

## Physiopathology and clinical management of one-lung ventilation\*

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During one-lung ventilation, the nonventilated lung is excluded from the ventilation, with all tidal volume directed into the ventilated lung. This technique facilitates viewing of intrathoracic structures, thereby providing optimal surgical conditions. However, this procedure has been associated with reduced arterial oxygen tension, principally in patients with a previous history of lung disease, since it reduces the surface area available for gas exchange and causes a loss of normal autonomic respiratory regulation. Therefore, maintaining sufficient oxygenation and elimination of carbon dioxide is the greatest challenge in the management of the one-lung ventilation. It is recommend that the tidal volume administrated to the ventilated lung be similar to that used during conventional mechanical ventilation and that high fractions of inspired oxygen be used. However, several alternative methods have been proposed in order to minimize hypoxemia during one-lung ventilation, including the correct positioning of the double-lumen tube, the use of positive end-expiratory pressure or continuous positive airway pressure, nitric oxide administration, and alveolar recruitment. The management of one-lung ventilation continues to be a challenge in clinical practice.

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## DEFINITION

One-lung ventilation consists of mechanical ventilation of the selected lung and exposure or intentional airway blocking of the other. This technique facilitates viewing of intrathoracic structures, thereby providing optimal surgical conditions, since adequate pulmonary exposure facilitates resection and reduces surgical time<sup>(1,2)</sup>.

## HISTORY

Selective intubation was described for the first time in 1932 by Gale and Waters, who aimed to open the thorax and surgically manipulate the lungs. The authors used a single-light tube that was inserted into the right or left mainstem bronchus<sup>(3)</sup>. Since then, various alternative methods have been proposed in order to make this technique safer and facilitate its practice.

The lung separation techniques previously described involve the use of bronchial tubes, bronchial blockers, or double-lumen tubes (the devices most commonly used in current surgical practice)<sup>(4)</sup>.

## INDICATIONS FOR USE

Situations in which one-lung ventilation are indicated may be divided into two groups: indications and relative indications. Indications include hemothorax, massive hemorrhage, unilateral cysts, bronchopleural fistulae and unilateral pulmonary diseases. Relative indications include pneumonectomies, lobectomies, esophageal resection and thoracoscopies<sup>(5)</sup>.

## COMPLICATIONS

The principal complications that arise from one-lung ventilation are hypoxemia, hemorrhage, hemodynamic instability, bronchial rupture caused by excessive inflation of the balloon on the tip of the double-lumen tube, and alveolar lesions caused by the use of fractions of inspired oxygen ( $\text{FiO}_2$ ) of 1.0<sup>(1)</sup>.

## PHYSIOLOGICAL REPERCUSSIONS OF ONE-LUNG VENTILATION

### Atelectasis of the nonventilated lung

Alveolar collapse results from the action of opposite forces on the pulmonary parenchyma. These include elastic recoil pressure and surface

forces of the alveolar air-liquid interface versus positive transpulmonary pressures. Positive basal alveolar pressure is fundamental to alveolar stabilization. When there is total collapse, as is the case for the nonventilated lung during one-lung ventilation, reversal of this state is not easily achieved and requires higher pressures to produce alveolar reopening. The term "time constant" cannot be applied to units that are in a state of collapse since these units are totally excluded from the process of distribution of the inspired air. This means that the air diffuses through an area that is less compliant, as compared with the lung as a whole.

Egan et al. demonstrated that the size of a pulmonary lobe may increase from three to four times, thereby maintaining the same inspiratory pressure<sup>(6)</sup>. When atelectasis of various pulmonary lobes is induced, the remaining lobe absorbs all the stress imposed by the high airway pressure. This is due to the fact that the resulting pleural pressure does not rise significantly. Since the other lobes cease to contribute to the increase in gas volume, the pleural pressures around the remaining lobe remain practically unaltered, thereby generating a high transpulmonary pressure over this lobe alone<sup>(6)</sup> (Figure 1).

### Blood flow distribution during one-lung ventilation

Thoracic surgeries are performed, for the most part, by placing the patient in the lateral decubitus position with the nondependent hemithorax compressed by the surgical field. When one-lung ventilation is instituted, the dependent lung is ventilated and the nondependent lung is not. As a result, the nondependent lung will be in total collapse, thereby presenting significant reduction in the surface area available for gas exchange, in addition to loss of normal autonomic respiratory regulation. Subsequently, a transpulmonary shunt is created in the nondependent lung and, even in the presence of similar  $\text{FiO}_2$  and comparable metabolic and hemodynamic conditions, arterial oxygen tension ( $\text{PaO}_2$ ) is lower than in traditional mechanical ventilation. In the lateral decubitus position, it is estimated that (in nonpathological conditions) 40% of the cardiac output is used for perfusing the nondependent lung, and the remaining 60% is directed to the dependent lung.

Two types of mechanisms (passive and active) minimize the blood flow into the nondependent

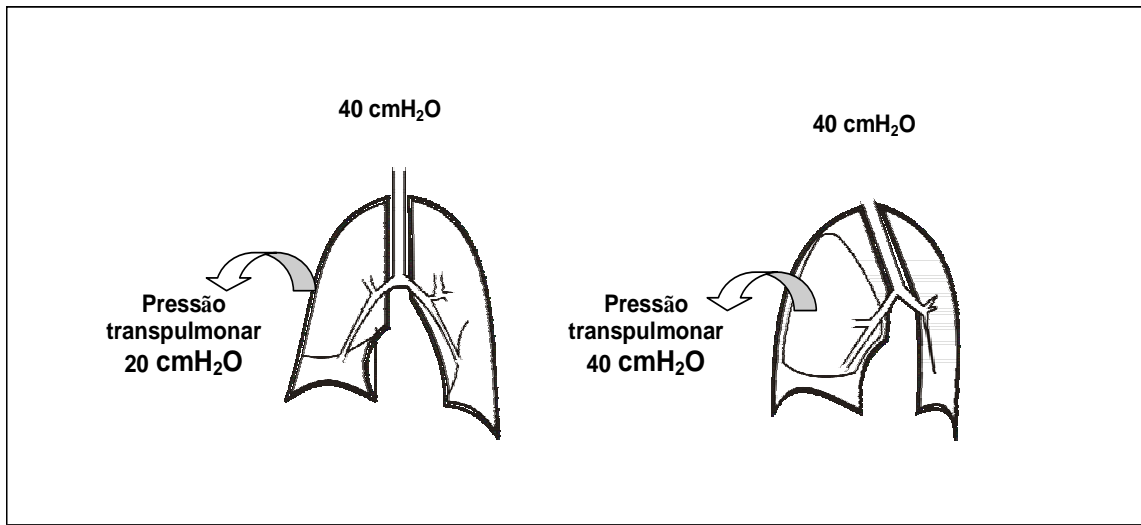


Figure 1 – Simplified diagram showing that, when the entire left lung is insufflated with a pressure of 40 cmH<sub>2</sub>O, the rib cage absorbs the stress generated by the applied pressure. The resulting transpulmonary pressure is 20 cmH<sub>2</sub>O. In the right lung, atelectasis was provoked in several pulmonary lobes by progressive bronchial obstructions. The sole remaining lobe absorbs all the stress imposed by the high airway pressure. This occurs because the pleural pressure does not increase significantly. Therefore, the other lobes cease to contribute to the increase in gas volume. This results in high transpulmonary pressure. (Modified from Egan EA. Lung inflation, lung solute permeability, and alveolar edema. *J Appl Physiol* 1982;53:121-5)

lung and thereby prevent the drop in PaO<sub>2</sub>. Passive mechanisms include gravity and aggressive surgical compression (direct compression of the pulmonary vessels)<sup>(7)</sup>. Gravity is the determining factor in the regional distribution of the blood flow. This distribution depends on airway pressures and the local relationship between arterial and venous pressures. Furthermore, gravity creates a vertical gradient in the distribution of the flow. Therefore, the blood flow in the nondependent lung is lower than that in the dependent lung<sup>(8)</sup>.

The main active mechanism is hypoxic pulmonary vasoconstriction (HPV). The normal response of the pulmonary vasculature to atelectasis is that of increasing pulmonary vascular resistance, which diverts the blood flow from the nondependent to the dependent lung, thereby minimizing the shunt. Subsequently, the HPV mechanism, occurring predominantly in arterioles and inferior pulmonary veins, has a protective effect. The main stimulus to HPV is the decrease in PaO<sub>2</sub> and in venous oxygen tension (PvO<sub>2</sub>).

When PvO<sub>2</sub> is normal, there is maximum vasoconstriction response, which diminishes when PvO<sub>2</sub> is increased or reduced. Cardiac output may also influence HPV, since changes in the former cause alterations in lung vascular pressures<sup>(9)</sup>. It is of note that reduced FiO<sub>2</sub> in the dependent lung increases the vascular resistance of this lung, thereby attenuating the diversion of the blood flow coming from the nondependent lung<sup>(10,11)</sup>.

Several factors, such as anesthetic agents<sup>(12)</sup>, vasodilators<sup>(13)</sup>, arterial carbon dioxide tension<sup>(9)</sup>, manipulation of the lung<sup>(7)</sup> and epidural anesthesia<sup>(14)</sup>, can affect HPV. These factors may either minimize or maximize its effects.

#### Arterial oxygenation

Hypoxemia is a complication that affects from 9% to 27% of patients undergoing one-lung ventilation and is influenced by several factors. Initially, soon after the beginning of one-lung ventilation, the blood flow in the nonventilated lung becomes deoxygenated. This reduces the

surface area available for gas exchange and consequently decreases  $\text{PaO}_2$ <sup>(11)</sup>.

Patient positioning during thoracic surgery is another significant factor affecting oxygenation. Studies show that oxygenation is more satisfactory when the patient is placed in the lateral decubitus, rather than the dorsal decubitus, position. Watanabe et al. demonstrated that alveolar oxygen tension decreases more rapidly in the dorsal decubitus position than in the lateral decubitus position, thereby leading to more accentuated hypoxemia<sup>(15)</sup>. Therefore, the lateral decubitus position is used in most studies aiming to minimize the effects of patient position on arterial oxygenation<sup>(7,15)</sup>.

## EXECUTION OF ONE-LUNG VENTILATION

### Choosing the size of the double-lumen tube and confirming its correct positioning

Currently, the technique most frequently used for separating the two lungs is that which employs the double-lumen tube. The main advantages of this technique are rapidity and ease of use. The double-lumen tube offers, if necessary, the possibility of shifting to traditional bilateral ventilation. In addition, it permits the concomitant use of several techniques to correct any possible hypoxemia (continuous positive airway pressure, insufflation of oxygen, etc)<sup>(16)</sup>.

The size of the tube must be proportional to the weight and height of the patient. In addition, it must permit free passage through the mainstem bronchus, with no resistance. Occlusion of the tube by inflation of the balloon must be taken into account in order to prevent air leaks<sup>(17)</sup>.

Correct positioning of the double-lumen tube is confirmed by fiberoptic bronchoscopy and pulmonary auscultation. The use of the fiberoptic bronchoscope was first described in 1982 by Watson et al.<sup>(18)</sup> and still seems to best meet the needs of surgeons<sup>(17,19)</sup>.

Improper positioning of the tube causes complications in 20% to 30% of patients undergoing thoracic surgery. Hypoxemia and hypercapnia, as well as elevations in the plateau and apical pressures, are indicative of incorrect positioning of the tube. The three most important studies on the monitoring of airway pressures during one-lung ventilation were carried out in

1995. Cohen fixed 40  $\text{cmH}_2\text{O}$  as the upper pressure limit during one-lung ventilation<sup>(20)</sup>. Slinger fixed 45  $\text{cmH}_2\text{O}$  as the highest apical pressure<sup>(21)</sup>. Ovassapian proposed that the apical pressure not surpass 150% of the basal value of traditional bilateral ventilation<sup>(22)</sup>. In a more recent study conducted by Szedi et al., it was demonstrated that there are quantifiable increases in the plateau and apical pressures, but that these values should not be considered in isolation since they present low sensitivity and poor diagnostic precision<sup>(23)</sup>.

In a retrospective study of 234 one-lung intubations, arterial oxygen saturation of less than 90% was observed in 9% of the patients, apical pressure above 40  $\text{cmH}_2\text{O}$  in another 9%, an intubation error during isolation of one of the lungs in 7%, and airway trapping in 2%. This demonstrates that, although fiberoptic bronchoscopy had initially been performed, thus ensuring the correct positioning of the tube, a shift during surgical manipulation may alter its position, resulting in airway obstruction and increased inspiratory pressure<sup>(24)</sup>.

### Tidal volume ( $V_T$ ) similar to that used during traditional mechanical ventilation

During one-lung ventilation, it is recommended that the dependent lung be ventilated with a tidal volume ( $V_T$ ) similar to that used when ventilating both lungs during traditional mechanical ventilation<sup>(2,25)</sup>. High  $V_T$ s are used in order to maintain arterial oxygenation<sup>(26)</sup>. Katz et al. have demonstrated that  $V_T$  levels of 8 to 15 ml/kg do not significantly affect either the pulmonary shunt or the  $\text{PaO}_2$ <sup>(27)</sup>. In addition, the authors reported that  $V_T$  levels of less than 8ml/kg resulted in a reduction in the residual functional capacity, thereby causing atelectasis in the dependent lung and consequent gas exchange impairment. It is clear that the choice of the  $V_T$  is solely based on improving oxygenation. However, little attention is given to the potential deleterious effects of high  $V_T$ s on patients undergoing one-lung ventilation.

Recent studies have demonstrated that mechanical ventilation alone may initiate or aggravate lung injury<sup>(28-30)</sup>. High  $V_T$ s may distend normal or previously injured alveoli, thereby causing direct injury to the lung parenchyma. The principal consequence of administering high  $V_T$ s is cellular injury caused by hyperdistension and scission. As a result, there is a rupture of the

alveolar-capillary membrane, a functional alteration of the cells, liberation of proinflammatory cytokines, an alteration in the ionic transport and a reduction in the surfactant secretion, constituting pulmonary injury<sup>(28-31)</sup>.

Although most of the patients undergoing one-lung ventilation do not present a previous history of lung disease, the administration of high  $V_T$ s may lead to lung parenchymal injury<sup>(26,32)</sup>. A reduction in  $V_T$ , in combination with the use of positive end-expiratory pressure (PEEP), may minimize these alterations<sup>(26,33)</sup>.

#### Use of high fractions of inspired oxygen

In addition to the use of high  $V_T$ s, an  $FiO_2$  of 1.0 is used in order to maintain satisfactory arterial oxygenation. This concentration of oxygen causes vasodilatation in the dependent lung, thereby increasing its capacity to accommodate the blood flow coming from the nondependent lung. Capan *et al.* showed that the use of an  $FiO_2$  of 1.0 resulted in shunt fractions of 25% to 30% and  $PaO_2$  values between 150 mmHg and 210 mmHg during one-lung ventilation<sup>(34)</sup>. More recently, Bardoczky *et al.* analyzed the effects of different concentrations of oxygen combined with positioning patients in the dorsal decubitus or lateral decubitus position and concluded that all of them presented an increase in the alveolar-arterial oxygen difference, regardless of the  $FiO_2$  values used. However, with an  $FiO_2$  of 1.0, the reduction in  $PaO_2$  was smaller and therefore did not cause hypoxemia. It is noteworthy that the reduction in  $PaO_2$  was greater in patients in the dorsal decubitus position than in those in the lateral decubitus position<sup>(35)</sup>.

High  $FiO_2$  values, on the other hand, cause several complications, such as absorption atelectasis, as well as alterations in vital capacity, respiratory rate, pH,  $PaO_2$  and in the pulmonary diffusing capacity for carbon monoxide. This leads to a later increase in the shunt fraction<sup>(36)</sup>.

#### Positive end-expiratory pressure

During one-lung ventilation, especially when in the lateral decubitus position, the functional residual capacity of the dependent lung is reduced due to factors related to the induction of general anesthesia, such as compression of the abdominal contents and the mediastinum<sup>(2,25)</sup>.

The application of PEEP to the dependent lung prevents alveolar collapse and increases functional residual capacity, thus improving the ventilation-

perfusion ratio and the compliance of this lung<sup>(25)</sup>. However, PEEP efficacy depends on the levels used. High PEEP levels may have deleterious effects on arterial oxygenation. This is due to the compression of the intra-alveolar vessels resulting from increased lung volume, thereby leading to an increase in pulmonary vascular resistance and a reduction in cardiac output<sup>(37)</sup>.

There is much controversy in the literature over the efficacy of PEEP in controlling  $PaO_2$  during one-lung ventilation. Cohen *et al.* demonstrated that the application of a PEEP level of 10 cmH<sub>2</sub>O to patients with low  $PaO_2$  increased the functional residual capacity to normal values, thereby reducing the pulmonary vascular resistance, improving the ventilation-perfusion ratio and increasing  $PaO_2$ <sup>(38)</sup>. On the other hand, Capan *et al.* provided evidence that oxygenation did not improve in the presence of PEEP<sup>(34)</sup>. More recently, Inomata *et al.* proposed an explanation for the conflicting results regarding the administration of PEEP during one-lung ventilation<sup>(39)</sup>. They ascertained that there was an increase in airway resistance and, as a result, patients presented auto-PEEP. In patients with no previous history of lung disease, arterial oxygenation, shunt fraction and cardiac rate were satisfactory when PEEP levels similar to those of auto-PEEP were used. Therefore, in order to apply an ideal PEEP level, it is recommended that auto-PEEP levels be determined<sup>(39)</sup>.

## ANESTHESIA

*In vitro* studies have shown that volatile anesthetics directly reduce the action of hypoxic vasoconstriction and may theoretically lead to increased perfusion of the nonventilated lung, thus increasing the shunt fraction and, as a result, reducing  $PaO_2$ <sup>(40)</sup>.

Bjertnaes *et al.* used scintigraphy to analyze the effects of ether, halothane, thiopental and fentanyl on HPV and ascertained that ether and halothane, when used in clinical concentrations, inhibited HPV, whereas the intravenous agents (thiopental and fentanyl) did not<sup>(41)</sup>. More recently, Groh *et al.* investigated the influence of isoflurane on hypoxic vasoconstriction by measuring pulmonary blood flow in rabbits. The authors demonstrated that isoflurane increased perfusion in the nonventilated lung since it inhibited hypoxic vasoconstriction<sup>(42)</sup>.

The effects of propofol on PaO<sub>2</sub>, shunt fraction, pulmonary perfusion and cardiac output have been analyzed in comparison to volatile anesthetics previously studied, and it was demonstrated that PaO<sub>2</sub> values, pulmonary perfusion and cardiac output were higher when propofol was used, and that the shunt fraction was significantly lower than that observed with the other volatile anesthetics<sup>(43,44)</sup>.

## ALTERNATIVE METHODS FOR MINIMIZING HYPOXEMIA DURING ONE-LUNG VENTILATION

### Continuous positive airway pressure

Continuous positive airway pressure is administered to the nondependent lung in order to maintain airway and alveolar patency, thereby making gas exchange possible, since the alveoli are not in total collapse. The pressure values for continuous positive airway pressure must be adjusted in order to maintain sufficient arterial oxygenation. Generally, the combination of continuous positive airway pressure with PEEP in the dependent lung produces more satisfactory results<sup>(45-47)</sup>.

### Nitric oxide

Nitric oxide (NO) is a key factor in endothelium-dependent relaxation. Endothelial NO release is induced by L-arginine and by increased concentrations of calcium in the cytoplasm. It diffuses through the intracellular site of the smooth muscle cells and binds the heme group that is present in the guanylate cyclase. This activation leads to smooth muscle relaxation by the synthesis of the 3',5'-cyclic guanosine monophosphate, which causes relaxation and vasodilatation. Its half-life ranges from 110 msec to 130 msec<sup>(48)</sup>.

Inhaled NO (5 to 80 ppm) selectively reduces pulmonary vascular resistance, that is, its effects are restricted to the pulmonary circulation, and, since it is deactivated by hemoglobin immediately after entering the circulation, it has no effect on systemic circulation<sup>(48)</sup>. This concept that pulmonary circulation may be modulated by the administration of NO had led to its utilization in attempts to reduce hypoxemia during one-lung ventilation. It is notable that NO inhalation only causes vasodilatation in ventilated areas, not affecting HPV in nonventilated areas. Administration of NO during one-lung

ventilation could theoretically improve oxygenation since it selectively reduces pulmonary vascular resistance and increases the blood flow into the ventilated lung<sup>(49)</sup>.

However, there is controversy over the results obtained by NO use during one-lung ventilation. Booth et al. administered NO (40 ppm) to nine patients, and reported improved oxygenation<sup>(50)</sup>. However, the authors of two other studies found no evidence of improved PaO<sub>2</sub> resulting from the use of NO<sup>(51,52)</sup>.

There are several theories that attempt to explain the lack of NO efficacy during one-lung ventilation. One is based on the fact that, in the lateral decubitus position, 75% to 80% of the cardiac output flows through the ventilated lung. This suggests that the pulmonary vessels in the ventilated lung are already dilated sufficiently to accommodate this increased flow, and additional dilation would therefore be impossible<sup>(52)</sup>.

## HIGH-FREQUENCY VENTILATION

High-frequency ventilation was initially developed in the 1970s and 1980s with the aim of ventilating patients with acute lung injury. The principal characteristics of high-frequency ventilation are the use of low tidal volumes (approximately 1.0 ml/kg), high respiratory rate, and low airway pressures – analogous to PEEP, although without the need to maintain high volumes in order to adequately eliminate carbon dioxide<sup>(53)</sup>.

As a result of the convection created by low levels and molecular diffusion (reduction in the carbon dioxide gradient from the alveolus to the conducting airways), carbon dioxide elimination during high-frequency ventilation is efficacious and is increased by the turbulence created by the convective flow (Taylor dispersion). These mechanisms make it possible to effectively eliminate carbon dioxide despite the use of tidal volumes lower than that of the pulmonary dead space<sup>(53)</sup>.

High-frequency ventilation promotes alveolar distension by increasing average airway pressure. This promotes alveolar recruitment and a consequent increase in the functional residual capacity, as well as a reduction in the number of areas with a low ventilation-perfusion ratio<sup>(54)</sup>. This technique has been widely used to ventilate the nondependent lung during one-lung ventilation,



with the aim of improving arterial oxygenation. Some studies have demonstrated its efficacy by supporting the hypothesis that PaO<sub>2</sub> normalizes, thereby improving surgical success rates<sup>(55,56)</sup>. Dikmen *et al.* analyzed PaO<sub>2</sub>, carbon dioxide tension, arterial pressure and cardiac rate in 15 patients undergoing elective thoracic surgery in the lateral decubitus position. High-frequency ventilation was applied to the nondependent lung. The authors concluded that this technique was effective in establishing normal values for the parameters analyzed<sup>(55)</sup>.

### ALVEOLAR RECRUITMENT

It is known that general anesthesia causes atelectasis in dependent pulmonary regions<sup>(57)</sup>. Based on that fact, Tusman *et al.* demonstrated, in 1999, that the alveolar recruitment maneuver improves oxygenation, reverses alveolar collapse and increases compliance during anesthesia<sup>(58)</sup>.

In 2002, the same group analyzed the effects of the alveolar recruitment maneuver during one-lung ventilation. They concluded that the use of this technique in the dependent lung promotes proper oxygenation, since it optimizes the ventilation-perfusion ratio and totally reverses the shunt<sup>(59)</sup>. However, further studies are needed in order to elucidate which mechanisms are involved in alveolar and capillary recruitment during one-lung ventilation.

### CONCLUSION

The execution of one-lung ventilation still constitutes a challenge in clinical and surgical practice. Many techniques have been developed with the aim of minimizing the related complications. However, further studies are warranted in order to find the ideal way to employ and monitor this technique.

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