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Hypoxemia during One-lung Ventilation

Prediction, Prevention, and Treatment

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When switching from two-lung to one-lung ventilation (OLV), shunt fraction increases, oxygenation is impaired, and hypoxemia may occur. Hypoxemia during OLV may be predicted from measurements of lung function, distribution of perfusion between the lungs, whether the right or the left lung is ventilated, and whether the operation will be performed in the supine or in the lateral decubitus position. Hypoxemia during OLV may be prevented by applying a ventilation strategy that avoids alveolar collapse while minimally impairing perfusion of the dependent lung. Choice of anesthesia does not influence oxygenation during clinical OLV. Hypoxemia during OLV may be treated symptomatically by increasing inspired fraction of oxygen, by ventilating, or by using continuous positive airway pressure in the nonventilated lung. Hypoxemia during OLV may be treated causally by correcting the position of the double-lumen tube, clearing the main bronchi of the ventilated lung from secretions, and improving the ventilation strategy.

ONE-LUNG ventilation (OLV) is required for a number of thoracic procedures, such as lung, esophageal, aortic, or mediastinal surgery. Although OLV is not mandatory for all such procedures, it almost always improves access to the operation field and expedites the process of operation. For this reason and because anesthesiologists' expertise in placement and monitoring of double-lumen tubes (DLTs) has increased, OLV is now used for almost all thoracic operations in which the lung is operated on or in which the collapse of the lung improves access to the operation field.

During OLV, although only one lung is ventilated, both lungs are perfused. Perfusion of the collapsed, nonventilated lung leads inevitably to transpulmonary shunting, to impairment of oxygenation, and, occasionally, to hypoxemia. In a recent study,[1] we found that hypoxemia during OLV, defined by a decrease in arterial hemoglobin oxygen saturation (Sa_{O_2}) to less than 90%, occurred in 4% of patients whose lungs were ventilated with a fraction of inspired oxygen (F_{IO_2}) greater than 0.5. Other studies[2–5] using similar definitions of hypoxemia place the rate at 5–10%. Hypoxemia during OLV may affect the safety of the patient and is a challenge for the anesthesiologist and for the surgeon. It is therefore important to predict, to prevent if possible, and to promptly treat hypoxemia during OLV.

Prediction of Hypoxemia during OLV

A number of factors may be helpful in predicting oxygenation during OLV. However, it must be kept in mind that none of these factors alone can accurately predict whether an individual patient will become hypoxemic during OLV.

Side of Operation

Because the right lung is larger than the left lung, it is not surprising that oxygenation during OLV is better during left thoracotomy (*i.e.*, when the larger right lung is the dependent, ventilated lung).[6] In a recent study,[1] we found that while ventilating with an F_{IO_2} of 1, mean arterial oxygen tension (Pa_{O_2}) during OLV was approximately 280 mmHg during left-sided thoracic surgery as compared with approximately 170 mmHg during right-sided operations. Slinger *et al.*[2] using regression analysis, found the side of operation to be one of the important factors in predicting hypoxemia during OLV.

Lung Function Abnormalities

Although lung function abnormalities may predispose to hypoxemia during OLV, not all measures of lung function are reliable indicators. Indeed, some studies show a clearly paradoxical effect: Some indicators of airway obstruction in lung function tests show a negative correlation with oxygenation during OLV, meaning that the more severe the obstruction is, the less likely it is that the patient will experience hypoxemia during OLV. In retrospective and prospective studies, Slinger *et al.*[2] found that the less the forced expiratory volume was in 1 s, the better the oxygenation was during OLV. One explanation provided for this paradoxical relation may be that air trapping in the ventilated lung may generate auto–positive end-expiratory pressure (PEEP) during OLV, thus decreasing the likelihood of atelectasis in the ventilated lung and improving oxygenation. Also, air trapping in the nonventilated lung may delay the onset of desaturation. However, other studies have not found any relation between degree of auto-PEEP and oxygenation during OLV,[7] and another recent study did not find

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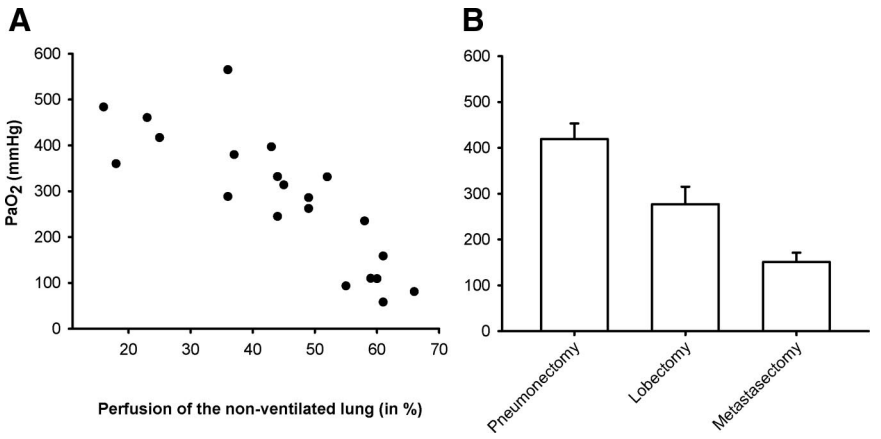

Fig. 1. Perfusion of the nonventilated lung affects oxygenation during one-lung ventilation. (*A*) Oxygenation 30 min after initiating one-lung ventilation increases with decreasing preoperatively measured perfusion of the nonventilated lung. The lowest (< 100 mmHg) arterial oxygen tension (Pa_{O_2}) occurs in patients with high perfusion levels in the nondependent lung. (*B*) Oxygenation 30 min after initiating one-lung ventilation for patients presenting for pneumonectomy, lobectomy, and metastasis resections. Mean preoperatively measured perfusion of the nonventilated lung was 55% in patients undergoing metastasectomy, 47% in patients undergoing lobectomy, and 32% in patients undergoing pneumonectomy. Modified with permission from Schwarzkopf *et al.*: Oxygenation during one-lung ventilation: The effects of inhaled nitric oxide and increasing levels of inspired fraction of oxygen. Anesth Analg 2001; 92:842–7.[1]

any meaningful relation between the preoperatively measured degree of bronchial obstruction (forced expiratory volume in 1 s) and oxygenation during OLV.[5]

Another frequently used surrogate measure of lung function in the preoperative workup is capillary or arterial blood gas analysis. Abnormally low arterial oxygen tension (Pa_{O_2}) as found by blood gas analysis during the preoperative workup or during two-lung ventilation before OLV may be a reliable indicator of abnormal lung function and predict hypoxemia during OLV. Slinger *et al.*[2] found that Pa_{O_2} levels during spontaneous ventilation, and even more during two-lung ventilation, were strongly and positively correlated with Pa_{O_2} during OLV.

Distribution of Perfusion

Distribution of perfusion between the two lungs is another important factor that may be measured preoperatively and may help to predict hypoxemia during OLV[8] (fig. 1A). Because transpulmonary venous shunting depends on the percentage of cardiac output that is not oxygenated, the less the perfusion of the nonventilated lung is and the more the perfusion of the ventilated lung is, the higher the Pa_{O_2} is during OLV.[2,5,4,8,9] Because a good number of patients presenting for major thoracic surgery may have perfusion scans in the workup for the operation, it is important that the anesthesiologist take the results of the scans into account.

Even without having access to perfusion scans, clinical presentation of the patients may offer some clues as to how good the perfusion of the nonventilated lung will be: Patients with large central tumors will most probably have less perfusion to the operated (nonventilated) lung as compared with patients with small peripheral masses. Large, more centrally located masses usually are treated surgically by lobectomy or pneumonectomy, whereas small peripheral lesions, usually metastases of nonpulmonary tumors, are treated by wedge resections. We[1] have found that patients undergoing lobectomy and pneumonectomy had a much better oxygenation during OLV than patients presenting for open or videoscopic metastasectomy (fig. 1B). Lung perfusion studies showed that perfusion of the nonventilated lung was more impaired in patients presenting for lobectomy and pneumonectomy than in patients presenting for metastasectomy.

Another factor affecting perfusion of the ventilated and nonventilated lung during OLV is gravity. In patients in the supine position, gravity affects both lungs equally. In the lateral decubitus position, however, gravity leads to a better perfusion of the lower, ventilated lung than of the upper, nonventilated lung. Because oxygenation increases as perfusion of the nonventilated lung decreases, oxygenation during OLV will be probably better with the patient in the lateral decubitus position as compared with the supine position (fig. 2). In one study[10] involving patients with chronic obstructive pulmonary diseases, Pa_{O_2} after 15 min of OLV during ventilation with an F_{IO_2} of 1 was 301 (215–422) mmHg during OLV in the supine position as compared with 486 (288–563) mmHg in the lateral decubitus position. The relatively high levels of Pa_{O_2} in this study may have resulted from an incomplete deairing of the nonventilated lung in patients with obstructive lung disease.

Prediction of hypoxemia is important not only for the anesthesiologist but also for the surgeon because measures to deal with hypoxemia during the procedure may

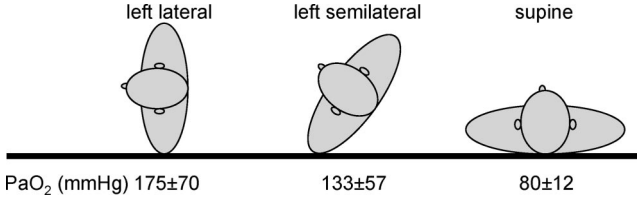

Fig. 2. Patient position may affect the perfusion of the ventilated lung and thus improve or worsen oxygenation during one-lung ventilation. Patients in lateral decubitus position have a much better oxygenation during one-lung ventilation than patients in semilateral or supine position. Pa_{O_2} = arterial oxygen tension. Modified with permission from Watanabe *et al.*: Sequential changes of arterial oxygen tension in the supine position during one-lung ventilation. Anesth Analg 2000; 90:28–34.[88]

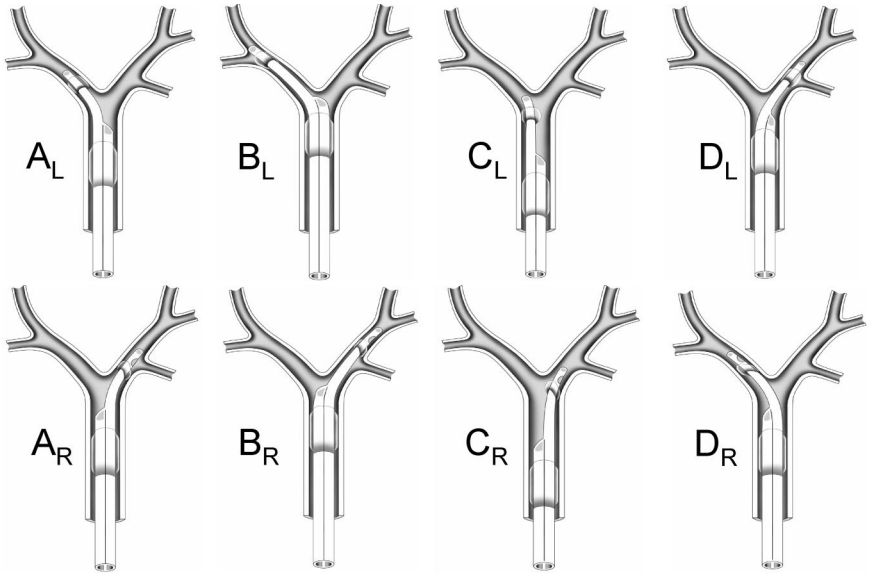

Fig. 3. Tube misplacement during one-lung ventilation may lead to hypoxemia. The correct position (A_L) and possible misplacements (B_L–C_L) of the left-sided double-lumen tube are shown. In the lower four figures, correct position (A_R) and possible misplacements (B_R–D_R) of the right sided double-lumen tubes are shown.

interfere with surgery. A patient who has poor oxygenation before surgery, even distribution of perfusion between the lungs, and is scheduled to undergo surgery in the supine position may very likely develop hypoxemia, and it may be helpful to discuss this point with the surgeon before the operation. An integrated approach using all patient and procedure information may therefore help to develop a sound surgical and anesthesiologic approach in an individual patient.

Prevention of Hypoxemia during OLV

Improving Preoperative Lung Function

Although not unequivocally proven by published data, it is probably safe to assume that improving the pulmonary function before the operation will most probably not only decrease postoperative pulmonary complications but also improve oxygenation during OLV. Improving preoperative lung function may involve physical therapy and drugs to dilate the bronchi and to loosen secretions.[11]

Monitoring Lung Separation

Using a DLT is the method of choice for lung separation and OLV for thoracic procedures. A DLT allows easy fiberoptic access to both lungs, which may be crucial if bleeding or secretions are a problem. However, both left- and right-sided DLTs are frequently misplaced during placement or dislodged later,[12] which may lead to impaired oxygenation and inadequate lung separation during surgery (fig. 3). Primary placement of the DLT as well as the danger of dislodgment due to patient positioning or surgical manipulation necessitates fiberoptic monitoring during thoracic surgery.[13] As much as 12% of all DLTs may be misplaced or dislodged during the operative period. A distal misplacement of a left-sided DLT during right thoracotomy may lead to hypoxemia in that, during OLV, only the left lower or the left upper lobe will be adequately ventilated through the bronchial limb, thus leading to insufficient lung surface for oxygenation (fig. $3B_L$). A proximal dislodgment of a left-sided tube may lead to ventilation problems while ventilating through the tracheal limb because the cuff of the bronchial limb may partially obstruct the trachea (fig. $3C_L$). Ventilating through the bronchial limb of a right-sided tube may also lead to hypoxemia if, in case of misplacement, the right upper lobe is not adequately ventilated, leading to a decrease in ventilation surface and an increase in shunt fraction (fig. $3B_R$). A recent retrospective analysis in 1,170 patients undergoing OLV found hypoxemia in 35 patients (3%), the majority of whom required a correction of tube position to alleviate the problem.[14] Because of inherent difficulties in the use of DLT, adequate monitoring and proper fixation of the tube may make hypoxemia less likely. Fiberoptic monitoring of DLTs is therefore required both after intubation and after patient positioning in the lateral decubitus position. A malposition of more than 1 cm in or out of the optimal positioning has been suggested as being clinically relevant and in need of correction.[13,15] Although this amount of malposition may not seem to obstruct bronchi or be associated with incomplete lung separation at the time of fiberoptic bronchoscopy, subsequent manipulation by the surgeon may lead to total malposition and an increased rate of hypoxemia.[15] For this reason, the tube should be optimally positioned as suggested by Klein *et al.*[13] at each fiberoptic inspection.

Good Ventilation Strategy in the Dependent Lung

Ventilation strategy is important if we are to decrease the incidence of hypoxemia during OLV. While ventilating the dependent lung in paralyzed patients in the

lateral decubitus position, we should consider three problems.

First, the expansion of the dependent lung is impeded by the weight of the mediastinum, by the pressure of the abdominal organs and cephalad displacement of the diaphragm, and by the pressure and noncompliance of the thoracic wall on the which the patient is lying.[16] For all these reasons, atelectasis may readily occur in the dependent, ventilated lung, leading to a decrease in ventilated lung surface. Atelectasis and alveolar collapse in the dependent lung activates hypoxic pulmonary vasoconstriction (HPV) and/or impedes perfusion to these lung areas, leading to a concomitant increase in resistance to flow in the dependent pulmonary artery, thus diverting more perfusion to the nonventilated lung and increasing shunt fraction. For these reasons, it is crucial to apply a ventilation strategy that decreases the occurrence of atelectasis in the dependent lung.

Second, whereas a moderate increase in lung volume (and ventilation pressure) is necessary to avoid development of atelectasis and to keep the dependent lung open, a large increase in dependent lung volume may impede perfusion of the ventilated lung, leading inevitably to an increase in perfusion of the nonventilated lung and an increase in venous shunting.

Third, poor ventilation strategy, at least in special groups of patients requiring OLV, may lead to lung injury.

Theoretically, depending on lung mechanics and perfusion status for any individual patient, there is a range of ventilation strategies that keep the lung open without impeding perfusion. Clinically, however, there are no viable means of determining this best ventilation strategy in an individual patient. Therefore, patient condition, physiologic reasoning, and best available clinical evidence must be used to tailor a ventilatory strategy that best fits the needs of the individual patient. Most studies on ventilation strategies are physiology based and are performed in a limited number of patients with mixed pathologies. Ideally, a physiology-based study should be performed in patients with minimal perfusion abnormalities, which would mean excluding most patients undergoing lobectomy and pneumonectomy. However, this is seldom the case in most studies. Transferable evidence is therefore limited.

Two strategies have been advocated to decrease the likelihood of hypoxemia and, possibly, atelectasis, during OLV: a high tidal volume (10–12 ml/kg) without PEEP[14,17] or a moderate tidal volume (6–8 ml/kg) with PEEP.[1,18,19] A large tidal volume will open the lung during the inspiration phase. Because a large tidal volume will need a longer time to expire, most of the lung may remain open during most of the expiration period. However, two less-optimal scenarios are also possible.

First, a large tidal volume may overdistend alveoli, hyperinflate the lung, and lead to acute lung injury in susceptible patients.[20,21] The Acute Respiratory Distress Syndrome Network study and a large number of animal studies have demonstrated the perils of using large tidal volumes and of cyclic atelectasis in injured or healthy lungs.[22,23] These studies show that oxygenation alone cannot be considered the sole sufficient endpoint in assessment of ventilatory strategies. Only limited information is available on the effects of ventilatory strategy during OLV on inflammatory reaction and on lung injury. Wrigge *et al.*[24] studied the effects of high tidal volume (12 ml/kg) without PEEP *versus* low tidal volume (6 ml/kg) with PEEP of 10 cm H_2O on the mediators of systemic and pulmonary inflammation measured 3 h after surgery and did not find any difference in plasma or tracheal aspirate tumor necrosis factor α, interleukin (IL)-1, IL-6, IL-8, IL-10, or IL-12 levels. This study suggests that in the normal noninjured lung, the inflammatory reaction to surgery will most probably override any difference an inflammatory reaction ventilation strategy would make. However, with previous lung injury and a long duration of OLV, large tidal volumes may well translate into clinically evident lung injury. In rats, we have shown[25] that a moderately injurious ventilation strategy did not lead to overt lung injury in control rats but caused considerable injury in rats challenged with a small dose of endotoxin. In a recent clinical study,[26] high tidal volume (9 ml/kg) without PEEP as compared with low tidal volume (5 ml/kg) with PEEP during OLV for esophagectomy increased systemic levels of cytokine and led to an increase in lung water measurements. However, it must be kept in mind that OLV was not the only insult on lung integrity: Half of the patients in this study had undergone previous chemotherapy and radiotherapy, the duration of surgery was 5 h, and esophagectomy disrupts lung lymph drainage. Therefore, high tidal volumes without PEEP may injure the dependent lung, at least in the setting of previous and concomitant lung injury and a very long duration of surgery, and low tidal volumes with PEEP may be more appropriate in similar settings.

Second, in patients with airway obstruction, a large tidal volume may not be expired before the end of the set expiration time, leading to intrinsic PEEP. The factors determining intrinsic PEEP are tidal volume, expiration time, resistance, and compliance.[27] Many patients undergoing lung surgery may have some level of airway obstruction, and intrinsic PEEP has been frequently described during OLV.[28–30] A low level of intrinsic PEEP may be of no further consequence and may even help to keep the lung open and avoid atelectasis. A high level of intrinsic PEEP may lead to hyperinflation and, consequently, to a decrease in perfusion of the ventilated lung, potentially decreasing oxygenation.

Of note, in the study by Wrigge *et al.*[24] which applied large tidal volumes without PEEP *versus* small tidal volumes with PEEP, oxygenation was not different between the two very different ventilation strategies. A much

older study focusing on oxygenation also did not show improvement in oxygenation during OLV while increasing tidal volume from 8 to 15 ml/kg.[31] Therefore, large tidal volumes, although potentially injurious to the lung, do not translate into better oxygenation during OLV as compared with moderate or low tidal volumes combined with PEEP.

Although hyperinflation is unlikely with small tidal volume, small tidal volumes, especially during high F_{IO_2}, may lead to more atelectasis and poor oxygenation.[32] Therefore, small tidal volumes must be applied with PEEP to avoid atelectasis. However, there is some debate on which level of PEEP under which circumstances would improve oxygenation during OLV. Some recent studies have documented that a low or modest level of PEEP (approximately 4–5 cm H_2O) during OLV may improve oxygenation but that increasing PEEP to 8–10 cm H_2O produces no further improvement and might even be counterproductive in some patients.[33–36] Other studies have documented that PEEP will not increase oxygenation, at least not in all patients. In a recent study, PEEP at 0, 5, 8, or 10 cm H_2O did not affect oxygenation during OLV.[37] In another study, PEEP has been advantageous in patients with low oxygenation during OLV or with low oxygenation during two-lung ventilation preceding OLV.[38] Still other studies have found that interactions of applied PEEP with auto-PEEP may determine whether applied PEEP will lead to an improvement in lung mechanics and, probably, oxygenation.[39] In support of this, Valenza *et al.*[40] demonstrated that patients with a high forced expiratory volume in 1 s, who are therefore less likely to develop auto-PEEP, may profit more from application of PEEP than those with low forced expiratory volume in 1 s. In a recent study, Slinger *et al.*[41] showed that PEEP is effective in increasing oxygenation if the end-expiratory pressure (equivalent to total PEEP) is in close proximity to the lower inflection point on the volume–pressure curve of the ventilated lung. These findings suggest that PEEP may improve oxygenation when there is a serious problem of atelectasis but not necessarily if intrinsic end-expiratory pressure keeps the lung open. It should at the same time be appreciated that intrinsic PEEP is not only dependent on intrinsic mechanical properties of the lung, but can be modified according to the ventilation strategy.[39,42] This means that during use of PEEP, it may be helpful to know whether the ventilation strategy has led to development of intrinsic PEEP. A clinically feasible means of assessing intrinsic PEEP is assessing the flow–time or the flow–volume curve, one of which is usually available in the monitoring module of most modern anesthesia (ventilation) machines: Expiration is complete and intrinsic PEEP is very unlikely when expiration flow is not interrupted by the next inspiration and reaches zero before the next inspiration cycle starts. Auto-PEEP will most probably be present when the next inspiration begins before the expiration flow is complete *i.e.*, is zero.[43]

Complex physiology, diversity in the underlying conditions of patients, and inconclusive studies make it difficult to define which combination of tidal volume, respiratory rate, and PEEP will decrease the likelihood of atelectasis in the ventilated lung without impeding its perfusion and remains a matter of debate and study. There may be many solutions to the problem, and it is difficult to analyze, compare, and integrate the results of all the studies (with diverse methodologies) into evidence-supported and clinically feasible advice. We will present a strategy we currently use in our patients: We ventilate the dependent lung pressure-controlled[44] with a peak pressure of 20–25 cm H_2O and a PEEP of 5 cm H_2O (tidal volumes will vary between 450–650 ml [6–8 ml/kg] depending on lung compliance and lung size). We increase or decrease peak pressure to achieve a tidal volume of 6–7 ml/kg in left lung or 7–8 ml/kg in the right lung without altering PEEP. Ventilation rate and inspiratory:expiratory ratio are altered to achieve an expiration flow at or near zero and end-tidal carbon dioxide of 30–35 mmHg. In a clinical trial,[1] we ventilated patients according to this protocol (peak pressure 30 and PEEP of 5 cm H_2O) and, with use of a rather strict hypoxemia criterion of measured arterial desaturation below 90%, found a rather low 4% hypoxemia rate while ventilating with F_{IO_2} greater than 0.5. Of note, the clinically more relevant pulse oximetric saturation did not decrease below 91% in any of the patients. We are aware that we may have studied a selected group of patients and that this method will need to be tailored to the individual patient.

Oxygen Administration to the Nondependent Lung

Oxygen administration to the nondependent lung is mostly used to treat hypoxemia during OLV but may also be used to prevent it. Oxygen may be administered with or without continuous positive end-expiratory pressure (CPAP) to the nondependent lung. CPAP is very effective in improving oxygenation during OLV, and CPAP levels of as little as 3 cm H_2O have been shown to be sufficient.[45,46] Some studies suggest that routine CPAP may not only improve oxygenation but also be beneficial in reducing injury to the nonventilated lung. It has recently been shown that reexpansion of the nonventilated lung after OLV leads to release of oxygen radicals,[47–50] findings probably related to reperfusion injury. Further studies are needed to investigate whether routine CPAP during OLV would attenuate oxygen radical release from the nonventilated, albeit open, lung and whether this will be relevant to postoperative outcome and to the general well-being of the patient. However, CPAP may not be tolerated during some thoracic procedures (*i.e.*, thoracoscopy), and many surgeons may find it a problem

during thoracotomy too. Another problem with routine CPAP is that its efficacy in providing good oxygenation may conceal tube dislocation and atelectasis in the ventilated lung. During OLV without CPAP, tube dislocation leading to a lobe not being adequately ventilated will be detected clinically by decreasing oxygen saturation. This will not be the case with routine CPAP. Oxygen administration without CPAP through a T piece has also been described[51,52] as a means of providing oxygenation or delaying desaturation and used with some success.[53]

Modulation of Perfusion

A number of studies have used drugs that may increase perfusion of the ventilated lung or decrease perfusion of the nonventilated lung. One strategy involved the use of nitric oxide during OLV. Nitric oxide is an endothelial-dependent vasorelaxing factor.[54] Because nitric oxide is a gas, it can be easily administered during anesthesia. We and others[1,55–58] studied whether inhaled nitric oxide, by selectively vasodilating the vessels of the ventilated lung, would increase its perfusion and thus improve oxygenation during OLV. In concentrations ranging from 5 to 40 ppm, nitric oxide did not improve oxygenation or decrease the occurrence of hypoxemia during OLV.

Another approach to modulation of perfusion is to decrease the perfusion of the nonventilated lung with appropriate drugs. One such drug is almitrine. Almitrine is thought to decrease the perfusion of the nonventilated lung by strengthening HPV.[59] HPV is a physiologic reflex that by arteriolar vasoconstriction decreases blood flow to hypoxic and atelectatic lung regions, thereby reducing the perfusion of the nonventilated lung, reducing shunt fraction, and improving oxygenation.[60,61] During OLV, any strengthening of HPV may further reduce perfusion of the nonventilated lung and improve oxygenation. In one study,[62] the authors administered 16 $\mu g \cdot kg^{-1} \cdot min^{-1}$ almitrine (in combination with nitric oxide) during OLV and demonstrated a greater than 130% increase in Pa_{O_2}. A more recent study has also used lower doses of almitrine with nitric oxide with similar results.[63] However, the effect of almitrine on oxygenation during OLV has remained an interesting finding and can be considered a proof of principle but of no immediate clinical impact. With the use of sound clinical practice, however, hypoxemia should occur in less than 5% of patients.[1,14] Moreover, clinicians may (or should) be reluctant to use almitrine on a routine basis not only because of its toxicity[64] but also because, should hypoxemia occur during OLV, there are simple, effective, and rather safe methods of treatment. Almitrine could be a last-resort prevention or treatment strategy in patients with high likelihood of developing hypoxemia during video-assisted thoracoscopy where CPAP and intermittent ventilation may not be possible to use.

Type of Anesthesia

Type of anesthesia does not seem to affect oxygenation much during OLV, although some experimental studies may point to the contrary. *In vitro*, all volatile anesthetics inhibit HPV, whereas most intravenous anesthetics do not.[61,65] Inhibition of HPV by anesthetics is not only an *in vitro* finding and occurs during OLV *in vivo*: In one controlled animal experiment, Domino *et al.* [66] ventilated the right lung with pure oxygen and the left lung with a hypoxic gas mixture. Increasing concentrations of isoflurane administered only to the hypoxic left lung increased intrapulmonary shunt and decreased Pa_{O_2} in a dose-dependent fashion. The objective of this study was to show that the *in vitro* determined dose-dependent effects of isoflurane on HPV are also operative *in vivo*. Some experimental studies in which volatile anesthetics are administered to the ventilated lung also suggest that volatile anesthetics may impair oxygenation when used during OLV.[67,68] Other experimental studies,[69,70] however, show not only no deterioration of oxygenation during increasing concentrations of volatile anesthetics, but also that shunt fraction and perfusion of the dependent lung actually decreased with increasing concentration of volatile anesthetics during OLV. In one experimental study,[69] increasing levels of inhalational anesthetic led to a decrease in perfusion of the nonventilated lung and to a decrease in shunt fraction with no change in oxygenation. In this study, volatile anesthetic–induced changes in cardiac output, differential lung perfusion, and venous oxygen saturation integrated to maintain oxygenation during OLV. Most clinical studies show no or only minimal and mostly clinically insignificant changes in oxygenation when comparing volatile (0.5–1 minimum alveolar concentration) with intravenous anesthetics.[34,71–74] These findings suggest that, clinically, direct affects of volatile anesthetics on HPV do not always translate to impairments in oxygenation, largely because they are modified by the concurrent effects of volatile anesthetics on global hemodynamics.[65,67,69,70]

Epidural anesthesia is frequently used for intraoperative and postoperative analgesia in thoracic surgical patients. In experimental studies, epidural anesthesia has not inhibited HPV.[75,76] However, one clinical study[77] shows that the combination of general anesthesia with propofol–fentanyl and thoracic epidural anesthesia with local anesthetics during OLV is associated with lower Pa_{O_2} (mean: approximately 120 mmHg during ventilation with oxygen) than with general anesthesia alone (mean: approximately 180 mmHg), whereas incidence of hypoxemia was comparable in the two groups. The most recent study[78] comparing general anesthesia with isoflurane and nitrous oxide *versus* epidural analgesia in combination with general anesthesia found no difference in oxygenation or in the frequency of hypoxemia between the two groups. The authors speculated that using epidural anesthesia will allow using lower levels of

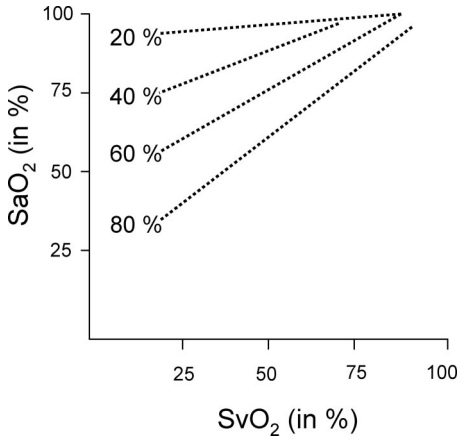

Fig. 4. In this graph, the shunt equation was modified and used to show the dependency of arterial oxygen saturation (Sao_2) on mixed venous oxygen saturation (Svo_2) at different shunt levels (*dotted lines*). It must be acknowledged that the graph represents a crude mathematical and hence a theoretical construct. However, it is useful in showing that the higher the shunt level is, the greater the effects are of decreasing levels of Svo_2 in shunted blood on oxygenation. Modified with permission from Dennehy *et al.* [89]

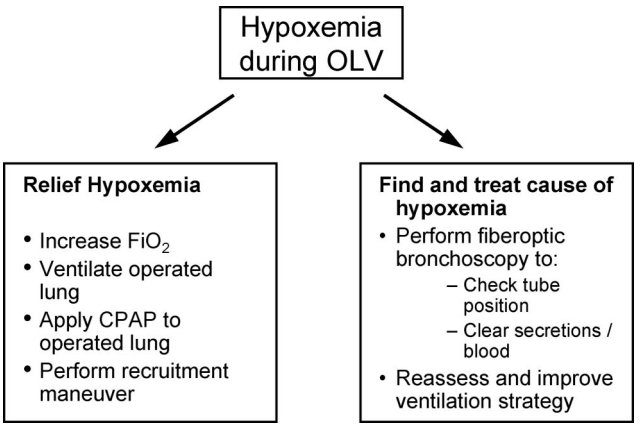

Fig. 5. Options in treating hypoxemia during one-lung ventilation (OLV). It is important to first relieve hypoxemia but then find the cause of hypoxemia. Fiberoptic bronchoscopy is important in correcting tube position and clearing secretions or blood in the ventilated lung and thus correcting the cause of hypoxemia during OLV. CPAP = continuous positive airway pressure; F_{IO_2} = fraction of inspired oxygen.

inhalational anesthetic during OLV, which would then potentially have less impact on HPV and thereby improve oxygenation. However, this speculation is not supported by a study in which epidural anesthesia did not affect oxygenation during total intravenous anesthesia: Von Dossow *et al.*[79] show that central and systemic hemodynamics were maintained and oxygenation was significantly better during epidural anesthesia with local anesthetics in combination with total intravenous anesthesia with propofol and remifentanil as compared with total intravenous anesthesia alone during OLV. In conclusion, type of anesthesia (inhalational *vs.* total intravenous anesthesia/epidural *vs.* no epidural) by itself does not affect oxygenation during OLV.

Hemoglobin Levels

In physiologic studies, Deem *et al.*[80] showed that shunt fraction increases and oxygenation decreases with low hemoglobin levels. Szegadi *et al.*[81] studied the effects of acute hemodilution on oxygenation in patients with and without chronic pulmonary obstructive disease undergoing OLV. They found that acute removal of 500 ml blood did not affect oxygenation in the normal population, whereas it decreased oxygenation in patients with chronic obstructive pulmonary disease. Unfortunately, shunt fraction was not calculated and mixed venous oxygen saturation was not measured, thus making interpretation difficult. One explanation may be that oxygenation during OLV depends not only on the magnitude of shunt fraction but also on the oxygenation of the shunted blood[69] (fig. 4). Factors leading to a decrease in oxygenation of the shunted (venous) blood are an increased oxygen extraction (low cardiac output or increased oxygen expenditure) and low hemoglobin levels. Therefore, the interaction of shunt fraction, cardiac output, oxygen expenditure, venous saturation, and hemoglobin levels may affect oxygenation.[82]

Treatment of Hypoxemia during OLV

Should hypoxemia occur during OLV, two strategies must be applied at the same time: First, hypoxemia must be effectively and immediately treated. Second, the cause of hypoxemia should be found and, if possible, corrected (fig. 5).

Increasing F_{IO_2}

Increasing F_{IO_2} is effective in immediately treating hypoxemia during OLV. Although increasing F_{IO_2} may not improve oxygenation with shunt fractions above 40%, this is seldom the case during OLV. Shunt fraction during OLV is usually in the range of 20–30%, leaving room for the efficacy of increasing F_{IO_2}. We have shown that oxygenation increases and rate of hypoxemia decreases when increasing F_{IO_2} from 0.3 to 0.5 and to 1.0.[1] Using an F_{IO_2} of 1.0 at all times during OLV is possible but may increase the risk of atelectasis[83,84] and would preclude the use of nitrous oxide. Moreover, in our clinical practice, decreases in oxygen saturation as measured by pulse oximetry while ventilating with an F_{IO_2} of approximately 0.5 serves as an early warning system that alerts the anesthesiologist to immediately increase in F_{IO_2} to 1.0, thereby improving oxygenation and allowing time to find the cause of decreasing oxygenation. This early warning system avoids the immediate necessity of ventilating the nonventilated lung and potentially disrupting the operative procedure.

Reexpansion of the Nonventilated Lung

If an increase in F_{IO_2} during hypoxemia does not improve oxygenation, the surgeon should be informed and

the operated lung should be expanded with pure oxygen. Although it may be sufficient to ventilate the operated lung by repeated hand ventilation every 3–5 min, the application of CPAP in the range of 3–10 cm H_2O is a more effective way of improving oxygenation by expanding the nonventilated lung and keeping it expanded. It may be easier for the surgeon to operate on an immobile albeit expanded lung than on a lung with frequent tidal ventilations. Many studies show that using CPAP of 5–10 cm H_2O improves oxygenation during OLV.[45,46] When CPAP levels between 5 and 10 cm H_2O are used, the improvement is attributed to the oxygen content of the CPAP fresh gas. During use of CPAP in the clinical practice, it should be appreciated that a pressure of 5–10 cm H_2O may not immediately inflate an already collapsed and atelectatic lung and may not be very helpful in increasing oxygenation. It is therefore necessary to reinflate the collapsed lung by applying a higher airway pressure and then using CPAP to keep the lung at a constant level of inflation. Although it may be tempting to use CPAP as a preventive measure in all patients undergoing OLV, not all surgeons and not all operative procedures will tolerate an expanded lung.[85]

High-frequency jet ventilation of the nondependent lung is another method to treat hypoxemia during thoracic surgery.[86,87] Because of the high respiratory frequency and the small tidal volumes, the operated lung during jet ventilation is almost immobile and does not interfere with surgery. However, widespread use has been hindered by the expense of the equipment, the need of expertise, and the danger of barotrauma.

Treating the Cause of Hypoxemia during OLV

Clinical experience suggests that the most common treatable causes of hypoxemia during OLV are dislodgment of the DLT, inadequate ventilation strategy leading to atelectasis in the ventilated lung, and occlusion of major bronchi of the ventilated lung with secretions or blood. Some of these problems can be dealt with immediately by using fiberoptic monitoring. If dislodgment has occurred or if secretion has occluded major bronchi, fiberoptic bronchoscopy can be used to correct the DLT position or to clear secretions. However, if DLT is not dislodged and no occlusion is found, the ventilation strategy should be reassessed. In our clinical experience, it is often helpful at this point to expand the ventilated dependent lung with high pressures to open up atelectasis and then to increase PEEP and/or tidal volume to keep the lung open. Recent studies suggest possible benefits of recruitment strategies on oxygenation during OLV.[18,19] Cinnella *et al.*[19] used a tidal volume of 6 ml/kg with no PEEP during OLV before recruitment and then performed a 1-min recruitment maneuver. After the maneuver, 5 cm H_2O PEEP was added to the ventilation strategy. The Pa_{O_2}/F_{IO_2} ratio improved from 235 mmHg to 351 mmHg, compliance improved, and although cardiac output and mean arterial pressure both decreased during the recruitment maneuver, they returned to baseline values soon after recruitment was over. The effect of the recruitment strategies on oxygenation during OLV will depend, among other factors, on whether the primary ventilation strategy was tailored to avoid atelectasis. In cases where recruitment improves oxygenation, the ventilation strategy should be modified by introducing or increasing PEEP or increasing tidal volumes after the recruitment maneuver to keep the lung open.

In our experience, in a small minority of patients no treatable cause for hypoxemia may be found and, depending on operative procedure, continuous or discontinuous CPAP of 5–10 cm H_2O may be used. In addition, to open the ventilated lung and keep it open, recruitment maneuvers and increasing PEEP up to 10 cm H_2O maybe be needed throughout the operation to achieve adequate oxygenation during OLV.

In conclusion, hypoxemia may occur in 5–10% of patients undergoing OLV. Preoperative lung function abnormalities, side of operation, and distribution of perfusion are important predictors of its occurrence. Prevention and treatment of hypoxemia during OLV involves fiberoptic monitoring of the DLT, using an appropriate ventilation strategy, increasing F_{IO_2}, and applying CPAP to the nonventilated lung.

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