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Original Article

The effects of acute hypervolemic hemodilution and conventional infusion in laparoscopic radical prostatectomy patients

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Abstract: Objective: To compare the effect of acute hypervolemic hemodilution and conventional infusion in prostate cancer patients undergoing laparoscopic radical prostatectomies. Methods: A total of 87 patients with prostate cancer who underwent laparoscopic radical prostatectomies in our hospital were retrospectively analyzed. The patients were randomly divided into a control group (the CNG, n=43, conventional infusion) and an observation group (the OG, n=44, acute hypervolemic hemodilution). Blood gas analyses were performed at different time points, and the patients' cognitive dysfunction was evaluated. Results: The intraoperative blood transfusion rates of the OG and the CNG were 11.36% and 30.23%. The average intraoperative blood transfusions in the OG and the CNG were (315.46±24.49) ml and (486.95±42.17) ml ($P < 0.05$). The CVP and JVP levels in the OG and the CNG at T2 and T3 were significantly higher than the levels at T0 ($P < 0.05$). The Hb levels of the CNG at T3 and T4 were lower than they were at T0 ($P < 0.05$), and the Hb level in the OG at T4 was lower than it was at T1 ($P < 0.05$). The Hb levels in the CNG at T3 and T4 were lower than they were at T1 ($P < 0.05$), and the Hb levels in the OG at T1 and T2 were lower than they were in the CNG ($P < 0.05$). The MMSE cognitive function scores were lower than the scores recorded on the day before the operations ($P < 0.05$). Conclusion: Acute hypervolemic hemodilution in laparoscopic radical prostatectomy patients can maintain their hemodynamics in a stable state, help reduce blood transfusion, improve the oxygen supply to the brain tissue to maintain the supply and demand balance, and reduce the impact on the patients' cognitive function.

Keywords: Prostate cancer, laparoscopic radical prostatectomy, acute hypervolemic hemodilution, conventional infusion, hemodynamics, effect

Introduction

Clinically, radical prostatectomy is the main treatment for prostate cancer, and the clinical application of laparoscopic technology reduces surgical trauma. However, prostate cancer operations are difficult, and there is significant bleeding during the operations, so a large number of allogeneic blood transfusions are required [1]. Acute hypervolemic hemodilution is widely used in perioperative blood protection, because it rapidly increases blood volume in a short period of time without significantly affecting circulation, and it also improves cerebral oxygen metabolism, effectively controlling the bleeding caused by the operation, and reducing the demand for allogeneic blood [2, 3].

Previous studies have focused more on the application of open radical prostatectomy. However, there is no consensus on whether the application of acute hypervolemic hemodilution is equally safe and effective in laparoscopic radical prostatectomy [4, 5]. Li et al. [6] found that acute hypervolemic hemodilution may increase the circulating blood volume, the cerebral blood flow, and the intracranial pressure, which will cause cerebral congestion and edema, abnormal brain oxygen metabolism, and reduce circulatory stability. In addition, Zhang et al. [7] found that due to the special position required for surgery and the established pneumoperitoneum, the application of acute hypervolemic hemodilution during laparoscopic radical prostatectomy may have more serious effects on the cerebral oxygen meta-

bolism and the stability of the body's circulation.

Based on this, this study selected 87 patients with prostate cancer in our hospital as the research cohort to specifically analyze the effect of acute hypervolemic hemodilution in laparoscopic radical prostatectomy patients and to compare the operation with conventional infusion to explore the clinical effectiveness of acute hypervolemic hemodilution.

Information and methods

Information

A total of 87 patients with prostate cancer diagnosed in our hospital from January 2018 to December 2019 were retrospectively analyzed and determined to undergo laparoscopic radical prostatectomy. The patients were randomly divided into a control group (CNG, n=43) and an observation group (OG, n=44). The patients in the CNG ranged from 55-75 years old, weighed 60-85 kg, and were 152-173 cm tall. The operation times ranged from 170-220 min, and the hemorrhaging during the operations ranged from 890-1240 ml. The patients in the OG ranged from 53-74 years old, weighed 62-85 kg, and were 150-175 cm tall. The operation times ranged from 160-225 min, and the hemorrhaging during the operation ranged from 895-1250 ml. (1) Inclusion criteria: Patients who met the diagnostic criteria for prostate cancer [8] and whose cancer was confirmed through pathology. The patients met the grades I-II classifications of the American Society of Anesthesiologists (ASA) [9]. Their hemoglobin levels were (hemoglobin, Hb) ≥ 120 g/L. Their hematocrit was (hematocrit, Hct) ≥ 35%. The patients or their guardians were informed of the contents of the study, and they signed a consent form. The study was approved by the ethics committee. (2) Exclusion criteria: Patients over 80 years old. Patients who were not candidates for a radical operation. Patients with organic heart disease. Patients with a history of cardiovascular or cerebrovascular diseases. Patients with renal dysfunction. Patients who were noncompliant with the study.

Methods

Anesthesia: The two groups of patients underwent total intravenous anesthesia. Patients were required to fast for 8 hours and not drink for 4 hours before their operations. After entering the operating room, the patients underwent ECG monitoring, and an upper extremity venous access was opened. After local anesthesia was administered, the right internal jugular vein and a radial artery were punctured and catheterized. The patients underwent a retrograde puncture at a position of 1 cm above the puncture point of the right internal jugular vein, and they were catheterized toward the base of the skull at depth of 10 m. During the operation, the parameters of the various vital signs such as diastolic blood pressure, systolic blood pressure, mean arterial pressure (MAP), heart rate (HR), pulse oximetry, electrocardiogram, end-expiratory carbon dioxide, *etc*. were monitored, and the patients' EEG bispectral indexes, central venous pressure (CVP), and jugular bulb pressure were also monitored. The patients in both groups were induced intravenously, and the medications were: 4 μg/kg fentanyl, 0.05 mg/kg midazolam, 0.6 mg/kg rocuronium, 1.5-2.0 mg/kg propofol. The patients were connected to an anesthesia ventilator after their oral tracheal intubation, and the intermittent positive pressure ventilation mode was used. During the operation, the tidal volume was maintained at 8-10 mg/kg, the respiratory rate at 12 bpm, and the end-tidal carbon dioxide at 30-40 cm H_2O. The anesthesia maintenance in the two groups was cis-atracurium besylate 1 μg/(kg·min), remifentanil 0.1 μg/(kg·min), propofol 8 mg/(kg·min), and the bispectral index of the EEG was controlled at about 50. During the operations, we kept the patients' heads low and feet highs, and we kept the pneumoperitoneum pressure at 12 mmHg.

Ten minutes after the induction of anesthesia, the OG underwent acute hypervolemic hemodilution. Lactated ringer's solution (crystals) and 6% hydroxyethyl starch (colloid) were mixed at a ratio of 1:1 and infused at a dose of 20 ml/kg, with the speed controlled at 50 ml/min. After the infusion, the lactated Ringer's solution was infused at a rate of 6-8 ml/min. The CNG was given continuous infusion of lactated Ringer's solution at a rate of 6-8 ml/min. The hemorrhaging during the patients' operations in the two groups was supplemented by the same amount of colloid. In addition, crystalloids were used to supplement the fluid lost due to mechanical ventilation, and the evapo-

Table 1. Comparison of general information between the observation group and the control group ($\overline{x}$ ± s)/[n (%)]

Information		Observation group (n=44)	Control group (n=43)	t/X^2	*P*
Gender	Male	24 (54.55)	25 (58.14)	0.114	0.735
	Female	20 (45.45)	18 (41.86)		
Age (years)		64.23±8.49	62.75±8.26	0.824	0.412
Height (cm)		161.85±9.68	162.38±10.43	0.246	0.807
Weight (kg)		71.35±6.35	70.56±5.92	0.600	0.550
Operation time (min)		189.68±20.43	194.68±23.74	1.054	0.295
Intraoperative blood loss (ml)		1054.34±124.70	1050.66±120.75	0.140	0.889

rating fluid and urine in the surgical field. The patients' arterial blood gas was regularly monitored. If the Hb level was lower than 80 g/L and the circulation could not be stabilized by fluid replacement treatment, red blood cell suspension infusions were given to maintain a stable circulation.

Indicator observation

(1) Blood gas analysis: A total of 5 time points including before hemodilution, 10 min after hemodilution, 10 min after the establishment of the pneumoperitoneum, 1 h after the establishment of the pneumoperitoneum, and 10 min after pneumoperitoneum recovery were regarded as T0-T4. Blood from the patients' radial artery and the right internal jugular venous bulb was collected for blood gas analyses to determine the patients' HR, Hb, MAP, jugular venous pressure (JVP) and CVP.

(2) Blood transfusion: The rates and volumes of the intraoperative blood transfusions were compared between the two groups.

(3) Adverse reactions: The incidence of pulmonary edema and water intoxication during and after operations were compared between the two groups.

(4) Cognitive dysfunction: Cognitive function evaluations were performed 1 day before the operations, 1 day after the operations, 3 days after operations, and 7 days after the operation. The Mini Mental State Examination (MMSE) was chosen [10] to evaluate the patients' cognitive function statuses. The content of the examination includes orientation, memory, attention and calculation abilities, recall abilities, and language abilities. The score range from 0-30 points, of which 27-30 points indicates no cognitive impairment, and less than 27 points indicates cognitive impairment (21-26 points indicates mild, 10-20 points indicates moderate, and 0-9 points indicates severe).

Statistical methods

The statistical analysis was performed using SPSS 22.0. The measurement data were expressed as the mean ± standard deviation, and the comparisons of the results between the two groups and within the groups were tested using independent sample *t* tests. The enumeration data were expressed as [n (%)], and the comparisons of the results between and within the groups was tested using X^2 *tests*. The figures were made using GraphPad Prism 8. $P < 0.05$ indicates that a difference is statistically significant.

Results

Comparison of the general information between the OG and the CNG

There were no significant differences in the proportion of males and females, the average ages, the average heights, the average weights, the average operation durations, or the average intraoperative blood losses between the two groups ($P > 0.05$) (**Table 1**).

Comparison of blood transfusion rates and the blood transfusion volumes between the OG and the CNG

Five patients in the OG needed blood transfusions during their operations, for a blood transfusion rate of 11.36%. Thirteen patients in the CNG needed blood transfusions during their operation, for a blood transfusion rate of

Table 2. Comparison of blood transfusion rate between the observation group and the control group [n (%)]

Group	Case	With blood transfusion	Without blood transfusion
Observation group	44	5 (11.36)	39 (88.64)
Control group	43	13 (30.23)	30 (69.77)
X^2		4.719	
P		0.030	

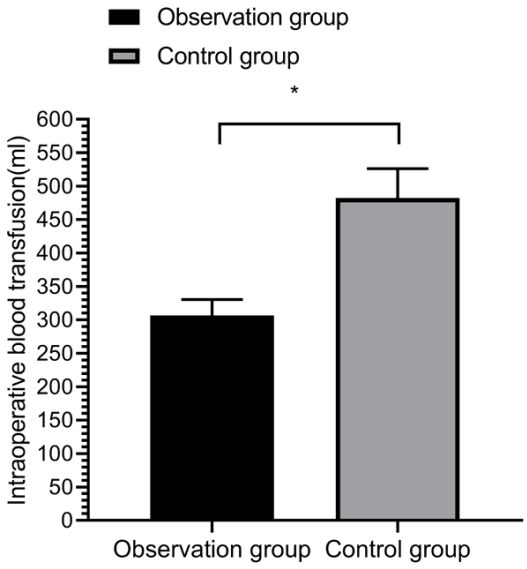

Figure 1. Comparison of the blood transfusion volumes between the observation group and the control group. The intraoperative blood transfusion volume in the observation group was significantly reduced compared to the control group ($P < 0.05$). * indicates a comparison between the two groups, $P < 0.05$.

30.23%. The difference was statistically significant ($P < 0.05$). The average intraoperative blood transfusion was (315.46±24.49) ml in the OG and (486.95±42.17) ml in the CNG, showing a statistically significant difference ($P < 0.05$) (**Table 2**; **Figure 1**).

Comparison of the hemodynamics between the OG and the CNG at different time points

The MAP levels in the OG from T0 to T4 were (92.35±10.46) mmHg, (96.45±11.38) mmHg, (97.58±10.23) mmHg, (95.27±10.28) mmHg, and (93.16±10.28) mmHg, respectively. The MAP levels in the CNG from T0 to T4 were (91.57±10.53) mmHg, (94.58±10.43) mmHg, (96.7±10.82) mmHg, (95.46±10.15) mmHg, and (92.13±10.37) mmHg, respectively. The HR levels in the OG from T0 to T4 were (81.34±10.46) beats/min, (82.57±10.65) beats/min, (82.67±10.13) beats/min, (85.27±10.46) beats/min, and (82.27±10.18) beats/min, respectively. The HR levels in the CNG from T0 to T4 were (80.34±10.46) beats/min, (85.49±10.76) beats/min, (83.25±10.27) beats/min, (84.75±10.16) beats/min, and (81.23±10.34) beats/min, respectively. The CVP and JVP levels in the OG and the CNG at T2 and T3 were significantly higher than the CVP and JVP levels at T0 ($P < 0.05$), and there were no significant differences at the other time points ($P > 0.05$). The Hb levels of the OG at T1-T4 were lower than the levels at T0 ($P < 0.05$), and the Hb levels of the CNG at T3 and T4 were lower than the levels at T0 ($P < 0.05$). The Hb level of the OG at T4 was lower than it was at T1 ($P < 0.05$). The Hb levels of the CNG at T3 and T4 were lower than the levels at T1 ($P < 0.05$), and the Hb levels of the OG at T1 and T2 were lower than the levels in the CNG ($P < 0.05$) (**Table 3**; **Figures 2**, **3**).

The incidence of adverse reactions in the OG and the CNG

In the OG, there were 3 patients with pulmonary edema during and after their operations, for an incidence rate of 6.82%. In the CNG, there were 4 patients with pulmonary edema during and after their operations, for an incidence rate of 9.30%. In the OG, there were 4 patients with water intoxication during and after their operations, for an incidence rate of 9.09%. In the CNG, there were 4 patients with water intoxication during and after their operation, for an incidence rate of 9.30% (**Table 4**).

Cognitive function comparisons between the OG and the CNG

The MMSE preoperative cognitive function scores in the OG and the CNG were (27.12±1.96) and (27.32±1.64). The MMSE cognitive function scores in the OG and the CNG at one day after the operations were (23.56±2.18) and (22.89±2.42). The MMSE cognitive function scores in the OG and the CNG at 3 days after the operations were (25.46±2.17) and (25.61±2.34). The MMSE cognitive function scores in the OG and the CNG at 7 days after the operations were (27.46±1.19) and (27.61±2.30). The MMSE cognitive function scores in the two groups at 1 and 3 days after the opera-

Table 3. Comparison of hemodynamics between the observation group and the control group at different time points ($\bar{x} \pm s$)

Indicator	Group	T0	T1	T2	T3	T4
CVP (cmH_2O)	Observation group	6.12±2.03	6.48±2.18	8.64±2.23*	8.87±2.51*	6.69±2.28
	Control group	6.32±2.15	6.07±1.89	8.57±2.34*	8.69±2.42*	6.57±2.13
JVP (mmHg)	Observation group	6.43±2.18	7.24±2.23	18.47±3.16*	18.27±3.09*	6.95±2.13
	Control group	6.53±2.05	6.35±2.13	18.57±3.34*	18.23±2.98*	6.95±2.05
Hb (g/L)	Observation group	131.35±12.59	120.42±10.57*,#	120.13±10.27*,#	120.59±10.37*	115.57±8.59*,&
	Control group	130.26±12.37	128.62±11.13	127.49±10.38	120.75±10.13*,&	112.28±8.62*,&

Note: Compared with T0, *$P < 0.05$; compared with T1, &$P < 0.05$; compared with the control group at the same time, #$P < 0.05$.

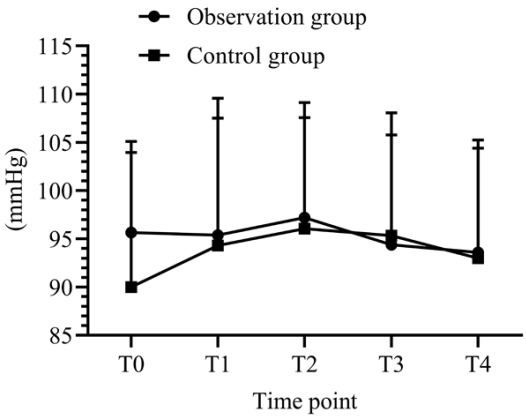

Figure 2. Comparison of the MAP levels between the observation group and the control group at different time points. Compared with the MAP levels in the control group at T0, the observation group's levels were only slightly different ($P > 0.05$). Compared with the MAP levels in the control group at T1, the observation group's levels were only slightly different ($P > 0.05$). Compared with the MAP levels in the control group at T2, the observation group's levels were only slightly different ($P > 0.05$). Compared with the MAP levels in the control group at T3, the observation group's levels were only slightly different ($P > 0.05$). Compared with the MAP levels in the control group at T4, the observation group's levels were only slightly different ($P > 0.05$).

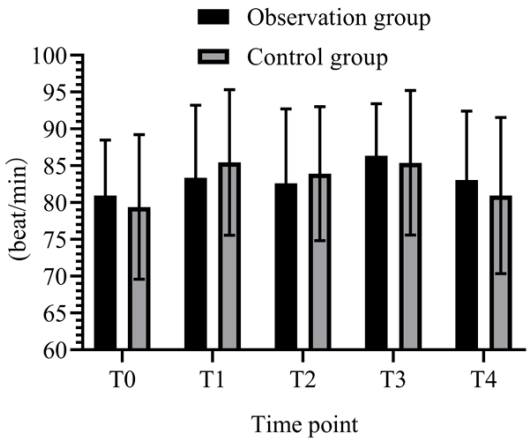

Figure 3. Comparison of the HR levels between the observation group and the control group at the different time points. Compared with the HR levels in the control group at T0, the observation group had only a slight difference ($P > 0.05$). Compared with the HR levels in the control group at T1, the observation group had only a slight difference ($P > 0.05$). Compared with the HR levels in the control group at T2, the observation group had only a slight difference ($P > 0.05$). Compared with the HR levels in the control group at T3, the observation group had only a slight difference ($P > 0.05$). Compared with the HR levels in the control group at T4, the observation group had only a slight difference ($P > 0.05$).

tions were significantly lower than the scores at 1 day before the operations ($P < 0.05$) (**Table 5**; **Figure 4**).

Discussion

Hemodilution is a type of blood protection method widely used during the perioperative period. It can significantly reduce the amount of intraoperative blood loss, help control the demand for allogeneic blood, reduce adverse reactions and disease transmission caused by blood transfusion, save blood resources, and reduce the medical burden of patients [11, 12]. The hemodilution methods include acute isovolumetric hemodilution and acute hypervolemic hemodilution, the latter of which is less difficult to perform, requires less equipment and fewer human resources, and it can effectively reduce the risk of blood contamination and damage to the blood components [13, 14].

Acute hypervolemic hemodilution refers to the rapid infusion of a certain dose of colloidal fluid or crystal fluid over a period of time, and it increases the circulating blood volume by approximately 20%-25% and reduces the effective blood component concentration [15].

Table 4. Comparison of the incidence of adverse reactions between the observation group and the control group [n (%)]

Group	Cases	Pulmonary edema	Water intoxication
Observation group	44	3 (6.82)	4 (9.09)
Control group	43	4 (9.30)	4 (9.30)
X^2		0.181	0.001
P		0.670	0.973

Table 5. Comparison of the incidence of cognitive dysfunction between the observation group and the control group at different times after operation

Group	1 day after operation	3 days after operation	7 days after operation
Observation group (n=44)	6 (13.64)	3 (6.82)	2 (4.55)
Control group (n=43)	5 (11.63)	4 (9.30)	2 (4.65)
X^2	0.079	0.181	0.001
P	0.778	0.670	0.981

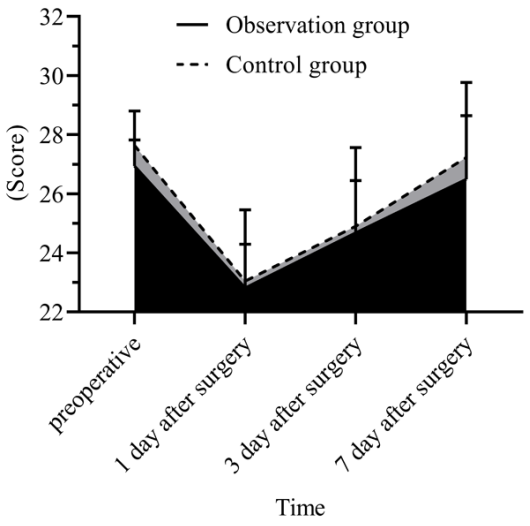

Figure 4. Comparison of the MMSE cognitive function scores between the observation group and the control group at the different time points. Compared with the preoperative MMSE cognitive function scores in the control group, the observation group had little difference ($P > 0.05$). Compared with the MMSE cognitive function scores in the control group at 1 day one after the operations, the observation group had little difference ($P > 0.05$). Compared with the MMSE cognitive function scores in the control group at 3 days after the operations, the observation group had little difference ($P > 0.05$). Compared with the MMSE cognitive function scores in the control group at 7 days after operation, the observation group had little difference ($P > 0.05$).

By performing acute hypervolemic hemodilution treatment, one is assured that under the premise of the same amount of bleeding, the loss of effective blood components can be significantly reduced, the patients will have a higher blood loss tolerance, and it helps maintain a balanced state of cerebral oxygen supply and demand [16]. At present, acute hypervolemic hemodilution is widely used in thoracic operations, spinal operations, aneurysm operations, gastrointestinal operations, liver operations, meningioma operations, urinary system operations, *etc.* [17], and the results have been proved to be satisfactory.

In this study, the OG underwent acute hypervolemic hemodilution. Compared with the CNG, the OG had little difference in its overall intraoperative blood loss, but the intraoperative blood transfusion rate was significantly lower and the volume of the intraoperative blood transfusion was significantly reduced. It shows that the use of acute hypervolemic hemodilution can significantly control the demand for allogeneic blood in patients undergoing laparoscopic radical prostatectomies, and can help reduce blood consumption during the perioperative period. A previous study also showed that acute hypervolemic hemodilution reduced patients' intraoperative blood transfusion rates (4% VS 13%) [5], which is consistent with this study. The results have shown that due to acute hypervolemic hemodilution, a certain dose of crystalloid and colloidal fluid is selected for high-speed infusion in a short time, and the blood volume of the body can be rapidly expanded to 20%-25%. The blood volume is controlled at a high level throughout the perioperative period, and the concentration of active ingredients in the blood is significantly reduced, which can help reduce the risk of intraoperative blood component loss, and the patients can obtain a higher tolerance for blood loss caused by the operation [18, 19].

The role of acute hypervolemic hemodilution in open radical prostatectomy has been widely demonstrated. For laparoscopic radical prostatectomy, it is necessary to consider whether increased blood volume resuscitation in a short period of time will affect cardiopulmonary function and hemodynamics during the implementation of acute hypervolemic hemodilution [20,

21]. Lu et al. [22] have found that acute hypervolemic hemodilution can maintain a stable state of intraoperative circulation and improve hemodynamic stability. Mielke et al. [23] studied hemodynamic monitoring and found that HR and blood pressure did not fluctuate significantly. Although the CVP is increased to a certain extent, the overall level was normal. Another study [24] also showed that acute hypervolemic hemodilution does not significantly affect the circulatory state of the body, but can keep the circulatory system at a stable level during an operation.

In this study, the MAP and HR levels in the OG and the CNG did not fluctuate significantly at the different time points during the perioperative period, and there were no significant differences between the groups. The CVP levels of the OG and the CNG increased significantly at T2 and T3, but there was still no significant difference between the groups. The analysis showed that due to the special head-down and foot-high posture adopted during the laparoscopic radical prostatectomies, the patients' return blood volume increased, but the overall level was at a normal level, and the burdens on the heart and lungs did not increase significantly, indicating that acute hypervolemic hemodilution does not have a significant effect on CVP. In addition, there was no significant difference between the OG and the CNG in the incidence of pulmonary edema or water intoxication during and after the operation, indicating that the implementation of acute hypervolemic hemodilution during laparoscopic radical prostatectomy can ensure safety.

In this study, there was no significant difference in the MMSE cognitive function scores between the two groups before the operations or at 1 day, 3 days, and 7 days after the operations ($P > 0.05$). The MMSE cognitive function scores of the two groups at 1 and 3 days after the operations were significantly lower than they were at 1 day before operations ($P < 0.05$). There was no significant difference in the incidence of cognitive dysfunction between the OG and the CNG at 1 day, 3 days, and 7 days after the operations ($P > 0.05$), and the incidence of cognitive dysfunction decreased gradually at 3 days and 7 days after the operation. A study pointed out that there was no significant difference in the incidence of cognitive impairment within 1 week after surgery between the group receiving acute hypervolemic hemodilution and the control group ($P > 0.05$) [25], which is consistent with our study. This indicated that acute hypervolemic hemodilution will not have a serious impact on the cognitive function of patients undergoing laparoscopic radical prostatectomies, and the patients' cognitive function can be basically restored to its preoperative levels at 1 week after the operation, confirming the safety of acute hypervolemic hemodilution.

In summary, acute high-volume hemodilution in patients undergoing laparoscopic radical prostatectomies can maintain a stable hemodynamic state, help reduce blood transfusions, improve the oxygen supply of the brain tissue, maintain the supply and demand balance, and reduce the impact on the patients' cognitive function. However, this study also has some shortcomings, which are reflected in the fact that it is a retrospective study, and the cohort is small, so the study content is not comprehensive enough. Therefore, prospective studies with a larger sample size, more comprehensive and in-depth research and analysis should be carried out in the future, so as to provide more useful guidance for improving the effect and safety of laparoscopic radical prostatectomy.

Disclosure of conflict of interest

None.

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