Influence of goal-directed fluid therapy guided by the Vigileo-FloTrac^{TM} system on intestinal mucosal barrier function in elderly patients with colorectal cancer

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Abstract

Introduction: *Colorectal cancer is a clinically common malignancy arising in the digestive tract.*
Aim: *To evaluate the influence of goal-directed fluid therapy (GDFT) guided by the Vigileo-FloTrac^{TM} system on intestinal mucosal barrier function in elderly patients with colorectal cancer.*
Material and methods: *A prospective study was conducted on 106 elderly patients with colorectal cancer. They were divided into control and research groups (n = 53) using a random number table, and subjected to conventional fluid therapy and Vigileo-FloTrac^{TM} system-guided GDFT, respectively. Their intraoperative indicators, postoperative indicators, and changes of haemodynamics, oxygen metabolism, intestinal mucosal barrier function at different time points, and incidence rates of complications were compared.*
Results: *Compared with the control group, the intraoperative urine volume, colloid fluid volume, crystalloid fluid volume, and total infusion volume were lower, and the first postoperative exhaust time, first postoperative feeding time, and hospital stay were shorter in the research group ($p < 0.05$). At T_1 and T_2, mean artery pressure, heart rate, central venous pressure, oxygen consumption, oxygen delivery, and oxygen extraction ratio in the research group were lower than in the control group, but all of them first rose and then fell in the 2 groups ($p < 0.05$). On the 3rd day after surgery, the levels of serum endothelin, diamine oxidase and D-lactate declined in both groups, and the decline was more obvious in the research group ($p < 0.05$).*
Conclusions: *GDFT guided by the Vigileo-FloTrac^{TM} system is beneficial to the prognosis of patients by effectively decreasing fluid infusion.*

Key words: *goal-directed fluid therapy, Vigileo-FloTrac^{TM} system, intestinal mucosal barrier function, colorectal cancer.*

Introduction

Colorectal cancer is a clinically common malignancy of the digestive tract, with high morbidity and mortality rates [1]. Currently, patients with colorectal cancer are mainly treated by laparoscopic surgery as the first-line therapy, which is typified by mild trauma and fast recovery [2, 3]. However, elderly patients are often complicated with other diseases and subjected to preoperative fasting, bowel preparation, postoperative trauma stimulation, establishment of the pneumoperitoneum, and inappropriate fluid therapy, so they have insufficient tissue perfusion and weakened immune function, and the prognosis is affected [4–6]. Therefore, an effective volume ther-

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apy is vital for elderly patients receiving colon cancer surgery.

The aims of traditional fluid replacement schemes are to maintain the stability of heart rate (HR), urine volume, and blood pressure during surgery. In these schemes, the fluid replacement volume is a predetermined amount, and there are no individual differences between age, gender, circulatory function, or basic diseases, so the outcomes are usually poor [7]. To date, urine volume, mean artery pressure (MAP), and central venous pressure (CVP) are often monitored to keep the fluid in a normal state, but these indicators have low accuracy and their application is complicated [8]. In recent years, goal-directed fluid therapy (GDFT) has been widely applied in the perioperative fluid therapy for thoracotomy and laparotomy, which can effectively maintain homeostasis and suppress stress responses [9, 10]. However, the frequent postural changes and the establishment of pneumoperitoneum during the laparoscopic radical resection of colorectal cancer result in pathophysiological changes, which makes perioperative volume management more difficult [11].

Established based on the monitoring indicators of peripheral arterial pressure waveforms such as stroke volume variability (SVV) and cardiac index (CI), the Vigileo-FloTrac^{TM} system is easy to operate and has high accuracy in predicting fluid responsiveness [12]. This system mainly records the changes of vascular compliance through its own statistical analysis, without needing other correction methods. Hamed *et al.* reported that the Vigileo-FloTrac^{TM} system was in good agreement with transoesophageal Doppler ultrasound [13].

Aim

The effect of GDFT guided by the Vigileo-FloTrac^{TM} system on the intestinal mucosal barrier function in elderly patients with colorectal cancer was assessed in this study, aiming to provide a reference for the development of fluid volume therapy in clinical practice.

Material and methods

General data

A prospective study was performed on 106 elderly patients with colorectal cancer, who were treated in our hospital from January 2021 to December 2021. These patients were divided into control and research groups (n = 53) using a random number table. The control group included 33 males and 20 females aged 60–87 years, with an average age of (70.21 ±4.27) years. In this group, there were 28 cases of colon cancer and 25 cases of rectal cancer. In terms of the tumour, node, and metastasis (TNM) stage, there were 21 cases of stage II and 32 cases of stage III. Regarding the tumour location, there were 20 cases of rectal cancer, 18 cases of ascending colon cancer, and 15 cases of descending colon cancer and sigmoid colon cancer. The research group consisted of 31 males and 22 females aged 61–89 years, with an average age of (70.49 ±4.52) years. In this group, there were 29 cases of colon cancer and 24 cases of rectal cancer. With regard to the TNM stage, 23 cases were at stage II and 30 cases at stage III. In terms of the tumour location, there were 22 cases of rectal cancer, 19 cases of ascending colon cancer, and 12 cases of descending colon cancer and sigmoid colon cancer. Differences in gender, age, TNM stage, and tutor location between the 2 groups were not statistically significant (p > 0.05). This study was approved by the Ethics Committee of our hospital.

Inclusion and exclusion criteria

Inclusion criteria were set as follows: 1) patients diagnosed with colorectal cancer in line with the diagnostic criteria [14] by surgery and pathology; 2) those aged 60–90 years; 3) those who signed the informed consent; 4) those at TNM stage II–III; and 5) those undergoing selective laparoscopic radical resection of colorectal cancer.

Exclusion criteria involved: 1) patients with immune system disorders or coagulation disorders; 2) those with severe heart, liver or kidney insufficiency; 3) those with history of distant metastasis or chemoradiotherapy; 4) those who required positive end-expiratory pressure during surgery; 5) those who had received infusion of blood products before surgery; and 6) those with poor compliance with research.

Anaesthesia methods

After inclusion, the HR and electrocardiograms of all patients were monitored by a Siemens Patient Monitoring System (Germany). Then the peripheral venous access was established, local anaesthesia was performed, and the left radial artery and right internal jugular vein were punctured with catheters. Anaesthesia induction drugs included 0.3–0.6 μg/kg sufentanil, 0.1 mg/kg midazolam, 0.2 mg/kg cisatracurium, and 0.2 mg/kg etomidate. Tracheal intubation parameters were set as follows: tidal volume: 8 ml/kg, oxygen flow: 2 l/min, and respiratory rate: 12 beats/min. Anaesthesia maintenance drugs consisted of 6–12 μg/(kg·h) remifentanil and 4–6 mg/(kg·h) propofol.

Treatment method for the control group

The control group underwent conventional fluid therapy to achieve a CVP of 8–12 cm H_2O, blood oxygen saturation (SpO_2) ≥ 75%, and urine volume ≥ 0.5 ml/(kg·h). 500 ml of crystalloid fluid was infused in the case of SpO_2 < 75%, after which if SpO_2 remained less than 75%, 250 ml of colloid fluid was infused.

Treatment method for the research group

The research group received GDFT guided by the Vigileo-FloTrac™ system (Edwards Lifesciences, USA). Specifically, the radial artery was punctured and connected to the Vigileo-FloTrac™ system to monitor SVV, CI, CVP, and other indicators, and to adjust the fluid replacement. When SVV > 12% and CVP < 15 cm H_2O, 3 ml/kg colloid fluid was infused for 10 min for volume expansion. If SVV < 12% or CI variation amplitude ≤ 10% after the expansion, whether the CI was greater than 2.5 l/(min·m^2) should be observed. If CI > 2.5 l/(min·m^2), re-evaluation would be performed after 5 min, but if CI ≤ 2.5 l/(min·m^2), 3 μg (kg·min), dopamine would be pumped until CI > 2.5 l/(min·m^2). During surgery, tachycardia indicated the need for intravenous injection of 15–20 mg of esmolol, hypertension indicated the need for intravenous injection of 12.5–25 mg of urapidil, bradycardia represented the need for intravenous injection of 0.5–1 mg of atropine, and hypotension suggested the necessity for intravenous injection of 0.5 μg/kg of dopamine.

Detection of related indicators

Examination of intraoperative indicators: Intraoperative blood loss, urine volume, colloid fluid volume, crystalloid fluid volume, and total infusion volume of the 2 groups were recorded.

Examination of postoperative indicators: The first postoperative exhaust time, first postoperative feeding time, and hospital stay of the 2 groups were recorded.

Examination of haemodynamics: At different time points [at 0 min before surgery (T_0), at 1 h after the beginning of surgery (T_1), and at 2 h after the beginning of surgery (T2)], changes of MAP, HR, and CVP in the 2 groups were detected using the NICAP-T18 non-invasive continuous blood pressure monitoring system (Zhejiang Mailian Medical Devices Co., Ltd.).

Detection of oxygen metabolism: Oxygen consumption (VO_2), oxygen delivery (DO_2), and oxygen extraction ratio (ERO_2) were detected at T0, T1, and T2.

Detection of intestinal mucosal barrier function: At 1 d before surgery and at 3 d after surgery, 3 ml of peripheral venous blood was collected from each of the 2 groups, and the levels of endotoxin (ET), diamine oxidase (DAO), and D-lactate (D-LA) were determined by an enzymatic method.

Detection of complications: The incidence rates of infection, anastomotic leakage, and intestinal obstruction in the 2 groups were measured.

Statistical analysis

Statistical analysis was performed using SPSS 23.0 software. Measurement data were expressed as ($\bar{x}$ ± s). Intergroup comparison was carried out by the independent samples *t*-test, intragroup comparison was conducted using the paired samples *t*-test, and comparison among multiple groups was performed using one-way analysis of variance. Count data were expressed as percentage and detected using the χ^2 test. $P < 0.05$ indicated a statistically significant difference.

Results

Detection results of intraoperative indicators

The intraoperative urine volume, colloid fluid volume, crystalloid fluid volume, and total infusion volume were lower in the research group than in the control group ($p < 0.05$) (Table I).

Detection results of postoperative indicators

The first postoperative exhaust time, first postoperative feeding time, and hospital stay in the research group were shorter than in control group ($p < 0.05$) (Table II).

Table I. Intraoperative indicators ($\bar{x}$ ± s, ml)

Group	Intraoperative blood loss	Urine volume	Colloid fluid volume	Crystalloid fluid volume	Total infusion volume
Control (*n* = 53)	115.69 ±15.61	508.74 ±84.08	1097.53 ±253.25	1589.38 ±305.21	2761.02 ±453.68
Research (*n* = 53)	117.06 ±16.37	356.36 ±58.63	795.61 ±124.06	1196.24 ±264.01	1996.25 ±395.16
t	0.441	10.823	7.794	7.092	9.254
P-value	0.660	< 0.001	< 0.001	< 0.001	< 0.001

Table II. Postoperative indicators ($\bar{x}$ ± s)

Group	First exhaust time [h]	First feeding time [h]	Hospital stay [days]
Control (*n* = 53)	65.09 ±9.52	41.85 ±7.23	18.87 ±5.67
Research (*n* = 53)	40.06 ±8.33	31.28 ±6.29	14.52 ±5.38
t	14.405	8.030	4.052
P-value	< 0.001	< 0.001	< 0.001

Examination results of haemodynamics indicators

At T_0, no statistically significant differences were found in MAP, HR, and CVP between the 2 groups. At T_1 and T_2, MAP, HR, and CVP in the research group were lower than in the control group, but all of them first rose then fell in the 2 groups ($p < 0.05$) (Table III).

Examination results of oxygen metabolism

At T_0, there were no statistically significant differences in VO_2, DO_2, and ERO_2 between the research group and the control group. At T_1 and T_2, VO_2, DO_2, and ERO_2 were up-regulated first and then down-regulated, and they were lower in the research group than in the control group ($p < 0.05$) (Table IV).

Table III. Examination results of haemodynamics ($\bar{x}$ ± s)

Group	Indicator	T_0	T_1	T_2	*F*	*P*-value
Control (*n* = 53)	MAP [mm Hg]	73.25 ±4.55	88.63 ±5.02	82.39 ±4.89	136.275	< 0.001
	HR [beat/min]	71.18 ±3.72	86.29 ±5.06	82.44 ±4.16	172.746	< 0.001
	CVP [mm Hg]	4.47 ±1.63	7.86 ±1.06	6.69 ±1.10	94.463	< 0.001
Research (*n* = 53)	MAP [mm Hg]	73.11 ±4.34	84.35 ±4.4^{3*}	78.15 ±4.3^{4*}	87.960	< 0.001
	HR [beat/min]	71.44 ±3.50	82.03 ±4.1^{4*}	76.74 ±3.2^{3*}	95.365	< 0.001
	CVP [mm Hg]	4.38 ±1.56	7.02 ±1.3^{9*}	5.71 ±1.2^{6*}	68.254	< 0.001

**P < 0.05 vs. control group at the same time point. CVP – Central venous pressure, HR – heart rate, MAP – mean artery pressure, T_0 – at 0 min before surgery, T_1 – at 1 h after beginning of surgery, T_2 – at 2 h after beginning of surgery.*

Table IV. Examination results of oxygen metabolism ($\bar{x}$ ± s)

Group	Indicator	T_0	T_1	T_2	*F*	*P*-value
Control (*n* = 53)	VO_2 [ml/(min·m^2)]	108.62 ±11.34	135.02 ±13.57	122.71 ±12.06	94.483	< 0.001
	DO_2 [ml/(min·m^2)]	442.68 ±38.95	598.64 ±40.37	549.25 ±38.52	218.152	< 0.001
	ERO_2 (%)	26.67 ±2.77	36.86 ±2.69	32.23 ±2.26	206.776	< 0.001
Research (*n* = 53)	VO_2 [ml/(min·m^2)]	109.51 ±10.54	129.05 ±12.0^{4*}	116.07 ±10.5^{8*}	42.727	< 0.001
	DO_2 [ml/(min·m^2)]	441.28 ±37.59	551.06 ±41.0^{9*}	502.47 ±37.5^{3*}	165.287	< 0.001
	ERO_2 (%)	26.18 ±2.56	34.62 ±2.1^{9*}	29.14 ±1.6^{5*}	148.561	< 0.001

**P < 0.05 vs. control group at the same time point. DO_2 – oxygen delivery, ERO_2 – oxygen extraction ratio, T_0 – at 0 min before surgery, T_1 – at 1 h after beginning of surgery, T_2 – at 2 h after beginning of surgery.*

Detection results of intestinal mucosal barrier function

At 1 d before surgery, the levels of serum ET, DAO, and D-LA were not statistically significantly different between the research group and control group. At 3 d after surgery, the levels of serum ET, DAO, and D-LA declined in both groups, and the decline was more evident in the research group ($p < 0.05$) (Table V).

Detection results of complications

The research group had a lower incidence rate of complications than the control group (1.89% vs. 15.09%, $p < 0.05$) (Table VI).

Discussion

Fluid management has always been a major concern of surgeons and anaesthesiologists. A good fluid therapy scheme can effectively maintain vascular content and homeostasis, improve organ and tissue perfusion, and reduce complications [15]. Intraoperative restrictive fluid replacement can trigger occult hypovolaemia and haemodynamic instability, thereby impairing organ function. In addition, excessive fluid treatment not only affects the recovery of intestinal peristalsis and cardiopulmonary function, but also suppresses tissue oxygenation and wound healing [16]. Therefore, it is of great significance to effectively evaluate the circulatory status of patients during surgery, to formulate a rational fluid therapy scheme.

GDFT is regarded as a scientific method for perioperative volume management. In contrast to traditional rehydration schemes, GDFT is a minimally invasive scheme that can achieve dynamic and continuous monitoring of different circulation indicators as well as dynamic fluid management in light of the specific conditions of patients during surgery [17]. Froghi *et al.* found that GDFT effectively decreased complications and facilitated the recovery of gastrointestinal function [18]. In this study, elderly patients undergoing colon cancer surgery received GDFT guided by the Vigileo-FloTract™ system. The results showed that the infusion volume of all kinds of fluids, postoperative indicators, haemodynamics, oxygen metabolism-related indicators, and complication rate in the research group were superior to those in the control group, indicating that GDFT guided by the Vigileo-FloTract™ system in elderly patients receiving colon cancer surgery can effectively decrease fluid infusion, stabilize haemodynamics, and improve oxygen metabolism, with fewer complications. This is because GDFT aims to optimize liquid infusion, which can not only reduce the incidence rate of haemodynamic instability owing to restricted infusion, but also prevent tissue oedema caused by excessive liquid infusion. Moreover, GDFT can maintain the volume of circulating blood, as well as the perfusion of tissues and organs and the oxygen supply for microcirculation [19]. The Vigileo-FloTrac™ system excels in continuous monitoring, displaying

Table V. Detection results of intestinal mucosal barrier function ($\bar{x} \pm s$)

Group	Indicator	1 day before surgery	3 days after surgery	*t*	*P*-value
Control (*n* = 53)	ET [EU/l]	75.47 ±7.88	45.53 ±6.18	21.765	< 0.001
	DAO [U/l]	18.18 ±2.96	12.37 ±2.06	11.729	< 0.001
	D-LA [mg/l]	13.47 ±2.59	9.86 ±2.11	7.867	< 0.001
Research (*n* = 53)	ET [EU/l]	74.88 ±7.93	28.35 ±5.4^{3*}	35.246	< 0.001
	DAO [U/l]	18.44 ±2.54	9.03 ±2.0^{4*}	21.028	< 0.001
	D-LA [mg/l]	13.18 ±2.23	6.62 ±1.3^{8*}	18.211	< 0.001

$^*P < 0.05$ vs. control group at the same time point. DAO – diamine oxidase, D-LA – D-lactate, ET – endotoxin.

Table VI. Incidence of complications [*n* (%)]

Group	Infection	Anastomotic leakage	Intestinal obstruction	Total
Control (*n* = 53)	3 (5.66)	2 (3.77)	3 (5.66)	8 (15.09)
Research (*n* = 53)	1 (1.89)	0	0	1 (1.89)
χ^2				4.835
P-value				0.028

convenience, accuracy, and rapidity. Connected with the peripheral arterial catheter, the system can effectively analyse the arterial pressure waveform and measure parameters such as CI and SVV in combination with individual differences such as patients' gender and age. SVV reflects the variability of stroke volume (SV) per heartbeat and the responsiveness of liquid therapy [20].

Clinically, elderly patients with colorectal cancer will experience impairment of the intestinal mucosa due to the disease itself, surgical trauma, and preoperative intestinal cleaning, thereby impairing intestinal mucosal barrier function, and good intestinal mucosal barrier function is key to facilitating the recovery and prognosis of patients. Additionally, the damage of intestinal mucosal barrier function will cause the translocation of intestinal flora, intestinal infection, and inflammatory responses, making the treatment more difficult. ET, a kind of lipopolysaccharide, is mainly present in the cell wall of G-Bacillus cells. Only a small amount of ET can pass through the vein via the intestinal mucosa under normal conditions, but it can participate in blood circulation through the intestinal mucosa when the intestinal mucosal barrier function is impaired. DAO, a cellular enzyme, is primarily present in the upper villi of the small intestinal mucosa of mammals. In the case of damaged intestinal mucosal barrier function, the level of DAO evidently rises. D-LA is the end product of intestinal metabolism, and it normally cannot penetrate the intestinal mucosal barrier. When the intestinal mucosal barrier function is impaired, the permeability of D-LA is enhanced, so it can be successfully delivered to the blood, resulting in an obvious increase in the content of D-LA in the blood. According to the results of this study, the levels of serum ET, DAO, and D-LA in the research group and the control group declined at 3 d after surgery, and they were lower in the research group than in the control group, which suggests that GDFT guided by the Vigileo-FloTrac™ system can dramatically promote the recovery of intestinal mucosal barrier function and improve the prognosis of patients.

Conclusions

GDFT guided by the Vigileo-FloTracTM system can effectively reduce fluid infusion, stabilize haemodynamics, improve oxygen metabolism, and promote the recovery of intestinal mucosal barrier function in elderly patients undergoing colon cancer surgery, with fewer complications, which is beneficial to the improvement of the prognosis of such patients. However, this study has a small sample size and a single data source, so the results may be biased. In the future, large-scale and multi-centre clinical research will be carried out for further exploration.

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Yunfeng Zhang and Linsen Zhan contributed equally to this study.

Conflict of interest

The authors declare no conflict of interest.

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