial; IS, incentive spirometry; VO<sub>2max</sub>, maximal oxygen consumption; V/Q, ventilation/perfusion ratio; PET, preoperative exercise therapy; BMI, body mass index; PEP, positive expiratory pressure; NIV, non-invasive ventilation; TENS, transcutaneous electrical nerve stimulation.

\* Corresponding author.

E-mail address: [fkendall@gmail.com](mailto:fkendall@gmail.com) (F. Kendall).

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complications and reduce the length of hospital stay, and the therapeutic targets are respiratory muscle training, bronchial hygiene and exercise training. For the perioperative period, breathing exercises for pulmonary expansion and bronchial hygiene, as well as early mobilization and deambulation, postural correction and shoulder range of motion activities, should be added. Finally, it can be concluded that in the postoperative phase exercise training should be maintained, and adoption of healthy life-style behaviours must be encouraged.

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## Introduction

For the early stages of non-small cell lung cancer (NSCLC) surgical resection is undoubtedly the *gold standard* treatment for candidates who are eligible; however, this procedure is associated with the occurrence of postoperative pulmonary complications (PPC) such as atelectasis and pneumonia, as well as pleural complications, which apart from the economic repercussions, may have an immediate impact in patients' recovery with long-term consequences on their quality of life.<sup>1</sup>

Only 15–20% of those patients diagnosed with lung cancer are candidates for surgery; it depends not only upon the histological characteristics of the tumour but also the preoperative staging according to the classification of malignant tumours TNM.<sup>1–3</sup> However, it is still necessary to assess the surgical risk, which is influenced by several factors, including age, co-morbidities, and cardiopulmonary function.

Physiotherapy has been widely used preoperatively and/or postoperatively to avoid surgical complications and enhance the recovery of these patients. However, there is a huge heterogeneity regarding the components of the proposed physiotherapy programs and the timing for their implementation (before and/or after surgery). Unfortunately, the available evidence regarding the effectiveness of physiotherapy interventions is heterogeneous, probably due to the variability in the program contents, along with the questionable quality of the studies design. Therefore, considering the inherent economic costs, physiotherapy intervention programs based on robust scientific evidence are required.

Taking into account the physiopathological changes induced by pulmonary surgery, this review aims to provide a literature and clinical overview of the role of physiotherapy interventions in patients undergoing lobectomy or pneumectomy, considering the preoperative, perioperative and the post-hospital discharge phases.

## Pulmonary surgery and risk factors for postoperative complications

Most often patients with lung cancer are smokers or ex-smokers and, therefore, presenting chronic obstructive pulmonary disease (COPD) and impaired pulmonary function.<sup>1</sup> Indeed, many patients with localized lung cancer up to IIIA stage, are excluded from pulmonary surgery due

to their impaired pulmonary function and increased risk for PPC.<sup>4</sup> Moreover, low postoperative predictive (ppo) values of forced vital capacity (FVC) and forced expiratory volume in first second (FEV<sub>1</sub>) are also used to exclude patients from surgery.<sup>5,6</sup> According to the joint ERS/ESTS clinical practice guidelines, the single evaluation of the predicted postoperative FEV<sub>1</sub> (ppo-FEV<sub>1</sub>) is not a strong predictor for PPC, especially in patients with FEV<sub>1</sub> < 70%. Despite the ppo-FEV<sub>1</sub> with cut-off of higher risk set at 40%, the recent improvements in surgical technique and in perioperative care lead experts to suggest changing the cut-off to 30%.<sup>7</sup> Traditionally, the diffusion capacity for carbon monoxide (DLCO) was only evaluated in patients with obstruction, but recent studies showed that even in patients with normal FEV<sub>1</sub> the DLCO is a strong predictor of PPC. The ppo-DLCO cut-off was 40%, and currently the experts suggest changing it to 30%.<sup>7</sup>

A recent meta-analysis concludes that increased exercise capacity is associated with less PPC, even in COPD patients.<sup>8</sup> According to Brunelli et al.<sup>5</sup> exercise testing can be divided into two types: the low-technology tests and the cardiopulmonary exercise test (CPET), being the later the gold-standard for the assessment of surgical candidates, especially for *borderline* patients. The authors<sup>5</sup> found that the correlation between the exercise capacity both with FEV<sub>1</sub> and DLCO is weak probably due to the existence of cardiovascular compensatory mechanisms to enhance tissue oxygen (O<sub>2</sub>) extraction. Indeed, the FEV<sub>1</sub> reduction induced by the lobectomy is significantly less marked in COPD patients than in those with normal pulmonary function, suggesting that, compared to exercise capacity, the pulmonary function parameters are not so sensitive and accurate in predicting the occurrence of PPC.<sup>9–11</sup> The surgical approach commonly used was the posterolateral thoracotomy, though in recent decades video-assisted thoracic surgery (VATS) has gained progressive popularity, despite the initial reservations concerning its oncologic reliability.<sup>12–14</sup> Seder et al.<sup>15</sup> clearly show in their retrospective study that VATS has been widely accepted in lung resections, probably due to the weakness of arguments about oncologic outcomes or the required prolonged periods of training to practice this surgical approach, as there are several important advantages of muscle-sparing techniques like VATS compared to the traditional posterolateral thoracotomy, related not only to fewer postoperative complications, shorter chest tube duration, with less pain and shoulder impairment, but also with higher overall annual survival rates.<sup>16,17</sup> Furthermore, VATS has shown to be advantageous for reduction of postoperative

inflammatory response, with less production of reactive oxygen species, which may have an important role in avoiding tumour proliferation.<sup>18</sup> Also interesting is a new technological improvement, the robotic video-assisted thoracic surgery (RVATS), which has been shown to be more effective than VATS regarding the image quality and allows a better control of movements. Despite these advantages, RVATS is a more expensive technique than VATS, requires more specialized training periods for all the surgical staff, and requires prolonged surgical operations. Additionally, there is still the same lack of clarity about its long-term oncologic efficacy, which has limited the use of this approach.<sup>19</sup>

All chest surgical approaches involve several organic injuries, and cause related respiratory muscle weakness.<sup>20–22</sup> After lung resection, considerable respiratory muscle weakness has developed, which was strongly associated to age and surgical approach, being more severe in older patients and in posterolateral thoracotomy, leaving little doubt that VATS offers the best surgical approach in terms of respiratory muscle weakness.<sup>20</sup> Indeed, postoperative pain is not the only reason for the respiratory muscle impairment; it is possible that chest wall muscular dysfunction might have an important influence on diaphragmatic function, and chest wall compliance. Bernard et al.<sup>23</sup> compared the postoperative maximal inspiratory pressure (MIP) in different surgical approaches, such as VATS, transaxillary thoracotomy or posterolateral thoracotomy, on the 2nd, 4th and 30th postoperative days, making all patients follow the same analgesic protocol. Overall, the results showed VATS as the best approach in relation to inspiratory muscle dysfunction and its recovery.

Other surgical consequences are the limitation of shoulder range of motion, with loss of strength, postural abnormalities, as well as general muscle weakness due to pain, and ambulation restriction during the thoracic drainage suction period.<sup>24</sup> The impairment of shoulder range of motion and strength on the side of the surgical incision are important limiting factors to daily living activities, requiring the use of analgesia. The advent of VATS and its advantages regarding the impact of trauma of this approach has been well documented, with patients submitted to VATS showing lower surgical injury repercussions compared to those undergoing posterolateral thoracotomy.<sup>25</sup>

Despite the surgeons' conservative concern regarding lung tissue, pneumonectomy is still required in a few patients.<sup>26</sup> Pneumonectomy is related to huge changes in pulmonary function beyond the compensatory hyperinflation of the remaining lung and consequent mediastinal shift. Moreover, diaphragmatic dysfunction could be also a consequence of costo-phrenic obliteration, intercostal space reduction and paradoxical diaphragmatic movement resulting from phrenic nerve injury. Some surgeons choose to perform a diaphragmatic plicature whenever the phrenic nerve is removed.<sup>27</sup> Compared to lobectomy, pneumonectomy is a procedure with higher risk, associated with higher mortality ratio, not only in-hospital but also in the six months after discharge; it is worth noting that right pneumonectomy compared to the left one is even worse in terms of the risk of morbidity and mortality.<sup>28</sup> All these data show that pneumonectomy might influence mortality and morbidity with an important loss of quality of life caused by deterioration of the respiratory function.<sup>28,29</sup>

## Potential physiotherapy targets for lung surgery patients

Traditionally, physiotherapy for lung surgery patients was focused on promoting chest expansion, bronchial clearance, postural correction and shoulder range of motion. Recently, the advent of lung volume reduction and lung transplant surgeries, in parallel with the slew of new studies of physiotherapy in COPD patients, brings a new perspective to the physiotherapy approach in pulmonary surgical candidates. Recent studies have suggested the beneficial effects of adding exercise training to traditional physiotherapy targets, complemented or not with inspiratory muscle training (IMT), not only in preoperative programs, but also postoperatively as a recovery and maintenance approach.<sup>22,30</sup>

In COPD patients, IMT has been widely studied in pulmonary rehabilitation programs.<sup>31–33</sup> In a meta-analysis Gosselink et al.<sup>33</sup> concluded that IMT might add clinically relevant improvements of inspiratory muscle strength and endurance, functional exercise capacity, dyspnoea and quality of life. In addition, respiratory muscle strength training shows better results compared to endurance training, which is a type of training that requires special care since it must be performed in a hospital environment in order to monitor and control the "normocapnic hyperpnoea" method. Conversely, strength training can be performed at home with a device to produce "inspiratory resistive breathing" and "threshold loading".<sup>33</sup>

Respiratory muscle weakness is a serious impairment in several surgeries, such as upper abdominal, cardiac or pulmonary surgery, due to muscular injury, to depressed central nervous system, and to pain.<sup>34</sup> Respiratory muscle weakness leads to inability to cough, to reduced lung compliance and dyspnoea, associated with postoperative immobilization, which in turn induce a generalized muscular weakness.<sup>20,35,36</sup> In order to avoid the occurrence of atelectasis and to prevent other PPC, it is imperative to remove secretions from the airways and promote distension of the lung tissue.<sup>22</sup> Thus, the association of deep breathing exercises with bronchial clearance and early patient mobilization must be part of the physiotherapy program.<sup>22</sup> Oddly enough, there are very few studies regarding respiratory muscle training in surgical patients particularly in pulmonary surgery, either preoperatively or postoperatively. It is possible to observe favourable results in the decrease of hospital length of stay (LOS) and PPC in other types of surgeries, such as cardiac and upper abdominal, especially if the muscular training is performed before surgery.<sup>37–41</sup> Two meta-analysis including only patients submitted to cardiac and upper abdominal surgery, show that preoperative IMT leads to a PPC and LOS reduction, as a result of a significant improvement of strength after IMT and throughout the early postoperative days.<sup>35,42</sup> A recent meta-analysis including cardiac and abdominal surgery patients, and also pulmonary surgical patients, have shown a more pronounced effect in pulmonary surgical patients both in PPC reduction (RR=0.45, 95%CI: 0.24, 0.82, 10.4) and LOS (MD=−4.52, 95%CI: −7.33, −1.70, 0.0).<sup>43</sup> Meantime, Brocki et al.<sup>44</sup> conducted a RCT aiming to investigate two weeks of postoperative IMT in addition to breathing exercises and early mobilization in high-risk patients after lung cancer surgery, showing a non-significant difference

in respiratory muscle strength, pulmonary volumes, physical performance, and dyspnoea. Relatively to PPC, only a significant reduction in hypoxaemia was observed, in the training group. Despite the small sample size this is a unique study investigating IMT in postoperative pulmonary surgery patients, and the associated risks. The absence of significant results for the majority of the outcomes could probably be related to the low load level.<sup>44</sup>

## Scientific evidences supporting physiotherapy interventions

### Preoperative period

Weiner et al.<sup>45</sup>, through a randomized control trial, studied the effect of specific inspiratory muscle training with incentive spirometry (IS) started two weeks before surgery and maintained until three months after. Compared to a control group that did not receive any respiratory training, the experimental group had significant improvements in FEV<sub>1</sub>, FVC, and MIP before surgery, which became even more pronounced at the end of the study. In this study, despite the apparent benefits of IMT, the weight of preoperative and postoperative training periods to the results was not ascertained.

Sekine et al.<sup>46</sup> obtained similar results in a preoperative study with COPD candidates for pulmonary surgery. Apart from the IS training, candidates were also advised to walk 5000 steps/day for two weeks prior to surgery. They were instructed about diaphragmatic breathing exercises, pursed-lip breathing, huffing and coughing for 15 min after nebulization with bronchodilation, five times a day. At baseline, the FEV<sub>1</sub> in the intervention group was significantly lower than in the control group composed by historical data ( $1.8 \pm 0.5$  L vs.  $2.0 \pm 0.45$  L, respectively;  $P=0.04$ ), and despite that the intervention group had a significant LOS reduction ( $21.0 \pm 6.8$  vs.  $29.0 \pm 9.0$   $P=0.0003$ ) and a lower rate of PPC (54.5% vs. 70%, respectively;  $P=0.202$ ). Despite the limitation inherent to the lack of a true control group, the results support the importance of physiotherapy intervention programs, particularly those involving physical exercise to prevent PPC. This was later reinforced by a study in severe COPD patients,<sup>47</sup> who did not meet the inclusion criteria for lung surgery due to their reduced maximal oxygen consumption (VO<sub>2max</sub>). Patients underwent a four-week program of peripheral muscle training on a cycle ergometer with an initial load of 50% of their maximum work load on CPET, and a weekly load increase of 10% until reaching 80%. Patients were also encouraged to practice breathing exercises and IS twice a day. Despite the absence of lung function improvements, the aerobic capacity was significantly enhanced after training, fitting the inclusion criteria for lung surgery. Interestingly, the initial VO<sub>2max</sub> of 13.5 ml/kg/min was enhanced to 16.3 ml/kg/min after training, being 15 ml/kg/min the accepted VO<sub>2max</sub> cut-off for pulmonary resection. However, the lack of a control group weakens the conclusions in this study regarding the true effect of the intervention.

More recently, Pehlivan et al.<sup>48</sup> in an RCT examined the effect of a short-time intensive program in patients awaiting pulmonary surgery. The program started one week before

surgery and was continued during the hospital stay, which was similar to others performed in the previous studies but with the advantage of assessing a larger range of variables and having a real control group. All patients were assessed before surgery for heart rate, performance in the six-minute walk test, and pulmonary function, including, FVC, FEV<sub>1</sub>, DLCO, oxygen arterial pressure, and carbon dioxide arterial pressure. The experimental group showed significant improvements in all parameters compared with the control group. Some patients from the intervention group were submitted to a ventilation/perfusion ratio (V/Q) scan, which was repeated one week after intensive training, and showed advantageous changes in the perfusion distribution. Indeed, the V/Q suffered a reduction around the tumour side and an improvement in the contra-lateral lung, probably modulated by the physiotherapy program. Although the *modus operandi* was unknown, the authors speculated that the exercise-training program might have induced a hypoxic constriction of the pulmonary arterial branches around the tumour, and a significant improvement in V/Q in the healthy lung, which would explain the better gas-exchange after the program. Regarding PPC and LOS, both were also significantly reduced in the intervention group.

According to Pouwels et al.<sup>49</sup> preoperative exercise therapy (PET) might be an important component to reduce PPC, mortality and LOS; and to improve physical fitness and quality of life. Curiously, the authors found two studies indicating a decreased incidence of persistent air leak, although it was not possible to assume a relationship with PET.

Based on the above, and similarly to what Bartels et al.<sup>50</sup> recommend for lung-volume reduction surgery, multidisciplinary interventions in the preoperative period should also be focused on smoking cessation and healthy lifestyle advice, pharmacological optimization, nutritional counselling, stress management, bronchial hygiene and an exercise training program.

### Perioperative period

Many studies have focused on physiotherapy treatment in the perioperative period. Some have attempted to analyse the importance of physiotherapy in patients undergoing pulmonary resection, but apparently, all have methodological flaws, such as the absence of control group. Indeed, regarding this subject, due to ethical reasons, it is difficult to conduct a study without any kind of approach or recommendation to patients who do not receive treatment. The study of Reeve et al.<sup>51</sup> has been frequently classified in the literature as the only true randomized controlled trial (RCT) in which the control group did not receive treatment for respiratory physiotherapy. In that study, the authors analysed the effectiveness of a postoperative physiotherapy program on PPC and LOS in patients submitted to different types of lung resection by posterolateral thoracotomy. They have concluded that routinely respiratory physiotherapy is not necessary in such patients. Nevertheless, this conclusion must be carefully analysed, because in this study the control group was not blinded towards physiotherapy, since before surgery the patients received a document explaining the need for breathing and coughing exercises, early deambulation, mobilization, and shoulder exercises. Moreo-

ver, although patients did not formally receive any physiotherapy intervention, they were encouraged to carry out exercises that they had learned before. Additionally, the exercise program in the treatment group consisted only of 20 repetitions of breathing exercises with three seconds apnoea in the end of inspiration, two forced expirations and coughing, walking 15 m, mobilization exercises, active or active-assisted shoulder mobilization, five repetitions of each exercise, shoulder flexion, horizontal abduction and adduction. These exercises lasted only 15 min, which can be considered the minimum treatment as the author stated. At baseline the groups were similar except for body mass index (BMI), which was higher in the treatment group with an average of 29 kg/m<sup>2</sup>, and 45% presented a value  $\geq 30$  kg/m<sup>2</sup>, while in the control group the average was 26.5 kg/m<sup>2</sup> and only 15% presented a value  $\geq 30$  kg/m<sup>2</sup>. In addition, all patients included in this sample showed good pulmonary function. Besides being widely accepted as a hallmark study, the above-mentioned methodological flaws, such as not controlling for BMI differences between groups at baseline, as well as the lack of recording of the frequency of autonomous training in both groups, seriously compromise the conclusions. Indeed, another study in this topic has been frequently criticized due to the lack of a real control group, which was composed by historical data.<sup>52</sup> Briefly, the study was conducted in a hospital unit that did not routinely perform respiratory physiotherapy interventions until 2002, but since then an intensive postoperative physiotherapy program has been implemented for all patients. For that reason, the control group encompassed the patients submitted to lung surgery prior to 2002. This physiotherapy program intervention consisted of maximal inspiratory manoeuvres, coughing and mobilization exercises of the upper limbs, and supervised exercise on cycle-ergometer or treadmill. The effectiveness of the program was evaluated for outcomes such as PPC, LOS and hospital costs. Regarding the preoperative assessed parameters, the groups were similar at baseline. The physiotherapy intervention did not bring any improvements in mortality rates or pneumonia when compared to controls, although there was a trend to a reduction in the physiotherapy group. Reinforcing this tendency, the physiotherapy group evidenced a significant reduction in the prevalence of atelectasis compared to the historical group.<sup>52</sup> Responding to methodological criticisms of the Varela et al. study, Novoa et al.<sup>53</sup> used the same data but with a different approach (i.e., through a propensity matched analysis), and clearly showed that the intensive physiotherapy program significantly reduced the patients' morbidity. This conclusion was based on 359 pairs of patients (before vs. after 2002) using a logistic regression where the dependent variable was the PPC, assessed by radiological analysis, leucocytosis and body temperature, the independent variables being age, BMI, FEV<sub>1</sub>% and ppoFEV<sub>1</sub>, the Charlson index, and the clinical T status. This quasi-experimental study supported by a solid analysis, weakens the criticisms made of the study of Varela et al.<sup>52</sup> and reinforces the importance of a regular and intensive physiotherapy program to avoid PPC, enhancing the recovery process of these patients.

Despite the scientific evidence supporting the physiotherapy programs performed routinely in surgical patients, uncertainties still remain regarding the advantages of external respiratory devices, such as IS, or PEP Mask, among

others, to the traditional chest physiotherapy interventions. For instance, it is common to associate the IS device with the chest physiotherapy program; however, this practice was questioned by Gosselink et al.<sup>54</sup> in a RCT that assessed patients submitted to lobectomy or to oesophageal resections. For each surgery the sample was divided into a control group, which received physiotherapy, and an intervention group that received both physiotherapy and the volumetric IS device. Patients started the program preoperatively, and continued after surgery until hospital discharge. As expected, there was a decline in pulmonary function in all patients immediately after surgery, but without differences between the groups in their recovery rate and in pulmonary complications. Additionally, Agostini et al.<sup>55</sup> reviewed the efficacy of the routine use of IS devices in patients submitted to thoracic surgery and corroborated the findings of Gosselink et al.<sup>54</sup> concluding that physiotherapy with or without IS is equally effective in reducing postoperative pulmonary complications and enhancing pulmonary function. Agostini et al.<sup>55</sup> also state that IS cannot replace nor significantly improve the physiotherapist's work. Thus, a well-organized and regular physiotherapy program seems to be the most effective approach for recovery and PPC prevention. Later, Agostini et al.<sup>56</sup> performed a RCT to investigate the effect of IS compared with deep breathing exercises in patients submitted to lung resections by thoracotomy in terms pulmonary function recover, PPC development and LOS, and also adjusted according to the patients' risk stratification and concluded that IS is not more effective in pulmonary function improvement or in the PPC reduction. However, it is possible to observe a tendency with no statistical significance of more favourable result for PPC frequency in the high risk patients.

Regarding the use of other external devices associated with physiotherapy treatment, the results reported in literature do not allow safe conclusions regarding its advantage/costs. Indeed, Orman et al.<sup>57</sup> conducted a systematic review of the effectiveness of using simple devices that allow breathing exercises with positive expiratory pressure (PEP) in postoperative abdominal and thoracic surgery. Although there are many devices available to achieve this goal, it is important to note that due to the scarcity of literature, this review only includes the blow-bottle system and the PEP-mask<sup>®</sup>. Moreover, from a methodological point of view and considering the PEDro scale, the low quality of these studies must be highlighted. From a conceptual point of view, it must be outlined that the positive expiratory pressure (PEP) can be used either to increase or to reduce lung volume, depending on the respiratory technique applied, and none of the included studies referred to the breathing pattern or the pressure applied. Consequently, well-designed studies about this issue are required in order to clarify the advantage of using these external devices in surgical patients. It would also be interesting to find out the extent to which the association of non-invasive ventilation (NIV) with a conventional physiotherapy program could be an asset to reduce PPC in patients undergoing pulmonary resection. Freynet et al.<sup>58</sup>, in a review article including five studies, reported that all were unanimous in demonstrating the effectiveness of NIV therapy in association with physiotherapy, either to treat or to prevent PPC after lung resection.

It is widely accepted that postoperative pain is highly restrictive to patients, particularly after posterolateral thoracotomy. Thus, pain control is necessary not only for the patients' comfort, but also, to assure better cooperation with physiotherapy treatment, and therefore to achieve faster improvements in their pulmonary function. It is worth noting that analgesic drugs as opioids may have a detrimental effect on pulmonary function and, therefore, it is now recommended to use analgesia in the form of ropivacaine and sufentanil via epidural catheter rather than intravenous morphine administration, with significant improvements in pulmonary function recovery after lung surgery.<sup>59</sup> Therefore, patients with epidural pain control had more rapid improvement in lung volume without increased airway resistance, reducing the likelihood of pulmonary complications such as atelectasis and pneumonia. Regarding the disadvantages of analgesia via epidural catheter, including hypotension, urinary retention, respiratory muscle weakness, and neurological injury risk, other analgesic alternatives have been used, such as thoracic paravertebral block, which proved to be a good and safe alternative for thoracotomy pain control. In a recent meta-analysis comparing thoracic epidural analgesia with thoracic paravertebral block, differences in terms of pain control efficacy and opioid consumption were not found between the two procedures. However, patients submitted to thoracic paravertebral block revealed a lower incidence of urinary retention and hypotension comparatively to those submitted to epidural analgesia.<sup>60</sup>

The use of analgesia by application of transcutaneous electrical nerve stimulation (TENS) can be an asset as a technical adjunct to control severe pain. This technique was effective in reducing the administration of opioid analgesics, and significantly increased FVC, positively influencing the cooperation of the patients with the physiotherapy treatment and improving the extent of chest and shoulder mobilization.<sup>61</sup> Since thoracotomy leads to shoulder functional limitations, with loss of shoulder mobility, strength, and pain, Reeve et al.<sup>24</sup> carried out a study in which all participants received an explanatory document about the importance of early mobilization and deambulation, changing position in bed regularly, as well as the importance of performing upper limb and breathing exercises. The intervention group was submitted to a daily physiotherapy program, including active-assisted shoulder mobilization. The program finished at hospital discharge, but patients were advised to continue the program by themselves. They also received a diary to record the exercises performed during the following three months. Patients were evaluated before surgery, on the day of hospital discharge, and one and three months after discharge. Pain, shoulder function, shoulder mobility and strength, and quality of life were evaluated. At hospital discharge the intervention group had substantially less pain, both at the shoulder and the chest. The same results were observed one month and three months after discharge. Shoulder function was also significantly better in this group, but with no significant differences in mobility, strength and quality of life. Oddly enough, this was the only article found that tested a shoulder treatment protocol after pulmonary resection.

## Postoperative and maintenance periods

After hospital discharge, patients still present dyspnoea, pain, fatigue, and changes in lung function, and they still are highly limited in their daily activities, with significant loss of their quality of life. Considering these issues, Cesario et al.<sup>62</sup> conducted a study with a physiotherapy program after-discharge. Unfortunately, this study loses strength in the evidence, since patients in the intervention group were enrolled by convenience, and therefore, the study was not a RCT. The intensive physiotherapy program lasted one month, five days/week, with session duration of 3 h. The program included a supervised incremental cycle ergometer exercise until the patient reach 30 min of continuous exercise at 70–80% of the load achieved in CPET at baseline. Exercises to strengthen the abdominal muscles, upper and lower limb training, inspiratory muscle training were included, as well as educational sessions on lung pathophysiology, pharmacology, nutrition, relaxation and stress management, principles of energy conservation, and breathing control. Since this program demanded a prolonged hospitalization of one month, it is interesting to note that only 25 out of the 211 eligible patients accepted to participate in the program, all of them being the ones with worse clinical status at baseline. The remaining 186 patients agreed to take part in the control group. Despite the better status of the control group at baseline, one month after hospital discharge there was an inversion in the condition of both groups, with the intervention group showing higher improvements in functional parameters in contrast to the impaired functionality observed in control group. Even with methodological limitations, it is clear that the physiotherapy program accelerated functional recovery, with improvement in dyspnoea and exercise tolerance, without compromising the adjuvant oncologic treatment.

After pulmonary resection patients are often submitted to additionally adjuvant therapies, such as chemotherapy and radiotherapy. Unfortunately, these therapies induce permanent changes in these patients. During the treatment period, fatigue is one of the most limiting factors and causes a significant negative impact on quality of life. It is not yet clear whether this symptomatology is directly related to the malignancy, to a side effect of these therapies, or if it arises from a combination of both.<sup>63</sup> Thus, like observations in other types of cancer/diseases with the same kind of limitations, such as COPD and heart failure, it is possible that an exercise training program applied to lung cancer patients might also be effective in controlling symptoms and improving work capacity.

Indeed, the application of an exercise program seems to have a positive impact on a wide variety of neoplasms, as described by McMillan et al.<sup>64</sup>, although lung cancer patients are not included in any of these studies. Regarding lung cancer, it might be expected that a positive impact of physical training on these patients would be seen because pulmonary surgical resection, in parallel with other factors, such as COPD and cardiac overload, tends to result in a decreased exercise tolerance. According to Nagamatsu et al.<sup>65</sup>, long-term recovery of lung function and exercise capacities seem to have different timings, because pulmonary function recovers faster as the pain gets progressively less severe. Lung

function seems to be regained in the first three months, while the recovery of exercise tolerance is slower, reaching a maximum after one year. Considering this subject, there are some doubtful results in literature presented by studies with several methodological flaws.<sup>66</sup> Nevertheless, there are studies supporting the beneficial effects of exercise training with robust methodology such as the one from Spruit et al.<sup>30</sup> These authors conducted a non-randomized pilot study of a multidisciplinary rehabilitation program of eight weeks in patients undergoing surgical treatment and complementary cancer therapy. The program was focused on general exercise training following the recommendations of the programs preconized for COPD patients.<sup>67</sup> All patients presented at baseline a restrictive lung function, with abnormalities in diffusion and exercise intolerance. After eight weeks, they showed no improvement in lung function, but in contrast showed significant improvements in exercise capacity. Worth noting are the late start of the exercise program, which was at least three months after completing intensive lung cancer treatment, and the absence of specific respiratory exercises on this training program. Consequently, improvements in the pulmonary function after such long time following surgery were not expected.

## Concluding remarks

Besides the need for physiotherapy programs based on evidence, there are only a few scientific studies which have enough quality to allow the definition of the best and feasible treatment strategies. Thus, to avoid methodological bias, allowing the strengthening of the evidence future experimental studies should be carefully designed, choosing the meaningful variables and controlling the potential bias. The available studies on the topic allow us to take several conclusions.

Physiotherapy programs should be individually designed regarding each phase and each subject's needs. The goals for lung cancer surgical subjects might be divided into four different phases according to the surgery timings: preoperative; perioperative; postoperative and maintenance.

In the preoperative period, the intervention should be targeted for healthy lifestyles advisement, respiratory expansion, and bronchial hygiene. IMT seems to be an interesting part of the program, not only in this phase but also in the perioperative phase to reduce PPCs and LOS. According to ERS/ESTS,<sup>7</sup> preoperative training programs reduced hospital stay and complications in COPD subjects with lung cancer. Exercise training seems to be an important tool to improve cardiopulmonary fitness and even to include candidates with poor  $VO_{2max}$ .<sup>7,47</sup>

In the perioperative phase, the main goals are to avoid PPC and reduce the LOS, through maximal inspiratory manoeuvres, coughing and mobilization exercises of the upper and lower limbs under supervision, and also to improve postural changes and shoulder impairment.<sup>24,52,53</sup>

In the postoperative phase, physiotherapy aims to make the transition between the perioperative and the maintenance phases, because as soon as the pain is reduced, the pulmonary function also recovers, but the exercise capacity takes longer to improve, and some patients still have to be submitted to co-adjuvant therapies, corroborating one of

the most limiting symptoms, the fatigue that reduces quality of life. But it is also true that exercise capacity has more potential to improve than pulmonary function. For that reason, it may be interesting to encourage and promote participation in exercise training programs after the adjuvant therapies, although there is a need for more powerful studies.

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## Authors' contribution

All authors have contributed for the conception of the problem, theorizing, and/or interpreting data as well as for drafting the article or revising it critically, approving the final version.

## Conflicts of interest

The authors have no conflicts of interest to declare.

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