

Comparison of Robot-assisted Versus Conventional Laparoscope on Incidence and Risk Factors of Postoperative Delirium for Patients undergoing radical prostatectomy: A single-center Retrospective Analysis

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Abstract

Background: Robot-assisted laparoscopic radical prostatectomy (RALRP) has better effects than conventional laparoscopic radical prostatectomy (LRP). However, there were few research focus on the incidence and risk factors of postoperative delirium for patients with different procedures.

Methods: Eighty-one cases of RLRP patients (group RALRP) and 71 cases of LRP patients (group LRP) under general anesthesia were collected from anesthesia information system from June 2013 to December 2019. Comparison of the time of preparation period before surgery (T_p), time of operation (T_o), time of anesthesia maintenance (T_a), time of anesthesia recovery (time from cessation of intravenous anesthetic to endotracheal extubation, T_r), time of endotracheal extubation (time from endotracheal extubation to discharge from post-anesthesia care unit, T_e), dosage of anesthetic (propofol, sufentanil, remifentanil), P_aCO_2 , plasma lactate level and airway pressure at different points (before pneumoperitoneum, post-pneumoperitoneum, after loosening pneumoperitoneum), the incidences of postoperative delirium and utilization of mannitol, IAP, dosage of vasoactive agents (ephedrine, methoxamine and atropine), fluid infusion volume, blood transfusion volume, blood loss, postoperative hospitalization time (T_h) and overall cost.

Results: The incidences of postoperative delirium and utilization of mannitol in group RALRP and LRP were (17.3% VS 32.4%, $P=0.03$; 7.4% VS 21.1%, $P=0.014$), T_r was (31.52 ± 9.89 VS 38.65 ± 16.32 min; $P=0.01$, 95% CI 2.72-11.54), IAP was (12.72 ± 1.87 VS 13.37 ± 1.12 mmHg; $P=0.01$, 95% CI 0.16-1.14), $PaCO_2$ at post-pneumoperitoneum and after loosening pneumoperitoneum were (47.89 ± 10.89 VS 38.65 ± 16.32 mmHg; $P < 0.001$, 95% CI 6.47-11.98; 40.77 ± 5.34 VS 43.57 ± 4.54 mmHg; $P=0.001$, 95% CI 1.17-4.37), the difference was statistically significant. T_p , T_o , T_a and overall cost of patients in the RLRP group were significantly longer than those in the LRP group ($P < 0.02$). No statistical difference was found in other observation variables. The incidence of postoperative delirium was considered as the dependent variable for binary logistic regression analysis. The result showed the incidence of postoperative delirium increased 1.17 times (95% CI 1.06-1.17), 1.13 times (95% CI 1.03-1.24), and 1.66 times (95% CI 1.02-2.70) for each unit increase in T_r , post-pneumoperitoneum $PaCO_2$ and IAP.

Conclusion: Compared with group LRP, patients in group RALRP had lower IAP, lower incidence of postoperative delirium and shorter recovery time, but the overall cost was higher. IAP is the main factor affecting the incidence of postoperative delirium.

Background

Today, robots pervade all aspects of our lives and industries, including, of course, healthcare. Da Vinci assisted laparoscopic system is widely used in radical prostatectomy. Previous Study has shown that compared with open surgery and laparoscopic radical prostatectomy, RALRP has fewer postoperative complications and can be safely used for radical prostatectomy [1]. However, in both RALRP and LRP group, patients need to be in CO_2 pneumoperitoneum and placed in Trendelenburg (ST) position to

provide effective operating space, which has a great influence on the physiology of patients during operation and may affect the incidence of postoperative delirium.

CO₂ pneumoperitoneum can promote the inflammatory response during surgery[2], which affects the patient's outcomes. At the same time, this effect varies with the change of intra-abdominal pressure(IAP) [3]. RALRP is similar to LRP, but the difference between the two procedures is that RALRP uses a computer to precisely control the robotic arm, the operation is more accurate and precise, and it can provide a better surgical field of vision and three-dimensional anatomical structure for the surgeon. Therefore, compared with LRP, RALRP requires shorter operation time, lower IAP, and have less impact on patients during operation, and patients recover faster. At present, there is few study in this field. Therefore, we carried out this retrospective study to compare the effects of these two different procedures on operation time, IAP, partial pressure of arterial CO₂ (P_aCO₂), postoperative outcomes and the incidence of postoperative delirium, and explored the risk factors for postoperative delirium.

Methods

Patients and groups

This study is a retrospective study, **approved by the General Hospital of Southern Theater command and registered with the China Clinical Trial Center with registration number: ChiCTR1900026479. All patients were not required to sign informed consent.** 152 patients undergoing radical prostatectomy performed in the Department of Anesthesiology of General Hospital of Central Theater Command from June 2013 to December 2019 were included. Overall cohort were divided into two group according to the surgical method they received,, 81 cases were included in the group RALRPand 71 cases were included in the group LRP,

Inclusion criteria: The anaesthesia documents was recorded in detail, including airway pressure, P_aCO₂ before pneumoperitoneum, post-pneumoperitoneum, and after loosening pneumoperitoneum. All surgical procedure were performed by the one surgeon. Exclusion criteria: Patients with heart, lung, liver, kidney, respiratory insufficiency, disturbance of consciousness, preoperative MMSE less than 27 points, or converted to open surgery during operation.

Measurements

Demographic variables(age, height, weight, ASA classification, blood pressure, heart rate), the time of preparation for surgery(T_p), time of operation(T_o), time of anesthesia maintenance (T_a), time of anesthesia recovery(time from cessation of intravenous anesthetic to endotracheal extubation, T_r), time of endotracheal extubation(time from endotracheal extubation to discharge from post-anesthesia care unit, T_e), dosage of anesthetic (propofol, sufentanil, remifentanil), P_aCO₂, plasma lactate level and airway pressure at different points (before pneumoperitoneum, post-pneumoperitoneum, after loosening pneumoperitoneum), the incidences of postoperative delirium and utilization of mannitol, IAP, dosage of

vasoactive agents (ephedrine, methoxamine and atropine), fluid infusion volume, blood transfusion volume, blood loss, time of postoperative hospitalization (T_h) and overall cost were recorded.

Methods of anesthesia

In the operating room, all patients were routinely monitored for electrocardiogram (ECG), pulse oxygen saturation (SpO_2), noninvasive blood pressure and partial pressure of end tidal carbon dioxide ($PetCO_2$). Open upper extremity vein for intraoperative infusion. A radial artery cannula was inserted under local anesthesia to monitor blood pressure directly and for arterial blood gas analysis. Nasopharyngeal temperature was monitored by nasal temperature probe. Neuromuscular function was measured using a TOF-Watch acceleromyograph. All patients were induced with etomidate 0.3 mg/kg, sufentanil 0.5 μ g/kg and rocuronium 0.9 mg/kg. When TOF ratio was at 0, intubation is performed. After intubation, ventilation was performed to maintain P_aCO_2 between 35 and 45 mmHg. General anesthesia was maintained with propofol, remifentanil and rocuronium. vasoactive drugs (ephedrine 5 mg or methoxy 0.5-1 mg) were administered when blood pressure was below basic 20%, and atropine 0.5 mg was administered when heart rate was below 45 beats/min. when the heart rate was higher than 100 beats/minutes, 5 mg of esmolol was administered, and when systolic blood pressure was more than 180 mmHg, peridipine 0.2–0.5 mg were administered. When hemoglobin was lower than 70 g/L, suspended red blood cells was infused. Stop the infusion of propofol 15 minutes before the end of the operation, and reduce the rate of remifentanil infusion. When the operation was over, stop the infusion of remifentanil, give patients dorastron 12.5 mg to prevent vomiting, 40 mg parecoxib sodium to relieve pain. Tracheal catheter was removed when the patient was conscious, spontaneous respiration recovered, TOF value > 90%, SpO_2 > 95%. After endotracheal extubation, the patients were continued to be monitored until they were fully conscious, able to cooperative, and vital signs were stable. If postoperative delirium was found, mannitol was given to dehydrate, or sedated with propofol.

Surgical Procedure

After general anesthesia, the patients were kept in the prone position, pneumoperitoneum was induced with CO₂ insufflation of 15 mmHg. Following the

insertion of trocars, an IAP of 8 mmHg was set from the previous 15 mmHg, and a remote control was used to place the patients in a ST position, and IAP was gradually increased until the surgeon was satisfied with the surgical space. The IAP was recorded.

Statistical analysis

Statistical analysis was performed using SPSS version 25.0. Measurement data are described as mean \pm standard deviation. Demographic variables, T_p , T_o , T_a , T_r , T_e , dosage of anesthetic (propofol, sufentanil, remifentanil), IAP, dosage of vasoactive drugs (ephedrine, methoxamine and atropine), infusion volume, blood transfusion volume, blood loss, T_h and overall cost were compared using unpaired Student *t* tests. P_aCO_2 , lactic acid value and airway pressure at different points are repeated measurement data, using repetitive measure analysis of variance. The incidence of postoperative delirium and utilization of

mannitol, and ASA scores are count data, using chi-square test. Binary logistic regression analysis was performed with postoperative delirium as the dependent variable, T_a , T_r , T_e , P_aCO_2 , and IAP as independent variables, to explore the risk factors for postoperative delirium. A P value < 0.05 was considered statistically significant.

Results

A total of 152 patients were assessed for eligibility. Demographic variables (age, weight, height, ASA grading, blood pressure and heart rate) of patients in the two groups showed no significant difference (Table 1).

Table 1
patients characteristics

	RALRP group	LRP group	statistics	P values	95% CI
sample	81	71			
age (yr)	67.56 \pm 6.82	68.85 \pm 6.37	1.20	0.232	-0.84–3.81
weight (kg)	68.04 \pm 10.13	66.68 \pm 9.06	0.86	0.389	-4.45–1.74
height (cm)	169.78 \pm 5.56	168.97 \pm 4.95	0.94	0.350	-2.50–0.89
ASA scores n(%)	28(34.6%)	31(43.7%)	1.32	0.251	
□	53(65.4%)	40(56.3%)			
□					
systolic pressure(mmHg)	146.59 \pm 17.03	142.85 \pm 18.93	1.29	0.201	-9.51–2.02
diastolic pressure(mmHg)	81.51 \pm 8.09	79.62 \pm 9.37	1.33	0.185	-4.68–0.91
heart rate (beats/min)	73.46 \pm 10.85	74.62 \pm 11.85	0.63	0.529	-2.48–4.80

T_p , T_o and T_a in group RALRP were significantly longer than those in group LRP; T_r was significantly shorter than that in group LRP; There was no statistical difference between T_e and T_h (Table 2).

Table 2
 Comparison of T_p , T_o , T_a , T_r , T_e , and T_h between two groups

	RALRP group	LRP group	statistics	P value	95% CI
sample	81	71			
T_p	39.10 ± 6.34	32.15 ± 6.95	6.44	<0.001	4.81–9.07
T_o	235.58 ± 38.21	216.82 ± 39.50	2.97	0.003	6.29–31.23
T_a	280.89 ± 41.55	264.56 ± 42.10	2.40	0.018	2.90–29.75
T_r	31.52 ± 9.89	38.65 ± 16.32	3.20	0.002	2.72–11.54
T_e	30.65 ± 10.07	32.37 ± 11.50	0.98	0.329	-1.74–5.17
T_h	13.11 ± 6.34	14.52 ± 8.07	1.21	0.230	-0.90–3.72

The dosage of propofol and remifentanyl in the group RALRP were higher than those in the group LRP; IAP was lower than that in the group LRP; overall cost was higher than that in group LRP. The incidence of delirium and utilization of mannitol were lower than those in group LRP. There was no significant difference in dosage of sufentanil, vasoactive agents, fluid infusion volume, blood transfusion volume, and blood loss (Table 3).

Table 3
Intraoperative and Postoperative Observation Indexes

	RALRP group	LRP group	statistics	<i>P</i> value	95% <i>CI</i>
sample	81	71			
propofol(g)	1.37 ± 0.27	1.26 ± 0.30	2.35	0.020	0.02–0.20
remifentanil(mg)	5.30 ± 1.10	4.68 ± 1.03	3.58	<0.001	0.28–0.97
sulfentanyl(μg)	49.51 ± 10.74	46.69 ± 10.79	1.61	0.110	-6.27–0.64
Vasoactive drugs	1.88 ± 3.33	2.13 ± 3.36	0.46	0.646	-0.82–1.32
ephedrine(mg)	0.06 ± 0.30	0.08 ± 0.25	0.35	0.727	-0.07–0.10
methoxamine(mg)	0.21 ± 0.28	0.28 ± 0.64	0.91	0.364	-0.08–0.23
atropine(mg)					
IAP(mmHg)	12.72 ± 1.87	13.37 ± 1.12	2.63	0.010	0.16–1.14
incidence of delirium(%)	14(17.3%)	23(32.4%)	4.69	0.030	
incidence of utilization of mannitol(%)	6(7.4%)	15(21.1%)	5.98	0.014	
Overall cost(Ten thousand RMB)	8.29 ± 5.55	5.18 ± 1.51	4.57	<0.001	1.77–4.45
infusion volume(ml)	2286.05 ± 581.44	2143.61 ± 473.44	1.65	0.10	-314.91–28.02
blood transfusion volum(ml)	51.85 ± 230.37	25.35 ± 87.37	0.91	0.362	-83.82–30.82
blood loss(ml)	183.33 ± 109.26	203.5 ± 123.15	1.07	0.286	-17.06–57.43

There was statistically significant difference of P_aCO_2 between groups; P_aCO_2 at time points of post-pneumoperitoneum and after loosening pneumoperitoneum in group RALRP was lower than that in group LRP (Fig. 1). There was no statistically difference of plasma lactate concentration between two groups, but there was statistically significant difference of plasma lactate concentration within groups and the change of that in group RALRP was smaller than that in group LRP(Fig. 2). There was no statistically difference of airway pressure between groups, but there was statistically significant difference of airway pressure within groups and the change of airway pressure in group RALRP was smaller than that in group LRP(Fig. 3).

Binary logistic regression analysis was performed with postoperative delirium as the dependent variable, T_a , T_r , T_e , P_aCO_2 (Pp, Alp), and IAP as independent variables. Using the Enter method, $P < 0.05$ was entered into the equation and $P > 0.1$ was removed from the equation. The results showed that T_r , $PaCO_2$ (Pp) and IAP were entered into the equation and the formula was obtained as follows: $\text{Logit}(P) = -18.55 + 0.11 \times T_r + 0.12 \times PaCO_2(Pp) + 0.50 \times IAP$. The result showed the incidence of postoperative delirium increased 1.17 times (95% CI/1.06–1.17), 1.13 times (95% CI/1.03–1.24), and 1.66 times (95% CI/1.02–2.70) for each unit increase in T_r , $PaCO_2(Pp)$ and IAP. With the prediction probability 0.5 as the cut-off point, the sensitivity of judging the incidence of postoperative delirium was 67.6%, the specificity was 95.7%, and the total correct rate was 88.8% (Table 4,5).

Table 4
The results of binary logistic regression

	<i>B</i>	<i>SE</i>	<i>Wald</i>	<i>P</i>	<i>OR</i>	<i>95% CI</i>
T_r	0.11	0.03	19.90	<0.001	1.12	1.06–1.17
$PaCO_2(Pp)$	0.12	0.05	6.49	0.011	1.13	1.03–1.24
IAP	0.50	0.25	4.07	0.044	1.66	1.02–2.70

Table 5
Model classification table with the prediction probability 0.5 as the cut-off point

		delirium		
Observed		NO	YES	Correct percentage(%)
delirium	NO	110	5	95.7
	YES	12	25	67.6
Overall Percentage(%)				88.8

Discussion

tumor of prostate is the one of most common disease in elderly patients over 60 years[5]. Open radical prostatectomy has been the reference standard for treatment of prostate cancer. Recently, surgical approaches to prostate cancer treatment have been replaced by minimally invasive techniques such as LRP and RALP[6]. Previous study has shown RALRP improves clinical effect comparing with open radical prostatectomy and LRP, the time of operation of RALRP was longer than that of LRP from 2000 to 2005, but the time of operation of RALRP was shorter than that of LRP from 2014 to 2016[1]. Meanwhile, our study found that the T_p , T_o , T_a of RALRP was significantly longer than that of LRP, which may be related to the surgical skill of the surgeon. Because our hospital started using Da Vinci surgical operating system

for RALRP only in September 2017, and surgeon have more than ten years of experience with hundreds of LRP operations, that may help to explain why the dosage of propofol and remifentanyl were higher in the group RALRP than that in the group LRP.

A study has shown that the incidence of postoperative delirium in robotic assisted esophageal surgery was about 30%, significantly lower than that in open surgery [8]. Our study found that the incidence of postoperative delirium in the group RALRP was 17.3%, which may be due to the need for single lung ventilation during esophageal surgery, which could increase the incidence of postoperative delirium. Meanwhile, our study showed that the incidence of postoperative delirium in group LRP was 32.4% significantly higher than that in group RALRP (17.3%). T_r in group RALRP and LRP was 31.52 ± 9.89 and 38.65 ± 16.32 min, respectively, which indicated that RALRP could significantly reduce the incidence of postoperative delirium and recovery time.

Similar to LRP, RALRP requires insufflation of the abdomen with carbon dioxide (CO₂) pneumoperitoneum and the steep Trendelenburg (ST) position to create an optimal surgical space, which are associated with a number of problems, including hypercapnia, brain edema and other complications. These complications affected the postoperative recovery and increase the incidence of postoperative delirium [9]. Rapid infusion and absorption of CO₂ and high pressure pneumoperitoneum increased intraabdominal pressure, led to internal and external organs ischemia, increased postoperative pain, and resulted in many physiological disorders [10]. Meanwhile, CO₂ harmed organs by promoting oxidative stress and inflammatory response [2]. Studies have shown that the incidence of postoperative delirium and cognitive dysfunction may be related to the inflammatory response of the central nervous system [15, 16]. Reducing IAP and P_aCO₂ could reverse this adverse effect [3]. Trendelenburg position could aggravate the mentioned adverse effect and change the intracranial hemodynamics subsequently increased intracranial pressure. Our study has found that post-pneumoperitoneum PaCO₂ and IAP in group RALRP were significantly lower than those in group LRP, which may be the explanation for the lower incidence of postoperative delirium and the short recovery time in group RALRP. Zhou [9] et al. showed that a small dose of mannitol can effectively improve cerebral oxygen metabolism and protect cognitive function after the operation. The author works in the same department as Zhou's. When patients had severe delirium after surgery, we first gave them a small dose of mannitol. We also sedated patients with propofol and gradually removed the endotracheal tube after the delirium remission. T_r in the group RALRP was significantly lower than that in the group LRP, which was associated with the low incidence of postoperative delirium in the group RALRP. However, there was no difference of T_e between RALRP and LRP, mainly because all patients were removed trachea tube with completely awake and without delirium. Meanwhile, the patients left the post-anesthesia care unit with the same standards, the vital signs of patients after endotracheal extubation were similar, and the dosage of vasoactive drugs in the two groups were similar.

There are many factors affecting delirium after surgery, and pain is one of the factors [18]. Studies have shown that low IAP can reduce pain in patients during laparoscopic surgery [19–21]. Our study found

that the IAP of patients in the group RALRP was significantly lower than that in the group LRP (12.72 ± 1.87 VS 13.37 ± 1.12 mmHg, $P < 0.05$), so the patients in group RALRP suffered less postoperative pain, resulting lower incidence of operative delirium. Meanwhile, through binary logistic regression analysis, our study found that each unit of IAP increased the postoperative delirium rate by 1.66 times.

RALRP is similar to LRP, surgeon need to use CO₂ to provide effective operating space. But the difference between the two procedures is that the computerized electromechanical controls give the surgeon much more precision and stability for the dissection of critical structures, and the console has tridimensional vision, which provides depth of field and helps immensely with regard to orientation and surgical precision[4]. Therefore, compared with LRP, RALRP needs a lower IAP to satisfy the surgeon's requirements for surgical space, which is the reason for why IAP in the group RALRP was significantly lower than in the group LRP. Our study did not find differences in postoperative hospital stay and blood loss between the two groups, which was different from other studies [1, 22]. The overall cost of patients in the RALRP group is higher than that in the LRP group, which may hinder the development of RALRP in China.

Conclusion

Our retrospective study showed that IAP was the most important factor affecting the incidence of postoperative delirium, and controlling IAP may help reduce the incidence of postoperative delirium. However, the underlying mechanism was not clear and needed to be discussed in future studies. In summary, compared with group LRP, patients in group RALRP had lower IAP, lower incidence of postoperative delirium and shorter recovery time, but the overall cost was higher.

Abbreviations

RALRP: Robot-assisted Laparoscopic Radical Prostatectomy

LRP: Laparoscopic Radical Prostatectomy

P_aCO₂: Partial Pressure of Arterial CO₂

IAP: Intra-abdominal Pressure

MMSE: Mini-mental State Exam

ASA: American Society of Anesthesiology

TOF: Train of Four Stimulation

Declarations

– Ethics approval and consent to participate

This study was approved by the General Hospital of Southern Theater command and written informed consent was obtained before study from all patients.

– Consent for publication

Not applicable

– Availability of data and material

The data used and/or analyzed during the current study are available from the corresponding author on reasonable request.

–Competing interests

The authors declare that they have no competing interests.

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–Authors' contributions

HGJ and XB contributions to study conception and design, data analysis and interpretation, and preparation of the manuscript. SWD, XMD, LBX and LL participated in data collection and analysis. All authors read and approved the final manuscript.

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Not applicable

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Figures

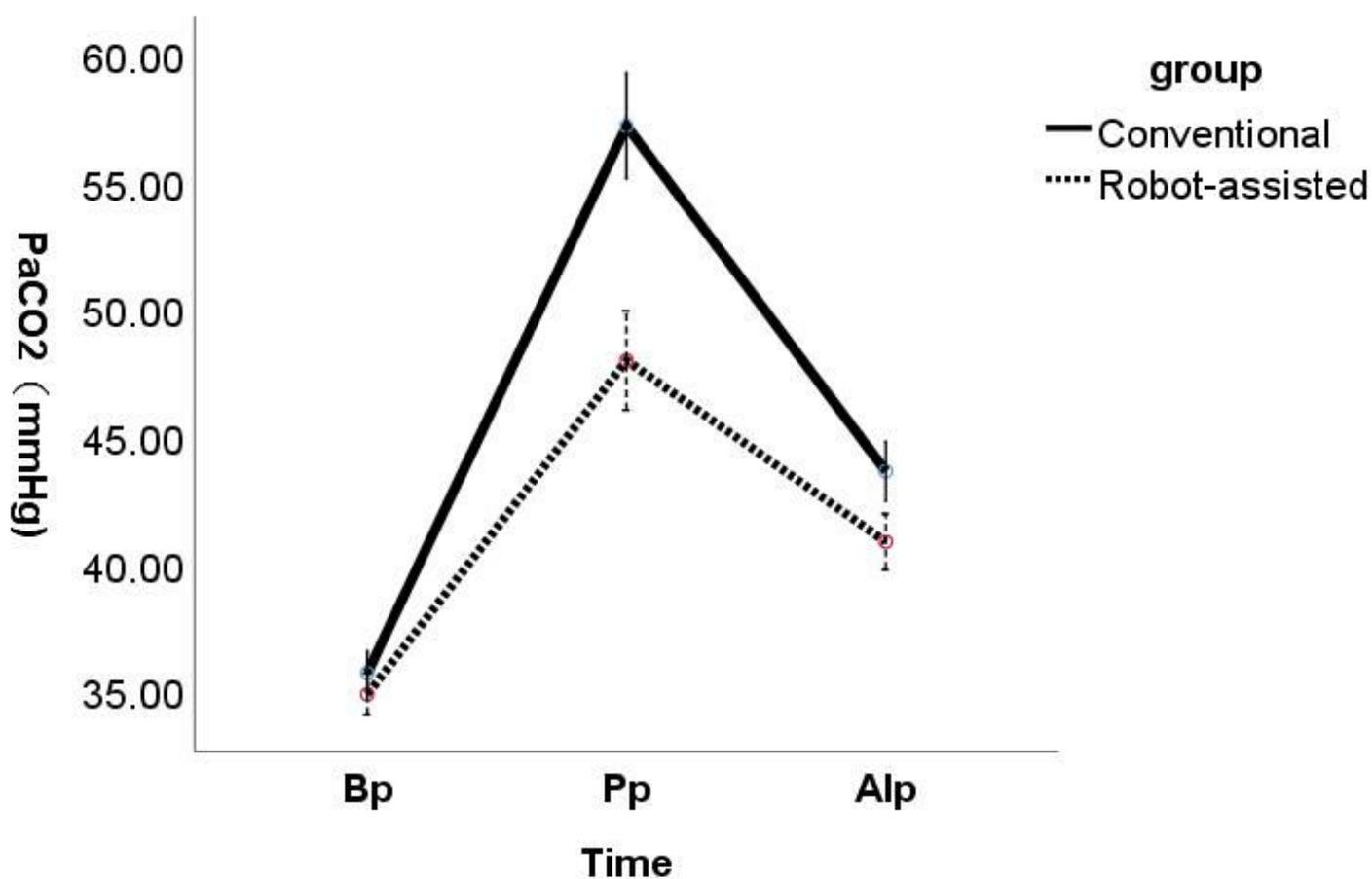


Figure 1

PaCO₂ at different time points in the two groups Bp = before pneumoperitoneum, PP = post-pneumoperitoneum, Alp = after loosening pneumoperitoneum

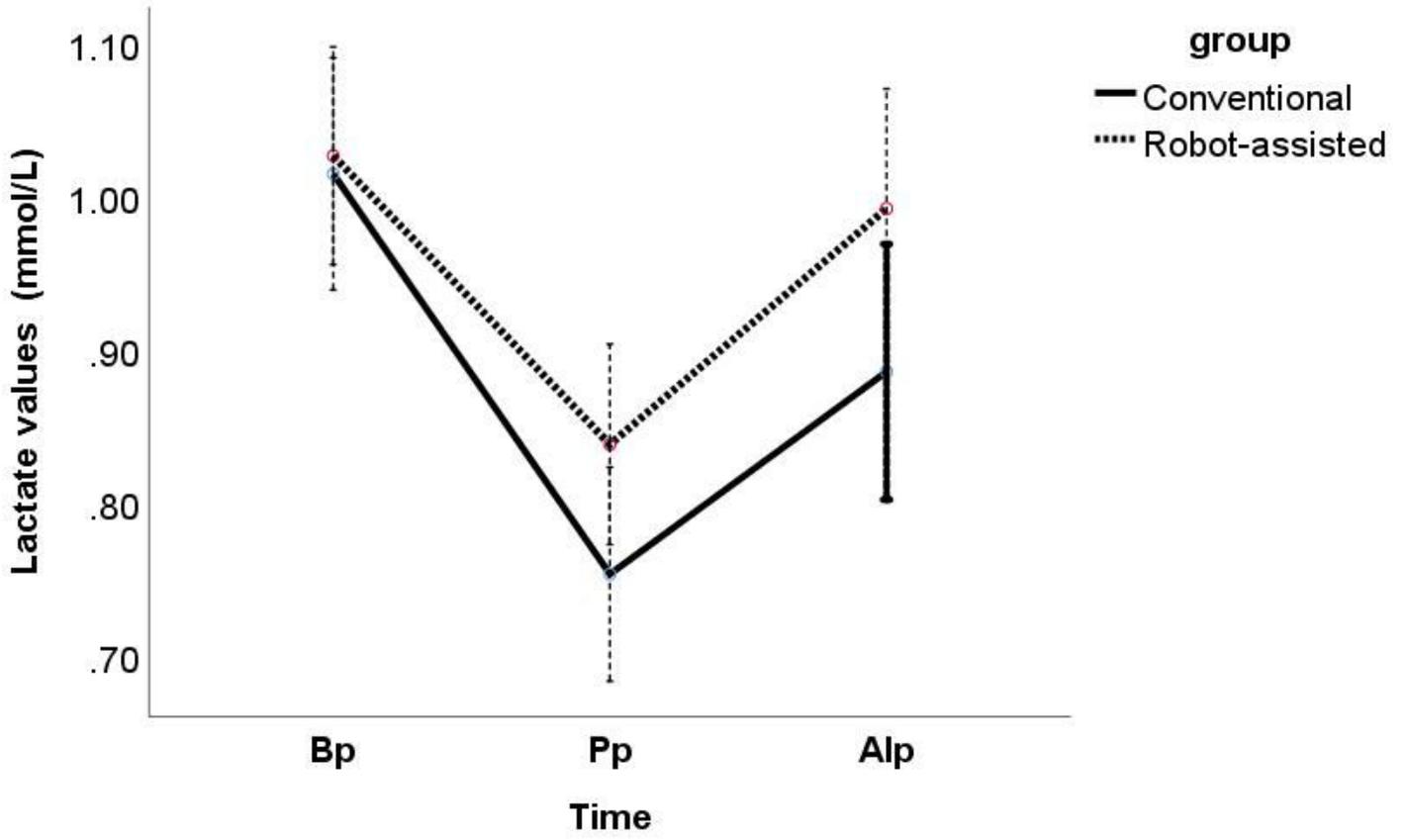


Figure 2

plasma lactate concentration at different time points in the two groups

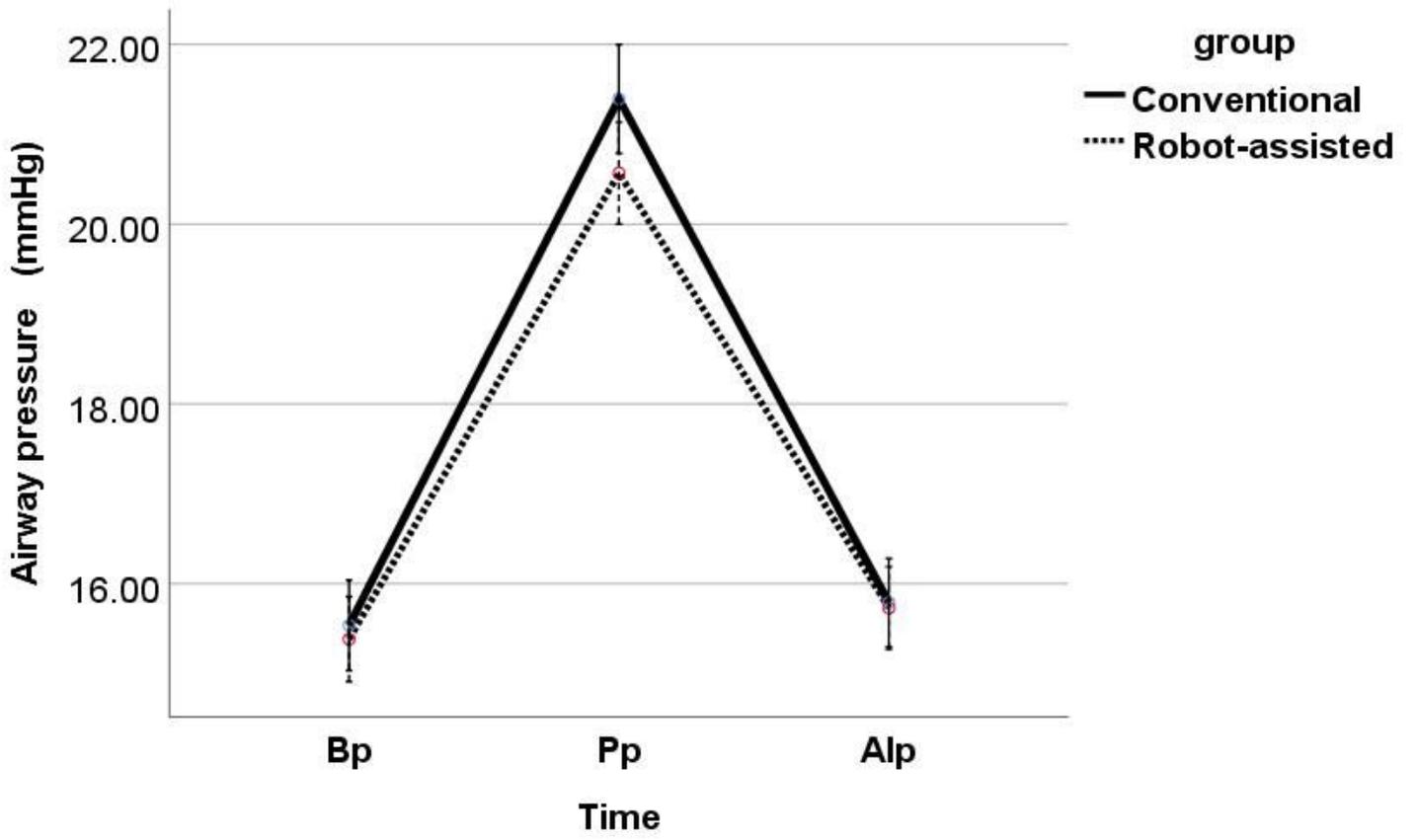


Figure 3

Airway pressure at different time points in the two groups