

# Respiratory complications in the postanesthesia care unit: A review of pathophysiological mechanisms

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General anesthesia and mechanical ventilation impair pulmonary function, even in normal individuals, and result in decreased oxygenation in the postanesthesia period. They also cause a reduction in functional residual capacity of up to 50% of the preanesthesia value. It has been shown that pulmonary atelectasis is a common finding in anesthetized individuals because it occurs in 85% to 90% of healthy adults. Furthermore, there is substantial evidence that atelectasis, in combination with alveolar hypoventilation and ventilation-perfusion mismatch, is the core mechanism responsible for postoperative hypoxemic events in the majority of patients in the postanesthesia care unit (PACU). Many concomitant factors also must be considered, such as respiratory depression from the type and anatomical site of surgery altering lung mechanics, the consequences of hemodynamic impairment and the residual effects of anesthetic drugs, most notably residual neuromuscular blockade. The appropriate use of anesthetic and analgesic techniques, when combined with meticulous postoperative care, clearly influences pulmonary outcomes in the PACU. The present review emphasizes the major pathophysiological mechanisms and treatment strategies of critical respiratory events in the PACU to provide health care workers with the knowledge needed to prevent such potentially adverse outcomes from occurring.

**Key Words:** *Alveolar hypoventilation; Atelectasis; Postanesthesia care unit; Pulmonary shunt; Respiratory complications; Ventilation-perfusion mismatch*

Respiratory complications in the postanesthesia period are an important area of concern because they are a major cause of morbidity and mortality. A critical respiratory event in the postanesthesia care unit (PACU) is the complex of major unanticipated ventilation problems, including hypoxemia (hemoglobin oxygen saturation <90%), hypoventilation (respiratory rate <8 breaths/min or arterial carbon dioxide [CO<sub>2</sub>] tension >50 mmHg) or upper-airway obstruction (laryngospasm or stridor), that require a physical or pharmacological intervention (eg, insertion of an oral/nasal airway, ventilation, tracheal intubation, opioid antagonism, muscle relaxant reversal) (1).

There is large variation in the incidence of critical respiratory events in the PACU, with several prospective observational studies reporting an incidence of between 0.8% and 6.9% (1-5). Multiple factors, including surgical, anesthetic and patient variables, contribute to the etiology of postoperative respiratory complications (2-4). Surgical risk factors include emergency surgery, long duration of surgery and type of surgery (2,4). Anesthetic causes include the use of opioids, neuromuscular blocking drugs and general anesthesia (2). Patient risk factors include chronic obstructive pulmonary disease (COPD), diabetes, obesity and nonmodifiable risk factors such as advanced age and male sex (2-4). The present article reviews the major mechanisms causing deterioration in gas exchange during the immediate postoperative period, the effects of anesthetic pharmacology and measures to improve oxygenation relevant to clinical practice.

## RISK FACTOR OVERVIEW AND CLINICAL GUIDELINE

Respiratory complications are as common as cardiac complications following noncardiac surgery in the PACU and beyond. Fleischmann

## Les complications respiratoires à l'unité de soins postanesthésiques : une analyse des mécanismes physiopathologiques

L'anesthésie générale et la ventilation mécanique nuisent à la fonction pulmonaire, même chez des personnes en santé, et entraînent une diminution de l'oxygénation pendant la période postanesthésique. Elles provoquent également une réduction de la capacité fonctionnelle résiduelle pouvant atteindre 50 % de la valeur obtenue avant l'anesthésie. Il a été démontré que l'atélectasie pulmonaire est courante chez les personnes anesthésiées. En effet, elle se produit chez 85 % à 90 % des adultes en santé. De plus, il est clairement démontré que l'atélectasie, associée à l'hypoventilation alvéolaire et à la discordance entre la ventilation et la perfusion, est le principal mécanisme responsable d'événements hypoxémiques postopératoires chez la majorité des patients de l'unité de soins postanesthésiques (USPA). Il faut également tenir compte de nombreux facteurs concomitants, tels que la dépression respiratoire causée par le type et le foyer anatomique des mécanismes pulmonaires modifiés par chirurgie, les conséquences d'une atteinte hémodynamique et les effets résiduels des médicaments anesthésiques, notamment le blocage neuromusculaire résiduel. Le recours pertinent aux techniques anesthésiques et analgésiques, associé à des soins postopératoires méticuleux, influe clairement sur les issues pulmonaires à l'USPA. La présente analyse fait ressortir les principaux mécanismes physiopathologiques et stratégies thérapeutiques d'événements respiratoires critiques à l'USPA pour transmettre aux dispensateurs de soins les connaissances nécessaires en vue d'éviter la survenue d'issues indésirables.

et al (6) found that the incidence of respiratory events was highly comparable with that of cardiac complications (2.7% versus 2.5%). However, they differ from cardiac complications in that surgical- and anesthesia-related factors are more predictive of respiratory complications than are patient-related factors (6).

The 2006 American College of Physicians (ACP) clinical guideline on risk assessment for and strategies to reduce perioperative respiratory complications in patients undergoing noncardiothoracic surgery (7-9) assigned letter grades to the risk factors based on the strength of evidence (Table 1). According to this guideline, surgical site was found to be the most important of any of the procedure- or patient-related risk factors, and the closer the incision is to the diaphragm, the greater the risk for postoperative respiratory complications (8). When considering the different types of procedures, thoracic, abdominal and aortic surgeries carry the highest risk (8). Furthermore, upper abdominal surgery carries a greater risk than lower abdominal surgery among abdominal procedures (8). Good evidence also supports the procedure-related risk factors of prolonged surgery and emergency surgery (8).

The most important of the patient-related risk factors identified in the ACP guideline are increasing age and increasing American Society of Anesthesiologists classification of comorbidity (8). The effect of advanced age becomes particularly notable at approximately 60 years of age and worsens from there (8). Of note, smoking and COPD were only minor risk factors in the ACP analysis (8).

A serum albumin level <35 g/L is the most powerful predictor among potential laboratory tests to stratify risk, and predicts risk to a similar degree as the most important patient-related risk factors (8).

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**TABLE 1**  
**Strength of evidence for association of risk factors with postoperative respiratory complications**

Level of evidence	Risk factor		
	Patient related	Procedure related	Laboratory tests
A (Good)	ASA class $\geq 2$	Thoracic surgery	Albumin level $<35$ g/L
	Cardiac failure	Abdominal surgery	
	Advanced age	Upper abdominal surgery	
	Functional dependence	Aortic aneurysm repair	
	Chronic obstructive pulmonary disease	Neurosurgery	
		Prolonged surgery	
		Emergency surgery	
		Vascular surgery	
		Head and neck surgery	
		General anesthesia	
B (Fair)	Impaired sensorium	Perioperative transfusion	Chest radiography
	Cigarette use		BUN level $>7.5$ mmol/L ( $>21$ mg/dL)
	Alcohol use		
	Weight loss		
	Abnormal findings on chest examination		

Table adapted from reference 8. ASA American Society of Anesthesiologists; BUN Blood urea nitrogen

### DIFFERENTIAL DIAGNOSIS OF ARTERIAL HYPOXEMIA IN THE PACU

There are several factors that can contribute to arterial hypoxemia in the immediate postoperative period (10). The most important mechanisms will be discussed at length.

#### Atelectasis

Atelectasis causes pulmonary shunt and, therefore, undoubtedly contributes to the impairment of gas exchange during general anesthesia. According to Lundquist et al (11), 20% to 25% of the lung tissue in basal regions or approximately 15% of the entire lung may be atelectatic in adults with healthy lungs, resulting in true pulmonary shunt.

A pulmonary shunt of 5% to 10% of cardiac output is found in adults during general anesthesia with mechanical ventilation (12,13). Although shunt does not increase with age, regions with poor ventilation in relation to their perfusion show a dependency on age (12). Furthermore, larger atelectatic areas are present in obese patients whereas patients with COPD may show less or even no atelectasis (14). Atelectasis appears immediately with induction of anesthesia and is present after muscle paralysis and during spontaneous breathing regardless of whether inhalational or intravenous anesthetics are used (11,15). The use of ketamine is the only exception to this rule (16).

Three possible mechanisms may cause atelectasis including gas resorption, impaired function of surfactant and compression atelectasis (17-19).

It has been shown that a lung unit will ultimately collapse if it is not ventilated (20). Hence, lung collapse may occur if induction of anesthesia results in an increased number of lung units with poor or no ventilation, and if such lung units are filled with an easily resorbed gas (21). Even short periods of breathing 100% oxygen near the residual volume may cause atelectasis (22). Therefore, if there is a concomitant increase in low ventilation/perfusion (V/Q), an increased inspired fraction of oxygen ( $FiO_2$ ) may promote the formation of atelectasis (23,24).

It is known, however, that there may be a decreased content of active forms of alveolar surfactant due to a lack of intermittent deep breaths, as is usual during mechanical ventilation (25). Furthermore, anesthesia and atelectasis per se may impede the function of surfactant (26). Such decreased function results in reduced alveolar stability and causes alveolar collapse. It may also contribute to liquid bridging in the airway lumen and cause airway closure (27).

The end-expiratory intrathoracic pressure is normally lower than the abdominal pressure because the diaphragm separates two spaces

with different pressures as well as vertical pressure gradients. In an awake patient, the vertical pressure gradient in the pleural space is  $0.2$  cmH<sub>2</sub>O/cm to  $0.4$  cm H<sub>2</sub>O/cm, whereas this gradient approximates  $1$  cm H<sub>2</sub>O/cm in the abdomen (28). This abdominal pressure will be transferred into the thoracic cavity if the diaphragm no longer acts as a rigid wall between these two spaces, thus increasing the pleural pressure in dependent lung regions. This process could result in compression atelectasis. This was indirectly reflected in a study by Tokics et al (16), who showed that no atelectasis developed during anesthesia with ketamine, a drug known to maintain respiratory muscle tone and rib cage function. Furthermore, several studies (29,30) showed a cephalad shift of the diaphragm with anesthesia and muscle paralysis.

The attenuation of hypoxic pulmonary vasoconstriction (31,32) may further contribute to impairment in gaseous exchange by increasing pulmonary shunt (because atelectasis is present throughout anesthesia). This effect may be apparent with the inhalational anesthetics (33) but is less prominent or even absent with intravenous anesthetics (33). Such an effect does not cause any disturbances in an otherwise normally functioning lung and is only relevant in the setting of V/Q mismatch or pulmonary shunt.

In summary, atelectasis is found in 85% to 90% of anesthetized adults, appears immediately after induction of general anesthesia and primarily causes pulmonary shunt (11). Two mechanisms most commonly involved in the perioperative formation of atelectasis are compression and resorption. The early formation of atelectasis and the increase in pulmonary shunt are unavoidable adverse effects of anesthesia leading to respiratory complications in the postanesthesia period (34).

#### Alveolar hypoventilation

CO<sub>2</sub> retention is the hallmark of hypoventilation and is always present. Review of the alveolar gas equation according to West (34) indicates that partial pressure of oxygen ( $PaO_2$ ) is both directly and inversely proportional to alveolar ventilation; therefore, when patients breath room air while hypoventilating, hypoxia results secondary to an increase in alveolar CO<sub>2</sub>. Furthermore, hypoxemia of pure hypoventilation can be readily improved by increasing the  $FiO_2$  (34). This is especially important when monitoring patients for airway or ventilation adequacy in the PACU. According to Stemp and Ramsay (35), a fall in arterial oxygen saturation on pulse oximetry in patients breathing room air is indicative of alveolar hypoventilation or possible airway obstruction. Rapid detection of this phenomenon in the PACU thus enables early intervention.

In the immediate postoperative period, causes of hypoventilation are myriad and include the following (34,36): depressed central respiratory drive secondary to drug overdose or the residual effects of opioids, sedative hypnotics and inhaled anesthetics and, possibly, due to metabolic derangements such as metabolic alkalosis and severe hypothyroidism; ventilatory muscle dysfunction and generalized weakness secondary to residual neuromuscular blockade or underlying neuromuscular disease such as Guillain-Barré syndrome or myasthenia gravis; ventilation failure attributable to chest wall abnormalities, such as severe kyphoscoliosis, injuries, such as rib fractures or flail chest, or postoperative thoracotomy pain; injudicious use of oxygen; and increased minute ventilation due to metabolic acidosis (common in patients receiving crystalloid resuscitation), sepsis, anxiety and agitation.

Obstruction of the upper airway secondary to hematoma formation or severe inflammation/infection can significantly increase respiratory muscle fatigue and the inspiratory work of breathing. Morbid obesity is another example of increasing inspiratory load on breathing leading to hypoventilation (36). Severe cases of pulmonary edema or obstructive airways disease can also cause respiratory muscle fatigue and hypercapnia (37).

In patients with COPD, V/Q inequalities contribute to hypercapnia (37). The associated hypoxemia is more severe in relation to hypercapnia than in other forms of hypoventilation. Furthermore, injudicious use of oxygen therapy in such patients can worsen hypercapnia and ventilatory failure. This effect is often attributed to a decrease in hypoxic ventilatory drive associated with this group of patients (38).

In most patients with hypoventilation, hypoxemia is reversed with supplemental oxygen therapy and the main focus of management is treating the cause of hypoventilation (34). It is important to note, however, that the use of supplemental oxygen in these settings can mask the progression of bradypnea to apnea, preventing the onset of hypoxemia as evidenced by pulse oximetry and, thus, can lead to unrecognized severe hypoventilation with potentially catastrophic consequences (35). In this situation, the pulse oximeter becomes an important tool for monitoring not only oxygenation but also the adequacy of ventilation when supplemental oxygen is not used (39).

#### V/Q mismatch

The mechanisms for V/Q mismatch during general anesthesia and mechanical ventilation involve changes in both the functional residual capacity (FRC) and the distribution of ventilation. According to several studies (40,41), FRC is reduced by approximately 20% during general anesthesia compared with the awake state. Such a reduction is caused by a change in rib cage configuration (42) and cranial shift of the diaphragm (mostly of its dependent parts) (43,44).

The magnitude of such changes depends on several factors including the type of anesthetic used and whether muscle relaxation is added. Rib cage contribution to normal tidal breathing is reduced (45) or unchanged with inhalation anesthetics (46), whereas ketamine, on the other hand, increases rib cage contribution (47) or may at least keep the contribution unchanged (48). A change in intrathoracic blood volume is an additional factor relevant to the decrease in FRC (49). These changes may also result in a change in regional ventilation. During spontaneous breathing, there is some gravity-dependent distribution of ventilation, with an increase in regional ventilation from nondependent to dependent lung regions (50), as well as marked gravity-independent inhomogeneity of regional ventilation (51,52).

There is a marked change in ventilation distribution with induction of anesthesia and muscle paralysis caused, at least, in part, by a change in the position and movement of the diaphragm (39). Inspiratory gas predominantly shifts to nondependent lung regions during normal tidal breathing, whereas dependent regions are less ventilated (53).

There is also a change in the distribution of pulmonary blood flow in addition to the change in ventilation distribution (54). Increased intrathoracic pressure, present during positive pressure ventilation,

may reduce cardiac output and affect pulmonary vascular resistance (55). This may result in decrease of blood flow to West's zone I lung region (37). There is also some change in distribution of pulmonary perfusion with induction of general anesthesia and mechanical ventilation, with the net result being a well-documented impairment in V/Q distribution (56). These changes contribute significantly to respiratory complications in the postanesthesia period.

Regional anesthesia, compared with general anesthesia, usually results in markedly less impairment of V/Q distribution (30,57).

#### Pulmonary shunt

Hypoxemia attributable to shunt is characterized by a decrease in arterial oxygen content in the setting of constant alveolar ventilation. Consequently, venous blood passes to the arterial system through areas of unventilated lung. An important diagnostic element of shunt is apparent in the shape of the oxygen-hemoglobin dissociation curve (36); the addition of supplemental oxygen cannot ameliorate the hypoxemia.

This is because the saturation of nonshunted blood is on the flat portion of the oxygen-hemoglobin dissociation curve and, thus, additional oxygen has little impact in raising the  $PaO_2$ . The  $PaO_2$  drops precipitously when this blood mixes with poorly oxygenated shunted blood. This is in contrast to arterial hypoxemia secondary to V/Q mismatch, hypoventilation or diffusion abnormality, which is easily resolved with oxygen therapy (34).

Furthermore, treatment with 100% oxygen in the postanesthesia period, which causes nitrogen washout, can result in alveolar collapse creating an area of low V/Q ratio and, therefore, worsening the hypoxemia characteristic of patients with V/Q abnormalities.

Pulmonary disorders, such as pulmonary edema (both cardiogenic and negative pressure), transfusion-related lung injury and pneumonia, represent potential causes of shunt commonly encountered in the PACU. The less common extrapulmonary causes of shunt may include congenital cardiac defects such as atrial septal defect, patent ductus arteriosus and ventricular septal defect, which are associated with increased right heart pressures.

#### Diffusion impairment

Diffusion impairment reflects the lack of equilibrium between  $PaO_2$  in the alveolar gas and pulmonary capillary blood. Such a situation can occur when the alveolar capillary membrane is thickened, thus limiting the rate of diffusion of oxygen between the capillary and alveoli (34). Underlying lung disease, such as emphysema, interstitial lung disease, primary pulmonary hypertension or pulmonary fibrosis, are classic examples. Damage or loss of whole lung units reduces alveolar capillary surface area and capillary volumes, resulting in a lack of equilibrium and decreased red cell transit time through alveolar capillaries. Such a decreased transit time through alveolar capillaries may be due to increases in cardiac output, as observed in sepsis for example, thus worsening arterial hypoxemia in the context of an already injured lung.

#### Increased oxygen extraction

Increased oxygen extraction typically refers to low cardiac output states and is due to the mixing of desaturated venous blood with oxygenated arterial blood. Typically only 2% to 5% of cardiac output is shunted through the lungs, and this shunted blood with a normal mixed venous saturation has a negligible effect on  $PaO_2$  (34,37). However, blood returns to the heart severely desaturated in low cardiac output states. Furthermore, the shunt fraction increases significantly in conditions that impede alveolar oxygenation such as pulmonary shunt or V/Q mismatch and mixing of desaturated shunted blood with saturated arterialized blood under these conditions decreases  $PaO_2$  (34,37).

### THE EFFECTS OF PHARMACOLOGY

General anesthesia and mechanical ventilation are facilitated by many drugs, mainly opioids, sedatives and neuromuscular blocking agents, that can impede the physiological control of breathing after the

weaning process. At the conclusion of surgery, it is therefore especially important that residual effects of anesthetic agents be adequately reversed or dissipated.

As long as the airway is maintained, adequate spontaneous ventilation is readily possible during surgical levels of anesthesia, but a picture resembling sleep apnea may be induced at lighter planes of anesthesia that requires control of the airway (58). Thus, many of the problems noted in the PACU are related to the loss of mechanical support of the upper airway.

Pharmacological effects are of little importance in the control of breathing throughout general anesthesia and mechanical ventilation; however, during and after the weaning process, any depression of ventilator control may require the reinstatement of mechanical ventilation.

Furthermore, the effects of these drugs on the control of breathing are complex and can affect breathing by alterations in: the chemoreflexes (both hypercapnic and hypoxic); the nonchemoreflex or the so-called 'wakefulness drive'; and upper airway tone. Because the control of ventilation is under both feedback and feedforward control, the effects of specific drugs can vary greatly, depending on the patient's physiological state (59,60). Thus, during periods of patient sedation in the PACU, adequate ventilation may depend solely on the chemoreflexes as opposed to when the patient is fully awake, when feedforward influences from the higher centres typically predominate (59,60). Ventilation may, therefore, be adequate when the patient is awake and aroused but may become inadequate during oversedation (61).

#### Opioids and sedatives

Opioids are commonly used for analgesia in the PACU and are mainstays in the treatment of acute severe pain. It is well known, however, that they are the classic respiratory depressants and produce a dose-related depression of total ventilation through a decrease in both respiratory frequency and tidal volume. The respiratory depressant effect of the opioid is a central  $\mu$  receptor action (62), and there is little benefit in recommending one opioid over another as far as this side effect profile is concerned. The pharmacokinetic characteristics of the different opioids may, however, have a profound impact and those that are short acting after a single dose may produce extended respiratory depression manifesting in the PACU after prolonged infusion in the operating room (63). Thus, the increase in  $\text{CO}_2$  secondary to the reduction in spontaneous minute ventilation when an opioid is given will tend to counter the depression of ventilation if the onset of the opioid is slow. On the other hand, a bolus of a rapid-onset opioid may induce apnea before the  $\text{CO}_2$  can increase sufficiently to stimulate ventilation (64).

Neuraxially administered opioids, either epidurally or intrathecally, depress both the hypoxic and hypercapnic responses even though the plasma levels are not significant and, thus, the route by which the opioid reaches the brainstem does not appear to be as important (65). Delayed respiratory depression must, however, be considered with neuraxial administration, particularly if lipophilic opioids are used. Thus, postoperatively, such opioid administration is potentially associated with upper airway obstruction and desaturation (66).

The effects of midazolam on the upper airway may be more important than its effects on decreasing respiratory drive (67). It reduces both the hypoxic and hypercapnic chemoreflexes, and it is the loss of the wakefulness drive that may account for the mild reduction in hypercapnic sensitivity (67). Both the sedative and respiratory depressant effects of midazolam can be reversed by flumazenil, although the sedation reversal may outlast reversal of the respiratory depression (68).

The combination of opioids and sedatives can be synergistic in the extent of respiratory depression produced (66). This synergism may result from the effect of the sedative on the wakefulness drive (a hypothesis originally proposed by Fink [69], that cerebral activity associated with wakefulness is a component of the normal respiratory drive) and the effect of the opioid on the chemoreflex and, thus, should be closely monitored in the PACU.

#### Neuromuscular blocking drugs

Neuromuscular blocking drugs are frequently used intraoperatively and residual neuromuscular blockade is commonly observed in the PACU. Approximately 33% to 64% of patients have evidence of inadequate neuromuscular recovery on arrival to the PACU (70,71), despite the application of techniques proven to limit the degree of residual paralysis such as pharmacological reversal and the use of intermediate-acting agents. Residual neuromuscular blockade may produce postoperative hypoxemia by several mechanisms. These include the deleterious effects on both chemoreception and upper airway patency in addition to their predictable effects on the phrenic nerve-diaphragm neuromuscular junction (72).

In an study by Eikermann et al (73), significant upper airway obstruction was detected in eight of 12 volunteers at a train-of-four (TOF) ratio of 0.50 and four of 12 volunteers at a TOF ratio of 0.83 (73). Similarly, other investigators have demonstrated significant pharyngeal muscle dysfunction in healthy volunteers at TOF ratios <0.90 (73,74) suggesting that residual neuromuscular blockade is a primary contributing factor to airway obstruction in the PACU.

At the receptor level, it is generally accepted that the neuromuscular blocking drugs act to block the neuromuscular junction nicotinic receptors, with little effect on neuronal nicotinic receptors. As a result, low doses of vecuronium appear to depress hypoxic ventilatory drive through depression of carotid body chemosensitivity in both rats (75) and humans (76).

#### Cardiovascular medications

Medications used to support the cardiovascular system can also have significant respiratory effects, but auspiciously, most of them do not cause major clinical problems in the PACU. Of these agents, dopamine has the most pronounced ventilator effects because even low doses significantly blunt the hypoxic ventilatory response (77). Several studies have demonstrated that a low-dose dopamine infusion has depressant effects on minute ventilation when given during hypoxia or during states with compromised oxygen delivery to tissues such as during exacerbation of congestive heart failure (78). Other cardiovascular drugs, such as digoxin and adenosine, have ventilatory effects that can be readily measured; however, there is no evidence that any of these effects are clinically significant (77).

#### PREVENTION AND TREATMENT OF ATELECTASIS

Atelectasis is clearly an important cause of postoperative hypoxemic events in the PACU. Identifying various procedures in the operating room that can prevent atelectasis or reopen collapsed alveoli are, therefore, worth mentioning. At the outset, using an anesthetic, such as ketamine, that enables maintenance of respiratory muscle tone will likely preclude the formation of atelectasis (17,18). Nonetheless, if combined with muscle paralysis, atelectasis will most likely develop (16).

In anesthetized adults with healthy lungs, alveolar recruitment reduces the amount of atelectasis and pulmonary shunt and, despite a concomitant increase in perfusion to poorly ventilated lung units, it also improves ventilatory efficiency as measured by  $\text{CO}_2$  elimination (79). A single recruitment breath may result in the release of surfactant (80), thus contributing to improved alveolar stability and preventing lung collapse. It has also been shown that recruitment attenuates bacterial growth and translocation in an animal model of pneumonia (81). However, in patients with COPD, anesthesia causes only a small amount of atelectasis, and impaired oxygenation is primarily caused by a V/Q mismatch (14). Therefore, any further expansion of lung tissue in these patients may be of limited value or may even be harmful because of possible regional overinflation. For that reason, one should carefully weigh the assumed benefits and possible risks before performing a recruitment manoeuvre (82).

The use of positive end-expiratory pressure (PEEP) is another approach to reopen the collapsed lung. PEEP reduces the amount of

atelectasis if used in patients with healthy lungs, but it has a variable effect on pulmonary shunt and often results in increased dead space (83). However, atelectasis redevelops within a few minutes after cessation of PEEP (84) and, therefore, if sustained reopening of atelectasis and reduction of pulmonary shunt are the main goals of a therapeutic measure, a vital capacity alveolar recruitment manoeuvre may be more appropriate than PEEP used alone (85). Alternatively, when used after a recruitment manoeuvre, PEEP significantly reduces the rate of renewed lung collapse even if a high  $FiO_2$  is used (86-88). PEEP may also be used to prevent formation of atelectasis and to prolong the time of nonhypoxic apnea during induction of anesthesia (89,90).

### TREATING THE CAUSES OF ARTERIAL HYPOXEMIA IN THE PACU

According to the oxygen dissociation curve (which defines the relationship between  $PaO_2$  and oxygen saturation [ $SaO_2$ ]), a  $PaO_2$  of 60 mmHg results in an  $SaO_2$  of approximately 90%. The main aim of supplemental oxygen therapy in the PACU is, therefore, to maintain a  $PaO_2 \geq 60$  mmHg (91) because any further decrease in  $PaO_2$  would result in a marked drop in  $SaO_2$ . Herein, we discuss the goals of oxygen therapy based on the causes of arterial hypoxemia in the PACU.

#### Alveolar hypoventilation

The level of hypoxemia in alveolar hypoventilation is usually not severe and is easily reversed by the use of oxygen. The main goals of the management of hypoventilation in the PACU are the recognition and treatment of its underlying cause. A major cause is COPD and V/Q mismatch plays a key role in the pathophysiology of the increased pressure of  $CO_2$  ( $PCO_2$ ) in these patients (37,92).

Oxygen should, therefore, be carefully titrated because too high an  $FiO_2$  can reduce hypoxic vasoconstriction or abolish hypoxic ventilatory drive, thereby leading to an increase in dead space (92) and, consequently, can contribute to dangerously high levels of  $PCO_2$  and ventilatory failure. Regardless of this concern, adequacy of tissue perfusion is the primary goal in these patients in the PACU.

It is not recommended, however, to sacrifice adequate arterial oxygen levels and tissue oxygen delivery to improve hypercarbia. Thus, if the  $PCO_2$  remains dangerously high after careful titration of oxygen in the PACU, as indicated by a patient's clinical status and arterial pH, and the oxygen saturation remains too low, then bilevel noninvasive positive pressure ventilation or even intubation and mechanical ventilation may be required.

#### V/Q mismatch

The use of supplemental oxygen increases  $PaO_2$  in the setting of V/Q mismatch, but the extent of increase depends on the predominant pattern of inequality. The response may, however, be unpredictable and could take many minutes (93). Treatment with 100% oxygen can potentially increase  $PaO_2$  to very high levels and subsequent nitrogen washout can cause alveolar collapse that can turn areas of low V/Q mismatch to true shunt.

Aside from the use of oxygen therapy in the PACU, treatment should be targeted at improving the V/Q abnormality. This includes the use of bronchodilators for patients with COPD and asthma, and PEEP for patients with acute lung injury and pulmonary edema.

#### Pulmonary shunt

Hypoxia caused by pulmonary shunt is less responsive to supplemental oxygen in and beyond the PACU. However, meaningful increases in  $PaO_2$  can occur with use of high concentrations of oxygen in these patients. At high  $PaO_2$ , there is significant additional dissolved oxygen (34,37) and, consequently, important increases in the arterial oxygen content and saturations can occur because the  $FiO_2$  is increased. However, with shunt fractions  $\geq 50\%$ , little benefit to high concentrations of supplemental oxygen is apparent.

#### Diffusion impairment

The use of supplemental oxygen in the PACU easily overcomes hypoxemia-associated diffusion impairment. The main reason for this is that the pressure difference between the capillary and the alveolus determines the rate of movement of oxygen across the alveolar-capillary membrane. Therefore, increasing the  $FiO_2$  will raise the driving pressure and, thus, improves the  $PaO_2$  (34,37).

#### Increased oxygen extraction

The benefit of supplemental oxygen during low cardiac output states (increased oxygen extraction) is that the use of high  $FiO_2$  increases the dissolved oxygen in the blood, thereby improving tissue oxygen delivery. This is fundamentally crucial because decreases in tissue oxygen delivery due to poor cardiac output or low arterial oxygen content can cause a reduction in mixed venous oxygen saturation. Such a situation can contribute to arterial hypoxemia because many of the disease processes causing inadequate tissue perfusion are often associated with V/Q abnormalities of the lung. Therefore, assessing and treating the underlying cause of decreased tissue perfusion with fluids, blood, vasopressors, inotropes and antibiotics are critical interventions that begin in the PACU.

### THE ROLE OF CONTINUOUS POSITIVE AIRWAY PRESSURE VENTILATION AND NONINVASIVE VENTILATION IN THE PACU

The use of continuous positive airway pressure ventilation (CPAP) in the PACU can potentially decrease hypoxemia due to atelectasis by alveolar recruitment. The subsequent increase in FRC decreases the work of breathing and improves pulmonary compliance. In 2005, Squadrone et al (94) conducted a randomized controlled trial involving 209 patients to determine the effectiveness of CPAP compared with standard treatment in preventing the need for intubation and mechanical ventilation in patients who develop acute hypoxemia after elective major abdominal surgery. The authors showed that the application of CPAP (at 7.5 cmH<sub>2</sub>O pressure) in the PACU in conjunction with oxygen versus oxygen alone significantly reduced the incidence of endotracheal intubation and other severe complications including pneumonia, infection and sepsis.

There will still be a number of patients who will require additional ventilatory support even with the application of CPAP in the PACU. There is a limited experience in the application of noninvasive ventilation (NIV) in the PACU despite being an effective alternative to endotracheal intubation in the treatment of both chronic and acute respiratory failure in the critical care setting (95-97).

The use of NIV was avoided in the immediate postoperative period in the past because of the potential for wound dehiscence, gastric distention and aspiration, which can occur in patients who have undergone gastric or esophageal surgery (98). In 2000, Tobias (99) reported the successful application of NIV in two patients, one after gastrostomy tube placement and another after cholecystectomy. Similarly, in a larger case series, Albala and Ferrigno (100) reported the successful use of NIV in a variety of rapidly reversible causes of postoperative respiratory failure in the PACU. Careful consideration of both surgical and patient factors is necessary, however, before making a decision to use NIV in the PACU.

Furthermore, relative contraindications to the use of NIV include altered mental status, high risk of aspiration, refractory hypoxemia, hemodynamic instability or life-threatening arrhythmias, and an inability to use nasal or facial mask such as after head and neck surgery (101).

### SPECIFIC SITUATIONS

#### Laparoscopic versus open surgery

Laparoscopic surgery has multiple benefits, such as a shorter recovery, and shorter hospital stay (102). It would, therefore, seem intuitive that laparoscopic procedures would reduce the risk for postoperative

pulmonary complications compared with open surgical procedures, especially because they are associated with less postoperative pain, thus potentially improving postoperative lung volumes and facilitating deep breathing.

Only a few studies, however, have reported the postoperative respiratory complication rates associated with laparoscopic versus open surgical procedures. Weller and Rosati (103) showed that the rate of postoperative pulmonary complications was nearly double if patients underwent open surgery as opposed to laparoscopic surgery in an analysis of 19,156 patients who underwent bariatric surgery. Two other studies have also shown a reduction in atelectasis and other postoperative pulmonary complications following laparoscopic surgery compared with open cholecystectomy and open sigmoid resection, respectively (104,105).

Despite these obvious advantages, marked intraoperative and postoperative cardiorespiratory dysfunction may also occur in certain patients secondary to the effects of pneumoperitoneum (106,107). Changes regarding the respiratory system that are most prominent during laparoscopic surgery include a cephalad displacement of the diaphragm, reduction of FRC with derangement of gas exchange (108) and a decrease in the compliance of the respiratory system by up to 50% (109). Obesity (110) and patient positioning (111) during the procedure further modify these effects.

Furthermore, there may be an increased alveolar-arterial CO<sub>2</sub> tension difference in patients with underlying cardiopulmonary disease (112,113) as a result of CO<sub>2</sub> absorption (113,114), V/Q mismatch and an increase in pulmonary shunt (115,116). Clinically relevant respiratory complications that can occur during laparoscopic surgery using CO<sub>2</sub> insufflation include gas embolism, CO<sub>2</sub> emphysema, pneumothorax, pneumomediastinum and pneumopericardium (114-116).

#### Obstructive sleep apnea

Patients with obstructive sleep apnea (OSA) should be carefully monitored in the PACU because they can present during the postoperative period with more frequent, more severe or more prolonged episodes of oxyhemoglobin desaturation often accompanied by new or worse hypercapnia (117).

In a series of 438 patients with known or suspected OSA, Bolden et al (117) demonstrated that the frequency of oxyhemoglobin desaturations to <90% during sleep occurred in 16% of cases, while oxyhemoglobin desaturation to <80% during sleep occurred in 7% of patients within the first 24 h to 48 h after the surgical procedure.

In a study by Hwang et al (118), 172 patients undergoing elective surgery underwent nocturnal oximetry before surgery and were divided into two groups based on number of desaturation episodes per hour. Markedly higher rates of postoperative respiratory complications (eight complications among 98 patients) were observed in patients with five or more desaturations as opposed to those with fewer than five desaturations (one complication among 74 patients). Furthermore, the presence of five or more desaturations was also associated with higher rates of bleeding as well as cardiac and gastrointestinal complications.

It is the early postoperative period (first 24 h) that can be especially tenuous for patients with OSA because they are particularly prone to airway obstruction and numerous factors that can exacerbate OSA are active during this time (119).

These patients are especially sensitive to opioids that inhibit the upper respiratory muscles and, therefore, have the potential to induce or worsen upper airway collapse (120,121). Sedatives, such as benzodiazepines, can have an even greater effect on pharyngeal muscle tone than opioids, and act synergistically with opioids to decrease central respiratory drive. Thus, their use in the perioperative setting can also contribute significantly to airway obstruction in the PACU (122).

Alternative strategies to reduce or eliminate the need for systemic opioids postoperatively include the use of regional analgesia and non-opioid analgesics (123). Neuraxial analgesia (both spinal and epidural analgesia) may also reduce the need for postoperative systemic opioids.

Caution should, however, be used because it can be complicated by sedation and respiratory depression if the medication extends too far cephalad (124). Using local anesthetics without the addition of opioids for neuraxial analgesia may reduce this risk (123).

Finally, patients with OSA should resume their oral appliance therapy or positive airway pressure therapy in the immediate postoperative period (123). Positive airway pressure therapy should be initiated at the level prescribed preoperatively and, if this is not known, it is reasonable to begin at an empirical level of 8 cmH<sub>2</sub>O to 10 cmH<sub>2</sub>O and then titrate the level until apneas, episodes of oxyhemoglobin desaturation and snoring are eliminated (123).

#### CONCLUSION

Pulmonary function is markedly altered both by general anesthesia with mechanical ventilation and by surgery. Significant atelectasis is found in most anesthetized adults and there is a marked increase in alveolar hypoventilation, V/Q inequalities and pulmonary shunt as early as with induction of anesthesia. These mechanisms are responsible for the majority of cases of arterial hypoxemia in the PACU. Many concomitant factors that contribute to postoperative hypoxemic events must be considered such as the type and anatomical site of surgery causing a change in lung mechanics, hemodynamic impairment and respiratory depression from residual effects of anesthetic drugs (125). Even patients treated with intermediate- and short-acting neuromuscular blocking drugs may manifest residual paralysis in the PACU despite what was deemed clinically adequate pharmacological reversal in the operating room (126).

A thorough understanding of the changes that occur during specific procedures, such as laparoscopic surgery, are prerequisites for adequate care and appropriate monitoring of these patients in the PACU.

Pulmonary outcomes may be significantly influenced by the appropriate choice and use of analgesic techniques. More beneficial effects have been demonstrated in terms of pulmonary morbidity when comparing the use of epidural opioids, epidural local anesthetics or patient-controlled analgesia with systemic opioids (127-129).

Clinical correlation should guide the workup of a postoperative patient who remains persistently hypoxemic in the PACU. The signs and symptoms may include tachypnea with increased minute ventilation, dyspnea, tachycardia and altered mental status. New-onset delirium or agitation secondary to acute hypoxemia can be confused with psychosis or 'sundowning' (increased agitation, and confusion in late afternoon, evening or night) in elderly patients. As hypoxemia worsens or its duration increases, respiratory distress, respiratory muscle paradox and arrhythmias ensue, with elevations in myocardial oxygen consumption. Ultimately, respiratory muscle fatigue, coma, and respiratory and cardiac arrest may occur (130). The provision of oxygen therapy in such postoperative acutely hypoxemic patients in the PACU is, therefore, critical and keeping the oxygen dissociation curve in mind can provide a conceptual reference regarding delivery of oxygen to the tissues. Ultimately, careful consideration of the cause of hypoxemia enables the appropriate titration of oxygen at the patient's bedside.

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