Cardio-respiratory physiology during one-lung ventilation: complex interactions in need of advanced monitoring

Ines Marongiu[1], Elena Spinelli[2], Tommaso Mauri[1,2]

[1]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy; [2]Department of Anesthesia, Critical Care and Emergency, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

Correspondence to: Tommaso Mauri. Department of Anesthesia, Critical Care and Emergency, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Via F. Sforza 35, 20122 Milan, Italy. Email: tommaso.mauri@unimi.it.

During thoracic surgery, patients are often positioned on the lateral decubitus with the surgical site exposed, while gas exchange is granted through one-lung ventilation (OLV) technique. OLV is widely used to selectively ventilate the dependent lung, while the non-dependent one is collapsed to facilitate surgery. Careful settings of OLV can be extremely challenging as they have multiple and sometimes conflicting goals. To better understand challenges of OLV, changes induced in patients' physiology should be understood thoroughly.

Changes in cardio-respiratory physiology during OLV

Oxygenation

The non-ventilated but still perfused lung generates a right-to-left shunt, which is only partially corrected by the hypoxic pulmonary vasoconstriction (HPV) and gravitational re-distribution of blood flow (1). The oxygenation capability of the dependent ventilated lung might be compromised as a consequence of de-recruitment. Lateral decubitus, dependent position, over-imposed mediastinum weight, and general anesthesia reduce functional residual capacity (FRC) of the ventilated lung, even below the airway opening pressure (2,3). High inspiratory oxygen fraction is applied to improve oxygenation but it predisposes to the development of re-absorption atelectasis (4). Finally, if positive pressure

ventilation and gas trapping (see below) decrease the cardiac output, systemic O_2 delivery will fall reducing mixed venous saturation and further impairing arterial oxygenation.

Mechanics

Decreased FRC, de-recruitment and atelectasis result in decreased lung inflation and increased elastance of the dependent ventilated lung (5). Airway resistance is increased due to the smaller total area of the bronchial tree. Gas trapping due to higher respiratory rate and increased resistance is common, further worsening mechanics by development of intrinsic positive end-expiratory pressure (PEEP) and regional overdistension (6). Partitioned mechanics showed interesting results with lung elastance predictably increasing during OLV in comparison to supine double-lung ventilation, while chest wall elastance is unchanged during OLV and reduced during thoracic surgery with open chest (7).

Right heart function

Patients undergoing thoracic surgery are at high risk of having poor right heart function and surgery might pose a significant new challenge to the heart (8). As mentioned above, during OLV, HPV is usually activated in the non-dependent non-ventilated lung to decrease right-to-left shunt: however, this will increase pulmonary vascular

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resistance (PVR) and the workload for the right ventricle. Atelectasis and de-recruitment might lead to some activation of HPV in the dependent ventilated lung, too. Positive pressure ventilation with high pressure due to impaired mechanics in the dependent lung may overcome atelectasis (and decrease HPV) but will further increase PVR by increasing regions with West's Zone 1 behavior.

Optimal mechanical ventilation settings during OLV

The goals of OLV are to maintain viable oxygenation while preventing excessive ventilation pressure. Clinical studies showed that achieving such goals during the intraoperative ventilation management is crucial to decrease the incidence of postoperative pulmonary complications (PPC).

Although baseline condition of the lungs can be widely different, the pathophysiological changes during OLV and those observed in the lungs of patients with the acute respiratory distress syndrome (ARDS) are similar and the concepts of protective lung ventilation have been translated to OLV (9).

Tidal volume (Vt) and respiratory rate

The use of relatively low Vt [4–6 mL/kg predicted body weight (PBW)] during OLV decreases local and systemic cytokines release and inflammation and reduces PPC (10). However, to avoid hypercarbia, ventilation with low Vt is combined with increased respiratory rate, leading to reduction of the expiratory time and to dynamic hyperinflation. During volume-controlled ventilation, hyperinflation will increase the inspiratory pressures, vanishing the benefits of lower Vt; in pressure-controlled mode, instead, hyperinflation will reduce Vt, arterial pCO_2 will increase and further increase of respiratory rate will be required (6,11). A simple solution could be to titrate Vt by balancing acceptable arterial CO_2 and pH with a respiratory rate that allows the expiratory airflow tracing to reach zero before the next breath.

PEEP

Reversal of atelectasis by PEEP improves the oxygenation by decreasing shunt and improves the mechanical properties of the ventilated lung (12). Conversely, use of excessive PEEP might induce lung overdistension and increase regional PVR. These phenomena may cause a diversion of

blood perfusion from the ventilated to the non-ventilated lung, increasing right-to-left shunt and the workload for the right ventricle. Moreover, increased intra-thoracic pressure can reduce venous return. PEEP level should be fine-tuned to keep the lung open while avoiding the negative impact of overdistension. The most effective and simple bedside method to personalize PEEP during OLV could resemble the open lung approach used in ARDS patients: PEEP is titrated to the best respiratory system compliance after a maximal recruitment maneuver (13). This method applied during OLV resulted in improved oxygenation and increased lung compliance compared to the use of fixed low PEEP levels (14,15). However, this method only assesses global respiratory mechanics and doesn't measure directly overdistension, collapse or the right heart function.

To overcome the risk for de-recruitment while applying a relatively low PEEP level, an unexplored field is the use of cyclic sustained re-expansion maneuver (sigh). Sigh could be applied by periodically increasing airway pressure to 30 cmH_2O for 2–3 seconds every 4–5 minutes during OLV.

Electrical impedance tomography (EIT) as a new tool to guide mechanical ventilation settings during OLV

The recent study conducted by Liu *et al.* (16) explored the feasibility of personalizing PEEP during OLV using EIT. EIT is a simple dynamic non-invasive radiation-free lung imaging tool, which allows bedside monitoring of regional ventilation distribution, measured by a belt applied to the thorax. EIT has the unique advantage to allow direct visualization of ventilation distribution within the lungs, which is affected by the degree of regional overdistension and collapse (17). Thus, the PEEP level that balances lung collapse and overdistension could be regarded as the personalized optimal PEEP, although based upon the assumption that the clinical effects of decreasing lung collapse and minimizing lung overdistension are quantitatively equivalent. In the study by Liu *et al.*, EIT-guided PEEP group was compared to a control group ventilated with a fixed PEEP of 5 cmH_2O. In the EIT group, PEEP was titrated after start of OLV by a recruitment maneuver and decremental trial: pixel-level compliances were calculated for all PEEP levels and each pixel was classified as collapsed if compliance worsened at lower PEEP or overdistended if compliance worsened at higher PEEP. EIT-guided PEEP was set at the point where the proportion of overdistended and collapsed pixels were

equal, minimizing the detrimental effects of both. PEEP, in the EIT group, ranged from 9 to 13 cmH$_2$O, being significantly higher than in the control group. Moreover, authors reported improved oxygenation and lung mechanics at subsequent timepoints in the EIT group without major adverse cardiovascular impact.

This pilot clinical trial offers many interesting insights. The study population (composed by elderly patients) could particularly benefit from individualized PEEP titration. In this subgroup, the FRC is often lower than alveolar closing volume, increasing the risk of atelectasis, and general anesthesia and OLV exacerbate the phenomenon, further impairing oxygenation. Interestingly, the improvement of oxygenation and respiratory mechanics were correlated during individualized PEEP titration for OLV. We might speculate that this parallelism is related to the fact that atelectasis is the main mechanism responsible for both right-to-left shunt and decreased compliance in the dependent ventilated lung during OLV. By contrast, the ARDS lung includes areas with poor aeration and low ventilation/perfusion ratio, which precludes a linear correlation between improvement of oxygenation and compliance. The mean level of personalized PEEP was quite high compared to more classical studies on titrated OLV (14), but this might be related to the surgical technique. Indeed, as stated above, the chest wall elastance is reduced during thoracotomy (7), while during modern minimally invasive thoracoscopic procedures, the chest wall elastance likely approximates the one of closed chest, requiring higher airway pressure to obtain similar transpulmonary pressure.

The study by Liu *et al.* has limitations, too. The starting level for the PEEP decremental trial was 15 cmH$_2$O, which may be considered excessively high. As EIT only measures relative changes of pixel compliance between PEEP levels, overdistension decrease might have been heavily affected by this choice, resulting in the selection of higher than optimal PEEP levels. PEEP was selected only at the beginning of surgery, but this PEEP level might not be optimal one throughout the whole surgical procedure, when manipulation may have changed the initial conditions. Ideally, continuous EIT monitoring would be needed, but this is still not technically feasible during thoracic surgery. Unfortunately, EIT monitoring wasn't implemented in the control group, and we don't know if the amount of collapse and overdistension were significantly different between the two groups. The incidence of PPC wasn't different between the two study groups, questioning the clinical impact of personalized PEEP titration by EIT. However, the PPC

considered were highly heterogeneous, varying from atelectasis to bronchopleural fistula and the study sample size was not powered to address this outcome. Finally, it should be noted that in this study the concept of personalized PEEP is emphasized while Vt was fixed at 6 mL/kg PBW during OLV. However, since over-distension as quantified by EIT depends both from PEEP and Vt (18,19), the latter could have been tailored to limit overdistension.

A last word should be spent on monitoring of hemodynamics and right heart function during OLV: indeed, upcoming applications of EIT include the assessment of central hemodynamics such as cardiac output, pulmonary artery pressure and ventilation/perfusion matching (20). In the setting of OLV, these measurements could increase bedside accuracy to assess cardio-respiratory physiology and to guide ventilation settings.

Conclusions

In conclusion, the type and degree of pathophysiological changes of the cardiac and respiratory functions induced by OLV are variable and difficult to predict, also as a consequence of underlying chronic lung disease. Complex pathophysiology combined with high risk of PPC should prompt the use of advanced monitoring techniques, like EIT, to personalize mechanical ventilation in these patients.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm.2020.03.179). TM reports personal fees from Drager, personal fees from Fisher and Paykel, personal fees from Mindray, outside the submitted work. The other authors have no conflicts of interest to declare.

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