

Low Tidal Volume Positive End-Expiratory Pressure versus High Tidal Volume Zero-Positive End-Expiratory Pressure and Postoperative Pulmonary Functions in Robot-Assisted Laparoscopic Radical Prostatectomy

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Significance of the Study

- In this study, patients ventilated with a high V_T and ZEEP were more prone to the unwanted effects of combined sT positioning and pneumoperitoneum compared to patients ventilated with a low V_T and a moderate end-expiratory pressure. The adaptation of a low V_T with moderate PEEP and lung protective ventilation in patients undergoing RALP was a major factor in outcome improvement. This finding could be extended to patients undergoing RALP.

Keywords

Pneumoperitoneum · Steep Trendelenburg · Low tidal volume · Positive end-expiratory pressure · Pulmonary function · Robot-assisted surgery

Abstract

Objective: The aim was to compare the effects of low tidal volume (V_T) and moderate positive end-expiratory pressure (PEEP) with high V_T and zero end-expiratory pressure (ZEEP) on postoperative pulmonary functions and oxygenation in patients undergoing robot-assisted laparoscopic radical prostatectomy. **Subjects and Methods:** Forty-four patients

were randomized into low V_T -PEEP and high V_T -ZEEP groups. The patients were ventilated with a V_T of 6 mL/kg and 8 cm H₂O PEEP in the low V_T -PEEP group and a V_T of 10 mL/kg and 0 cm H₂O PEEP in the high V_T -ZEEP group. Preoperative and postoperative spirometric measurements were done and chest X-rays were evaluated using the radiological atelectasis score (RAS). $p < 0.05$ was considered statistically significant.

Results: The intraoperative and postoperative arterial partial pressure of oxygen and arterial oxygen saturation values were significantly higher in the low V_T -PEEP group than in the high V_T -ZEEP group. At all times, the arterial-to-alveolar oxygenation gradients were significantly lower in the low V_T -PEEP group than in the high V_T -ZEEP group. Preoperative

RAS were similar in both groups, but the postoperative RAS was significantly lower in the low V_T -PEEP group ($p < 0.001$). Forced vital capacity, forced expiratory volume in 1 s, and peak expiratory flow rate recorded postoperatively were significantly lower in the high V_T -ZEEP group ($p < 0.001$). **Conclusions:** Postoperative pulmonary functions were less impaired in patients ventilated with a V_T of 6 mL/kg and 8 cm H₂O PEEP than in patients ventilated with a V_T of 10 mL/kg and ZEEP.

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Introduction

Prostate cancer is the sixth most common cancer in the world and a frequent cause of cancer-related deaths [1]. Radical prostatectomy (RP) is an effective surgical treatment for localized prostate cancer; robot-assisted laparoscopic RP (RALP) is the newest, most minimally invasive and technologically advanced surgical alternative [2]. In the last 10 years, RALP has been the most extensively used procedure for removal of prostate cancer, and the frequency of RALP has increased from 1 to approximately 70% [3, 4]. The advantages of RALP are the easy access to difficult anatomical structures through smaller incisions, decreased blood loss and transfusion requirements, less pain, and the short hospital stay [5]. However, RALP has several problems due to pneumoperitoneum and steep Trendelenburg (sT) positioning [6]. Pneumoperitoneum and sT positioning result in cranial displacement of the diaphragm, reducing the functional residual capacity and compliance and increasing airway resistance and ventilation-perfusion mismatch [7]. Hence, the aim of this study was to compare the effects of low tidal volume (V_T) and moderate positive end-expiratory pressure (PEEP) with high V_T and zero end-expiratory pressure (ZEEP) on postoperative pulmonary functions and oxygenation during prolonged pneumoperitoneum and sT positioning in patients undergoing RALP.

Subjects and Methods

This prospective, observational clinical trial was carried out at the Umraniye Education and Research Hospital, Istanbul, Turkey, between January and November 2011. The Institutional Review Board approved this study, written informed consent was obtained from patients, and this study was conducted in accordance with Declaration of Helsinki including current revisions and Good

Clinical Practice guidelines. A total of 50 consecutive patients with American Society of Anesthesiologists (ASA) physical status I or II undergoing RALP were enrolled into this study. The patients were assigned to either a low V_T -PEEP group or a high V_T -ZEEP group using the sealed-envelope system. Patients in the low V_T -PEEP group were ventilated with a V_T of 6 mL/kg ideal body weight and 8 cm H₂O PEEP, while patients in the high V_T -ZEEP group were ventilated with a V_T of 10 mL/kg ideal body weight and 0 cm H₂O PEEP in group. The exclusion criteria were: cardiovascular and respiratory diseases (forced expiratory volume in 1 s [FEV₁] <50% of the predicted value and forced vital capacity [FVC] <50% of the predicted value), acute asthma exacerbation, obesity (BMI >40), and home oxygen therapy. Fifty-five patients were assessed for eligibility to be included in this study. However, 50 patients gave written informed consent to participate. Four patients were not able to undergo preoperative spirometric testing. Two patients could not undergo postoperative spirometric testing. In total, 44 participants were included in the analysis, i.e., 24 in the low V_T -PEEP group and 20 in the high V_T -ZEEP group. A power analysis showed that 20 patients per group were required for with a power of 80% and a p value of 0.05.

Preoperative spirometric measurements were performed using the standards of the American Thoracic Society with a Microlab 3000 series bedside spirometer (Micro Medical Ltd, Rochester, UK) [8]. All measurements were performed in the supine position with the head elevated 30°. Diet was restricted to only clear liquids 1 day prior to surgery, and ranitidine orally and low-molecular-weight heparin subcutaneously were administered the evening before the surgery. No premedication was given.

In the operating room, electrocardiography, invasive arterial blood pressure, pulse oximetry, bispectral index, end-tidal anesthetic gas, and end-tidal carbon dioxide (ETCO₂) monitorings were performed. Anesthesia was induced intravenously with remifentanyl 1 $\mu\text{g} \cdot \text{kg}^{-1}$, propofol 2–2.5 $\text{mg} \cdot \text{kg}^{-1}$, and rocuronium 0.6 $\text{mg} \cdot \text{kg}^{-1}$. Following endotracheal intubation, anesthesia was maintained with desflurane 4–6% (end-tidal concentration) and remifentanyl 0.1–0.3 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and adjusted to keep BIS values between 40 and 60%. Rocuronium was administered to maintain deep neuromuscular block according to clinical need. The train-of-four ratio was used for neuromuscular block monitoring. A ratio greater than 0.9 was required prior to extubation. Volume-controlled ventilation (Dräger Medical, Lübeck, Germany) was delivered with an inspiratory-to-expiratory time ratio of 1:2 at an inspired oxygen fraction of 0.5. Air was used as a carrier gas. The respiratory rate was adjusted to maintain ETCO₂ between 35 and 40 mm Hg, and plateau pressures were kept lower than 30 cm H₂O. No recruitment maneuvers were performed.

At the end of the surgery, patients were extubated when fully awake. Postoperative intravenous patient-controlled analgesia with morphine chloride was provided. Postoperative pain was evaluated using a numerical rating scale (NRS) of 0–10 as follows: no pain, 0; mild pain, 0–2; milder pain, 3–4; and severe pain, 5–10. Intramuscular diclofenac sodium was administered as a rescue analgesic when the NRS score was ≥ 3 .

Patients were placed on an egg crate mattress that was attached to the bed, and their lower extremities were placed in padded lithotomy stirrups. Shoulder braces covered with foam gel pads were used as additional safety devices to prevent brachial plexus or ulnar nerve injury. Pneumoperitoneum was induced with carbon dioxide, and the intra-abdominal pressure was set at 10–20 mm

Table 1. Patient characteristics and operative data

		Low V _T -PEEP (n = 24)	High V _T -ZEEP (n = 20)	p value
Age, years		62.17 ± 6.54	61.75 ± 4.47	0.59
BMI		28.23 ± 3.35	28.50 ± 4.24	1.0
Duration of the operation, h		3.42 ± 0.21	3.40 ± 0.26	0.78
Duration of the pneumoperitoneum, h		2.66 ± 0.32	2.61 ± 0.43	0.67
Mean arterial pressure, mm Hg	T ₁	80.09 ± 11.10	82.25 ± 8.54	0.28
	T ₂	80.52 ± 10.13	82.25 ± 8.54	0.55
Heart rate, beats/min	T ₁	72.43 ± 10.20	72.25 ± 7.67	0.94
	T ₂	74.35 ± 10.52	76.15 ± 7.30	0.51
AaDO ₂	T ₁	129.12 ± 36.06	155.57 ± 29.58	0.02
	T ₂	123.57 ± 29.58	143.36 ± 26.82	0.03

AaDO₂, arterial-to-alveolar oxygenation gradient; V_T, tidal volume; PEEP, positive end-expiratory pressure; ZEEP, zero end-expiratory pressure; T₁, 60 min after a 40° Trendelenburg position with pneumoperitoneum; T₂, 120 min after a 40° Trendelenburg position with pneumoperitoneum.

Hg, with da Vinci Robot Surgical System (Intuitive Surgical, Sunnyvale, CA, USA). Thereafter, the 40° Trendelenburg position was established. Arterial blood gas analysis was performed preoperatively (T₀), 1 h after a 40° Trendelenburg position with pneumoperitoneum (T₁), 2 h after a 40° Trendelenburg position with pneumoperitoneum (T₂), and 24 h after the operation (T₄). Arterial-to-alveolar oxygenation gradients were calculated 60 min after a 40° Trendelenburg position with pneumoperitoneum (T₁) and 120 min after a 40° Trendelenburg position with pneumoperitoneum (T₂).

The alveolar-to-arterial (A-a) oxygen gradient was the difference between the amount of the oxygen in the alveoli (i.e., the alveolar oxygen tension [PAO₂]), and the amount of oxygen dissolved in plasma (PaO₂) was calculated as: A-a oxygen gradient = PAO₂ - PaO₂.

PaO₂ was measured by arterial blood gas, while PAO₂ was calculated using the alveolar gas equation: PAO₂ = (FiO₂ × [P_{atm} - P_{H₂O}]) - (PaCO₂/R), where FiO₂ is the fraction of inspired oxygen, P_{atm} is the atmospheric pressure, P_{H₂O} is the partial pressure of water, PaCO₂ is the arterial carbon dioxide tension, and R is the respiratory quotient.

At the 24th hour of surgery, chest X-ray and spirometric testing were repeated. Spirometric testing was only performed if NRS scores at rest were lower than 3. If not, the pain was relieved before spirometric measurements. Three measurements of FVC, FEV₁, and peak expiratory flow rate (PEF) were done, and the highest values were taken into consideration for statistical analysis.

Pre- and postoperative chest X-rays were evaluated using the radiological atelectasis score (RAS) [9] (with a 5-point scale) by a single radiologist who was blinded to this study as follows: clear lung fields, 0; plate-like atelectasis or slight infiltration, 1; partial atelectasis, 2; lobar atelectasis, 3; and bilateral atelectasis, 4.

Statistical Analysis

Statistical analysis was performed using MedCalc Statistical Software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium; <http://www.medcalc.org>). The normality of continuous

variables was investigated using the Shapiro-Wilk test. Descriptive statistics are presented as means ± SD for normally distributed variables and medians (IQR) (25th to 75th percentile) for nonnormally distributed variables. Student's *t* test was used for comparisons of 2 normally distributed groups. Nonparametric statistical methods were used for values with a skewed distribution. For comparison of 2 nonnormally distributed groups, the Mann-Whitney U test was used. Dependent and nonnormally distributed continuous variables were analyzed using the Wilcoxon signed-rank test. *p* < 0.05 was considered statistically significant.

Results

All operations were performed without complications and without conversion to an open technique. The baseline characteristics of the patients and the operative data are presented in Table 1. There were no significant differences between the 2 groups in terms of patient characteristics or hemodynamic variables. Overall the pneumoperitoneum duration was 2.66 ± 0.32 h in the low V_T-ZEEP group and 2.61 ± 0.43 h in the high V_T-PEEP group. At all times, the arterial-to-alveolar oxygenation gradients were significantly lower in the low V_T-PEEP group than in the high V_T-ZEEP group (*p* = 0.02 and *p* = 0.03, respectively). Intraoperative and postoperative PaO₂ and SaO₂ values were significantly higher in the low V_T-PEEP group than in the high V_T-ZEEP group (Table 2).

A comparison of the spirometric measurements is presented in Table 3. The preoperative FVC, FEV₁, and PEF values were similar between the 2 groups (i.e., 92.5 vs. 91;

Table 2. Arterial blood gases of the patients

		Low V _T -PEEP (n = 24)	High V _T -ZEEP (n = 20)	p value
pH	T ₀	7.38±0.03	7.37±0.03	0.85
	T ₁	7.25±0.04	7.25±0.03	1.0
	T ₂	7.25±0.03	7.23±0.05	0.93
	T ₃	7.33±0.05	7.32±0.03	0.78
	T ₄	7.38±0.05	7.38±0.04	1.0
PaCO ₂ , mm Hg	T ₀	36.17±3.14	36.88±2.88	0.21
	T ₁	48.04±4.92	49.96±3.51	0.07
	T ₂	49.35±4.82	52.98±8.22	0.06
	T ₃	37.55±5.58	38.41±4.38	0.28
	T ₄	35.62±3.94	36.52±3.68	0.21
PaO ₂ , mm Hg	T ₀	89.68±14.97	82.37±8.82	0.97
	T ₁	179.33±33.94	150.97±34.27	0.009
	T ₂	184.88±30.45	160.15±27.34	0.008
	T ₃	85.01±16.89	70.62±11.70	0.003
	T ₄	77.68±16.86	65.09±15.21	0.014
HCO ₃ , meq/L	T ₀	22.12±1.70	21.60±1.74	0.83
	T ₁	19.73±1.87	19.96±1.39	0.32
	T ₂	19.70±1.64	19.67±1.68	0.52
	T ₃	19.79±1.85	19.91±1.67	0.41
	T ₄	22.08±2.11	22.34±2.54	0.35
BE	T ₀	-2.80±2.06	-3.35±2.28	0.79
	T ₁	-5.35±3.27	-5.34±1.83	0.49
	T ₂	-6.00±2.33	-5.36±3.03	0.21
	T ₃	-5.67±2.46	-5.39±2.20	0.34
	T ₄	-2.40±3.01	-2.50±3.26	0.54
SaO ₂ , %	T ₀	97.54±1.08	97.03±1.13	0.93
	T ₁	99.29±0.45	98.67±0.64	0.001
	T ₂	99.25±0.62	98.78±0.60	0.016
	T ₃	96.47±2.04	93.77±3.47	0.007
	T ₄	96.12±2.33	93.71±2.62	0.003

pH, potential of hydrogen; PaCO₂, arterial carbon dioxide pressure; PaO₂, arterial oxygen pressure; HCO₃, bicarbonate; BE, base excess; SaO₂, arterial oxygen saturation; T₀, preoperative; T₁, 60 min after a 40° Trendelenburg position with pneumoperitoneum; T₂, 120 min after a 40° Trendelenburg position with pneumoperitoneum; T₃, 2 h after the operation; T₄, 24 h after the operation.

99 vs. 98.5; and 93.5 vs. 91.5, respectively). A significant reduction in FVC, FEV₁, and PEF was recorded postoperatively in both groups ($p < 0.001$). However, postoperative FVC, FEV₁, and PEF values were significantly lower in the high V_T-ZEEP group than in the low V_T-PEEP group ($p < 0.001$).

The pain significantly decreased over time in all groups after surgery. NRS scores and morphine consumption were similar between the 2 groups (Table 4).

Preoperative RAS were similar in both groups, but the postoperative RAS was significantly lower in the low V_T-PEEP group than in the high V_T-ZEEP group ($p < 0.001$) (Table 5).

Discussion

In this RALP study, postoperative pulmonary functions were less impaired in patients ventilated with 6 mL/kg V_T and 8 cm H₂O PEEP than in those ventilated with 10 mL/kg V_T and ZEEP. No patient experienced intraoperative respiratory complications, but intraoperative oxygenation was significantly reduced in patients ventilated with a high V_T-ZEEP than in those with a low V_T-PEEP and there were no differences in ETCO₂, PAP, or hemodynamic parameters. In the postoperative period, although significant reductions in FVC, FEV₁, PEF, and partial arterial oxygen concentrations were observed in both groups, the reductions were smaller in the low V_T-PEEP group compared to the high V_T-ZEEP group.

In this study, the PaO₂ and SaO₂ values of the patients were significantly lower in the high V_T-ZEEP group compared to the low V_T-PEEP group, whereas the intraoperative A-a (DO₂) was lower in the low V_T-PEEP group. Intraoperative oxygenation was significantly reduced in patients ventilated with a high V_T-ZEEP than those with a low V_T-PEEP. The significance remained constant during the first 24 h. These results favor the use of 6 mL/kg V_T and 8 cm H₂O PEEP during RALP. There is some evidence for the benefits of intraoperative lung protective ventilation both in thoracic and in major abdominal [9–13] and laparoscopic surgeries [14]. The major difference in RALP versus other laparoscopic surgeries is the sT positioning. Pulmonary pathophysiological effects of sT positioning together with pneumoperitoneum include further decreases in functional residual capacity, compliance, and vital capacity resulting in an altered gas exchange. Prevention of these unwanted effects requires intraoperative use of PEEP. The recommended PEEP level remains over 5 cm H₂O in patients undergoing laparoscopic surgery [15], but the optimal level of PEEP has not yet been determined in the sT position by earlier studies. According to our study, 8 cm H₂O might be the optimal level of PEEP for patients undergoing laparoscopic surgery with sT positioning.

Although the PaO₂ decreased significantly in the postoperative period in both groups, at the 24th h it returned to preanesthetic values in the low V_T-PEEP group, indicating the benefits of moderate PEEP. Even though patients in the low V_T-PEEP group had fewer decreases in

Table 3. Comparison of spirometric measurements

		Low V _T -PEEP (n = 24)	High V _T -ZEEP (n = 20)	p value
FVC	preoperative	92.5 (86–97)	91 (87.75–94.5)	0.500
	postoperative	64 (57–68)	51 (45.75–54)	<0.001
	p	<0.001	0.001	
FEV ₁	preoperative	99 (97–103)	98.5 (96.25–103.75)	0.849
	postoperative	70 (67.25–77.75)	54.5 (44.25–57)	<0.001
	p	<0.001	0.001	
PEF	preoperative	93.5 (90–96.5)	91.5 (87.5–98.5)	0.768
	postoperative	65.5 (60–70)	44.5 (40.5–47.75)	<0.001
	p	<0.001	<0.001	

Values are medians and IQR (25th to 75th percentiles) unless otherwise stated. V_T, tidal volume; PEEP, positive end-expiratory pressure; ZEEP, zero end-expiratory pressure; FVC, forced vital capacity; FEV₁, forced expiratory volume in 1 s; PEF, peak expiratory flow rate.

Table 4. NRS scores and total morphine consumption

	NRS score at 2 h	NRS score at 6 h	NRS score at 18 h	NRS score at 24 h	Total morphine consumption, mg
Low V _T -PEEP (n = 24)	2 (2–3)	2 (2–3)	1 (1–3)	1 (0–2)	20 (18–25)
High V _T -ZEEP (n = 20)	2 (1–3)	2 (1–2)	1 (0–2)	1 (0–2)	20 (17–26.25)
p	0.948	0.932	0.804	0.663	0.804

Values are presented as medians (range) unless otherwise stated. NRS, numerical rating scale; V_T, tidal volume; PEEP, positive end-expiratory pressure; ZEEP, zero end-expiratory pressure.

PaO₂, the decreases in the postoperative PaO₂ in both groups should remind us that PEEP alone did not have a long-lasting effect. Thus, application of PEEP or CPAP after surgery might be an alternative approach to preventing decreases in postoperative oxygenation [13, 16].

Pulmonary function testing is valuable in predicting postoperative pulmonary complications, especially atelectasis [17]. FVC, FEV₁, and PEF were significantly decreased in the postoperative period in both groups, but the values measured were in the normal ranges in the low V_T-PEEP group. The decreases in FVC, FEV₁, and PEF were significantly lower in the low V_T-PEEP group compared to the high V_T-ZEEP group, emphasizing the benefit of PEEP application in the intraoperative period of RALP. Kilic et al. [18] stated that postoperative vital capacity and FEV₁ values were reduced in patients without COPD, returning to normal levels only after 5 days. In our patients, we measured pulmonary functions at the 24th postoperative hour.

Table 5. Comparison of RAS between groups

	Preoperative RAS	D ₁ RAS
Low V _T -PEEP (n = 24)	0 (0–1)	1 (1–2)
High V _T -ZEEP (n = 20)	0.5 (0–1)	3 (2–3)
p	0.989	<0.001

Values are presented as medians (range) unless otherwise stated. RAS, radiological atelectasis score; D₁, day 1; V_T, tidal volume; PEEP, positive end-expiratory pressure; ZEEP, zero end-expiratory pressure.

The limitations of this study included that: we did not measure the intraoperative functional residual capacity and compliance; we did not ensure that atelectasis was not underdiagnosed on the chest X-ray; the postoperative evaluation of pulmonary functions was limited to the first 24 h.

Conclusion

In this study, patients ventilated with a high V_T and ZEEP were more prone to the unwanted effects of combined sT positioning and pneumoperitoneum in RALP compared to patients ventilated with a low V_T and moderate PEEP.

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Disclosure Statement

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