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

Paolo Pelosi1 and Cesare Gregoretti2

1. Associate Professor, Department of Environment, Health and Safety, University of Insubria, Varese; 2. Director, Anaesthesia and Intensive Care Services, Maria Adelaide Hospital, Turin

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

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.1 Complications following major surgery are leading cause of morbidity and mortality.2,3 Previous sickness before surgery is second only to cardiovascular disease in terms of associated short-term complications and increased mortality.4 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).5 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.6,7 PPCs may also be more likely than cardiac complications to predict long-term mortality after surgery, particularly among older patients.8 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 reintroduction 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 to fraction of inspired oxygen = 300mmHg and acute respiratory distress syndrome [ARDS] if lower than 200mmHg);
  - new bilateral pulmonary infiltrates on two consecutive days; or
  - new or worsening hypoxaemia with a ratio of arterial oxygen to fraction of inspired oxygen = 300mmHg and acute respiratory distress syndrome [ARDS] if lower than 200mmHg));
- 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;
Respiratory and Airway Management

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

![Schematic diagram showing the relationship between anaesthesia, intra-operative atelectasis, post-operative atelectasis, pain, hypoxaemia, V/Q mismatch, ARF, and handling of viscera.]

**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°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 multifocal 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 or difficulty initiating spontaneous breathing, 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.²

**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; inclusion of cases with prevalent risk factors for ALI; lack of a clear definition of post-operative ALI; restriction to specific age groups; and examination of only in-hospital mortality as an end-point. Moreover, 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. 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.²³ 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: oxygenhaemoglobin saturation measured by pulse oximetry while patients breathe air in a supine position, and a positive cough test. When oxygenhaemoglobin 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.²⁰

**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.²² 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.
- High oxygen fraction – higher (>80%) oxygen fraction delivered during induction and maintenance of mechanical ventilation has been shown to promote increased atelectasis.²⁰,²ⁱ
always be performed only when a volaemic and haemodynamic
on haemodynamics. In any case, the recruitment manoeuvre should
hand, an application for a relatively short period of time (six seconds) is
manoeuvre. The superiority of one or more of these different
alveoli, airway pressures up to 60cmH₂O are necessary. On the other
achieve a transpulmonary pressure high enough to re-open collapsed
volumes; and fraction of inspired oxygen (FiO₂) lower than 0.8. This may
respiratory circle. In general, to ventilate a lung showing a tendency
during general anaesthesia is to ‘keep the lung open’ during the entire
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 alveolar bronchiolar attachments;32 damage
of endothelial cells, leading to right ventricular dysfunction with
increased microvascular leakage;33 peripheral airway injury34 and
fragmentation of the extracellular matrix35 not mediated by the
pro-inflammatory process.36 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.37

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
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 (FiO₂) 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;36 use of tidal volumes lower than 10ml/kg
ideal body weight;37 application of PEEP after a recruitment
manoeuvre.38 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).39 To
achieve a transpulmonary pressure high enough to re-open collapsed
alveoli, airway pressures up to 60cmH₂O 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 10cmH₂O of PEEP
during anaesthesia and paralysis may be an optimal compromise
between oxygenation improvement and alveolar recruitment without
negative effects on haemodynamics.39 This suggested ventilator setting
has been proved to be effective also during laparoscopic surgery.40,41
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; 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-
neumonectomy respiratory failure, independently of PEEP level.41 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. 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-α (TNF-α) in the plasma
and bronchoalveolar lavage fluid compared with a tidal volume of
12ml/kg. Similarly, a protective ventilatory strategy (tidal volume
8ml/kg and PEEP 10cmH₂O versus tidal volume 10–12ml/kg and PEEP
2–3cmH₂O) intra-operatively reduced inflammatory response in
cardiac surgery patients.42 Reis Miranda et al.43 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 10cmH₂O)
that conventional ventilation (tidal volume 6–8ml/kg and PEEP
5cmH₂O). 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.44 Choi
et al.45 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 10cmH₂O.
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,46 a tidal volume of 9ml/kg
during two-lung ventilation or 5ml/kg during one-lung ventilation with
a PEEP of 5cmH₂O decreased pro-inflammatory systemic response,
improved lung function and allowed earlier extubation compared with
conventional ventilatory strategy (tidal volume 9ml/kg during two-lung
Respiratory and Airway Management

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

Post-operative Period

Continuous Positive Airway Pressure in the Figure 2: The Helmet to Provide Non-invasive Respiratory and Airway Management

20

perceived efficacy than on scientific evidence.53–58 This may be respiratory dysfunction, but their use is often based more on non-invasive continuous positive airway pressure (nCPAP). Physiotherapy and incentive spirometry are widely used either alone and one-lung ventilation, with no PEEP). By contrast, in other randomised studies64–65 including a heterogenous 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.66 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.67

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.68 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.69,70 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.71 Alternative techniques are incentive spirometry and application of 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.

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.72–73 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.74 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.75 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 PaO2/FiO2 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 (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.,76 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 PaO2 after treatment were predictive of nPPV failure.
Peri-operative Respiratory Complications and the Post-operative Consequences

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. Conti et al., in a matched-controlled study, reported nPPV success rate of 80% in the helmet and of 52% in the facial mask group. Antoñel et al. 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. 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.

Paolo Pelosi is an Associate Professor in the Department of Environment, Health and Safety at the University of Insubria, Varese, and also practises at the Intensive Care Unit of the Servizio di Anestesia B Dipartimento di Circolo, Varese. His main research interests include respiratory physiology during anaesthesia and acute respiratory failure. Dr Pelosi has developed numerous collaborations with European and extra-European countries for research in the mechanical ventilation field. He is actively involved in the fellow and resident educational programme at the University of Insubria, Varese, and serves also as Co-Fellowship Director. Dr Pelosi is a member of the Board of Directors of the European Society of Anaesthesiology (ESA), Chair of the ESA Research Grant Committee and ESA Nomination Committee and President Elect of the ESA. He is the author or co-author of over 158 medical and scientific peer-reviewed papers and 60 book chapters, and has lectured at more than 730 national and international meetings on ventilation management during the peri-operative period and on the pathophysiology and treatments of acute respiratory failure.

Cesare Gregoretti is Director of Anaesthesia and Intensive Care Services at Maria Adelaide Hospital in Turin. He also lectures in anaesthesia and intensive care at the post-graduate school of the University of Turin and Novara. His main research interests include invasive and non-invasive mechanical ventilation in acute and chronic respiratory failure. Dr Gregoretti is the author or co-author of many medical and scientific peer-reviewed papers and book chapters, and has lectured at major national and international meetings on ventilation management and treatment of acute respiratory failure.