Original Article
The accuracy and effectiveness of goal directed fluid therapy in plateau-elderly gastrointestinal cancer patients: a prospective randomized controlled trial

Guoliang Zhao*, Peihua Peng*, Yinyan Zhou, Junjie Li, Haiyan Jiang, Jianlin Shao

Department of Anesthesiology, The First Affiliated Hospital of Kunming Medical University, Kunming, People’s Republic of China. * Equal contributors and co-first authors.

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Abstract: Gastrointestinal cancer, a common disease with high mortality in the world, happens in Yun-Gui Plateau region of China with high morbidity and mortality. The purpose of this study is using dynamic parameters (provided by the Vigileo FloTrac system) to evaluate the accuracy and effectiveness of goal directed fluid therapy (GDFT) in the perioperative period for plateau-elderly gastrointestinal cancer patients. This prospective, randomized and controlled study was conducted among 88 participants from Yun-Gui Plateau of China, aged over 60 years, undergoing elective radical correction of gastrointestinal cancer. They were randomly allocated into two equal groups: GDFT group, using FloTrac/Vigileo system to obtain blood flow dynamic indices Visual analog scale; routine fluid infusion group (control group), routine fluid infusion according to blood pressure during the surgery. Surveillance indicators contained the following contents: the total fluid infusion volume, the amount of crystalloid and colloid, the urine output, the blood loss volume, the time of first bowel movement after surgery, the postoperative discharge time and the medical care costs. The crystalloid quantity infused in GDFT group was markedly less than that in control group [(1269.32 ± 332.4) vs (1670.45 ± 348.8) ml, P < 0.05]. The colloid quantity infused in GDFT group was significantly more than that in control group [(892.64 ± 413.87) vs (1140.91 ± 271.36) ml, P < 0.01]. The incidence of pulmonary complications post of the operation in GDFT group was much lower. In GDFT group, the first time of intestinal peristalsis was substantially earlier than that in control group [(81.51 ± 33.2) vs (107.66 ± 31.81) min, P < 0.05]. Moreover, the hospitalization days after surgery in GDFT group were much shorter than that in control group. Medical cost in GDFT group was much lower than that in control group. In conclusion, GDFT used in the perioperative period could improve the prognosis of old patients undergoing radical correction of gastrointestinal cancers and reduce the incidence of postoperative complications. On the other hand, patients with this treatment will be happy for cost savings.

Keywords: Plateau, goal-directed fluid therapy (gdft), svv, gastroenteric operations, advanced age

Introduction
Gastrointestinal cancer, a common disease with high mortality in the word [1], happens in Yun-Gui Plateau region of China with high morbidity and mortality [2]. At present, gastrointestinal cancer treatment is still based on surgical treatment, and perioperative fluid management has been shown to be a major determinant of postoperative outcomes. During the perioperative period, the amount of administered fluid depends on multiple factors such as preoperative hydration, intraoperative blood loss, hemodynamic stability, and anesthesiologists and surgeons. Owing to the decline of elderly patients physiological functions, the hemodynamics in the perioperative period is so vulnerable as to be unstable, thereby increasing the operation risk in the perioperative period [3].

The traditional mode of fluid infusion is a routine one based on experience, which may not satisfy individualized demands and may lead to excessive or insufficient fluid infusion. The former may result in tissue edema and increase the load of the heart and lungs. The latter may lead to the deficiency of effective circulating blood volumes that may contribute to organs...
and tissues hypo-perfusion, and ultimately increasing the incidence of postoperative complications and mortality [4, 5].

The goal directed fluid therapy (GDFT) was based on clinical treatment experience. Mythen et al. [6] used transesophageal Doppler ultrasound to optimize the liquid treatment for the first time in patients undergoing coronary artery bypass grafting. The results showed that liquid optimal treatment can significantly improve intestinal perfusion and reduce occurrence of complications. FloTrac/Vigileo monitoring is one of the perioperative GDFT detection methods. The FloTrac/Vigileo system requires radial arterial puncture without calibration, and can consistently obtain stroke volume variation (SVV) or pulse pressure variability (PPV). It has been reported that when using SVV as the main index in fluid infusion therapy, the incidence of complications following the operation and mortality would be greatly reduced. However, dynamic parameters provided by FloTrac/Vigileo system, are derived from calculating and analyzing invasive arterial pressure waveform data and heart rate [3, 7-9]. Because SVV is a reliable indicator for predicting fluid responsiveness, so clinically the first to pass liquid reaction method is to make SVV or PVV < 13%, and then use inotrope agents to achieve the predetermined value of CI or DO₂ [8, 10].

In highland district, human arteries blood pressure and heart rate change because of the effects of high altitude [11, 12]. The accuracy and effectiveness of dynamic hemodynamic parameters in patients living in high altitudes, especially elderly patients have not been proven as yet. In this study, we chose elderly patients who have lived more than 10 years in Yun-Gui Plateau (altitude about 2000 meter) and underwent radical operation of gastrointestinal cancer as subjects, and used dynamic parameters (provided by the FloTrac/Vigileo system) to evaluate the accuracy and effectiveness of GDFT used in plateau-elderly gastrointestinal cancer patients in the perioperative period.

Materials and methods

Subjects

The study has been approved by the Ethics Committee of the First Affiliated Hospital of Kunming Medical University, and written informed consents have been provided by all patients in our hospital from February to October 2016 enrolled in this prospective, randomized and double-blind study.

The inclusion criteria were: (1) aged over 60 years; (2) patients conformed to American Society of Anesthesiologist (ASA) physical status class II or III; and (3) those scheduled for radical operations of gastrointestinal cancers (stomach, colon or rectum). The exclusion criteria were: (1) suffered from severe aortic regurgitation or rapid arrhythmia (atrial fibrillation, ventricular tachycardia); (2) patients conformed to American Society of Anesthesiologist (ASA) physical status class I or IV; and (3) those needed intra-aortic counterpulsation. All participants were randomly and equally assigned to routine fluid infusion group (control group) and GDFT group.

Administration and management in perioperative period

Before anesthesia induction, all patients were administered 250 ml compound formula of electrolytes (Baxter, UK) to provide volume expansion. Patients were given peneyclidine (0.5 mg) 15 min before the operation via intravenous push. Under local anesthesia, arterio-puncture of radial artery was conducted, and a cannula was placed into the radial artery. As for the anesthesia induction, fentanyl (3 μg·kg⁻¹) (Yichang Humanwell Pharmaceutical, China), propofol (2 mg/kg) (AstraZenecaUK) and cisatracurium besilate (Glaxo Smith Kline, UK) were administered.

In control group the fluid infusion therapy was conducted according to blood pressure changes. That is, MAP was maintained ≥ 65 mmHg, or, if in hypertension patients, the blood pressure during the operation should be maintained to the level of 30% beyond the basal blood pressure. Heart rate (HR) was maintained at 60-90 beats/min. If it is necessary to give compound formula electrolytes and Hydroxyethyl Starch 130/0.4 and Sodium Chloride Injection (Hes, Fresenius Kabi Deutschland Gmbh), their volume ratio was maintained as 2:1.

In GDFT group, FloTrac/Vigileo system was employed to obtain blood flow dynamic indices including SVV. The 3 ml/kg/hr dosage of compound formula electrolytes was used as maintenance fluids. In this group, SVV value on the FloTrac/Vigileo system was remained below
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13%. When SVV > 13% (lasting beyond 5 min), 250 ml 6% hetastarch 130/0.4 should be administered intravenously within 15 min, or 250 ml Wan Wen was additionally administered when current fluid challenge showed positive (SV increased by 10% or more). Vasoactive agents could be administered as appropriate by the anesthesiologist. The body temperature was maintained ≥ 36°C, the hemoglobin was maintained ≥ 80 g/L. When hemoglobin was < 80 g/L, suspended red blood cells were infused. Following the operation, all patients underwent self-control venous analgesia.

Outcome variables

Arterial blood was drawn at different time points to perform blood gas analysis. The total fluid intake, quantity of crystalloid and colloid, urine output, blood loss volume and dose of vasoactive agent of the two groups was recorded, respectively. Time to first bowel movement, postoperative hospitalization and total cost were recorded as well.

Statistical analysis

Data was analyzed by using SPSS 17.0 software. All data were expressed as \( \bar{x} \pm s \). The comparison of two independent samples was performed by using t-test. The comparison of enumeration data, such as general data and the incidence of postoperative complications, was performed by using chi square test or continuous correction formula or Fisher's Exact Test. A level of \( P < 0.05 \) was considered as statistically significant.

Results

Comparison of the general data

Between February and October 2016, there were 88 patients undergoing elective radical operations of gastrointestinal cancers in the First Affiliated Hospital of Kunming Medical University. A total of 0 patient was excluded, including age less than 60 years old (n = 0), patients suffered from severe aortic regurgitation or rapid arrhythmia and needed intra-aortic counterpulsation (n = 0), American Society of Anesthesiologist (ASA) physical status class I or IV (n = 0). The total 88 patients were randomly divided into control group (n = 44) and GDFT group (n = 44) (Figure 1). There was no significant difference in gender, age, and body mass index (BMI) and ASA grade between the two groups (\( P > 0.05 \)) (Table 1).

Comparison of fluid intake and output volumes

In our study, the results showed that the fluid intake of GDFT group was significantly less than that of the control group. There was no significant difference in the number of transfusion patients between control group (8, 8.2%) and GDFT group (10, 22.7%) (\( P > 0.05 \)); but the average amount of blood transfusion in GDFT group was significantly higher than that in control group (885.00 ± 377.16 ml vs 443.75 ± 139.99 ml). Compared with control group, the
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Table 2. Comparison of fluid input and output volume and vasoactive agent dose between two experimental groups (X \( \pm \) s, n = 44)

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>GDFT group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystalloid (ml)</td>
<td>1670.45 ( \pm ) 348.8</td>
<td>1269.32 ( \pm ) 332.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Colloid (ml)</td>
<td>1140.91 ( \pm ) 271.36</td>
<td>892.64 ( \pm ) 413.87</td>
<td>0.001</td>
</tr>
<tr>
<td>Total (ml)</td>
<td>2888.64 ( \pm ) 571.91</td>
<td>2375.59 ( \pm ) 814.03</td>
<td>0.001</td>
</tr>
<tr>
<td>Urine (ml)</td>
<td>550 ( \pm ) 271.94</td>
<td>553.41 ( \pm ) 309.61</td>
<td>0.956</td>
</tr>
<tr>
<td>Blood loss (ml)</td>
<td>140.45 ( \pm ) 117.12</td>
<td>170.57 ( \pm ) 308.37</td>
<td>0.546</td>
</tr>
<tr>
<td>Urine plus blood Loss (ml)</td>
<td>685 ( \pm ) 344.96</td>
<td>1043.3 ( \pm ) 1598.75</td>
<td>0.15</td>
</tr>
</tbody>
</table>

GDFT: goal directed fluid therapy.

Table 3. Comparison of first evacuating time after operation, total hospital days, hospital days post of operation and the medical care costs between two experimental groups (X \( \pm \) s, n = 44)

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>GDFT group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative time (h)</td>
<td>3.70 ( \pm ) 1.20</td>
<td>3.68 ( \pm ) 1.47</td>
<td>0.955</td>
</tr>
<tr>
<td>Extubation time (h)</td>
<td>1.79 ( \pm ) 5.8</td>
<td>3.38 ( \pm ) 7.18</td>
<td>0.256</td>
</tr>
<tr>
<td>PCA time (h)</td>
<td>3.32 ( \pm ) 10.2</td>
<td>7.21 ( \pm ) 16.88</td>
<td>0.196</td>
</tr>
<tr>
<td>Time of exsufflation (min)</td>
<td>107.66 ( \pm ) 31.81</td>
<td>81.51 ( \pm ) 33.2</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Postoperative discharge time (d)</td>
<td>16 ( \pm ) 5.05</td>
<td>13.82 ( \pm ) 6.6</td>
<td>0.085</td>
</tr>
<tr>
<td>Days in hospital (d)</td>
<td>26.16 ( \pm ) 7.12</td>
<td>21.93 ( \pm ) 9.34</td>
<td>0.019</td>
</tr>
<tr>
<td>Medical expense (CNY)</td>
<td>48263.25 ( \pm ) 13242.63</td>
<td>38848.23 ( \pm ) 11453.4</td>
<td>0.001</td>
</tr>
</tbody>
</table>

GDFT: goal directed fluid therapy.

average volume of crystalloid in GDFT group was markedly lower (P < 0.05) while the average volume of colloid was significantly higher (P < 0.01). There was no significant difference in total fluid volume, urine output and blood loss between the two groups (P > 0.05) (Table 2).

Comparison of surgical related indicators

There was no significant difference between the two groups in operation time (P > 0.05) (Table 3), even some parameters were monitored in GDFT group. At the same time, we compared the extubation time, PCA time and the first exhaust time. The exhaust time in GDFT group was significantly earlier than that in control group (81.51 \( \pm \) 33.2 min vs 107.66 \( \pm \) 31.81 min) (Table 3) as well as the postoperative discharge time. The postoperative hospital days in GDFT group (13.82 \( \pm \) 6.6 days) were significantly less than that in control group (16 \( \pm \) 5.05 days). The first bowel movement after operation in GDFT group was significantly earlier than that in control group (P < 0.05). Hospitalization cost is another issue worthy of attention except for postoperative recovery. In our study, we found that the hospitalization cost in GDFT group (38848.23 \( \pm \) 11453.4 CNY) was significantly lower than that in control group (48263.25 \( \pm \) 13242.63 CNY) (P < 0.05) (Table 3).

Comparison of complications after operation

The incidence of complications occurred before discharge between the two groups was compared, and there was no statistical difference. However, the incidence of wound infection and wound dehiscence in GDFT group was significantly higher than that in control group. The probability of postoperative hypotension in GDFT group was higher than that in control group (Table 4). At the same time, our data showed that the incidence rate of heart failure and pulmonary edema in GDFT group were both lower than those in control group, but with no statistical significance.

Discussion

Low oxygen partial pressure, hypoxia, severe acidosis and increased capillary permeability, which caused by high altitude conditions, often be accompanied by pulmonary hypertension and can reduce the body’s tolerance to fluid [13]. Pulmonary edema and heart failure can be occurred if standard methods are used to determine fluid treatment capacity [12, 14].
This is a prospective study in which the FloTrac/Vigileo system was used to monitor perioperative hemodynamic parameters in the perioperative period to direct GDFT when elderly patients at high altitude were undergoing radical operations of gastrointestinal cancers. The accuracy and effectiveness of GDFT was evaluated by measuring the total fluid intake during the operation, the quantity of crystalloid and colloid, the urine volume, the blood loss, the dose of vasoactive agents, and the postoperative recovery, occurrence of complications, and cost of hospitalization.

In clinical work, fluid infusion therapy during surgery is always one of the most important issues that attracting more attention of anesthesia doctors [15-17]. The harmful sequelae of severe patients and patients undergoing complex operations have a close relation to fluid overload or fluid deficiency [18]. GDFT could maintain the stability of hemodynamics during surgery, increase the oxygen delivery and reduce the incidence of post operation complications and mortality [8, 19]. Li et al. [20] revealed that GDFT could make the body achieve the optimal circulating functional state through fluid loading by a study on 60 cases of radical resection of gastric cancer in elderly hypertension patients. In this study, patients undergoing GDFT accepted lower total fluid intake during the operation. And GDFT could provide more stable hemodynamics and enhance tissue perfusion and oxygen metabolism throughout the body [3], so ScvO₂ was markedly higher than that in routine fluid infusion group at four time points throughout the periprocedural phase. It has been indicated that GDFT could maintain the balance oxygen delivery and consumption. These suggest that the use of GDFT in the perioperative period helps the smooth progress of radical operation for plateau-elderly gastrointestinal cancer patients.

Furthermore, the results of our study have shown that the incidence of pulmonary complications in control group was markedly higher than that in GDFT group, which may be attributed to the fact that the crystalloid quantity infused in control group was more than that in GDFT group in the perioperative period. It has been demonstrated that 20% of crystalloid solution infused into the human body stayed in the blood vessels while the remainder dispersed into the interstitial fluid, which results in the edema of the interstitial fluid and incidence of pulmonary complications. There exists major controversy regarding the selection of fluid applied for treatment during operations. We found in this study that, compared with the control group, the quantity of colloid infusion was less in GDFT group, which was in line with previous reports. Mayer et al. [8] revealed that in GDFT group, the quantity of colloid infused was more than that administered in routine method from a study of 60 cases of major abdominal surgery, whereas the quantity of crystalloid was less than the latter. This study suggested that the colloid solution was preferred to be used in fluid administration in the perioperative period. To attain identical effect of fluid expansion, the quantity of the crystalloid solution needed was 2.5-3 folds than that of the colloid one. And a large amount of crystalloid infused during the operation raises the extent of interstitial edema, increases the incidence of pulmonary and gastrointestinal tract complications, and meanwhile increases the incidence of nausea and vomiting post of operation [21].

It was reported that hetastarch may exert an influence on renal function and coagulation function leading to augmentation of bleeding volume [22]. However, recent studies have demonstrated that hetastarch 130/0.4 had no significant influence on renal function and coagulation function [23, 24]. Demir A et al. [23] compared the security and efficiency between the gelofusine solution and hetas-

<table>
<thead>
<tr>
<th>Table 4. Comparison of complications after operation between two experimental groups (%) (X ± s, n = 44)</th>
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<tbody>
<tr>
<td>Control group</td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td>Complications</td>
</tr>
<tr>
<td>Wound infection</td>
</tr>
<tr>
<td>Wound dehiscence</td>
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<tr>
<td>Abdominal incisional hernia</td>
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<tr>
<td>Anastomotic fistula</td>
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<tr>
<td>Adhesive ileus</td>
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<tr>
<td>Retroperitoneal hemorrhage</td>
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<tr>
<td>Postoperative hypertension</td>
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<tr>
<td>Postoperative hypotension</td>
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<tr>
<td>Arrhythmia</td>
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<tr>
<td>Pneumonia</td>
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<tr>
<td>Pulmonary atelectasis</td>
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<tr>
<td>Pneumonnedema</td>
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GDFT: goal directed fluid therapy.
tarch 130/0.4 when used in elective operations. The results showed that in the elective operation, usage of 6% hetastarch 130/0.4 is safe and effective. Simultaneously, hetastarch could enhance the perfusion of the microcirculation, reduce the inflammatory reaction and decrease the vascular permeability. Hiltebrand et al. [25] conducted a study regarding roles of different categories of fluid in tissue perfusion in animal models. They found that when the colloid solution was predominantly used in operations as GDFT therapy, it would remarkably raise the volume of blood flow and oxygen supply in tissues. Therefore, in patients undergoing elective operations, it is secure and feasible that the colloid solution be selected for fluid expansion. More importantly, it reduces the incidence of post operation complications and reduces mortality that the colloid solution was predominantly used in operations as GDFT therapy.

Consistent with the results of previous research [5, 7, 8], this study found GDFT could reduce the hospital stay post of the operation for old aged gastrointestinal cancer patients who underwent operations. Although the patients’ medical care cost was raised due to the use of the FloTrac/Vigileo system, the total medical care cost was still less than that of patients administered with routine fluid infusion owing to the reduction of hospital stay post of the operation for GDFT administration, which saved valuable medical resources.

Conclusion

In this study, we found that GDFT can satisfy individualized fluid infusion requirements in elderly patients living at high altitude who were subjected to gastrointestinal cancer operations. Moreover, in the patients treated by GDFT, their prognosis would be improved. We also found the hospital stay post of the operation and medical care costs of these patients dramatically reduced. Our results may shed a new light on the development of fluid infusion therapeutic strategies. In this study, however, we did not find the significant difference in the incidence of such complication of operations as cardiovascular complications, anastomotic stoma fistula, adhesive intestinal obstruction, pulmonary edema and heart failure, which might be attributed to the small samples of this study. Larger samples could be involved in the future studies in a manner of multi-centric research.

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Disclosure of conflict of interest

None.

Address correspondence to: Jianlin Shao, Department of Anesthesiology, The First Affiliated Hospital of Kunming Medical University, 295 Xichang Road, Kunming 650032, People’s Republic of China. Tel: +86-13888586162; Fax: +86-871-65324888; E-mail: janelinshaow@163.com

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