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Pneumoperitoneum at 8 versus 12 mmHg and cerebral haemoglobin dynamics during robot-assisted radical prostatectomy: a sequential observational cohort study

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Abstract

Background

Pneumoperitoneum pressure is a modifiable component of robot-assisted radical prostatectomy (RALP), but its association with cerebral haemodynamics during prolonged steep Trendelenburg positioning remains incompletely defined. We examined whether pneumoperitoneum at 8 versus 12 mmHg was associated with differences in NIRS-derived cerebral haemoglobin dynamics, optic nerve sheath diameter (ONSD), and postoperative patient-reported visual function.

Methods

This sequential observational cohort study included 72 patients undergoing RALP. The low-pressure group (8 mmHg; n = 36) was derived from a previously published prospective cohort that had addressed a different physiological research question, whereas a subsequent standard-pressure cohort (12 mmHg; n = 36) was prospectively recruited using the same eligibility criteria, perioperative management, monitoring protocol, and outcome assessment. Cerebral haemodynamics were assessed using bilateral NIRS-derived haemoglobin indices and ONSD ultrasonography. Postoperative visual function was assessed using Catquest-9SF Rasch analysis. Inverse probability of treatment weighting (IPTW) was used as a sensitivity analysis for measured differences in surgical complexity.

Results

Standard-pressure pneumoperitoneum was associated with greater ONSD enlargement and greater changes in deoxygenated haemoglobin (ΔHHbi) and regional cerebral oxygen saturation (ΔrSO_2) than low-pressure pneumoperitoneum. These differences remained directionally consistent after IPTW adjustment for measured surgical-complexity variables. The postoperative change in Catquest-9SF Rasch score was greater in the 12-mmHg cohort, whereas the incidence of self-reported visual disturbances did not differ significantly between groups.

Conclusions

Compared with 8 mmHg, pneumoperitoneum at 12 mmHg was associated with a greater increase in cerebral deoxygenated haemoglobin and ONSD during RALP, a physiological pattern compatible with greater impairment of cerebral venous drainage. Because the cohorts were sequential and non-randomised, these findings require confirmation in randomised studies.

1. INTRODUCTION

Robot-assisted radical prostatectomy (RALP) requires prolonged steep Trendelenburg positioning combined with CO_2 pneumoperitoneum [1]. Once the robot is docked, changing patient position is cumbersome; insufflation pressure therefore remains one of the principal modifiable intraoperative variables [2, 3].

Low-pressure pneumoperitoneum can provide adequate surgical exposure in selected patients, but no single optimal pressure has been established for RALP [4] [5]. The relevant trade-off is between surgical workspace and the physiological burden of increased intra-abdominal pressure.

Pneumoperitoneum and steep Trendelenburg affect the cerebrovascular compartment [6]. Higher insufflation pressure has been associated with increased intracranial and intraocular pressure, while optic nerve sheath diameter (ONSD) provides a non-invasive surrogate of intracranial pressure[7–10]. These effects are relevant because transient visual-field abnormalities and rare ischaemic optic neuropathy have been reported after RALP [10].

The pressure–volume relationship of the insufflated abdomen is nonlinear, with diminishing workspace gains at higher pressures [11]. Randomised and observational studies support the feasibility of lower-pressure strategies in laparoscopic and robotic surgery [12, 13]. This raises the possibility that reducing pressure may decrease physiological effects without compromising exposure in appropriately selected patients.

Conventional cerebral near-infrared spectroscopy (NIRS) reports regional cerebral oxygen saturation (rSO_2), which may increase during pneumoperitoneum and Trendelenburg positioning [14–16]. Device-derived oxygenated and deoxygenated haemoglobin indices (ΔO_2Hbi and ΔHHbi) may provide complementary information on cerebral haemoglobin dynamics [17]. A pattern of increasing ΔHHbi without a parallel increase in ΔO_2Hbi has been described as compatible with acute cerebral venous congestion [18].

Our previous prospective cohort characterised phase-dependent NIRS and ONSD changes during RALP performed at low insufflation pressure [19], but did not compare pressure strategies. The present sequential observational study therefore asked whether sustained pneumoperitoneum at 8 versus 12 mmHg is associated with different cerebral haemoglobin dynamics, ONSD responses, and postoperative patient-reported visual function.

2. MATERIALS AND METHODS

2.1 Study Design and Ethics Approval

This sequential observational cohort study was conducted at Nuovo Ospedale di Prato, Prato, Italy, in accordance with the Declaration of Helsinki. The study was conducted under the approval of the Ethics Committee of Area Vasta Toscana Centro (no. 25336, July 2024), which covered data collection for both

cohorts as part of routine clinical practice, and written informed consent was obtained from all participants.

The present analysis combines patients from a previously collected low-pressure cohort with a subsequently recruited standard-pressure (12-mmHg) cohort. Both cohorts were recruited under the original ethics approval; the low-pressure cohort had originally been studied to address a different physiological research question, whereas the 12-mmHg cohort was recruited using the same eligibility criteria, perioperative management, monitoring protocol, and outcome assessment.

Seventy-two adults (ASA physical status I–III) undergoing RALP with the da Vinci V robotic system (Intuitive Surgical, CA, USA) in 30° steep Trendelenburg were included: 36 in the 8-mmHg cohort and 36 in the subsequently recruited 12-mmHg cohort. Patients with ophthalmic or neurological disease were excluded.

The 8-mmHg cohort was recruited from January to March 2025 and the 12-mmHg cohort from April to June 2025.

The cohorts were not randomised. Pressure reflected clinical practice and anticipated surgical difficulty. Four predefined complexity factors were recorded: previous inframesocolic abdominal surgery, prostate volume ≥ 100 g, BMI ≥ 30 kg/m^2, and planned extended pelvic lymph-node dissection. Because higher pressure was more often selected when greater surgical difficulty was anticipated, confounding by indication was addressed in a sensitivity analysis using inverse probability of treatment weighting (IPTW).

The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines; the completed checklist is provided as Supplementary Material.

A generative AI language model was used for language editing and manuscript shortening. All scientific content, interpretation, data, and final wording were reviewed and approved by the authors.

2.2 Sample Size Calculation

The sample size assessment was based on the primary endpoint, defined as the between-group difference in ΔHHbi at T3, and used data from the previously studied 8-mmHg cohort. The assumed common standard deviation of 5.6 units was estimated from the observed variability of ΔHHbi at T3 in that cohort. As no established minimal clinically important difference was available for ΔHHbi, a between-group difference of 5 units was considered clinically meaningful based on investigator judgment. Assuming a two-sided α of 0.05 and 80% power, the calculation yielded a required sample size of 20 patients per group. The target sample size was increased to 36 patients per group to improve precision and account for exclusions and missing NIRS recordings.

2.3 Surgical Procedure and Pneumoperitoneum Management

After patient positioning, the abdomen was insufflated with CO_2 and the patient was placed in mild Trendelenburg position for trocar placement. Patients were then positioned in 30° steep Trendelenburg. Pneumoperitoneum was delivered using a valveless AirSeal® system (ConMed Corporation, Utica, NY, USA), selected to provide stable intra-abdominal pressure and continuous smoke evacuation.

Low-pressure exposure was defined as an 8-mmHg target maintained for > 80% of insufflation time and standard-pressure exposure as a 12-mmHg target maintained for > 80%. Brief surgeon-requested increases were permitted for specific steps, with return to target as soon as feasible.

The AirSeal® target was set at the start of the procedure. Operative phases and brief pressure increases were timed manually by the anaesthesia team. These timings supported the > 80% exposure criterion, but no time-stamped console log was retrieved.

At the end of the procedure, the table was returned to the neutral position and pneumoperitoneum was released.

2.4 Anaesthetic Management

Standard monitoring was applied upon arrival in the operating room, including electrocardiography, pulse oximetry, non-invasive arterial blood pressure, train-of-four neuromuscular monitoring, oesophageal temperature monitoring, and processed electroencephalography (Patient State Index).

General anaesthesia was induced with propofol 1–2 mg/kg, fentanyl 1–2 µg/kg, and rocuronium 0.6 mg/kg, followed by orotracheal intubation. Anaesthesia was maintained with sevoflurane at 1–1.5 minimum alveolar concentration in 40% oxygen/air. Analgesia was provided by continuous remifentanil infusion (0.05–0.2 µg/kg/min). Magnesium sulphate (2 g) and lidocaine (1 mg/kg) were administered as part of a multimodal analgesic strategy. Forty minutes before the anticipated end of surgery, acetaminophen 1 g, ketorolac 30 mg, tramadol 1.0–1.5 mg/kg, and ondansetron 4 mg were administered intravenously. Neuromuscular blockade was maintained with continuous rocuronium infusion and monitored at the adductor pollicis using TOF and PTC. Rocuronium was titrated to deep blockade (TOF 0; PTC 1–2) throughout pneumoperitoneum and steep Trendelenburg in both cohorts, and reversed with sugammadex 2–4 mg/kg according to TOF recovery.

Individual TOF/PTC measurements were used for intraoperative titration but were not transcribed into the study case-report form. The proportion of operative time within target and cumulative rocuronium dose beyond the stated infusion rate are therefore unavailable.

Mechanical ventilation was delivered in volume-controlled mode with a tidal volume of 8 mL/kg ideal body weight. Respiratory rate was adjusted to maintain end-tidal carbon dioxide between 35 and 45 mmHg. Positive end-expiratory pressure (PEEP) was 6 cmH_2O, and recruitment manoeuvres were not performed. Normothermia was maintained using forced-air warming. Intraoperative fluid therapy consisted of balanced crystalloid solutions at 6 mL/kg/h. Mean arterial pressure was maintained above 65 mmHg; intravenous ephedrine 5 mg was administered when required.

No recruitment manoeuvre was performed during pneumoperitoneum. Any routine manoeuvre after desufflation and return to the neutral position was not prospectively documented and was not included in the study analysis.

2.5 Outcome Measurements

2.5.1 Optic nerve sheath diameter

Bilateral optic nerve sheath diameter (ONSD) was assessed by ocular ultrasonography using a 7.5-MHz linear transducer. Measurements were obtained in the transverse plane, 3 mm posterior to the globe, at five predefined time points: T0 (baseline, pre-pneumoperitoneum, neutral position), T1 (45 minutes after establishment of pneumoperitoneum and steep Trendelenburg), T2 (120 minutes after steep Trendelenburg positioning), T3 (during vesicourethral anastomosis), and T4 (before extubation, after return to neutral position).

ONSD measurements were obtained according to a standardised protocol by an experienced examiner, with a second examiner present during image acquisition to ensure adherence to the protocol. Three separate image acquisitions were obtained for each eye at each time point, with ONSD measured independently on each image; the mean of the three measurements was used for analysis.

An ONSD threshold of 5.0 mm was explored as a secondary categorical marker associated in previous studies with increased intracranial pressure. Because absolute ONSD thresholds vary with technique and population, change from baseline was considered the more informative measure for between-group comparison.

2.5.2 Cerebral oximetry

All patients underwent continuous bilateral cerebral oximetry (Root O3, Masimo Corporation, Irvine, CA, USA), providing regional cerebral oxygen saturation (rSO_2) and device-derived oxygenated, deoxygenated and total haemoglobin indices (ΔO_2Hbi, $\Delta HHbi$ and $\Delta cHbi$).

These indices are manufacturer-defined relative changes in spectral absorption referenced to the start of monitoring and are reported in arbitrary units rather than as haemoglobin concentrations. Accordingly, the Δ symbol is part of the device nomenclature and does not denote a change calculated between study timepoints.

2.5.3 Visual function assessment

Visual function was assessed preoperatively and on postoperative day 1 using the Catquest-9SF, a nine-item patient-reported outcome measure. Responses were converted to interval-level Rasch scores (theta, logits) using Winsteps software. Because Catquest-9SF was developed for cataract-related visual disability and has not been validated for transient symptoms after non-ocular surgery, this outcome was considered exploratory [20, 21].

2.6 Outcomes

The primary outcome was the between-group difference in device-reported ΔHHbi at T3, representing prolonged cumulative exposure to pneumoperitoneum and steep Trendelenburg. ONSD at T3 was a complementary non-invasive intracranial-pressure surrogate [22, 23].

Secondary outcomes were ONSD enlargement; between-group differences in change-from-baseline rSO_2 and ΔO_2Hbi; associations between NIRS-derived indices and ONSD; change in Catquest-9SF Rasch score from baseline to postoperative day 1; and self-reported postoperative visual disturbances. The latter visual outcomes were exploratory.

NIRS-derived indices and ONSD were interpreted as complementary physiological measures; neither was considered a direct measurement of cerebral venous pressure or proof of a causal mechanism.

2.7 Statistical Analysis

Statistical analyses were performed using R software version 4.4.0 (R Foundation for Statistical Computing, Vienna, Austria).

2.7.1 Primary analysis

Longitudinal changes in optic nerve sheath diameter (ONSD), regional cerebral oxygen saturation (rSO_2), oxygenated haemoglobin index (ΔO_2Hbi), and deoxygenated haemoglobin index (ΔHHbi) were analysed using linear mixed-effects models. For each outcome, the model included fixed effects for treatment group (low-pressure pneumoperitoneum [LPP] versus standard-pressure pneumoperitoneum [SPP]), timepoint (T0–T4), the group × timepoint interaction, and the adjustment covariates age, body mass index (BMI), and ASA physical status. A random intercept for each patient was included to account for within-patient correlation across repeated measurements, and time was modelled as a categorical variable.

The primary contrast was the adjusted between-group difference in ΔHHbi at T3. The group × timepoint interaction was used to assess whether longitudinal trajectories differed between pneumoperitoneum groups. Adjusted between-group contrasts at individual timepoints were derived from the fitted models. As a sensitivity analysis, the mixed-effects models were additionally adjusted for surgical duration.

2.7.2 Secondary analyses

Within-group temporal changes were evaluated using the Friedman test. Between-group comparisons at individual timepoints were performed using the Mann–Whitney U test because most variables were not normally distributed according to the Shapiro–Wilk test. Because baseline rSO_2 values differed significantly between groups, between-group comparisons of rSO_2 were performed using change-from-baseline values (ΔrSO_2).

Spearman rank correlation coefficients (ρ) were calculated to assess the association between ONSD and each NIRS-derived parameter (rSO_2, ΔO_2Hbi, and ΔHHbi), separately for each hemisphere and pneumoperitoneum group. These correlation analyses were considered exploratory. Postoperative visual

disturbances were summarised using frequency distributions and compared between groups using Fisher's exact test.

2.7.3 Sensitivity analysis: inverse probability of treatment weighting

Because treatment allocation was not randomised, inverse probability of treatment weighting (IPTW) was performed as a sensitivity analysis. Propensity scores were estimated using a logistic regression model including four predefined surgical difficulty factors: previous inframesocolic abdominal surgery, prostate volume ≥ 100 g, BMI ≥ 30 kg/m [2], and planned extended pelvic lymph-node dissection.

Stabilised inverse probability weights were calculated to generate a weighted pseudo-population in which the four included surgical difficulty factors were balanced between treatment groups. To limit the influence of extreme weights, stabilised weights were truncated at the 99th percentile. Covariate balance before and after weighting was assessed using absolute standardised mean differences (SMD), with an absolute SMD below 0.10 considered indicative of adequate balance.

For the IPTW analysis, ONSD was evaluated as change from baseline to T3 (ΔONSD=T3 − T0) to account for the between-group difference observed at baseline. ΔrSO_2 was likewise analysed as change from baseline.

IPTW-weighted comparisons of continuous outcomes were performed using weighted regression with robust variance estimation. The IPTW analysis evaluated whether the observed between-group differences remained consistent after adjustment for the four measured components of baseline surgical complexity [24] [25].

2.7.4 Multiple comparisons

Longitudinal between-group differences across timepoints were primarily assessed using the group-by-time interaction terms of the linear mixed-effects models. Between-group comparisons at individual timepoints were considered secondary exploratory analyses and are reported as such in the relevant tables and table footnotes (Tables 4–5–6). No adjustment for multiple comparisons was applied to these exploratory analyses. All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant.

3. RESULTS

Seventy-two patients were included in the final analysis: 36 in the low-pressure pneumoperitoneum group (LPP, 8 mmHg) and 36 in the standard-pressure pneumoperitoneum group (SPP, 12 mmHg). The study flow diagram is presented in Fig. 1.

Of the 40 patients included in the previously published low-pressure cohort, 36 were included in the present comparative analysis. Four patients were excluded because consistent exposure to the intended

8-mmHg pneumoperitoneum strategy throughout the procedure could not be ascertained.

Forty-three patients were assessed for eligibility for the 12-mmHg cohort. Five patients did not meet the inclusion criteria, and two declined to participate. Therefore, 36 patients were included in the final comparative analysis.

3.1 Baseline Characteristics

Baseline demographic, clinical, intraoperative, and haemodynamic characteristics are summarised in Table 1. Age, ASA physical status, smoking history, baseline haemoglobin concentration, surgical duration, time in steep Trendelenburg, ephedrine use and fluid administration were similar between groups. BMI and several predefined surgical-complexity variables were higher in the 12-mmHg cohort. End-tidal carbon dioxide remained within the predefined target range and mean arterial pressure was maintained above 65 mmHg in both groups.

Table 1
Baseline demographic, clinical, haemodynamic, and surgical characteristics.

Variable	**LPP (n = 36)**	**SPP (n = 36)**	***P***
Age, years	70.0 ± 6.5	70.1 ± 6.2	0.94
BMI, kg/m²	25.9 ± 3.2	30.7 ± 4.1	< 0,001
ASA class	2.22 ± 0.42	2.36 ± 0.49	0.19
Hypertension, n (%)	10 (27.8)	12 (33.3)	0.79
Diabetes, n (%)	8 (22.2)	12 (33.3)	0.43
Smoking, n (%)	12 (33.3)	14 (38.9)	0.80
Haemoglobin, g/dL	12.0 ± 1.1	12.0 ± 1.2	1.00
Mean $EtCO_2$, mmHg	35 ± 2.1	36 ± 2.2	0.06
Surgery duration, min	182.4 ± 41.3	186.7 ± 39.7	0.65
Steep Trendelenburg, min	130 ± 10.1	135 ± 10.4	0.41
Ephedrine use, n (%)	12 (33.3)	14 (38.9)	0.80
Fluids, L	1.5 ± 0.3	1.4 ± 0.2	0.10

Values are mean ± SD or n (%). BMI, body mass index; ASA, American Society of Anesthesiologists; $EtCO_2$, end-tidal carbon dioxide.

The distribution of preoperative surgical difficulty factors is summarised in Table 2. Prostate volume > 100 g, BMI > 30 kg/m, planned extended pelvic lymph-node dissection were significantly more frequent in

the SPP group. In contrast, the prevalence of previous inframesocolic abdominal surgery, was similar between groups (16.7% versus 22.2%, P = 0.767).

Table 2
Distribution of preoperative surgical difficulty factors by pneumoperitoneum pressure group.

Factor	LPP (n = 36)	SPP (n = 36)	P
Previous inframesocolic abdominal surgery (excluding pelvic surgery), n (%)	6 (16.7)	8 (22.2)	0.767
Prostate volume > 100 g, n (%)	11 (30.6)	24 (66.7)	0.004
BMI > 30 kg/m², n (%)	8 (22.2)	20 (55.6)	0.007
Planned extended pelvic lymph-node dissection, n (%)	6 (16.7)	18 (50.0)	0.005

Values are n (%). BMI, body mass index; LPP, low-pressure pneumoperitoneum; SPP, standard-pressure pneumoperitoneum. P values were calculated using Fisher's exact test.

3.2 Optic Nerve Sheath Diameter

ONSD progressively increased throughout pneumoperitoneum and steep Trendelenburg positioning in both groups, with significantly greater enlargement in the SPP group at all intraoperative timepoints (Tables 3 and 4).

In the SPP group, right-sided ONSD increased from 3.76 ± 0.35 mm at baseline (T0) to 4.55 ± 0.40 mm at T3, and left-sided ONSD from 3.74 ± 0.40 mm to 4.60 ± 0.38 mm. Clinically relevant ONSD enlargement (> 5.0 mm) was observed in 8 of 36 patients (22.2%) at T3. After pneumoperitoneum release (T4), ONSD partially decreased but remained above baseline. No significant right-versus-left hemispheric differences were observed at any timepoint (all P > 0.05).

In the LPP group, ONSD changes were more modest. Right-sided ONSD increased from 3.52 ± 0.31 mm to 4.03 ± 0.39 mm at T3, and left-sided ONSD from 3.55 ± 0.34 mm to 4.08 ± 0.41 mm. No patient in the LPP group exceeded the 5.0 mm threshold.

Table 3
Between-group comparison of right ONSD (mm).

Time	LPP (8 mmHg)	SPP (12 mmHg)	*P*
T0	3.52 ± 0.31	3.76 ± 0.35	0.003
T1	3.71 ± 0.33	4.06 ± 0.37	0.008
T2	3.89 ± 0.36	4.35 ± 0.41	< 0.001
T3	4.03 ± 0.39	4.55 ± 0.40	< 0.001
T4	3.68 ± 0.34	4.07 ± 0.37	0.024

Values are mean ± SD. Within-group temporal changes: Friedman test (both groups: all P < 0.001).

Table 4
Between-group comparison of left ONSD (mm).

Timepoint	LPP (8 mmHg)	SPP (12 mmHg)	P
T0	3.55 ± 0.34	3.74 ± 0.40	0.03
T1	3.76 ± 0.35	4.10 ± 0.34	< 0.001
T2	3.95 ± 0.37	4.43 ± 0.38	< 0.001
T3	4.08 ± 0.41	4.60 ± 0.38	< 0.001
T4	3.72 ± 0.35	4.09 ± 0.38	0.003

Values are mean ± SD. Within-group temporal changes: Friedman test (both groups: all P < 0.001).

3.3 Cerebral haemoglobin dynamics and findings suggestive of venous congestion

3.3.1 Deoxygenated haemoglobin index (ΔHHbi)

Device-reported ΔHHbi values increased during sustained pneumoperitoneum and steep Trendelenburg positioning. In the SPP group, right-sided ΔHHbi increased from 1.1 ± 1.1 at T0 to 15.2 ± 6.7 at T3, whereas left-sided ΔHHbi increased from 0.9 ± 1.2 to 14.5 ± 5.5. At T3, ΔHHbi was significantly greater in the SPP group than in the LPP group on both the right (P < 0.001) and left sides (P = 0.011; Table 5). Additional between-group differences were observed bilaterally at T0 and for left-sided ΔHHbi at T2 and T4; however, these timepoint-specific comparisons were secondary exploratory analyses. The principal longitudinal analysis demonstrated a significant group × time interaction for bilateral mean ΔHHbi (P < 0.001), indicating distinct temporal trajectories according to pneumoperitoneum pressure.

Table 5
Phase-dependent raw values of the device-reported change in deoxygenated haemoglobin index (ΔHHbi).

Timepoint	LPP Right	SPP Right	P value	LPP Left	SPP Left	P value
T0	0.6 ± 2.1	1.1 ± 1.1	0.017	0.3 ± 1.5	0.9 ± 1.2	0.001
T1	11.2 ± 6.7	9.1 ± 6.9	0.079	10.0 ± 6.5	9.5 ± 6.9	0.408
T2	11.5 ± 5.6	13.1 ± 5.5	0.228	10.0 ± 5.9	13.1 ± 6.6	0.032
T3	9.4 ± 6.1	15.2 ± 6.7	< 0.001	10.2 ± 6.2	14.5 ± 5.5	0.011
T4	1.9 ± 4.4	2.9 ± 2.9	0.287	1.4 ± 3.8	4.2 ± 2.5	0.012

Values are presented as mean ± SD and represent ΔHHbi values reported directly by the monitoring device rather than changes calculated from the study timepoint measurements. Between-group comparisons at individual timepoints were performed using the two-sided Mann–Whitney U test and should be considered secondary exploratory analyses. The principal longitudinal inference was based on the group × time interaction obtained from the linear mixed-effects model.

3.3.2 Regional cerebral oxygen saturation (rSO_2)

Baseline rSO_2 values were significantly lower in the SPP group (right: 63.8 ± 3.9% vs 70.8 ± 4.7%, P < 0.001; left: 64.3 ± 5.2% vs 69.8 ± 4.8%, P < 0.001). Therefore, between-group comparisons were performed using change-from-baseline values (ΔrSO_2). Both groups demonstrated the characteristic paradoxical increase in rSO_2 following establishment of pneumoperitoneum and steep Trendelenburg positioning. The increase was significantly greater in the SPP group at all intraoperative timepoints, with the greatest between-group difference observed at T3 (ΔrSO_2: +11.5% vs + 3.5%, P < 0.001). These observations were supported by linear mixed-effects analysis, which demonstrated a significant group × time interaction for bilateral mean rSO_2 (P < 0.001), indicating distinct longitudinal trajectories according to pneumoperitoneum pressure. Phase-dependent changes in ΔrSO_2 are summarised in Table 6.

Table 6
Phase-dependent changes in regional cerebral oxygen saturation from baseline (ΔrSO_2).

Time	ΔR 8 mmHg	ΔR 12 mmHg	P value	ΔL 8 mmHg	ΔL 12 mmHg	P value
T1	+ 0.0 ± 4.5	+ 7.7 ± 5.1	**< 0.001**	+ 1.3 ± 4.8	+ 7.3 ± 6.4	**< 0.001**
T2	+ 1.5 ± 5.4	+ 10.0 ± 6.1	**< 0.001**	+ 2.0 ± 5.5	+ 9.9 ± 8.3	**< 0.001**
T3	+ 2.9 ± 5.5	+ 11.3 ± 6.6	**< 0.001**	+ 3.2 ± 5.6	+ 11.0 ± 8.1	**< 0.001**
T4	+ 1.5 ± 3.4	+ 7.1 ± 4.4	**< 0.001**	+ 1.6 ± 3.1	+ 6.9 ± 6.4	**< 0.001**

Values represent mean change from baseline (T0). Positive values indicate an increase in regional cerebral oxygen saturation relative to baseline. P values refer to between-group comparisons at each intraoperative timepoint. Linear mixed-effects analysis demonstrated a significant group × time interaction for bilateral mean rSO_2 (P < 0.001).

3.3.3 Oxygenated haemoglobin index (ΔO_2Hbi)

ΔO_2Hbi increased in both groups after establishment of pneumoperitoneum and steep Trendelenburg positioning, reaching peak values at T1–T2 before gradually returning towards baseline. No statistically significant between-group differences were observed at any intraoperative timepoint after Bonferroni correction (Table 7). A nominally significant difference was observed in the left hemisphere at T1 (P = 0.040), but this did not remain significant after correction for multiple comparisons. These observations were supported by linear mixed-effects analysis, which demonstrated no significant group × time interaction for bilateral mean ΔO_2Hbi (P = 0.144), indicating similar longitudinal trajectories between the two pneumoperitoneum groups.

Table 7
Phase-dependent changes in oxygenated haemoglobin index (ΔO_2Hbi).

Timepoint	LPP (8 mmHg) Right	SPP (12 mmHg) Right	P value	LPP (8 mmHg) Left	SPP (12 mmHg) Left	P value
T0	1.5 ± 3.4	0.7 ± 2.1	0.24	0.6 ± 2.0	0.8 ± 2.5	0.71
T1	12.8 ± 7.0	14.3 ± 8.5	0.40	12.3 ± 6.8	15.4 ± 7.2	0.040
T2	13.5 ± 5.7	14.6 ± 6.0	0.35	12.5 ± 5.8	15.0 ± 6.8	0.057
T3	13.2 ± 5.8	12.8 ± 5.0	1.00	12.0 ± 5.6	14.2 ± 6.8	0.21
T4	2.4 ± 5.8	3.3 ± 3.0	0.51	1.5 ± 5.3	3.4 ± 2.2	1.00

Values are presented as mean ± SD. The principal longitudinal inference was based on the group-by-time interaction obtained from the linear mixed-effects model. Individual between-group comparisons at each timepoint were performed using the Mann–Whitney U test and were considered secondary exploratory analyses. Within-group temporal changes were assessed using the Friedman test and were significant in both cohorts (all $P < 0.001$). The linear mixed-effects model demonstrated no significant group-by-time interaction for bilateral mean ΔO_2Hbi ($P = 0.144$).

3.3.4 Linear mixed-effects analysis

Longitudinal changes in bilateral mean rSO_2, ΔO_2Hbi, ΔHHbi, and ONSD were further evaluated using linear mixed-effects models adjusted for age, BMI, and ASA physical status. Significant group × time interactions were observed for bilateral mean rSO_2 (global interaction $P < 0.001$), bilateral mean ΔHHbi ($P < 0.001$), and bilateral mean ONSD ($P < 0.001$), indicating differential longitudinal trajectories according to pneumoperitoneum pressure.

In contrast, no significant group × time interaction was observed for mean bilateral ΔO_2Hbi ($P = 0.144$). Adjusted between-group contrasts demonstrated significantly greater increases in rSO_2 in the SPP group at all intraoperative timepoints (T1–T4; all $P < 0.001$). For ΔHHbi, the largest adjusted between-group difference was observed at T3 (adjusted difference 4.56 μM, 95% CI 2.27–6.84, $P < 0.001$), whereas differences at earlier timepoints were not statistically significant. ONSD likewise showed progressively greater enlargement in the SPP group throughout the procedure. Sensitivity analyses additionally adjusted for surgical duration yielded essentially identical results, confirming the robustness of the findings.

3.3.5 Integrated physiological findings

The simultaneous increase in rSO_2, the absence of a consistent between-group increase in oxygenated haemoglobin, and greater accumulation of deoxygenated haemoglobin in the 12-mmHg cohort form a physiological pattern compatible with altered cerebral blood volume and impaired venous drainage rather than necessarily improved cerebral oxygen delivery. The accompanying increase in ONSD provides a complementary pressure-related surrogate. These findings remain associative: neither NIRS-derived

haemoglobin indices nor ONSD directly measures cerebral venous pressure, cerebral blood flow, or cerebral oedema.

3.4 Correlation Between Cerebral Oxygenation and ONSD

Repeated-measures correlation analysis was used to evaluate within-patient associations between ONSD and NIRS-derived variables across the intraoperative timepoints (Table 8; Figs. 3). This approach accounted for the non-independence of repeated observations obtained from the same patient.

In the LPP group, rSO_2 showed weak positive within-patient correlations with ONSD (right: r_{rm} = 0.190, P = 0.022; left: r_{rm} = 0.179, P = 0.032). ΔO_2Hbi and ΔHHbi showed positive correlations with ONSD bilaterally, with coefficients ranging from 0.285 to 0.415 (all P < 0.001).

In the SPP group, stronger positive correlations were observed between rSO_2 and ONSD (right: r_{rm} = 0.640; left: r_{rm} = 0.597; both P < 0.001). ΔO_2Hbi was moderately correlated with ONSD (right: r_{rm} = 0.468; left: r_{rm} = 0.486; both P < 0.001), whereas ΔHHbi showed stronger positive correlations (right: r_{rm} = 0.624; left: r_{rm} = 0.638; both P < 0.001). These findings describe within-patient associations and should not be interpreted as evidence of causality. Differences in correlation magnitude between groups were descriptive because no formal between-group comparison of the coefficients was performed.

Table 8
Repeated-measures correlations between NIRS-derived variables and ONSD.

Group	Variable	r_{rm} Right	P Right	r_{rm} Left	P Left
LPP (8 mmHg)	rSO_2	0.190	0.022	0.179	0.032
LPP (8 mmHg)	ΔO_2Hbi	0.394	**< 0.001**	0.285	**< 0.001**
LPP (8 mmHg)	ΔHHbi	0.397	**< 0.001**	0.415	**< 0.001**
SPP (12 mmHg)	rSO_2	0.640	**< 0.001**	0.597	**< 0.001**
SPP (12 mmHg)	ΔO_2Hbi	0.468	**< 0.001**	0.486	**< 0.001**
SPP (12 mmHg)	ΔHHbi	0.624	**< 0.001**	0.638	**< 0.001**

Values are repeated-measures correlation coefficients (r_{rm}), calculated after accounting for the non-independence of observations obtained from the same patient. Positive coefficients indicate that within-patient increases in the NIRS-derived variable were associated with increases in ONSD.

3.5 Visual Outcomes

3.5.1 Incidence of postoperative visual disturbances

Visual disturbances were reported by 5 of 36 patients (13.9%) in the LPP group and 7 of 36 patients (19.4%) in the SPP group on postoperative day 1 (absolute risk difference, 5.5 percentage points; Fisher's exact test, P = 0.53). The most frequently reported symptoms were blurred vision, difficulty with near-focus tasks, and transient visual field alterations. All visual disturbances were self-limiting and resolved within 72 hours. No cases of ischaemic optic neuropathy were observed.

3.5.2 Catquest-9SF visual function scores

Preoperative Catquest-9SF Rasch scores were comparable between groups (LPP: −2.8 ± 1.2 logits versus SPP: −2.6 ± 1.4 logits; P = 0.54), indicating similar baseline visual function. On postoperative day 1, both groups demonstrated deterioration in visual function; however, the decline was significantly greater in the SPP group (Δθ: −1.4 ± 0.8 versus − 0.7 ± 0.6 logits; P = 0.002), indicating greater postoperative visual impairment after standard-pressure pneumoperitoneum.

3.5.3 Predictors of postoperative visual disturbances

Univariate analysis identified pneumoperitoneum pressure group, duration of steep Trendelenburg positioning, peak ONSD, and peak ΔHHbi as candidate predictors of postoperative visual disturbances (all P < 0.10). Age, body mass index, ASA physical status, and baseline Catquest-9SF Rasch score were not significantly associated with postoperative visual disturbances.

3.6 IPTW Sensitivity Analysis

3.6.1 Propensity score estimation and covariate balance

The propensity-score model included four preoperative surgical difficulty factors: previous inframesocolic abdominal surgery, prostate volume ≥ 100 g, BMI ≥ 30 kg/m [24], and planned extended pelvic lymph-node dissection. After application of stabilised inverse probability weights truncated at the 99th percentile, all four covariates included in the propensity-score model achieved adequate balance (absolute SMD < 0.10; Table 9).

Table 9
Covariate balance before and after inverse probability of treatment weighting.

Covariate	Standardized Mean difference (unweighted)	Standardized mean difference (weighted)
Prostate volume > = 100 g'	0.775	0.039
BMI > = 30 kg/m2'	0.728	0.011
Extended pelvic lymph-node dissection'	0.756	0.001
Previous inframesocolic surgery'	0.141	0.051

BMI, body mass index; IPTW, inverse probability of treatment weighting; SMD, standardised mean difference. An absolute SMD < 0.10 after weighting indicates adequate covariate balance.

3.6.2 IPTW-weighted between-group comparisons

After IPTW adjustment, the between-group differences in ΔHHbi, ΔrSO_2, and ONSD at T3 remained statistically significant and directionally consistent with the unweighted analyses (Table 10). For ΔHHbi, the IPTW-adjusted between-group differences remained significant in both the right (P = 0.002) and left hemispheres (P = 0.036). Differences in ΔrSO_2 and ONSD at T3 also remained significant bilaterally (all P < 0.001). Overall, these findings indicate that the observed differences persisted after adjustment for the measured baseline components of surgical complexity.

Table 10
Between-group comparisons: unweighted versus IPTW-weighted analysis.

Outcome	Unadjusted p_value	IPTW-adjusted p_value
'ΔHHbi at T3 (right hemisphere)'	'<0.001'	'0.002'
'ΔHHbi at T3 (left hemisphere)'	'0.022'	'0.036'
'ΔrSO2 at T3 (right hemisphere)'	'<0.001'	'<0.001'
'ΔrSO2 at T3 (left hemisphere)'	'<0.001'	'<0.001'
'ONSD at T3 (right eye)'	'<0.001'	'<0.001'
'ONSD at T3 (left eye)'	'<0.001'	'<0.001'

Unadjusted P values were calculated using the two-sided Mann–Whitney U test. The corresponding IPTW-adjusted P values were obtained from weighted regression with robust variance estimation, using stabilised weights truncated at the 99th percentile. IPTW, inverse probability of treatment weighting; ΔHHbi, change in deoxygenated haemoglobin index; ΔrSO_2, change in regional cerebral oxygen saturation; ONSD, optic nerve sheath diameter.

4. DISCUSSION

This sequential observational comparison found that 12-mmHg pneumoperitoneum was associated with greater ΔHHbi accumulation and ONSD enlargement than an 8-mmHg strategy during RALP. The low-pressure cohort overlaps with our previous physiological study [19], whereas the present analysis adds a subsequently recruited 12-mmHg cohort to address insufflation pressure as the exposure of interest. The findings therefore show association, not causality.

4.1 Pneumoperitoneum Pressure and Intracranial Pressure

The unweighted analysis demonstrated greater ONSD enlargement from baseline in the SPP group at the intraoperative timepoints, with 22.2% of patients exceeding the clinically relevant 5.0-mm threshold

compared with none in the LPP group. These findings suggest an association between standard insufflation pressure and greater intracranial pressure surrogates during prolonged steep Trendelenburg positioning. This observation is consistent with the invasive intracranial pressure measurements reported by Kamine et al. [8], who demonstrated a linear dose–response relationship between insufflation pressure and intracranial pressure, with a mean increase of 7.2 cmH_2O at 15 mmHg.

After IPTW adjustment for the four predefined surgical difficulty factors, the between-group differences in ONSD enlargement from baseline to T3 remained statistically significant. Compared with the LPP group, the SPP group showed a greater adjusted increase in ONSD of 0.43 mm in the right eye (95% CI 0.27–0.59; $P < 0.001$) and 0.52 mm in the left eye (95% CI 0.28–0.76; $P < 0.001$). The consistency between the unweighted and weighted analyses indicates that the association between standard-pressure pneumoperitoneum and greater ONSD enlargement persisted after adjustment for the measured components of baseline surgical complexity. However, residual confounding and confounding by indication cannot be excluded.

The findings are physiologically plausible in view of the sigmoid intra-abdominal pressure–volume relationship, which provides diminishing workspace gains as pressure rises [8]. Operative duration and time in steep Trendelenburg were similar between cohorts, and previous trials support the feasibility of low-pressure pneumoperitoneum in selected patients [13] [12]. Because allocation was not randomised, however, this study cannot establish equivalent surgical feasibility across levels of operative complexity [26].

The valveless AirSeal system may have facilitated stable low-pressure exposure; therefore, these findings may not be fully generalisable to conventional insufflation systems [27, 28].

4.2 NIRS-derived haemoglobin patterns suggestive of impaired venous drainage

Composite rSO_2 increased during pneumoperitoneum in both groups, which in isolation might be interpreted as improved cerebral oxygenation. The haemoglobin subspecies showed a different pattern: ΔO_2Hbi did not differ materially between groups, whereas ΔHHbi accumulated more in the 12-mmHg cohort. This resembles the pattern described by Calderone et al. [17] and is compatible with impaired cerebral venous drainage [29].

Accordingly, an increase in rSO_2 should not automatically be interpreted as improved perfusion in this setting. ΔHHbi remains a physiological index, not a diagnostic measure of venous congestion, and no validated intervention threshold exists.

The robustness of the NIRS-derived findings was supported by the IPTW analysis. After adjustment for baseline surgical complexity, the between-group differences in ΔHHbi at T3 remained statistically significant for both the right hemisphere (weighted mean difference 6.11; $P = 0.006$) and the left hemisphere (weighted mean difference 4.34; $P = 0.026$). Differences in change-from-baseline rSO_2 also

remained significant bilaterally after weighting (both P < 0.001). Among the physiological outcomes evaluated, the NIRS-derived indices therefore provided the most consistent evidence of an association with pneumoperitoneum pressure after adjustment for measured confounders.

Current cerebral NIRS algorithms mainly trigger intervention for decreases in rSO_2 and do not address potentially abnormal haemoglobin dynamics when rSO_2 remains normal or elevated [12]. This limitation may be relevant during prolonged steep Trendelenburg.

Chen et al. [30]reported that 52% of elderly patients undergoing RALP developed internal jugular valve incompetence during Trendelenburg positioning and that all seven cases of postoperative delirium in their cohort occurred among patients with jugular valve incompetence, despite normal or elevated rSO_2 values. Lopez et al. [31] showed in cardiac surgery that intraoperative hyperoxic cerebral reperfusion was independently associated with increased odds of postoperative delirium per 10%·hour (OR 1.65, 95% CI 1.12–2.44; P = 0.01). A recent systematic review and meta-analysis also found that cerebral oxygen saturation monitoring alone does not consistently reduce perioperative neurocognitive disorders in non-cardiac surgical patients [32]. These observations support the hypothesis that composite rSO_2 values may provide an incomplete representation of cerebral haemodynamic changes during RALP and that subspecies-level analysis may offer complementary physiological information.

Because baseline rSO_2 differed between groups and cerebral oximetry shows substantial inter-individual variability, rSO_2 was compared using change-from-baseline values rather than absolute measurements.

4.3 Visual Outcomes: A Surgeon-Relevant Complication

The incidence of self-reported visual disturbances did not differ significantly between groups (19.4% vs 13.9%, P = 0.53). The Catquest-9SF Rasch score showed a greater postoperative change in the 12-mmHg cohort; however, Catquest-9SF was developed for cataract-related visual disability and has not been validated for transient postoperative visual symptoms after non-ocular surgery. Accordingly, the questionnaire finding should be considered exploratory and described as a difference in patient-reported visual-function score rather than evidence of ocular injury.

Visual complications after RALP are uncommon but clinically important [10] [7]. Symptoms in this study were transient, but the study was not powered for rare ocular injury and did not include sensitive structural testing such as optical coherence tomography.

The positive correlation between ΔHHbi and ONSD (ρ = 0.54–0.63; all P < 0.001) indicates that greater deoxygenated haemoglobin accumulation was associated with greater optic nerve sheath enlargement. The different correlation patterns between rSO_2 and ONSD across groups—weak in the LPP group (ρ = 0.16–0.21) and moderate in the SPP group (ρ = 0.46–0.54) —provide further physiological support for the interpretation that increases in composite rSO_2 during standard-pressure pneumoperitoneum may occur alongside changes consistent with cerebral venous congestion rather than necessarily reflecting improved cerebral perfusion. These correlations should nevertheless be interpreted as associations and not as evidence of causality.

4.4 Toward Individualised Pneumoperitoneum: A Collaborative Surgical–Anaesthetic Strategy

A practical implication is to investigate individualised pneumoperitoneum as a collaborative surgical–anaesthetic strategy. Previous work has shown that pressure titration combined with measures such as deep neuromuscular blockade can permit lower operating pressures in many patients [33] [34].

The present findings suggest that NIRS-derived haemoglobin indices could potentially provide physiological feedback for future individualised pneumoperitoneum protocols [35] [36].

Future protocols could combine the lowest pressure compatible with safe surgical exposure with physiological monitoring. The present NIRS indices warrant further study as markers of cerebral tolerance but should not be interpreted as direct measures of venous pressure, congestion, or cerebral oedema [37, 38].

No ΔHHbi intervention threshold can be derived from this study. Until clinically relevant thresholds are validated prospectively, haemoglobin-subspecies monitoring should remain investigational and adjunctive to clinical assessment.

Individualised pressure may be particularly relevant in patients with limited cerebrovascular reserve, obesity, glaucoma, or prolonged expected operating time. Future studies should integrate surgical exposure, patient characteristics, and physiological responses rather than assuming a single optimal pressure [15, 16].

5. LIMITATIONS

This study has several limitations that should be considered when interpreting the findings.

First, treatment allocation was non-randomised and reflected anticipated surgical difficulty. IPTW balanced four measured complexity factors, but residual and unmeasured confounding remain possible; weighted estimates therefore do not establish causality.

Second, cohorts were recruited sequentially rather than concurrently, so temporal changes in patient selection, surgical experience, anaesthetic management, or other practice may have contributed to between-group differences.

Ventilatory conditions can influence cerebral venous drainage and ONSD. Although ventilation and PEEP were protocolised, undocumented end-of-procedure recruitment manoeuvres cannot be analysed and remain a potential source of variability.

Third, the sample size was based on the primary ΔHHbi endpoint and was insufficient for definitive inference on all secondary outcomes, particularly categorical visual events.

Fourth, Catquest-9SF is validated for cataract-related visual function, not transient symptoms after non-ocular surgery. The visual findings are therefore exploratory; objective ophthalmological testing and longer follow-up would be required to detect subclinical or persistent injury [21, 39, 40].

Fifth, ONSD is a surrogate rather than a direct measurement of intracranial pressure, and its association with NIRS-derived indices does not establish mechanism [41] [22].

ONSD measurements were obtained by an experienced examiner according to a standardised protocol. However, the examiner was not blinded to pneumoperitoneum pressure, which may have introduced measurement bias.

Sixth, ΔHHbi and ΔO_2Hbi are device-derived physiological indices, not direct measurements of cerebral blood flow or venous pressure. Their interpretation as markers of impaired venous drainage remains inferential, and no intervention threshold is established.

Sixth, this was a single-centre study involving experienced robotic surgical and anaesthetic teams. Consequently, the generalisability of the findings to other centres, surgical settings, and patient populations remains to be established.

Postoperative neurocognitive outcomes were not assessed and should be included, together with objective ophthalmological endpoints, in future studies.

6. CONCLUSIONS

In this sequential observational cohort study of RALP, 12-mmHg pneumoperitoneum was associated with greater ΔHHbi accumulation and ONSD enlargement than an 8-mmHg strategy, a pattern compatible with greater impairment of cerebral venous drainage.

The associations persisted after weighting for measured surgical-complexity factors, but residual, indication-related and temporal confounding cannot be excluded.

These findings support prospective evaluation of the lowest pressure compatible with safe surgical exposure and suggest that haemoglobin-subspecies monitoring may provide information not captured by composite rSO_2 alone. Visual-function findings remain exploratory.

Randomised studies with standardised ventilation and objective neurological and ophthalmological outcomes are required before pressure selection can be guided by these physiological indices.

Declarations

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Y. Santoro is an employee of Masimo Corporation, the manufacturer of the Root® O3 cerebral oximetry system used in this study. Statistical analysis was performed by Y. Santoro in collaboration with L. Campiglia and I. Cappellini.

B. Matta is Chief Medical Officer of Masimo International and a consultant in anaesthesia and neurocritical care at Cambridge University Hospitals, Cambridge, UK.

Masimo Corporation provided no funding for the study and had no role in the study design, data collection, data interpretation, manuscript preparation, or decision to submit the manuscript for publication.

J.P. Mulier reports honoraria from Medec International outside the submitted work and is co-founder of MT4L, a company developing airway-related medical devices unrelated to the present study.

The academic investigators had full access to the study data and retained final responsibility for the integrity of the data, the accuracy of the analysis, and the decision to submit the manuscript for publication.

All remaining authors declare no relevant financial or non-financial interests.

Ethics approval

The study was performed in accordance with the Declaration of Helsinki. The original low-pressure cohort was approved by the Institutional Ethics Committee of Area Vasta Toscana Centro (approval/registration no. 25336, July 2024).

Consent to participate

Written informed consent was obtained from all individual participants included in the study.

Author contributions

All authors contributed to the study conception and design. Material preparation, data collection, and statistical analysis were performed by L. Campiglia, I. Cappellini, and D. Modafferi. Optic nerve sheath diameter measurements were performed by (L.C. e D.M.). Surgical procedures were performed by G. Vignolini and A. Gavazzi. L. Campiglia wrote the first draft of the manuscript. J. P. Mulier contributed to the critical revision of the manuscript. All authors critically reviewed and revised the manuscript, read and approved the final version, and agreed to be accountable for the work.

Data availability

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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Figures

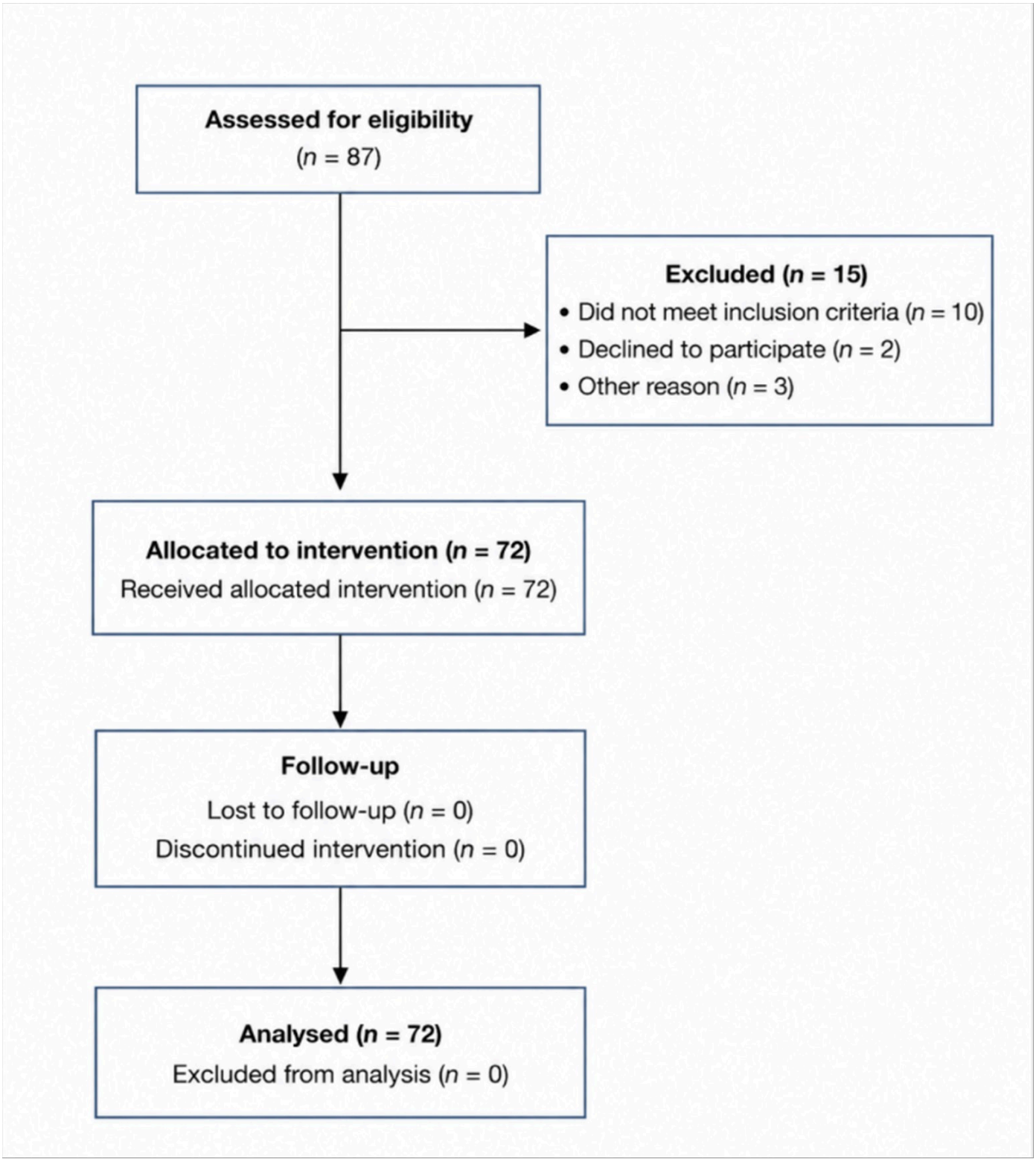


Figure 1

Study flow diagram (total n=72).

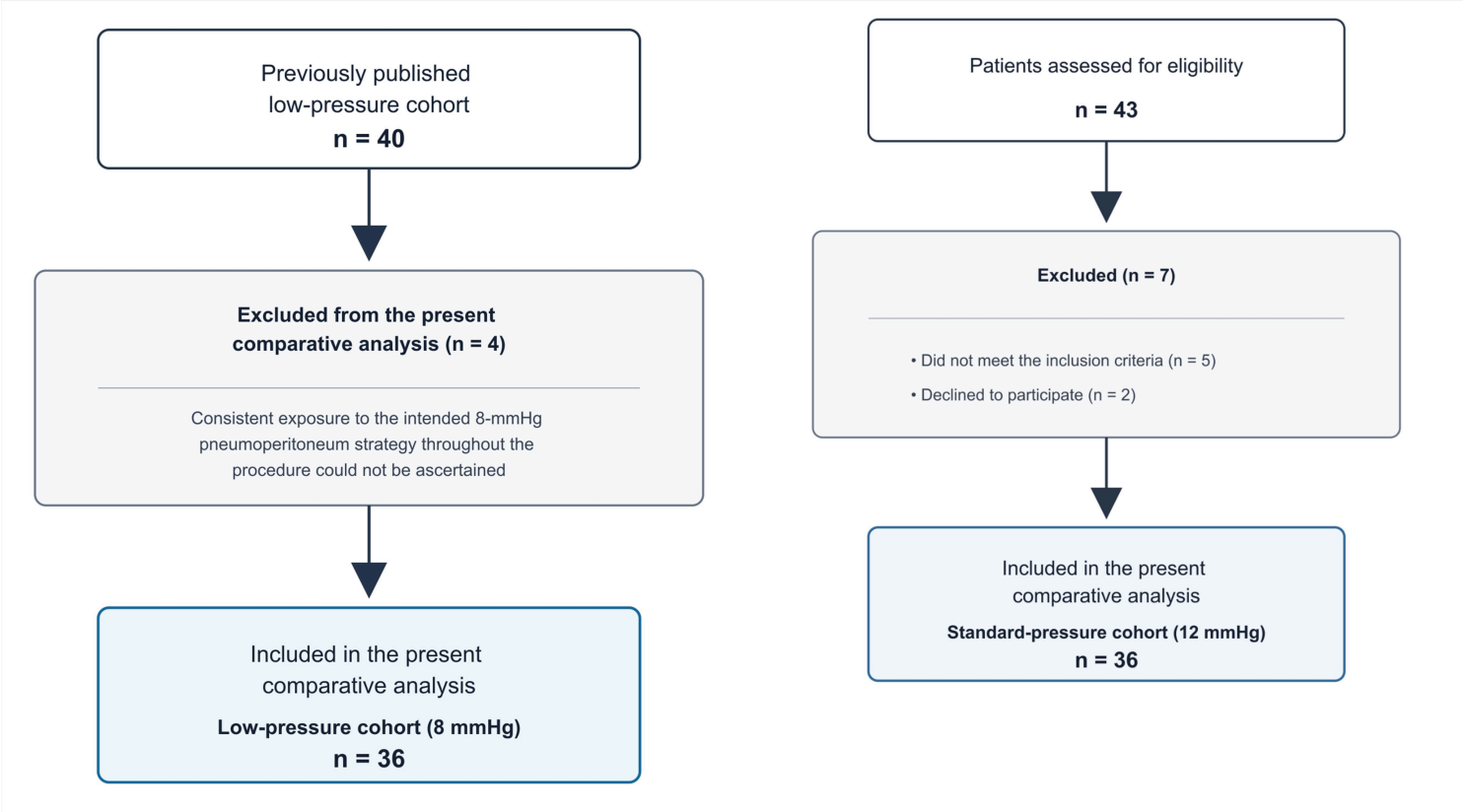


Figure 2

Figure 1. Study flow diagram for the two cohorts. The previously published low-pressure cohort comprised 40 patients, of whom 36 were included in the present comparative analysis; four were excluded because consistent exposure to the intended 8-mmHg pneumoperitoneum strategy throughout the procedure could not be ascertained. For the 12-mmHg cohort, 43 patients were assessed for eligibility; five did not meet the inclusion criteria and two declined to participate, leaving 36 patients for the comparative analysis. The final study population therefore comprised 72 patients.

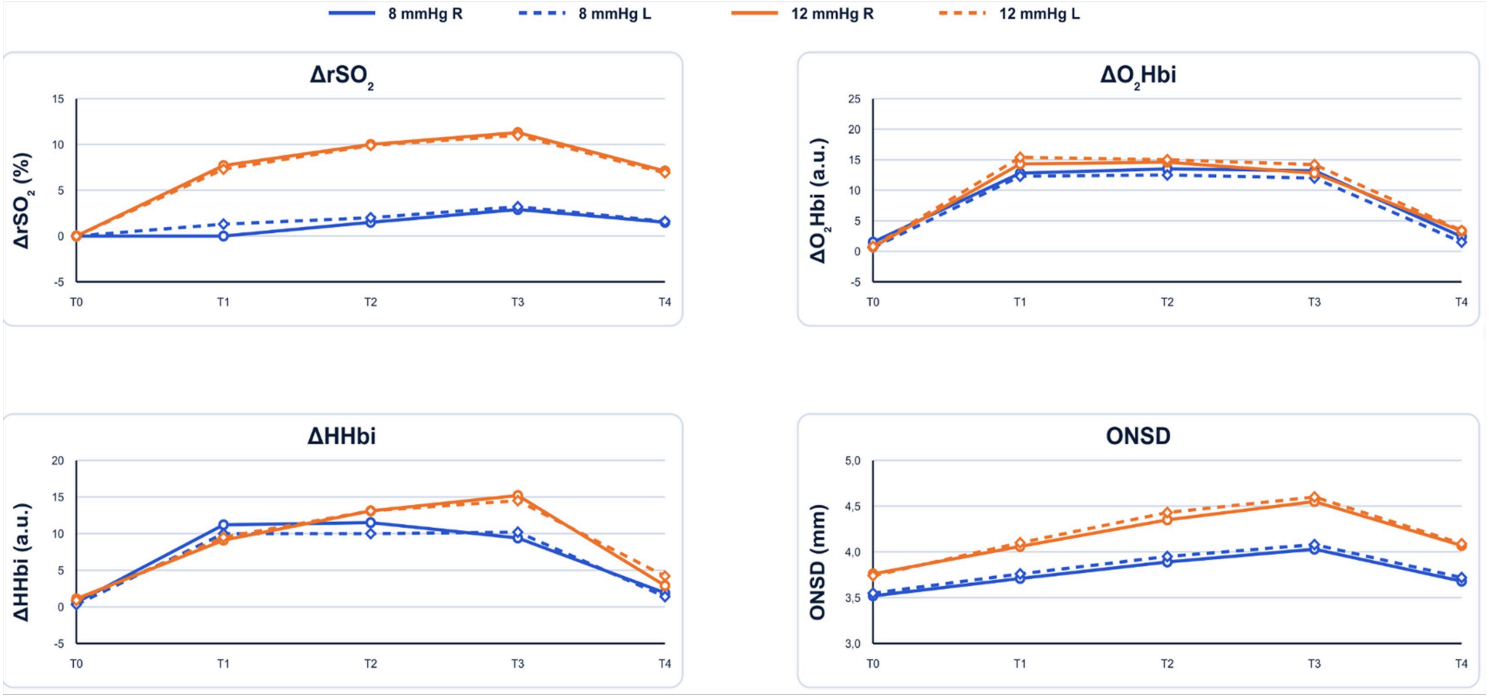


Figure 3

Fig.2 Time-course comparison of changes in regional cerebral oxygen saturation (ΔrSO_2), oxygenated haemoglobin index (ΔO_2Hbi), deoxygenated haemoglobin index ($\Delta HHbi$), and optic nerve sheath diameter (ONSD) during pneumoperitoneum at 8 versus 12 mmHg. Solid lines indicate the right side and dashed lines the left side.

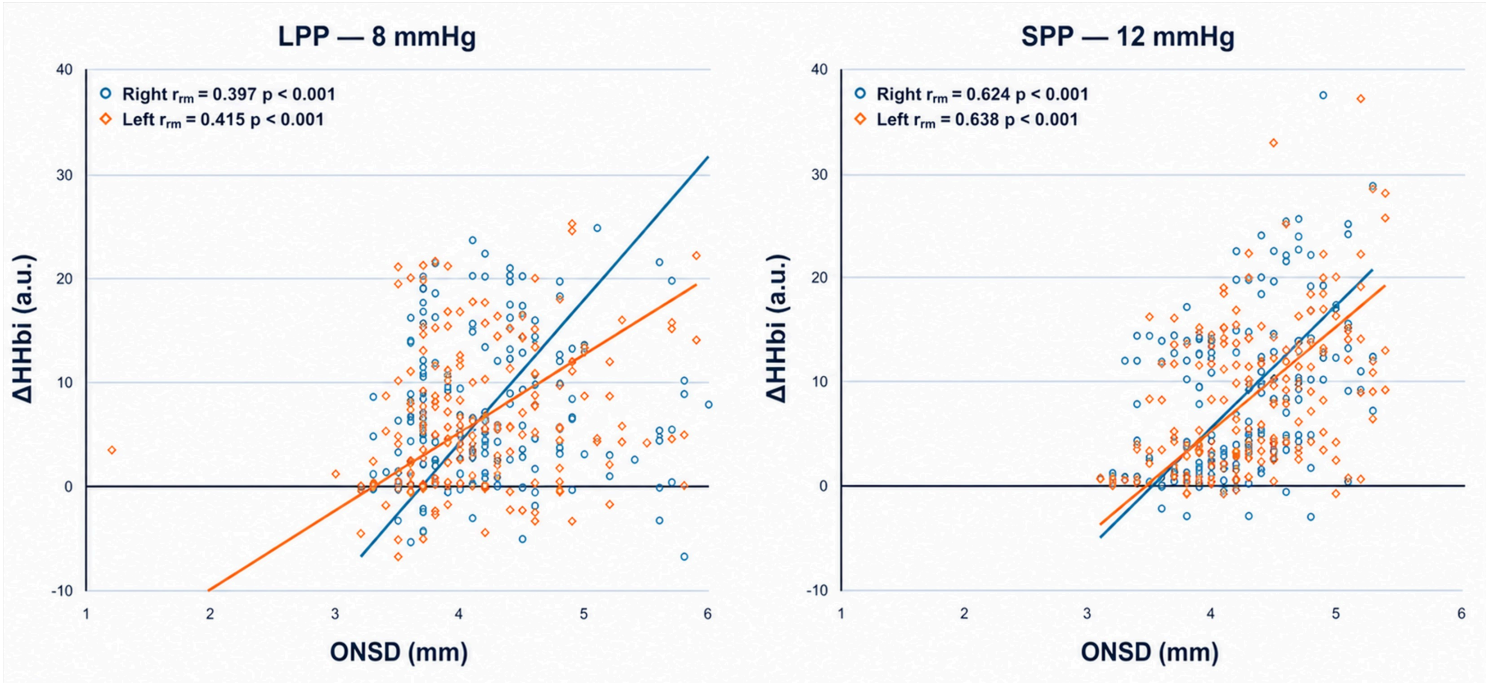


Figure 4

Fig. 3 Repeated-measures correlations between optic nerve sheath diameter (ONSD) and deoxygenated haemoglobin index (ΔHHbi) across intraoperative timepoints (T0–T4), stratified by pneumoperitoneum pressure. Associations are shown separately for the right and left sides. The within-patient association was stronger in the standard-pressure group (SPP, 12 mmHg) than in the low-pressure group (LPP, 8 mmHg). Lines represent repeated-measures correlation fits