Approaches to hypoxemia during single-lung ventilation

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Modern techniques to isolate the lungs, coupled with accurate continuous non-invasive monitoring, have made single-lung ventilation safe and easy to perform. Most patients maintain an adequate arterial oxygen tension during single-lung ventilation. In order to maximize oxygenation, efforts are directed towards optimizing perfusion and ventilation to the ventilated lung or increasing the oxygen content of blood returning from the collapsed lung. Curr Opin Anaesthesiol 14:71–76. © 2001 Lippincott Williams & Wilkins.

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Abbreviations

CPAP	continuous positive airway pressure
F_{iO_2}	fraction of inspired oxygen
FRC	functional residual capacity
HFV	high-frequency ventilation
HPV	hypoxic pulmonary vasoconstriction
iNO	inspired nitric oxide
NO	nitric oxide
P_{aO_2}	arterial oxygen tension
PEEP	positive end-expiratory pressure
P_{vO_2}	mixed venous oxygen tension
PVR	pulmonary vascular resistance
S_{aO_2}	arterial oxyhemoglobin saturation
SLV	single-lung ventilation
TIVA	total intravenous anesthesia
TLV	two-lung ventilation
V/Q	ratio of ventilation to blood flow in the lung

Introduction

This article focuses on recent work on the causes and management of hypoxemia during single-lung ventilation (SLV). For more detailed discussions, the reader is directed to comprehensive reviews of this subject [1,2].

Thoracic operations are usually performed with the patient in the lateral position with selective ventilation of the dependent lung. The intentionally collapsed non-dependent lung continues to be perfused. The extent of this wasted perfusion, or 'shunt', is determined by many factors [3•]. Blood flow to the dependent lung usually increases during SLV, but even under the best of circumstances, shunt is between 20 and 25% of cardiac output. Therefore, in order to maximize oxygenation, efforts are directed towards either optimizing the matching of ventilation with perfusion (V/Q) in the dependent ventilated lung or increasing the oxygen content of blood returning from the collapsed lung (see Table 1).

Effect of gravity on shunt

Gravity is a major determinant of shunt and perfusion. Two recent studies [4••,5•] examined changes in arterial oxygen tension (P_{aO_2}) with patients in different positions.

In the first study [4••], patients undergoing right thoracotomy were divided into three groups. One group was supine, one group was placed in the left semi-lateral decubitus position, and the third group was placed in the left full-lateral position. All patients were ventilated with 100% oxygen, and arterial blood gas samples were analysed every 5 min after intentional collapse of the right lung. P_{aO_2} progressively decreased in all groups after two-lung ventilation (TLV) was discontinued. Nine out of 11 patients in the supine group experienced an arterial oxyhemoglobin saturation (S_{aO_2}) of less than 90% and had to have TLV re-instituted. Only one out of nine patients in the semi-lateral group and one out of 13 patients in the full-lateral group experienced that degree of hypoxemia. The time for P_{aO_2} to decrease to 200 mmHg after the start of SLV was very rapid: (354 s) in the supine group compared with 583 s in the semi-lateral group and 794 s in the full-lateral group.

The second study [5•] compared the effects of position and fraction of inspired oxygen (F_{iO_2}) during thoracic surgery. Randomly assigned patients were ventilated with a F_{iO_2} of 0.4, 0.6 or 1.0 during periods of TLV and SLV in the supine and lateral positions. P_{aO_2} decreased

Table 1. Strategies to maximize oxygenation during single-lung ventilation

Operated lung
   Oxygenate shunt blood
- Continuous oxygen insufflation
- Intermittent single breath with oxygen
- CPAP
- CPAP$_{(upper-lung)}$/PEEP$_{(dependent\ lung)}$
- High-frequency ventilation

   Decrease shunt
- Vasoconstriction (phenylephrine, noradrenalin, almitrine)
- Pulmonary artery obstruction

Non-operated lung
   Optimize ventilation
- High Fio_2
- Large tidal volume ventilation
- Pressure-controlled ventilation
- PEEP

   Improve perfusion
- Selective vasodilation (iNO, prostacyclin)

CPAP, Continuous positive airway pressure; Fio_2, fraction of inspired oxygen; iNO, inspired nitric oxide; PEEP, positive end-expiratory pressure.

more during SLV compared with TLV in all groups in both positions. In all three groups Pao_2 was significantly higher during SLV in the lateral than in the supine position.

Those studies demonstrated that, during SLV with a patient in the lateral position, gravity augments the re-distribution of perfusion to the ventilated lung, resulting in a better V/Q match and a higher Pao_2.

Hypoxic pulmonary vasoconstriction and anesthetic agents

Regional hypoxia in the lung causes arteriolar constriction, with diversion of the blood flow away from the hypoxic segment to normal areas of lung (hypoxic pulmonary vasoconstriction; HPV). By redistributing cardiac output from poorly ventilated hypoxic areas to better-ventilated regions, V/Q is maximized. Under experimental conditions, HPV is an important regulator of blood flow to atelectatic lung.

It has been known for many years from in-vitro animal studies that all intravenous anesthetic and sedative agents (examples: barbiturates, benzodiazepines, opioids, ketamine, droperidol) do not alter the HPV response [6]. More recent experiments have reconfirmed these findings, and have shown that propofol may actually potentiate HPV [7,8]. In contrast, in-vitro studies [9] demonstrated that inhaled halogenated anesthetic agents all inhibit HPV in a dose-dependent manner.

In intact animals and patients, there is no inhibition of HPV by intravenous anesthetic agents. However, a wide range of effects is seen with inhalational anesthetic agents.

The conflicting results between in-vitro and in-vivo studies of inhalational anesthetic agents may be caused by their complex effects on cardiac output and shunt, oxygen consumption and mixed venous oxygen tension (Pvo_2), and by other mechanical factors (surgical manipulation of the lung, the use of positive end-expiratory pressure; PEEP) in patients undergoing operations.

All inhalational anesthetic agents directly increase shunt through partial inhibition of HPV, producing a modest reduction in Pao_2 [10]. However, an anesthetic agent that lowers cardiac output more than it decreases oxygen consumption will also lower Pvo_2 producing a potent stimulus for HPV. A decrease in cardiac output will result in less blood flow to the collapsed lung because of the higher pulmonary vascular resistance (PVR) already present in that lung. These actions counter the direct depression of HPV by the anesthetic agent.

This was demonstrated in anesthetized pigs using desflurane [11•]. In that study, pigs initially received total intravenous anesthesia (TIVA) with propofol, and then were ventilated with different concentrations of desflurane once the propofol was discontinued. With increasing concentrations of desflurane, Pvo_2, mean arterial pressure, cardiac output and shunt fraction all decreased in a dose dependent manner during SLV. Pao_2 remained unchanged. The authors concluded that increasing concentrations of desflurane have hemodynamic effects that negate its direct inhibitory effect on HPV.

There is no clinical advantage during SLV in terms of oxygenation with any of the inhalational anesthetic agents. When desflurane was compared with isoflurane in patients undergoing thoracotomy, there were no differences in mean arterial pressure, heart rate or Pao_2 [12,13•].

Choice of anesthetic agent for thoracic surgery

If HPV is clinically important, then the depressive effects of inhalational anesthetic agents would be a disadvantage during SLV. Because intravenous agents maintain HPV, some anesthesiologists continue to recommend TIVA for procedures requiring SLV [14].

In a study of 50 patients undergoing SLV for pulmonary resection [15], one group received TIVA and the second group received an inhalation anesthetic agent. Blood pressure, heart rate and arterial carbon dioxide tension levels were similar in both groups. As a group, the TIVA patients had higher Pao_2 levels during SLV than those receiving inhalation anesthesia, but patients in both groups maintained adequate oxygenation.

For most patients, the clinical effects of intravenous and inhalational anesthetic agents on HPV and oxygenation are more theoretical than real. Concerns about anesthetic effects on HPV are even less important during surgery than under experimental conditions, because surgical manipulation of the lung releases vasoactive substances (thromboxane and prostacyclin) that cause local vasodilation that blunts HPV [16]. As Conacher [17••] emphasized in a recent editorial, the use of 100% oxygen, optimizing dependent lung functional residual capacity (FRC), manipulating ventilatory parameters, and the application of PEEP or continuous positive airway pressure (CPAP) are clinically far more important than the effects (or lack of effects) of anesthetic agents on HPV.

Ventilation during single-lung ventilation

General anesthesia normally decreases FRC. When the patient is in the lateral position the intra-abdominal contents shift the diaphragm cephalad, further reducing dependent lung FRC. During lateral thoracotomy the dependent lung may have areas of low V/Q and areas that are totally atelectatic.

It is my practice not to decrease tidal volume at the commencement of SLV. Patients are ventilated with the same tidal volume as they were during TLV. The ventilator rate is adjusted to keep arterial carbon dioxide tension between 36 and 40 mmHg. The dependent lung is ventilated with a FiO$_2$ of 1.0 and a tidal volume of 10–12 ml/kg. This tidal volume will recruit dependent lung alveoli. Tidal volumes of less than 8 ml/kg result in a further decrease in FRC, with increased areas of dependent lung atelectasis. Tidal volumes greater than 15 ml/kg over-distend the alveoli and increase PVR in the dependent lung, resulting in an increase in shunt to the non-dependent lung.

Even with a shunt as high as 25%, a FiO$_2$ of 1.0 and large tidal ventilation usually results in a PaO$_2$ greater than 150 mmHg during SLV [18]. At this PaO$_2$, arterial hemoglobin is 100% saturated. A high FiO$_2$ causes vasodilation of the vessels in the dependent lung that increases perfusion of that lung and further decreases shunt.

There is concern that tidal volumes even as small as 10 ml/kg may cause excessive inflation pressures and barotrauma to the lungs, and may be responsible for some pulmonary complications after thoracotomy [19,20].

Pressure-controlled ventilation has been suggested as an alternative. Pressure-controlled ventilation is associated with lower peak airway pressure, lower shunt and higher PaO$_2$ than conventional volume-controlled ventilation during SLV [21].

Another technique experiencing renewed interest is high-frequency ventilation (HFV). In one retrospective clinical study [22•] there were no differences in SaO$_2$ or end-tidal carbon dioxide between patients who had conventional SLV and those receiving HFV.

Although the mechanism of lung injury is unknown, in animals even a short period of injurious mechanical ventilation can lead to a decrease in compliance that is associated with a large influx of proteins into the alveoli and alteration in pulmonary surfactant [23].

If ventilation is interrupted for any reason during SLV, hypoxemia can rapidly ensue [24•]. Baraka *et al.* [24•] compared the rate of apnea-induced hemoglobin desaturation in six patients undergoing thoracotomy and thoracoscopy. Their lungs were ventilated with a FiO$_2$ of 1.0 during TLV and then SLV. SaO$_2$ was monitored and recorded after intentional apnea. The mean time for apnea-induced hemoglobin desaturation from a SaO$_2$ of 100 to 95% after TLV was 6.3 ± 1.2 min compared with 3.2 ± 0.5 min ($P < 0.05$) after SLV.

Optimizing oxygenation during single-lung ventilation

If hypoxemia occurs during SLV it is usually as a result of an inadequate FiO$_2$, alveolar hypoventilation, or a large alveolar to arterial oxygen tension gradient from continued perfusion of the deflated lung.

The position of the double-lumen tube or endobronchial blocker should be immediately re-confirmed. Other mechanical problems (tube obstruction, bronchospasm) should be ruled out. Decreased perfusion of the ventilated lung from hemodynamic causes (hypotension, arrhythmia) should also be considered.

As discussed earlier, there is a reduction of FRC in the dependent lung during SLV in the lateral position. In the presence of decreased FRC, PEEP (5–10 cm water) will recruit collapsed and under-inflated alveoli and improve oxygenation.

Not all patients show an improvement with PEEP. Each patient's pre-existing lung disease determines their response [25]. During mechanical ventilation some patients have expiratory gas flow halted by the start of the next inspiration. This phenomenon (called 'auto-PEEP' or 'instrinsic PEEP') increases FRC. Although there is a greater degree of auto-PEEP generated in patients with emphysema during SLV, it is measurable in normal patients [26]. Applied PEEP may not improve or may even decrease oxygenation in patients who already have significant auto-PEEP and normal or high FRC [27]. In these patients, the application of PEEP will increase alveolar airway pressure and dependent

lung PVR, which in turn will divert blood flow to the non-ventilated lung increasing hypoxemia. For a patient with chronic obstructive pulmonary disease and a high level of auto-PEEP, the addition of PEEP combined with large tidal volume ventilation can lead to pulmonary hyperinflation and cardiopulmonary compromise [28•].

The reader is directed to a comprehensive review of the special anesthetic considerations of patients with advanced emphysema [29••]. This subject is particularly pertinent because of the increasing number of such patients who are undergoing lung volume reduction procedures [30].

If hypoxemia occurs, the collapsed lung can be partly or fully re-expanded. A single breath to the operated lung will temporarily oxygenate shunt blood. The lung will eventually re-collapse from absorption atelectasis, and so it must be re-expanded approximately every 5 min.

Insufflation with 100% oxygen to the non-ventilated lung is usually unsuccessful because oxygen fails to reach and recruit collapsed alveoli. However, insufflation by CPAP with 100% oxygen to the non-ventilated lung is an effective means of correcting hypoxemia. CPAP maintains the patency of alveoli with oxygen, so shunt blood becomes oxygenated. Any increased airway pressure in that lung from CPAP may further increase PVR, which will divert blood flow to the ventilated lung.

The combination of PEEP (5–10 cm water) applied to the ventilated lung and CPAP (5–10 cm water) to the non-ventilated lung has been described [31]. In my experience, this maneuver is unnecessary because upper-lung CPAP or just intermittent re-expansion of the collapsed lung predictably reverses hypoxemia during SLV.

During pneumonectomy, ligation of the pulmonary artery completely eliminates shunt, thereby maximizing the dependent lung V/Q relationship. Clamping the pulmonary artery during lobectomy will direct blood to the ventilated lung. This maneuver should be avoided because re-perfusion after total interruption of pulmonary artery blood flow may injure the lung [32•].

Pharmacological management of single-lung ventilation

If shunt is decreased, then V/Q matching in the ventilated lung will improve. In animal studies [33], direct infusion of prostaglandin F_{2a}, a potent pulmonary vasoconstrictor, into the pulmonary artery of the non-ventilated lung causes a significant decrease in shunt and an increase in PaO$_2$. Phenylephrine has also been used as a non-specific pulmonary vasoconstrictor to improve oxygenation [34].

Another approach is to increase blood flow directly to the dependent lung. There is considerable interest in using nitric oxide (NO), a potent vascular smooth muscle vasodilator, in this role [35••].

In one study [36], 60 patients undergoing pulmonary resection in the lateral position were divided into two groups. If a patient became hypoxemic during SLV, either inspired NO (iNO) 20 ppm or nitrogen was added to the inspired gas mixture. Eight patients in each group experienced hypoxemia. Oxygenation improved in two patients in the iNO group and two patients in the control group. The majority (75%) of patients receiving iNO showed no benefit. The authors concluded that 20 ppm iNO was not superior to nitrogen in the treatment of hypoxemia during SLV, and that iNO was not a practical alternative to the conventional management of hypoxemia during SLV.

Similarly, iNO (40 ppm) to the ventilated lung did not decrease mean pulmonary artery pressure in patients with normal PVR. Oxygenation was not improved because shunt remained unchanged [37]. The effects of iNO are directly proportional to the degree of PVR present when it is administered [38•]. The majority of patients undergoing pulmonary resection have normal or only slightly elevated PVR.

For patients with increased PVR, iNO in combination with another vasoactive agent can improve oxygenation. For example, aerosolized prostacyclin improves gas exchange and pulmonary shunt by redistributing pulmonary blood flow from non-ventilated to aerosol-accessible ventilated lung regions [39•]. The combination of inhaled prostacyclin and iNO decreases elevated pulmonary artery pressure [40]. Intravenous prostacyclin and iNO resulted in a marked decrease in pulmonary artery pressure, with an increase in cardiac output and an improvement in PaO$_2$ in a patient with severe adult respiratory distress syndrome and pulmonary hypertension [41]. Although potentially useful, the combination of iNO and prostacyclin has not yet been used during SLV.

Administering iNO to increase perfusion to well ventilated lung and almitrine bismesylate (a potent pulmonary vasoconstrictor) to decrease shunt to poorly ventilated lung increases oxygenation in animals [42] and in patients with acute respiratory distress [43]. Several years ago there was excitement over a study that successfully used this combination during thoracoscopy [44]. That report has not been followed by any further clinical studies.

Pharmacological interventions to improve oxygenation during SLV may play a role during procedures such as

thoracoscopy or bronchopulmonary lavage [45•] because conventional management strategies (re-inflation of the operated lung, application of CPAP) are not practical in these cases.

Conclusion

During SLV ventilation with 100% oxygen and optimization of dependent lung FRC will produce a safe $PaO2$ for most patients. If hypoxemia does occur, manipulation of ventilatory parameters and the application of PEEP to the dependent lung or CPAP to the collapsed lung will usually correct the problem. In the future, pharmacological manipulation may be helpful during SLV, but to date such interventions have not been very successful.

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