

## Postoperative Pulmonary Complications: An Epidemiological, Risk Factors and Prevention Review

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### Abstract

**Introduction:** Current knowledge suggests that pulmonary complications are a frequent entity in the postoperative period, with special risk after lung surgery. They are associated with high rates of morbidity and mortality and acute respiratory distress syndrome is a common cause of respiratory failure. These complications have a significant impact on the economy with prolonged hospital stay and increased number of hospital readmissions.

**Objectives:** To conduct a non-systematic literature review related to the topic of postoperative pulmonary complications, regarding its epidemiology and clinical impact, modifiable and non-modifiable risk factors and preventive strategies.

**Methods:** Electronic databases such as PubMed, Medline and Google scholar, were used with the keywords listed below. The MeSH terms used were: postoperative complications, acute respiratory distress syndrome and acute lung injury. Accordingly, the review was conducted between the years 2009 and 2015.

**Results:** The etiology of postoperative pulmonary complications is multifactorial. Modifiable risk factors (smoking and drinking habits, respiratory infection in last month, prolonged surgery) or non-modifiable (advanced age, chronic obstructive pulmonary disease, congestive heart failure) may be involved in the development of postoperative pulmonary complications and should be recognized early to assess the patients' risk. Preventive strategies can be instituted pre, intra or postoperatively, acting on modifiable risk factors (such as cessation of alcohol consumption and smoking habits) and optimizing those which are not, by training inspiratory muscles preoperatively or using ventilatory strategies such as low tidal volume and incentive spirometry.

**Conclusion:** The clinical and social consequences of postoperative pulmonary complications are huge and the prevention of its high incidence continues to be a growing challenge. Preventive strategies should be systematically applied in order to achieve better results.

**Keywords:** Postoperative pulmonary complications; Acute respiratory distress syndrome; Risk factors; Prevention

### Introduction

Despite all the medical and surgical technological advances in recent years, postoperative pulmonary complications (PPCs) are the most frequently encountered following lung resections. The incidence of PPCs may vary from 2 to 40%, depending on the context in which they are inserted. These complications are associated with a serious increase in morbidity and mortality, having a significant influence on the economy with long periods of hospitalization or hospital readmissions [1-3]. The Acute Respiratory Distress Syndrome (ARDS) is a heterogeneous entity with complex pathology that can have multiple etiologies [4,5]. In the postoperative period it has an incidence estimated at approximately 3% and it is a common cause of respiratory failure [6]. The identification of those patients who are at risk of developing PPCs becomes thus an important step in reducing the future population of these comorbidities [7]. PPCs can result from

the interaction of various risk factors, whether related to the patient or the procedure [8]. The study of these risk factors and therefore the stratification of patients are fundamental measures to predict complications, although it is a difficult task to predict whether a patient will develop them [1,9]. Prevention of PPCs is one of the most important goals of treatment of surgical patients, and preventive strategies can be implemented pre, intra or postoperatively, although some of them can be better supported by evidence [3,8,10]. This review is intended to assess the epidemiology, risk factors and prevention strategies PPCs, with discussion of issues that have proved more controversial.

### Methods

The bibliography used in this review was searched in electronic databases such as PubMed, Medline and Google scholar, using the keywords postoperative pulmonary complications, acute respiratory distress syndrome, risk factors, prevention. The MeSH terms were used postoperative complications, acute respiratory distress syndrome and

acute lung injury. Accordingly, a review was conducted between the years 2009 and 2015.

## Results

### Epidemiology

The PPCs incidence rate varies widely from 2 to 40%, differing from hospitals and procedures, and may reach values as high as 48%. The incidence of these events is much higher in thoracic surgery (37.8%), in comparison to upper abdominal (12.2%) or peripheral surgeries (2.2%) [3].

These PPCs are associated with increased mortality and serious morbidity, increased length of stay, increased number of admissions to the Intensive Care Unit (ICU) and therefore to higher costs [3,7,11]. In fact, the costs of PPCs can double or increase up to twelve times [3].

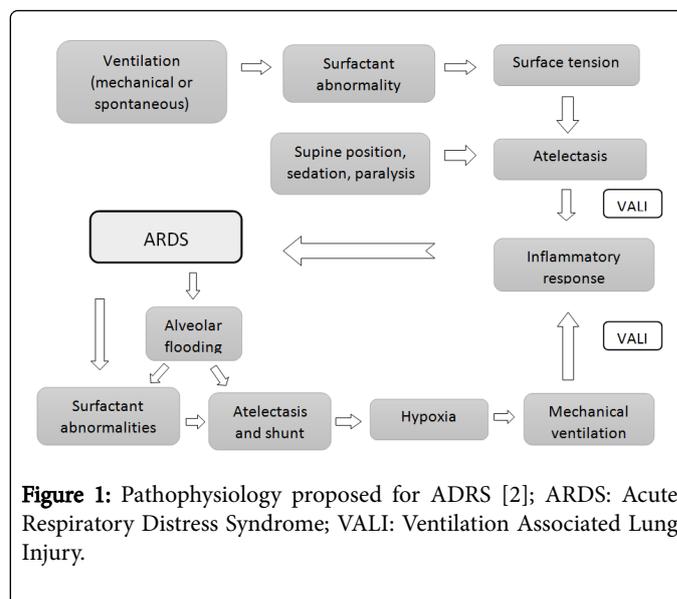
ARDS, which was last set in 2012 by the Berlin Consensus, is a clinical syndrome that has different events in its pathogenesis and it develops in patients with predisposing conditions [5,6] (Table 1). It has an approximate incidence in postoperative of about 3%, representing a frequent cause of lethal respiratory failure (35%) [6].

Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
Chest Imaging <sup>a</sup>	Bilateral opacities – not fully explained by effusions, lobar/lung collapse or nodules
Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g. echocardiography) to exclude hydrostatic edema if no risk factor present
Oxygenation <sup>b</sup>	Mild - $200 \text{ mm Hg} < \text{PaO}_2/\text{FiO}_2 \leq 300 \text{ mm Hg}$ with PEEP or CPAP $\geq 5 \text{ cm H}_2\text{O}$
	Moderate - $100 \text{ mm Hg} < \text{PaO}_2/\text{FiO}_2 \leq 200 \text{ mm Hg}$ with PEEP $\geq 5 \text{ cm H}_2\text{O}$
	Severe - $\text{PaO}_2/\text{FiO}_2 \leq 100 \text{ mm Hg}$ with PEEP $\geq 5 \text{ cm H}_2\text{O}$
CPAP: Continuous Positive Air Pressure; FiO <sub>2</sub> : Fraction of Inspired Oxygen; PaO <sub>2</sub> : Partial Pressure of Arterial Oxygen; PEEP: Positive End-Expiratory Pressure. <sup>a</sup> Chest radiograph or computed tomography scan. <sup>b</sup> If altitude is higher than 1000m, the correction factors should be calculated as follow ( $\text{PaO}_2/\text{FiO}_2 \times (\text{barometric pressure}/760)$ ). <sup>c</sup> This may be delivered noninvasively in the mild acute respiratory distress syndrome group.	

**Table 1:** The Berlin definition for ARDS adapted from [1].

### Risk factors

There are many risk factors associated with the development of an acute lung injury and it may be assumed a multifactorial theory to their appearance [10] (Figure 1).

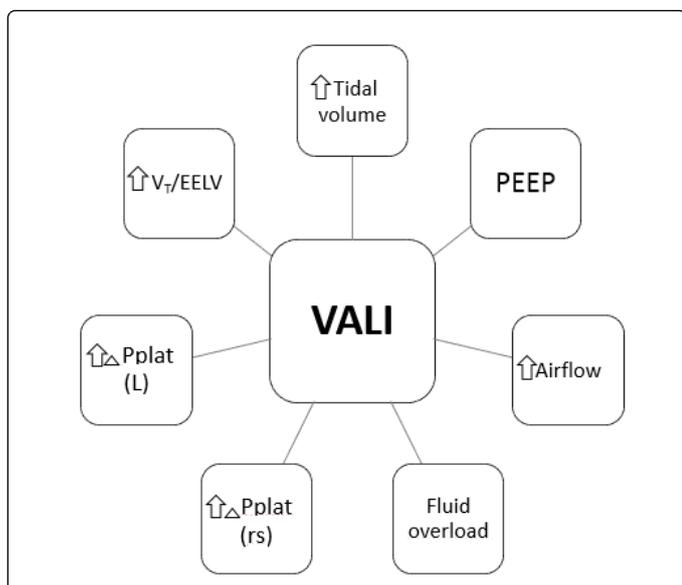


**Figure 1:** Pathophysiology proposed for ARDS [2]; ARDS: Acute Respiratory Distress Syndrome; VALI: Ventilation Associated Lung Injury.

### Factors related to the procedure

Mechanical ventilation, or artificial positive pressure ventilation is often essential to ensure oxygenation in patients during general anesthesia, on the other hand, it can lead to Ventilation Associated Lung Injury (VALI) [10]. This phenomenon is a well-recognized pulmonary complication that can exacerbate lung disease or make it appear in healthy lungs [12,13]. Pathological changes can occur by direct effect of high lung pressure -barotrauma-, by pulmonary distension -volutrauma-, by repetitive cycles of inflation and alveolar collapse-atelectotrauma or by activating cytokines that trigger the inflammatory cascade-biotrauma [14-16]. Several variables are therefore responsible for the development VALI [17] (Figure 2).

VALI occurs frequently in patients undergoing one-lung ventilation (OLV) and therefore the latter is another important predictor of PPCs. It is required in thoracic surgical procedures where there is exclusion from the respiratory activity of a lung to facilitate surgical approach [8]. Because only one lung being ventilated (baby lung), but both perfused, a change in ventilation/perfusion arises and it may be associated with hypoxemia [8,18]. Thus, it is important that the fraction of inspired oxygen (FiO<sub>2</sub>) ensures effective oxygenation but it is only necessary because the formed oxygen free radicals can sustain lung inflammation [19]. It is known that the greater the length of the OLV and the resection area, the greater the oxidative damage and inflammatory response [20]. Some recent laboratory studies in animal models show that even in spontaneous breathing, either supplemental oxygen ventilation bipulmonary [21] or OLV per se [22] are factors associated with a more intense lung inflammatory response.



**Figure 2:** Variables associated with VALI [5]; EELV: End-Expiratory Lung Volume; PEEP: Positive End-Expiratory Pressure; Pplat(L): Changes in Lung Plateau Pressure; Pplat(rs): Changes in Respiratory System Plateau Pressure; VALI: Ventilation-Associated Lung Injury.

A major lung surgery is usually associated with a systemic inflammatory response induced by surgical trauma, such as in lung resection [8]. Emergency procedures and surgeries lasting more than three hours are both risk factors consistently mentioned [3,23]. Some authors stated that laparoscopic surgery has a decreased risk of PPCs in comparison to conventional surgery [3]. However, Cook et al. say it is not clear that it lowers the risk, but only that the recovery is faster [23].

**Risk factors related to the patient**

In addition to the risk associated with surgery, individual conditions play a key role in the PPCs [8].

A study by Agostini et al. showed five significant risk factors: over 75 years old, body mass index (BMI) greater than 30 kg/m<sup>2</sup>, classification according to the American Society of Anesthesiology (ASA) ≥3, smoking and Chronic Obstructive Pulmonary Disease (COPD), and that the higher the severity of COPD, the greater the risk of PPCs [1,23,24]. Smoking and drinking habits have been associated with PPCs in several investigations as significant morbidity factors [3,25]. In fact, chronic alcohol consumption has been shown to be one of the most important risk factors in the PPCs [8].

The low weight or recent weight loss and low serum albumin are directly related to the nutritional status and the risk of developing PPCs. Alone, obesity is not a significant risk factor except in certain types of surgery, if morbid or comorbidities associated with obesity.

In a prospective study by Canet et al. [7] anemia, which may increase the risk in three times, and low preoperative O<sub>2</sub> saturation were identified as PPCs predictors, the latter being for the first time reported as a risk factor.

The upper respiratory infection in the month prior to surgery increases bronchial reactivity and the risk of broncho and laryngospasm, and is also a predisposing factor for the development of these complications, as well as congestive heart failure [3,7,11].

Genetic factors have been proposed in recent studies as having a role in development of PPCs. Genes encoding angiotensin converting enzyme (ACE), the surfactant protein B, and myosin light chain kinase and a factor of macrophage migration inhibitory appear to be involved in this phenomenon [8].

Table 2 presents risk factors classified by the American College of Physicians (ACP) [3].

Non-modifiable patient-related factors	Non-modifiable procedure-related factors	Non-modifiable preoperative testing
Congestive heart failure	High risk procedures: aortic aneurysm, thoracic, upper abdominal, abdominal, neurosurgery, vascular, head and neck	Genetic variations
ASA ≥3	Procedures with high risk for ALI/ARDS	Alterations in chest radiograph
Advanced age	Procedures with high risk for UEPI	High blood urea
COPD	Emergency surgery	
Functional dependence		
Impaired sensorium		
GERD		
Diabetes mellitus		
Obstructive sleep apnea		
Hypertension		
Liver disease		
Cancer		

ALI: Acute Lung Injury; ARDS: Acute Respiratory Distress Syndrome; ASA: American Society of Anesthesiologists; COPD: Chronic Obstructive Pulmonary Disease; GERD: Gastro Esophageal Reflux Disease; SpO<sub>2</sub>: Oxygen saturation as measured by Pulse Oximetry; UEPI: Unanticipated Early Postoperative Intubation

**Table 2:** Risk factors classified by American College of Physicians [6].

**Prevention Strategies**

**Preoperative**

Prior to surgery, one of the goals is to identify and act on risk factors, for the stratification of patients [8].

Preoperative strategies include the delay surgery if there was a respiratory infection in the previous month, the cessation of alcohol consumption (more than two weeks) and smoking habits [3]. About the latter, it was shown that long periods of smoking cessation before

surgery largely reduce PPCs compared to shorter periods [26]. Reducing the frequency of these complications cannot be detected if the withdrawal period does not exceed two months [1]. For patients with a history of smoking or dyspnea undergoing a cardiac surgery, upper abdominal or pulmonary resection, it is recommended to perform spirometry [27]. Still, patients with COPD may benefit from the training of preoperative inspiratory muscles and removal of airway secretions in high-risk patients [8].

Anemia can be modified pre operatively using drug therapy, although the cut-point of the hemoglobin value that confers increased risk is not properly identified [3]. The level of albumin should be measured in patients suspected of having hypoalbuminemia, but the total parenteral or enteral nutrition for patients who are malnourished or have low serum albumin levels should not be used alone [11].

A recent study identified predisposing conditions for ARDS, validating a model to identify patients at high risk of developing ARDS at admission. Thus Lung Injury Score Prediction (LIPS) appeared (Table 3) where a cutoff at least 4 indicates a positive predictive value of 18% and negative of 97%. Although the predictive accuracy is not ideal, the LIPS is involved in other clinical trials for the prevention of ARDS, as LIPS-A - Lung Injury Prevention Study with Aspirin and LIPS-B - Lung Injury Prevention Study With budesonide and Beta Agonist formeterol. Several models have been suggested, but in most of them, the diversity of the population is high, which can result in large variability and the predictive accuracy decreases [6].

### Intraoperative

Lately, an important progression is represented by Chang the basic mechanical respiratory support for protective ventilation or ultra-protective [28].

### Protective ventilation strategies

Good strategy ventilation should offer the best possible blood oxygenation, limiting lung injury [8].

Investigations suggested a form of protection VALI with low tidal volume (VT) and/or high levels of positive end-expiratory pressure (PEEP), reducing the incidence of pulmonary dysfunction in the postoperative period and providing satisfactory gas exchange [15,16,29].

Several meta-analyzes showed that the protective ventilation with low VT reduces VALI, it is beneficial in patients who require long term ventilation ARDS, as well as for patients without ARDS [15]. Some data show that a reduction in VT to values near the physiological volumes decreases lung inflammatory response, as well as the mortality rate of patients with ARDS. However, controversy exists when one questions the volume that should be used [8,17,28]. The study Acute Respiratory Distress Network (ARDnet) showed a reduced mortality of 22%, which can be obtained with the use of VT 6 ml/kg ideal weights, instead of 12 ml/kg [28]. Actually, the use of VT of 10 ml/kg of ideal body weight raises atelectrauma markers and barotrauma [30].

Moreover, PEEP helps keep the alveoli open in the end of expiration, promoting oxygenation and preventing atelectasis [8]. The value of PEEP should be minimized to prevent hemodynamic changes and lung over-distention, but should be high enough to induce cellular recruitment [17,31]. Meta-analysis showed that there is a reduction in hospital mortality with the use of high levels of PEEP compared to low levels in patients with PaO<sub>2</sub>:FiO<sub>2</sub><200 mm Hg [28]. The application of

PEEP will be in accordance with the classification of ARDS, according to Berlin Definiton, with higher PEEP levels being applied, when the severity of the syndrome is higher: 5-10 cm H<sub>2</sub>O PEEP in patients with mild ARDS, 10-15 cm H<sub>2</sub>O in patients with moderate and 15-20 cm H<sub>2</sub>O in patients with severe [32,33]. Although Gattinoni et al. state that the better the PEEP, the better the oxygenation, they also say that the best PEEP does not exist [32]. In addition to these benefits, Hedenstierna reports its negative effects which are the collapse of the alveoli after discontinuation and the reduction in cardiac output, since this prevents venous return [34].

Predisposing conditions		LIPS points
Shock		2
Aspiration		2
Sepsis		1
Pneumonia		1.5
High risk surgery	Orthopedic spine	1
	Acute abdomen	2
	Cardiac	2.5
	Aortic vascular	3.5
High risk trauma	Traumatic brain	2
	Smoke inhalation	2
	Near drowning	2
	Lung contusion	1.5
	Multiple fractures	1.5
Risk modifiers		LIPS points
Alcohol abuse		1
Obesity (BMI>30)		1
Hypoalbuminemia		1
Chemotherapy		1
FiO <sub>2</sub> >0.35 (>4 L/min)		2
Tachypnea (RR>30)		1.5
SpO <sub>2</sub> <95%		1
Acidosis (pH<7.35)		1.5
Diabetes mellitus		-1
FiO <sub>2</sub> : Fraction inspired oxygen concentration RR: respiratory rate SpO <sub>2</sub> : Oxygen saturation by pulse oximetry; <sup>a</sup> Add 1.5 points if emergency surgery; <sup>b</sup> Only if sepsis present.		

**Table 3:** Lung Injury Prediction Score (LIPS)[2].

Permissive hypercapnia is often used as ventilatory strategy in patients with severe respiratory failure [35]. In this phenomenon, the increase of arterial CO<sub>2</sub> is accepted to minimize VALI and it has demonstrated better results in ARDS. Permissive hypercapnia has multiple effects in the lungs, heart and brain. In the lungs, moderate hypercapnia improves ventilation/perfusion through high CO<sub>2</sub> alveolar

pressure and increased parenchymal compliance and, on the other hand, increases alveolar surfactant secretion. Also, it decreases pulmonary vascular resistance and improves the function of the right ventricle. However, there are no clinical trials that show the direct effect of hypercapnia in patients with ARDS [35].

During OLV it is important to prevent atelectasis in the non-surgically approached lung, a phenomenon that already occurs in the other lung. Thus, some authors argue that the VT will be used wider (10 mg/kg) to reduce the likelihood of lung shunt, despite certain inflammatory markers may increase in both lungs [36,37]. Moreover, given the weakness of the ventilated lung -baby lung-, the use of too high VT may cause mechanical damage in this lung [18]. Other strategies to minimize the consequences of OLV reside in the correct use of a double-lumen endotracheal tube and sevoflurane, a general anesthetic that somehow modulates this effect [8,38]. The body pronation can also help minimize VALI in different ways [28]. Regarding the value of fraction of inspired O<sub>2</sub> (FiO<sub>2</sub>), this should be as low as possible but enough to promote a satisfactory peripheral O<sub>2</sub> saturation [8].

Together, these strategies favor a system of "open lung" in the intraoperative period, in which the PPCs reduction would be significant [28,39].

### Ultra protective ventilation strategies

When mechanical ventilation becomes unsafe, the extracorporeal support can be introduced [18]. Body techniques such as extracorporeal membrane oxygenation (ECMO) and extracorporeal removal of CO<sub>2</sub> (ECCO<sub>2</sub>R) promote adequate gas exchange in patients with ARDS. Theoretically, all patients receiving ventilatory support would benefit from non-invasive strategies [28]

It was studied the clinical efficacy, safety and cost-effectiveness of ECMO compared to conventional ventilation in the study Conventional Ventilation or ECMO for Severe Adult Respiratory Failure (CESAR). There was a significant improvement in survival without severe disability at 6 months in patients who were transferred to a specialised in this technic center. This result was attributed to the fact that ECMO have supported the patient's life in an acute lung failure during more time, permitting diagnosis, treatment and recovery [18,28].

The use of low VT can lead to increased PaCO<sub>2</sub> and pH reduction where ECCO<sub>2</sub>R can be a solution to this problem [40]. These devices have been developed to offer less resistance to blood flow and are increasingly available [35,40]. ECCO<sub>2</sub>R facilitates lung protective ventilation, allowing a greater reduction in VT [35]. In fact, researchers demonstrate the feasibility of combining ECCO<sub>2</sub>R with VT 3ml/kg and report that ventilation with very low tidal volumes is feasible, safe and easy to implement with this technique [35,40,41].

Although they have promising benefits, strategies in patients with ARDS still require confirmation in clinical trials [28].

### Postoperative

As well as some of the previous, postoperative strategies lack any scientific evidence. A program postoperatively organized by the Pulmonary Care Working Group, appointed by the acronym I COUGH, which means Incentive spirometry, Coughing and deep breathing, Oral care, Understanding (patient and family education), Getting out of bed frequently and Head-of-bed elevation reduced the

incidence of postoperative pneumonia, as well as unplanned intubation.

Deep breathing exercises, incentive spirometry and electrical neuromuscular stimulation can improve gas exchange, the quality of life and a shorter postoperative hospitalization [3]. Still, for postoperative nausea and vomiting can be used a nasogastric tube [11]

In Table 4 is summarized possible techniques to reduce pulmonary complications according to several authors. Table 4: Possible techniques to reduce pulmonary complications adapted from [3,8,11,27-29,35].

Preoperative	Intraoperative	Postoperative
Smoking cessation	Low VT and/or high PEEP	Incentive spirometry
Delay surgery if there was respiratory infection in last month	Permissive hypercapnia	Deep breathing exercises
Alcohol cessation	Body pronation	Nasogastric tube (for nausea and vomiting)
Spirometry <sup>1</sup>	Enough FiO <sub>2</sub>	Electrical neuromuscular stimulation
Training of inspiratory muscles <sup>2</sup>	ECMO	
Serum albumin measurement <sup>3</sup>	ECCO <sub>2</sub> R	
Hemoglobin measurement	Higher VT during OLV	

ECMO: Extracorporeal Membrane Oxygenation; ECCO<sub>2</sub>R: Extracorporeal Removal of CO<sub>2</sub>; OLV: One-Lung Ventilation; PEEP: Positive End-Expiratory Pressure; VT: Tidal Volume. <sup>1</sup>For patients with a history of smoking or dyspnea undergoing a cardiac surgery, upper abdominal or pulmonary resection; <sup>2</sup>in patients with COPD; <sup>3</sup>in patients suspected of having hypoalbuminemia

Table 4: Possible techniques to reduce pulmonary complications.

### Discussion

Hereunder, topics that have been observed as the most controversial in literature review will be presented for discussion, namely: The Berlin Definition, PEEP level and Tidal Volume.

	Score				
	0	1	2	3	4
Chest X-ray, number of quadrants	None	1	2	3	4
Oxygenation, P/F ratio	≥300	225-299	175-224	100-174	<100
PEEP, cm H <sub>2</sub> O	≤5	6-8	9-11	12-14	≥15
Lung compliance, ml/cm H <sub>2</sub> O	≥80	60-79	40-59	20-39	≤19

PEEP: Positive End-Expiratory Pressure.

Table 5: Lung Injury Score [3].

### Berlin definition

In 1988, a definition for acute lung injury (ALI) and ARDS (Table 5) was proposed, consisting of 4 different scales punctuated from 1 to 4. The definition also included the presence or absence of risk factors and non-pulmonary dysfunction. The ARDS was defined as a score higher than 2.5 [42]. Table 5: Lung Injury Score adapted from [42].

Another ALI and ARDS settings was made in 1994 by the American European Consensus Conference (AECC) (Table 6), in an attempt to standardize and clarify both [42]. Although researchers have known that PEEP could affect oxygenation, they decided not to include this as a criterion, because they considered that the response to PEEP was not consistent and was time-dependent [42]. Table 6: Criteria for ALI and ARDS by the AECC adapted from [43].

	Timing	Oxygenation	Radiological abnormalities	Pulmonary artery wedge pressure
ALI	Acute onset	≤ 300 regardless of PEEP	Bilateral infiltrates on frontal chest radiograph	≤ 18 mm Hg when measured or no clinical evidence of left atrial hypertension
ARDS	Acute onset		Bilateral infiltrates on frontal chest radiograph	≤ 18 mm Hg when measured or no clinical evidence of left atrial hypertension

ALI: Acute Lung Injury; ARDS: Acute Respiratory Distress Syndrome

**Table 6:** Criteria for ALI and ARDS [4].

This definition was accepted, however, aspects of the AECC criteria began to emerge, notably the lack of explanation for what is defined as acute and the value of the cutoff of PaO<sub>2</sub>/FiO<sub>2</sub> selected [42] [5] (Table 7). On the other hand, the existence of a broad category designated

ALI brought some confusion, because patients with ARDS (PaO<sub>2</sub>/FiO<sub>2</sub> ≤ 200 mm Hg) or less critical illness (200 mm Hg < PaO<sub>2</sub>/FiO<sub>2</sub> ≤ 300 mm Hg) were covered by this definition. Generally, the professionals used the term ALI for patients with ALI without ARDS [42].

	AECC Definition	AECC Limitations	Addressed in Berlin Definition
Timing	Acute onset	No definition of acute	Acute time frame specified
ALI category	All patients with PaO <sub>2</sub> <300 mm Hg	Misinterpreted as PaO <sub>2</sub> / FiO <sub>2</sub> =201-300 leading to confusing ALI/ARDS term	3 mutually exclusive subgroups of ARDS by severity ALI term removed
Oxygenation	PaO <sub>2</sub> /FiO <sub>2</sub> ≤ 300 mm Hg (regardless of PEEP)	Inconsistency of PaO <sub>2</sub> /FiO <sub>2</sub> ratio due to the effect of PEEP and/or FiO <sub>2</sub>	Minimal PEEP level added across subgroups; FiO <sub>2</sub> effect less relevant in severe ARDS group
Chest radiograph	Bilateral infiltrates observed on frontal chest radiograph	Poor inter-observer reliability of chest radiograph interpretation	Chest radiograph criteria clarified; example radiographs created
PAWP	≤18 mm Hg when measured or no clinical evidence of left atrial hypertension	High PAWP and ARDS may coexist; poor inter-observer reliability of PAWP and clinical assessments of left atrial hypertension	PAWP requirement removed; Hydrostatic edema not the primary cause of respiratory failure; Clinical vignettes created to help exclude hydrostatic edema
Risk factor	None	Not formally included in definition	Included; When none identified, need to objectively rule out hydrostatic edema

AECC: American European Consensus Conference; ALI: Acute Lung Injury; ARDS: Acute Respiratory Distress Syndrome; FiO<sub>2</sub>: Fraction Of Inspired Oxygen; PaO<sub>2</sub>: Arterial Pressure Of Oxygen; PAWP: Pulmonary Artery Wedge Pressure; PEEP: Positive End-Expiratory Pressure

**Table 7:** The AECC Definition- Limitations and methods to address these in the Berlin Definition [1].

In 2012, a new definition - the Berlin Definition - suggested by the European Society of Intensive Care Medicine emerged to help address these limitations of reliability and validity of AECC [5] (Table 7). In short, the authors claim that the current Berlin definition brought improvements and simplification compared to the previous one, with better predictive validity for mortality [5,42]. Despite this improved validity, the overall incidence of morbidity and mortality rates have not changed substantially since 2012 [44,45]. In fact, in Europe, the incidence of ARDS has not changed significantly over the past decade [45]. Table 7: The AECC Definition - Limitations and methods to address these in the Berlin Definition adapted from [5].

### PEEP

In 1938, Barach et al. described the physiology of the PEEP and its use has been widespread in the clinical by Gregory et al., becoming routine in the treatment of ARDS. In the 90s the concept of PEEP emerged as lung protective strategy, which is based in the idea of "open the lung and keep it open," to prevent lung collapse [32].

Initially, the experiments that compared the administration of low and high levels of PEEP in ARDS patients showed no differences in mortality [28].

Downs et al. have suggested that PEEP value should be so high as to obtain a PaO<sub>2</sub> ideal value, but without hemodynamic instability. Later, this led to Kirby et al. to recommend very high levels of PEEP (as 60

cm H<sub>2</sub>O) to decrease the shunt, which culminated in lung distension [33].

The PEEP as protective mechanical ventilation started with Webb and Tierney, who reported that rats ventilated with PEEP of 45 cm H<sub>2</sub>O for an hour suffered fulminant lung injury, rats ventilated with 30 cm H<sub>2</sub>O had an intermediate lung injury and those ventilated with 14 cm H<sub>2</sub>O did not suffered injury [32,46].

Many approaches have been proposed to select the most appropriate PEEP value and, in general, it was found that hypoxemia rates were lower when higher levels of PEEP were used [28,33]. Currently, the selection of the PEEP can be taken according to the severity of ARDS, as mentioned [32,33].

### Tidal volume

The combination of high VT of 12-15 ml/kg ideal weight with a 5-10 cm H<sub>2</sub>O PEEP was advised in 1970 to prevent hypoxemia and atelectasis [18,29]. Moreover, high tidal volumes showed, in the past, improved oxygenation and reduced shunt [14].

With the evolution of knowledge, investigations show that higher VT in patients with ARDS and VALI would be associated with the worsening of a pre-existing lung injury, with development of new injury and also with an increased mortality [29,47]. Another series of studies indicate that low VT are related with decrease of inflammatory mediators and PPCs, being accepted in general, the amount of 6 ml/kg of ideal weight [14,18].

After several years it is suggested that the use of low VT and sufficient levels of PEEP help to protect VALI [13,15,39].

### Study limitations

The Berlin definition adopted a single entity that describes the imbalance of the expected oxygenation regarding a determined inspired oxygen fraction. The acute lung injury notion has been outdated and a three level of gravity ARDS has been assumed. Since no randomized controlled studies using this definition solely have been published, this review may experience some limitation due to this fact. Clearly, further studies are dimly necessary to confirm previous assumptions on this topic.

### Conclusion

The PPCs add morbidity and mortality to surgical patients, essentially after lung surgery, with important clinical and economic impacts. ARDS is a serious complication after surgery and despite the Berlin definition it remains an arduous task to predict their appearance individually.

Several risk factors related to the patient or the procedure, modifiable and non-modifiable, contribute to the development of the PPCs. The prevention of these has been increasingly recognized and strategies can be performed in the preoperative, intraoperative or postoperative period, which are associated with a reduced incidence of PPCs.

Given the epidemiological, clinical and economic relevance of these complications, it will be of great importance, in the future, to systematically implement preventive strategies to reduce its occurrence, particularly with an early detection and action on modifiable risk factors.

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