



The effects of respiratory physiotherapy after lung resection: Protocol for a systematic review



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ABSTRACT

Background: The main treatment of lung cancer (stage 1 and 2) is lung resection surgery. The risk of postoperative pulmonary complications is high and therefore standard postoperative care involves respiratory physiotherapy. The purpose of this systematic review is to create an overview of the evidence on respiratory physiotherapy after lung resection surgery on mortality rate (within 30 days) and postoperative pulmonary complications.

Methods and analysis: The review will include randomized or quasi-randomized controlled studies investigating the effect of all types of respiratory physiotherapy on mortality and postoperative pulmonary complications after lung resection surgery. Furthermore, the effect of respiratory physiotherapy is evaluated on secondary outcomes such as length of hospital stay, lung volumes and function, and adverse events. The method of the planned review is described in this paper. The literature search will include the databases PubMed, Cochrane (Central), Embase, Cinahl and PEDro. The literature search is being performed in 2017. If meta-analyses are not undertaken, a narrative synthesis of the available data will be provided. The protocol was registered in PROSPERO on the 10th of October 2016 (registration number CRD42016048956).

Ethics and dissemination: Conclusion of this systematic review is expected available in the second half of 2017.

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1. Background

1.1. Description of the condition

Lung resection surgery is the primary treatment for patients at stage I and II lung cancer [1]. Despite an increasing survival rate for lung cancer, it is still the leading cause of cancer death and the main reason for performing lung resection surgery [2]. Cigarette smoking remains the predominant risk factor for lung cancer, and it is estimated that as much as 90% of the disease is related to the use of tobacco [1,3]. Data on patient demographics show that lung resection surgery is performed almost equally on men and women, and that the median age is 63 years. Roughly a fourth of the population are diagnosed with chronic obstructive

pulmonary disease (COPD) and, dependent on the type of surgery, 24–32% had hypertension and 5–10% had coronary artery disease [4,5]. Regarding patients undergoing lobectomy, preoperative chemotherapy or radiation therapy was provided for 8.5% and 2.3%, respectively [4]. In 2014 878 patients underwent lung surgery at Danish hospitals. Of these, 80% were lobectomy, 12% wedge resection, 4% pneumonectomy, 3% segment resection, and 1% explorative surgery. The thoracic procedures were in 60% of the cases performed by video-assisted surgery (VATS). Overall, the median length of hospital stay (LOS) was 4 days (with maximum LOS of 59 days) [5].

Lung resection surgery reduces health-related quality of life for months, in particular physical functioning, and one of the major concerns for patients is the possibility to resume an acceptable lifestyle [6]. Lung surgery involves a high risk of sustaining postoperative pulmonary complications (PPC) that may impair patient recovery [7–9]. PPC imply considerable economical and patient related consequences, as PPC are associated with increased LOS,

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intensive care unit admission, and increased mortality [10]. The incidence rate of PPC differs from 14.5%–37%. The difference in rate of incidence is primarily caused by variation in definition criteria of PPC [7,8,10]. Additionally, factors such as extended resection, type of lung resection, preoperative chemotherapy and comorbidity (e.g. COPD, peripheral vascular disease, and coronary artery disease) are associated with increased risk of PPC [11]. PPC include, i.a., significant hypoxia and atelectasis, pneumonia, exacerbation of COPD, various types of upper airway obstruction, pulmonary edema, and tracheal re-intubation [10,12]. Physiologically, pulmonary complications can lead to reduced lung volumes and subsequent low oxygenation [13]. Retained pulmonary secretion and physically compression of lung tissue during surgery are often the cause of atelectasis [14]. Furthermore, the risk of developing pneumonia, which may cause purulent secretion and hypoxia, is higher in patients undergoing lung resection surgery because the normal defense mechanism of the lungs is compromised [10,14]. This is due to a higher occurrence of atelectasis, pain-related depression of the cough mechanism, and direct passage for microorganisms to lower airways through the endotracheal tube [14]. The incidence of postoperative pneumonia varies depending on risk factors ranging from 1.5% to as high as 15.3% [10]. When considering the source of infection and preventive strategies it is important to distinguish between community-acquired pneumonia and hospital-acquired (≥ 48 h post-hospital admission) or ventilator-acquired pneumonia (>48 – 72 h post-intubation) [10]. The distinction between the types of pneumonia is likewise relevant to take into account when deciding the optimal time of outcome measurement when examining the effect of preventive strategies [10].

1.2. Description of the intervention

Respiratory physiotherapy is an important adjuvant in fast-track regimen following lung resection surgery because respiratory care, as well as pain control and supplemental oxygen requirement, are factors that reduce PPC, limit LOS, and improve patient outcomes [9,15,16]. The central aim for respiratory physiotherapy is to optimize ventilation and clear airway secretions in order to improve gas exchange and make breathing easier. Respiratory physiotherapy covers many different treatment techniques and the utilization of these techniques varies to a great extent [17,18]. Ambulation and frequent position change (position change in bed and sitting out of bed) are central parts of postoperative recovery programs and are both considered an interdisciplinary teamwork responsibility and an important aspect of respiratory physiotherapy [15,17]. Respiratory physiotherapy also comprises techniques that promote increasing lung volumes such as deep breathing exercises with or without devices (e.g. incentive spirometry), positive expiratory pressure breathing (PEP), intermittent positive pressure breathing, or continuous positive airway pressure breathing (CPAP) [19,20]. Other techniques focus on airway clearance; postural drainage, percussion, vibration and shaking, active circle of breathing techniques including forced expiration, high-frequency chest wall oscillation, intrapulmonary percussive ventilation, huffing, and coughing [21]. Furthermore, some physiotherapists use different exercises for the upper extremities, soft-tissue release techniques to lengthen individual tight muscles, or osteopathic manipulative treatments to enhance thorax mobility (e.g. bilateral rib rising, myofascial release of diaphragm or restrictive connective tissue) [22].

1.3. How the intervention might work

Ambulation, position change and breathing techniques may improve respiratory function postoperatively by increasing func-

tional residual capacity (FRC) and ventilation, and by minimizing closing volumes [20]. The change in breathing pattern caused by positive expiratory pressure has been shown to decrease expiratory flow and increase expiratory time which leads to a smaller exhaled volume and an increase in FRC [20]. Also, the increased positive pressure during breathing is believed to reinflate collapsed alveoli by allowing air to be redistributed through collateral channels, allowing pressure to build up distal to the obstruction, and by promoting the movement of pulmonary secretions towards larger airways [21]. Some airway clearance techniques include different types of vibration which is believed to decrease collapsibility of the airways and to promote loosening pulmonary secretions [21]. Exercises for the upper extremities and thorax mobility techniques are believed to enable a more freely chest wall excursion necessary for a normal breathing pattern and thereby improving oxygenation [22].

To our knowledge, the only review investigating the effect of respiratory physiotherapy on PPC and mortality after lung resection so far was conducted by Varela et al. (2011). The authors conclusion was unclear due to a lack of well designed clinical trials [23]. The review, however, did not include descriptions of a systematic method and search strategy, why it is uncertain if all relevant literature was identified. Furthermore, new studies on the subject may have been published since then. A systematic review from 2014 concluded that CPAP initiated during the postoperative period following major abdominal surgery might reduce postoperative atelectasis, pneumonia and re-intubation but its effect on mortality, hypoxia and invasive ventilation were uncertain [12]. Another systematic review from 2010 investigating the effect of PEP after abdominal and thoracic surgery showed uncertain effect of the treatment [24]. These systematic reviews also included patients undergoing abdominal and cardiac surgery, respectively, which could influence the outcome of respiratory physiotherapy on PPC and mortality. Overall, we find it relevant to conduct a systematic review concerning only patients undergoing lung surgery.

1.4. Why is it important to do this review?

Lung surgery is frequently associated with PPC and hence, substantial resources are spent on respiratory physiotherapy in order to prevent PPC and thereby reduce mortality and enhance health-related quality of life by facilitating patient recovery [9]. Accordingly, it is relevant to compose a better overview of the literature investigating the effect of respiratory physiotherapy specifically following lung surgery in order to evaluate whether we should continue using respiratory physiotherapy for this group of patients [17]. If possible, we will evaluate different types of respiratory physiotherapy and the effect on different risk groups of PPC.

2. Objectives

The objective is to investigate the effects of respiratory physiotherapy after lung resection surgery on mortality rate (within 30 days) and postoperative pulmonary complications.

3. Methods

PRISMA guidelines will be followed in this review [25].

3.1. Criteria for considering studies for this review

3.1.1. Types of studies

The review will include randomised and quasi-randomised controlled trials only.

Table 1
Literature search strategy for PubMed.

AND			
	Population	Intervention	Study design ^a
OR	Pulmonary surgical procedure [mh] [tiab] (p) Thoracotomy [tiab] (p) Thoracic surgery [mh] [tiab] (p) Video-assisted thoracic surgery [mh] [tiab] (p) Video-assisted thoracoscopic surgery [tiab] (p) Lung surgery [tiab] (p) Lung resectional surgery [tiab] (p) Lung resection [tiab] (p) Lung volume reduction surgery [tiab] (p) Lobectomy [tiab] (p)	Respiratory physiotherapy [tiab] Respiratory physical therapy [tiab] Chest physiotherapy [tiab] Chest physical therapy [tiab] Lung physiotherapy [tiab] Lung physical therapy [tiab] Continuous positive airway pressure [mh] [tiab] Noninvasive ventilation [mh] [tiab] Bilevel positive airway pressure [tiab] Biphasic positive airway pressure [tiab] Positive expiratory pressure [tiab] Intermittent positive pressure breathing [mh] [tiab] Inspiratory muscle training [tiab] Airway clearance technique [tiab] (p) Breathing exercises [mh] [tiab] (p) Incentive spirometry [tiab] Sustained maximal inspiration [tiab] Postural drainage [tiab] Autogenic drainage [tiab] Bronchial drainage [tiab] Bronchial hygiene [tiab] ELTGOL [tiab] Forced expiratory technique [tiab] (p) Early ambulation [mh] [tiab] Early mobilization [tiab]	Randomized controlled trial [pt] Controlled clinical trial [pt] Randomized [tiab] Randomised [tiab] Placebo [tiab] Randomly [tiab] Trial [tiab] Groups [tiab] Control group [tiab] NOT Animals [mh] not (humans [mh] and animals [mh])

AND, OR, NOT = boolean operators.

[mh] = MeSH term.

[sh] = MeSH subheading.

[tiab] = title and abstract.

[pt] = publication type.

(p) = term searched both in single and plural.

^a Reference: Cochrane Highly Sensitive Search Strategy for identifying randomised trials. Available from: Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. Cochrane Handbook for Systematic Reviews of Interventions. Higgins, HPT; Green, S ed. Chichester (UK): John Wiley & Sons; 2008. p. 96–149.

3.1.2. Types of participants

The review will include all adults (18 years of age and older) who receive respiratory physiotherapy after lung resection surgery by open thoracotomy or VATS. Patients who received heart or esophagus surgery or lung transplantation will be excluded. Studies addressing all thoracic surgeries will be included if data provided for lung resection are reported separately.

3.1.3. Types of intervention

The intervention is any type of respiratory physiotherapy that is applied in the postoperative period, for example deep breathing exercises with or without devices (e.g. incentive spirometry), positive expiratory pressure breathing (PEP), intermittent positive pressure breathing, continuous positive airway pressure breathing (CPAP), postural drainage, percussion, vibration and shaking, active circle of breathing techniques including forced expiration, high-frequency chest wall oscillation, intrapulmonary percussive ventilation, huffing, coughing, and exercises for the upper extremities.

The comparison may be standard care (defined by the individual studies), sham treatment, or no treatment.

3.1.4. Types of outcome measures

Primary outcomes

1. Mortality (within 30 days)
2. Postoperative pulmonary complications (as defined in the individual studies)

Secondary outcomes

1. Length of stay in hospital (days)
2. Lung volumes and function (FVC, FEV¹)
3. Adverse events (any undesired outcome due to the intervention)

Pulmonary secretion is not included as an outcome measure, because it can be interpreted as both a positive (successfully airway clearance) and a negative outcome (severe infection with increased pulmonary secretion). Furthermore, it is very difficult to measure the amount of pulmonary secretion [21].

3.2. Search methods for identification of studies

3.2.1. Bibliographic databases

The search for literature will include Cochrane Central Register of Trials (CENTRAL), PubMed, EMBASE, Cinahl and the Physiotherapy Evidence Database (PEDro). No language or date limits will be used.

We will search trial registers (ClinicalTrials.gov and ISRCTN registry) for ongoing and completed but unpublished randomised controlled trials.

The following search strategy (Table 1) will be used to search PubMed and is reviewed by a health information specialist. This search strategy includes a search strategy for randomized controlled trials constructed and validated by Cochrane [26]. The search strategy will be adapted to search in the above mentioned databases.

3.2.2. Searching other resources

We will consult the reference lists of relevant articles found by searches for additional studies as described in Section 3.2.1.

3.3. Data collection and analysis

3.3.1. Selection of studies

The first selection of studies will be performed by three review authors (KSA, BS and AKP) based on titles and abstracts. Studies

considered potentially relevant by any of the authors are read independently in full text in order to determine the eligibility for this review. Disagreements between reviewers will be discussed and a majority vote used to make a final decision.

The reference management software Refworks is chosen for managing the records retrieved from searches of electronic databases.

3.3.2. Data extraction and management

Three review authors will independently extract data using a standard data collection form and will resolve any disagreements by discussion and consensus. As recommended by the *Cochrane Handbook for Systematic Reviews of Interventions* the standard data collection form will include the following information [27]:

- 1) Methodological details (including design, method of randomisation, total number of withdrawals, and dropouts).
- 2) Description of participants (total sample, age, gender, type of surgery, country, setting, trial inclusion, and exclusion criteria)
- 3) Description of intervention (details of respiratory physiotherapy and comparison, including type, frequency, intensity, and timing)
- 4) Description of outcomes (including type of measurements, baseline measures, and time of follow-up)

Before the beginning of this process the standard data collection form will be tested by the participating authors to ensure comparability of the extracted data. Articles in a language other than English will be examined along with an interpreter. The lead author (KSA) will enter the data into RevMan. Multiple reports of the same study will be collated and considered as one study.

3.3.3. Assessment of risk of bias in included studies

The Cochrane tool for risk of bias (RoB) will be used and the following domains will be considered:

- 1) Random sequence generation
- 2) Allocation concealment
- 3) Blinding of participants and personnel
- 4) Blinding of outcome assessment
- 5) Incomplete outcome data
- 6) Selective reporting
- 7) Other bias

The study will be classified as low risk of bias if all these domains are considered adequate. The study will be classified as high risk of bias if one or more of these domains are inadequate and plausible biases seriously weakens confidence in the results. If one or more of these domains are considered unclear and plausible biases raise some doubt about the results the study will be evaluated as unclear risk of bias [28].

3.3.4. Measures of treatment effect

In case of dichotomous outcomes the treatment effect will be measured as risk ratios (RR) using 95% confidence intervals (CIs). Continuous outcomes will be measured as mean differences (MDs) with 95% CIs or as standardized mean differences (SMDs) if different methods of measurements are used in the studies.

3.3.5. Unit of analysis issues

Studies with multiple intervention groups will be included in the meta-analysis by treating each intervention group as a separate study and by dividing the control group out on each of the intervention groups.

3.3.6. Dealing with missing data

We will contact trial authors in order to request additional information and obtain missing data. Assumptions will be made on whether missing data in the included studies are random and whether the authors have dealt with missing data appropriately. Sensitivity analysis will be performed to assess how sensitive results are to changes. The potential impact of missing data on the results will be addressed in the discussion section of the review [29].

3.3.7. Assessment of heterogeneity

The data will be assessed in aspects of clinical, methodological and statistical heterogeneity. Clinical heterogeneity will be evaluated by the degree of differences of intervention or patient characteristics. Methodological heterogeneity will be evaluated by the variation in risk of bias.

The Quantity of statistical heterogeneity will be evaluated by I^2 statistic with the thresholds:

- 0%–40%: might not be important
- 30%–60%: may represent moderate heterogeneity
- 50%–90%: may represent substantial heterogeneity
- 75%–100%: considerable heterogeneity

3.3.8. Assessment of reporting biases

Funnel plot will be used to assess potential reporting bias if the number of studies is sufficient (>10 studies). Furthermore, the Clinical Trial Register at the International Clinical Trials Registry Platform of the World Health Organization will be screened for published studies. If available, the trial protocol will be compared to the published report in order to evaluate outcome reporting bias in the individual study.

3.3.9. Data synthesis

The software RevMan 5.3 will be used to combine the results in a meta-analysis if considered possible. The fixed-effect model will be used if data are considered homogeneous. Presumably, we will use the random-effects model to summarize the results due to expected clinical and methodological heterogeneity or if the I^2 statistic is >50%. If meta-analyses are not undertaken, a narrative synthesis of the available data will be provided in text and tables to summarize characteristics and findings of the included studies. The narrative synthesis will consider the questions: What is the direction of the effect? What is the size of the effect? Is the effect consistent across studies? What is the strength of evidence for the effect?

3.3.10. Subgroup analysis and investigation of heterogeneity

The plan is to conduct the following subgroup analyses:

1. Techniques (breathing exercises with or without device, positive pressure breathing exercises, osteopathic, or other manual techniques)
2. Low versus high risk population

3.3.11. Sensitivity analysis

If sufficient data, sensitivity analyses will be carried out on the following:

1. Study quality (high risk of bias versus low risk of bias)
2. Missing data (observed and imputed data versus observed data only)
3. Study size (stratified by sample size)
4. Allocation concealment (high risk of bias versus low risk of bias)
5. Assessor blinding (high risk of bias versus low risk of bias)

6. Characteristics of the comparator care (large differences in usual care, small difference in treatment between control and intervention)
7. Characteristics of the intervention (range of dose and timing)

Potential conflict of interest

There are no conflicts of interest for the authors conducting this review.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.isjp.2017.03.001>.

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