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Effect of Intraoperative Lung-Protective Ventilation on Postoperative Pulmonary Complications in Adult Patients Undergoing Elective Craniotomy: A Double-Blind Randomized Controlled Trial

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Abstract

Background

Mechanical ventilation is essential during general anesthesia; however, conventional ventilation strategies may contribute to ventilator-induced lung injury and postoperative pulmonary complications (PPCs). Lung-protective ventilation (LPV), incorporating low tidal volumes and positive end-expiratory pressure (PEEP), may improve pulmonary outcomes. Its application during elective craniotomy remains controversial because of concerns regarding intracranial pressure and surgical brain relaxation. This study aimed to compare the effects of intraoperative lung-protective and conventional ventilation on PPCs in adult patients undergoing elective craniotomy.

Methods

This prospective, randomized, controlled trial included 160 adult patients with American Society of Anesthesiologists physical status I-II undergoing elective craniotomy under general anesthesia. Patients were randomly allocated to receive either LPV group (Group A; tidal volume 6 mL/kg predicted body weight (PBW) with PEEP of 6 cmH_2O) or conventional ventilation (CV) group (Group B; tidal volume 10 mL/kg PBW without PEEP). The primary outcome was the incidence of PPCs during the first seven postoperative days. Secondary outcomes included respiratory mechanics, arterial blood gas parameters, brain relaxation scores, hemodynamic variables, and duration of neurosurgical intensive care unit stay.

Results

Baseline demographic and perioperative characteristics were comparable between the groups. The incidence of PPCs was significantly lower in the LPV group than in the CV group ($p < 0.001$). LPV was associated with higher dynamic lung compliance, lower driving pressure, a lower respiratory index, and improved oxygenation. Although brain relaxation scores were slightly better in the CV group, moderate PEEP did not adversely affect surgical exposure or postoperative neurological outcomes. The duration of neurosurgical intensive care unit stay was significantly shorter in the LPV group. No ventilation-related adverse events, including barotrauma or pneumothorax, were reported.

Conclusion

Intraoperative LPV using low tidal volumes and moderate PEEP reduced PPCs and improved respiratory mechanics in adults undergoing elective craniotomy, without clinically significant impairment of surgical brain relaxation. These findings support its potential use in appropriately selected neurosurgical patients.

Categories: Pharmacology, Neurosurgery, Anesthesiology
Keywords: craniotomy, lung-protective ventilation, mechanical ventilation, neurosurgery, positive end-expiratory pressure, postoperative pulmonary complications

Introduction

Mechanical ventilation is an essential component of general anesthesia and is required to maintain adequate oxygenation and carbon dioxide elimination during surgery. However, inappropriate ventilatory settings may contribute to ventilator-induced lung injury (VILI) through alveolar overdistension, repetitive alveolar collapse and reopening, and pulmonary inflammation, thereby increasing the risk of postoperative pulmonary complications (PPCs). PPCs, including atelectasis, pneumonia, and respiratory failure, are important causes of perioperative morbidity and mortality and may lead to prolonged intensive care unit (ICU) stay, increased healthcare costs, and delayed postoperative recovery [1-6].

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Conventional intraoperative ventilation has traditionally involved relatively high tidal volumes with little or no positive end-expiratory pressure (PEEP), with the aim of maintaining adequate gas exchange and preventing hypoxemia. However, evidence suggests that this approach may expose the lungs to excessive alveolar stretch and cyclic alveolar collapse, even in patients without pre-existing pulmonary disease. Experimental and clinical studies have demonstrated that conventional mechanical ventilation may promote pulmonary inflammation, whereas lower tidal volumes combined with appropriate PEEP may help preserve alveolar stability and reduce ventilator-associated lung injury (VALI) [3,7-10].

Lung-protective ventilation (LPV), generally characterized by lower tidal volumes and appropriate PEEP, has become an important strategy for minimizing VILI. Although initially established in the management of acute respiratory distress syndrome (ARDS), this approach has increasingly been investigated in patients undergoing general anesthesia without pre-existing lung injury. Randomized controlled trials and meta-analyses have evaluated the effects of intraoperative LPV on respiratory mechanics, pulmonary inflammation, PPCs, and recovery following major surgery. Collectively, these studies support the potential benefits of LPV, although the effects may vary according to the ventilation protocol, surgical population, and clinical setting [3,9-16].

Despite these encouraging findings, the application of LPV during neurosurgical procedures remains an area of clinical interest. The use of PEEP during craniotomy has traditionally raised concerns regarding increased intrathoracic pressure, impaired cerebral venous drainage, elevation of intracranial pressure, reduced cerebral perfusion pressure, and deterioration of surgical brain relaxation. These concerns are particularly relevant during intracranial surgery, where satisfactory brain relaxation is essential for surgical exposure and safe operative conditions. Previous studies have investigated the relationship between PEEP, intracranial pressure, cerebral hemodynamics, and brain relaxation; however, the optimal balance between pulmonary protection and neurosurgical requirements remains incompletely established [17-20].

Patients undergoing elective craniotomy may be vulnerable to PPCs because of prolonged surgery, postoperative immobility, neurological impairment, compromised airway protective reflexes, and the potential requirement for postoperative mechanical ventilation in an intensive care setting. Although previous investigations have examined pulmonary complications following intracranial surgery and the physiological effects of different ventilation strategies, evidence regarding the impact of LPV on clinically relevant postoperative pulmonary outcomes and intraoperative brain relaxation remains limited [5,6,18,21].

Therefore, the present study aimed to compare LPV using a tidal volume of 6 mL/kg predicted body weight (PBW) with PEEP of 6 cmH_2O against conventional ventilation using a tidal volume of 10 mL/kg PBW without PEEP in adult patients undergoing craniotomy under general anesthesia. The primary outcome was the incidence of PPCs. Secondary outcomes included respiratory mechanics, arterial blood gas parameters, hemodynamic variables, intraoperative brain relaxation, and duration of ICU stay.

Materials And Methods

Study design and ethical approval

This prospective, randomized, controlled trial was conducted in the Department of Anesthesiology in collaboration with the Department of Neurosurgery at Vardhman Mahavir Medical College (VMMC) and Safdarjung Hospital, New Delhi, between 11 December, 2020 and 10 June, 2022. The study protocol was approved by the Institutional Protocol Review Committee (IPRC) of VMMC and Safdarjung Hospital. The ethics approval letter was dated 10 December, 2020 with a reference number IEC/VMMC/SJH/Thesis/2020-11/CC-58, and the trial was prospectively registered with the Clinical Trials Registry-India (CTRI/REF/2021/02/031326). The study was conducted under the supervision of Dr. Ranju Gandhi, Professor, Department of Anaesthesia. Written informed consent was obtained from all participants before enrolment. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki (2013).

Participants

A total of 160 adult patients aged 18-70 years with American Society of Anesthesiologists (ASA) physical status I or II, scheduled to undergo elective craniotomy under general anesthesia, were included in the study [22]. The ASA Physical Status Classification System was used to describe the preoperative physical status of the participants.

The inclusion criteria were age between 18 and 70 years, ASA physical status I or II, elective craniotomy under general anesthesia, and provision of written informed consent.

Patients with chronic pulmonary disease, severe cardiac dysfunction, morbid obesity (body mass index >35 kg/m^2), pregnancy, anticipated difficult airway, previous thoracic surgery, emergency craniotomy, or refusal to participate were excluded.

Randomization and allocation

A total of 160 eligible patients were randomly allocated in a 1:1 ratio to either the LPV group (Group A, n = 80) or the conventional ventilation (CV) group (Group B, n = 80). Randomization was performed using a computer-generated sequence. Allocation concealment was achieved using sequentially numbered, opaque, sealed envelopes prepared by an investigator who was not involved in patient recruitment or outcome assessment.

The anesthesiologist responsible for intraoperative ventilation was aware of the assigned intervention. Patients, operating neurosurgeons, postoperative assessors, and investigators responsible for data collection and statistical analysis remained blinded to group allocation.

Anesthetic management

Upon arrival in the operating room, standard intraoperative monitoring was instituted, including electrocardiography (ECG), pulse oximetry (SpO_2), non-invasive blood pressure monitoring, invasive arterial blood pressure monitoring, end-tidal carbon dioxide ($EtCO_2$) monitoring, and temperature monitoring. Arterial blood gas analysis was performed at predefined time points during the study period. All monitoring and anesthetic management were conducted according to standard institutional protocols.

General anesthesia was induced using intravenous fentanyl, propofol, and vecuronium to facilitate endotracheal intubation. Anesthesia was maintained with an oxygen-air mixture, sevoflurane, intermittent doses of vecuronium, and fentanyl according to the institutional protocol. Mechanical ventilation was adjusted to maintain $EtCO_2$ between 30 and 35 mmHg throughout the surgical procedure.

Ventilation protocol

Patients allocated to the LPV group received volume-controlled ventilation with a tidal volume of 6 mL/kg PBW and PEEP of 6 cmH_2O throughout the procedure.

Patients allocated to the CV group received volume-controlled ventilation with a tidal volume of 10 mL/kg PBW without PEEP.

The inspired oxygen concentration, inspiratory-to-expiratory ratio, and fresh gas flow were maintained similarly in both groups. Recruitment maneuvers were not routinely performed. Ventilatory management was continued according to the assigned protocol, with the aim of maintaining adequate gas exchange and the target $EtCO_2$ range.

Monitoring and outcome assessment

The following intraoperative variables were recorded at predefined intervals: heart rate (HR), mean arterial pressure (MAP), peak airway pressure, plateau airway pressure, dynamic lung compliance, driving pressure, respiratory index, and oxygen index.

Arterial blood gas analysis was performed at predetermined time points to assess arterial pH, partial pressure of oxygen (PaO_2), partial pressure of carbon dioxide ($PaCO_2$), bicarbonate concentration, and oxygen saturation.

Brain relaxation was assessed by the operating neurosurgeon immediately after dural opening using a four-point brain relaxation scale with lower scores indicating better surgical conditions.

The primary outcome was the incidence of PPCs during the first seven postoperative days. PPCs included atelectasis, pneumonia, bronchospasm, respiratory failure requiring ventilatory support, pulmonary infiltrates, and pleural effusion. Their diagnosis was based on predefined clinical and radiological criteria.

Secondary outcomes included dynamic lung compliance, driving pressure, respiratory index, oxygen index, arterial blood gas parameters, brain relaxation scores, intraoperative hemodynamic variables, duration of neurosurgical ICU stay, and total hospital stay. Postoperative neurological complications, reoperation, in-hospital mortality, and ventilation-related adverse events were also assessed.

Sample size calculation

The study by Futier et al. [14] observed that PPCs occurred in 10.5% of LPV and 27.5% of nonprotective ventilation. Taking these values as a reference, the minimum required sample size, with 80% power of study, 5% level of significance, and allowing for possible dropouts, was 160 (80 per group).

Statistical analysis

Data were analyzed using IBM SPSS Statistics for Windows version 22.0 (released 2013; IBM Corp., Armonk, NY, USA). Continuous variables were compared using the independent-samples Student's t-test or the Mann-Whitney U test, as appropriate. Categorical variables were compared using the chi-square test or

Fisher's exact test, as appropriate. The relevant test statistic (t, χ^2, or U) and two-sided p-value are reported for each comparison where applicable. For Fisher's exact test, the exact p-value is reported. A p-value <0.05 was considered statistically significant.

Results

Patient enrolment and baseline characteristics

A total of 176 patients were assessed for eligibility. Sixteen patients were excluded before randomization, and the remaining 160 patients were randomly allocated equally to the LPV group (Group A, n = 80) and the CV group (Group B, n = 80). All randomized patients completed the study and were included in the final analysis (Figure *1*).

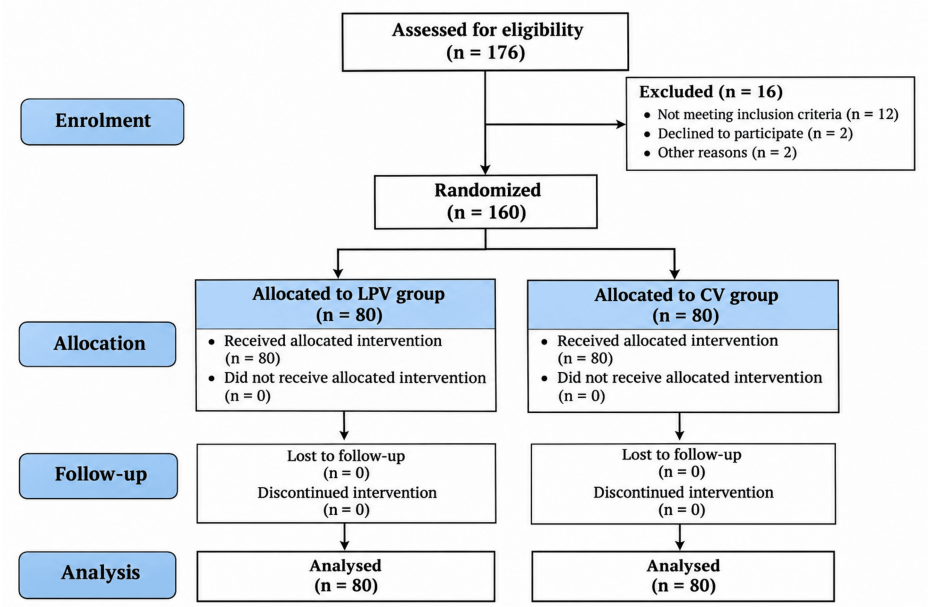


FIGURE 1: CONSORT flow diagram of study participants.

A total of 176 patients were assessed for eligibility. Sixteen patients were excluded before randomization. The remaining 160 patients were randomly allocated in a 1:1 ratio to the lung-protective ventilation (LPV) group (n = 80) or the conventional ventilation (CV) group (n = 80). All randomized patients completed the study and were included in the final analysis. The figure was created using Canva (Canva Pty Ltd., Sydney, New South Wales, Australia).

CONSORT: Consolidated Standards of Reporting Trials; LPV: lung-protective ventilation; CV: conventional ventilation

The baseline demographic and clinical characteristics were comparable between the two groups (Table *1*). The mean age was 39.16 ± 12.97 years in the LPV group and 41.40 ± 11.90 years in the CV group (t = -1.137, p = 0.2574). The mean body mass index (BMI) was 22.40 ± 2.12 kg/m² in the LPV group and 22.92 ± 2.04 kg/m² in the CV group (t = -1.577, p = 0.1168). The Glasgow Coma Scale (GCS) scores recorded in the master-chart analysis were 14.82 ± 0.96 and 14.94 ± 0.56, respectively; the between-group comparison was not statistically significant (U = 3119.500, p = 0.3127). The mean duration of surgery was 200.69 ± 44.95 minutes in the LPV group and 211.69 ± 40.67 minutes in the CV group (t = -1.623, p = 0.1066). There were no statistically significant between-group differences in sex distribution (χ^2 = 1.616, p = 0.2036) or ASA physical status (χ^2 = 1.406, p = 0.2357).

Variable	LPV (Group A), n = 80	CV (Group B), n = 80	Statistical test	Test statistic	p-Value
Age (years), mean ± SD	39.16 ± 12.97	41.40 ± 11.90	Student's t-test	-1.137	0.2574
BMI (kg/m²), mean ± SD	22.40 ± 2.12	22.92 ± 2.04	Student's t-test	-1.577	0.1168
GCS, mean ± SD as recorded	14.82 ± 0.96	14.94 ± 0.56	Mann-Whitney U test	3119.5	0.3127
Duration of surgery (min), mean ± SD	200.69 ± 44.95	211.69 ± 40.67	Student's t-test	-1.623	0.1066
Sex (male/female), n	32/08	30/10	Pearson's chi-square test	1.616	0.2036
ASA physical status (I/II), n	61/19	67/13	Pearson's chi-square test	1.406	0.2357

TABLE 1: Baseline demographic and clinical characteristics of patients in the lung-protective ventilation and conventional ventilation groups

Continuous variables are presented as mean ± standard deviation (SD), and categorical variables as numbers (n). Independent-samples Student's t-tests were used to compare age, BMI, and duration of surgery. The Mann-Whitney U test was used for GCS, and Pearson's chi-square test was used for sex and ASA physical status. All p-values are two-sided. A p-value < 0.05 was considered statistically significant.

LPV: lung-protective ventilation; CV: conventional ventilation; BMI: body mass index; ASA: American Society of Anesthesiologists; GCS: Glasgow Coma Scale; SD: standard deviation

Postoperative clinical findings

Postoperative clinical features were assessed in the post-anesthesia care unit (PACU) and at subsequent postoperative time points (Table *2*). In the PACU, fever, cough, or both were recorded in four patients (5.0%) in the LPV group and five patients (6.3%) in the CV group. The difference was not statistically significant (χ^2 = 0.118, p = 0.7315). At 24 hours, fever, cough, or both were recorded in eight patients (10.0%) in the LPV group and five patients (6.3%) in the CV group. Fever with shortness of breath was recorded in none of the LPV patients and 10 CV patients (12.5%). The distribution of clinical features differed significantly between the groups (χ^2 = 11.050, p = 0.0040). At 48 hours, fever, cough, or both were recorded in 12 patients (16.2%) in the LPV group, compared with none in the CV group. Fever with shortness of breath was recorded in none of the LPV patients and 17 CV patients (21.8%). The between-group difference was statistically significant (χ^2 = 28.923, p = 0.0001). At 72 hours, fever, cough, or both were recorded in seven patients (13.0%) in the LPV group and two patients (3.4%) in the CV group. Fever with shortness of breath was recorded in none of the LPV patients and 16 CV patients (27.1%). The distribution differed significantly between the groups (χ^2 = 19.003, p = 0.0001). At 96 hours, fever, cough, or both were recorded in two patients (8.0%) in the LPV group and none in the CV group. Fever with shortness of breath was recorded in none of the LPV patients and 15 CV patients (35.7%). The between-group difference was statistically significant (χ^2 = 13.902, p = 0.0010). At 120 hours, the difference in clinical-feature distribution was not statistically significant (χ^2 = 4.886, p = 0.0869). Similarly, the comparisons at 144 hours (χ^2 = 5.878, p = 0.0529) and 168 hours (χ^2 = 1.750, p = 0.4169) did not reach statistical significance. At 144 hours, the difference in clinical-feature distribution was not statistically significant (χ^2 = 5.878, p = 0.0529). Similarly, the comparison at 168 hours did not reach statistical significance (χ^2 = 1.750, p = 0.4169).

Assessment time	Clinical feature	LPV (Group A), n (%)	CV (Group B), n (%)	Statistical test	Test statistic	p-Value
PACU	Fever, cough, or both	4 (5.0)	5 (6.3)	Pearson's chi-square test	0.118	0.7315
	Asymptomatic	76 (95.0)	75 (93.8)			
24 hours	Fever, cough, or both	8 (10.0)	5 (6.3)	Pearson's chi-square test	11.05	0.004
	Fever with shortness of breath	0 (0.0)	10 (12.5)			
	Asymptomatic	72 (90.0)	65 (81.3)			
48 hours	Fever, cough, or both	12 (16.2)	0 (0.0)	Pearson's chi-square test	28.923	0.0001
	Fever with shortness of breath	0 (0.0)	17 (21.8)			
	Asymptomatic	62 (83.8)	61 (78.2)			
72 hours	Fever, cough, or both	7 (13.0)	2 (3.4)	Pearson's chi-square test	19.003	0.0001
	Fever with shortness of breath	0 (0.0)	16 (27.1)			
	Asymptomatic	47 (87.0)	41 (69.5)			
96 hours	Fever, cough, or both	2 (8.0)	0 (0.0)	Pearson's chi-square test	13.902	0.001
	Fever with shortness of breath	0 (0.0)	15 (35.7)			
	Asymptomatic	23 (92.0)	27 (64.3)			
120 hours	Fever, cough, or both	2 (25.0)	2 (8.7)	Pearson's chi-square test	4.886	0.0869
	Fever with shortness of breath	0 (0.0)	9 (39.1)			
	Asymptomatic	6 (75.0)	12 (52.2)			
144 hours	Fever, cough, or both	2 (50.0)	1 (7.1)	Pearson's chi-square test	5.878	0.0529
	Fever with shortness of breath	0 (0.0)	8 (57.1)			
	Asymptomatic	2 (50.0)	5 (35.7)			
168 hours	Fever, cough, or both	1 (25.0)	1 (10.0)	Pearson's chi-square test	1.75	0.4169
	Fever with shortness of breath	0 (0.0)	3 (30.0)			
	Asymptomatic	3 (75.0)	6 (60.0)			

TABLE 2: Comparison of postoperative clinical features between the lung-protective ventilation and conventional ventilation groups

Data are presented as number (percentage). Percentages use the number of patients assessed at each time point as the denominator. The reported test statistics and p-values are from the available master-chart analysis. A two-sided p-value < 0.05 was considered statistically significant.

LPV: lung-protective ventilation; CV: conventional ventilation; PACU: post-anesthesia care unit; POD: postoperative day

Postoperative chest radiographic findings and ICU stay

Chest radiographic findings at 24 and 48 hours and the duration of ICU stay are summarized (Table 3). At 24 hours, all 80 patients in each group were recorded as having no chest X-ray abnormality. There was no between-group difference in the distribution of findings ($\chi^2 = 0.000$, $p = 1.0000$). At 48 hours, 78 patients (97.5%) in the LPV group and 63 patients (78.8%) in the CV group had no recorded chest X-ray abnormality.

Patchy opacities were recorded in one patient (1.3%) in the LPV group and 14 patients (17.5%) in the CV group. Pleural effusion was recorded in one patient (1.3%) in the LPV group and two patients (2.5%) in the CV group, while atelectasis was recorded in none of the LPV patients and one CV patient (1.3%). The distribution of chest X-ray findings differed significantly between the groups ($\chi^2 = 14.196$, p = 0.0027). The mean duration of ICU stay was 2.17 ± 1.61 days in the LPV group and 3.33 ± 1.91 days in the CV group. The difference was statistically significant (t = -4.109, p = 0.0001), with a shorter mean ICU stay in the LPV group.

Variable	LPV (Group A), n = 80	CV (Group B), n = 80	Statistical test	Test statistic	p-Value
Length of ICU stay (days), mean ± SD	2.17 ± 1.61	3.33 ± 1.91	Independent-samples Student's t-test	-4.109	0.0001
Chest X-ray findings at 24 hours, n (%)			Pearson's chi-square test	0	1
Normal (no abnormality detected)	80 (100.0)	80 (100.0)			
Chest X-ray findings at 48 hours, n (%)			Pearson's chi-square test	14.196	0.0027
Normal (no abnormality detected)	78 (97.5)	63 (78.8)			
Patchy opacities	1 (1.3)	14 (17.5)			
Pleural effusion	1 (1.3)	2 (2.5)			
Atelectasis	0 (0.0)	1 (1.3)			

TABLE 3: Comparison of postoperative pulmonary complications, chest radiographic abnormalities, and neurosurgical intensive care unit stay between the study groups

Continuous data are presented as mean ± standard deviation (SD), and categorical data as number (percentage). An independent-samples Student's t-test was used to compare ICU length of stay. Pearson's chi-square test was used to compare the distribution of chest X-ray findings between groups. A two-sided p-value < 0.05 was considered statistically significant.

LPV: lung-protective ventilation; CV: conventional ventilation; ICU: intensive care unit; SD: standard deviation

Intraoperative respiratory mechanics and ventilatory parameters

Dynamic lung compliance was numerically higher in the LPV group than in the CV group at the first three assessment points, although none of the between-group differences reached statistical significance (Figure *2*). At T1, the between-group comparison yielded t = 1.493 (p = 0.1373); at T2, t = 1.803 (p = 0.0732); and at T3, t = 1.563 (p = 0.1201). At T4, the difference was also not statistically significant (t = -1.238, p = 0.2288).

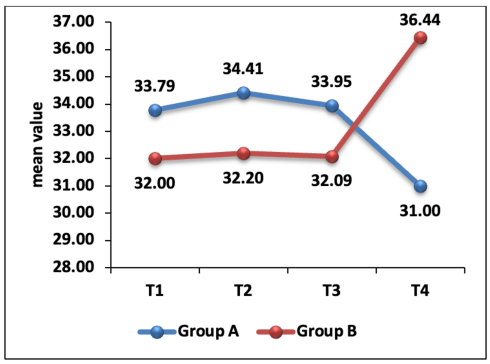


FIGURE 2: Comparison of intraoperative dynamic lung compliance between the lung-protective ventilation and conventional ventilation groups at predefined intraoperative time points.

Data are presented as mean ± standard deviation. Between-group comparisons at each time point were performed using independent-samples Student's t-tests. The test statistics and two-sided p-values were: T1, t = 1.493, p = 0.1373; T2, t = 1.803, p = 0.0732; T3, t = 1.563, p = 0.1201; and T4, t = -1.238, p = 0.2288. A p-value < 0.05 was considered statistically significant. The figure was created using Canva (Canva Pty Ltd., Sydney, New South Wales, Australia).

LPV: lung-protective ventilation; CV: conventional ventilation; T1: before changing the ventilator setting, after hemodynamic stabilization following intubation; T2: one hour after changing the ventilatory strategy; T3: at the end of surgery; T4: immediately after extubation

The respiratory index was significantly lower in the LPV group at T1 (t = -2.591, p = 0.0105), T2 (t = -4.697, p < 0.0001), and T3 (t = -5.279, p < 0.0001) (Figure *3*). At T4, the difference between groups was not statistically significant (t = -0.651, p = 0.5216).

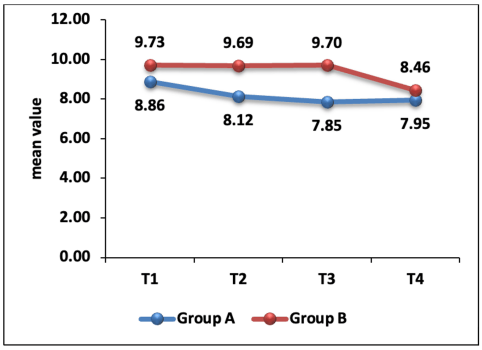


FIGURE 3: Comparison of intraoperative respiratory index between the lung-protective ventilation and conventional ventilation groups at four predefined intraoperative time points.

Data are presented as mean ± standard deviation. Between-group comparisons at each time point were performed using independent-samples Student's t-tests. The test statistics and two-sided p-values were: T1, t = -2.591, p = 0.0105; T2, t = -4.697, p < 0.0001; T3, t = -5.279, p < 0.0001; and T4, t = -0.651, p = 0.5216. A p-value < 0.05 was considered statistically significant. The figure was created using Canva (Canva Pty Ltd., Sydney, New South Wales, Australia).

LPV: lung-protective ventilation; CV: conventional ventilation; T1: before changing the ventilator setting, after hemodynamic stabilization following intubation; T2: one hour after changing the ventilatory strategy; T3: at the end of surgery; T4: immediately after extubation

The oxygen index differed significantly between the groups at all four assessment points (Figure *4*). The between-group comparisons yielded t = 2.004 (p = 0.0468) at T1, t = 3.274 (p = 0.0013) at T2, t = 2.275 (p = 0.0243) at T3, and t = 5.086 (p < 0.0001) at T4.

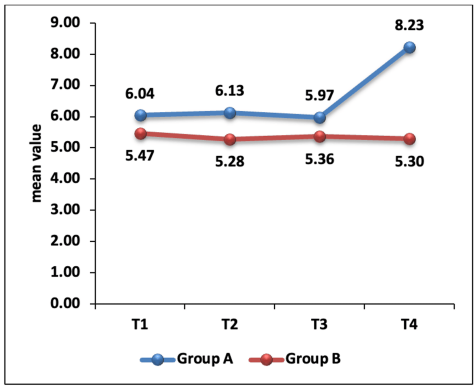


FIGURE 4: Comparison of intraoperative oxygen index between the lung-protective ventilation and conventional ventilation groups at four predefined intraoperative time points.

Data are presented as mean ± standard deviation. Between-group comparisons at each time point were performed using independent-samples Student's t-tests. The test statistics and two-sided p-values were: T1, t = 2.004, p = 0.0468; T2, t = 3.274, p = 0.0013; T3, t = 2.275, p = 0.0243; and T4, t = 5.086, p < 0.0001. A p-value < 0.05 was considered statistically significant.

LPV: lung-protective ventilation; CV: conventional ventilation; T1: before changing the ventilator setting, after hemodynamic stabilization following intubation; T2: one hour after changing the ventilatory strategy; T3: at the end of surgery; T4: immediately after extubation

Driving pressure differed significantly between the groups at T2 (t = -9.869, p < 0.0001) and T3 (t = -8.644, p < 0.0001) (Figure 5). The differences at T1 (t = -1.875, p = 0.0626) and T4 (t = -1.268, p = 0.2174) were not statistically significant.

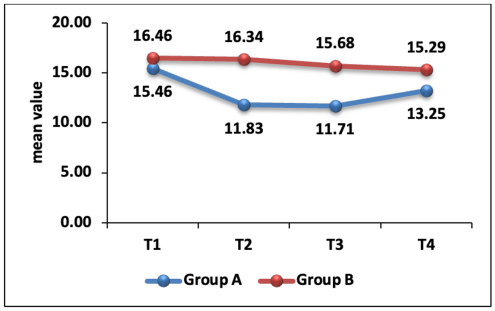


FIGURE 5: Comparison of intraoperative driving pressure between the lung-protective ventilation and conventional ventilation groups at four predefined intraoperative time points.

Data are presented as mean ± standard deviation. Between-group comparisons at each time point were performed using independent-samples Student's t-tests. The test statistics and two-sided p-values were: T1, t = -1.875, p = 0.0626; T2, t = -9.869, p < 0.0001; T3, t = -8.644, p < 0.0001; and T4, t = -1.268, p = 0.2174. A p-value < 0.05 was considered statistically significant. The figure was created using Canva (Canva Pty Ltd., Sydney, New South Wales, Australia).

LPV: lung-protective ventilation; CV: conventional ventilation; T1: before changing the ventilator setting, after hemodynamic stabilization following intubation; T2: one hour after changing the ventilatory strategy; T3: at the end of surgery; T4: immediately after extubation

Brain relaxation

Brain relaxation scores differed significantly between the LPV and CV groups at the assessed intraoperative time points (Table 4). At dural opening, brain bulging was recorded in 60 patients (75.0%) in the LPV group and five patients (6.3%) in the CV group. Firm brain relaxation was observed in 20 patients (25.0%) in the

LPV group and 54 patients (67.5%) in the CV group, while satisfactory relaxation was recorded in 21 patients (26.3%) in the CV group and none in the LPV group (χ^2 = 83.160, p = 0.0001). At 60 minutes, brain bulging was observed in 28 patients (35.0%) in the LPV group and none in the CV group. Satisfactory relaxation was recorded in nine patients (11.3%) in the LPV group and 61 patients (76.3%) in the CV group. The distribution of brain relaxation scores differed significantly between the groups (χ^2 = 77.874, p = 0.0001). At 120 minutes, brain bulging was observed in seven patients (8.8%) in the LPV group and none in the CV group. Satisfactory relaxation was recorded in 26 patients (32.5%) in the LPV group and 66 patients (82.5%) in the CV group. The between-group difference remained statistically significant (χ^2 = 52.221, p = 0.0001). At 180 minutes, brain relaxation scores also differed significantly between the groups (χ^2 = 54.566, p = 0.0001). Complete relaxation was recorded in three patients (3.8%) in the LPV group and 29 patients (37.2%) in the CV group, while firm relaxation was recorded in 35 patients (44.9%) and three patients (3.8%), respectively. At 240 minutes, the distribution of brain relaxation scores differed between the groups (χ^2 = 11.203, p = 0.0037). Five patients were assessed in the LPV group and 24 in the CV group at this time point. The small numbers assessed should be considered when interpreting this comparison.

Assessment time	Brain relaxation score	LPV (Group A), n (%)	CV (Group B), n (%)	Statistical test	Test statistic	p-Value
At dural opening	Satisfactory	0 (0.0)	21 (26.3)	Pearson's chi-square test	83.16	0.0001
	Firm	20 (25.0)	54 (67.5)			
	Bulging	60 (75.0)	5 (6.3)			
At 60 minutes	Complete	0 (0.0)	1 (1.3)	Pearson's chi-square test	77.874	0.0001
	Satisfactory	9 (11.3)	61 (76.3)			
	Firm	43 (53.8)	18 (22.5)			
	Bulging	28 (35.0)	0 (0.0)			
At 120 minutes	Complete	2 (2.5)	6 (7.5)	Pearson's chi-square test	52.221	0.0001
	Satisfactory	26 (32.5)	66 (82.5)			
	Firm	45 (56.3)	8 (10.0)			
	Bulging	7 (8.8)	0 (0.0)			
At 180 minutes	Complete	3 (3.8)	29 (37.2)	Pearson's chi-square test	54.566	0.0001
	Satisfactory	35 (44.9)	46 (59.0)			
	Firm	35 (44.9)	3 (3.8)			
	Bulging	5 (6.4)	0 (0.0)			
At 240 minutes	Complete	0 (0.0)	6 (25.0)	Pearson's chi-square test	11.203	0.0037
	Satisfactory	2 (40.0)	17 (70.8)			
	Firm	3 (60.0)	1 (4.2)			

TABLE 4: Comparison of brain relaxation scores between the lung-protective ventilation and conventional ventilation groups at predefined intraoperative time points

Data are presented as number (percentage). Percentages are calculated using the number of patients assessed at each time point as the denominator. Pearson's chi-square test was used to compare the distribution of brain relaxation scores between groups at each assessment time. A two-sided p-value < 0.05 was considered statistically significant.

LPV: lung-protective ventilation; CV: conventional ventilation

Adverse events

No ventilation-related adverse events, including barotrauma, pneumothorax, or severe intraoperative hypoxemia, were reported in either group.

Discussion

The present study compared LPV using a tidal volume of 6 mL/kg PBW with PEEP of 6 cmH_2O against CV using a tidal volume of 10 mL/kg PBW without PEEP in adult patients undergoing elective craniotomy. The principal finding was a significantly lower incidence of PPCs in the LPV group. PPCs occurred in 0 of 80 patients (0%) receiving LPV, compared with 16 of 80 patients (20%) receiving CV. LPV was also associated with more favorable respiratory mechanics and a shorter ICU stay. These findings suggest that lower tidal volumes combined with moderate PEEP may provide pulmonary benefits in appropriately selected neurosurgical patients.

PPCs remain an important source of morbidity following major surgery and are associated with prolonged hospitalization, increased healthcare utilization, delayed recovery, and mortality. Anesthesia and mechanical ventilation may promote atelectasis, reduce functional residual capacity, and impair ventilation-perfusion matching. CV involving relatively high tidal volumes and little or no PEEP may further contribute to alveolar overdistension and repetitive alveolar collapse. These mechanisms provide a physiological rationale for using LPV during surgery [4-10].

The reduction in PPCs observed in the present study is consistent with previous investigations of protective ventilation during general anesthesia. Meta-analyses and randomized controlled trials have reported that lower tidal volumes combined with appropriate PEEP can reduce pulmonary complications in selected surgical populations. Studies involving abdominal and other major surgical procedures have also demonstrated improvements in postoperative pulmonary function with protective ventilation strategies. The present findings extend this clinical question to patients undergoing elective craniotomy, in whom potential pulmonary benefits must be considered alongside cerebral and surgical requirements [11-16].

Patients receiving LPV demonstrated higher dynamic lung compliance and more favorable driving pressure and respiratory index measurements than those receiving CV. These findings suggest improved respiratory mechanics with the combination of low tidal volume and moderate PEEP. PEEP may help maintain end-expiratory alveolar recruitment, while lower tidal volumes may reduce excessive cyclic alveolar strain. Driving pressure has also received considerable attention as a measure of the mechanical stress applied to the respiratory system and as a potential predictor of PPCs. These observations support the importance of considering the overall ventilatory strategy rather than tidal volume or PEEP in isolation [8,13,15,21,23-25].

The use of moderate PEEP may help reduce dependent alveolar collapse and improve ventilation-perfusion matching. Previous studies have investigated the role of PEEP and recruitment strategies in preventing atelectasis during general anesthesia, while research on protective ventilation has examined their effects on pulmonary function and postoperative respiratory outcomes. In the present study, oxygenation-related respiratory indices were more favorable with LPV, although intraoperative arterial blood gas parameters were broadly comparable between groups. This distinction suggests that improvements in respiratory mechanics do not necessarily translate into statistically significant differences in every intraoperative gas-exchange measurement [8,12,13,25,26].

An important consideration during craniotomy is whether the application of PEEP compromises brain relaxation or cerebral hemodynamics. Increased intrathoracic pressure may influence cerebral venous drainage and intracranial pressure, particularly in susceptible patients. In the present study, brain relaxation findings were not uniformly better with LPV. Brain bulging was more frequent in the LPV group immediately after dural opening, and the CV group demonstrated better relaxation at several subsequent assessment points. These findings should be acknowledged rather than interpreted as evidence that the two strategies produced equivalent brain relaxation. Nevertheless, the observed differences in surgical brain relaxation need to be considered in the context of the overall operative assessment and the absence of neurological deficits attributed to the ventilation strategy at extubation. Previous neurosurgical studies have similarly highlighted the need to balance pulmonary-protective strategies with cerebral physiological considerations [17-21].

The shorter duration of ICU stay in the LPV group represents another clinically relevant finding. Mean ICU stay was 2.17 ± 1.61 days in the LPV group and 3.32 ± 1.91 days in the CV group. A lower burden of PPCs may contribute to improved postoperative recovery and reduced requirements for respiratory support or intensive monitoring. Previous studies of intraoperative protective ventilation have also examined postoperative respiratory outcomes and healthcare utilization. However, the relationship between ventilation strategy and ICU duration may be influenced by several factors, and the present findings alone cannot establish that the reduction in ICU stay was mediated exclusively by the lower incidence of PPCs [11,13-15].

The study has several strengths. It directly compared two clearly defined ventilation strategies in adults undergoing craniotomy and assessed both pulmonary outcomes and neurosurgery-specific considerations. In addition to the primary outcome, the evaluation included respiratory mechanics, arterial blood gas measurements, hemodynamic variables, brain relaxation, and ICU stay. This multidimensional assessment provides a broader understanding of the potential benefits and trade-offs of LPV in this clinical setting.

Several limitations should also be acknowledged. The findings may not be generalizable to patients

undergoing emergency neurosurgery or those with substantial cardiopulmonary comorbidities. Brain relaxation is a subjective surgical assessment, and intracranial pressure was not directly measured. Furthermore, the observed differences in PPCs should be interpreted in the context of the study population, the definitions used for individual complications, and the ventilation protocol evaluated. Larger multicenter studies would help establish the reproducibility of these findings and clarify the effects of LPV on cerebral hemodynamics, surgical brain relaxation, and longer-term postoperative outcomes.

Overall, the findings support the potential role of LPV during elective craniotomy. However, the ventilation strategy should be individualized according to pulmonary status, cerebral physiology, and surgical requirements rather than applied without consideration of the patient's intracranial condition.

Conclusions

Intraoperative LPV using a tidal volume of 6 mL/kg PBW with 6 cmH_2O of PEEP reduced the incidence of PPCs, improved respiratory mechanics, and shortened ICU stay compared with CV using a tidal volume of 10 mL/kg PBW without PEEP in adult patients undergoing craniotomy under general anesthesia. Although brain relaxation was comparatively better in the CV group at several assessment points, LPV was not associated with neurological deficits attributable to the ventilation strategy at extubation. Thus, LPV may be a beneficial strategy for improving postoperative pulmonary outcomes in appropriately selected neurosurgical patients.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Vardhman Mahavir Medical College and Safdarjung Hospital Institutional Ethics Committee issued approval IEC/VMMC/SJH/Thesis/2020-11/CC-58. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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