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Original Article

Effect of different ventilation modes on postoperative cognitive dysfunction in elderly patients undergoing laparoscopic abdominal wall herniorrhaphy

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Abstract: Objective: To compare the effects of three ventilation modes - pressure-controlled ventilation (PC), volume-controlled ventilation (VC), and pressure-regulated volume control ventilation (PRVC) - on postoperative cognitive dysfunction (POCD) in elderly patients undergoing laparoscopic abdominal wall hernia repair. Methods: In this prospective study, 485 elderly patients undergoing laparoscopic abdominal wall hernia repair were randomly assigned to one of three ventilation groups: PC, VC, or PRVC. Cognitive function was assessed using the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA) at baseline (D0), and on postoperative days 1 (D1) and 3 (D3). Intraoperative physiological indicators, including mean arterial pressure (MAP), heart rate (HR), $PaCO_2$, central venous pressure (CVP), dynamic lung compliance (Cdyn), and optic nerve sheath diameter (ONSD), were recorded at five perioperative time points (T1-T5). Plasma concentrations of brain injury biomarkers (Aβ1-40, S-100β) and inflammatory cytokines (IL-1β, IL-6, TNF-α) were measured at baseline and serial postoperative time points (TI-TV). Results: The incidence of POCD differed significantly among the three ventilation groups on both postoperative day 1 ($P = 0.040$) and day 3 ($P = 0.034$). On day 3, post-hoc analysis revealed that the POCD rate in the PRVC group was significantly lower than in the PC group ($P < 0.0167$). Regarding potential mechanisms, PRVC was associated with improved dynamic lung compliance and a lower optic nerve sheath diameter compared to both PC and VC groups. Furthermore, PRVC significantly reduced plasma concentrations of the inflammatory cytokines IL-1β and IL-6 (all $P < 0.05$). Conclusion: In elderly patients undergoing abdominal wall hernia repair, PRVC ventilation reduced the incidence of early POCD, particularly compared to PC ventilation. This neuroprotective effect appears to be linked to improved respiratory mechanics and an attenuated systemic inflammatory response. Therefore, PRVC represents a preferable ventilation strategy for this vulnerable patient population.

Keywords: Abdominal wall hernia, elderly patients, postoperative cognitive dysfunction, ventilation modes

Introduction

Postoperative cognitive dysfunction (POCD) is a frequent and serious complication in elderly patients after major surgery [1-3]. The landmark International Study of Post-operative Cognitive Dysfunction (ISPOCD1) found that POCD affected 25.8% of patients one week after non-cardiac surgery [4]. Although this incidence has declined, it highlights the substantial early burden of the condition. Elderly patients undergoing abdominal wall hernia repair are particularly susceptible due to age-related physiological decline and surgical stress [5]. The clinical consequences of POCD are profound, ranging from impaired short-term memory and attention to increased long-term mortality risk [6-8]. In some vulnerable patient populations, the five-year mortality rate has reportedly reached as high as 70%. The multiple factors that cause POCD have led researchers to identify neuroinflammation from perioperative stress as the primary pathophysiologic mechanism [9, 10]. The peripheral release of pro-inflammatory cytokines leads to blood-brain barrier compromise which allows these cytokines to activate central glial cells and results in neuronal damage and cognitive

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decline [2, 11, 12]. The clinical research now focuses on minimizing this inflammatory cascade by optimizing modifiable intraoperative factors including ventilation strategies.

Among these factors, the role of mechanical ventilation is under increasing scrutiny as a possible independent contributor to remote organ injury, particularly through the "lung-brain axis". The concept of ventilator-induced brain injury (VIBI) has been established through preclinical evidence which shows that mechanical ventilation can cause neuroinflammation and neuronal damage without affecting the primary disease process [13, 14]. The injury occurs through two main pathways where the first pathway involves "biotrauma" from mechanical stress that leads to inflammatory mediator release into the circulation [15] and the second pathway involves direct physiological disruption through altered arterial CO_2 levels that affect cerebral blood flow and oxygenation [16, 17]. Consequently, adopting "brain-protective" ventilation strategies has emerged as a promising avenue for POCD prevention. Modern ventilation modes, particularly pressure-controlled ventilation (PC) and its advanced hybrid mode, pressure-regulated volume control (PRVC), have shown clear advantages over traditional volume-controlled ventilation (VC) for improving respiratory mechanics by lowering airway pressures [18, 19]. However, a critical knowledge gap remains. While the superiority of these modes for lung mechanics is well-documented, it is largely unknown whether these benefits translate into reduced neuroinflammation and a lower incidence of POCD in a clinical setting [13].

Based on this mechanistic framework, this study was designed to bridge this gap by directly comparing the effects of VC, PC, and PRVC on the incidence of POCD in elderly patients undergoing laparoscopic abdominal wall hernia repair. We hypothesized that the PRVC mode would most effectively attenuate the systemic inflammatory response and cerebral injury, ultimately resulting in a lower incidence of POCD. To test this hypothesis, we evaluated the perioperative effects of these ventilation modes on cognitive function, respiratory mechanics, and plasma biomarkers of inflammation and brain injury.

Patients and methods

Ethical approval and informed consent

This prospective, randomized, double-blind trial was designed to compare the effects of three ventilation modes - PC, VC, and PRVC - on the incidence of POCD in elderly patients undergoing laparoscopic abdominal wall hernia repair. The trial protocol was approved by the Clinical Research Ethics Committee of Inner Mongolia Baogang Hospital (2024-MER-322) and registered on ClinicalTrials.gov (registration number: NCT06772558). All patients or their legal representatives provided written informed consent before enrollment. The research followed the principles established by the Declaration of Helsinki. The research assistants who managed the data maintained both data confidentiality and integrity. The attending physician had the authority to request emergency unblinding or study termination when a patient developed a serious adverse event.

Study population

This study enrolled elderly patients scheduled for elective laparoscopic abdominal wall hernia repair at Inner Mongolia Baogang Hospital between January 2025 and May 2025. Inclusion criteria: 1. Age: 65-90 years. 2. American Society of Anesthesiologists (ASA) Physical Status: II-III. 3. Cognitive function: Able to complete neuropsychological tests. 4. Surgical procedure: Elective laparoscopic abdominal wall hernia repair under general anesthesia. Exclusion criteria: 1. Neurological: Pre-existing neurological disorders or hearing impairment. 2. Substance use: History of chronic opioid or other psychotropic substance dependence. 3. Medical history: Anesthetic allergy or prior brain surgery. 4. ASA physical status: Preoperative ASA Physical Status > III. 5. Organ dysfunction: Dialysis-dependent renal failure or liver transaminase levels exceeding 1.5 times the upper limit of normal. 6. Transfusion: Perioperative red blood cell transfusion exceeding 3 units. 7. Surgical factors: Emergency surgery or requirement for multiple surgeries during the same hospitalization.

Randomization and blinding

Patients were randomly assigned in a 1:1:1 ratio to the PC, VC, and PRVC Groups using a

random number table generated by SPSS 25.0 software. Block randomization was employed with a block size of 6. Group assignments were revealed to a non-blinded anesthesiologist, uninvolved in the study, by opening a sealed envelope one hour before the induction of anesthesia. Peripheral blood samples were collected by a blinded anesthesiologist, trained before the study, who was not involved in group assignment. Patients and the researchers assessing cognitive function remained blinded to group assignments, reinforcing the double-blind design. The group assignments remained sealed in opaque envelopes until study completion. During the study, the attending physician retained the right to request unblinding or withdraw a patient if their condition unexpectedly deteriorated.

Anesthesia management

No pre-operative anti-anxiety medications were administered. Upon operating room arrival, peripheral intravenous access was established with an 18-gauge catheter, and standard monitoring was initiated, including non-invasive blood pressure (NIBP), 5-lead electrocardiography (ECG), peripheral oxygen saturation (SpO_2), and Bispectral Index (BIS) (Mindray, Shenzhen, China). After performing internal jugular vein and radial artery catheterization under ultrasound guidance, crystalloid fluids were administered based on physiological requirements.

Following 5 minutes of pre-oxygenation with 100% oxygen, anesthesia was induced with etomidate (0.3-0.5 mg/kg), sufentanil (0.3-0.5 μg/kg), rocuronium (0.6 mg/kg), and a target-controlled infusion of propofol initiated at 3.0 μg/mL. Tracheal intubation was performed once the BIS value reached a target range of 40-50.

Anesthesia was maintained with target-controlled infusions (TCI) of propofol (target concentration: 2-5 μg/mL) and remifentanil (target concentration: 2-5 ng/mL) to keep the BIS between 40 and 60. Pneumoperitoneum pressure was maintained at 12-14 mmHg. Hypotension (defined as systolic blood pressure [SBP] < 90 mmHg or a > 20% decrease from baseline for > 1 min) was treated with intravenous boluses of ephedrine (6 mg). Bradycardia (heart rate [HR] < 50 beats/min) was treated with atropine (0.2 mg).

At the end of the procedure, neuromuscular blockade was antagonized with neostigmine (0.05 mg/kg) and atropine (0.01 mg/kg). The tracheal tube was removed once patients regained consciousness (BIS > 80), demonstrated adequate spontaneous ventilation (respiratory rate > 12 breaths/min, tidal volume > 5 mL/kg), and could follow commands. Patients were then transferred to the Post-Anesthesia Care Unit (PACU) for continued monitoring. Patients were transferred from the PACU to the general ward after meeting discharge criteria, which included maintaining SpO_2 > 95% on room air and showing no evidence of active bleeding or airway obstruction.

Ventilation management

Following tracheal intubation, all patients were mechanically ventilated using a Mindray A9 anesthesia machine (Mindray, Shenzhen, China). Tidal volume (TV) was calculated based on ideal body weight (IBW). Common ventilatory parameters for all three groups were initially set as follows: an inspiratory-to-expiratory (I:E) ratio of 1:2 and a positive end-expiratory pressure (PEEP) of 5 cmH_2O. The respiratory rate was adjusted throughout the procedure (range: 10-18 breaths/min) to maintain end-tidal carbon dioxide ($EtCO_2$) between 32 and 38 mmHg. The fraction of inspired oxygen (FiO_2) was initially set at 0.5 and was subsequently adjusted to maintain $SpO_2 \geq 95\%$.

The specific management strategy for each group was as follows: 1. PC group: The initial inspiratory pressure (Pinsp) was set to 12 cmH_2O. The Pinsp was then titrated in 1-2 cmH_2O increments to achieve a target tidal volume of 6-8 mL/kg IBW. This mode delivers breaths with a decelerating flow pattern. 2. VC group: The tidal volume was set to 8 mL/kg IBW with a constant flow pattern. An upper airway pressure limit alarm was set at 35 cmH_2O. If the peak inspiratory pressure (Ppeak) persistently exceeded this limit, the tidal volume was reduced in 1 mL/kg increments until Ppeak was below the threshold. 3. PRVC group: The target tidal volume was set to 8 mL/kg IBW. PRVC is a dual-controlled, hybrid ventilation mode that combines the advantages of volume-controlled and pressure-controlled ventilation. In this mode, the ventilator delivers an initial test breath to determine the patient's respi-

ratory mechanics, specifically the dynamic compliance. It then automatically adjusts the inspiratory pressure on a breath-by-breath basis to deliver the preset target tidal volume using a decelerating flow pattern and the lowest possible airway pressure.

Data collection

We recorded baseline demographic and clinical characteristics, including age, sex, education level, body mass index (BMI), and preoperative comorbidities. The ASA physical status was determined by the attending anesthesiologist during preoperative assessment, classifying patients based on systemic disease severity (Class I-III, ranging from a healthy patient to one with severe systemic disease). Comorbidity burden was quantified using the Charlson Comorbidity Index, a weighted index where higher scores indicate a greater risk of mortality. Cardiac functional status was evaluated using the New York Heart Association (NYHA) classification (Class I-IV), which categorizes patients based on limitations to physical activity. Preoperative functional independence was measured with the Barthel Index (score range: 0-100; higher scores indicate greater independence in activities of daily living). Preoperative cognitive function was assessed using two validated instruments. The Mini-Mental State Examination (MMSE) (a 30-point questionnaire) provided a global assessment of cognitive domains. The Montreal Cognitive Assessment (MoCA) (a 30-point test) was also used, as it is considered more sensitive for detecting mild cognitive impairment, particularly in executive function and attention.

Intraoperative data collected included anesthesia induction time, anesthesia maintenance time, surgery duration, BIS values, anesthetic drug dosages, estimated blood loss, and total intraoperative fluid administration. Hemodynamic and respiratory parameters were recorded at five prespecified intraoperative time points (T1-T5): T1 (5 minutes after anesthesia induction), T2 (10 minutes after pneumoperitoneum), T3 (30 minutes after pneumoperitoneum), T4 (50 minutes after pneumoperitoneum), and T5 (after abdominal desufflation). These parameters included mean arterial pressure (MAP), HR, partial pressure of arterial carbon dioxide ($PaCO_2$), central venous pressure (CVP), dynamic lung compliance (Cdyn), and optic nerve sheath diameter (ONSD). ONSD was measured by an experienced sonographer, blinded to group assignment, using a 7.5 MHz linear transducer. During ONSD measurement, the ventilation mode settings interface was obscured by an opaque covering. Following application of ultrasound gel, the linear transducer was secured to the patient's closed eyelid using a transparent Tegaderm dressing. Gentle adjustment of the transducer angle allowed visualization of the vitreous body, optic disc, and hypoechoic optic nerve sheath. ONSD was measured bilaterally 3 mm posterior to the optic disc in both sagittal and transverse planes using electronic calipers. The average of these four measurements was used for analysis. Each measurement was completed within one minute. For each measurement, the operator directly recorded the following data in an electronic spreadsheet: measurement time, patient identification number, left and right eye ONSD values, and the calculated average. Ultrasound images were archived within the ultrasound system's storage.

Venous blood samples (3-5 mL) were collected into lithium heparin tubes at five perioperative time points (TI-TV): TI (baseline, upon operating room arrival), TII (30 minutes after pneumoperitoneum), TIII (after extubation), TIV (1 hour postoperatively), and TV (24 hours postoperatively). Samples were immediately centrifuged at 1500 × g for 10 minutes at 4°C. Aliquots of the resulting supernatant plasma were then carefully collected and stored at -80°C until analysis. Plasma concentrations of brain injury biomarkers (S-100 calcium-binding protein B [S-100β] and amyloid beta peptide 1-40 [Aβ1-40]) and pro-inflammatory cytokines (interleukin-1β [IL-1β], interleukin-6 [IL-6], and tumor necrosis factor-alpha [TNF-α]) were measured. All analytes were quantified using commercial enzyme-linked immunosorbent assay (ELISA) kits (Nanjing Jiancheng Bioengineering Institute, Nanjing, China) according to the manufacturer's protocols. All samples were assayed in duplicate. Reasons for any missing intraoperative data were documented. Patients with > 10% missing data were excluded from the analysis. Missing values for the remaining patients were handled using multiple imputation.

Cognitive function assessment

Cognitive function was assessed at baseline (one day before surgery, D0) and on postoperative days 1 (D1) and 3 (D3). All assessments

were conducted in a quiet environment by trained researchers using the Beijing version of the MMSE and the MoCA [4, 6]. The MMSE is the most widely used cognitive screening test and a widely accepted measure in clinical practice. The MoCA is a validated and practical cognitive screening tool with high sensitivity and the ability to assess multiple cognitive domains [12, 13]. The Beijing version of the MoCA has been standardized for use in Chinese populations. Each assessment could be completed in 5-15 minutes. The diagnosis of POCD was determined using an established Z-score methodology. For each patient and each test, a Z-score was calculated to quantify the change from their own baseline relative to the cohort's variability. The formula was: Z-score = (Patient's Postoperative Score - Patient's Baseline Score)/Standard Deviation of the entire cohort's baseline scores. A patient was diagnosed with POCD if they demonstrated a decline of 1.5 standard deviations or more (i.e., a Z-score ≤ -1.50) on both the MMSE and the MoCA. This dual-test criterion was employed to enhance diagnostic specificity and minimize the risk of false-positive classifications [20, 21].

Sample size calculation

The primary outcome of this study was the incidence of POCD on postoperative days 1 and 3. The ISPOCD1 reported a 25.8% incidence of POCD one week after major non-cardiac surgery in elderly patients, which decreased to 9.9% at 3 months, consistent with findings by Zhang et al [4]. A sample size of 155 patients per group was calculated using PASS 2021 statistical software, assuming a two-sided design, a significance level of 5% ($\alpha = 0.05$), and a power of 80% ($1-\beta = 0.8$). To account for a potential 20% loss to follow-up, the sample size was increased to 194 patients per group, resulting in a total sample size of 582 patients [6, 7, 14]. A sensitivity analysis was performed to assess the robustness of the sample size calculation, assuming a range of plausible POCD incidence rates (20%-30%). This analysis confirmed that the sample size was sufficient to meet the required power.

Statistical analysis

Statistical analyses were performed using SPSS (Version 25.0; IBM Corp., Armonk, NY, USA) and GraphPad Prism (Version 9.0; GraphPad Software, San Diego, CA, USA). The normality of data distribution was assessed using the Shapiro-Wilk test. Continuous data were presented as mean ± standard deviation (SD) for normally distributed variables and as median [interquartile range, IQR] for non-normally distributed variables. Categorical data were presented as counts (n) and percentages (%). Group comparisons were performed using one-way ANOVA or the Kruskal-Wallis H test for continuous variables, and the chi-square (χ^2) test or Fisher's exact test for categorical variables. Post-hoc pairwise comparisons were performed using Tukey's test following ANOVA, Dunn's test following the Kruskal-Wallis test, and a Bonferroni correction for significant χ^2 results. A *P*-value < 0.05 was considered significant.

Results

Patient characteristics

Between January 13 and May 3, 2025, 582 patients were screened for eligibility, of whom 97 were excluded. 485 patients were enrolled and randomized, 471 completed intraoperative monitoring, and 465 completed neuropsychological testing on postoperative day 3 (**Figure 1**). The final follow-up for the last randomized patient occurred on May 6, 2025. The results were reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines. The three groups were well-matched with respect to baseline characteristics, including age, BMI, sex, education level, ASA Physical Status, NYHA classification, preoperative comorbidities, Charlson Comorbidity Index, Barthel Index, MoCA and MMSE (all *P* > 0.05, **Table 1**). A comparison of baseline cognitive scores among the three groups, using the Kruskal-Wallis test, revealed no statistically significant differences in either the MMSE scores (*P* = 0.604) or the MoCA scores (*P* = 0.069) (**Figure 2**). There were no significant differences among the three groups with respect to intraoperative clinical characteristics, including anesthesia time, surgical duration, anesthetic dosages, vasoactive drug requirements, estimated blood loss, or total intraoperative fluid administration (all *P* > 0.05, **Table 2**).

Comparison of the MAP and HR

Comparison of the vital signs between and within groups revealed that the MAP and HR

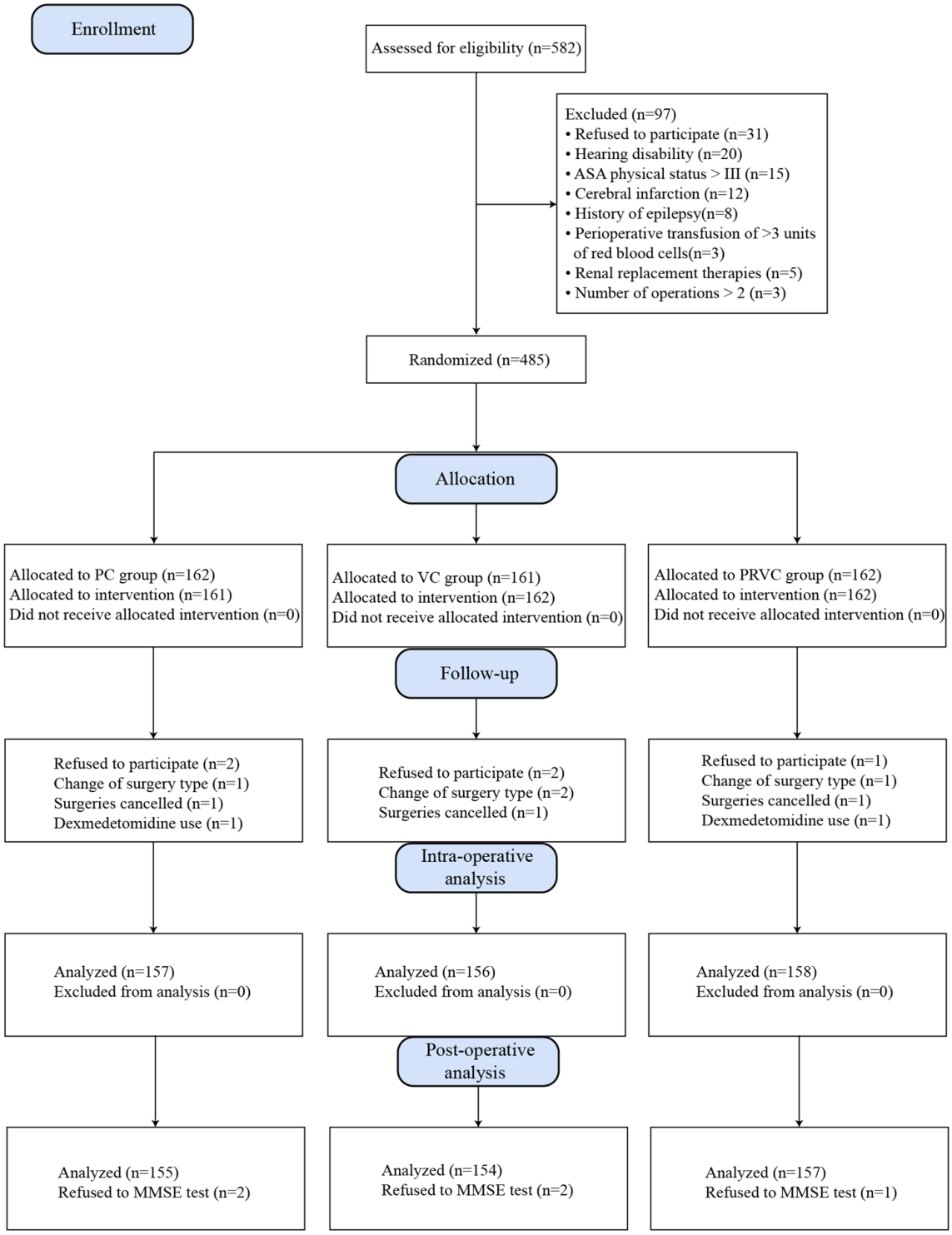

Figure 1. Flow chart depicting patient enrollment. This flowchart illustrates the process of patient screening, enrollment, allocation to the three ventilation groups, follow-up, and analysis according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines.

significantly increased 30 minutes after pneumoperitoneum in the PC Group, VC Group, and PRVC Group ($^{a}P < 0.05$), whereas there were no statistically significant differences in the MAP 30 minutes after pneumoperitoneum in the PRVC Group ($^{b}P > 0.05$). The MAP was signifi-

Table 1. Baseline demographic and clinical characteristics of patients

	PC Group (n = 157)	VC Group (n = 156)	PRVC Group (n = 158)	*P*-value
Age (yr)	74.9±5.3 (65-89)	74.3±4.7 (65-87)	74.3±5.2 (65-87)	0.523
Body mass index (kg/m^{-2})	23.1±2.0	23.6±2.2	23.4±2.0	0.089
Male gender	141 (90%)	138 (88%)	143 (91%)	0.833
Education (yr)	7.3±3.2	7.1±3.5	7.2±2.9	0.829
ASA physical status				0.493
1	18 (11%)	14 (9%)	24 (15%)	
2	114 (73%)	119 (76%)	114 (72%)	
3	25 (16%)	23 (15%)	20 (13%)	
NYHA classification				0.771
I	100 (64%)	109 (70%)	107 (68%)	
II	52 (33%)	44 (28%)	48 (30%)	
III	5 (3%)	3 (2%)	3 (2%)	
Comorbidities				
Hyperlipidaemia	79 (50%)	66 (42%)	76 (48%)	0.341
Coronary artery disease	19 (12%)	23 (15%)	16 (10%)	0.459
Diabetes mellitus	30 (19%)	37 (24%)	38 (24%)	0.500
History of malignancy	3 (2%)	3 (2%)	6 (4%)	0.473
Chronic smoking*	117 (75%)	121 (78%)	106 (67%)	0.098
Alcoholism†	51 (32%)	40 (25%)	44 (28%)	0.393
Charlson comorbidity index	3.48±0.7	3.47±0.68	3.42±0.74	0.722
Barthel Index	92.7±8.63	94.4±7.2	94.2±7.6	0.104
MMSE	24 (IQR: 24-29)	24 (IQR: 24-29)	24 (IQR: 24-29)	0.604
MoCA	26 (IQR: 28-30)	26 (IQR: 28-30)	26 (IQR: 28-30)	0.069

Note: Data are expressed as mean ± standard deviation, n (%), or median (quartiles). Statistical comparisons were performed using the one-way ANOVA for continuous normally distributed data, the Kruskal-Wallis test for non-normally distributed data (MMSE, MoCA), and the chi-square or Fisher's exact test for categorical data. ASA, American Society of Anesthesiologists; BI, Barthel Index; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; NYHA, New York Heart Association. *Indicates smoking of half a pack of cigarettes per day for at least 2 yr, either former or current smoker. †Daily consumption of the equivalent of 80 g of alcohol for at least 5 yr.

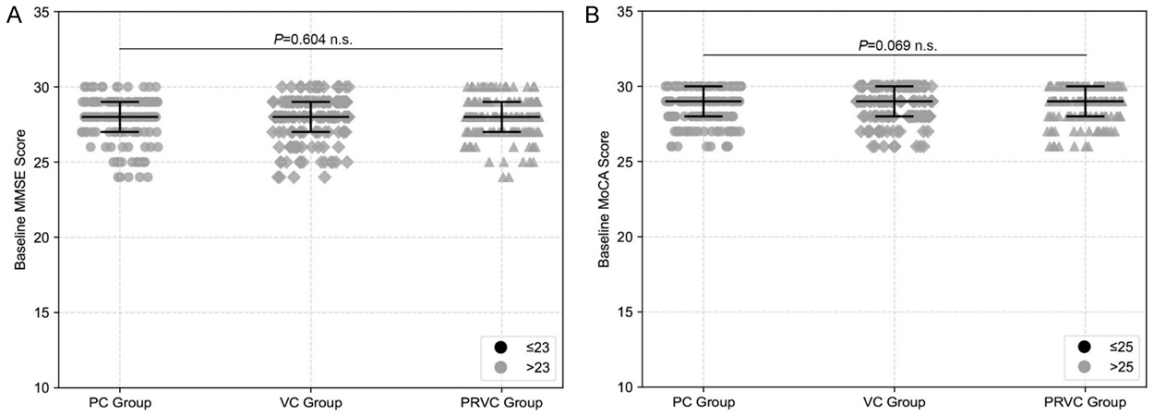

Figure 2. Baseline cognitive scores among the three ventilation groups. A. Comparison of baseline Mini-Mental State Examination (MMSE) scores. B. Comparison of baseline Montreal Cognitive Assessment (MoCA) scores. Data are presented as individual scores, with the median and interquartile range overlaid. The Kruskal-Wallis test was used to compare the scores among the three groups. PC, pressure-controlled ventilation; VC, volume-controlled ventilation; PRVC, pressure-regulated volume control; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; n.s., not significant.

Table 2. Intraoperative and anesthetic data

	PC Group (n = 157)	VC Group (n = 156)	PRVC Group (n = 158)	*P*-value
Anesthesia				
Time of induction (min)	5.9 (5.7-6.2)	6.0 (5.7-6.1)	5.8 (5.6-6.0)	0.646
Duration of anesthesia (min)	78.1 (76.4-79.9)	80.2 (78.4-82.0)	80.6 (78.5-82.7)	0.148
Operative time (min)	58.7 (57.1-60.3)	61.2 (59.3-63.0)	58.6 (56.5-60.7)	0.083
BIS	48.6±3.0	49.2±3.0	49.0±3.3	0.153
Dose of anaesthetics				
Propofol (mg)	508.4±83.9	494.4±85.2	491.9±86.6	0.183
Etomidate (mg)	19.5±1.6	19.8±2.4	19.5±1.3	0.675
Sufentanil (μg)	24.7±2.0	24.7±3.0	24.4±1.7	0.298
Remifentanil (mg)	0.71±0.1	0.69±0.1	0.69±0.1	0.102
Rocuronium bromide (mg)	39.0±3.1	38.3±4.7	38.5±2.6	0.204
Total intraoperative infusion (ml)	540±64.9	537±68.4	536±63.1	0.851
Estimated blood loss (ml)	82.3±16.2	83.0±17.3	85.4±13.9	0.177
Vasoactive vascular drug				
Atropine, n (%)	71 (45%)	79 (51%)	93 (59%)	0.114
Ephedrine, n (%)	104 (66%)	93 (60%)	113 (72%)	0.084
Norepinephrine, n (%)	78 (50%)	68 (44%)	86 (54%)	0.157
Nitroglycerin, n (%)	13 (8%)	11 (7%)	9 (6%)	0.668

Note: Data are presented as mean ± standard deviation, mean (95% confidence interval), or n (%). Statistical comparisons were performed using one-way ANOVA, the Kruskal-Wallis test, or the chi-square test as appropriate. BIS, Bispectral Index.

Table 3. Comparison of hemodynamic dynamics (MAP and HR) among the three groups

	PC Group (n = 157)	VC Group (n = 156)	PRVC Group (n = 158)	*P*-value
MAP (mmHg)				
T1	76.4±4.4	78.6±7.4	77.6±8.6	< 0.05
T2	77.6±8.6	82.2±8.4	79.2±5.3	< 0.0001
T3	93.2±9.6[a]	100.3±10.3[a]	84.4±7.9[a,c]	< 0.0001
T4	92.0±9.3	97.0±11.1	87.1±7.9[b,c]	< 0.0001
T5	89.0±9.9	100.2±9.4	89.4±15.7[c]	< 0.0001
HR (bpm)				
T1	74.0±6.3	75.4±8.6	77.1±8.3	< 0.01
T2	75.3±6.7	80.4±6.9	77.2±5.3[d]	< 0.0001
T3	90.7±9.2[a]	92.2±9.4[a]	81.8±9.6[a,d]	< 0.0001
T4	92.4±10.8	93.1±7.3	79.1±5.5[d]	< 0.0001
T5	91.4±6.3	89.3±8.4	76.5±7.0[d]	< 0.0001

Note: Compared to T1, [a]$P < 0.05$. Comparison between T3 and T5, [b]$P > 0.05$. Compared to VC Group, [c]$P < 0.01$. Compared to the PC Group and VC Group, [d]$P < 0.05$.

cantly lower in the PRVC Group than in the VC Group at all time points 10 minutes after pneumoperitoneum ([c]$P < 0.05$). The HR was significantly lower in the PRVC Group than in the PC and VC Group at all time points 10 minutes after pneumoperitoneum ([d]$P < 0.05$) (**Table 3**).

Comparison of CVP and Cdyn

CVP significantly increased and Cdyn significantly decreased after pneumoperitoneum in all groups ([a]$P < 0.05$). At time points T1-T5, CVP was significantly lower in the PRVC Group than in the VC Group ([b]$P < 0.05$). At time points T3 and T5, CVP was significantly lower in the PRVC Group than in the PC Group ([c]$P < 0.05$). At time points T4-T5, CVP was significantly lower in the PC Group than in the VC Group ([d]$P < 0.05$). At time points T1-T5, Cdyn was significantly higher in the PRVC Group than in the PC and VC Groups ([e]$P < 0.05$) (**Table 4**).

Comparison of the ONSD and $PaCO_2$

In the within-group comparison between the PC, VC, and PRVC Groups, the ONSD at T2 was significantly higher than that at T1 ([a]$P < 0.05$), whereas there was no statistically significant difference between the ONSDs of the PRVC Group at any of the times from T3 to T5 ([b]$P >$

Table 4. Comparison of respiratory mechanics (Cdyn) and central venous pressure (CVP)

	PC Group (n = 157)	VC Group (n = 156)	PRVC Group (n = 158)	*P*-value
CVP (cmH_2O)				
T1	7.1±1.4	7.3±1.5	7.0±1.5[b]	< 0.05
T2	13.1±1.9[a]	13.4±1.4[a]	12.7±2.1[a,b]	< 0.01
T3	12.8±2.2	12.6±2.6	12.0±1.3[b,c]	< 0.001
T4	11.4±1.6[d]	11.9±1.4	11.1±2.3[b]	< 0.001
T5	8.9±1.2[d]	9.2±1.0	8.3±1.9[b,c]	< 0.001
Cdyn (mL/cmH_2O)				
T1	40.3±2.8	38.4±2.0	41.3±2.5[e]	< 0.001
T2	36.3±2.3[a]	34.2±2.0[a]	37.9±2.5[a,e]	< 0.001
T3	33.1±2.1	31.7±1.8	34.5±1.6[e]	< 0.001
T4	27.9±2.6	25.2±2.1	29.9±1.6[e]	< 0.001
T5	34.5±2.2	32.4±1.4	37.2±2.4[e]	< 0.001

Note: [a]$P < 0.0001$ compared to T1. [b]$P < 0.0001$ compared to VC Group. [c]$P < 0.0001$ compared to PC Group. [d]$P < 0.0001$ compared to VC Group. [e]$P < 0.0001$ compared to both PC and VC Groups.

Table 5. Comparison of optic nerve sheath diameter (ONSD) and $PaCO_2$ levels

	PC Group (n = 157)	VC Group (n = 156)	PRVC Group (n = 158)	*P*-value
ONSD (mm)				
T1	5.49±0.42[a]	5.54±0.35[a]	5.49±0.38[a]	0.444
T2	5.82±0.35	5.92±0.17	5.57±0.44[b,c]	< 0.0001
T3	6.07±0.21	6.07±0.43	5.72±0.25[c]	< 0.0001
T4	6.20±0.29	6.19±0.37	5.78±0.30[c]	< 0.0001
T5	6.23±0.20	6.33±0.22	5.81±0.23[c]	< 0.0001
$PaCO_2$ (mmHg)				
T1	39.1±2.7	38.5±2.8	38.6±3.0	0.091
T2	40.3±3.2	39.0±4.1	39.5±3.3	< 0.001
T3	48.7±5.4[d]	48.4±5.4[d]	40.4±3.2[e]	< 0.0001
T4	51.3±4.5	52.9±5.1	41.1±2.6	< 0.0001
T5	49.8±5.9	51.3±4.9	42.1±3.0	< 0.0001

Note: Compared to T2, [a]$P < 0.05$. Compared to 30 minutes each time point after pneumoperitoneum, [b]$P > 0.05$. Compared to PC Group and VC Group, [c]$P < 0.05$. Compared to T2, [d]$P > 0.05$. Comparison to T2 and T4, [e]$P < 0.05$.

0.05). The ONSD of the PRVC Group was significantly lower than that of the PC and VC Groups at all time periods after pneumoperitoneum ([c]$P < 0.05$). Comparison of carbon dioxide metabolism between and within the PC and VC Groups revealed that $PaCO_2$ was significantly higher in T3 ([d]$P < 0.05$), but there was no significant difference in $PaCO_2$ in the PRVC Group after pneumoperitoneum ([e]$P > 0.05$) (**Table 5**).

Comparison of plasma biomarker profiles: Aβ1-40, S-100β, IL-1β, IL-6, and TNF-α dynamics across treatment groups

There were no significant differences in plasma concentrations of Aβ1-40, S-100β, IL-1β, IL-6, or TNF-α between the groups at T I. At T II, T III, T IV, and T V, the plasma concentrations of Aβ1-40 and S-100β were significantly lower in both the PRVC and PC Groups compared to the VC Group ([a]$P < 0.05$). There were no significant differences in plasma Aβ1-40 concentrations at any time point in the PRVC Group compared with the PC Group. Compared to T I, plasma Aβ1-40, and S-100β concentrations were significantly higher at all time points in all three groups. However, in the PRVC Group, Aβ1-40 concentrations remained stable from T III to T V ([b]$P > 0.05$). Plasma concentrations of S-100β were significantly different in the PC and VC Groups at T V compared with T I, but not in the PRVC Group at T V ([c]$P > 0.05$). Plasma IL-1β concentrations were significantly lower in the PRVC Group than in the PC and VC Groups at T II, T III, T IV, and T V ([d]$P < 0.05$). At T III, T IV, and T V, plasma IL-6 concentrations were significantly lower in the PRVC Group than in the PC and VC Groups ([e]$P < 0.05$). At T II, T III, T IV, and T V, plasma TNF-α concentrations were significantly lower in the PRVC Group than in the VC Group ([f]$P < 0.05$). There was no significant difference in plasma concentration of TNF-α at T V in the VC Group compared to T I ([g]$P > 0.05$), but no significant difference was observed between the PC and PRVC Groups at T V (**Table 6**).

Comparison of cognitive outcomes and POCD incidence on D1 and D3

The baseline cognitive scores (MMSE and MoCA) were comparable among the three groups prior to surgery ($P > 0.05$) (**Table 1**). On

Table 6. Comparison of plasma biomarker profiles: Aβ1-40, S-100β, IL-1β, IL-6, and TNF-α dynamics across treatment groups

	PC Group (n = 157)	VC Group (n = 156)	PRVC Group (n = 158)	*P*-value
Aβ1-40 (pg·mL^{-1})				
T I	338.0±42.6	341.0±32.8	336.3±39.8	0.557
T II	408.4±76.0[a]	468.0±63.6	397.2±72.3[a]	< 0.0001
T III	402.4±69.7[a]	474.7±66.8	412.6±58.5[a,b]	< 0.0001
T IV	414.5±67.9[a]	501.5±59.8	397.8±62.5[a]	< 0.0001
T V	391.4±55.3[a]	430.8±58.00	382.1±61.1[a,b]	< 0.0001
S-100β (pg·mL^{-1})				
T I	217.5±23.4	216.2±23.3	220.0±20.5	0.176
T II	280.3±30.3[a]	288.4±32.6	252.8±26.2[a]	< 0.0001
T III	285.8±30.3[a]	301.4±29.9	262.8±32.7[a]	< 0.0001
T IV	290.9±31.2[a]	301.9±34.1	268.7±27.2[a]	< 0.0001
T V	252.8±24.1[a]	269.2±27.0	227.4±30.8[a,c]	< 0.0001
IL-1β (pg·mL^{-1})				
T I	12.24±1.36	12.40±1.35	12.49±1.05	0.197
T II	16.80±2.25	18.41±2.66[d]	14.68±2.38	< 0.0001
T III	17.58±1.98	18.87±1.96[d]	15.12±2.58	< 0.0001
T IV	17.20±1.81	18.44±2.16[d]	14.56±1.97	< 0.0001
T V	15.09±2.01	15.51±2.69[d]	13.57±1.86	< 0.0001
IL-6 (pg·mL^{-1})				
T I	18.22±2.58	18.54±2.17	18.40±2.65	0.505
T II	22.38±2.90	24.06±2.53	21.36±2.20	< 0.0001
T III	25.79±3.76	26.29±2.27[e]	24.33±2.68	< 0.0001
T IV	24.10±2.62	24.50±2.18[e]	22.69±1.98	< 0.0001
T V	21.78±3.19	22.47±2.49[e]	20.13±2.12	< 0.0001
TNF-α (pg·mL^{-1})				
T I	13.82±2.32	14.22±2.02	14.37±1.98	0.372
T II	15.16±2.53	17.26±2.09[a]	16.14±2.13[f]	< 0.0001
T III	19.43±2.17	20.23±2.76[a]	19.04±2.76[f]	< 0.0001
T IV	22.62±3.17	22.96±2.36[a]	20.42±1.97[f]	< 0.0001
T V	18.42±2.35	19.22±1.95[a,g]	17.68±2.11[f]	< 0.0001

Note: Compared to the VC Group, [a]$P < 0.05$. Compared to the T III, [b]$P > 0.05$. Compared to the T I, [c]$P > 0.05$. Compared to the PC Group and VC Group [d]$P < 0.05$. Compared to the PC Group and VC Group, [e]$P < 0.05$. Compared to the VC Group, [f]$P < 0.05$. Compared to the T1, [g]$P > 0.05$.

Table 7. Comparison of POCD incidence in three groups

	Time	PC Group (n = 155)	VC Group (n = 154)	PRVC Group (n = 157)	χ^2	*P*-value
POCD+	D1	39 (25.2%)	32 (20.8%)	22 (14.0%)*	6.422	0.040
	D3	24 (15.5%)	17 (11.0%)	10 (6.4%)*	6.789	0.034

Note: Pairwise comparisons were performed using the Chi-square test with a Bonferroni correction. $P < 0.0167$ was considered significant. *Compared to the PC group.

D1, there was a significant difference in the overall incidence of POCD among the three groups ($\chi^2 = 6.422$, $P = 0.040$; **Table 7**). The incidence was lowest in the PRVC Group (14.0%), compared to the PC Group (25.2%) and the VC Group (20.8%). This finding was further explored by analyzing the raw cognitive test scores. For the MMSE, a Kruskal-Wallis test revealed a significant difference among the groups, with post-hoc analysis showing that median scores in the PRVC Group were significantly higher than in the PC Group ($P = 0.029$; **Figure 3A**). However, for the MoCA, there was no significant difference in median scores among the three groups on D1 ($P = 0.571$; **Figure 4A**).

By D3, the significant difference in overall POCD incidence persisted ($\chi^2 = 6.789$, $P = 0.034$; **Table 7**). Post-hoc analysis confirmed that the incidence in the PRVC group (6.4%) remained significantly lower than in the PC Group (15.5%; $P < 0.0167$). The difference between the PRVC and VC Groups (11.0%) was not significant. The analysis of individual test scores on D3 provided strong corroborating evidence for these findings. Median MMSE scores in the PRVC group were significantly higher than in the PC group ($P = 0.020$; **Figure 3B**). Even more pronounced, median MoCA scores in the PRVC Group were significantly higher than in both the PC Group ($P < 0.001$) and the VC Group ($P = 0.046$; **Figure 4B**).

Discussion

With an aging global population, the incidence of inguinal hernia is rising, reaching up to 45% in men over 75 years of age [1, 22, 23]. The

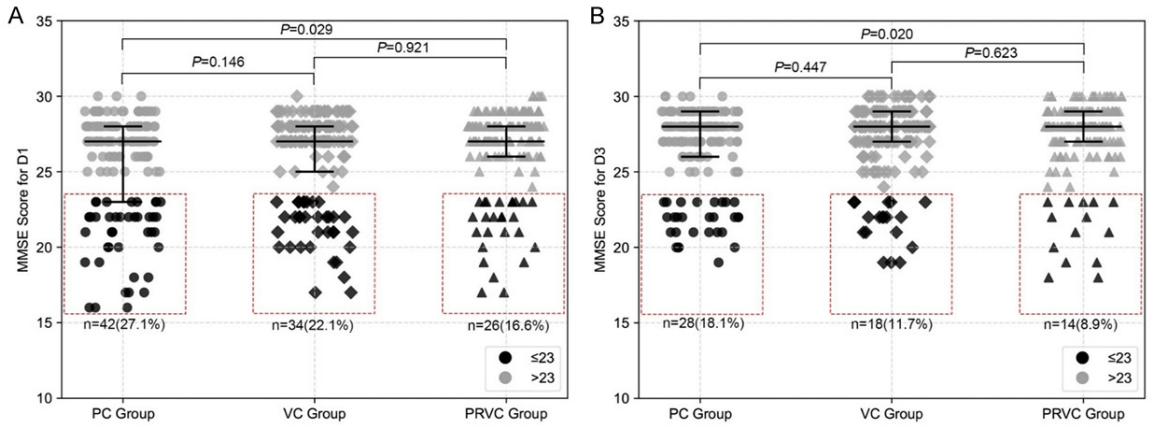

Figure 3. Comparison of MMSE scores on postoperative days 1 and 3. A. MMSE scores on postoperative day 1 (D1). B. MMSE scores on postoperative day 3 (D3). Data are presented as individual scores, with the median and interquartile range overlaid. The number (n) and percentage (%) of patients in each group meeting the cutoff for cognitive impairment (score ≤ 23) are highlighted. *P*-values for pairwise comparisons were derived from the Dunn's post-hoc test following a significant Kruskal-Wallis test.

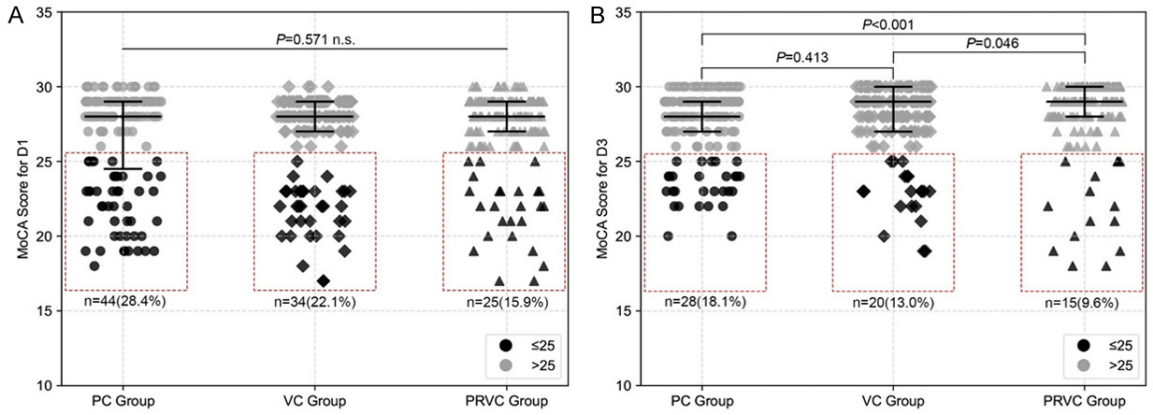

Figure 4. Comparison of MoCA scores on postoperative days 1 and 3. A. MoCA scores on postoperative day 1 (D1). B. MoCA scores on postoperative day 3 (D3). Data are presented as individual scores, with the median and interquartile range overlaid. The number (n) and percentage (%) of patients in each group meeting the cutoff for cognitive impairment (score ≤ 25) are highlighted. *P*-values for pairwise comparisons were derived from the Dunn's post-hoc test following a significant Kruskal-Wallis test.

primary treatment is laparoscopic abdominal wall hernia repair. This method shows increasing use in this demographic, thus emphasizing the need to optimize perioperative care for this vulnerable population [24-26]. POCD represents a common severe complication that affects recovery and life quality of these patients [5, 7, 11]. The incidence of POCD continues to be a major clinical challenge despite multiple treatment approaches. Our research investigates the direct effect of intraoperative ventilation mode selection on early cognitive results in patients. Our primary finding is that PRVC ventilation confers a neuroprotective advantage as early as D1, on which the PRVC Group exhibited a significantly lower POCD incidence and higher MMSE scores compared to the PC Group. This advantage became more pronounced by D3, at which point the POCD incidence in the PRVC Group was significantly lower than in both the PC and VC Groups. This was further corroborated by the more sensitive MoCA, on which D3 scores in the PRVC Group were superior to those in both the PC and VC Groups. The research findings demonstrate that PRVC represents a hybrid ventilation mode

which provides better protection against early neurocognitive decline for elderly patients during this procedure.

The main protective effect of PRVC against brain damage stems from its optimal control of respiratory functions during pneumoperitoneum. The PRVC Group achieved better dynamic lung compliance results, which matches previous research showing that PRVC mode decreases both peak and plateau airway pressures [27]. The PRVC mode successfully maintained stable $PaCO_2$ levels which prevented the major increases seen in the PC and VC Groups. The literature shows mixed results about how different ventilation strategies affect $PaCO_2$ because of patient population differences and monitoring duration [28] but our study proves that PRVC provides better $PaCO_2$ stability during laparoscopy in elderly patients. The stable exchange of gases represents a fundamental requirement for preventing hypercapnia and its harmful effects on cerebral blood flow which serves as the first protective mechanism of PRVC. The aging brain faces increased vulnerability because natural neurogenesis and synaptic plasticity decline with age thus making it more sensitive to perioperative stressors including neuroinflammation [29, 30]. Surgical procedures together with anesthesia administration trigger a body-wide inflammatory response that results in the release of IL-1β and IL-6 and TNF-α pro-inflammatory cytokines. The blood-brain barrier permeability of these cytokines allows them to trigger neuroinflammatory responses that act as the primary pathological mechanisms behind POCD [11, 31].

The procedure of laparoscopy produces elevated intracranial pressure (ICP) through increased intrathoracic and CVP levels. The elderly population with weakened compensatory abilities will experience greater ONSD elevation which serves as an ICP indicator [32-34]. The PRVC Group demonstrated a substantial reduction in CVP increase when compared to the VC Group, according to our study findings. The intrathoracic pressure optimization through PRVC appears to reduce cerebral perfusion pressure effects which is supported by our observation of decreased ONSD values in this group. The reduction in physiological stress became evident through serum biomarker results. The PRVC Group showed decreased postoperative levels of S-100β and Aβ1-40, which serve as established surrogate markers of brain injury when compared to the PC Group [7, 35]. The plasma levels of IL-1β, IL-6, and TNF-α remained lower in PRVC patients at various postoperative measurement points. The large body of evidence shows that blocking these specific cytokine pathways leads to cognitive impairment prevention [35-37]. The observed findings demonstrate reduced inflammation and cerebral stress which supports the better cognitive results achieved through PRVC.

This study has several limitations. First, our findings may have limited generalizability since the study was conducted in a single center and included only patients undergoing a specific surgical procedure (laparoscopic abdominal wall hernia repair). Second, our follow-up period was limited to the early postoperative phase (up to day 3), precluding any conclusions about the long-term neurocognitive trajectory of these patients. Therefore, large-scale, multicenter randomized controlled trials are warranted to validate our findings across diverse surgical populations and to assess the long-term effect of these ventilation strategies on cognitive recovery.

Conclusion

In elderly patients undergoing laparoscopic abdominal wall hernia repair, the use of PRVC ventilation was associated with a significantly lower incidence of POCD compared to PC ventilation. While the overall incidence of POCD was significantly reduced in the PRVC Group on both postoperative days 1 and 3, the protective effect was most pronounced and comprehensive by day 3, where PRVC demonstrated superiority over both PC and VC modes on the more sensitive MoCA. These clinical benefits were accompanied by improved dynamic lung compliance, attenuated systemic inflammatory responses, and reduced surrogate markers of brain injury. Therefore, PRVC represents a preferable ventilation strategy for mitigating early neurocognitive decline in this vulnerable patient population.

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Disclosure of conflict of interest

None.

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