

# Effects of tidal volume on physiology and clinical outcomes in patients with one-lung ventilation undergoing surgery: A meta-analysis of randomized controlled trials

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Received May 8, 2023; Accepted February 16, 2024

DOI: 10.3892/br.2024.1761

**Abstract.** There is no detailed study on how tidal volume (VT) affects patients during one-lung ventilation (OLV). The present study conducted a meta-analysis to assess the effect of VT on physiology and clinical outcomes in OLV patients. Databases until February 2023 were retrieved from PubMed, Cochrane Library and Web of Science. Randomized controlled trials comparing the application of low and high VT ventilation in adults with OLV were performed. Demographic variables, VT, physiology, and clinical outcomes were retrieved. The random-effects model calculated the summary of odds ratios with 95% confidence intervals (CI) and mean difference with standard deviation. A total of 12 studies involving a total of 876 participants met the inclusion criteria. Low VT ventilation was associated with decreased risk of acute lung injury [relative risk 0.50, 95% CI (0.28, 0.88),  $P=0.02$ ]. Low VT ventilation decreased the driving pressure ( $\Delta P$ ) and peak pressure (Ppeak) and improved arterial oxygen pressure ( $PaO_2$ )/fraction of inspired oxygen ( $FiO_2$ ). Furthermore, the present study suggested that a significant difference in blood IL-6 was observed between low and high VT ventilation [mean

difference, -35.51 pg/ml, 95% CI (-66.47, -4.54 pg/ml),  $P=0.02$ ]. A decrease in the length of stay at the hospital occurred in the low VT group when set to 4-5 ml/kg. In the OLV patients, low VT ventilation decreased the risk of acute lung injury, blood IL-6,  $\Delta P$  and Ppeak, and improved  $PaO_2/FiO_2$ . Furthermore, when low VT was set to 4-5 ml/kg, the length of stay at the hospital decreased.

## Introduction

Lung complications are common after general anesthesia surgery, significantly increasing mortality and morbidity (1,2). Low tidal volume (VT) mechanical ventilation in anaesthetized patients undergoing abdominal surgery can minimize the chances of postoperative pulmonary complications (3). Initial evidence of protective ventilation with low VT ventilation has been obtained from acute respiratory distress syndrome (ARDS) (4). Research has shown consistent results concerning applying low VT ventilation to the surgical population without ARDS (5). Patients undergoing thoracic surgery with one-lung ventilation (OLV) face physiologically and clinically challenging circumstances that complicate lung-protective ventilation application with low VT.

Due to the significant physiological changes caused by OLV, the clinical prognosis of patients is affected. These changes include the following (6-8): The obligate collapse of the non-dependent lung and overdistention of the dependent lung indicate an inflammatory cascade and can be related to high airway pressures; increase in shunt fraction when ventilation is switched from two-lung to OLV, resulting in hypoxemia; frequent occurrence of pulmonary atelectasis owing to lower chest wall compliance due to lateral decubitus position compared with two-lung ventilation. Therefore, patients undergoing thoracic surgery with OLV are vulnerable to ventilator-induced lung injury and an ultimate increase in the length of their hospital stay.

Mostly, OLV studies involve small-sized samples and primarily focus on reporting physiological outcomes. Furthermore, owing to the paucity of evidence, anesthesiologists

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**Abbreviations:** VT, tidal volume; ARDS, acute respiratory distress syndrome; OLV, one-lung ventilation; PEEP, positive end-expiratory pressure; RCT, randomized controlled trials;  $\Delta P$ , driving pressure; Ppeak, peak pressure; RR, relative risk; CI, confidence interval;  $FiO_2$ , fraction of inspired oxygen; RM, recruitment manoeuvres

**Key words:** low tidal volume, one-lung ventilation, physiology, clinical outcomes, meta-analysis

have tried implementing various ventilation strategies during OLV (9). A study demonstrated the improvement in physiological outcomes in OLV for thoracic surgery through lung-protective ventilation with recruitment maneuvers and positive end-expiratory pressure (PEEP) (10). However, it is still unclear if low VT improves the clinical outcomes when used during OLV in patients undergoing thoracic surgery. In 2017, El Tahan *et al* (11) noted that low VT of OLV did not affect the length of hospital stay, while a subsequent study (12) showed that the duration of hospital stay was shorter in the low VT group. The present study assessed the effects of low VT on the physiological and clinical outcomes of surgery in adults undergoing OLV.

## Materials and methods

The methods used for writing the meta-analysis were according to the guidelines provided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (13).

**Search strategies and study screening.** PubMed (<https://pubmed.ncbi.nlm.nih.gov/>), EMBASE (<https://www.embase.com/>) and Cochrane Library databases (<https://www.cochranelibrary.com>) were extensively searched from inception to February 2023. Studies were related to the intraoperative use of OLV with low VT in patients undergoing thoracic surgery. This was not limited to articles published in just one language. The terms searched included 'protective ventilation or low tidal volume' and 'one-lung ventilation or thoracic surgery'. In addition, the authors manually searched the reference lists of relevant studies.

Then two reviewers (FX and ZL) independently assessed all the titles and abstracts and excluded irrelevant studies. Further, according to the inclusion and exclusion criteria, the full texts of the remaining articles were independently reviewed. The inclusion criteria were as follows: i) Patients receiving OLV undergoing surgery; ii) a clear report of VT; iii) different VT compared during intraoperative ventilation of patients; iv) randomized controlled trials (RCT). Studies involving children, lung transplantation, cardiopulmonary bypass, airway device comparison, indefinite time of measurement and patients with COVID-19 were excluded. The discrepancies were resolved through agreement and after discussion with a third reviewer to reach a consensus on inclusion. The included studies defined low and high VT as 3-6 and 8-10 ml/kg of ideal body weight, respectively. These studies were analyzed to identify outcome measures.

**Data extraction and quality assessment.** Two authors (FX and JJ) performed data extraction according to a standardized author-developed data extraction form in Microsoft Excel. The following data were extracted from the included trials: Year of publication, first author, type of patients, operating side, VT category, PEEP setting, fraction of inspired oxygen (FiO<sub>2</sub>) during OLV, recruitment maneuver, and physiology or clinical outcomes. The primary outcome was the risk of acute lung injury and the length of stay at the hospital. Secondary outcomes were focused on physiology outcomes, including the driving pressure ( $\Delta P$ ), peak pressure (Ppeak), arterial oxygen pressure (PaO<sub>2</sub>)/FiO<sub>2</sub>, atelectasis

and blood IL-6. Acute lung injury was defined as the sudden onset of respiratory distress and impaired oxygenation with a PaO<sub>2</sub>/FiO<sub>2</sub> ratio of <300 mm Hg. Atelectasis was defined as new pulmonary infiltrates on a chest radiograph. The data presented as a median range was converted to mean standard deviation (14).

The evaluation of the present study involved RCTs using the Cochrane Risk of Bias tool, which included the following items: Random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and other biases (15). Visual inspection of funnel plots was applied for the evaluation of publication bias. Data extraction and bias assessment of the included studies were performed by JJ and confirmed by FX. In case of discrepancy, a consensus was reached by discussion.

**Statistical analysis.** All statistical pooling of the meta-analysis was conducted using RevMan (version 5.1; The Nordic Cochrane Centre). Physiology outcomes for the meta-analysis of VT were blood IL-6,  $\Delta P$ , Ppeak, PaO<sub>2</sub>/FiO<sub>2</sub>, and atelectasis. Clinical outcomes for meta-analysis of VT were the length of stay at the hospital and the incidence of acute lung injury. Subgroup analyses were conducted with stratification by TV of predicted body weight (6 ml/kg vs. <6 ml/kg). Relative risk (RRs) with 95% corresponding confidence intervals (CIs) were calculated for dichotomous outcomes. The random-effects model was considered for clinical heterogeneity (16). The author quantified the existence of heterogeneity between the studies using the I<sup>2</sup> statistic (17). One study was excluded from sensitivity testing and the process was repeated to analyze the robustness of the aggregated results. P<0.05 was considered to indicate a statistically significant difference.

## Results

**Search results.** A total of 2,842 relevant articles were initially retrieved and 25 additional records were identified through other sources. The titles and abstracts were screened to eliminate duplicates, which left 1,023 records. Among these, 943 publications were discarded for being irrelevant. The full text of the remaining 80 publications was assessed. Based on the exclusion criteria, 68 publications were excluded. Finally, 12 studies were included in the meta-analysis (Fig. 1).

**Study characteristics.** The included 12 studies compared low and high VT in patients undergoing thoracic surgery with OLV. The characteristics of each study are listed in Table I. Basic characteristics of patients are provided in Table SI. The included studies were published between 2005 and 2023. The analysis involved individual studies on 876 participants using different sample sizes that ranged between 26 and 343. Low and high VT varied between 3-6 and 8-10 ml/kg of ideal body weight, respectively. In 10 studies PEEP was applied varying from 3-8 cm H<sub>2</sub>O in the low VT groups, whereas PEEP was set to zero in the high VT groups. The FiO<sub>2</sub> applied in eight studies during the surgery was adjusted based on oxygen saturation or protocol. Three and two studies administered

Table I. Characteristics of included studies.

First author, year	Type of surgery	Low VT					High VT					Main outcomes	(Refs.)			
		Number of patients	Time of ventilation (min)	Vt (ml/kg) IBW	PEEP (cm H <sub>2</sub> O)	RM	FiO <sub>2</sub>	Number of patients	Time of ventilation (min)	Vt (ml/kg) IBW	PEEP (cm H <sub>2</sub> O)			RM	FiO <sub>2</sub>	Time of measurement
Ahn, 2012	Video-assisted thoracic surgery	25	108.6±36.5	6	5	NA	0.5	25	115.9±44.0	10	0	NA	1	60 min after OLV	IL-6; atelectasis; ALI; hospital length of stay	(18)
Jung, 2014	Video-assisted thoracostomy	30	NA	6	8	Yes	1	30	NA	10	0	No	1	45 min after OLV	PaO <sub>2</sub> /FiO <sub>2</sub> ; Ppeak	(19)
Kim, 2019	Thoracoscopic lobectomy	20	121±34	6	5	No	Adjusted according to oxygen saturation	20	131±40	10	0	No	Adjusted according to oxygen saturation	OLV end	IL-6; PaO <sub>2</sub> /FiO <sub>2</sub> ; ΔP; Ppeak; atelectasis	(20)
Lin, 2008	Esophagectomy	20	142±21	5-6	3-5	NA	NA	20	154±32	10	0	NA	NA	120 min after OLV	IL-6; PaO <sub>2</sub> /FiO <sub>2</sub> ; Ppeak	(21)
Marret, 2018	Lung cancer surgery	172	NA	5	5-8	Yes	According to local protocol	171	NA	10	0	Yes	According to local protocol	20 min after OLV	FiO <sub>2</sub> ; Ppeak; ΔP; Ppeak; atelectasis; ALI; Hospital	(12)
Maslow, 2013	Elective pulmonary resection	16	42±8.3	5	5	NA	Adjusted according to oxygen saturation	16	46±9.5	10	0	NA	Adjusted according to oxygen saturation	20 min after OLV	length of stay ΔP; Ppeak; atelectasis; hospital	(22)
Michelet, 2006,	Esophagectomy for cancer	26	85±29	5	5	NA	Adjusted according to oxygen saturation	26	85±29	9	0	NA	Adjusted according to oxygen saturation	OLV end	length of stay IL-6; ALI	(23)
Qutub, 2014	Video-assisted thoracic surgery	13	NA	4	5	Yes	Adjusted according to oxygen saturation	13	NA	8	5	Yes	Adjusted according to oxygen saturation	15 min after OLV	PaO <sub>2</sub> /FiO <sub>2</sub> ; atelectasis; ALI; hospital length of stay	(24)

Table I. Continued.

First author, year	Type of surgery	Low VT					High VT					Main outcomes	(Refs.)			
		Number of patients	Time of ventilation (min)	Vt (ml/kg) IBW	PEEP (cm H <sub>2</sub> O)	RM	FiO <sub>2</sub>	Number of patients	Time of ventilation (min)	Vt (ml/kg) IBW	PEEP (cm H <sub>2</sub> O)			RM	FiO <sub>2</sub>	Time of measurement
Schilling, 2005	Thoracic surgery	16	68±71.9	5	0	NA	Adjusted to achieve a PaO <sub>2</sub> >80 mm Hg	16	71±60.7	10	0	NA	Adjusted to achieve a PaO <sub>2</sub> >80 mm Hg	30 min after OLV	ΔP; Ppeak	(25)
Shen, 2013	Esophagectomy	53	72.2±23.6	5	5	NA	Adjusted according to oxygen saturation	48	75.0±18.8	8	0	NA	Adjusted according to oxygen saturation	18-h postoperative	PaO <sub>2</sub> /FiO <sub>2</sub> ; hospital length of stay	(26)
Yang, 2011	Lung cancer surgery	50	120±41	6	5	NA	Adjusted according to oxygen saturation	50	126±53	10	0	NA	1	60 min after OLV	ΔP; Ppeak; atelectasis; ALI; hospital length of stay	(27)
Ye, 2011	Lung cancer surgery	10	NA	6	5	NA	1	10	NA	8	0	NA	1	70 min after OLV	Ppeak	(28)

VT, tidal volume; RM, recruitment maneuvers; NA, not available; OLV, one-lung ventilation; ALI, acute lung injury; Ppeak, peak airway pressures; ΔP, driving pressure; PaO<sub>2</sub>, oxygen pressure; FiO<sub>2</sub>, fraction of inspired oxygen.

VT, tidal volume; RM, recruitment maneuvers; NA, not available; OLV, one-lung ventilation; ALI, acute lung injury; Ppeak, peak airway pressures; ΔP, driving pressure; PaO<sub>2</sub>, oxygen pressure; FiO<sub>2</sub>, fraction of inspired oxygen.



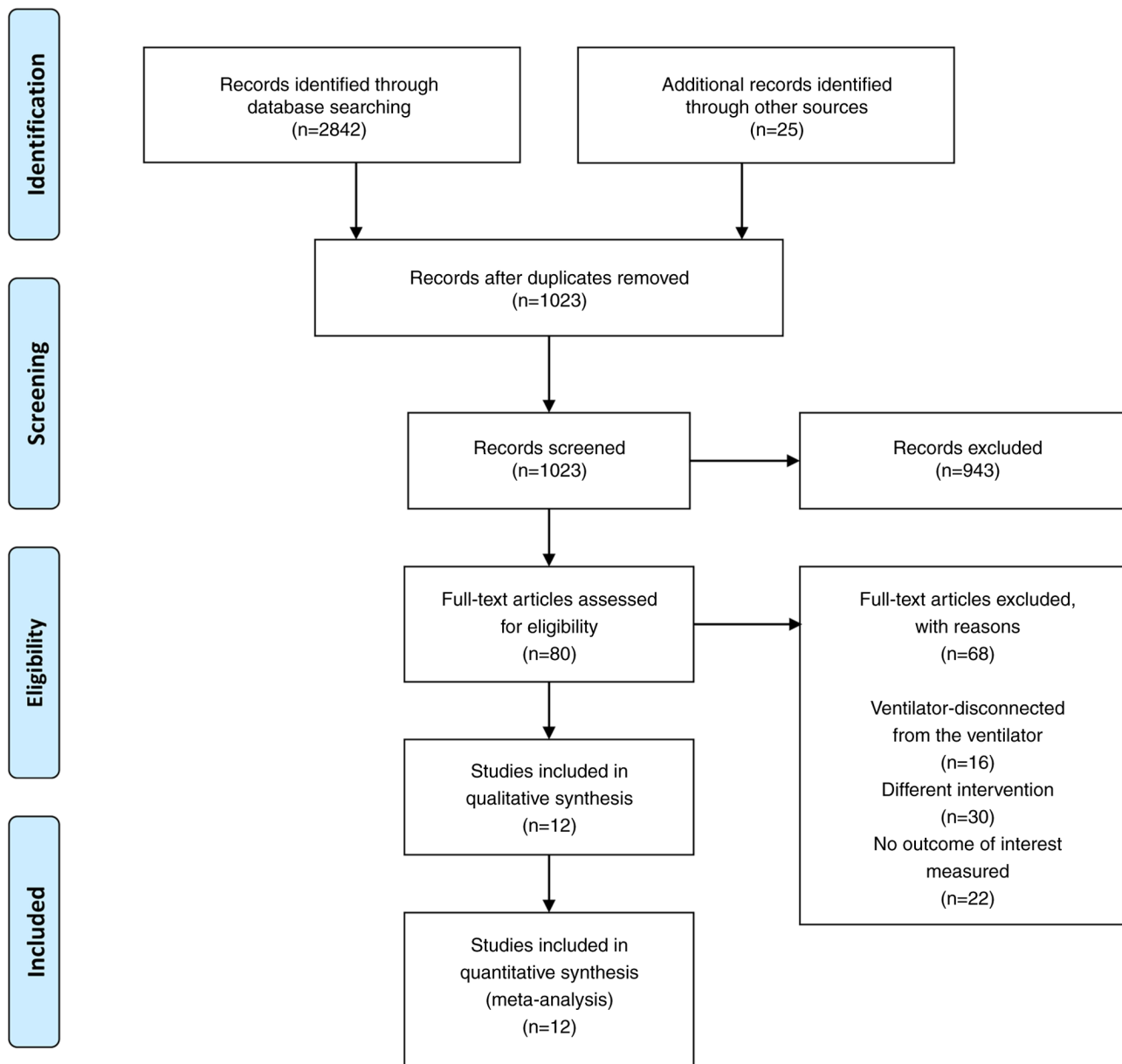


Figure 1. PRISMA flow diagram of the selected trials.

recruitment manoeuvres (RM) in the low and high VT groups, respectively. A total of 12 (12,18-28) of the studies reported data on physiology outcomes (IL-6,  $\Delta P$ , Ppeak,  $PaO_2/FiO_2$  and atelectasis) and seven studies (12,18,22-24,26,27) included data on clinical outcomes (length of stay at the hospital and the incidence of acute lung injury). The details of the bias assessment risk are outlined in Fig. 2.

**Physiology outcomes.** A total of 12 studies with 876 participants reported the effect of low VT on physiology outcomes, including IL-6,  $\Delta P$ , Ppeak,  $PaO_2/FiO_2$  and atelectasis. The results suggested that OLV with low VT was associated with decreased IL-6 [mean difference (MD), -35.51 pg/ml; 95% CI (-66.47, -4.54 pg/ml);  $P=0.02$ ; Fig. 3A],  $\Delta P$  [MD, -6.02 cmH<sub>2</sub>O; 95% CI (-8.32, -3.72 cmH<sub>2</sub>O);  $P<0.0001$ ; Fig. 3B], Ppeak [MD, -2.88 cmH<sub>2</sub>O; 95% CI (-4.60, -1.16 cmH<sub>2</sub>O);  $P=0.001$ ; Fig. S1] and increased  $PaO_2/FiO_2$  [MD, 32.27 mmHg; 95% CI (19.54, 45.01 mmHg);  $P<0.00001$ ; Fig. 3C]. Furthermore, the risk of

atelectasis [RR, 0.79; 95% CI (0.53, 1.17);  $P=0.24$ ; Fig. S2] with low VT did not show any increase.

During the analysis of IL-6, for those who received a low VT of below 6 ml/kg, there was a significant decrease in the low VT group compared with the high VT group [MD, -74.62 pg/ml, 95% CI (-110.73, -38.51 pg/ml),  $P<0.0001$ ; Fig. 3A], with possible moderate heterogeneity ( $I^2=32\%$ ). However, for those who received a low VT of 6 ml/kg, there was no significant difference in IL-6 between both the groups [MD, -4.08 pg/ml, 95% CI (-11.08, 2.93 pg/ml),  $P=0.25$ ; Fig. 3A]. There was also a possibility of substantial heterogeneity ( $I^2=84.7\%$ ) between the subgroups (Fig. 3A).

**Clinical outcomes.** A total of 13 studies reported acute lung injury and length of stay at the hospital as clinical outcomes. Overall, there was a significant decrease in the risk of acute lung injury with low VT [RR, 0.50; 95% CI (0.28, 0.88);  $P=0.02$ ; Fig. 4A]. A possibility of low heterogeneity ( $I^2=0\%$ ) existed

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Ahn 2012	+	?	+	+	+	+	+
Jung 2014	+	?	+	+	+	+	+
Kim 2019	+	?	+	+	+	?	+
Lin 2008	?	?	+	+	+	?	+
Marret 2018	+	+	+	+	+	+	+
Maslow 2013	+	+	+	+	+	+	+
Michelet 2006	+	+	+	+	+	+	+
Qutub 2014	+	+	+	+	+	+	+
Schilling 2005	+	?	+	+	+	?	+
Shih 2013	+	+	+	+	+	?	+
Yang 2011	+	+	+	+	+	+	+
Ye 2011	?	?	+	+	+	+	+

Figure 2. Risk of bias summary of the included studies. The reviews' judgments about seven risks of bias item for each study. Red indicates high risk; yellow indicates uncertain risk; green indicates low risk.

between the low and high VT groups (Fig. 4A). Meanwhile, the results suggested that low VT was not associated with the length of stay at the hospital [MD, -0.53 days; 95% CI (-1.09, -0.03) days;  $P=0.06$ ; Fig. 4B].

In the low VT group, four studies with a VT of 4-5 ml/kg showed a shorter length of stay at the hospital [MD, -0.78 days; 95% CI (-1.45, -0.11) days;  $P=0.02$ ; Fig. 4B], whereas two studies with a VT of 6 ml/kg showed no difference compared with the high VT group [MD -0.06 days; 95% CI (-0.96, 1.08) days;  $P=0.91$ ; Fig. 4B]. A possibility of low heterogeneity existed between the two subgroups ( $I^2=45.4\%$ ; Fig. 4B).

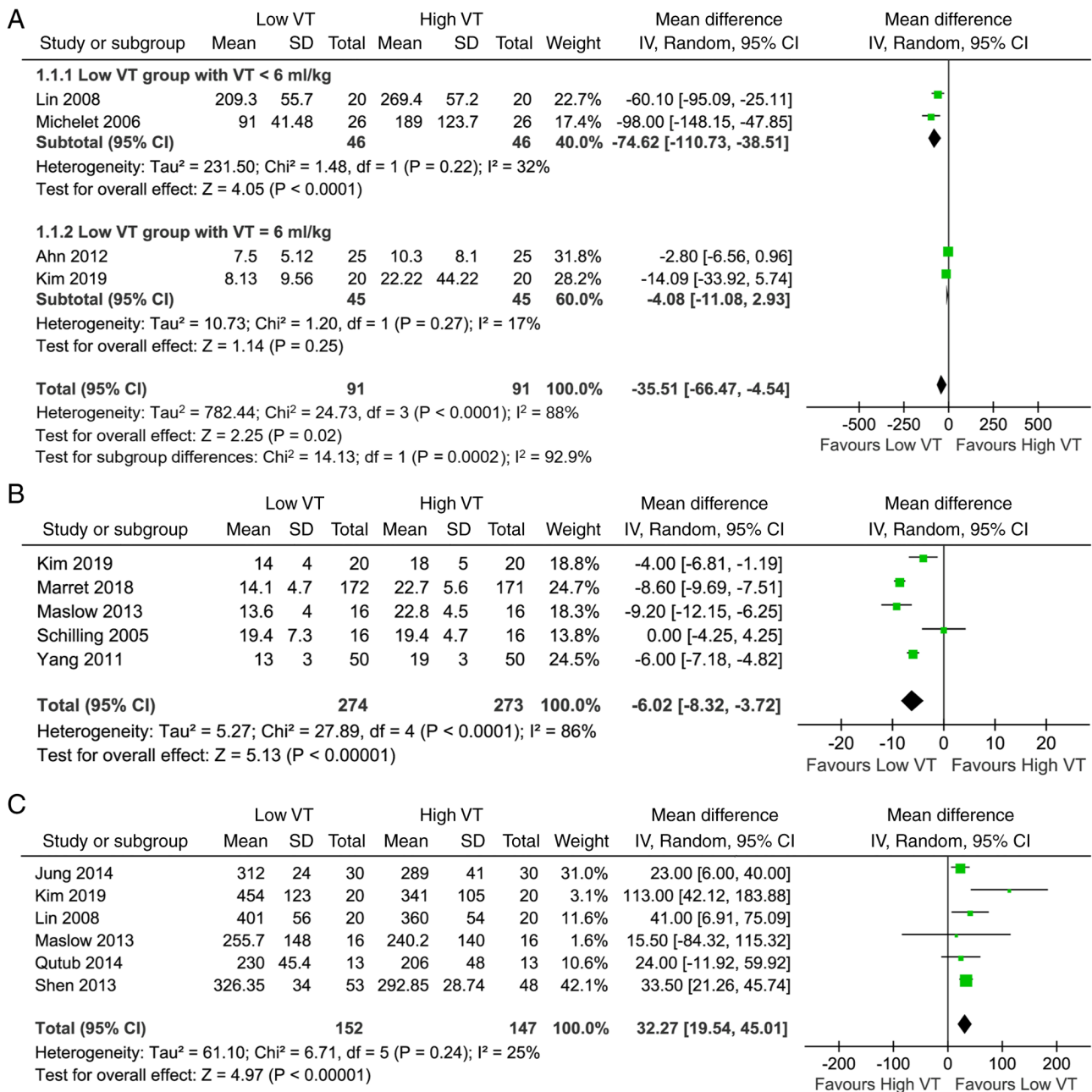
## Discussion

Meta-analysis was conducted to elaborate on the physiology and clinical impacts of VT in patients undergoing thoracic surgery with OLV. The results demonstrated that low VT ventilation during OLV significantly improves  $\text{PaO}_2/\text{FiO}_2$  and decreases blood IL-6,  $\Delta\text{P}$ , Ppeak and the risk of acute lung injury. Furthermore, the length of stay at the hospital decreases in low VT ventilation with VT set to 4-5 ml/kg. Meanwhile, low VT ventilation does not impact the risk of atelectasis.

Low VT ventilation strategy aims at limiting lung overdistension, leading to a reduction in the incidence of ALI along with a shorter hospital stay. Two-lung ventilation is a conventional VT technique that may lead to overdistension of the aerated lung and increase the shear forces generated owing to the repetitive opening and collapse of the atelectatic areas. In comparison, a low VT ventilation strategy is beneficial for both the injured lungs (4) and anaesthetized patients (3). However, large-sample randomized controlled studies do not exist to evaluate the effect of low VT on ALI. According to Hu and Du (29), the incidence of ALI was low when patients had one-lung ventilation during the surgery. However, this study did not explore the length of stay at the hospital. This limitation was overcome in the present study, which noted that the length of stay at the hospital decreased when VT was set to 4-5 ml/kg. However, this factor did not differ between the ventilatory strategies in Lee *et al* (30) and this could be attributed to using the actual body weight to set VT in their research. Ahn *et al* (18) showed that low VT did not have any positive effect on the length of stay at the hospital. In the present study, the negative results could be attributed to the fact that although ventilated with low VT, the platform pressure is  $<20 \text{ cmH}_2\text{O}$ . This result implies that pressure during ventilation needs to be taken into account while determining the factors affecting the outcomes of OLV patients.

In a retrospective study, Amato *et al* (31) identified the risk of high  $\Delta\text{P}$  as an outcome in ARDS patients. Among the surgical population, either two-lung (32) or one-lung (33,34) ventilation,  $\Delta\text{P}$  is identified as a risk factor for the development of postoperative pulmonary complications.  $\Delta\text{P}$  equals elastance times the VT. Thus, it may serve as a surrogate for dynamic alveolar injury. The results of the present study show that low VT significantly reduces both the  $\Delta\text{P}$  and Ppeak. Therefore, it can be hypothesized that low VT ventilation is associated with postoperative pulmonary complications in patients. Further studies are needed to clearly understand the relationship between VT,  $\Delta\text{P}$  and patient outcomes. In addition, the results of the present study give strong indications that lung injury is attenuated by the application of low VT. These 12 studies excluded patients with chronic obstructive disease and obstructive pulmonary dysfunction, possibly mainly considering that the tolerance and efficacy of low TV may vary depending on the background conditions of the lungs. Unfortunately, only five studies mentioned the proportion of smokers among the included patients, while the remaining studies did not (Table SII). From a pathophysiological perspective, a smoking history may be related to the patient's tolerance to low VT.

High VT is associated with deformation of the alveolar epithelium and cyclic opening of collapsed areas during



OLV, which leads to local production and release of inflammatory mediators resulting in ALI. Inflammatory biomarkers directly assess lung damage. The inflammatory response was observed to decrease in healthy lungs after low VT ventilation compared with conventional VT (35). A previous meta-analysis (11) evaluated the impact of low VT without the use of inflammatory biomarkers. In the present study, in the patients who received low VT ventilation, serum IL-6 was found to decrease, which was indicated as a useful marker of induced injury (36). The present study was consistent with previous findings (23) of patients undergoing esophagectomy. This referred to VT of 5 ml/kg being combined with PEEP 5 cm H<sub>2</sub>O during one-lung ventilation, which resulted in the release

of low levels of IL-6 into the serum after the surgery. However, Kim *et al* (20) did not observe a difference in plasma IL-6. This could be attributed to the calculation of the sample size of the study not being based on postoperative outcomes, resulting in its small size. Therefore, the clinical impact on the severity of the surgical trauma needs to be further investigated. In addition to IL-6, commonly used inflammatory markers also include C-reactive protein (CRP) and white blood cell (WBC). Unfortunately, none of the four studies mentioned (18,20,21,23) detected CRP and WBC. One possible reason is that in these studies, the total surgical time was between 120 and 300 min; IL-6 was tested before surgery, during single lung ventilation and 15 min-2 h postoperatively, with only one study retesting

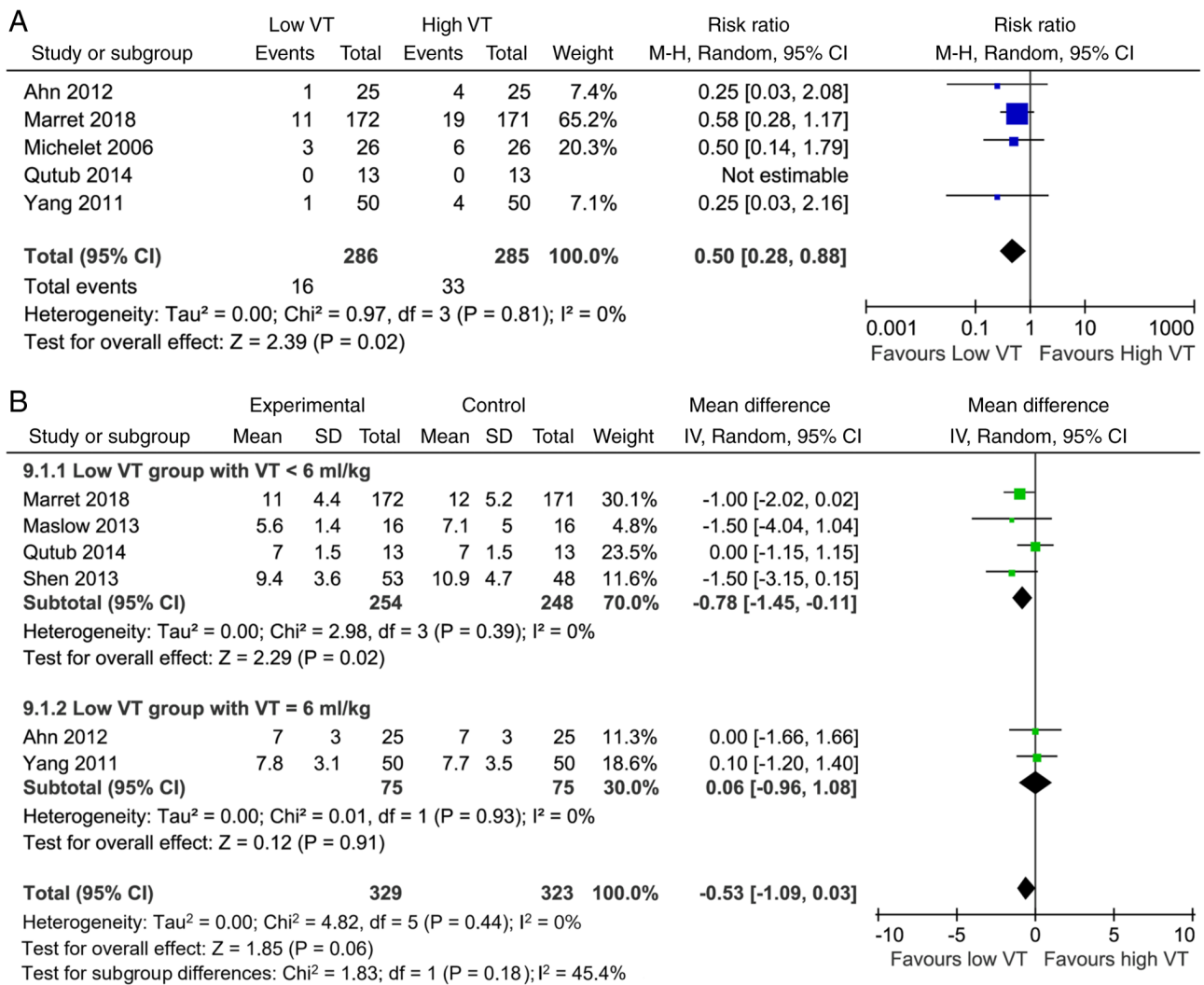


Figure 4. Clinical effects of low VT. (A) The association of low VT ventilation and the risk of acute lung injury in patients with one-lung ventilation undergoing surgery. (B) The association of low VT ventilation and length of stay at hospitals in patients with one-lung ventilation undergoing surgery. M-H, Mantel-Haenszel; SD, standard deviation; CI, confidence interval; df, degrees of freedom; IV, inverse variance; VT, tidal volume.

IL-6 at 18 h postoperatively. It is known that IL-6 is one of the earliest inflammatory factors to appear in the acute phase of inflammation, reaching its peak within 2 h with a half-life of only 1 h, which can reflect the rapid changes in inflammation in a timely manner (37). However, CRP is induced by IL-6 and reaches its peak ~48 h, while white blood cells begin to rise as early as 6-24 h after inflammation. Therefore, researchers may consider that IL-6 gives an improved reflection of the early inflammatory status of surgical patients. If CRP and WBC data can be reported in these studies, it will help a more comprehensive and detailed evaluation of the patient's inflammatory status.

Hypoxemia during OLV can be prevented by applying a ventilation strategy that can avoid alveolar collapse while minimally impairing perfusion of the dependent lung. The use of low VT and PEEP to the ventilated lung and titrating inspired  $\text{FiO}_2$  to maintain a pulse oximetric oxygen saturation can serve as strategies to improve the ventilation/perfusion ratio and maintain arterial oxygen tension during OLV (8) in thoracic surgery. In the present study,  $\text{PaO}_2/\text{FiO}_2$  was improved under low VT ventilation. These results are consistent with

Lee *et al* (30); that low VT ventilation is associated with improved oxygenation compared with conventional ventilation requiring OLV. In Liu *et al* (38), owing to the comparison of different modes rather than different VTs of ventilation, there is no difference in  $\text{PaO}_2/\text{FiO}_2$  between pressure-controlled ventilation and volume-controlled ventilation. Therefore, in this case, compared with low VT, high VT, which is potentially injurious to the lung, did not translate into improved oxygenation. Low VT ventilation, which keeps the lung open without impeding perfusion, improves oxygenation during OLV.

It has also been found that postoperative atelectasis is not evident in the low VT group compared with the conventional VT group. During intraoperative ventilation, atelectasis may occur due to ventilator-associated lung injuries (39,40), leading to a reduction in the functional residual capacity consequent to OLV and muscle paralysis. A previous study (30) has shown that lung atelectasis can be reduced by low VT ventilation when assessed using lung ultrasound.

The main complication of low VT is atelectasis, which also leads to an increase in arterial oxygen pressure ( $\text{PaO}_2$ ) level and an increase in dead space fraction due to atelectasis. In



nine studies, PaCO<sub>2</sub> levels were compared between two groups, with three studies showing higher PaCO<sub>2</sub> levels in the low VT group and the remaining studies showing no significant difference between the two groups. Only one study compared the VD/VT between two groups, and the results showed no significant difference (Table SIII).

Apart from VT, the application of 3-8 cm H<sub>2</sub>O PEEP (41) in the low VT group contributed to the prevention of atelectasis. This physiological level of PEEP is mainly aimed at reversing the sustained opening of the glottis caused by tracheal intubation, in order to maintain physiological positive airway pressure and functional residual air volume. In only one study (25), the low VT group was not given PEEP and the results showed no increase in the incidence of atelectasis. However, the number of cases in this study is small (16/16) and more research results are needed to confirm whether low TV without PEEP increases the risk of atelectasis.

The present meta-analysis also has some limitations. First, the magnitude of hypoxemia generally peaks ~20 min after OLV begins. However, in the present study, data were collected for times between 15 min and 2 h from the different studies, which would overestimate the effect of low VT on oxygenation. Second, heterogeneity was identified in the use of PEEP and RM between the two groups for the included studies. In most studies, low VT ventilation during OLV is often accompanied by PEEP, and the actual effect of PEEP cannot be separated from low VT to a certain extent. The current study cannot clearly demonstrate the specific advantages of low VT ventilation in the absence of other ventilation strategies (PEEP and recruitment maneuvers). Therefore, analyses need to be cautiously interpreted due to heterogeneity. Third, the risk of bias and publication bias was assessed, but may be affected by the study design and outcome reported of the original article.

The present study assessed the physiology and clinical impact of low VT ventilation during OLV. In OLV patients, low VT improves PaO<sub>2</sub>/FiO<sub>2</sub> and decreases blood IL-6, ΔP, Ppeak, and risk of acute lung injury. Furthermore, low VT can reduce the length of hospital stay when set to 4-5 ml/kg, implying that low VT should be applied in patients with OLV. However, further research on this might be required for confirmation.

## Acknowledgements

Not applicable.

## Funding

The present study was supported by a grant from the National Natural Science Foundation of China (grant no. 81871602).

## Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article.

## Authors' contributions

All authors made substantial contributions to the present study. FX and FG designed the study. JJ was the main contributor to the work. ZL and YT participated in the collection and analysis

of clinical data. HQ was involved in writing the original draft. JJ has completed the manuscript revision work. YY was involved in reviewing and substantial editing of the paper. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication. All authors read and approved the final manuscript. Data authentication is not applicable.

## Ethics approval and consent to participate

Not applicable.

## Patient consent for publication

Not applicable.

## Competing interests

The authors declare that they have no competing interests

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