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The influence of goal-directed fluid therapy on the prognosis of elderly patients with hypertension and gastric cancer surgery

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Purpose: We aimed to investigate the influence of perioperative goal-directed fluid therapy (GDFT) on the prognosis of elderly patients with gastric cancer and hypertension.

Methods: Sixty elderly patients (>60 years old) with primary hypertension who received gastric cancer radical surgery and who were American Society of Anesthesiologists (ASA) class II or III were enrolled in the current study. Selected patients were divided randomly into two arms, comprising a conventional intraoperative fluid management arm (arm C, n=30) and a GDFT arm (arm G, n=30). Patients in arm C were infused with crystalloids or colloids according to the methods of *Miller's Anesthesia* ([illegible]th edition), while those in arm G were infused with 200 mL hydroxyethyl starch over 15 minutes under the FloTrac/Vigileo monitoring system, with stroke volume variation between 8% and 13%. Hemodynamics and tissue perfusion laboratory indicators of patients were recorded continuously from 30 minutes before the operation to 24 hours after the operation.

Results: Compared with arm C, the average intraoperative intravenous infusion quantity in arm G was significantly reduced (2,732±488 mL versus 3,135±346 mL, $P<0.05$), whereas average colloid fluid volume was significantly increased (1,235±360 mL versus 760±280 mL, $P<0.05$). In addition, there were more patients exhibiting intraoperatively and postoperatively stable hemodynamics and less patients with low blood pressure in arm G. Postoperative complications were less frequent, and the time of postoperative hospital stay shorter, in arm G. No significant differences were observed in mortality between the two arms.

Conclusion: Our research showed that GDFT stabilized perioperative hemodynamics and reduced the occurrence of postoperative complications in elderly patients who underwent gastric cancer surgery.

Keywords: stroke volume variation, gastric cancer, the elderly

Introduction

Fluid therapy is an integral part of daily anesthesia, as well as one of the most debated issues in perioperative management. With the aging of the population, more and more patients are in need of large-scale noncardiac surgery.[1–3] Elderly hypertensive patients with hypovolemia and hypoxia are often unable to tolerate such surgery due to postoperative complications. The traditional methods normally introduce more liquid, but easily lead to tissue edema and postoperative low blood pressure. These methods also slow tissue healing and increase the incidence of complications such as pulmonary infection. Furthermore, rapid rehydration loading within a short time can easily lead to acute pulmonary edema and heart failure, which is often life threatening.[4–7] Therefore, more stringent standards are required for fluid administration in elderly patients, and anesthetists should operate with great cautiousness. Since there are no

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instruments that can accurately assess blood volume or tissue perfusion, or accurately predict liquid overload, most studies[8–11] have focused on the selection of types of blood for the perioperative treatment. Clinically, the decision regarding the amount of liquid to use during the surgery still depends on the anesthesiologist's experience and patient's tolerance.

Stroke volume variation (SVV) is an accurate and easy parameter by which to measure fluid responsiveness and functional hemodynamic parameters. It can be used to guide fluid therapy in mechanically ventilated patients. In the present study, we aimed to investigate the effect of goal-directed fluid therapy (GDFT) on prognosis in elderly hypertensive patients receiving gastric cancer surgery. The purpose is to provide a more objective basis for intraoperative fluid therapy and further refine the technique to improve outcomes for elderly patients.

Materials and methods

Patient selection

This study was approved by the ethics committee of Fujian Medical University, Fuzhou, People's Republic of China. All patients signed consent forms. Between March 2011 and December 2012, 60 elderly hypertensive patients (older than 60 years) undergoing abdominal cancer surgery were enrolled in the study. All patients had normal preoperative blood pressures. According to the standards of the American Society of Anesthesiologists (ASA), the preoperative conditions of patients were classed as grades II or III. The averaged body mass index (BMI) was <30 kg/m^2, and the averaged preoperative hematocrit level was >0.3[illegible]/L. Patients were excluded if they had secondary hypertension, severe cardiopulmonary diseases (coronary heart disease, congenital heart disease, pneumonia, tuberculosis, pulmonary malignant tumors, etc), liver and kidney dysfunctions, or clear arrhythmia. The diagnostic criteria for hypertension were based on *Chinese Hypertension Prevention Guide*, 2010.[12] All patients received regular preoperative antihypertensive treatments. Using random selection, patients were divided into two arms: a conventional infusion arm (arm C, n=30) and a GDFT group (arm G, n=30).

Perioperative management

Preparation before anesthesia

All patients received a restricted diet preoperatively. After entering the operation room, local anesthesia was administered by left radial artery catheterization guided by Doppler ultrasound (SKK24-S6 xk 9/1; Zhongxi Yuanda Technology Co., Ltd., Beijing, People's Republic of China). Using a multifunction monitor (Datex-Ohmeda S/5™ type), heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), central venous pressure (CVP), oxygen saturation (SpO_2), end-tidal carbon dioxide partial pressure ($PETCO_2$), and other indicators were continuously monitored. The FloTrac/Vigileo system (version 1.10; Edwards Lifesciences, Irvine, CA, USA) was used to obtain cardiac output/cardiac index (CI), stroke volume (SV)/stroke index, SVV, and other hemodynamic parameters.

Maintaining anesthesia

The patients in both arms underwent the same anesthetic procedure with drug application before surgery. Anesthesia was induced by midazolam (Jiangsu Nhwa Pharmaceutical Co., Ltd., Xuzhou, People's Republic of China) 0.06 mg/kg, fentanyl (Yichang Humanwell Pharmaceutical Co., Ltd., Yichang, People's Republic of China) 4 µg/kg, etomidate (German Braun Corporation, Southborough, Germany) 0.3 mg/kg, cis-atracurium (GlaxoSmithKline plc, London, UK) 0.2 mg/kg, followed by intravenous injection. Intubation was completed through video-assisted laryngoscopy. After intubation, a Datex-Ohmeda 7,100 ventilator was used to control breathing during anesthesia. All patients were supplied with 8 mL/kg tidal volume mechanical ventilation to maintain a respiratory ratio (times of inhale:times of exhale) of 1:2 and respiratory rate of 10 to 14 breaths per minute, to ensure a $PETCO_2$ level of ~35–45 mmHg. The airway pressure was kept at less than 25 cm H_2O. The anesthesia was maintained with inhalation of 1.5% to 3% sevoflurane (Jiangsu Nhwa Pharmaceutical Co., Ltd.), in air mixed with 50% O_2. Intermittent boluses of cis-atracurium 0.04 mg/kg and fentanyl 1 µg/kg were administered. A bispectral index of between 40 and 60 was also maintained.

Volume management

The FloTrac/Vigileo device was used to measure SVV and other hemodynamic parameters. Patients in arm C underwent conventional fluid therapy management according to the methods of *Miller's Anesthesia* (6th edition).[13] The management objective for arm G was to induce 200 mL of 6% hydroxyethyl starch within 15 minutes each time, with SVV between 8% and 13%, under the monitoring of the FloTrac/Vigileo system. When the measured SVV was 13% above the normal level (lasting for 5 minutes), or the current subtest reaction was positive (SV increased more than 10%), an additional 200 mL of Voluven® was introduced. Intraoperatively, insulation blankets and a continuous heating device were used to maintain patient temperatures at above 36°C. Blood transfusion was conducted if bleeding constituted more than one-quarter of the total blood volume. Finally, all patients were treated postoperatively by the same team of physicians.

Monitoring indicators

Basic indicators

Patients were scheduled preoperative visits and vital information was collected, which included sex, age, weight, height, blood pressure classification, ASA classification, BMI, hemoglobin levels (Hb), preoperative complication type, etc.

Hemodynamics

All patients were continuously monitored in terms of conventional hemodynamic parameters, including HR, SBP, DBP, MAP, CVP, SpO_2, and other indicators. The FloTrac/Vigileo system was used to obtain cardiac output/CI, SV/stroke index, SVV, and other hemodynamic parameters. Hemodynamic indexes of MAP, HR, and CVP were recorded at the following time points: 30 minutes before surgery (T_0); at the beginning of surgery (T_1); 1 hour after the initial surgery (T_2); at the onset of surgery (T_3); 6 hours after surgery (T_4); 12 hours after surgery (T_5); and 24 hours after surgery (T_6). Also, the perioperative hypotensive events, defined as SBP <90 mmHg, DBP <50 mmHg, or a >30% drop in blood pressure compared with baseline blood pressure, were recorded. Once hypotensive events occurred, ephedrine was administrated to accelerate the infusion rate. We also recorded patients' undergoing crystal volumes, colloids, blood losses, and urine output.

Central venous oxygen saturation ($ScvO_2$) and arterial blood lactate (Lac)

Blood samples were collected from the jugular vein and radial artery in all patients at T_0, T_1, T_2, T_3, T_4, T_5, and T_6. $ScvO_2$ and Lac were then measured by a blood gas analyzer.

Postoperative conditions

The postoperative exhaust times were recorded. If any of postoperative nausea and vomiting, low blood pressure, cardiac arrhythmia, oliguria, anastomotic fistula, or other complications occurred multiple times, patients were immediately transferred to the intensive care unit. Postoperative complications were observed by physicians who were blinded to the two arms in combination with patient self-reports.

Statistical analysis

Data were analyzed by SPSS 18.0 software. Normal distribution was assessed with mean ± standard deviation. Within arms, data were assessed by using two-factor repeated measures analysis of variance. Analysis between arms used Student's *t*-test. Ridit analysis was used to assess ordinal data. Counts were done by using the χ^2 test or Fisher's exact test. $P<0.05$ was considered statistically significant.

Results

There were no significant differences in sex ratio, age, hypertension classification, ASA classification, BMI, Hb, or other general information of the patients between the two arms ($P>0.05$), as shown in Table 1.

There were no significant differences in the HR or CVP values of patients between the two arms. However, MAP values were statistically different between the two arms. For patients of the same arm, the values of MAP, HR, and CVP varied at different time points. There were cross-effects between arms and time points. Thus, it can be considered that the values and rates of change of MAP, HR, and CVP were different at different time points.

Compared with arm C, CVP values were higher at T_4, T_5, and T_6, and HR values were higher at T_3, T_4, T_5, and T_6, in arm G.

From the time point of view, MAP began to rise 1 hour after surgery and then began to decline to the levels from 30 minutes before surgery, continuing to decline until 12 hours after the operation. HR began to decline after surgery, then to rise 6 hours after surgery, reaching peak 12 hours after surgery. CVP began to rise after the start of surgery, rose to the highest value during surgery, and then began to decline 24 hours after the operation to the level from the beginning of the operation (Table 2).

Table 1 Basic information of the patients (n=30)

Arm	Sex (M/F)	Age (years)	Hypertension classification (I/II/III)	ASA classification (II/III)	BMI (kg/m²)	Hb (g/L)	Operation time (h)
C	29/11	67.2±4.3	7/14/9	32/8	24.1±3.3	129.2±4.6	4.3±1.2
G	31/9	66.6±3.9	6/14/10	31/9	24.4±4.2	131.2±6.8	4.1±1.3

Notes: Arm C received conventional infusion; arm G received goal-directed fluid therapy. Data are presented as number or mean ± standard deviation.
Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; Hb, hemoglobin.

Table 2 Comparison of hemodynamics of patients between the two arms (n=30)

Time point	MAP (mmHg)		HR (bpm)		CVP (cm H_2O)	
	Arm C	**Arm G**	**Arm C**	**Arm G**	**Arm C**	**Arm G**
T_0	106.5±8.2	106.9±6.1	71.8±6.2	75.5±10.5	7.4±1.7	7.0±1.7
T_1	107.5±7.9	107.3±6.0	68.8±5.4	71.8±11.3	8.3±1.9	7.9±1.7
T_2	109.2±7.9	110.8±6.5	70.5±5.1	70.3±8.4	10.0±2.2	9.3±1.8
T_3	100.2±7.5	110.9±7.5*	71.8±5.0	68.5±8.1	11.1±1.7	11.9±2.0
T_4	95.3±7.3	109.6±6.8*	74.4±3.8	70.0±8.0*	9.1±1.3	10.9±1.6*
T_5	93.9±6.1	106.0±6.2*	75.5±4.0	71.2±8.7*	7.8±1.2	9.9±1.3*
T_6	92.1±5.3	106.1±4.8*	76.6±4.1	71.9±8.6*	7.0±0.9	8.6±1.4*

Notes: Data are presented as mean ± standard deviation. Arm C received conventional infusion; arm G received goal-directed fluid therapy. T_0 =30 minutes before surgery; T_1 = at the beginning of surgery; T_2 =1 hour after the initial surgery; T_3 = at the onset of surgery; T_4 =6 hours after surgery; T_5 =12 hours after surgery; T_6 =24 hours after surgery. *$P<0.05$ compared to arm C.
Abbreviations: CVP, central venous pressure; HR, heart rate; MAP, mean arterial pressure.

The average volume of intravenous infusion in arm G (2,732±488 mL) was significantly lower than the value in arm C (3,135±346 mL). The amount of colloids was higher in arm G (1,235±360 mL) than in arm C (760±280 mL). There were no differences in intraoperative blood losses and urine outputs between the two arms. Arm G had a lower incidence of hypotensive events, thus patients in this arm had a smaller chance of requiring ephedrine (Table 3).

$ScvO_2$ values between the two arms were statistically different. The difference in Lac value was significant between the two arms. At different time periods, the values of $ScvO_2$ and Lac varied and there were cross-effects between arms and time points.

Compared with arm C, the averaged values of $ScvO_2$ were higher at T_2, T_3, T_4, and T_5 in arm G. The Lac values at T_3, T_4, and T_5 were lower in arm G. From the time point of view, $ScvO_2$ was slightly elevated before surgery, remained stable during surgery, started to increase after surgery, and then began to decline 12 hours after surgery to the preoperative levels. The values of Lac began to decrease during surgery to a minimum level 1 hour after surgery, then began to rise to the preoperative levels and remained stable thereafter (Tables 4 and 5).

Patients in arm G exhibited earlier onset of exhaust time than patients in arm C. The averaged postoperative start time of defecation in arm G was 3.6±1.4 days, and was 4.3±1.9 in arm C. The postoperative hospitalization time was shorter in arm G. The incidences of nausea, vomiting, and hypotension were lower in arm G than in arm C. There were no statistical differences in delirium, arrhythmia, pulmonary infection, pulmonary edema, pulmonary embolism, wound infection/dehiscence, anguria, intestinal fistula, mortality, and other complications between the two arms (Table 6).

Discussion

The debate about appropriate perioperative fluid treatment strategy has been going on for nearly half a century. Studies have reported a number of inconsistent or even contradictory points of views. Although clinical trials or meta-analysis with large sample sizes have been reported, researchers have failed to prove that one method has overwhelming advantages over others.[1–4] Recently, some researches proposed an ideal perioperative state of the loop.[5–15] These literatures showed that for patients at high risk for death, perioperative fluid load or the combination with dobutamine could increase the CI and oxygen delivery index (DO_2I) to extraordinary values (CI >4.5 L/[min·m^2], DO_2I >650 mL/[min·m^2]), significantly reducing patient hospital stay times or mortality. Subsequently, the GDFT term was introduced in many perioperative fluid-management studies.[16]

In recent years, more and more studies have started to reveal that the amount of perioperative transfusion is critical for maintaining the body's fluid balance.[17] Studies showed that the colloid and crystalloid solutions were not exchangeable,

Table 3 Liquid intake and intraoperative administration of vasoactive drugs (n=30)

Arm	Intravenous infusion volume (mL)	Colloids (mL)	Blood loss (mL)	Urine output (mL/[kg·h])	Hypotensive events (n)
C	3,135±346	760±280	473±156	1.77±0.42	9
G	2,732±488*	1,225±360*	482±168	1.82±0.35	2*

Notes: Data are presented as mean ± standard deviation. Arm C received conventional infusion; arm G received goal-directed fluid therapy. *$P<0.05$ compared to arm C.

Table 4 Comparison of $ScvO_2$ and Lac between the two arms (n=30)

Time point	$ScvO_2$ (%)		Lac (mmol/L)	
	Arm C	Arm G	Arm C	Arm G
T_0	71.4±6.2	69.5±4.8	1.2±0.5	1.1±0.3
T_1	72.8±5.6	73.7±3.3	1.1±0.5	1.1±0.3
T_2	71.4±5.4	75.7±3.0*	1.0±0.5	1.0±0.3
T_3	73.5±5.2	78.5±2.9*	1.4±0.6	0.9±0.2*
T_4	71.6±4.8	75.8±2.4*	1.4±0.5	1.0±0.2*
T_5	70.8±4.8	74.1±2.3*	1.3±0.5	1.0±0.2*
T_6	70.9±4.2	72.3±3.0	1.2±0.5	1.1±0.2

Notes: Data are presented as mean ± standard deviation. Arm C received conventional infusion; arm G received goal-directed fluid therapy. T_0 =30 minutes before surgery; T_1 = at the beginning of surgery; T_2 =1 hour after the initial surgery; T_3 = at the onset of surgery; T_4 =6 hours after surgery; T_5 =12 hours after surgery; T_6 =24 hours after surgery. $^*P<0.05$ compared to arm C.
Abbreviations: Lac, arterial blood lactate; $ScvO_2$, central venous oxygen saturation.

Table 6 Comparison of postoperative complications between the two arms

Indicators	Arm C (n=30)	Arm G (n=30)
Onset of exhaust time (days)	4.3±1.9	3.6±1.4*
Postoperative hospitalization (days)	12.2±2.4	10.8±1.9*
Fever	8	3
Nausea and vomiting	9	2*
Delirium	6	2
Hypotension	8	1*
Arrhythmia	5	1
Heart failure	0	0
Oliguria	[illegible]	2
Pulmonary infection	4	2
Pulmonary edema	0	0
Pulmonary embolism	0	0
Wound infection/fracture	2	1
Intestinal anastomosis	1	1
Death	0	0

Notes: Arm C received conventional infusion; arm G received goal-directed fluid therapy. $^*P<0.05$ compared to arm C. Data are presented as number or mean ± standard deviation.

even with an appropriate proportion such as 1:3 to 1:5.[18–20] Using a crystal liquid supplement may retain most of the crystals in the blood vessels. However, it is not always ideal to use a colloidal solution, as surgeons need to consider various factors, such as drug indications, contraindications, and side effects.[21–23]

The results of our study showed that, although the patients in arm G received a significantly lower amount of intravenous infusion, they also received a much higher amount of colloids. Although patients in arm C received more crystalloids, there was no significant difference in the amount of bleeding between the two arms. Compared with arm C, MAP values were higher at T_4, T_5, and T_6, and HR values lower at T_3, T_4, T_5, and T_6, in arm G. For patients in arm G, the probability of having postoperative hypotension was lower, thus these patients were more likely to maintain more stable hemodynamics and good tissue perfusion condition.

Studies have shown that GDFT intervention can not only lower the Lac levels within 24 hours after surgery, but also reduce the incidence of infection.[24–31] In the present study, we discovered that Lac concentrations in arm G were lower at T_3, T_4, and T_5 as compared to the values in arm C ($P<0.05$), in line with previous results.[32] Studies on GDFT also showed that $ScvO_2$ was a reliable parameter to predict postoperative effect, with accuracies of 64.4% and 73%.[33,34] In the present study, the values of $ScvO_2$ were higher at T_2, T_3, T_4, and T_5 in arm G, compared to arm C.

GDFT achieves the goal of optimal oxygen delivery by maintaining or increasing cardiac output. Thus, the immune cells can be free of the risk of preoperative hypoperfusion or intestinal disorder-associated lymphoid tissue damage, thus promoting tissue healing and reducing infection rates. The traditional treatment programs often use a large number of crystal liquid, which can easily lead to tissue edema and postoperative low blood pressure. Postoperative side-effects may affect tissue healing and increase the incidence of complications such as severe pulmonary infections. In the present study, patients in arm G experienced shorter postoperative hospital stay, better postoperative recovery, and faster bowel movement recovery. Also, the incidences of postoperative complications

Table 5 Comparison of different indicators between Arm G and Arm C by ANOVA

Indicators	Arm		Time		Arm × time	
	F-value	*P*-value	*F*-value	*P*-value	*F*-value	*P*-value
MAP (mmHg)	23.98	0.00	81.50	0.00	54.35	0.00
HR (bpm)	0.65	0.42	30.26	0.00	31.60	0.00
CVP (cm H_2O)	3.38	0.07	195.90	0.00	30.80	0.00
$ScvO_2$ (%)	5.81	0.02	52.38	0.00	25.93	0.00
Lac (mmol/L)	3.05	0.09	9.89	0.00	24.31	0.00

Abbreviations: ANOVA, analysis of variance; CVP, central venous pressure; HR, heart rate; Lac, arterial blood lactate; MAP, mean arterial pressure; $ScvO_2$, central venous oxygen saturation.

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such as nausea, vomiting, and hypotension were significantly lower in patients in arm G than in those in arm C. Interestingly, there were no differences in the incidences of delirium, arrhythmia, pulmonary infection, pulmonary edema, pulmonary embolism, wound infection/dehiscence, oliguria, intestinal fistula, mortality, and other complications between the two arms. One possible explanation is that the type and amount of infusion may affect patients' prognosis, as 6% of hydroxyethyl starch solution was found to be more likely to maintain gastrointestinal microcirculation perfusion and oxygen tension than the crystal.[35,36]

Study limitations

There were some shortcomings in this study. The observation time of the patients participating in this study was short. In addition, the experiment was a small, single-center study. A larger-sample-size multicenter study would certainly help investigation of the potential of full-scale implementation of GDFT.

Conclusion

Overall, this study showed that GDFT application in elderly hypertensive patients can stabilize the perioperative hemodynamic situation, improve tissue perfusion, reduce the incidence of postoperative complications, and shorten hospital stays.

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Disclosure

The authors report no conflicts of interest in this work.

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