Efficacy of Goal-Directed Fluid Therapy Monitored by Pulse-Pressure Variation During Parathyroidectomy in Patients With End-Stage Renal Failure

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Abstract

There are no well-recognized guidelines for intraoperative fluid management in patients with end-stage renal failure (ESRF). Goal-directed fluid therapy (GDFT) is a new concept of perioperative fluid management that has improved patients' prognoses. Dynamic indicators may better predict fluid response than static indicators. In this study, we assessed a GDFT protocol with monitoring of pulse-pressure variation (PPV) in patients with ESRF undergoing parathyroidectomy. The study included 102 patients who underwent elective parathyroidectomy. They were randomized to a control group (Group C, n = 51) that was managed with a restricted fluid regimen or a PPV group (Group P, n = 51) that was given a normal saline infusion and was monitored for change in PPV during the intraoperative period. If PPV reached >13%, 250 mL colloid was administered in 15 min. Ephedrine was infused to keep mean arterial pressure >65 mm Hg if needed. Hemodynamic variables in the perioperative period were recorded. The volume of saline infused during the intraoperative period was 364 (219–408) mL in Group P and 27 (50–50) mL in Group C (P = .001). Ephedrine was given to 16/51 (29.4%) of Group P patients and 27/51 (52.9%) of Group C patients (P = .027). From 30–60 min to 120 min of operation or until the end of operation, systolic blood pressure was significantly lower, heart rate was significantly higher, and PPV was significantly higher in Group C patients compared to Group P patients (P < .05). Use of goal-directed fluid therapy with the dynamic PPV indicator in patients with ESRF undergoing parathyroidectomy guided the administration of infused fluids, with reduced incidence of hypotension.

Background

There are no guidelines or consensus concerning perioperative fluid therapy for patients with end-stage renal failure (ESRF). Nearly all the studies of perioperative fluid therapy have excluded patients with ESRF because of their physical condition.

Vascular disease such as atherosclerosis predisposes patients with secondary hyperparathyroidism (SHPT) to dramatic fluctuation of blood pressure in the perioperative period. Hypotension may be caused by restriction of intravenous fluid therapy and the circulatory inhibition of anesthesia. The administration of propofol and remifentanil may accentuate these problems. Rational administration of drugs may help avert the hypotension, but this measure may be insufficient [1].

For patients with SHPT, infusion volumes, which are based mainly on preoperative solute loads, should be carefully monitored. To assess fluid status, noninvasive hemodynamic monitoring, as recorded with a continuous non-invasive arterial pressure monitoring system (CNAP) may be used [2]. CNAP can improve the control of blood pressure during dialysis, with resultant reduction in hospitalizations and without patient discomfort or vascular injury [3].

Goal-directed fluid therapy (GDFT), based on changes of stroke volume (SV) and cardiac output (CO), has attracted much attention recently. GDFT optimizes hemodynamics and oxygen delivery. Monitoring pulse-pressure variation (PPV) may be more accurate than monitoring cardiac preload in patients on

mechanical ventilation. Many experts recommend that GDFT with PPV be used for all operations [4]. Pulse pressure (PP) is defined as the difference between systolic pressure and diastolic arterial pressure. PPV is the variation in PP (Psystolic-Pdiastolic) caused by inspiration and expiration. Several factors can affect the accuracy of PPV, such as arrhythmia, spontaneous breathing, and peripheral vascular resistance. PPV does not predict fluid responsiveness during an endotoxin-induced acute increase in pulmonary artery pressure and right ventricular loading [5]. However, no studies have confirmed the impact of pathological changes in ESRF patients, including changes in increased pulmonary capillary permeability, calcification abnormalities, and cardiovascular dysfunction on the use of PPV.

We know of no research on the volumes of infused fluid given to patients with SHPT during surgery, let alone the use of CNAP in the perioperative period. GDFT, which can facilitate fluid management according to individual demographics and medical status, may be useful for such patients.

The purpose of this study was to determine the intraoperative fluid volume given to patients with SPTH and ESRF undergoing parathyroidectomy. We aimed to determine the safety and effectiveness of PPV in patients with ESRF and optimize the infusion strategy by dynamic fluid management with CNAP-PPV.

Methods

2.1 Patients population

The study protocol was approved by the Ethics Committee for Clinical Trials of The Second Affiliated Hospital of Anhui Medical University, Hefei, China (approval NO.: PJ-YX2018-008(F1). Written informed consent was obtained from each patient. This trial was registered with the Chinese Clinical Trial Registry (ChiCTR1800017302). This manuscript adheres to the applicable Consolidated Standards of Reporting Trials (CONSORT) guidelines. We selected 102 ESRF patients with SHPT who were scheduled for parathyroidectomy in our hospital from August to December 2018. All patients were receiving hemodialysis thrice weekly or daily peritoneal dialysis. The patients had American Society of Anesthesiologists physical status II or III. Patients were randomized into two equal groups by a computerized random-number generator; a control group, managed with a restricted-fluid regimen Group C), and a PPV group (Group P) that was given normal saline infusion and monitored for change in PPV (Figure 1). Patients with primary hyperparathyroidism, severe pulmonary hypertension, arrhythmia, arteriosclerosis, aortic stenosis, or chronic cardiac dysfunction were excluded from the study. Patients with upper limb edema or malformation, or with blood pressure difference >10 mm Hg between the arms, also were excluded. In total, three patients were excluded from this study. The same operative team performed all operations.

2.2 Anesthesia and mechanical ventilation

No sedative or analgesic drugs were administered before the induction of anesthesia. Dialytic therapy was performed on the day before surgery. After their arrival in the operating room, patients received

routine monitoring, including pulse oximetry (SPO_2), electrocardiogram, bispectral index, and end-tidal CO_2. CNAP was established and calibrated to measure blood pressure and other hemodynamic variables.

General anaesthesia was induced in all patients with bolus infusion of propofol (Fresenius Kabi AB, Macclesfeld, UK), with a goal of plasma concentration of 3.0–3.5 μg/mL; bolus remifentanil 1.5 μg/kg (Yichang Humanwell Pharmaceutical Co., Ltd., Yichang, China); and cisatracurium besylate 0.15 mg/kg (Jiangsu Hengrui Medicine Co., Ltd., Jiangsu, China). After tracheal intubation, ventilation was established with 6–8 mL/kg tidal volume, and respiratory rate was adjusted to target end-tidal CO_2 of 35–45 mm Hg. Anesthesia was maintained with IV remifentanil (0.2–0.3 μg/kg/min), target-controlled infusion propofol, and cisatracurium besylate (0.1 mg/kg/min). During the operation, bispectral index values were maintained within 45 ± 5 by regulating the infusion rate of propofol. Thirty minutes before the end of the surgery, cisatracurium besylate infusion was stopped. Propofol and remifentanil were turned off in both groups after wound closure.

The endotracheal tube was removed when patients were able to follow verbal commands to open their eyes and the T4/T1 ratio was 90%. Patients were kept in the post-anesthesia care unit for one hour.2.3 Fluid management

In Group C, only vasoactive agents were administered, without fluid infusion. Bradycardia (HR < 40 beats/min) was treated with 0.5 mg intravenous atropine. Hypotension was defined as a decrease of >20% of the baseline systolic blood pressure. If hypotension occurred, ephedrine was given at increments of 6 mg. Infusion of dopamine was considered if the total ephedrine dose exceeded 40 mg. Hypertension (systolic blood pressure [SBP] >20% of the baseline SBP) was treated by infusion of 10 mg urapidil.

In Group P, intravenous fluid therapy and the use of vasoactive agents was determined according to the change of PPV and other hemodynamic variables (Figure 2). If PPV was >13%, 250 mL normal saline was administered over 1 min. Ephedrine was given at increments of 6 mg to keep mean arterial pressure > 65 mm Hg. Use of phenylephrine was avoided because of its propensity to induce intense vasoconstriction. Cardiac index (CI) was maintained above 2.5 L/min/m by pumping 3–5 μg/kg/min dobutamine intravenously, if needed. Fluid challenge status was evaluated every 15 minutes. Additional details of intraoperative fluid management are illustrated Figure 2.

2.4 Study parameters

In both patient groups, demographic data, dialysis history, preoperative complications, duration of operation, total volume of anesthetics (propofol, remifentanil and cisatracurium besylate) used, and intraoperative fluid and vasoactive agents infused were recorded. Postoperative complications, including hypotension, hypertension, pulmonary edema, infection, incision disunion and arteriovenous fistula occlusion, also were recorded.

Vital signs and weight were recorded before and after the last dialysis and before the administration of anesthesia. Values were considered “maximum,” “minimum,” or “baseline.” Hemodynamic variables were

continually recorded at the beginning of mechanical ventilation (T1); before incision (T2); 30 min, 60 min, and 90 min during the operation (T3, T4, T5); and 120 min during the operation or at the end of the operation if the operative time was > 120 min (T6).

Blood samples were taken from the femoral artery before and 30 min after the operation and analyzed for brain naturietic peptide, blood gases, hemoglobin/hematocrit, lactate and electrolytes.

The primary endpoints of this study were the total volume of fluid administered, the doses of vasopressors used, and the incidence of postoperative complications. The secondary endpoints were abnormalities in blood gas values and electrolyte concentrations.

2.5 Data and statistical analysis

The sample size was determined based on our institutional records. A sample of 43 patients in each group was required to detect a 30% reduction in hypotension during and after operation at a significance level of 0.05. Considering a possible 20% dropout rate, a sample with a minimum of 51 per group was calculated.

Statistical analyses were performed with SPSS version 21.0 (SPSS Inc., Chicago, IL, USA). The data were tested for normal distribution with Kolmogorov-Sminov and for homogeneity of variances with Levene [6]. Normally distributed continuous data were presented as mean ± standard deviation, and abnormal distributions were expressed as median (25–75th percentile). Categorical variables were expressed as number (%). Independent-samples *t*-test was used to compare continuous variables between the two groups, and repeated-measures one-way ANOVA was used for in-group comparisons. All enumeration data were compared via chi-squared test. Comparisons between ranked data were made with the Kruskal-Wallis test or the Wilcoxon test. Binary logistic regression was used to determine the influence of age, gender, body mass index, and baseline hematocrit on the average PPV in the control group. $P < .05$ was considered statistically significant.

Results

3.1 Patient characteristics

One hundred five ESRF and SHPT undergoing parathyroidectomy were initially included in the study; 3 were excluded, as illustrated in Figure 1. Thus, 102 patients were enrolled (51 in Group C and 51 in Group P) and completed the study protocol. Patients in the two study groups had similar baseline characteristics and co-morbidities (Table 1).

3.2 Intraoperative profiles

The patients received total parathyroidectomy and re-implantation of a small parathyroid fragment into the subcutaneous of anterolateral femoral to maintain normal hormone levels. Their intraoperative profiles are listed in Table 1. Median duration of operation was similar in the two groups (Group P, 122 ±

18.3 min; Group C, 117 ± 15.5 min. Patients in the Group P received significantly more saline infusion (median 364 mL, range 219–408 mL) than did patients in Group C (median 27, range 50–50; the need for infusion of intravenous anesthetics) (P = 0.001). Patients in Group C received more vasoactive drugs than did those in Group P; 27/51 (52.9%) received ephedrine compared with 16/51 (29.4%) (P = 0.027). Three patients in Group C (5.9%) also required continuous intravenous infusion of dopamine, whereas none in Group P needed this medication. The total volume of anesthetics used was similar in the two groups. There was no significant difference in blood loss between the groups, and no patient required transfusion.

Figure 3 illustrate the perioperative hemodynamic changes that occurred in the two patient populations undergoing parathyroidectomy. Compared with the baseline values, changes in hemodynamic variables at the time of mechanical ventilation (T1) were mostly similar in the two groups; SBP was slightly but statistically significantly lower, but diastolic blood pressure (DBP), mean blood pressure (MBP), and heart rate (HR) were not. After initiation of mechanical ventilation, the PPV value was similar between the two groups [12.63 ± 6.02% vs 11.55 ± 7.28%; P > .05], but after three fluid challenges (T3), the PPV was lower in Group P than in Group C (8.92 ± 2.79% vs 11.63 ± 5.11%; P < .001). The PPV remained lower in Group P than in Group C through 120 min or until the end of the operation (T6) (7.49 ± 2.12% vs 11.43 ± 5.27%; P < .001). SBP, DBP and MBP were significantly lower through much or all of the operative period (T2–T6 or T4) in both patient groups than at T0. Through periods T2–T6, SBP was significantly higher in Group P than in Group C, whereas HR was higher in Group C than in Group P; PPV was significantly higher in Group C than in Group P during these times. CO was significantly higher in Group P patients than in Group C patients at T3, T4 and T6.

3.3 Postoperative outcomes

Table 2 summarizes the postoperative complications. The total incidence of complications was lower in Group P (18/51; 35.3%) than in Group C (31/51; 61.8%) (P < .01). Hypotension and arteriovenous fistula occlusion were more frequent in Group C than in Group P, but these differences did not reach statistical significance. The incidence of hypertension in the two groups was nearly identical. No patient suffered complications due to fluid overload (pulmonary edema, infection, or incision disunion).

3.4 Baseline and postoperative laboratory tests

Baseline and postoperative values are presented in Table 3. A mild but statistically significant drop in hematocrit occurred in Group P patients (39.49 ± 5.47 to 37.24 ± 5.14, P < .05), whereas no drop occurred in Group C patients. No significant differences in other laboratory tests were recorded.

Discussion

In this study, we aimed to optimize fluid management in patients with SPTH and ESRF undergoing parathyroidectomy. Thus, we applied the CNAP system to guide GDFT during the perioperative period. These strategies provided fluid responsiveness to help regulate venous return and CO to reduce the

incidence of hypotension and subsequent adverse events. Previous GDFT studies used invasive monitors under mechanical ventilation, whereas we used a noninvasive system. With our protocol, hemodynamics was well maintained, use of vasoconstrictive drugs was reduced, and complications were fewer than in patients managed with conventional fluid administration. The protocol is feasible in the fluid management hemodialysis patients.

Parathyroidectomy is a reasonable treatment for patients with SHPT. The operation can delay progression of the disorder and improve the quality of life for patients with SHPT. However, long-term hypertension and hypercalcemia accelerate atherosclerosis, which, in SHPT patients, can accentuate their propensity to dramatic fluctuation of blood pressure in the perioperative period, especially after the induction. In this study, more patients in the control group than in the P group had hypotension during and after the operation, an experience that is like that in a study that reported an incidence of 19% [7]. Due to preoperative fasting, dialysis and non-urinary fluid loss, even patients with ESRF may have intraoperative hypovolemia. Thus, restricted intravenous fluid therapy makes such patients susceptible to hypotension, which can be aggravated by circulatory inhibition via anesthesia, especially when using propofol and remifentanil. Moreover, eight patients in our control group had arteriovenous fistula occlusion compared with none in the P group. Although this difference did not reach statistical significance (likely because of an inadequate number of patients), it is consistent with evidence that vascular occlusion is one of the most serious complications due to hypotension and unstable blood pressure during the surgery [8,9]. Thus, adequate volume expansion to maintain stable hemodynamics microcirculatory perfusion is critical.

Controversy exists over the strategy of fluid management of patients with SHPT during anesthesia. Some doctors choose no infusion because of fear of fluid overload. However, since SHPT patients have a range of sensibility to vasoactive drugs, the incidence of hypertension and/or hypotension in them is high [10,11].In addition, some drugs, such as phenylephrine, may reduce the oxygen supply to vital organs [12]. Thus, rational drug use is necessary but may not be enough to maintain normal hemodynamics. Therefore, some scholars advocate moderate transfusion during the surgery for patients with SHPT. The main goal of the perioperative fluid management is optimal microcirculatory perfusion, which can be achieved with well-controlled blood pressure and adequate volume expansion.

The types of intraoperative infusion and total volume administered should be carefully chosen. Sodium lactate Ringer’s solution is not recommended since its sodium and chlorine content are low and potassium plentiful. Excessive infusion of 0.9% saline can result in hypernatremia and hyperchloremia, which can be corrected by dialysis after surgery [13]. In our study, there were no disturbances in preoperative and postoperative electrolyte concentrations.

Infusion volume is mainly determined by the preoperative state of solute loads. Thus, it is important to know patients’ actual weight and dry weight. Dry weight is the lowest weight that can be safely attained after dialysis without hypotension developing [14]. Prolonged low diastolic pressure is one of the independent risk factors for cardiovascular complications [15]. The risk of postoperative pulmonary

edema and hypertension is increased in patients whose weight is higher than their dry weight; this imbalance can impede wound healing and increase the chance of infection. These complications caused by fluid under/over-load are the focus of our research.

To achieve and maintain dry weight, the use of noninvasive hemodynamic monitoring, such as with a CNAP monitoring system to monitor the water load in hemodialysis, has been advocated [16]. It first measures arterial blood pressure through the upper-arm calibration system and blood volume and pressure signal through double fingertip-sensors continuously. Then, using the vascular unload technique and VERIFI algorithm, it eliminates the contract artifact [17]. CNAP can improve blood pressure control in-between dialysis sessions and limit hospitalizations [18].In our study, the CNAP system provided consistent hemodynamic measurements without causing patient discomfort.

However, the exact volume of fluid expansion needed is difficult to predict and varies among individuals. GDFT, by providing individualized fluid management, may help solve this problem. Currently, GDFT based on changes of PPV has attracted much attention. A large PPV or an increase in PPV can be interpreted as operating on the steep portion of Frank–Starling curve warning the responsible physician to counteract further fluid depletion to avoid hemodynamic instability [19].Changes in PPV seem more accurate than other indicators in determining cardiac preload for patients on mechanical ventilation, and some authorities recommend using this simple therapy during all operations [20]. CNAP can provide real-time PPV monitoring, and CNAP-PPV has identical sensitivity and accuracy to that of invasive methods [21,22].

In our study, GDFT strategies via CNAP-PPV enabled fluid responsiveness to optimize venous return and CO to reduce the incidences of hypotension and subsequent adverse events. The GDFT strategies we used in our study reduced the total dosages of vasopressors administered, thus reducing the heart rate, which can be increased using ephedrine and dopamine. Further, after moderate fluid expansion, hematocrit decreases and hemoconcentration seems to be improved. As verified by our data, the excessive use of vasoconstriction drugs without adequate fluid loading may further induce vasoconstriction, which may cause serious complications after surgery, similar to arteriovenous fistula.

We acknowledge that this study has limitations: 1) Since there is little bleeding and the operation time is short with parathyroidectomy, the results may not be applicable to major operations. 2) Some hemodialysis patients have arteriovenous fistulae on both arms or severe arrhythmia, so our protocol will not apply to them. 3) The relatively small sample size probably prevented detection of significant differences in the rates of hypotension and arteriovenous shunt occlusion.

In conclusion, we show that dynamic responsiveness GDFT with the CNAP system in parathyroidectomy in ESRF patients is reliable and feasible. The GDFT protocol reported in this study maintained hemodynamic stability, reduced the requirements of vasopressors, and decreased postoperative adverse events. ESRF patients had a shortage of fluid loads before surgery, and this condition persisted during and after operation if fluid infusion was not given.

Declarations

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Author Contributions

Jie Song: This author helped design the study, conduct the study, analyze the data, and write and revise the paper.

Xiaofen Liu: This author helped analyze the data.

Weiwei Jiang: This author helped conduct the study.

Jiayou Wang: This author helped conduct the study.

Yun Li: This author helped design the study.

Hong Chen: This author helped conduct the study.

Ye Zhang: This author helped design the study and write and revise the paper.

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Compliance with ethical standards

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical

standards.

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Tables

Table 1. Patient Characteristics and Intraoperative Profiles

Characteristic	Group P (n = 51)	Group C (n = 51)	*P*
Gender (M/F)	36/15	32/19	.401
Age (y)	47.49 ± 7.56	46.59 ± 6.65	.524
Weight (kg)	163.47 ± 7.62	165.49 ± 8.13	.199
Height (cm)	58.92 ± 10.52	62.73 ± 12.1	.093
BMI (kg/m^2)	22.01 ± 3.21	23.44 ± 5.44	.108
History of dialysis (y)	7.55 ± 3.16	7.73 ± 2.32	.749
Comorbidities			
Hypertension	38 (74.5%)	36 (70.6%)	.657
Cardiac disease (except hypertension)	8 (15.7%)	5 (9.8%)	.373
Pulmonary disease	14 (27.5%)	17 (33.3%)	.518
Diabetes mellitus	13 (25.5%)	10 (19.6%)	.477
Gastrointestinal disease	19 (37.3%)	20 (39.2%)	.839
Anemia	39 (76.5%)	34 (66.7%)	.272
Fasting duration (hours)	10.2 ± 2.1	36 (70.6%)	.416
Operation time (min)	122.02 ± 18.32	116.84±15.46	.126
Total volume of normal saline (mL)	363.7 (219.1–407.9)	50 (50–50)	.001
Frequency of vasoactive drugs given			
Ephedrine	16 (29.4%)	27 (52.9%)	.027
Dopamine	0	3 (5.9%)	.241
Total volume of anesthetics (mg)			
Propofol	438 ± 68	441 ± 78	.836
Remifentanil	2.1 ± 1.2	2.4 ± 0.8	.141
Cisatracurium besylate	9.8 ± 2.1	10.2 ± 1.7	.292

Values are given as mean value ± SD, median (25–75th percentile), or percentages.

Table 2. Postoperative Complications

	Group C (n = 51)	Group P (n = 51)	P (χ^2 test)
Hypotension	6 (11.76%)	0	ns
Hypertension	17 (33.3%)	18 (35.29%)	ns
Infection	0	0	ns
Incision disunion	0	0	ns
Arteriovenous fistula occlusion	8 (15.69%)	0	ns
Pulmonary edema	0	0	ns
Others	1 (1.96%)	0	ns
Total	31 (60.78%)	18 (35.29%)	.01

Table 3. Baseline and Postoperative Laboratory Tests			
Parameter	**Group P**	**Group C**	***P* (*t*-test)**
pH			
Baseline	7.41 ± 0.07	7.4 ± 0.05	.128
Post-operation	7.36 ± 0.05	7.37 ± 0.05	.560
PaO_2			
Baseline	466.25 ± 54.41	463.73 ± 56.03	.818
Post-operation	456.47 ± 40.37	462.24 ± 46.25	.504
$PaCO_2$			
Baseline	43.33 ± 5.52	43.94 ± 4.46	.541
Post-operation	44.98 ± 5.81	45.8 ± 5.84	.477
HCO_3^-			
Baseline	25.99 ± 2.57	26.09 ± 2.06	.822
Post-operation	25.86 ± 2.46	25.63 ± 2.07	0.608
Hematocrit			
Baseline	39.12 ± 5.35	39.35 ± 5.25	.823
Post-operation	37.24 ± 5.14	39.49 ± 5.47	.034
Hemoglobin			
Baseline	97.2 ± 13.4	98.2 ± 11.1	.682
Post-operation	96.3 ± 12.2	97.7 ± 12.4	.567
Lactate			
Baseline	1.06 ± 0.49	0.95 ± 0.41	.188
Post-operation	1.03 ± 0.46	1.06 ± 0.43	.774
BNP			
Baseline	280.2 ± 253.3	299.3 ± 212.3	.681
Post-operation	278.5 ± 391.9	286.3 ± 298.7	.910
Serum sodium			
Baseline	137.18 ± 2.21	137.61 ± 2.45	.352
Post-operation	136.22 ± 3.64	137.1 ± 2.61	.163

Serum potassium			
Baseline	4.21 ± 0.5	4.37 ± 0.39	.071
Post-operation	4.42 ± 0.74	4.48 ± 0.62	.666
Serum calcium			
Baseline	1.17 ± 0.09	1.17 ± 0.12	.953
Post-operation	1.16 ± 0.1	1.16 ± 0.09	1.000
Serum chloride			
Baseline	101.3 ± 2.1	101.5 ± 1.8	.607
Post-operation	100.5 ± 1.9	100.9 ± 1.4	.229

BNP, brain naturietic peptide. Values are given as mean value ± SD. *P* values in the table indicate the statistical significance between the two groups.

Figures

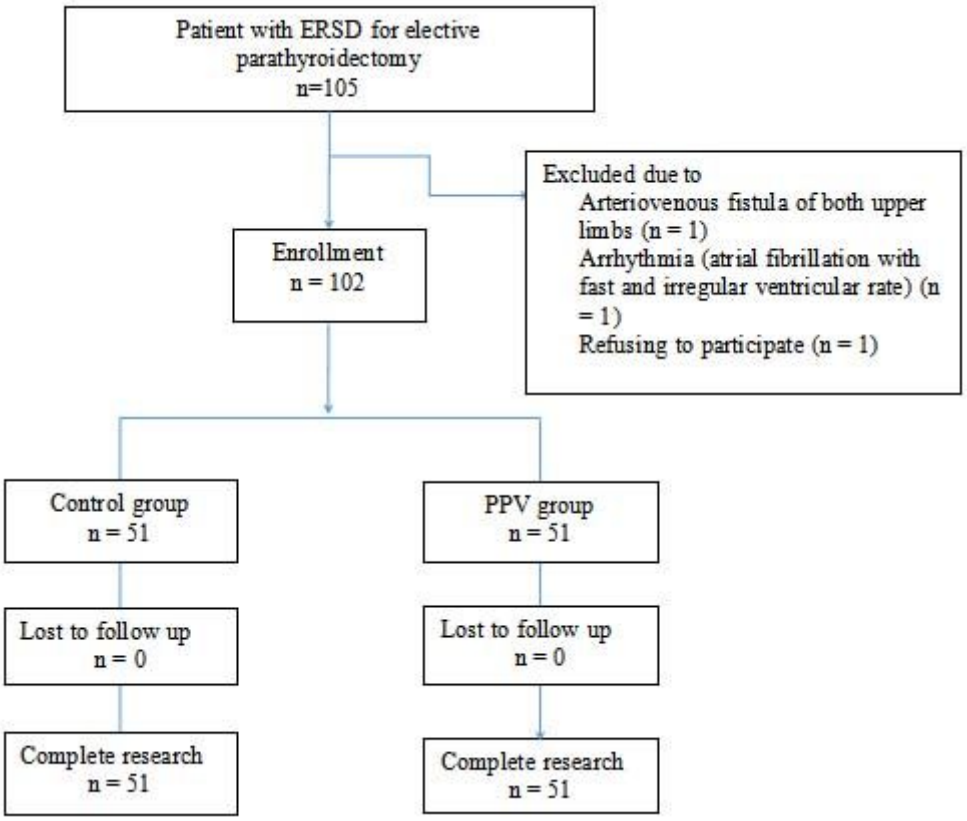

Figure 1

Patient recruitment flow chart.

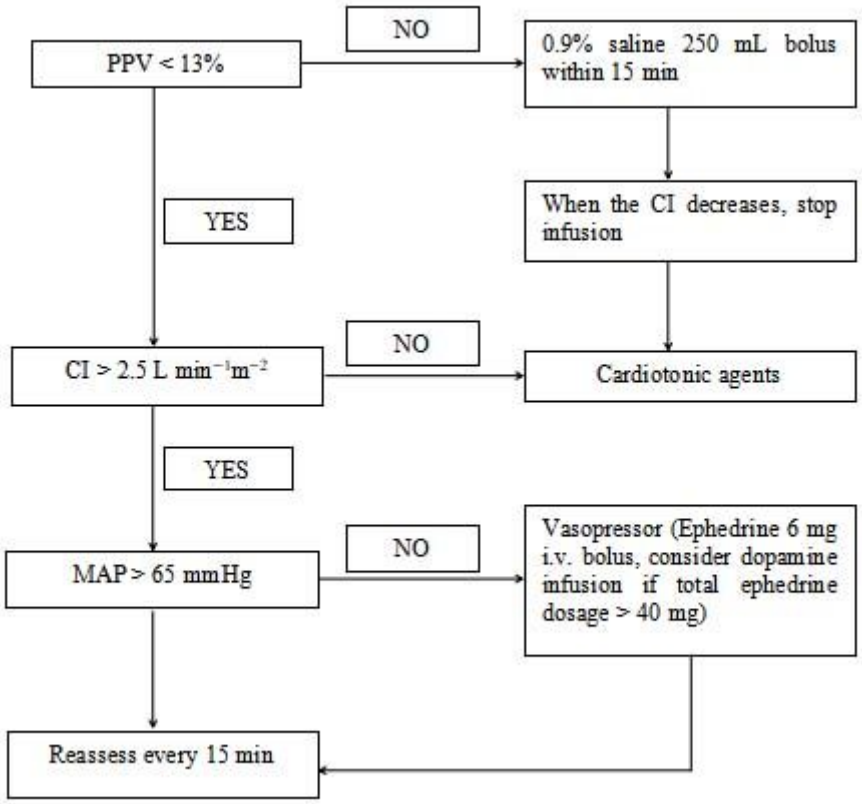

Figure 2

Protocols for PPV goal-directed fluid therapy. PPV, pulse-pressure variation; MAP, mean arterial pressure; CI, cardiac index.

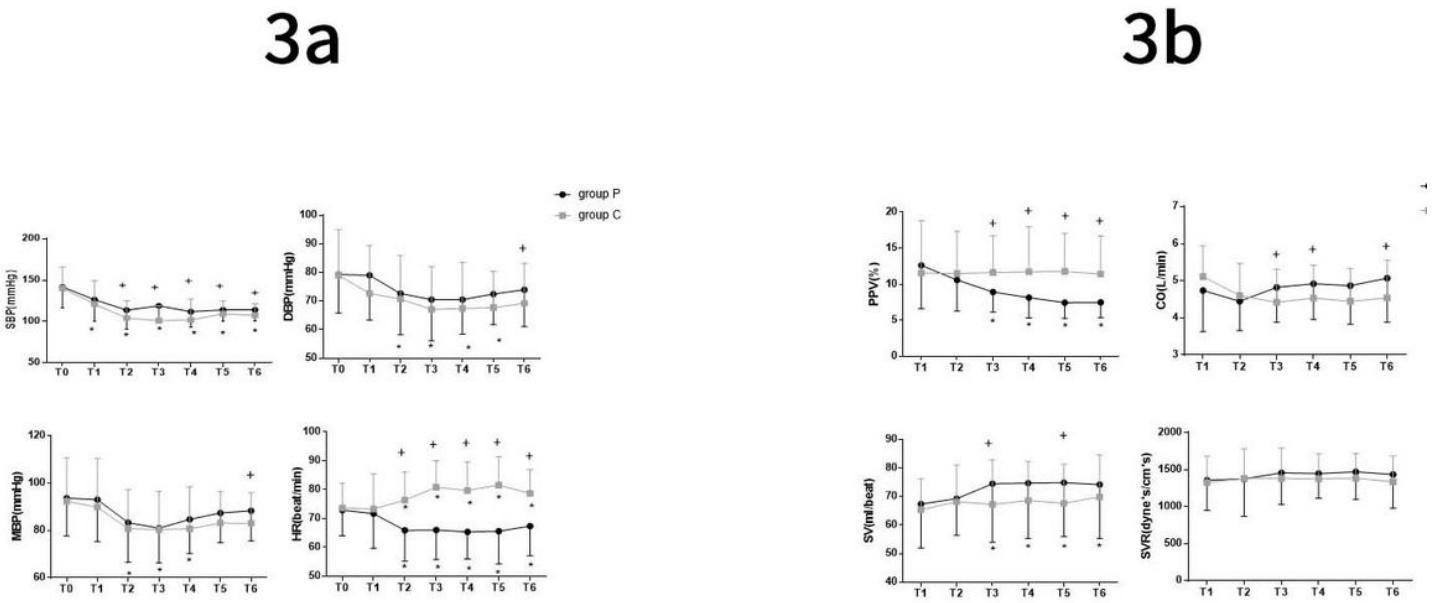

Figure 3

Differences in hemodynamic variables between the two groups at times during the perioperative period. SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; HR, heart rate; CO, cardiac output; SV, stroke volume; SVR, systemic vascular resistance. T1, at the beginning of mechanical ventilation; T2, before incision; T3, 30 min, T4, 60 min, T5, 90 min during surgery; T6, 120 min during surgery or at the end of the surgery if the surgery time was less than 120 min. *Significant difference, at $P < .05$, from baseline (T0) for SBP, DBP, MBP, and HR, and from beginning of ventilation (T1) for PPV, CO, SV and SVR. + Significant difference, at $P < .05$, between the two groups.