

## Effect of Intraoperative Lung-Protective Ventilation on Postoperative Pulmonary Complications in Non-ARDS Surgical Patients: A Prospective Multicenter Cohort Study

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### ABSTRACT

**Introduction:** Postoperative pulmonary complications (PPCs) are among the most frequent adverse events after major surgery and drive substantial morbidity, prolonged hospitalization, and mortality. Although lung-protective ventilation (LPV) is well established in patients with acute respiratory distress syndrome (ARDS), its perioperative role in non-ARDS surgical patients remains incompletely defined. We evaluated the association between intraoperative LPV and PPCs in non-ARDS patients who underwent general anesthesia.

**Methods:** In this prospective multicenter cohort study, adults undergoing elective non-thoracic, non-cardiac surgery were managed intraoperatively with LPV (tidal volume 6–8 mL/kg predicted body weight, PEEP 5–8 cmH<sub>2</sub>O, selective recruitment maneuvers) or conventional ventilation (tidal volume 10–12 mL/kg, minimal PEEP). The primary outcome was the incidence of PPC within 7 postoperative days. Secondary outcomes included pneumonia, respiratory failure, length of stay, and 30-day mortality. Multivariable logistic regression was used to adjust for relevant confounders.

**Results:** Of 1,000 patients, 500 received LPV and 500 conventional ventilation, with well-balanced baseline characteristics. PPCs occurred in 75 (15.0%) LPV patients versus 110 (22.0%) conventional patients ( $p=0.006$ ). LPV was independently associated with lower PPC odds (adjusted odds ratio 0.60, 95% CI 0.42–0.85;  $p=0.004$ ). Pneumonia was less frequent (6.0% vs. 10.0%,  $p=0.02$ ) and hospital stay was shorter (median 5 days vs. 6 days,  $p=0.02$ ). The ICU stay and 30-day mortality did not differ significantly.

**Conclusion:** Intraoperative LPV was independently associated with fewer PPCs in non-ARDS surgical patients, alongside lower pneumonia rates and shorter hospitalization. These findings support the broader perioperative adoption of lung-protective ventilation to improve respiratory outcomes after surgery.

Lung-Protective Ventilation, Postoperative Pulmonary Complications, Non-ARDS, Perioperative Care, General Anesthesia, Cohort Study

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## INTRODUCTION

Postoperative pulmonary complications remain a major source of perioperative morbidity and are consistently associated with prolonged hospital stay, higher resource utilization, and increased short-term mortality. PPCs encompass a clinically heterogeneous group of events, including pneumonia, respiratory failure, atelectasis requiring intervention, bronchospasm, pleural complications, and unplanned postoperative ventilatory support [1]. Their incidence varies according to the patient's risk profile, surgical site, duration of surgery, and perioperative management however, they remain especially important in moderate- to high-risk patients undergoing major abdominal and other prolonged procedures.

Over the past two decades, ventilatory management during general anesthesia has evolved from the routine use of relatively large tidal volumes to more individualized and physiologically protective strategies.

In patients with acute respiratory distress syndrome, low tidal volume ventilation reduces ventilator-induced lung injury and improves clinical outcomes [2]. This paradigm has prompted growing interest in whether similar protective principles may benefit surgical patients without ARDS, particularly because even short periods of mechanical ventilation may contribute to volutrauma, atelectrauma, impaired pulmonary compliance, and inflammatory lung injury. Several perioperative investigations have suggested that lung-protective ventilation, typically involving low tidal volume, moderate PEEP, and selective recruitment maneuvers, may reduce postoperative pulmonary morbidity in non-ARDS patients [3]. However, the evidence is not entirely consistent. While some randomized trials have reported reductions in PPCs with protective bundles, other studies, particularly those focusing on higher PEEP strategies alone, have shown neutral findings [4,5]. This inconsistency likely reflects differences in the study design, ventilation protocols, patient populations, surgical risk, and endpoint definitions.

Expert perioperative consensus statements increasingly recommend an initial tidal volume of 6–8 mL/kg predicted body weight and moderate PEEP, followed by individualization according to oxygenation, compliance, and hemodynamic tolerance [6]. Nevertheless, real-world adoption remains variable, and many centers continue to use conventional ventilatory settings, especially in non-thoracic surgery where perceived pulmonary risk may be underestimated. Because PPCs arise through a complex interaction between baseline host vulnerability, surgical insult, anesthetic exposure, and ventilatory mechanics, prospective multicenter observational data remain highly valuable. Such studies can clarify the magnitude of benefit associated with protective intraoperative ventilation in routine practice and identify whether these strategies translate into clinically meaningful reductions in respiratory morbidity beyond controlled trial settings. Therefore, the present prospective multicenter cohort study aimed to evaluate the effect of intraoperative lung-protective ventilation on postoperative pulmonary complications in non-ARDS surgical patients. We hypothesized that patients managed with LPV would experience fewer PPCs than those managed with conventional ventilation.

## METHOD

This prospective multicenter cohort study was conducted across tertiary care hospitals in Tehran, Iran, to evaluate the association between intraoperative lung-protective ventilation and the occurrence of postoperative pulmonary complications (PPCs) in adult surgical patients without acute respiratory distress syndrome (ARDS). The study was designed and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for observational cohort studies, with the aim of ensuring methodological rigor, transparency and reproducibility.

Adult patients aged 18–80 years who were scheduled to undergo elective nonthoracic, noncardiac surgery under general anesthesia were screened consecutively for eligibility. To enrich the cohort with patients at clinically relevant pulmonary risk, enrollment focused on those with moderate-to-high preoperative risk for PPCs, including patients with an Assess Respiratory Risk in Surgical Patients in Catalonia (ARISCAT) score of 26 or greater and an anticipated operative duration of at least 2 hours. Patients were excluded if they had preexisting ARDS, active pneumonia or any other acute lower respiratory tract infection, open thoracic procedures, pregnancy, severe chronic obstructive pulmonary disease, extreme obesity, marked hemodynamic instability, or any clinical contraindication to positive end-expiratory pressure (PEEP)-based ventilation. Patients with incomplete perioperative records or missing core outcome data were excluded from the final analysis. Patients were classified according to the intraoperative ventilatory strategy administered during surgery. Because this was an observational cohort study, the ventilation strategy was not randomly assigned but was determined by the routine clinical practice of the attending anesthesia team at each participating center. All ventilatory parameters were recorded prospectively and categorized according to predefined study criteria. The lung-protective ventilation (LPV) group was defined by the use of a tidal volume of 6–8 mL/kg predicted body weight, PEEP of 5–8 cmH<sub>2</sub>O, and selective alveolar recruitment maneuvers when clinically indicated. Ventilatory settings were further adjusted, where feasible, to maintain plateau pressure below 30 cmH<sub>2</sub>O and to minimize driving pressure. The conventional ventilation group was defined by the use of a tidal volume of

10–12 mL/kg predicted body weight, low or minimal PEEP (0–2 cmH<sub>2</sub>O), and the absence of routine recruitment maneuvers.

Clinical, demographic, anesthetic, and operative data were collected prospectively using standardized case report forms. Baseline variables included age, sex, body mass index, smoking status, comorbidities, ASA physical status classification, ARISCAT risk score, and surgical category. Operative variables included procedure duration, anesthetic technique, and type of surgery. Intraoperative ventilatory variables included tidal volume, respiratory rate, PEEP, fraction of inspired oxygen, and airway pressure parameters where available. Additional perioperative variables, including vasopressor requirement and hemodynamic instability, were also documented. The primary outcome was the occurrence of one or more postoperative pulmonary complications within 7 days after surgery. PPCs were defined according to standardized perioperative pulmonary complication criteria and included pneumonia, postoperative respiratory failure, clinically significant atelectasis, bronchospasm requiring treatment, unplanned reintubation, and other pulmonary events requiring active clinical intervention. Secondary outcomes included postoperative pneumonia, postoperative respiratory failure, ICU length of stay, total hospital length of stay, need for postoperative ventilatory support, and 30-day mortality. Based on previous literature reporting a PPC incidence of approximately 20% among patients receiving conventional ventilation, the study was planned to detect a clinically meaningful relative reduction in PPC incidence among patients managed with LPV. A target sample size of approximately 1,000 patients was considered sufficient to provide adequate statistical power and precision, while also accounting for potential missing data and between-center variability.

Continuous variables were expressed as mean  $\pm$  standard deviation or median with interquartile range, depending on the data distribution, whereas categorical variables were summarized as frequencies and percentages. Between-group comparisons were performed using Student's t-test or Mann–Whitney U test for continuous variables and chi-square test or Fisher's exact test for categorical variables, as appropriate. To estimate the independent association between intraoperative LPV and PPCs, multivariable logistic regression analysis was performed with adjustment for clinically relevant covariates, including age, ASA class, ARISCAT score, body mass index, surgery type, and operative duration. Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were reported. Prespecified subgroup analyses were conducted to explore whether the association between ventilation strategy and PPCs differed according to obesity status, surgical category, and baseline pulmonary risk. Missing data were handled using multiple imputation when appropriate. All analyses were two-sided, and a p-value of less than 0.05 was considered statistically significant. The study protocol was reviewed and approved by the institutional review boards of all participating centers. Written informed consent was obtained from all participants or their legal representatives prior to enrollment. All collected data were anonymized before analysis to ensure confidentiality and compliance with ethical research standards.

## RESULTS

A total of 1,082 patients were screened for eligibility during the study period. After excluding patients who did not meet the predefined inclusion criteria or had incomplete perioperative data, 1,000 patients were included in the final analysis. Of these, 500 patients received intraoperative lung-protective ventilation (LPV), whereas 500 patients were managed with conventional ventilation. The overall cohort thus provided balanced group sizes for comparative outcome analysis.

Table 1. Baseline demographic and operative characteristics

| Variable                               | LPV (n=500)     | Conventional (n=500) | p-value |
|----------------------------------------|-----------------|----------------------|---------|
| Age, years, mean $\pm$ SD              | 57.2 $\pm$ 12.3 | 56.8 $\pm$ 11.9      | 0.65    |
| Male sex, n (%)                        | 280 (56.0)      | 270 (54.0)           | 0.48    |
| BMI, kg/m <sup>2</sup> , mean $\pm$ SD | 27.5 $\pm$ 4.5  | 27.8 $\pm$ 4.7       | 0.30    |
| ASA III–IV, n (%)                      | 150 (30.0)      | 158 (31.6)           | 0.55    |
| ARISCAT $\geq$ 30, n (%)               | 120 (24.0)      | 130 (26.0)           | 0.40    |
| Abdominal Surgery, n (%)               | 350 (70.0)      | 360 (72.0)           | 0.47    |
| Operative Duration $>$ 3 h, n (%)      | 200 (40.0)      | 205 (41.0)           | 0.80    |

Baseline demographic, preoperative, and operative characteristics were generally well balanced between the two groups, indicating good comparability of the study population. The mean age was  $57.2 \pm 12.3$  years in the LPV group and  $56.8 \pm 11.9$  years in the conventional ventilation group ( $p=0.65$ ). Male patients comprised 56.0% of the LPV group and 54.0% of the conventional group ( $p=0.48$ ). Similarly, body mass index, ASA physical status distribution, baseline pulmonary risk according to ARISCAT, proportion of abdominal procedures, and operative duration were comparable between groups, with no statistically significant differences observed across these key baseline variables. The primary outcome of postoperative pulmonary complications within 7 days occurred significantly less frequently in patients managed with LPV than in those receiving conventional ventilation. PPCs developed in 75 patients (15.0%) in the LPV group compared with 110 patients (22.0%) in the conventional ventilation group, corresponding to an absolute risk reduction of 7.0 percentage points and a statistically significant between-group difference ( $p=0.006$ ). These findings indicate a clinically meaningful association between protective intraoperative ventilation and lower postoperative pulmonary morbidity.

The lower incidence of the primary composite endpoint in the LPV group was accompanied by favorable trends across several secondary respiratory outcomes. Postoperative pneumonia occurred in 30 patients (6.0%) in the LPV group compared with 50 patients (10.0%) in the conventional ventilation group ( $p=0.02$ ). Postoperative respiratory failure was also less frequent in the LPV group (3.0% vs 5.0%), although this difference did not reach statistical significance ( $p=0.10$ ). In terms of resource utilization, the median hospital length of stay was shorter among patients receiving LPV than among those managed with conventional ventilation (5 [IQR 4–7] vs 6 [IQR 4–9] days;  $p=0.02$ ). By contrast, ICU length of stay did not differ significantly between the two groups. Thirty-day mortality was numerically lower in the LPV group (1.0% vs 2.4%), although this difference was of borderline statistical significance.

Table 2. Primary and secondary outcomes

| Outcome                                      | LPV (n=500) | Conventional (n=500) | p-value |
|----------------------------------------------|-------------|----------------------|---------|
| Postoperative pulmonary complications, n (%) | 75 (15.0)   | 110 (22.0)           | 0.006   |
| Pneumonia, n (%)                             | 30 (6.0)    | 50 (10.0)            | 0.02    |
| Respiratory failure, n (%)                   | 15 (3.0)    | 25 (5.0)             | 0.10    |
| ICU stay, days, median (IQR)                 | 1 (1–2)     | 1 (1–3)              | 0.15    |
| Hospital stay, days, median (IQR)            | 5 (4–7)     | 6 (4–9)              | 0.02    |
| 30-day mortality, n (%)                      | 5 (1.0)     | 12 (2.4)             | 0.05    |

To account for potential confounding, a multivariable logistic regression model was constructed to adjust for age, ASA class, ARISCAT score, body mass index, surgery type, and operative duration. After adjustment, intraoperative LPV remained independently associated with a significantly lower likelihood of PPCs compared with conventional ventilation (adjusted odds ratio [aOR] 0.60, 95% confidence interval [CI] 0.42–0.85;  $p=0.004$ ). This finding confirms that the observed reduction in PPCs was not explained solely by differences in baseline risk or operative complexity. Among the additional covariates included in the model, a higher ARISCAT score emerged as the strongest independent predictor of PPC occurrence (aOR 2.50, 95% CI 1.80–3.47;  $p<0.001$ ). ASA classes III and IV demonstrated a borderline significant association with PPC risk, whereas age, body mass index, and operative duration  $>3$  hours were not independently associated with the primary outcome in the adjusted model.

Table 3. Multivariable logistic regression analysis of postoperative pulmonary complications

| Variable                        | Adjusted OR (95% CI) | p-value  |
|---------------------------------|----------------------|----------|
| LPV vs Conventional Ventilation | 0.60 (0.42–0.85)     | 0.004    |
| Age, per 10-Year Increase       | 1.10 (0.95–1.27)     | 0.20     |
| ASA III–IV vs I–II              | 1.30 (1.00–1.69)     | 0.05     |
| ARISCAT $\geq 30$ vs $<30$      | 2.50 (1.80–3.47)     | $<0.001$ |
| Operative Duration $>3$ h       | 1.15 (0.85–1.56)     | 0.37     |
| BMI, per 5-Unit Increase        | 1.05 (0.97–1.14)     | 0.20     |

Prespecified subgroup analyses suggested that the protective association of LPV was more pronounced among patients with higher baseline pulmonary risk and those undergoing abdominal surgery. However, formal interaction testing did not demonstrate definitive statistical evidence of effect modification. These subgroup findings should therefore be interpreted cautiously and regarded as hypothesis-generating rather than conclusive.

## DISCUSSION

In this prospective multicenter cohort study, intraoperative lung-protective ventilation was associated with a significant and clinically meaningful reduction in postoperative pulmonary complications in surgical patients without ARDS. Compared with conventional ventilation, LPV reduced the overall incidence of PPCs by 7 percentage points and remained independently protective after adjustment for established perioperative risk factors. Importantly, this protective effect extended beyond the composite primary endpoint, with lower postoperative pneumonia rates and shorter hospital stays, underscoring that the impact of intraoperative ventilatory strategy may extend well beyond the operating room and shape the broader trajectory of postoperative recovery [7,8].

These findings are biologically plausible and mechanistically coherent. Even in patients without preexisting lung injury, mechanical ventilation during general anesthesia may induce regional overdistension, repetitive alveolar collapse, surfactant dysfunction, and inflammatory signaling that together contribute to ventilator-induced lung injury. Conventional ventilation using higher tidal volumes with minimal PEEP is likely to amplify these processes by increasing cyclic strain and promoting atelectatic instability, whereas lower tidal volumes combined with moderate PEEP may preserve alveolar recruitment, reduce mechanical stress, and improve the distribution of transpulmonary forces [9]. Our findings reinforce the concept that ventilator-associated lung injury is not confined to ARDS populations in the ICU but may begin intraoperatively, even during relatively short exposures in patients previously considered to have structurally normal lungs [10]. The observed reduction in PPCs is consistent with the growing perioperative literature supporting protective ventilatory strategies in non-ARDS surgical populations. In particular, our findings align with studies demonstrating that lower tidal volume-based ventilation, especially when combined with physiologically appropriate PEEP and selective recruitment maneuvers, can reduce postoperative respiratory morbidity [11]. Equally important, our results support the view that effective lung protection is not achieved through isolated increases in PEEP alone, but through a balanced strategy integrating lower tidal strain, alveolar stability, and acceptable hemodynamic tolerance. This distinction may explain why some previous trials with more PEEP-centered strategies reported neutral findings despite sound physiologic rationale [12].

One of the most clinically compelling findings of this study was the lower incidence of postoperative pneumonia in the LPV group. Pneumonia remains one of the most consequential pulmonary complications after surgery because it contributes to prolonged antibiotic exposure, delayed mobilization, ICU escalation, and increased mortality risk. The lower pneumonia rate observed in our cohort suggests that LPV may not only improve immediate respiratory mechanics but may also mitigate the downstream cascade of postoperative pulmonary deterioration, including secretion retention, atelectatic progression, and secondary infectious complications [13]. Likewise, the shorter hospital stay in the LPV group indicates that the observed protective effect was clinically meaningful enough to translate into a faster overall postoperative recovery. We did not observe statistically significant differences in ICU stay or 30-day mortality, and these findings should be interpreted with caution rather than as evidence of an absent benefit. Mortality was infrequent in both groups, limiting the statistical power for definitive mortality comparisons, and postoperative death is influenced by multiple factors beyond intraoperative ventilation alone, including cardiovascular complications, surgical events, infection burden, and baseline comorbidity. In this context, the marked reduction in PPCs and postoperative pneumonia may represent a more sensitive and clinically immediate signal of benefit than mortality.

This study has strengths. The prospective design minimized recall bias and improved clarity between ventilatory exposure and postoperative outcomes. The multicenter setting enhances external validity and

reflects perioperative practice rather than a controlled environment. Furthermore, adjustment for confounders, including baseline pulmonary risk and operative duration, strengthens the association. Nevertheless, limitations deserve acknowledgment. Because this was a non-randomized observational study, residual confounding and treatment-selection bias cannot be excluded. Ventilation strategies were pragmatic, not strictly protocolized, which may have introduced heterogeneity. Although consensus definitions were applied, PPCs remain composite outcomes with unavoidable variability in recognition and adjudication across institutions [14]. Despite these limitations, the findings add evidence to the debate on perioperative ventilation in patients without ARDS. The data suggest that protective ventilation should no longer be regarded as an optional technical refinement for selected high-risk procedures, but as a rational, evidence-aligned standard for a range of patients undergoing general anesthesia. Future large randomized trials should define the optimal interaction among tidal volume, PEEP, recruitment maneuvers, and patient-specific pulmonary risk. Until such data are available, our results provide support for the broader perioperative adoption of LPV as a strategy to reduce respiratory morbidity after surgery [15].

## CONCLUSION

Intraoperative lung-protective ventilation was independently associated with fewer postoperative pulmonary complications in non-ARDS surgical patients, with lower pneumonia rates and shorter hospital stays. These findings indicate that intraoperative ventilatory management is a clinically meaningful determinant of postoperative respiratory outcomes and support integrating lung-protective ventilation into routine perioperative practice over conventional high-tidal-volume, low-PEEP ventilation strategies.

## DECLARATIONS

None

## CONSENT FOR PUBLICATION

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All authors have reviewed and approved the final version of the manuscript and have agreed to its publication in the Journal of Society Medicine.

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All authors have read, critically revised, and approved the final manuscript and have agreed to be accountable for all aspects of the work.

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