

## Peri-operative Respiratory Complications and the Post-operative Consequences – Atelectasis and Risk Factors

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### Abstract

Post-operative pulmonary complications (PPCs) play a significant role in the risks of surgery and anaesthesia. The definition of PPCs is not definitely established and may vary between different studies. Potential patient-related risk factors for PPCs are: age; chronic lung disease; cigarette use; congestive heart failure; functional dependence; American Society of Anesthesiologists (ASA) classification; obesity; asthma; obstructive sleep apnoea; impaired sensorium, abnormal findings on chest examination, alcohol use and weight loss; and exercise capacity, diabetes and HIV infection. Risk factors not related to the patient's clinical characteristics are surgical site, duration of surgery, anaesthetic technique and emergency surgery. The most important and morbid PPCs are atelectasis, pneumonia and respiratory failure, which contribute to increased morbidity, mortality and hospital length of stay. An appropriate ventilation setting during mechanical ventilation for general anaesthesia may reduce intra-operative atelectasis, with beneficial effects in the post-operative period. Lung expansion modalities, mainly physiotherapy and non-invasive continuous positive airway pressure (CPAP), may help reducing PPCs in patients at higher risk. Further studies are warranted to better define peri-operative clinical management to prevent and/or reduce PPCs.

### Keywords

Post-operative pulmonary complications, atelectasis, non-invasive respiratory support, physiotherapy, acute lung injury, acute respiratory distress syndrome, ventilator-induced lung injury

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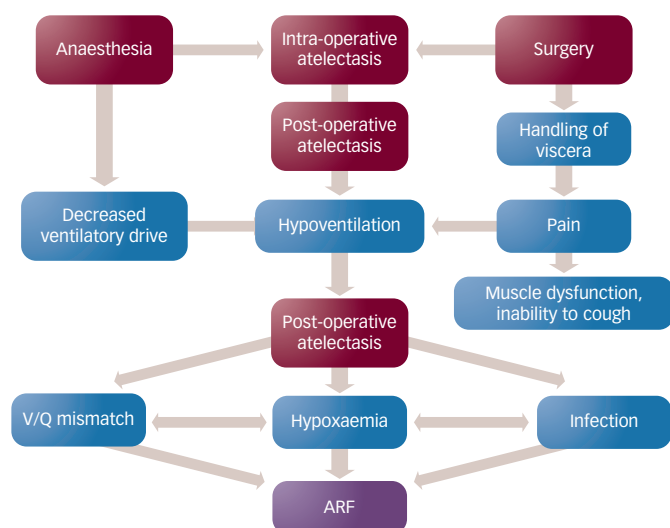
The high-risk non-cardiac surgical population represents a major global healthcare challenge. Recent estimates suggest that 234 million major surgical procedures are performed worldwide each year.<sup>1</sup> Complications following major surgery are a leading cause of morbidity and mortality.<sup>2,3</sup> Previous sickness before surgery is second only to cardiovascular disease in terms of associated short-term complications and increased mortality.<sup>2</sup> Recent evidence showed that the use of a surgical safety checklist may be helpful for reducing complications, but it was not associated with a reduction in post-operative pulmonary complications (PPCs).<sup>4</sup> PPCs play a significant role in the risks of surgery and anaesthesia. The most important and morbid PPCs are atelectasis, pneumonia, respiratory failure and exacerbation of underlying chronic lung disease, all of which contribute to increased morbidity, mortality and length of stay.<sup>5,6</sup> PPCs may also be more likely than cardiac complications to predict long-term mortality after surgery, particularly among older patients.<sup>7</sup> In this brief review we will discuss: the definition of PPCs; the prevalence of PPCs and possible risk factors; the main pathophysiological mechanisms leading to PPCs; the experimental and clinical evidence for lung injury during mechanical ventilation; and specific interventions to reduce PPCs.

### Definition of Post-operative Pulmonary Complications

The definition of PPCs is not definitely established and may vary among different studies. The most common definitions of PPCs include:

- post-operative respiratory failure:
  - the need for mechanical ventilation for greater than 48 hours post-operatively; or
  - the need for reinstitution of mechanical or non-invasive ventilation after extubation;
- acute lung injury:
  - new or worsening hypoxaemia with a ratio of arterial oxygen to fraction of inspired oxygen (acute lung injury [ALI] if lower than 300mmHg and acute respiratory distress syndrome [ARDS] if lower than 200mmHg) on two consecutive days;
  - new bilateral pulmonary infiltrates on two consecutive days; or
  - no evidence of left atrial hypertension (pulmonary capillary wedge pressure (18mmHg, when available) – the diagnosis of ALI/ARDS is mandatory if it persists for more than 24 hours;
- hydrostatic pulmonary oedema:
  - radiographic (diffuse bilateral pulmonary infiltrates);
  - haemodynamic (pulmonary artery occlusion pressure <18mmHg or echocardiographic evidence of left ventricular or right ventricular dysfunction and elevated ventricular filling pressures);
  - laboratory (brain natriuretic peptide >350pg/ml); and
  - documented physical findings (gallop, jugular venous distension);
- pneumonia as:
  - new or progressive pulmonary infiltrate or consolidation in the chest radiograph and one or more of the following: new onset of purulent sputum or change in the character of sputum;

**Figure 1: A Schematic Representation of the Pathophysiological Mechanisms Leading to Post-operative Pulmonary Complications**



V/Q = ventilation/perfusion; ARF = acute respiratory failure.

sputum cultures showing a respiratory pathogen; isolation of pathogen from specimen obtained by transtracheal aspirate or bronchial brushing/lavage; or

- three or more of the following: fever (temperature  $>38.5^{\circ}\text{C}$ ); rales or rhonchi on chest auscultation; new onset of purulent sputum or change in the character of sputum; sputum cultures showing a respiratory pathogen; isolation of pathogen from specimen obtained by transtracheal aspirate or bronchial brushing/lavage;
- atelectasis: lobar or multilobar atelectasis on chest radiograph and requiring bronchoscopic intervention;
- pneumothorax if newly present on chest radiograph and requiring chest tube placement;
- bronchospasm, defined as newly detected expiratory wheezing treated with bronchodilators; and
- aspiration pneumonitis, defined as ALI/ARDS after the inhalation of regurgitated gastric contents.

Recently, scores to be calculated at the bedside have been proposed to identify PPCs early, such as the Clinical Pulmonary Infection Score (CPIS), including or not microbiological data. These scores have also proved useful for monitoring the clinical evolution of PPCs and their response to treatment.<sup>8</sup>

## Prevalence of and Risk Factors for Post-operative Pulmonary Complications

The incidence of PPCs depends on the definition used and the type of patients and surgery considered. There are several limitations of existing studies addressing the incidence and prognosis of post-operative ALI, including: retrospective design;<sup>9–13</sup> inclusion of cases with prevalent risk factors for ALI;<sup>10,14</sup> lack of a clear definition of post-operative ALI;<sup>15,16</sup> restriction to specific age groups;<sup>17</sup> and examination of only in-hospital mortality as an end-point.<sup>18,19</sup> Furthermore, none of the published studies to date has provided an assessment of the relative contribution of ALI in determining post-operative respiratory failure and long-term post-operative survival. Several studies have shown that, according to the American Society of Anesthesiologists (ASA), PPCs varied from 1.2% for patients classified as ASA I to 10.9% for those

classified as ASA IV.<sup>5</sup> In a recent match-controlled study, it was reported that ALI occurred in 3% of high-risk elective surgeries and was the most common cause of post-operative respiratory failure. Compared with matched controls, patients with ALI-associated post-operative respiratory failure had markedly lower post-operative survival and longer length of hospital stay.<sup>6</sup> Potential patient-related risk factors for PPCs fell into the following general categories: age; chronic lung disease; cigarette use; congestive heart failure; functional dependence; ASA classification; obesity; asthma; obstructive sleep apnoea; impaired sensorium, abnormal findings on chest examination, alcohol use and weight loss; and exercise capacity, diabetes and HIV infection. Other factors not related to the patients' clinical characteristics must be taken into consideration, such as: surgical site (increased risk for PPCs reported in aortic aneurysm repair, thoracic surgery, abdominal surgery, upper abdominal surgery, neurosurgery, prolonged surgery, head and neck surgery, emergency surgery and vascular surgery); duration of surgery (increased risk when surgery is longer than 2.5 hours); anaesthetic technique (increased risk with general anaesthesia); and emergency surgery. In our clinical practice we also take into account two other clinical signs: oxyhaemoglobin saturation measured by pulse oximetry while patients breathe air in a supine position, and a positive cough test. When oxyhaemoglobin saturation measured in an upright position by pulse oximetry is lower than 95% in air and a cough test is positive, i.e. the patient has repeated coughing after the first cough attempt, the patient is considered at higher risk of PPCs, regardless of the type of surgery. Again, some scores have been identified and may be easily collected during the pre-operative anaesthetic visit to help identify patients with increased risk of PPCs.<sup>20</sup>

## Pathophysiological Mechanisms Leading to Post-operative Pulmonary Complications

A schematic representation of the pathophysiological mechanisms involved in PPCs is shown in *Figure 1*. Decreased lung volumes and atelectasis may be the first events in a cascade leading to PPCs, and are maintained in the post-operative period. They may be related to several factors, such as surgery-related shallow breathing, bed rest, diaphragmatic dysfunction, pain and impaired mucociliary clearance.

Atelectasis is a common finding in patients undergoing general anaesthesia and is reported to appear in around 90% of all patients. By using computed tomography (CT) it has been possible to identify an average atelectatic area near the diaphragm of around 3–7% of the total lung area, which in some cases can exceed 15–20% of total lung area. Atelectasis appears after intravenous or inhalational anaesthesia, and even during spontaneous breathing, and is not further increased by the administration of neuromuscular blockade agents. Thus, 15–20% of the lung is regularly collapsed at the base of the lung during uneventful anaesthesia, before any surgery has been performed.<sup>21</sup> Different mechanisms may promote reduced lung volume and atelectasis during mechanical ventilation and general anaesthesia:

- Loss of muscle tone – the use of anaesthetics allowing maintenance of respiratory muscle tone may prevent formation of atelectasis. The only intravenous anaesthetic not associated with atelectasis formation is ketamine, likely maintaining adequate respiratory muscle tone.<sup>22</sup>
- High oxygen fraction – higher ( $>80\%$ ) oxygen fraction delivered during induction and maintenance of mechanical ventilation has been shown to promote increased atelectasis.<sup>23,24</sup>

- Heart weight – the heart weighing down on the most dependent lung regions promotes progressive squeezing and collapse of the lower lobes.<sup>25</sup>
- Increased intra-abdominal pressure – in a supine position, this favours loading on the diaphragm, reduction of lung volume and atelectasis formation.<sup>26</sup>

Atelectasis that develops during anaesthesia may last for several days in the post-operative period,<sup>27</sup> likely promoting PPCs.

### Experimental Evidence for Lung Injury During Mechanical Ventilation

Mechanical ventilation is essential to sustain respiratory function during general anaesthesia; however, mechanical ventilation may also seriously damage the lung structure, leading to ventilator-induced lung injury even in previously healthy lungs. Damage to different lung structures has been reported as a consequence of mechanical ventilation at 'physiological' (6–8ml/kg) low tidal volume and in the absence of positive end-expiratory pressure (PEEP) in otherwise previously healthy lungs: injuries of epithelial cells with leukocyte infiltration in the alveolar septa and increase in the percentage of abnormal alveolarbronchiolar attachments;<sup>28</sup> damage of endothelial cells, leading to right ventricular dysfunction with increased microvascular leakage;<sup>29</sup> peripheral airway injury;<sup>30</sup> and fragmentation of the extracellular matrix<sup>31</sup> not mediated by the pro-inflammatory process.<sup>32</sup> The lesional effect of mechanical ventilation on the extracellular matrix of the lung and other pulmonary structures may depend on several factors: increased transpulmonary pressure; reversed distribution of intrathoracic pressures; heterogeneous distribution of ventilation; and reduction of pulmonary lymphatic drainage.<sup>33</sup>

### How to Set Mechanical Ventilation During General Anaesthesia

As a consequence of respiratory modifications induced by general anaesthesia and paralysis, the main aim of mechanical ventilation during general anaesthesia is to 'keep the lung open' during the entire respiratory circle. In general, to ventilate a lung showing a tendency to collapse we must provide: inspiratory pressure, such as to open up the collapsed lung regions (recruitment pressure); a high enough PEEP to keep the lung open at end-expiration associated with low tidal volumes; and fraction of inspired oxygen (FiO<sub>2</sub>) lower than 0.8. This may counteract negative effects induced by reduction in lung volume, airway closure and atelectasis. To approach the respiratory system alterations that occur during general anaesthesia, the following ventilation settings may be proposed: use of lower inspiratory oxygen fractions to induce anaesthesia and during surgery to maintain physiological oxygenation;<sup>24</sup> use of tidal volumes lower than 10ml/kg ideal bodyweight;<sup>33,34</sup> and application of PEEP after a recruitment manoeuvre.<sup>35</sup> The superiority of one or more of these different ventilatory settings in comparative studies has never been investigated. Adequate opening pressure can be obtained by applying periodic large, manually performed lung inflations (recruitment manoeuvres).<sup>35</sup> To achieve a transpulmonary pressure high enough to re-open collapsed alveoli, airway pressures up to 60cmH<sub>2</sub>O are necessary. On the other hand, an application for a relatively short period of time (six seconds) is recommended to avoid, as much as possible, potential negative effects on haemodynamics. In any case, the recruitment manoeuvre should always be performed only when a volaemic and haemodynamic stabilisation is reached after induction of anaesthesia. The recruitment

manoeuvre should be repeated every half an hour in the absence of PEEP. The role of PEEP in anaesthesia is still controversial; this is likely due to the opposite effects induced by PEEP on oxygenation in different patients. PEEP can resolve atelectasis, if present, and prevent small airways collapse, improving ventilation–perfusion matching and oxygenation. On the other hand, increasing PEEP may lead to negative effects on the ventilation–perfusion ratio and pulmonary shunt, if alveolar overstretching and cardiac output reduction or redistribution become the prevalent phenomena. The final effect on oxygenation of PEEP application depends on the balance between positive and negative effects in any given patients. We found that 10cmH<sub>2</sub>O of PEEP during anaesthesia and paralysis may be an optimal compromise between oxygenation improvement and alveolar recruitment without negative effects on haemodynamics.<sup>26</sup> This suggested ventilator setting has been proved to be effective also during laparoscopic surgery.<sup>36,37</sup> Further studies are needed to define the optimal levels of PEEP and tidal volume during general anaesthesia in different categories of patients and types of surgery to avoid atelectasis intra-operatively and keep the lung open post-operatively.

### Clinical Evidence

Low-tidal-volume ventilation and PEEP has been accepted as the standard ventilation treatment in patients with ALI/ARDS;<sup>38</sup> less evidence is available in patients with healthy lungs undergoing mechanical ventilation and general anaesthesia. Recent studies in patients investigated the effects of protective ventilation strategies – that is, a low tidal volume or PEEP – during general anaesthesia. Mechanical ventilation with high intra-operative tidal volume (8.5 versus 6.5ml/kg) was associated with an increased risk of post-pneumectomy respiratory failure, independently of PEEP level.<sup>11</sup> In another study conducted in post-operative patients, use of a tidal volume of 6ml/kg was associated with a reduction in the incidence of pulmonary infection and duration of intubation compared with a tidal volume of 12ml/kg.<sup>39</sup> In cardiac surgery, the use of a tidal volume of 6ml/kg with PEEP levels set according to current recommendations resulted in decreased tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ) in the plasma and bronchoalveolar lavage fluid compared with a tidal volume of 12ml/kg.<sup>40</sup> Similarly, a protective ventilatory strategy (tidal volume 8ml/kg and PEEP 10cmH<sub>2</sub>O versus tidal volume 10–12ml/kg and PEEP 2–3cmH<sub>2</sub>O) intra-operatively reduced inflammatory response in cardiac surgery patients.<sup>41</sup> Reis Miranda et al.<sup>42</sup> found that, in patients undergoing elective cardiopulmonary bypass, interleukin-8 (IL-8) levels decreased more rapidly at three days after the operation by using lung-protective ventilation (tidal volume 4–6ml/kg and PEEP 10cmH<sub>2</sub>O) than conventional ventilation (tidal volume 6–8ml/kg and PEEP 5cmH<sub>2</sub>O). Furthermore, they found that recruitment during surgery associated with higher levels of PEEP and lower tidal volume resulted in significantly higher lung volumes and fewer episodes of hypoxaemia after extubation than with conventional mechanical ventilation.<sup>43</sup> Choi et al.<sup>44</sup> randomly assigned patients scheduled for an elective surgical procedure to mechanical ventilation with either large tidal volume (12ml/kg) and no PEEP or lower tidal volume and PEEP of 10cmH<sub>2</sub>O. The use of a larger tidal volume promoted pro-coagulant changes, potentially leading to fibrin depositions within the airways; with a lung-protective lower tidal volume, these pro-coagulant changes were largely prevented. During oesophagectomy,<sup>45</sup> a tidal volume of 9ml/kg during two-lung ventilation or 5ml/kg during one-lung ventilation with a PEEP of 5cmH<sub>2</sub>O decreased pro-inflammatory systemic response, improved lung function and allowed earlier extubation compared with conventional ventilatory strategy (tidal volume 9ml/kg during two-lung

**Figure 2: The Helmet to Provide Non-invasive Continuous Positive Airway Pressure in the Post-operative Period**



and one-lung ventilation, with no PEEP). By contrast, in other randomised studies<sup>46,47</sup> including a heterogeneous group of major thoracic and abdominal surgical procedures, protective mechanical ventilation was not associated with a decrease in intra-pulmonary and systemic inflammation. Furthermore, there was no evidence that protective ventilation prevented lung adverse effects or decreased systemic cytokine levels in cardiac surgery.<sup>48</sup> However, adoption of a low tidal volume in patients without pre-existing lung injury may favour the development of atelectasis; hence, use of low tidal volume in the absence of recruitment or PEEP in anaesthetised patients without lung injury is not generally recommended.<sup>49</sup>

## Specific Interventions to Reduce the Risk of Post-operative Pulmonary Complications

Different strategies have been proposed to reduce the risk of PPCs. Among those proved to have beneficial effects are post-operative lung expansion modalities, selective post-operative nasogastric decompression and short-acting neuromuscular blockade. Other proposed interventions have not clearly been associated with reduced PPCs, such as laparoscopic (versus open) operation, smoking cessation, intra-operative neuraxial blockade, post-operative epidural analgesia, immunonutrition, routine total parenteral or enteral nutrition and right-heart catheterisation.<sup>50</sup> More recently, it has been definitively demonstrated that higher inspired oxygen fraction used in the peri-operative period is not associated with decreased risk of PPCs and more rapid wound healing,<sup>51,52</sup> thus inspiratory oxygen fraction should be titrated in the peri-operative period to achieve physiological oxygenation.

## Physiotherapy

Physiotherapy, including early mobilisation, stimulation of coughing, deep breathing exercises, postural drainage, percussion and vibration, aims to expand the lungs and to prevent secretion accumulation.<sup>5</sup> Alternative techniques are incentive spirometry and application of non-invasive continuous positive airway pressure (nCPAP). Physiotherapy and incentive spirometry are widely used either alone or in combination to prevent post-operative atelectasis formation and respiratory dysfunction, but their use is often based more on perceived efficacy than on scientific evidence.<sup>53-58</sup> This may be

explained because no large-scale multicentre randomised trial has clearly demonstrated their clinical advantage, and considerable controversy remains over which technique is superior to the other to prevent post-operative respiratory dysfunction when applied after surgery. Considering that these interventions may have different side effects on cardiovascular function, the expected benefit may vary considerably between patients with and without cardiac surgery. In addition, regular physiotherapy in the peri-operative period markedly increases the required human and financial resources.

## Non-invasive Respiratory Support

Non-invasive respiratory support refers to techniques allowing respiratory support without the need for an invasive airway. Two types of non-invasive respiratory support are commonly used: nCPAP and non-invasive positive pressure ventilation (nPPV). Non-invasive respiratory support may be an important tool to prevent (preventative treatment) or to treat acute respiratory failure avoiding intubation (curative treatment). The aims of non-invasive respiratory support are to partially compensate for the affected respiratory function by reducing the work of breathing; to improve alveolar recruitment with better gas exchange (oxygenation and ventilation); and to reduce left ventricular afterload, increasing cardiac output and improving haemodynamics.

## Preventative Non-invasive Respiratory Support

Few prospective randomised trials investigated nCPAP with oxygen and physiotherapy in the post-operative period with acceptable quality after abdominal surgery.<sup>59,60</sup> Despite the limited number of studies, all of them reported that nCPAP was advantageous for the reduction of atelectasis formation in non-cardiac surgery patients. In non-cardiac surgery patients, a reduction of pneumonia but not hospital length of stay was reported in two studies.<sup>61,62</sup> A further study demonstrated benefit of nasal CPAP to reduce atelectasis formation, pneumonia and hospital length of stay in patients with thoraco-abdominal aortic aneurysms.<sup>63</sup> CPAP is the easiest method of respiratory assistance compared with ventilation, especially if performed in the ward or in the surgical department. CPAP should be always administered in the post-operative period when the  $\text{PaO}_2/\text{FiO}_2$  ratio falls below 300, and maintained for a prolonged period of time during the day. The use of a helmet instead of a mask can improve the efficacy of the treatment and the comfort of the patient<sup>64</sup> (see Figure 2). The aim is to give ventilatory support to more rapidly restore lung volumes to pre-operative values, improving oxygenation and reducing the work of breathing. Moreover, for several days after surgery, patients should remain in a semi-recumbent position (30–45°) to reduce abdominal pressure on the diaphragm. These data suggest that a more physiological approach to respiratory treatment in the post-operative period could be useful to improve respiratory and clinical outcome.

## Curative Non-invasive Respiratory Support

Patients suffering from post-operative acute respiratory failure have been included among other types of patients in studies evaluating non-invasive respiratory support to treat respiratory failure of multiple causes. In these studies, no comparison has been made between patients presenting with medical or surgical acute respiratory failure because of the heterogeneity and small numbers of patients included. Jaber et al.,<sup>65</sup> in an observational study, demonstrated the feasibility, good tolerance and safety of nPPV for the treatment of acute respiratory failure after digestive surgery. More severe initial hypoxaemia and lower improvement of  $\text{PaO}_2$  after treatment were predictive of nPPV failure.



These results were confirmed by a recent study that included 72 patients who developed acute respiratory failure after abdominal surgery, where 42 patients (58%) avoided intubation with nPPV.<sup>66</sup> Conti et al.,<sup>67</sup> in a match-controlled study, reported nPPV success rate of 80% in the helmet and of 52% in the facial mask group. Antonelli et al.<sup>68</sup> showed in a controlled randomised trial that in organ transplant recipients with hypoxaemic acute respiratory failure, nPPV reduced the rate of intubation, the incidence of fatal complications and intensive care unit (ICU) mortality compared with the provision of supplemental oxygenation alone. More recently, Michelet et al.<sup>69</sup> showed that nPPV was associated with a lower intubation rate, a lower frequency of ARDS and anastomotic leakage and a reduction in ICU length of stay in patients with acute respiratory failure after oesophagectomy.

## Conclusions

In conclusion: PPCs are frequent after general surgery, particularly in high-risk patients undergoing major abdominal surgery; reduction in lung volume and atelectasis formation in the peri-operative period may be the main factors promoting PPCs; an appropriate ventilation setting during mechanical ventilation for general anaesthesia may reduce intra-operative atelectasis with beneficial effects in the post-operative period; and lung expansion modalities, mainly physiotherapy and nCPAP, may help to reduce PPCs. Further studies are warranted to better define peri-operative clinical management to prevent and/or reduce PPCs. ■



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