

The Society for Translational Medicine: clinical practice guidelines for mechanical ventilation management for patients undergoing lobectomy

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Abstract: Patients undergoing lobectomy are at significantly increased risk of lung injury. One-lung ventilation is the most commonly used technique to maintain ventilation and oxygenation during the operation. It is a challenge to choose an appropriate mechanical ventilation strategy to minimize the lung injury and other adverse clinical outcomes. In order to understand the available evidence, a systematic review was conducted including the following topics: (I) protective ventilation (PV); (II) mode of mechanical ventilation [e.g., volume controlled (VCV) versus pressure controlled (PCV)]; (III) use of therapeutic hypercapnia; (IV) use of alveolar recruitment (open-lung) strategy; (V) pre- and post-operative application of positive end expiratory pressure (PEEP); (VI) Inspired Oxygen concentration; (VII) Non-intubated thoroscopic lobectomy; and (VIII) adjuvant pharmacologic options. The recommendations of class II are non-intubated thoroscopic lobectomy may be an alternative to conventional one-lung ventilation in selected patients. The recommendations of class IIa are: (I) Therapeutic hypercapnia to maintain a partial pressure of carbon dioxide at 50–70 mmHg is reasonable for patients undergoing pulmonary lobectomy with one-lung ventilation; (II) PV with a tidal volume of 6 mL/kg and PEEP of 5 cmH₂O are reasonable methods, based on current evidence; (III) alveolar recruitment [open lung ventilation (OLV)] may be beneficial in patients undergoing lobectomy with one-lung ventilation; (IV) PCV is recommended over VCV for patients undergoing lung resection; (V) pre- and post-operative CPAP can improve short-term oxygenation in patients undergoing lobectomy with one-lung ventilation; (VI) controlled mechanical ventilation with I:E ratio of 1:1 is reasonable in patients undergoing one-lung ventilation; (VII) use of lowest inspired oxygen concentration to maintain satisfactory arterial oxygen saturation is reasonable based on physiologic principles; (VIII) Adjuvant drugs such as nebulized budesonide, intravenous sivelestat and ulinastatin are reasonable and can be used to attenuate inflammatory response.

Keywords: Mechanical ventilation; lobectomy; guideline; tidal volume

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Introduction

Anesthesia for lobectomy in thoracic surgery is a great challenge because it requires single contralateral lung ventilation with collapse of the ipsilateral lung. Collapse of the operated lung and ventilation of the other lung may induce an inflammatory response (1). The ventilated lung is hyperperfused, receiving most of the cardiac output and may be damaged by mechanical ventilation. The collapsed lung is exposed to ischemia, reperfusion injury and shear stress on reexpansion and postresection ventilation. As a result, patients who undergo lobectomy postoperatively may develop compromised lung function. Acute lung injury, reduced lung compliance and hypoxemia and an increase in pro-inflammatory cytokines, all are reported (2-6). The aim of mechanical ventilation during one-lung ventilation is (I) to facilitate carbon dioxide elimination; (II) to maintain oxygenation; and (III) to minimize postoperative lung dysfunction. There have been numerous investigations performed to determine the most appropriate means of mechanical ventilation. In this study we systematically searched the literature and the evidence for each graded recommendation.

Materials and methods

Literature review

Systematic search was performed to identify articles related to mechanical ventilation settings in patients undergoing lobectomy (((((((("2000/01/01"[Date - Publication] : "3000"[Date - Publication]) AND Clinical Trial[ptyp])) AND (anesthesia AND Clinical Trial[ptyp])) AND (((ventilation) OR ventilator) OR tidal volume)) AND ((surgery) OR resection OR operation OR lobectomy)) AND ((pulmonary) OR lung)). Studies were considered to be eligible if they fulfill the following criteria: (I) the study population involved patients who underwent lobectomy; (II) the primary intervention involved mechanical ventilation strategy; (III) articles were published after January 1st, 2000.

Classification and levels of evidence were graded according to American College of Cardiology/American Heart Association (ACC/AHA) rules (Available at: http://assets.cardiosource.com/Methodology_Manual_for_ACC_AHA_Writing_Committees.pdf).

Results

Evidence synthesis

Our initial search identified 461 citations. Four hundred and ten were excluded because in 176 studies the investigated patients underwent operations other than lobectomy, 84 studies did not investigate mechanical ventilation and 100 were unrelated studies. The remaining 51 citations were considered to be eligible for the present review.

Therapeutic hypercapnia

One-lung ventilation has long been associated with inflammatory response manifested as imbalance between pro-inflammatory and anti-inflammatory cytokines (7,8). Such systemic inflammatory response may cause complications such as acute lung injury and therefore, therapeutic strategy to prevent the inflammatory response may be potentially beneficial to patients.

Hypercapnia, secondary to reduced alveolar ventilation has been noted as a component of protective lung ventilation in clinical practice (9). It has been shown in both clinical and experimental studies that therapeutic hypercapnia can ameliorate severity of sepsis, injury induced by mechanical ventilation, and acute respiratory distress syndrome (10-13). In patients undergoing lobectomy with one-lung ventilation, hypercapnia facilitates inhibition of local and systemic inflammatory responses (REF?). Postoperative respiratory function, assessed by peak plateau pressure and dynamic compliance, was improved by hypercapnia induced by inhaled CO₂ (14). Hypercapnia has been shown to reduce systemic vascular resistance, increase cardiac index and pulmonary vascular resistance (15). Although these pilot studies are randomized controlled trials, they are small in sample size and will require more study in larger cohorts before stronger recommendations can be made. However, we can assume that hypercarbia is not harmful, except in the face of pulmonary hypertension, possibly cardiac arrhythmia and high intracranial pressure.

Recommendation

Permissive/therapeutic hypercapnia, to maintain a partial pressure of carbon dioxide of 50-70 mmHg potentially may be beneficial in patients undergoing single lung ventilation during pulmonary lobectomy operations (class IIa, level B).

Table 1 Studies investigating protective ventilation

Studies	Sample size	Protective ventilation	Control	Intermediate variable	Clinical outcomes
Qutub 2014	39	TV: 4 mL/kg; PEEP: 5 cmH ₂ O	TV: 6-8 mL/kg; PEEP: 5 cmH ₂ O	PV results in less pulmonary water content.	No difference in the incidences of postoperative acute lung injury, atelectasis, pneumonia, morbidity, hospitalization and 30-day mortality
Yang 2011	100	TV: 6 mL/kg; PEEP: 5 cmH ₂ O	TV: 10 mL/kg; PEEP: 0 cmH ₂ O	NA	PV has less incidence of lung injury, infiltrates and atelectasis
Ahn 2012	62	TV: 6 mL/kg; PEEP: 5 cmH ₂ O	TV: 10 mL/kg; PEEP: 0 cmH ₂ O	No difference in IL-6 and malondialdehyde	No difference in incidence of lung injury and abnormality on Chest X-ray
Ye 2011	30	TV: 6 mL/kg; PEEP: 5 cmH ₂ O	TV: 8 mL/kg; PEEP: 0 cmH ₂ O	F(A)/F(I) changes increased with PV	NA
Maslow 2013	32	TV: 5 mL/kg; PEEP: 5 cmH ₂ O	TV: 10 mL/kg; PEEP: 0 cmH ₂ O	Control had lower arterial carbon dioxide tension, less arterial carbon dioxide tension-end-tidal carbon dioxide gradient, lower alveolar dead space ratio, and higher dynamic pulmonary compliance	No difference in morbidity and hospital stay
Kim 2012	60	TV: 6 mL/kg; PEEP: 5 cmH ₂ O	TV: 10 mL/kg; PEEP: 0 cmH ₂ O	PV had higher incidence of hypoxemia	NA

PV, protective ventilation; TV, tidal volume; PEEP, positive end expiratory pressure; NA, not applicable.

Protective mechanical ventilation

Although low mechanical ventilation rate, higher levels of positive end-expiratory pressure (PEEP) and low inspired oxygen levels are considered to be “protective”, the primary components of protective ventilation (PV) include low tidal volume (LTV, tidal volume 6–8 mL/kg) and limited peak airway pressure, with or without PEEP. The landmark study by Amato and coworkers found that low tidal volume ventilation can effectively reduce mortality in patients with acute respiratory distress syndrome (ARDS) (16). Recent evidence also suggests potential beneficial effect of low tidal volume ventilation during general anesthesia for patients undergoing non-thoracic operative procedures (17-20).

During operative lobectomy with one-lung ventilation, results of PV in improving patients’ outcomes are confusing (Table 1) (21,22). Several studies failed to identify beneficial effects with PV strategy (21,23,24). Another randomized controlled trial favored the use of high tidal volume (HTV; 10 mL/kg) ventilation, as it resulted in less hypercarbia, less dead space, better dynamic compliance, and less postoperative atelectasis (25). However, in this small study

(n=34 patients) there was no difference in postoperative morbidity, or length of stay with LTV or HTV. In another study, LTV was found to be associated with increased risk of arterial hypoxemia (26).

Arterial hypoxemia in the presence of an elevated inspired oxygen concentration (FIO₂) is caused by right-to-left intrapulmonary shunting of blood, likely secondary to atelectasis. Low tidal volume ventilation has long been known to result in atelectasis, especially when FIO₂ is high, as it usually is during one-lung ventilation. Therefore, when LTV is applied, basic physiologic principles and some reports support application of a recruitment maneuver, followed by application of PEEP and lower FIO₂ (27,28).

This paragraph is out of place. There is no mention of FIO₂ in the recommendation. Further, “protective ventilation” advocates do not mention FIO₂ except as a mechanism to maintain PaO₂ in the face of low PEEP. I recommend this be a part of the “open lung” discussion.

Recommendation

PV with tidal volume of 6–8 mL/kg and a PEEP of 5 cmH₂O

is reasonable based on current evidence (class IIa, level B).

Alveolar recruitment (open lung)

Alveolar recruitment is traditionally used to open collapsed lungs, which typically occur in acute respiratory distress syndrome, but there is scarce evidence to support the use of alveolar recruitment in patients undergoing lobectomy with one-lung ventilation. In a feasibility study, Downs and colleagues reported that open lung ventilation (another term used for alveolar recruitment), which is performed by initially setting the PEEP to 30 cmH₂O, then adjusting the amount needed to maximize compliance, is safe and effective. A novel form of ventilation was applied to maintain the lung “open”. Apneustic anesthesia ventilation (AAV), similar to airway pressure release ventilation (APRV), utilized a continuous positive airway pressure (CPAP) of 15–30 cmH₂O. Ventilation was accomplished by decreasing airway pressure for 1–2 s to allow exhalation of a tidal volume of 6 mL/kg, but not long enough to permit lung collapse. Further, patients did not receive supplemental O₂, even on induction of general anesthesia, prior to extubation, or in the recovery room. Use of LTV, CPAP titrated to maximize lung-thorax compliance, FIO₂ =0.21, low ventilator rate (6–8 BPM) and mild hypercarbia (48–52 mmHg) were associated with no PPC. In this cohort of 12 patients, there was no atelectasis or infiltrates, and there was no complication or mortality (29).

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Recommendation

Alveolar recruitment (open lung ventilation) may be potentially beneficial in patients undergoing lobectomy with one-lung ventilation (class IIb, level C). Low FIO₂ may prevent absorption atelectasis.

Mode of mechanical ventilation

Different mode of mechanical ventilation may produce

different pulmonary mechanics for patients during surgical procedures. For instance, volume controlled ventilation (VCV) guarantees the tidal volume of inspired gas, whereas pressure controlled ventilation (PCV) provides a preset pressure to the airway. In a crossover study, involving patients undergoing open thoracotomy with one lung ventilation, PCV offered improved right ventricle (RV) function compared with the use of VCV. No other clinical outcomes were reported in this study (30). In other studies, PCV did not provide any beneficial effect, except for reduced peak airway pressure during ventilation (31–33). In a small pilot study involving 30 patients, the pressure-controlled volume-guaranteed (PCV-VG) mode appeared to offer clinical benefits in terms of lung mechanics and pro-inflammatory cytokines (34). However, other long-term outcomes were not investigated in these studies. In elderly patients with compromised pulmonary function, PCV and PCV-VG were found to have significant beneficial effects on intraoperative oxygenation and airway pressure (35–37).

Recommendation

PC or PCV-PG is recommended over VCV and can be used in patients undergoing lung resection with single-lung ventilation (class IIa, level B).

Pre-and post-operative noninvasive ventilation

CPAP is commonly used for patients with respiratory failure. Patients undergoing lung resection are at increased risk of postoperative acute lung injury. In a recent randomized controlled trial, CPAP applied for 6 h after operation was able to improve the oxygenation index at 24 h as compared to supplemental oxygen through a Venturi mask. Other clinical outcomes such as postoperative pulmonary complications and duration of stay in the post-anesthesia care unit (PACU) and hospital were not different between groups (38). Similar results are found in another study with smaller sample size (39). CPAP can be delivered via Boussignac CPAP system and helmet. In patients with a preoperative FEV₁ <70%, pre- and post-operative use of pressure support ventilation significantly reduced pulmonary dysfunction following lobectomy (40).

Recommendation

CPAP can be used in patients undergoing lobectomy and one lung ventilation, and is beneficial in improving short-term oxygenation (class IIa, level A).

Non-intubated thoroscopic lobectomy

In recent years, some authors have reported the use of thoroscopic lobectomy performed under epidural anesthesia, intrathoracic vagal blockade, sedation and spontaneous breathing, without tracheal intubation. Non-intubated patients had significantly shorter duration of anesthesia and other clinical outcomes were comparable (41). Occasionally, conversion to conventional one-lung ventilation is necessary (42). One retrospective study reported a conversion rate of 5.5% (13/238) (43). The technique is feasible, and there were no severe complications reported. Safety and efficacy need to be investigated in larger trials (44,45). To date, no randomized controlled trial investigating the efficacy and safety of this technique has been published. The technique is feasible, and there were no severe complications reported. Safety and efficacy need to be investigated in larger trials (44,45).

Recommendation

Thoroscopic lobectomy without tracheal intubation may be an alternative to conventional one-lung ventilation, in selected patients (class II, level C).

Inspiratory to expiratory ratio (I:E)

The setting of I:E ratio in controlled mechanical ventilation has been shown to have clinical important clinical impact on patients undergoing lobectomy with one-lung ventilation. A study involving 56 patients showed that setting I:E ratio to 1:1 as compared to 1:2 can reduce airway pressures and improve pulmonary compliance, but cannot significantly improve arterial oxygenation (46). Similar findings were reported in patients with low diffusion capacity of lung for carbon monoxide (47). AAV reported by Bratzke and Downs utilized an I:E of 2:1 to 4:1, as discussed earlier, with no PPC (48).

Recommendation

Controlled mechanical ventilation with I:E ratio of 1:1, or greater, is reasonable in patients undergoing one-lung ventilation (class IIa, level B).

Low inspired oxygen concentration

There is a pervasive, but scientifically unsupported assumption that higher inspired oxygen concentrations yield

a protective and beneficial effect during thoracic surgical procedures. However, absorption atelectasis rapidly occurs within minutes of induction of general anesthesia with high FIO₂ and detection of deterioration in lung function may be delayed significantly (27).

Few clinical trials have even mentioned FIO₂, a variable that likely has a profound influence on atelectasis, postoperative work of breathing, and, possibly, PPCs (49,50).

Recommendation

Application of the lowest FIO₂ necessary to maintain satisfactory arterial oxygen saturation is reasonable (REF Downs).

Adjuvant drug use

Preoperative nebulized budesonide was found to be effective in reducing peak and plateau pressure during mechanical ventilation. The effects of the drug lasted to the postoperative period where lung compliance was improved and pro-inflammatory cytokines were reduced after lung re-expansion (51). The use of intravenous sivelestat, a selective neutrophil elastase inhibitor, was effective in limiting inflammatory response and improving oxygenation (52,53). In a single RCT it was reported that preoperative injection of ulinastatin at 5,000 U/kg could attenuate local pulmonary inflammatory response in one-lung ventilation (54).

Recommendation

Adjuvant drugs such as nebulized budesonide, intravenous sivelestat and ulinastatin may have beneficial effect in attenuating inflammatory response following one-lung ventilation (class IIa, level B).

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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