COMPLICAÇÕES RESPIRATÓRIAS NO PÓS-OPERATÓRIO E ESTRATÉGIAS PARA A SUA PREVENÇÃO NO PERÍODO PERIOPERATÓRIO: UMA REVISÃO

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Palavras-chave:
- Anestesia;
- Avaliação de Resultados;
- Complicações Pós-Operatórias / prevenção e controlo;
- Doenças do Pulmão/prevenção e controlo;
- Fatores de Risco;
- Período Perioperatório

Resumo

Introdução: As complicações respiratórias pós-operatórias são as complicações mais frequentes após cirurgia torácica ou abdominal superior, desempenhando um papel determinante no risco dos doentes submetidos a cirurgia não-cardiotorácica. Estas complicações, definidas como qualquer alteração pulmonar que ocorra no período pós-operatório e que resulte em efeitos adversos, são tão prevalentes como as complicações cardíacas, contribuindo de forma semelhante para eventos adversos. Tendo em conta o significativo impacto clínico e económico das complicações respiratórias pós-operatórias, a sua prevenção e tratamento são aspetos da maior relevância para os profissionais de saúde.

Objetivo: Com este artigo, pretende-se rever a literatura mais recente relativamente às complicações respiratórias pós-operatórias, com destaque para a sua fisiopatologia e estratégias para a sua prevenção.

Material e Métodos: Esta revisão foi efetuada com recurso à base de dados PubMed, focando-se na literatura dos últimos 5 anos acerca deste tema.

Resultados: Têm sido utilizadas diversas estratégias de prevenção de complicações respiratórias pós-operatórias, com graus variáveis de sucesso. Entre estas incluem-se intervenções pré-operatórias, intra-operatórias e pós-operatórias, algumas delas bastante simples e pouco dispendiosas. Os estudos mais recentes sugerem que a estratégia mais eficaz será uma abordagem combinada, incluindo uma avaliação e educação pré-operatórias, uma prática anestésica baseada na evidência, o recurso a procedimentos minimamente invasivos, a implementação de uma analgesia eficaz e a instituição de alimentação e deambulação precoces.

Conclusões: Atendendo ao seu enorme impacto nos desfechos pós-operatórios, na morbilidade, mortalidade e consumo de recursos de saúde, as complicações respiratórias pós-operatórias são definitivamente uma área onde são necessárias medidas de prevenção eficazes. Este tipo de abordagem combinada parece ser uma área interessante para pesquisas futuras, com grande potencial em termos de melhoria dos cuidados prestados aos doentes e de otimização dos sistemas de saúde.

POSTOPERATIVE PULMONARY COMPLICATIONS AND STRATEGIES TO PREVENT THEM IN THE PERIOPERATIVE PERIOD: A REVIEW

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Keywords:
- *Anesthesia;*
- *Lung Diseases / prevention and control;*
- *Patient Outcome Assessment;*
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- *Risk Factors*

Abstract

Background: *Postoperative respiratory complications are the most frequent postoperative complications following thoracic and upper abdominal surgery, playing an important role in the risk for patients undergoing noncardiothoracic surgery. These complications, defined as any pulmonary abnormality occurring in the postoperative period that adversely influences outcomes after surgery, are as prevalent as cardiac complications and contribute similarly to adverse outcomes. Given the high clinical and economical impact of postoperative pulmonary complications, prevention and treatment are issues of major importance for the healthcare team. In this study, we aim to review the most recent literature about postoperative pulmonary complications, focusing on their pathophysiology and suggesting perioperative strategies to prevent them.*

Material and Methods: *This review was performed using the PubMed database, focusing on the literature of the last 5 years.*

Results: *As far as postoperative respiratory complications are concerned, several strategies of prevention have been used in the last years, with varying degrees of success. These include preoperative, intraoperative and postoperative interventions, some of them really simple and inexpensive. Recent studies suggest that the most effective strategy may be a combined approach, including preoperative assessment and education, evidence based practice in anesthesia, minimally invasive procedures, effective analgesia and early feeding and ambulation.*

Conclusions: *Due to its enormous impact on postoperative outcomes, morbidity, mortality and healthcare resources consumption, postoperative respiratory complications are definitely an issue where efficient prevention is needed and must be implemented. This kind of combined approach seems an interesting area for future research, with a great potential of improving patient care and helping healthcare systems.*

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INTRODUCTION

Postoperative respiratory complications (PRC) are common events,[1] with recent reports stating that they occur in 5% to 10% of surgical patients[2] depending on the hospital and on the procedure,[3] and are the most frequent postoperative complications following thoracic and upper abdominal surgery.[4] They are also responsible for an increased hospital length of stay and hospital readmission rate within the first 30 postoperative days, being the main source of postoperative morbidity and mortality[5] and thereby significantly increasing the consumption of healthcare resources.[6] In fact, PRC may have an impact on outcomes following surgery as great as that resulting from cardiac or other postoperative complications[7] and increase the average costs of an elective surgery, increasing the length of stay and the rate of admissions to Intensive Care Units (ICU),[8] even after adjusting for different patient characteristics.[1]

PRC are defined as any pulmonary abnormality occurring in the postoperative period,[9] adversely influencing outcomes after surgery. They can range from self-limited alterations in respiratory function, such as mild atelectasis or bronchospasm, to severe conditions associated with increased morbidity and mortality, such as severe atelectasis, postoperative pneumonia or acute respiratory failure (ARF).[1] As a group, they include atelectasis, bronchospasm, bronchitis, pneumonia, exacerbation of chronic obstructive pulmonary disease (COPD), pulmonary edema, acute lung injury (ALI), ARF and various forms of upper airway obstruction,[3] among others.[10] Several different complications can be present in the same patient,[11] but atelectasis are the most common PRC, and pneumonia and ARF are the main responsibles for the increased mortality.[11,12]

Given the high clinical and economical impact of PRC, prevention and treatment are issues of major importance for the healthcare team.[4] Fortunately, with a careful history and physical examination, many PRC can be anticipated and potentially prevented.[13,14] This is even more important as surgery is now being offered to patients at an increasingly higher risk, such as the elderly or those with comorbidities,[15] who need specific preoperative strategies to reduce the associated risk, as well as an appropriate surgical and anesthetic management.[10,16,17]

In the present manuscript, we aim to review the most recent literature about PRC, focusing on understanding their pathophysiology and suggesting perioperative strategies to prevent them.

MATERIAL AND METHODS

Search strategy

This review was performed during the last months of 2014 and focused on the literature of the last 5 years. The Pubmed database was searched using the following keywords: "postoperative complications", "respiratory", "pulmonary", "acute lung injury", "aspiration pneumonitis", "pneumothorax", "pneumonia", "bronchospasm", "pulmonary edema", "atelectasis", "respiratory failure", "prevention", "risk factors" and "ventilation". The final query can be found in the appendices (appendix **1)**. All references were also reviewed for completion of the research.

Exclusion and inclusion criteria

We included studies published during the last five years (from 01/01/2010 to 31/10/2014), in English or in Portuguese, and involving humans. Clinical Trials, reviews and systematic reviews were included. Studies about postoperative complications after a very specific type of surgery (for example pancreatoduodenectomy) were also excluded.

Selection strategy

Our search yeald a total of 657 articles. The first selection was performed by screening the titles, taking into account our exclusion criteria, and 470 articles were excluded. Then we conducted a second selection by reading the sumaries of the remaining articles. Forty one papers were excluded in this phase. From the remaining 146 articles, 61 papers were excluded after careful reading. Forty-eight articles were included after careful revision of the references of selected literature. Appendix 2 ilustrates the process of screening and selection of the information.

PATHOPHYSIOLOGY OF POSTOPERATIVE RESPIRATORY COMPLICATIONS

PRC are multifactorial events, with varying contributions from several factors:

• **General anesthesia**[1]**:** Almost all anesthetics (with the exception of ketamine) lead to a decrease in functional residual capacity (FRC), due to the loss of muscle tone in the chest wall with subsequent reduction in chest and lung volume,[18] anesthesia also leads to a decrease in lung compliance and an increase in airway resistance secondary to the decrease in lung volume.[19] Moreover, anesthetics, analgesics and other perioperative drugs[4] also have effects on the central regulation of breathing, changing the neural drive of the upper airway and chest wall muscles, thereby further increasing the risk of PRC. The immunosuppressive effects of anesthesia and intraoperative blood transfusion may also contribute to these poor outcomes.[13]

• **Respiratory muscle dysfunction:** There are two types of muscles involved in respiration: upper airway dilators (counterbalance the negative inspiratory pressure during inspiration in order to permit airflow) and respiratory pump muscles (responsible for generating inspiratory and expiratory forces in the thorax). Respiratory muscle dysfunction[9] is an important determinant in the development of postoperative respiratory failure and can result from several causes:[20] factors related to surgery[4,13] (displacement of the diaphragm to a more cephalic position,[1] functional disruption of respiratory muscle movements due to incisions, limitation of respiratory moviments due to pain or reflex inhibition of the phrenic and other nerves that innervate respiratory muscles due to stimulation of viscera[13,18,20]), impaired respiratory arousal (because of sedation, certain anesthetics, opioids, REM sleep rebound and endogenous impairment of consciousness), postoperative residual curarization (with increased risk of colapse of upper airway dilators), systemic inflammation, mechanical ventilation[21] and patient related factors [age,[22] obesity, obstrutive sleep apnea (OSA), obstructive respiratory pathology and smoking]. This dysfunction leads to a difficulty in increasing postoperative lung volumes.[18]

• **Postoperative pain:** Postoperative pain also contributes to PRC[4,13,22] due to its effects in impairing lung expansion[9] and in difficulting increases in lung volumes.[18]

• **Decreased lung and chestwall compliance**[1,23]

All these factors lead to a reduction in FRC and total lung capacity, with a resultant restrictive syndrome,[24] failure of the cough mechanisms[25] and ventilation-perfusion mismatch.[1,9] This leads to shunt, dead space, hypoxemia[13,19,25,26] and atelectasis,[19,27] with subsequent increased risk of other PRC.

COMMON POSTOPERATIVE RESPIRATORY COMPLICATIONS

Atelectasis

Atelectasis are the most common PRC,[11] occuring in more than 90% of anesthetized patients immediately after induction,[28] during either spontaneous breathing or positive pressure ventilation,[27] and are predominantly located in dependent lungs (aproximately 15-20% of the parenquima).[1,9,28,29] Three mechanisms contribute to the generation of atelectasis: compression of lung tissue[30] (due to supine positioning[4,18] and surgical material[31]), absorption of alveolar air,[30] and impairment of surfactant function.[13] In many instances atelectasis do not have a great clinical impact, as they may be transient and self-resolving; however, they cannot be ignored due to its associated increased work of breathing[30] and therefore increased risk of PRC.[9,15,18,25,27,30,32] This risk can be even higher if several perioperative factors are presente, such as excessive fluids, transfusion-related acute lung injury, inflammation, sepsis, and aspiration.[26]

Hypoxemia

Hypoxemia is a common intra and postoperative finding, and one of the most feared events in these settings,[33] with a reported incidence of 19% in the post anesthesia care unit (PACU).[34] In fact, it is the major problem associated with intraoperative atelectasis and consequent V/Q mismatch;[30] other contributing factors include hypoventilation due to pain or residual anesthetics, lung edema due to fluid overload, exacerbation of chronic obstructive pulmonary disease, laryngospasm or bronchospasm. This condition can have a serious impact on outcome, as it can be responsible for complications in other systems beside the respiratory.[27]

Pneumonia

Pneumonia is effectively one of the most frequent PRC, responsible for the highest morbidity and mortality rates,[3] along with ARF.[12] Pneumonia occurs when bacteria reach the lower respiratory tract, which should be sterile. This colonization is facilitated not only by impaired host defenses secondary to anesthesia-induced respiratory changes but also by the presence of invasive devices, medications altering gastric emptying and pH, contaminated water and respiratory therapy equipment.[3] Postoperative pneumonia can be further classified in hospital-acquired or ventilator-associated.[3,27] Once it is diagnosed, empirical therapy should be readily instituted while awayting results from cultures, and possible resistant agents should be adequately covered. When these results are available, therapy can be tailored to the agent in an effort to avoid excessive medication.[3]

Acute respiratory failure

Postoperative ARF is commonly defined as failure to wean from mechanical ventilation within 48 hours of surgery or unplanned reintubation in the postoperative period, and is significantly associated with increased 30-day mortality after surgery.[35] The severity of this condition can range from transient hypoxemia in the early postoperative period to the life-threatening acute respiratory disease syndrome (ARDS). Thus, it can be classified based on the PaO_2/FiO_2 relationship (partial pressure of oxygen in arterial blood divided by the fraction of inspired oxygen) as mild ($PaO_2/FiO_2 < 300$ mmHg but >200 mmHg), moderate (PaO_2/FiO_2 < 200 mmHg but > 100 mmHg), or severe (PaO_2/FiO_2 < 100 mmHg).[12] ARF in the postoperative setting can be caused by failure to oxygenate (hypoxemic respiratory failure, type 1) or failure to ventilate (hypercapnic respiratory failure, type 2). Hypoxemic respiratory failure is more common and occurs when there is a problem at the pulmonary capillary/alveolar interface, usually associated with fluid filling or colapse of alveolar units. Hypercapnic respiratory failure can be due to a central loss of ventilation, decreased activity of the diaphragm or accessory muscle after mechanical injury to the chest, or obesity.[3] In this setting, ARF occurs usually as a consequence of several other PRC such as large atelectasis, pneumonia, ARDS and diaphragmatic paralysis.[18,26]

Ventilator-associated lung injury

Postoperatively ventilator-associated lung injury (VALI) leads to local and systemic adverse effects[36] and may present as ALI or ARDS.[27] These pathophysiological changes occur from the direct effect of high pressure on the lung (barotrauma), damage caused by lung overdistension (volutrauma) and the shear stress of repetitive opening and closing of alveoli (atelectotrauma).[36,37] All these factors lead to the release of proinflammatory mediators with activation of circulating neutrophils that alter endovascular permeability.[27,36,38]

If a PRC is suspected, arterial blood gas assessment, sputum culture, chest x-rays and an electrocardiogram should be ordered. Aggressive treatment should readily be instituted, including the combination of antibiotics, physical therapy and ventilatory support.[13]

PREVENTION OF POSTOPERATIVE RESPIRATORY COMPLICATIONS

Taking into account the high impact of PRC on morbidity, mortality and economics, it is essential to implement all the possible measures to prevent them. In recent years, the management of the surgical patient has changed and a multi-modal effort to enhance postoperative recovery has been adopted, combining the preoperative preparation, intraoperative period and postoperative care.[39] Reduction of the incidence of PRC will require a multifaceted approach involving many clinical disciplines operating at different moments.[1]

1. Preoperative interventions:

a) Identifying patients with a higher risk of PRC

In the preoperative period, the first strategy to prevent PRC should be stratifying the individual risk of the patient, to allow a correct allocation of resources and treatment.[40] A detailed clinical history (with focus on preexisting respiratory diseases, smoking, respiratory symptoms and medications) and a physical examination seem to be the best strategies to predict the risk of PRC [13]. Spirometry findings do not correlate well with the risk of PRC in individual patients, so it is not routinely recommended and should be used only in specific settings.[14] The same is true for cough tests.[13]. Pulmonary function tests are also not useful as a general screening tests to assess risk the of PRC,[17] being important only in patients undergoing lung resection surgery.[13,14] Currently, evidence suggests that chest radiograph only rarely provides new information that influences preoperative management, and therefore it should not be routinely ordered.[13,14]

Therefore, the identification of patients at an higher risk of PRC remains largely dependent on the presence of certain risk factors, which permit a quick assessment and subsequent planning of the possible optimization.[3]

***Patient factors:** Advanced age,[4,18,31,41] obesity,[18,31,41] lung disease,[4,13,18,31,41-44] smoking history (as it leads to reduced lung capacity, increased inflammation, reduced mucus and reduced ciliary function),[4,6,18,41] congestive heart failure,[4,13] OSA,[4,42,45] obesity-hypoventilation syndrome,[42] functional dependence,[4] renal insufficiency (due to impaired excretion of anesthetic agents with a subsequent longer duration of action) and hypoalbuminemia (a marker of poor metabolic reserve)[44] may all be associated with an increased risk of PRC. Preoperative smokers, in particular, can have up to 2.5 times the risk of developing PRC when compared to nonsmokers, along with a significantly increased risk of admission to an ICU.[46]

***Surgery:** Type of surgery (higher risk for open and agressive procedures such as thoracoabdominal surgery,[4,13,18,22,44,47] and non-midline incisions;[40] in general, risk increases with increases in the proximity to the diaphragm[48]), duration of the procedure,[4,13,31,44] emergency cases[44] and situations associated with great blood losses[13] may also increase the risk of PRC.

***Anesthesia:** Neuromuscular blockers (particularly long acting[22,49] and aminosteroid derivatives[44]) are known to increase the risk of PRC, as well as an higher ASA physical status (III or more),[4,41,44]. Moreover, a recent study has sugested a higher impairment on postoperative respiratory function from total intravenous anesthesia when compared to balanced anesthesia with sevoflurane.[50]

A study from Canet ***et al***[51] included 2464 patients and identified seven independent predictors of PRC: Age (particularly if older than 80 years), low preoperative SpO_2, preoperative anemia, acute respiratory infection in the previous month, intrathoracic or upper abdominal surgery, longer duration of procedure, and emergency surgery. With these seven variables, the authors developed a score to assess the PRC risk of an individual patient. Alcohol intake, snoring, obesity, diabetes, immunosuppression, intraoperative fluid therapy, and postoperative pain did not show any correlation with PRC in this study. In a recent study from Brueckmann *et al*,[52] the authors investigated risk factors for PRC and developed a 11 point score to predict severe PRC with need of reintubation. The variables used in this score are ASA class (3 points if ≥

III), need for emergency surgery (3 points), staying in a high-risk surgical service (2 points), history of congestive heart failure (2 points) and chronic pulmonary disease (1 point).

These models may be useful in assessing which patients are at a higher risk of PRC, so that they can be adequately informed and specific preventive strategies can be implemented, including modifying or postponning the procedure if necessary.

Finally, a recent review from Canet J and Gallart L[5] on prediction of PRC in the general population ilustrated the miriad of possible risk factors, suggesting that several ones may be important although they are not included in the American College of Physicians guidelines.

Specific risk calculators:

In the specific setting of postoperative pneumonia, a recent retrospective study[7] developed a risk calculator for this outcome based on seven risk factors: dependent functional status, age, ASA class, COPD, preoperative sepsis, smoking history within 1 year before operation, and type of surgery. Although some of these risk factores are not modifiable, there are some in which it is possible to intervene, for exemple by advising smoking cessation, optimizing COPD patients and lowering ASA class if possible.[7,13] The same is true for postoperative ARF, for which Gupta *et al* [35] developed a risk calculator based on several preoperative variables: ASA physical status classification, dependent functional status, emergency procedure, preoperative sepsis, and type of surgery (brain, foregut/hepatopancreatobiliary and aortic surgeries associated with the highest risk).

b) General measures

Several easy strategies can be adopted in the preoperative period in order to reduce the risk of PRC. Smoking cessation is a well documented way of preventing not only PRC but also other types of postoperative complications,[14,46,48] showing more benefit as the period of smoking abstinence increases.[53,54] Some previous studies suggested that quitting smoking is effective only if done at least 8 weeks before surgery,[3,39] because of a possible greater risk of PRC due to increases in cough and mucous production in the first weeks after cessation.[55] However, recent studies have not confirmed this hypothesis: a systematic review and methanalysis of 9 studies with 889 patients[56] concluded that stopping smoking within 8 weeks before surgery does not lead to poorer postoperative outcomes when compared to continuous smoking; and another systematic review and methanalysis from Wong *et al*[54] included 25 studies and showed a reduction of 23% in the risk of PRC when cessation occurred more than 4 weeks before surgery and of 47% when cessation occurred more than 8 weeks before surgery. The authors confirmed previous findings that smokers have an increased risk of PRC but did not find any evidence that abstinence from smoking for a period shorter than four weeks before surgery increases or decreases the risk of PRC.

Patients with previous pulmonary disease should be managed accordingly, as they have an higher risk of PRC due to an increased susceptibility to sudden changes in arterial oxygen concentration; therefore, the preoperative evaluation of these patients is of major importance.[17] Therefore, in COPD patients the pulmonary function should be optimized by using combinations of bronchodilators, antibiotics and systemic glucocorticoids[14,57]; in the case of asthma, the patient should be evaluated about the need of a step-up in the therapy,[57] of an eventual postponing of the surgery or of special considerations concerning anesthetic management.[49]

c) Physiotherapy

The benefits of preoperative physiotherapy remain largely unknown, with most of the studies in this subject refering to patients awayting thoracic surgery.[57] In this setting, Pehlivan *et al*[58] demonstrated that preoperative physiotherapy with breathing, coughing exercises and treadmill walking reduced the incidence of PRC and length of hospital stay when compared to no physiotherapy. In another article from Nagarajan *et al*,[59] the authors concluded that preoperative physiotherapy is useful in optimising exercise capacity in patients with lung cancer with eventual impact in reducing PRC. Altough some studies suggest a benefit from this intervention, such services are actually offered by very few hospitals,[60] and these benefits have not been confirmed in other settings.[61] Therefore, a review from Canet *et al*[13] concluded that currently there is no clinical evidence supporting routine preoperative physiotherapy, although it may be useful in some settings.[14,62]

d) Inspiratory muscle training

Inspiratory muscle training (IMT) aims to increase inspiratory muscle strength and endurance by applying an increased load to inspiration.[63] IMT has proved to be useful in increasing inspiratory muscle strength in healthy volunteers[64] and several patient populations, including patients weaning from mechanical ventilation,[65] patients undergoing bariatric surgery[66] and patients awaiting for elective surgery.[67] Two meta-analysis have also demonstrated the utility of preoperative IMT in reducing the incidence of PRC after major abdominal or thoracic surgery.[63,68] Thereby, IMT in patients at high risk for PRC is recommended[57] and defering surgery in order to allow for a short period of IMT seems perhaps a good strategy for this group.[67]

e) Exercise training

Currently, there is substantial evidence of the association between physical fitness and outcome following major surgery, with less fit patients having poorer outcomes than well fit patients.[69,70] Cardiopulmonary exercise testing (CPET) is a clinical tool used to evaluate the performance of the cardiorespiratory system and to assess the individual's functional capacity. CPET has been increasingly adopted as a preoperative risk stratification tool, helping in decisions related to the type of surgery, perioperative management and postoperative care.[69] Preoperative exercise training has shown benefits in terms of reducing PRC after abdominal surgery,[71] with a meta-analysis from Valkenet *et al* suggesting that this technique can be helpful in decreasing PRC rates and length of hospital stay after cardiac or abdominal surgery.[68] However, the beneficial effects of these strategies on postoperative outcomes have not been confirmed in other studies.[72,73] Moreover, more studies are needed in order to establish the optimal duration and type of exercises.

2. Intraoperative interventions

a) General measures

Prevention of PRC is also needed in the intraoperative period. Surgery induces a stress response from the organism which contributes to postoperative complications, so the first step in reducing it is by choosing surgical techniques as minimally invasive as possible,[12-14,47] such as laparoscopic surgery when possible[49] Several substances have been proposed to reduce perioperative stress response, like glucocorticoids, growth factors, hormones, cytokine antagonists or free oxygen-radical scavengers,[39] but evidence about their possible benefit is still lacking.

Particularly in patients at high risk for PRC (such as patients with OSA[42]), general anesthesia should be avoided whenever possible in order to decrease the formation of atelectasis, as general anesthesia and endotracheal intubation with muscle paralysis may decrease lung volumes.[13,14,49] Epidural anesthesia/analgesia has the potential to improve perioperative respiratory function[14,47] by blocking reflexes that inhibit diaphragmatic function, by reducing pain (thereby permiting early mobilization, deep breathing and cough), by decreasing the need of systemic opioids with their associated respiratory depression and by reducing the stress response to surgery with less postoperative immunosuppression and infection.[74] Altough some studies state that this remains a controversial area still with insufficient evidence,[13,22] a recent review concluded that these tecnhniques may effectively be of benefit in reducing the incidence of postoperative pneumonia and mortality.[75]

Volatile anesthetics have anti-inflammatory and antiapoptotic effects in several organs, with evidence suggesting that the choice of these substances for mantaining anesthesia may be an effective way of attenuating the proinflammatory response of the lungs to a variety of insults.[47,49,76] Whether or not this translates into a decreased rate of PRC remains unclear.[76]

Neuromuscular blocking agents may also influence PRC, with short-acting or intermediate agents being associated with a significant reduction in the incidence of these complications when compared to long-acting agents.[14]

The use of oxygen supplementation intra and postoperatively is an easy and inexpensive way of improving tissue oxygenation,[39] although further studies are necessary to clearly define role, dose and duration of oxygen supplementation.

During surgery, it is also important to maintain normothermia, as it has been linked to the development of several postoperative complications.[39]

Liberal fluid therapy has also been associated with a higher incidence of postoperative ALI and/or ARDS after thoracic surgery, being one of the intraoperative factors that can contribute to this outcome.[77,78] To avoid it, a conservative strategy of maximum administration of 1–2 mL/kg/h in the intra and postoperative periods and a maximum positive fluid balance of 1.5L has been recommended[12,77]; as evidence concerning fluid management is still lacking, some authors advocate the use of an individualized strategy (goal directed therapy) based on objective parameters predictive of the patient's fluid requirements balanced with the individual risk of PRC.[49]

Transfusion-related acute lung injury is another complication that can occur in the perioperative period, and highlights the importance of avoiding unnecessary transfusion of blood products.[12,13,29]

b) Lung recruitment manouvers

Lung recruitment manouvers (LRM) have long been performed during general anesthesia, even without understanding its benefits. In the present, they may be performed by the ventilator and aim at reopening the colapsed lung through the use of a forceful high plateau pressure[19]; therefore, they normalize arterial PO_2 and improve CO_2 elimination.[37] After LRM, recolapse can be prevented by the use of positive end-expiratory pressure (PEEP). LRM are indicated in all intubated patient except those with a very low likelihood of developing atelectasis (healthy, young and thin patients undergoing minor surgery). These manouvers are contraindicated in hemodynamically unstable patients, if a proper anesthetic level is not present, in the case of bronchospasm, pneumothorax/bronchopleural fistula or elevated intracranial pressure and when lung colapse is not the cause of the alteration of gas exchange.[37]

LRM have been evaluated and proved to be useful during induction and maintenance of anesthesia in several settings such as bariatric surgery[79] and surgical ICU patients requiring endotracheal intubation.[80] However, when applied only near the end of anestesia, no significant improvement in postoperative oxygenation has been demonstrated.[81] Moreover, although LRM have been shown to improve atelectasis temporarily, this benefit does not persist durably into the postoperative period,[81] and therefore this strategy alone does not seem to have a great impact in reducing PRC.

c) Continuous positive airway pressure

Application of continuous positive airway pressure (CPAP) and/or PEEP prior to and during anesthetic induction may help in the prevention of compression atelectasis due to their effects in maintaining sufficient positive pressure within the airways and alveoli, thereby reducing the loss of functional residual capacity. These effects are even more useful when used in combination with intraoperative LRM.[10,19] PEEP, as well as most medical interventions, has the potential to do both harm and good, but is easily implemented and its use does not represent a significant cost,[31] making this strategy important and useful during the maintenance of anesthesia. During emergence from anesthesia, CPAP has a proved beneficial effect by maintaining the lungs free from colapse and thereby reducing postoperative complications.[37] This is especially important in patients with OSA, who need early resuming or initiation of CPAP after surgery.[42,45]

d) Fraction of inspired oxygen

During the induction of anesthesia, supplemental levels of oxygen are used to avoid the ocurrence of hypoxemia (preoxygenation phase). However, high concentration of oxygen may lead to resorption atelectasis.[19,28] Decreasing the fraction of inspired oxygen (FiO_2) during the preoxygenation phase decreases the incidence of atelectasis,[37] but also the security and apnea tolerance time for intubation. Moreover, a high FiO_2 has been shown to have some benefits unrelated to respiratory function[37] and this reduction in atelectasis is not maintained during surgery, probably because of adsorption of the oxygen in the closed alveoli.[19] Effectively, in a study from Mackintosh *et al*,[82] high FiO_2 (more than 90%) in patients with normal pulmonary function were not associated with increased oxygen requirements after extubation, and the authors therefore conclude that the extent of absorption atelectasis induced by a high FiO_2 is probably not enough to induce postoperative hypoxemia beyond that secondary to anesthesia/surgery.

e) Intraoperative mechanical ventilation

Mechanical ventilation is essential during general anesthesia.[83] It is well known that conventional mechanical ventilation with high tidal volumes, high plateau pressures and no PEEP can lead to lung injury in previously healthy but partially collapsed lungs[27,83] and has the potential to aggravate it in critically ill patients:[47,84,85] high tidal volumes may overstretch normal lung tissue, and the absence or institution of only low levels of PEEP may promote atelectasis leading to a cyclic colapse and reopening of alveoli.[86] This cyclic alveolar overdistension can initiate a local inflamatory response with polymorphonuclear leukocyte recruitment, that can evolve not only to acute lung injury but also to remote organ dysfunction.[47,87] Although the causes of perioperative ALI are clearly multifactorial, hyperinflation and repetitive inflation/deflation cycles of lung units may contribute to injury, and excessive tidal volume is associated with these insults in susceptible patients.[27,83]

Several studies have shown clear benefits in terms of PRC with the use of other strategies of ventilation ("lung-protective ventilation"),[4] notably in the management of patients with ALI/ARDS.[12,78] Lung protective ventilation usually combines low tidal volumes in order to minimize mechanical stress, recruitment manoeuvres to open colapsed alveoli and PEEP to prevent reformation of atelectasis;[23,37] the aims of this type of ventilation are to minimize lung trauma by avoiding overdistension and associated elevated pressure,[36,37] thereby improving gas exchange and minimizing the risk of ventilator-induced lung injury.[88] This ventilatory strategy has proved to be useful not only in reducing ALI and atelectasis but also in decreasing the incidence of postoperative pulmonary infections.[83] The use of intraoperative PEEP does not assure maintenance of lung reexpansion because there is a gradual decrease in respiratory system compliance during surgery with subsequent risk of re-colapse; the use of frequent LRM may be useful in this setting, due to its ability to open collapsed alveoli,[88] thereby improving oxygenation[23,89] and respiratory system compliance.[90] A recent Cochrane review showed that the aplication of PEEP during surgery decreased immediate postoperative atelectasis and improved arterial oxygenation on the first postoperative day; however, the authors concluded that current evidence is insufficient to coment on the postoperative benefits of intraoperative PEEP.[31] Derecruitment of lung tissue, impaired CO_2 elimination, and dynamic hyperinflation may occur during lung-protective ventilation.[29] This state of "mild permissive hypercapnia" may be beneficial in terms of intestinal perfusion, tecidual oxygen tension and better postoperative cognition,[88] and may also have benefits in terms of decreasing neutrophil recruitment, systemic cytokine concentrations, cell apoptosis and free radical injury.[91] Moreover, clinicians need to be aware of potential negative hemodynamic consequences due to the elevated intrathoracic pressures secondary to PEEP and LRM, which can lead to decreased venous return; therefore, potential hemodynamic effects should be closely monitored.[27]

Several retrospective and prospective studies have shown possible beneficial effects of a "lung protective ventilation" strategy during mechanical ventilation in the setting of surgery.[83,84,86-88,92-94] Two studies in cardiac surgery patients found that protective ventilation with low tidal volumes was associated with decreased postoperative morbidity and mortality.[87,94] Similar findings have been demonstrated with the use of low tidal volumes plus PEEP and LRM after abdominal surgery, [86,92] in elderly patients undergoing elective surgery[88] and in mechanicaly ventilated patients without previous ALI.[84] Another study using computed tomography to evaluate postoperative lung has confirmed that a protective ventilation strategy with preceding LRM, reduced tidal volume and sufficient PEEP ensures oxygenation and may decrease the mechanical stress associated with cyclic alveolar collapse.[93] Finally, a meta-analysis including eight articles with a total of 1669 patients has also confirmed the benefits of low tidal volumes and PEEP in postoperative outcomes.[83]

Therefore, although the potential benefits of lung-protective ventilation need to be replicated in larger and diverse groups of patients, this seems to be an effective and easy way of preventing PRC, thereby reducing the associated costs and improving patient care.[4,95]

3. Postoperative interventions

a) General measures

In the postoperative period, prevention of PRC remains an important part of patients management. In this setting, some measures have proved to be eficient. Potentialy difficult tracheal extubation should be antecipated, so that patients at risk can be correctly managed in order to reduce the risk of injury or death due to anesthesia.[95]

Oxygen suplemmentation during transport to the PACU is also a controversial topic, due to the heterogeneity of the literature published on this topic and lack of established guidelines. However, a recent study evaluating episodes of dessaturation in the PACU found that the most important predictors of this situation were transport without supplemental oxygen, low respiratory rate and sedation score. Therefore, the use of supplemental oxygen during transport to the PACU seems a simple and effective strategy of preventing postoperative hypoxemia.[34] After that, postoperative oxygen therapy should not be used routinely. Routine continuous pulse oximetry during the first postoperative hours is an important tool to monitorize patients,[13] as it is useful to detect hypoxemia and early pulmonary events; this strategy is even more important in patients with an increased risk of PRC, like those with OSA.[42,45] However, its effect on improving outcomes remains unknown.[33] High-flow nasal cannula has been sugested as a better strategy than conventional postoperative oxygen therapy to reduce the risk of PRC in cardiac surgery patients,[96] but more evidence is needed before its recommendation as a routine measure. Post-oxygenation with high inspired fractions of oxygen and suctioning of the airways at the end of surgery has been suggested as a routine strategy to improve postoperative oxygenation, but recent evidence suggests that it can have more deleterious effects than benefits and should therefore be avoided,[19] possibly due to oxygen toxicity.[29]

Postoperative nausea and vomiting are significant risk factors for postoperative complications, namely aspiration pneumonitis, and therefore should be prevented as far as possible.[39] Postoperatively, when the airway is unprotected and mainly in patients at higher risk of aspiration, it is recommended to carefully monitor administration of sedation and to avoid oral alimentation.[22] Nasogastric tubes should not be routinely used as they may increase the risk of pneumonia,[13] and when needed they should be removed as soon as possible. Conversely, there is some evidence that routine nasogastric decompression after abdominal surgery may be of benefit in reducing the incidence of postoperative vomits and PRC.[14,49] Therefore, more evidence is needed in this setting.[49]

Effective pain control is also extremely important, as it permits earlier mobilization[97] and contributes to adequate pulmonary toilet, thereby reducing the risk of pneumonia[3] and ARF.[12] Opioids can affect respiratory function through several mechanisms: direct depression of the central respiratory drive, sedation and depression of consciousness, and reduction of upper airway muscle tone. This ventilatory dysfunction usually occurs when initial doses are too high, when titration is too fast or when opioids are combined with other depressing agents,[98] and particularly in patients with ASA physical status of IV-V.[97] The avoidance of these agents as analgesics, for exemple through the implementation of an epidural catheter, seems a useful way of reducing the impact of opioids on respiratory function and thereby reducing the incidence of PRC,[49,62,99] and is of greatest importance in patients at higher risk, such as those with OSA.[42,45]

Residual paralysis after emergence from anesthesia (defined as a train-of-four ratio < 0.9[100]) is a common problem, with incidences ranging from 5 to 85% depending on the centres,[101] and occurs mainly when long-acting agents are used.[102] The most common adverse outcome associated with this situation is the ocurrence of PRC[100] due to its association with muscular weakness and subsequent airway collapse,[100,102] oxygen desaturation, respiratory impairment and ARF, thereby increasing postoperative morbidity and mortality.[100,101] These findings ilustrate the importance of careful patient monitoring in order to avoid residual paralysis with all its adverse consequences;[12,49,101,102] in adittion, reversal agents such as neostigmine or sugammadex can be used in more severe cases.[49,102]

In the specific setting of pneumonia, several preventive strategies have been suggested; in a study from Wren *et al*,[103] the authors achieved a 81% reduction in postoperative hospital-acquired pneumonia by implementing measures such as education of health profissionals, postoperative incentive spirometer, chlorhexidine oral hygiene, early ambulation, and head-of-bed elevation. As far as ventilator-associated pneumonia is concerned, the most important preventive measure is avoidance of intubation or reduction of the duration of mechanical ventilation.[3] Noninvasive ventilation may be an effective way to achieve this if evidence exists to support its use,[26] with the aditional benefit of decreasing atelectasis.[27] Besides this strategy, usual infection-control principles should be instituted,[12] as well as specific measures aimed at reducing bacterial colonization of the respiratory tract and decreasing the incidence of aspiration.[3] These measures include adoption of a semirecumbent position or eventually a lateral-horizontal position,[104] implementation of intermittent aspiration of subglottic secretions [105] and use of oral chlorhexidine gluconate.[103] Multistrategy programs including several of these measures may be of greater effectiveness in this setting.[106]

b) Incentive spirometry

Incentive spirometry is a commonly used strategy[107] in which the patient performs slow, deep breathings and sustain maximal inspiration[108] through a device that offers visual feedback, with the aims of mobilizing secretions and re-expanding areas of postoperatively collapsed lung by stretching the tissue.[109] It has the potential of decreasing pleural pressure and promoting lung expansion and better gas exchange, so it has been proposed as a way of preventing or reversing perioperative atelectasis with repetitive treatment on a regular basis.[48] There is not much evidence on the use of incentive spirometry during the preoperative period, and in general this strategy is not recommended due to a lack of benefits.[108] Conversely, several studies have adressed the effects of incentive spirometry in the postoperative period. As far as thoracic surgery is concerned, postoperative incentive spirometry does not seem to improve respiratory function or outcomes when compared to conventional thoracic expansion exercises[109] or to cough and deep-breathing regimens; the same is true for abdominal surgery.[110] Similar findings have been demonstrated in three recent systematic reviews evaluating the effects of incentive spirometry after upper abdominal[111] and cardiac/thoracic surgery,[11,112] and therefore its routine use in these settings is not recommended.[4,107] Current guidelines[113] confirm that routine incentive spirometry alone is not recommended for prevention of PRC, either pre or postoperatively.

c) Postoperative physiotherapy

In the past, chest physiotherapy with percussion, postural drainage, coughing, deep breathing exercises and mechanical devices was used as a preventive strategy to decrease the risk of PRC, based on its effects in increasing lung volumes and mobilizing secretions.[4,107] Chest physiotherapy is also routine in the management of ICU patients, with different combinations of the various techniques, depending on the physiotherapist.[114] As far as the postoperative period is concerned, chest physiotherapy has proved to be better than conventional care in improving outcomes in several settings.[114,115] Conversely, oposing results have been found in other studies.[60,116] Breathing exercises are one of the most commonly used strategies, and this techique in particular has proved to be beneficial in improving pulmonary function tests when used after upper abdominal surgery; however, its effects on postoperative outcomes remain unknown.[117] Therefore, based on the available evidence, which is mostly old, there is currently no indication for the postoperative routine use of chest physiotherapy,[112] except probably in case of retained secretions.[4,118] The availability of several techniques and the lack of evidence in favour of one over another dictates that this approach should be tailored to the individual patient according to experience of the professional.[25]

d) Early mobilization

Several studies have shown that postoperative bed rest can be detrimental to patient recovery[62] and that early patient mobilization can reduce the incidence of PRC, [20,39,40,103,119,120] so this strategy is generally recommended to reduce them and to promote airway clearance in the postoperative period.[57,107] The benefits may be evident even with once daily mobilization, if a moderate level of exertion is achieved, and this strategy should be implemented as early as possible.[120] Early mobilization may also be of benefit even in mechanicaly ventilated patients as a mean of preventing weakness and improving patients' status at the time of discharge, although more evidence is needed in this setting.[62] The addition of breathing exercises to early mobilization does not seem to be essential to improve postoperative outcomes. [120]

e) Exercise training

Postoperative pulmonary rehabilitation with exercise training has been shown to be beneficial following some surgical procedures[121] and in some special populations like COPD patients,[49] but these benefits have not been systematically confirmed.[122] Currently, there is insufficient evidence to conclude that exercise training is definitely of benefit prior to or after surgery. However, there is encouraging evidence that physical capacity and quality of life can be improved with prehabilitation and post-rehabilitation, so more studies are needed to establish if this will translate into a real improvement in outcomes [121.]

f) Multistrategy approaches

Lung expansion modalities such as chest physiotherapy, deep breathing exercises and incentive spirometry may be helpful in the postoperative setting, but evidence is insufficient to recommend them in a systematic way.[13,22] However, when the benefits of a specific intervention are small, there is a chance of combinig different strategies in order to improve an outcome.[57] In the case of PRC, Cassidy *et al*[119] proposed a system called I COUGH (incentive spirometry, coughing and deep breathing, oral care, understanding, getting out of bed, and head of bed elevation) as a way of reducing PRC. The results showed a reduction in the incidence of postoperative pneumonia and unplanned intubations. Although these were not statistically significant, they suggest a possible benefit from the combination of simple measures and thereby incentivate future trials with strategies like this in order to find effective ways of preventing or treating PRC.[4] Incentive spirometry plus positive expiratory airway pressure is another combination that has shown benefits over conventional care after cardiac surgery,[123] further supporting more investigation in multistrategy approaches (see tables 1 and 2, on the appendices section).

g) Noninvasive ventilation

When ARF develops, there is a need of maintaining adequate oxygenation by using external ventilation. Traditionally, invasive endotracheal ventilation has been the prefered approach, but it has also been associated with some complications such as ventilator-associated pneumonia.[3] Therefore, in recent years the interest in the use of noninvasive ventilation (NIV) has increased,[10] especially in patients presenting with COPD exacerbations or with acute cardiogenic pulmonary edema.[18,124] NIV has also shown eficiency in several other situations such as allowance of earlier extubation in patients with COPD,[124,125] discontinuation of mechanical ventilation in patients with resolving hypoxemic respiratory failure, management of immunocompromised patients who develop ARF and management of obesity-hypoventilation syndrome, some cases of acute asthma and some of comunity-acquired pneumonia.[124] The use of NIV as a facilitator to weaning from mechanical ventilation is controversial, as different conclusions have resulted from several studies.[125]

As far as anesthesia and surgery are concerned, postoperative NIV has proved to be useful in preventing or treating hypoxemia, thereby improving postoperative gas exchange and outcome,[9,24,95] and permits an increase in lung volumes without requiring effort from patient, thereby reducing atelectasis.[18,24] It is also a useful strategy to improve respiratory function by improving alveolar ventilation, reducing the work of breathing and reducing left ventricular afterload, with subsequent improvements in hemodynamics.[26] Moreover, NIV has the potential of decreasing the use of sedatives and endotracheal tubes, thereby reducing the number of pneumonias and improving patient comunication and functional status.[24]

NIV as a prophylatic strategy is specially important in high-risk patients (elderly, obese, COPD, and heart disease)[9,26,30] and has been demonstrated as a useful way of improving postoperative lung function in obese patients and in patients undergoing cardiac,[126] abdominal,[127] and several other types of surgery.[10] It also seems a beneficial approach once postoperative ARF has developed,[10,126] which occurs mainly after upper abdominal, cardiac, thoracic, and bariatric surgery,[30] and with a potential benefit over traditional mechanical ventilation.[9,26,30] However, when ARF develops, the first approach should be treating the cause (obstruction, central respiratory depression, residual neuromuscular blockade, ventilation-perfusion mismatch due to retained secretions and/or atelectasis, pulmonary embolism or obstruction). Then, if still needed, NIV should be considered.[30] In the specific setting of cardiothoracic surgery, the use of NIV has proved to be useful both as a preventive and as a therapeutic tool for ARF, with improved respiratory function and postoperative outcomes.[18,126,128-131] Hemodynamic changes induced by NIV may be of benefit in this setting,[126] as they lead to a reduced myocardial oxygen consumption[130] and improved pump function of the heart.[129] Postoperative NIV also appears to improve oxygenation in morbidly obese patients who undergo bariatric surgery,[132] with greater benefits if instituted immediately after extubation.[133] In a systematic review from Chiumello *et al*, the authors included 29 articles and concluded that NIV should be used postoperatively both as a preventive and as a therapeutic approach to improve gas exchange after several types of surgery.[9]

The decision to use NIV in the postoperative period as a prophylactic measure for high-risk patients should be taken taken preoperatively.[30] Currently, there is no evidence that BiPAP is superior to CPAP in these setting.[30] Studies of NIV as a treatment for ARF in the postoperative setting have also shown favorable results for both NIV types.[26] Studies have also demonstrated that NIV is more effective if instituted as early as possible[133] and in a continuous way, not in an intermitent approach.[10] Although a variety of interfaces are available, the oronasal mask is considered by some authors as the best initial interface in terms of leak prevention and patient confort.[124] The most important issue in this setting is to choose the best interface for the individual patient, even if that requires trying various types.[9,24,26] Improved comfort is associated with adequate synchrony and increased success of NIV.[124]

Conclusion

Due to its enormous impact on outcomes after surgery, morbidity, mortality and healthcare resources consumption, PRC are definitely an issue where efficient prevention is needed and must be implemented. Several strategies have been proposed with this goal, some of them with promising results, others still needing more studies to provide sufficient evidence of their benefits. However, it is certain that prevention of PRC should not rely on one specific measure, but should instead be considered as a whole process combining pre, intra and postoperative interventions, taking advantage of all the possible strategies for that individual patient. In this sense, fast-track programs have gained increased interest in the last years. These kind of approaches usually combine preoperative assessment and education, evidence based practice in anesthesia, minimally invasive procedures, effective analgesia and early feeding and ambulation; the goals are enhancing and accelerating postoperative recovery, thereby reducing morbidity. Currently, they have been adopted in several types of surgery with promising results, and therefore this seems an interesting area for future research, with a great potential of improving patient care and helping healthcare systems.

Conflicts of interest

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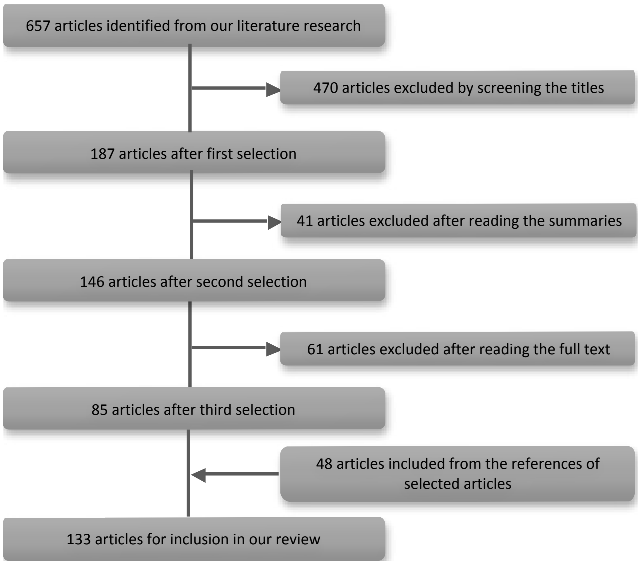
Appendices and tables

Appendix 1: query used in our research.



("postoperative complications"[All Fields] AND ("respiratory"[All Fields] OR "pulmonary"[All Fields] OR "acute lung injury"[All Fields] OR "aspiration pneumonitis"[All Fields] OR "pneumothorax "[All Fields] OR "pneumonia"[All Fields] OR "bronchospasm"[All Fields] OR "pulmonary edema"[All Fields] OR "atelectasis"[All Fields] OR "respiratory failure"[All Fields]) AND ("prevention"[All Fields] OR "risk factors"[All Fields] OR "ventilation"[All Fields])) AND ((Clinical Trial[ptyp] OR Review[ptyp] OR systematic[sb]) AND "humans"[MeSH Terms] AND (English[lang] OR Portuguese[lang]) AND ("2010/01/01"[PDAT] : "2014/12/31"[PDAT]))

Appendix 2: selection strategy (see text for details).

Table 1. Proposed combination strategies to keep the lungs open during the perioperative period.

- Pre-oxygenation with a FiO_2 of 100% (eventually 80% followed by a gentle inflation of the lung in nonobese patients with healthy lungs and no anticipated difficulty in airway management); - Perform a LRM or, alternatively, use CPAP/PEEP during the induction phase; after the first LRM, repeat it at every 30 minutes or use a PEEP of 7 to 10 cmH_2O during maintenance of anesthesia; - If possible, maintain a low FiO_2 during surgery, ideally 30 to 40% or even less; - Do not use post-oxygenation and airway suctioning as routine strategies. [19]	- Induction of anesthesia using a pre-oxygenation with a FiO_2 of 80 to 100% to allow for a longer safety time in case of a difficult intubation; - Perform an early LRM increasing the airway pressure to 40 cmH_2O during 10 seconds; - During surgery, keep the FiO_2 around 30 to 40%; if there is any oxygen problem, repeat a LRM with following PEEP of 7 to 10 cmH_2O; - Before extubation, consider performing another LRM and decide about post-oxygenation according to the individual patient, as this may promote atelectasis formation with persistence into the postoperative period. [28]

Table 2. Example of a multiapproach strategy to reduce PRC.[27]

Preoperative	1. Preoperative respiratory muscle training
Intraoperative	2. Application of CPAP during anesthesia induction 3. Reversal of anesthesia-induced atelectasis after intubation by a recruitment maneuver in combination with sufficient levels of PEEP and a low FiO_2 4. Repeating recruitment maneuvers as indicted by decrease in oxygenation and respiratory system compliance 5. Tracheal extubation using low FiO_2 and CPAP during emergence from anestesia 6. Use of CPAP and low FiO_2 immediately after extubation
Postoperative	7. Promotion of lung expansion through early mobilization, frequent changes in body position and coughing and support for the expectoration of mucus by sighs in conjunction with chest physiotherapy