

Efficacy of Goal-Directed Fluid Therapy Monitored by Pulse-Pressure Variation Using a Continuous Non-Invasive Arterial Pressure Monitoring System (the CNAP™ System) During Parathyroidectomy in Patients with End-Stage Renal Failure - A randomized trial

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Abstract

Background: 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 concept of perioperative fluid management that improves patients' prognosis. Dynamic indicators better predict fluid response than static indicators. **Aim:** In this study, we assessed a GDFT protocol with monitoring of pulse pressure variation (PPV) in patients with ESRF undergoing parathyroidectomy. **Methods:** The study included 102 patients who underwent elective parathyroidectomy. They were randomized to a control group (restrictive group, n = 51) that was managed with a restricted fluid regimen or a PPV group (GDFT group, 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 normal saline was administered over 15 min. Ephedrine was given at increments of 6 mg to keep mean arterial pressure >65 mmHg. Hemodynamic variables in the perioperative period were recorded. The primary endpoint was the occurrence of postoperative hypotension. **Results:** The occurrence of postoperative hypotension in the GDFT group was lower than in the restrictive group (0 vs. 11.67%, P = 0.027). The patients with complications in the GDFT group was lower than in the restrictive group (35.3% vs. 54.9%, P = 0.047). The volume of saline infused during the intraoperative period was 364 (219-408) mL in the GDFT group and 50 (50-50) mL in the restrictive group (P = 0.001). Ephedrine was given to 16/51 (29.4%) of the GDFT group and 27/51 (52.9%) of the restrictive group (P = 0.027). **Conclusion:** The use of goal-directed fluid therapy with the dynamic PPV indicator in patients with ESRF undergoing parathyroidectomy guides the administration of infused fluids, with reduced incidence of postoperative hypotension.

Background

There are no guidelines concerning perioperative fluid therapy for patients with end-stage renal failure (ESRF) [1]. Nearly all the studies of perioperative fluid therapy excluded patients with ESRF because of their physical condition [1-10].

Vascular diseases such as atherosclerosis predispose patients with secondary hyperparathyroidism (SHPT) to dramatic fluctuation of blood pressure in the perioperative period [11, 12]. Hypotension may be caused by restriction of intravenous fluid therapy and by the inhibitory effects of the anesthesia drugs on circulation, which could aggravate hypotension [11]. The administration of propofol and remifentanyl may accentuate these problems [13]. Rational administration of drugs may help avert hypotension, but this measure may be insufficient [13].

For patients with SHPT, infusion volumes, which are based mainly on preoperative solute loads, should be carefully monitored [14]. To assess fluid status, noninvasive hemodynamic monitoring, as recorded with a continuous non-invasive arterial pressure monitoring system (CNAP) may be used [14]. CNAP can improve the control of blood pressure during dialysis, with resultant reduction in hospitalizations and without patient discomfort or vascular injury [15].

Goal-directed fluid therapy (GDFT), based on changes in stroke volume (SV) and cardiac index (CI), has attracted much attention recently [16, 17]. GDFT optimizes hemodynamics and oxygen delivery [16, 17]. Monitoring pulse-pressure variation (PPV) may be more accurate than monitoring cardiac preload in patients on mechanical ventilation [16, 17]. Many experts recommend that GDFT with PPV be used for all operations [18]. Pulse pressure (PP) is defined as the difference between systolic pressure and diastolic arterial pressure [19]. 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 [19]. No studies 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.

GDFT, which can facilitate fluid management according to individual demographics and medical status, may be useful for such patients. Therefore, 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 by observing the occurrence of postoperative hypotension and optimize the infusion strategy by dynamic fluid management with CNAP-PPV.

Methods

Patients population

We recruited 105 ESRF patients with SHPT who were scheduled for parathyroidectomy at our hospital between August and December 2018. Patients with primary hyperparathyroidism, severe pulmonary hypertension, arrhythmia, atherosclerosis, aortic stenosis, or chronic cardiac dysfunction were excluded. Patients with upper limb edema or malformation, or with blood pressure difference >10 mm Hg between the arms, were excluded. In total, three patients were excluded from this study. All patients were receiving hemodialysis thrice weekly or daily peritoneal dialysis. The patients had an American Society of Anesthesiologists physical status of III. Patients were randomized into two equal groups by a computerized random-number generator (managed by a third-party statistician): a control group, managed with a restricted-fluid regimen (restrictive group), and a PPV group (GDFT group) that was given normal saline infusion and monitored for change in PPV (Figure 1). The same operative team performed all operations.

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 (SPO₂), electrocardiogram, bispectral index (MedTronic, Minneapolis, MN, USA), and end-tidal CO₂. CNAP was established and calibrated to measure blood

pressure and other hemodynamic variables. We used the CNAP™ system (CNSystem, Medizintechnik, Graz, Austria).

General anesthesia was induced in all patients with bolus infusion and a target-controlled infusion of propofol (Fresenius Kabi AB, Macclesfield, UK) for a plasma concentration of 3.0-3.5 µg/mL; bolus of remifentanil (Yichang Humanwell Pharmaceutical Co., Ltd., Yichang, China) 1.5 µg/kg infused over 30 s; 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 CO₂ of 35-45 mmHg. Since the operation was performed and completed under endoscopy and in order to avoid excessive high airway pressure during the operation, we maintained the tidal volume at 8 ml/kg, which was lowered (but still >6 ml/kg) only when the airway pressure was too high. Since the patient's PaCO₂ had to remain within 35-45 mmHg, it did not achieve the criteria of permissive hypercapnia. Anesthesia was maintained with target-controlled infusion propofol (target concentration: 2.5-3.5 µg/ml), IV remifentanil (0.2-0.3 µg/kg/min), and cisatracurium besylate (0.05 mg/kg/min, intermittent intravenous injection). The intermittent injection of cisatracurium was based on the patients' muscle tone during the operation. During the operation, bispectral index values (MedTronic, Minneapolis, MN, USA) were maintained within 45 ± 5 by regulating the infusion rate of propofol. Thirty minutes before the end of the surgery, the 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, after checking for spontaneous respiration, swallowing, fist boxing, and keeping the head up before extubation, and the T7/T4 ratio was 90%. Patients were kept in the post-anesthesia care unit for one hour.

Fluid management

In the restrictive group, only vasoactive agents were administered, without fluid infusion. In the GDFT group, intravenous fluid therapy and the use of vasoactive agents were determined according to the change of PPV and other hemodynamic variables. If PPV was >13%, 250 mL of normal saline was administered over 15 min. Fluid responsiveness was evaluated every 15 min.

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 were recorded.

Vital signs and weight were recorded before and after the last dialysis and before the administration of anesthesia. Baseline SBP was the SBP measured after the last dialysis before surgery. The measurements were taken in the hemodialysis ward before transfer to the operating room. The SBP was measured in the supine position. Values were considered “maximum,” “minimum,” or “baseline.” Hemodynamic variables were continually recorded at baseline (T0); before induction (T1); after induction (T2); immediately after intubation (T3); beginning of mechanical ventilation (T4); before incision (T5); 30 min, 60 min, and 90 min during the operation (T6, T7, T8); and 120 min during the operation or at the end of the operation if the operative time was > 120 min (T9).

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

In order to preserve the integrity of the arteriovenous fistula, we avoided any blood pressure monitoring and puncture in the arm with the fistula. We used the lower extremity venous access, placed the arm with the arteriovenous fistula on the side of the body, and the nurse repeatedly confirmed that there was no compression of the venous fistula. Any abnormality of the arteriovenous fistula pulsation was assessed before and after the operation, in order to ensure functional integrity.

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

Regarding complications, hypotension was considered when blood pressure is lower than the baseline blood pressure by 20%. Hypertension was considered when blood pressure is higher than basic blood pressure by 20%. Pulmonary edema was considered in the presence of hypoxemia, foamy sputum, auscultation of double lung wet rales, and confirmation by chest X-ray. Infections were confirmed by elevated C-reactive protein levels. Poor wound healing was defined as incision edema.

Data and statistical analysis

According to the records of the research center, postoperative hypotension rarely occurs in patients receiving dynamic fluid replacement, while postoperative hypotension is prone to occur with conventional surgery. Therefore, the difference in postoperative complications between the two groups was estimated at about 20%. Postoperative hypotension was also considered in the calculation process of the minimum sample size. A sample of 44 patients in each group was required to detect a 20% reduction in postoperative hypotension at a significance level of 0.05 and power of 80%. Considering a possible 20% dropout rate, a sample with a minimum of 53 per group was required.

Statistical analyses were performed with SPSS version 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp). The data were tested for normal distribution with the Kolmogorov-Smirnov test and for homogeneity of variances with the Levene test [20]. Normally

distributed continuous data were presented as mean \pm standard deviation, and those with abnormal distributions were expressed as median (25–75th percentile). Categorical variables were expressed as number (%). The independent-samples *t*-test was used to compare continuous variables between the two groups, and repeated-measures one-way ANOVA was used for within-group comparisons. All enumeration data were compared using the chi-squared test or Fisher's exact test. Comparisons between ranked data were made with the Kruskal-Wallis test or the Wilcoxon test.

Ethics

The study was a single-blind randomized controlled trial, which was conducted at The Second Affiliated Hospital of Anhui Medical University, Hefei, China between August and December 2018. The protocol approved by the Ethics Committee for Clinical Trials of The Second Affiliated Hospital of Anhui Medical University (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.

Results

Patient characteristics

One hundred and five patients with ESRF and SHPT undergoing parathyroidectomy were initially recruited in the study between August and December 2018; three were excluded, as illustrated in Figure 2. Thus, 102 patients were randomized (51 in the restrictive group and 51 in the GDFT group) and completed the study. Patients in both groups had similar baseline characteristics and comorbidities (Table 1).

Intraoperative profiles

The patients received total parathyroidectomy and re-implantation of a small parathyroid fragment subcutaneously in the femoral area to maintain normal hormone levels. Their intraoperative profiles are listed in Table 1. The median duration of operation was similar in the two groups (GDFT group, 122 \pm 18.3 min; restrictive group, 117 \pm 15.5 min. Patients in the GDFT group received significantly more saline infusion (median 364 mL, range 219-408 mL) than did patients in the restrictive group (median 50 mL, range 50-50 mL; the need for infusion of intravenous anesthetics) ($P = 0.001$). Patients in the restrictive group received more vasoactive drugs than did those in the GDFT group; 27/51 (52.9%) received ephedrine compared with 16/51 (29.4%) ($P = 0.027$). Three patients in the restrictive group (5.9%) also required continuous intravenous infusion of dopamine (they received 10, 20, and 38 mg, respectively), whereas none in the GDFT group 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 illustrates the perioperative hemodynamic changes that occurred in the two patient populations undergoing parathyroidectomy. Hemodynamic variables had no significant difference at baseline (T0) or before induction (T1). Compared with the baseline values, changes in hemodynamic variables at the time of after induction (T2), immediately after intubation (T3) were mostly similar in the two groups. At the time of mechanical ventilation (T4), 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 [$12.6 \pm 6.0\%$ vs. $11.6 \pm 7.3\%$; $P = 0.417$], but after three fluid challenges (T6), the PPV was lower in the GDFT group than in the restrictive group ($8.9 \pm 2.8\%$ vs. $11.6 \pm 5.1\%$; $P < 0.001$). The PPV remained lower in the GDFT group than in the restrictive group through 120 min or until the end of the operation (T9) ($7.5 \pm 2.1\%$ vs. $11.4 \pm 5.3\%$; $P < 0.001$). SBP, DBP, and MBP were significantly lower through much or all of the operative period (T5-T9 or T7) in both patient groups than at T0. Through periods T5-T9, SBP was significantly higher in the GDFT group than in the restrictive group, whereas HR was higher in the restrictive group than in the GDFT group; PPV was significantly higher in the restrictive group than in the GDFT group at these time points. CI was significantly higher in the GDFT group than in the restrictive group at T6, T7, and T9.

Postoperative complications

As the primary endpoint, the occurrence of postoperative hypotension was lower in the GDFT group (0/51; 0%) than in the restrictive group (6/51; 11.7%) ($P=0.027$). Postoperative hypertension in the GDFT group (18/51; 35.3%) and the restrictive group (17/51; 33.3%) did not reach statistical significance ($P=0.500$). Arteriovenous fistula occlusion was lower in the GDFT group (0/51; 0%) than in the restrictive group (8/51; 15.7%) ($P=0.006$). Among those eight patients, one had preoperative diarrhea, two had a long history of hypotension (mean systolic blood pressure 70-80 mmHg), one had long operation time (>3 h), one had preoperative damage of arteriovenous fistula, and one had diabetes-related vascular disease; the reason could not be identified in the remaining two patients. In addition, one patient suffered from myocardial infarction after surgery in the restrictive group. Although this was not a complication as per study design, this could be related to intraoperative hemodynamic changes. The patients with complications were less in the GDFT group (18/51; 35.3%) than in the restrictive group (28/51; 54.9%) ($P=0.047$). No patient suffered from complications due to pulmonary edema, infection, or incision disunion (Table 2).

Baseline and postoperative laboratory tests

Baseline and postoperative values are presented in Table 3. A mild but statistically significant drop in hematocrit occurred in the GDFT group (from 39.5 ± 5.5 to 37.2 ± 5.1 , $P = 0.034$), whereas no drop occurred in the restrictive group. No significant differences in other laboratory tests were recorded.

Discussion

Parathyroidectomy is the most frequently performed operation in ESRF patients [21], but there are no well-recognized guidelines for intraoperative fluid management. 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 CI to reduce the incidence of hypotension and subsequent adverse events. Previous GDFT studies used invasive monitors under mechanical ventilation [22, 23], whereas we used a noninvasive system. With our protocol, the hemodynamics were well maintained, the use of vasoconstrictive drugs was reduced, and the complications were fewer than in patients managed with conventional fluid administration. The protocol is feasible in the fluid management of hemodialysis patients.

Parathyroidectomy can delay the progression of the disorder and improve the quality of life for patients with SHPT [24]. Long-term hypertension and hypercalcemia in SHPT patients can accentuate their propensity to dramatic fluctuation of blood pressure in the perioperative period, especially after induction [11, 12]. In this study, more patients in the restrictive group than in the GDFT group had hypotension after operation, as supported by a previous study that reported an occurrence of 19% [25]. Due to preoperative fasting, dialysis and non-urinary fluid loss, even patients with ESRF may have intraoperative hypovolemia [11, 12]. Thus, restricted intravenous fluid therapy makes such patients susceptible to hypotension, which can be aggravated from anesthesia, especially when using propofol and remifentanyl [13].

High blood viscosity, low blood volume, endovascular intima damage, thrombosis, and improper care, among others, are all possible reasons for arteriovenous fistula occlusion [26], which is a dismal complication because it can complicate future dialysis. Eight patients in our restrictive group had arteriovenous fistula occlusion compared with none in the GDFT group. It is consistent with evidence that vascular occlusion is one of the most serious complications due to hypotension and unstable blood pressure during surgery [27, 28]. Thus, adequate volume expansion to maintain stable hemodynamics and perfusion is critical. Despite significant associations between the use of GDFT and the lower occurrence rate of postoperative hypotension and arteriovenous fistula occlusion, the exact causal relationship remains to be determined.

Controversy exists over the strategy of fluid management of patients with SHPT during anesthesia [29, 30]. Some physicians choose no infusion because of fear of fluid overload. Since SHPT patients have a range of sensibility to vasoactive drugs, the incidence of hypertension and/or hypotension in them is high [31, 32]. In addition, some drugs used for anesthesia may reduce the oxygen supply to vital organs [33]. Thus, rational drug use is necessary but may not be enough to maintain normal hemodynamics. Therefore, some authors advocate individualized fluid management during the surgery for patients with SHPT [34, 35]. Recent studies revealed associations between hypotension and adverse outcomes such as myocardial injury, depending on the extent and duration of hypotension [36-38]. In non-cardiac surgery, the most common cardiac complication is myocardial infarction, which may be caused by an imbalance

between myocardial oxygen supply and demand [36-38]. A meta-analysis based on multiple cohort studies showed that intraoperative hypotension increased postoperative major cardiovascular events (OR=1.56), especially for myocardial injury (OR=1.67) [37]. Salmasi et al. [38] found that MAP below the absolute value of 65 mmHg or a decrease of >20% of baseline can increase the risk of postoperative myocardial damage. The main goal of perioperative fluid management is optimal microcirculatory perfusion, which can be achieved with well-controlled blood pressure and adequate volume expansion [39]. Some authors suggest that the right amount of fluid can be input during parathyroidectomy, but the absolute amount of liquid should not be fixed [38]. If the amount of dehydration of the last hemodialysis ≥ 3 kg, patients with normal cardiac function are often accompanied by different degrees of dehydration, but in patients with cardiac insufficiency, there is still the problem of extracellular fluid overload [38]. Therefore, if there is insufficient capacity before the start of anesthesia, the blood volume should be replenished in time, and the cardiac function should be considered. Otherwise, huge hemodynamic fluctuations will occur after anesthesia.

The infusion volume is mainly determined by the preoperative state of solute loads [40, 41]. Thus, it is important to know the patients' actual weight and dry weight [41]. The dry weight is the lowest weight that can be safely attained after dialysis without hypotension developing [42]. Prolonged low diastolic pressure is one of the independent risk factors for cardiovascular complications [43]. 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 [44]. 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 [45]. 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 contrast artifact [46]. CNAP can improve blood pressure control between dialysis sessions and limit hospitalizations [47]. In our study, the CNAP system provided consistent hemodynamic measurements without causing patient discomfort.

Nevertheless, the exact required volume of fluid expansion is difficult to predict and varies among individuals [40, 41]. By providing individualized fluid management, GDFT may help solve this problem. A large PPV or an increase in PPV can be interpreted as operating on the steep portion of the Frank-Starling curve, warning the responsible physician to counteract further fluid depletion to avoid hemodynamic instability [48]. By monitoring non-invasive parameter PPV, this indicator could efficiently assess the fluid requirements of patients with general anesthesia and mechanical ventilation [49]. MAP, PPV, CI, SVR, and other parameters should be considered comprehensively in patients under general anesthesia with mechanical ventilation in order to accurately assess liquid reactivity [50, 51]. CNAP can provide real-time PPV monitoring, and CNAP-PPV has identical sensitivity and accuracy to that of invasive methods [52, 53].

In the present study, GDFT strategies via CNAP-PPV enabled fluid responsiveness to optimize venous return and CI to reduce the occurrence 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. Furthermore, 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.

Limitations of the study

We acknowledge that this study has limitations. Since there is little bleeding and the operation time is short with parathyroidectomy, the results may not be applicable to major operations. Some hemodialysis patients have arteriovenous fistulae on both arms or severe arrhythmia, so our protocol will not apply to them. The dry weight of the patients and their weight gain after surgery were not recorded. Our anesthesia team only observed the condition of hemodialysis on the first day after surgery, and subsequent observation and treatment were not included in the study. This study did not observe a correlation between postoperative complications and the duration of surgery.

Conclusions

In the current study, we show that PPV-guided GDFT with the CNAP system during parathyroidectomy in ESRF patients is feasible and reliable. The GDFT protocol reported in this study maintained hemodynamic stability, reduced the requirements of vasopressors, and decreased postoperative adverse events.

Declarations

Ethics approval and consent to participate

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. The protocol approved by the Ethics Committee for Clinical Trials of The Second Affiliated Hospital of Anhui Medical University (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.

Consent to publish

There are no details on individuals reported within the manuscript.

Availability of data and materials

The datasets used and/or analysed 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

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.

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Tables

Table 1. Patient Characteristics and Preoperative Profiles

Characteristic	GDFT group (n = 51)	Restrictive group (n = 51)	P
Sex (M/F)	36/15	32/19	0.401
Age (years)	47.49 ± 7.56	46.59 ± 6.65	0.524
Height (cm)	163.47 ± 7.62	165.49 ± 8.13	0.199
Weight (kg)	58.92 ± 10.52	62.73 ± 12.1	0.093
BMI (kg/m ²)	22.01 ± 3.21	23.44 ± 5.44	0.108
History of dialysis (years)	7.55 ± 3.16	7.73 ± 2.32	0.749
Comorbidities			
Hypertension	38 (74.5%)	36 (70.6%)	0.657
Cardiac disease (except hypertension)	8 (15.7%)	5 (9.8%)	0.373
Pulmonary disease	14 (27.5%)	17 (33.3%)	0.518
Diabetes mellitus	13 (25.5%)	10 (19.6%)	0.477
Gastrointestinal disease	19 (37.3%)	20 (39.2%)	0.839
Anemia	39 (76.5%)	34 (66.7%)	0.272
Fasting duration (hours)	10.2 ± 2.1	10.6±2.8	0.416
Systolic blood pressure	142±25	140±26	0.745
Diastolic blood pressure	79±13	79±16	0.931
Mean blood pressure	99.7±16.0	99.4±18.2	0.926
Heart rate	73±9	74±9	0.667

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

Table 2. Intraoperative Profiles

Characteristic	GDFT group (n = 51)	Restrictive group (n = 51)	<i>P</i>
Operation time (min)	122 ± 18	117±15	0.126
Total volume of normal saline (mL)	363.7 (219.1-407.9)	50.0 (50-50)	0.001
Stroke volume (mL)			
T1	68.73±10.88	68.01±11.07	0.741
T2	66.74±11.35	67.91±11.98	0.614
T3	68.76±10.67	69.56±11.22	0.713
T4	65.39±10.90	67.39±15.43	0.452
T5	68.18±12.87	69.29±12.81	0.661
T6	67.29±15.60	74.51±20.51	0.048
T7	68.63±13.73	73.73±19.40	0.129
T8	67.63±13.70	72.90±18.87	0.109
T9	69.90±14.710	73.24±18.92	0.323
Frequency of vasoactive drugs given			
Ephedrine	16 (29.4%)	27 (52.9%)	0.027
Dopamine	0	3 (5.9%)	0.241
Total volume of vasoactive drugs			
Ephedrine (mg)	0 (0-12)	12(0-24)	0.008
Dopamine (mg)	0	20 (10-38)	0.609
Total volume of anesthetics			
Propofol (mg)	438.00 ± 68.00	441.00 ± 78.00	0.836
Remifentanil (mg)	2.10 ± 1.20	2.40 ± 0.80	0.141
Cisatracurium besylate (mg)	9.80 ± 2.10	10.20± 1.70	0.292

Values are given as mean value \pm SD, median (25–75th percentile), median (range) or percentages

Table 3. Postoperative Complications

	GDFT group	Restrictive group	<i>P</i>
	(n = 51)	(n = 51)	
Hypotension	0	6 (11.8%)	0.027
Hypertension	18 (35.3%)	17 (33.3%)	0.500
Arteriovenous fistula occlusion	0	8 (15.7%)	0.006
Others	0	1 (2.0%)	1.000

Table 4. Baseline and Postoperative Laboratory Tests

Parameter	GDFT group	Restrictive group	<i>P</i>
pH			
Baseline	7.41 ± 0.07	7.4 ± 0.05	0.128
Post-operation	7.36 ± 0.05	7.37 ± 0.05	0.560
PaO ₂ (mmHg)			
Baseline	466.25 ± 54.41	463.73 ± 56.03	0.818
Post-operation	456.47 ± 40.37	462.24 ± 46.25	0.504
PaCO ₂ (mmHg)			
Baseline	43.33 ± 5.52	43.94 ± 4.46	0.541
Post-operation	44.98 ± 5.81	45.8 ± 5.84	0.477
HCO ₃ ⁻ (mmol/L)			
Baseline	25.99 ± 2.57	26.09 ± 2.06	0.822
Post-operation	25.86 ± 2.46	25.63 ± 2.07	0.608
Hematocrit (mm)			
Baseline	39.12 ± 5.35	39.35 ± 5.25	0.823
Post-operation	37.24 ± 5.14	39.49 ± 5.47	0.034
Hemoglobin (g/L)			
Baseline	97.20 ± 13.40	98.20 ± 11.10	0.682
Post-operation	96.30 ± 12.20	97.70 ± 12.40	0.567
Lactate (mmol/L)			
Baseline	1.06 ± 0.49	0.95 ± 0.41	0.188
Post-operation	1.03 ± 0.46	1.06 ± 0.43	0.774
BNP (pg/mL)			
Baseline	280.20 ± 253.30	299.30 ± 212.30	0.681
Post-operation	278.50 ± 391.90	286.30 ± 298.70	0.910
Serum sodium (mmol/L)			
Baseline	137.18 ± 2.21	137.61 ± 2.45	0.352
Post-operation	136.22 ± 3.64	137.10 ± 2.61	0.163

Serum potassium (mmol/L)

Baseline	4.21 ± 0.50	4.37 ± 0.39	0.071
Post-operation	4.42 ± 0.74	4.48 ± 0.62	0.666

Serum calcium (mmol/L)

Baseline	1.17 ± 0.09	1.17 ± 0.12	0.953
Post-operation	1.16 ± 0.1	1.16 ± 0.09	1.000

Serum chloride (mmol/L)

Baseline	101.30 ± 2.10	101.50 ± 1.80	0.607
Post-operation	100.50 ± 1.90	100.90 ± 1.40	0.229

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

Figures

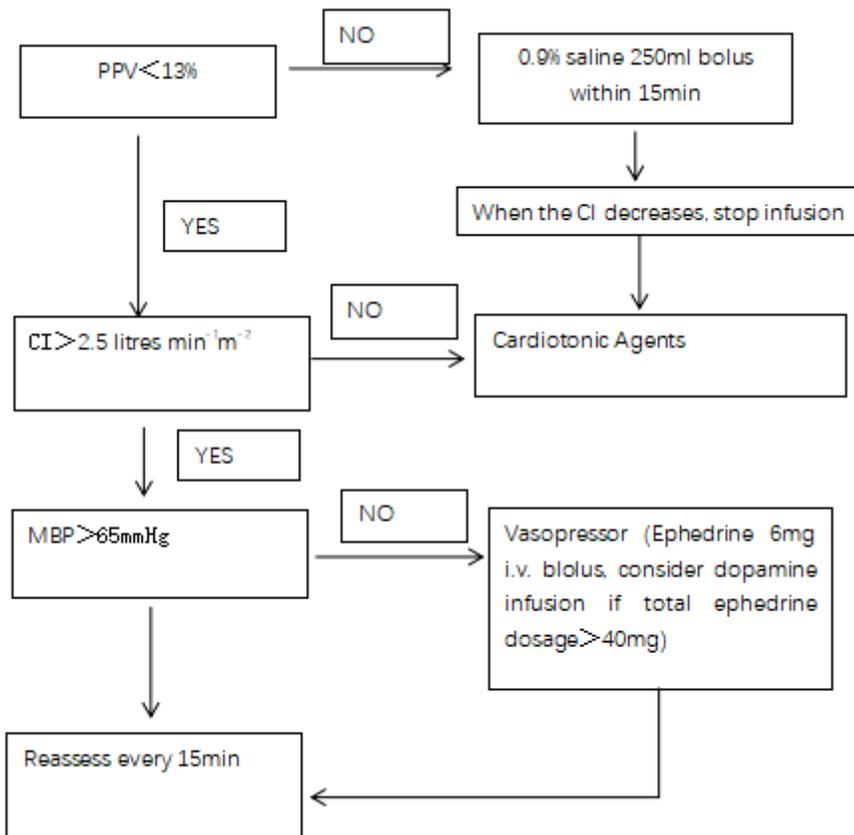


Figure 1

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

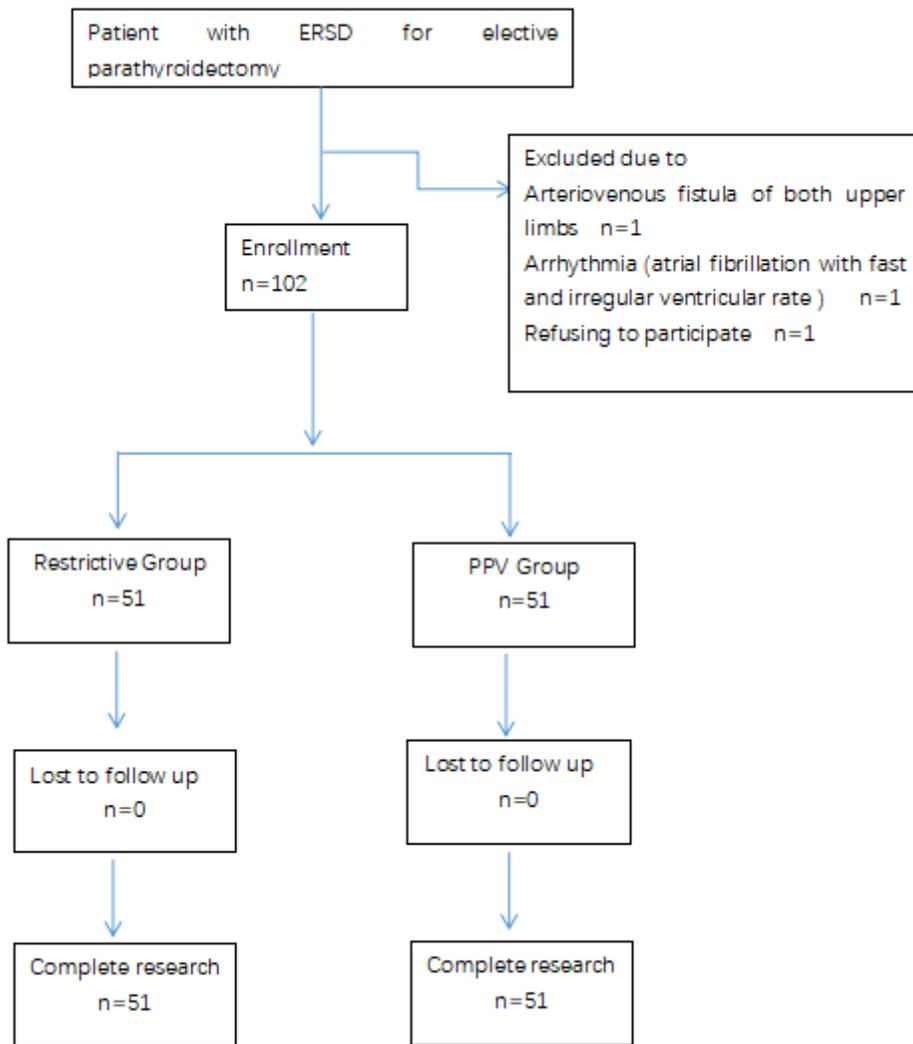


Figure 2

Patient recruitment flow chart.

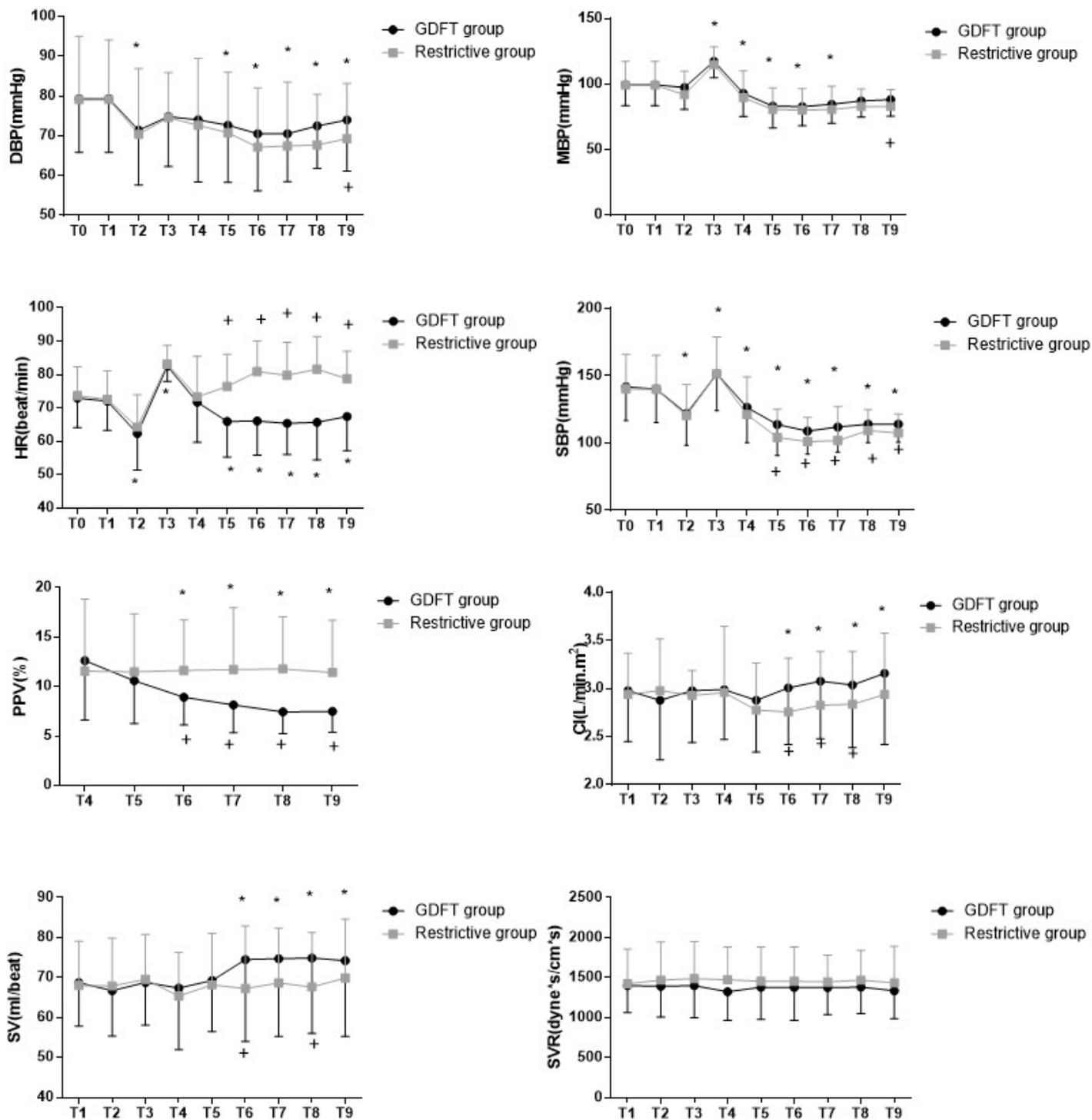


Figure 3

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; CI, cardiac index; SV, stroke volume; SVR, systemic vascular resistance. T0, baseline; T1, before induction; T2, after induction; T3, immediately after intubation; T4, at the beginning of mechanical ventilation; T5, before incision; T6, 30 min, T7, 60 min, T8, 90 min during surgery; T9, 120 min during surgery or at the

end of the surgery if the surgery time was less than 120 min. *Significant difference, at $P < 0.05$, from baseline (T0) for SBP, DBP, MBP, and HR, and from the beginning of ventilation (T4) for PPV, CI, SV, and SVR. + Significant difference, at $P < 0.05$, between the two groups (details in Supplementary Material).

Supplementary Files

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