Editorial

Lung-protective ventilation during one-lung ventilation: known knowns, and known unknowns

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More than 230 million patients undergo major surgical procedures every year worldwide (1), among whom 16% to 18% will develop major postoperative complications (2,3), which negatively affect morbidity, mortality, healthcare cost, and quality of life. Patients undergoing thoracic surgery are at a higher risk of postoperative complications, especially those involving the respiratory system. Potential pathophysiology leading to postoperative pulmonary complications (PPCs) includes depressed central respiratory drive, changes in end-expiratory muscle tone, reduced lung volume (including functional residual capacity), abnormal regional distribution of ventilation, and atelectasis (4).

Among all the modifiable risk factors for postoperative complications, inappropriate intraoperative ventilation strategies may lead to tidal hyperinflation and tidal recruitment; i.e., major mechanisms associated with ventilator-induced lung injury. This is particularly true during one-lung ventilation for thoracic surgery, when more than one-third of anesthesiologists will not actively minimize tidal volume (5), which is inevitably associated with increased stress and strain. As a result, the concept of lung-protective ventilation (LPV) has been introduced from intensive care settings to the operating theater.

In the Pulmonary Surgery with Protective Ventilation (PPV) trial (6), which was a prospective, double-blind, randomized controlled trial in 13 thoracic surgical centers over a 33-month study period, patients undergoing lobectomy or pneumonectomy for lung cancer were randomly assigned to either LPV [tidal volume 5 mL/kg ideal body weight (IBW), and positive end-expiratory pressure (PEEP) 5 to 8 cmH_2O] or conventional ventilation (tidal volume 10 mL/kg IBW without PEEP) during anesthesia. Lung recruitment maneuvers (RMs) were performed in both groups at the discretion of the anesthesiologists in charge. The primary outcome included major pulmonary and non-pulmonary complications or death within 30 days after surgery. The study was stopped prematurely after enrollment of only 346 patients (about one-third of the predicted sample size of 900 patients) due to slow recruitment. In a modified intention-to-treat analysis, 23 patients (13.4%) in the LPV group developed major postoperative complications, compared with 38 patients (22.2%) in the control group [(odds ratio (OR) 0.54, 95% confidence interval (CI): 0.31 to 0.95, P=0.03)]. In addition, duration of hospital length of stay was significantly shorter in the LPV group (median 11 *vs.* 12 days, P=0.048). Despite limitations such as underestimation of complication rate in the control group, premature termination of the trial, and non-standardized RMs, the authors concluded that the PPV trial provided preliminary evidence supporting LPV during one-lung ventilation.

Apart from the PPV trial, there have been several other studies comparing LPV and conventional ventilation during one-lung ventilation. We have searched PubMed with the following strategy: ((low tidal [Title/Abstract] OR protective [Title/Abstract])) AND (one-lung [Title/

Table 1 Characteristics and ventilator settings of included studies

Studies	Sample size	Age	Male (%)	LPV group				Control group			
				n	Vt	PEEP	RR	n	Vt	PEEP	RR
Ahn 2012 (7)	50	58	NA	25	6	5	NA	25	10	0	NA
Cai 2013 (8)	60	22.8	53	30	3-5	NA	NA	30	8–10	NA	NA
Lin 2008 (9)	40	55	78	20	5–6	3–5	13	20	10	0	11
Maslow 2013 (10)	32	65.4	41	16	5	5	14	16	10	0	7
Michelet 2006 (11)	52	60.5	83	26	5	5	15	26	9	0	12
Shen 2013 (12)	101	58.9	71.3	53	5	5	NA	48	8	0	NA
Yang 2011 (13)	100	59	62	50	6	5	12.8	50	10	0	9.4
Kim 2018 (14)	60	57	45	40	6	5	12	20	10	0	10
Marret 2018 (6)	343	63	71.9	171	5	5	17	172	10	0	10.8

LPV, lung-protective ventilation; NA, not available; PEEP, positive end-expiratory pressure; RR, respiratory rate; Vt, tidal volume.

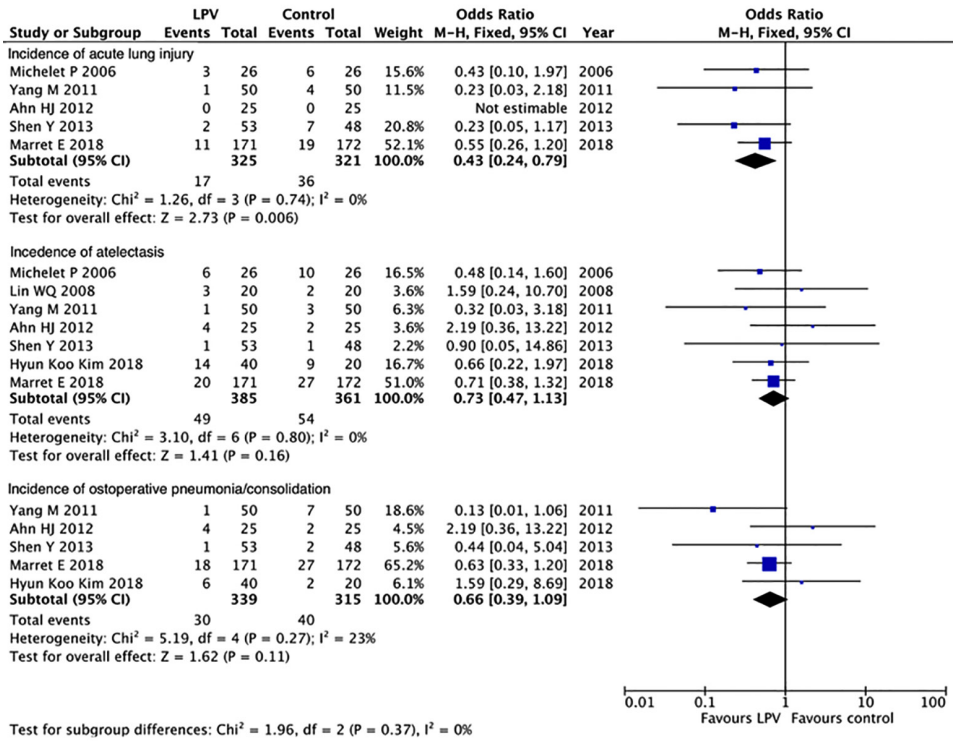

Figure 1 Forest plot of the meta-analyses.

Abstract] OR thoracic surgery [Title/Abstract]). This search identified 9 trials (6-14) (*Table 1*). A meta-analysis of these 9 trials using a fixed-effects model showed a significant decrease in acute lung injury (OR 0.43, 95% CI: 0.24 to 0.79, P=0.006), a nonsignificant reduction in atelectasis (OR 0.73, 95% CI: 0.47 to 1.13, P=0.16) and postoperative pneumonia/consolidation (OR 0.66, 95% CI: 0.39 to 1.09, P=0.11) (*Figure 1*).

Despite all these efforts to delineate the effects of LPV to prevent postoperative complications, especially PPCs, the importance of individual components of LPV (low tidal volume, PEEP, and RM) remains to be addressed.

Interestingly, an international prospective randomized controlled trial enrolling 900 patients at risk for PPCs undergoing elective open abdominal surgery compared high PEEP (12 cmH_2O) with RM and low PEEP (2 cmH_2O) without RM during low tidal volume (8 mL/kg IBW) ventilation (15). The study showed a similar prevalence of PPCs between the two groups, suggesting that the beneficial effects of LPV might be attributable to low tidal volume ventilation rather than high PEEP. This viewpoint was also supported by findings of an individual patient data meta-analysis (16). In contrast, a retrospective cohort study of 1,019 patients undergoing thoracic surgery with one-lung ventilation concluded that, without adequate PEEP, low tidal volume did not prevent PPCs (17).

There are even more questions to be answered. First, for those who cannot be extubated in the operating theatre, how should LPV be continued in the intensive care unit? Second, with regards to the ventilator settings, should we adopt a one-size-fits-all approach (as tested in almost all studies) or an individualized approach? And, if the latter approach is appropriate, how should we determine the appropriateness of tidal volume and/or PEEP? For example, how should we set PEEP level during one-lung ventilation, and why? From the previous experience in ventilating ARDS patients, we understand that gas exchange may not be the answer as it is very often, if not always, dissociated from lung protection under these circumstances (18). Therefore, can lung mechanics or imaging investigations provide convincing answers? Although it is true that further studies are needed to address the above questions, we would rather believe that these studies should be designed based on a robust and well-defined pathophysiology.

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Footnote

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

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