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Acute Hypervolemic Infusion Can Improve Splanchnic Perfusion in Elderly Patients During Laparoscopic Colorectal Surgery

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: There is no adequate evidence on how the long duration of laparoscopic surgery affects splanchnic perfusion in elderly patients or the efficacy of acute hypervolemic fluid infusion (AHFI) during the induction of anesthesia. Our aim was to observe the effects of AHFI during the induction of general anesthesia on splanchnic perfusion.

Material/Methods: Seventy elderly patients receiving laparoscopic colorectal surgery were randomly divided into three groups: lactated Ringer's solution group (group R), succinylated gelatin group (group G), and hypertonic sodium chloride hydroxyethyl starch 40 injection group (group H). Thirty minutes after the induction of general anesthesia, patients received an infusion of target dose of these three solutions. Corresponding hemodynamic parameters, arterial blood gas analysis, and gastric mucosal carbon dioxide tension were monitored in sequences.

Results: In all three groups, gastric-arterial partial CO_2 pressure gaps ($P_{g-a}CO_2$) were decreased at several beginning stages and then gradually increased, $P_{g-a}CO_2$ also varied between groups due to certain time points. The pH values of gastric mucosa (pHi) decreased gradually after the induction of pneumoperitoneum in the three groups.

Conclusions: The AHFI of succinylated gelatin (12 ml/kg) during the induction of anesthesia can improve splanchnic perfusion in elderly patients undergoing laparoscopic surgery for colorectal cancer and maintain good splanchnic perfusion even after a long period of pneumoperitoneum (60 minutes). AHFI can improve splanchnic perfusion in elderly patients undergoing laparoscopic colorectal surgery.

MeSH Keywords: **Gelatin • Infusions, Intravenous • Splanchnic Circulation**

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Background

Laparoscopy is an advanced minimally invasive surgical technique. It has efficacy similar to that of traditional surgery, and has the advantages of minimal invasiveness, quick recovery, better cosmetic outcomes, and cost-effectiveness [1,2]. In the past decade, laparoscopy has developed quickly in the field of general surgery, and it is not only applied in simple procedures involving, for example, the biliary tract or abdominal external hernia, but is also extended to larger surgeries involving the thyroid, gastrointestinal tract, liver, and pancreas, and has even been used for almost all malignant tumors in the digestive system except during liver transplantation. The technical feasibility and safety of laparoscopy have been widely affirmed [3]. The extension of its application now allows for many patients who are in inoperable condition, such as elderly patients, to receive endoscopic surgeries and to enjoy the benefits they bring; however, the increased numbers of such patients also places a higher demand on perioperative anesthesia management. The increased intra-abdominal pressure caused by CO_2 pneumoperitoneum, hypercapnia, and the consequent neuroendocrine response during laparoscopy can all greatly influence the hemodynamic stability and intraperitoneal splanchnic perfusion [4,5]. Therefore, knowing how to adjust patients' circulatory volume status during laparoscopy is particularly important [6].

Intraoperative volume management is an important task of clinical anesthesia. Good volume management not only ensures perioperative cardiovascular stability and creates a better surgical condition for patients, but also improves the prognosis of patients [7], which is particularly important for those who are elderly. Acute hypervolemic fluid infusion (AHFI) during anesthesia induction is one of the methods of intraoperative volume management. Its main advantages include: reduced blood viscosity, improved tissue oxygen supply, blood protection, stable hemodynamics during anesthesia, actual loss of blood volume, and easy operation [8]. The fluid used is mainly isotonic fluid – namely, isotonic crystalloid and/or artificial colloid. As a new type of synthetic hypertonic colloid solution, hypertonic sodium chloride hydroxyethyl starch 40 injection [9] is composed of 4.2% sodium chloride and 7.6% hydroxyethyl starch 40. It is mainly used for anti-shock, perioperative volume therapy, and emergency rescue for brain trauma or brain edema. Its application in AHFI during anesthesia induction, and especially the feasibility, safety, and efficacy of its application in elderly patients, remains to be further investigated.

In order to ensure the safety and reliability of volume management, real-time, highly sensitive, and highly specific monitoring methods are required during anesthesia to quickly and accurately determine the amount of circulating blood volume and its effect on circulating oxygen supply. Gastric tonometry is the only monitor approved by the United States Food and Drug Administration for clinical gastrointestinal perfusion, and its principle of measurement is to continuously monitor the PCO_2 in the system by infrared spectroscopy with a closed carbon dioxide circulation system. The values and curves are displayed simultaneously on the monitor, and the required balancing time is within 10 minutes. In the case of ischemia and hypoxia, in order to ensure the blood supply of vital organs, the body often sacrifices the tissue perfusion in non-vital organs such as gastrointestinal tract; thus, gastrointestinal mucosal oxygen metabolism can be used as a sensitive indicator of insufficient tissue perfusion. Studies have shown that gastrointestinal mucosa is very sensitive to ischemia and hypoxia, and that low blood volume can cause acidosis at the early stage. Even after an aggressive volume restoration, the recovery of gastrointestinal mucosa is slower than other organs. The use of this phenomenon developed by gastric tonometry created based on the above phenomenon is a technology that monitors partial carbon dioxide tension in gastrointestinal mucosa, and sensitively and promptly reflects visceral blood perfusion and oxygenation status. It can also give early indications of the presence of gastric mucosal acidosis, and provide certain references for the prognosis of the disease [10].

So far, there is no adequate evidence on how the long duration of laparoscopic surgery affects splanchnic perfusion in elderly patients, or the efficacy of hypervolemic fluid infusion of different plasma products during the induction of anesthesia in elderly patients. Therefore, the present study observed the effects of AHFI of crystalloid and synthetic colloid fluid during the induction of general anesthesia using gastric tonometry in elderly patients undergoing laparoscopic colorectal surgery, as well as to provide a research basis and clinical operation approach for more complete and proper volume management regimens.

Material and Methods

Case selection and grouping

Elderly patients of both genders undergoing elective laparoscopic colorectal surgery with ASA I~II level, with ages of 65 to 85 years and BMI <30 kg/m², were included. Patients who met one of the following criteria were excluded from the study: hematocrit (Hct) <30%, hemoglobin (Hb) <10g/L, obvious cardiac, hepatic, or renal dysfunction, abnormal coagulation function, history of allergy to hydroxyethyl starch or gelatin. According to these criteria, a total of 72 patients were selected, of which two patients were removed from the study due to severe illness and an intraoperative change in surgical approach (changed to open surgery), resulting in a total of 70

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patients who were eventually included in the subsequent statistics analysis. All patients were randomly divided into three groups: a balance solution group (group R, n=25), succinylated gelatin group (group G, n=21), and a hypertonic sodium chloride hydroxyethyl starch 40 injection group (group H, n=24). During the experiment, additional cases were excluded due to the following situations: cases whose baseline values were not collected or whose data collection was interfered with and statistical analysis could not be conducted, cases whose monitoring could not continue due to damages of laboratory equipment and supplies, and cases with Hct <20% in any blood gas test.

Operation procedure

Method of anesthesia

This study was approved by the Ethics Committee of the Ruijin Hospital, Shanghai Jiao Tong University School of Medicine. All patients or their designated representatives were fully informed of the objectives of the study and the possible risks, and all signed the informed consent form. All patients maintained the right to terminate their participation in the study at any stage of the experiment.

Patients were routinely barred from drinking and eating prior to surgery. No preoperative medication was used. Once the patient was moved into the operating room, a Datex S/5 monitor (Absolute Medical Equipment, Stony Point, NY, USA) was used for noninvasive monitoring of blood pressure, electrocardiogram, pulse, and blood oxygen saturation. Intravenous infusion was established at the left forearm, and a single dose of midazolam 0.04 mg/kg was injected intravenously. The gastric tonometer was placed through the nose of patients in waking state (Tonometrics™ Catheter, TONO-16F, Datex-Ohmeda, Finland), and the position of the tonometer was confirmed by auscultation at the surface projection area of the stomach after air inflation, or by the presence of gastric contents after aspiration, and then the gastric tonometry module was connected. The focal skin was cleaned by alcohol for defatting, and the electrode sheets were placed according to the instruction of the BioZ.com instrument (CardioDynamics Company, USA). The cuff was placed on the left upper arm, and the BioZ.com instrument was connected for noninvasive hemodynamic monitoring.

Thirty minutes after entering the operation room, patients received an intravenous infusion of 10 ml·kg^{-1} balance solution to supplement the restrained food and evaporation before the surgery. The catheter was placed in the left radial artery under local anesthesia, and the blood samples were collected. Catheterization of the right internal jugular vein was performed under local anesthesia, and a double-lumen central venous catheter was placed. The infusion system was then connected and the central venous pressure (CVP) was monitored continuously. After the completion of fluid replacement, each monitoring index was recorded as the basic value. At the same time, arterial blood gas analysis was conducted, and the laboratory data were entered into the gastric tonometry-monitoring module to calculate the relevant values.

After the above procedures, the patients took a 5-minute rest, followed by the induction of general anesthesia. Rapid intravenous induction was used: fentanyl 2 μg/kg, vecuronium bromide 0.1 mg/kg, and propofol 1.5 mg/kg. Pure oxygen was manually delivered to the patients for 3 minutes to remove nitrogen, and secretions were removed. After endotracheal intubation, the anesthesia machine was connected for positive pressure mechanical ventilation (Tidal volume 10 ml/kg, respiratory rate 12 times/min, I: E 1: 2). During the operation, intravenous administration of propofol TCI (2μg/ml) and inhalation of desflurane 0.6MAC were combined to maintain anesthesia, and intermittent intravenous injection of fentanyl and vecuronium were given, based on the surgical process to maintain a stable depth of anesthesia.

AHFI method

Patients were randomly divided into three groups by envelope method, and within 30 minutes of the induction of the general anesthesia, 12 ml/kg balance solution (sodium lactate Ringer's solution, Baxter, Deerfield, IL, USA; group R), 12 ml/kg succinylated gelatin (GELATIN, B Braun, Germany; group G), or 3.5 ml/kg hypertonic sodium chloride hydroxyethyl starch 40 injection (Worldbest Treeful Pharmaceutical, Shanghai, China; group H) was infused. Afterward, the three groups all received infusion of the balance solution at the speed of 7 ml/kg/h. During the surgery, the amount of bleeding was closely monitored, and if the blood loss was estimated to be greater than 200 ml, the appropriate amount of succinylated gelatin was supplemented.

Data collection

The following data were collected at the following time points: prior to the induction (T_0); at the end of AHFI (T_1); 5 minutes, (T_2), 15 minutes (T_3), 30 minutes (T_4), and 60 minutes (T_5) after pneumoperitoneum induction; and 5 minutes (T_6), 15 minutes (T_7), and 25 minutes (T_8) after the release of pneumoperitoneum.

iSTAT arterial blood gas analysis: arterial blood pH (pHa), carbon dioxide partial pressure ($PaCO_2$), bicarbonate concentration (HCO_3), plasma base excess (BE), sodium ions (Na^+), potassium ions (K^+), ionized calcium concentration (iCa^{2+}).

Hemodynamic indexes: heart rate (HR), systolic blood pressure (SBP), central venous pressure (CVP), cardiac index (CI),

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Table 1. General data of patients in the three groups ($\overline{\chi}$±s).

Category	Group R	Group G	Group H
Number (male/female)	25 (14/11)	21 (15/6)	24 (17/7)
Age(yrs)	73±7	73±5	73±7
Weight(Kg)	66±10	62±11	64±8
Weight index(Kg/m²)	24±3	24±3	23±4

P>0.05, the differences among the groups were not statistically significant.

Table 2. Comparisons in the anesthesia duration, post AHFI hemodilution, blood loss, and urine amount among the three groups ($\overline{\chi}$±s).

Category	Group R	Group G	Group H
Post AHFI hemodilution (%)	14±6	17±9	13±5
Anesthesia duration (min)	89±36	94±50	88±43
Blood loss(ml)	81±49	103±38	93±80
Urine amount(ml)	582±484	526±332	732±571

P>0.05, the differences among groups were not statistically significant.

systemic vascular resistance index (SVRI), acceleration index (ACI), thoracic fluid content (TFC).

Gastric mucosal blood flow indices: carbon dioxide partial pressure in gastric mucosa ($PgCO_2$), gastric mucosal pH (pHi), gastric-arterial carbon dioxide partial pressure gap ($P_{g-a}CO_2$), colloid osmotic pressure (COP).

Hemodilution after AHFI: The hemodilution after AHFI during the induction of anesthesia was calculated using the following formula: hemodilution=$HctT_0–HctT_1/HctT_0$, which aims to reflect the level of hemodilution by the degree of change of Hct.

At the end of the operation, the patient's intraoperative blood loss, urine amount, and total operation duration were recorded. If the urine amount was less than 40 ml/h, 5-10 mg furosemide was injected intravenously.

Statistical analysis

The experimental data were analyzed by SPSS 13.0 software (IBM, Armonk, NY, USA), and the normally distributed measurement data were presented as mean ±SD. One-way ANOVA was used for the comparisons of the measurement data between groups, and the S-N-K method was used for pairwise comparisons. Count data were presented by the median, and chi-square test was used for the comparison between groups. A P value <0.05 was considered to be statistically significant, and a P value <0.01 was considered to be very statistically significant.

Results

According to the inclusion and exclusion criteria of the study, a total of 72 patients were initially enrolled in this study. Of the 72 cases, the surgical method was changed during the operation in two patients who were excluded from the study. Eventually, a total of 70 patients were included in the statistical analysis. After a random grouping, the sample numbers of the three groups were: 25 cases in the group of sodium lactate Ringer's solution (group R), 21 cases in the group of succinylated gelatin (group G), and 24 cases in the group of hypertonic sodium chloride hydroxyethyl starch 40 injection (group H).

Table 1 lists the general epidemiological data of the three groups of patients. There were no significant differences in age, weight, or body mass index among the patients of the three groups. Table 2 lists the hemodilution, the total anesthesia duration, intraoperative blood loss, and urine amount after AHFI. Among them, the hemodilution, anesthesia duration, and blood loss in patients of the group G were slightly higher than those of patients in groups R and H (17%, 94 min, and 103 ml, respectively), but the differences were not statistically significant. Perioperative urine amount in the patients of group H was the most (732 ml), which was about 150 ml and 200 ml higher than those in patients of group R group and group G, respectively. These differences between the groups were also not statistically significant.

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Table 3. Comparisons of hemodynamic parameters at different time points among the three groups ($\overline{\chi}$±s).

Index	Group	T_0	T_1	T_2	T_3	T_4	T_5	T_6	T_7	T_8
HR (bpm)	R (*n*=10)	84±10	80±18	73±4$^{a)}$	77±12	75±8	67±7$^{a)}$	72±8$^{a)}$	68±7$^{a)}$	70±9$^{a)}$
	G (*n*=10)	79±15	73±11	72±8	73±7	77±8	72±9	73±10	71±10$^{a)}$	64±10$^{a)}$
	H (*n*=10)	79±15	79±18	75±15	81±15	71±6	74±9	76±11	72±6	76±11
SBP (mmHg)	R (*n*=10)	132±10	121±14$^{a)}$	133±11	127±16	122±9$^{a)}$	121±9$^{a)}$	109±13$^{b)}$	104±10$^{b)}$	101±9$^{b)}$
	G (*n*=10)	136±18	118±9$^{b)}$	132±32	132±20	132±20	123±6$^{b)}$	120±18$^{b)}$	120±16$^{b)c)}$	120±13$^{b)c)}$
	H (*n*=10)	134±18	123±15$^{a)}$	134±10	128±13	122±8$^{a)}$	122±3$^{a)}$	118±12$^{a)}$	130±13$^{d)}$	132±10$^{d)}$
CVP (cm H_2O)	R (*n*=10)	5±2	12±2$^{b)}$	17±4$^{b)}$	16±5$^{b)}$	13±3$^{b)}$	12±3$^{b)}$	8±1$^{b)}$	7±1$^{a)}$	7±1$^{a)}$
	G (*n*=10)	6±3	11±3$^{b)}$	18±2$^{b)}$	18±1$^{b)}$	17±2$^{b)c)}$	14±3$^{b)}$	10±2$^{b)c)}$	9±2$^{a)}$	9±2$^{a)}$
	H (*n*=10)	6±2	11±2$^{b)}$	18±1$^{b)}$	18±5$^{b)}$	16±4$^{b)}$	14±3$^{b)}$	10±2$^{b)c)}$	10±3$^{b)c)}$	9±3$^{a)}$
CI [L/(min·m)]	R (*n*=10)	3.1±0.3	3.0±0.6	2.6±0.3$^{b)}$	2.8±0.4	2.7±0.6$^{a)}$	2.0±0.4$^{b)}$	2.7±0.5$^{a)}$	2.5±0.6$^{b)}$	2.1±0.6$^{b)}$
	G (*n*=10)	3.4±1.0	3.0±0.8	3.1±0.8	2.8±0.3	2.8±0.3	2.6±0.2$^{c)}$	2.9±0.3	2.7±0.2	2.3±0.1$^{a)}$
	H (*n*=10)	3.0±0.3	2.9±.5	2.8±0.5	3.2±0.5	2.8±0.6	2.7±0.4$^{c)}$	2.9±0.7	2.7±0.5	2.4±0.2
SVRI (dyne·s·cm^{-5})	R (*n*=10)	2350±167	2200±594	2942±423$^{b)}$	2521±440	2755±611	2932±312$^{b)}$	2209±523	2455±532	2970±556$^{b)}$
	G (*n*=10)	2451±761	2260±516	2872±397	2715±305	2762±211	2606±174	2305±344	2431±205	2761±110
	H (*n*=10)	2560±537	2051±350$^{a)}$	2648±492	2301±334$^{e)}$	2437±432	2605±440	2240±623	2578±619	2784±413
ACI (100^{-1}·s^{-2})	R (*n*=10)	81±27	70±14	63±17$^{a)}$	78±24	73±22	47±9$^{b)}$	78±22	62±19$^{a)}$	60±27$^{a)}$
	G (*n*=10)	84±18	86±26	94±35$^{c)}$	101±32	91±27	83±21$^{c)}$	92±22	73±15$^{a)}$	75±39
	H (*n*=10)	85±22	85±22	93±17$^{c)}$	106±29$^{a)}$	99±30	86±16$^{d)}$	89±25	81±21	69±13$^{a)}$
TFC	R (*n*=10)	33±8	36±7$^{a)}$	38±6$^{b)}$	39±6$^{b)}$	39±8$^{b)}$	36±8$^{a)}$	40±10$^{b)}$	44±5$^{b)}$	42±3$^{b)}$
	H (*n*=10)	36±6	37±6	39±6$^{a)}$	40±7$^{a)}$	37±9	38±9	40±7$^{a)}$	43±7$^{b)}$	43±2$^{b)}$
	G (*n*=10)	35±3	37±3	39±2$^{a)}$	40±4$^{b)}$	39±6$^{a)}$	43±5$^{b)}$	40±6$^{b)}$	42±5$^{b)}$	39±5$^{a)}$

Compared with the baseline value, $^{a)}$ P<0.05; $^{b)}$ P<0.01;compared with Group R, $^{c)}$ P<0.05; $^{d)}$ P<0.01; compared with Group G, $^{e)}$ P<0.05.

Comparison of the monitoring data at different time points among patients of the three groups

Hemodynamics, Table 3: Compared with T_0, in patients of all three groups, SBP decreased at T_1 and CVP increased at T_{1-8}. In patients of group R, CI decreased at T_2 and $T_{4\text{-}8}$, and ACI decreased at $T_{2,5,7,8}$. SVI increased at $T_{2,5}$, and T_8 in patients of group R, but decreased at T_1 in patients of group H (P<0.05 or P<0.01). Compared with patients of group R, in patients of groups G and H, CVP increased at T_6, CI increased at T_5, and ACI increased at T_2 and T_5 (P<0.05 or P<0.01). Compared with patients of group G, SVRI decreased at T_3 in patients of group H (P<0.05).

Blood gas analysis and electrolytes, Table 4: Compared with T_0, the arterial blood pH value (pHa) decreased at T_{2-8} in patients of the three groups, and both $PaCO_2$ and HCO_3^- increased. Blood sodium concentration (Na+) increased at T_{1-7} in patients of group H, and blood potassium concentrations (K+) at T_{1-2} in groups R and G, and at T_{1-3} in group H, decreased (P<0.05 or P<0.01). Compared with groups R and G, the levels of blood HCO_3^- at $T_{2,3,4}$ and T_6 in group H decreased (P<0.05), while Na + at T_{1-7} increased (P <0.01). The base excess (BE) at T_{2-3}, T_{5-6}, and T_8 in group H was similar to or lower than the lower limit of the normal values.

Gastric mucosal blood flow indices, Table 5: Compared with T_0, pHi at T_{4-8} in group R, at T_{5-8} in groups G and H, and at T_{5-8} in Groups R and H was lower than 7.32, while pHi at all time points in group G was higher than 7.32. $PgCO_2$ at $T_{2\text{-}8}$ in all three groups increased and $P_{g-a}CO_2$ at T_1 and 2 in groups G and H decreased, while $P_{g-a}CO_2$ at T_{4-7} in group R and at T_6 in group H was higher than the baseline (P<0.05 or P<0.01). Compared with in group R, pHi at T_5 and T_8 in group G increased, while $PgCO_2$ at T_5 decreased and $P_{g-a}CO_2$ at T_2 decreased (P <0.05). Compared with group G, the pHi at T_8 in group R decreased (P <0.05).

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Table 4. Comparisons of the arterial blood gas tests at different time points among the three groups ($\overline{\chi}$±s).

Index	Group	T_0	T_1	T_2	T_3	T_4	T_5	T_6	T_7	T_8
pHa	R (*n*=10)	7.38±0.03	7.37±0.06	7.31±0.03[b]	7.30±0.03[b]	7.29±0.04[b]	7.26±0.05[b]	7.27±0.06[b]	7.29±0.04[b]	7.30±0.03[b]
	G (*n*=10)	7.40±0.03	7.39±0.04	7.32±0.07[a]	7.33±0.06[a]	7.28±0.02[b]	7.26±0.03[b]	7.28±0.06[b]	7.30±0.04[b]	7.29±0.01[b]
	H (*n*=10)	7.40±0.03	7.38±0.02	7.32±0.03[a]	7.30±0.03[b]	7.30±0.03[b]	7.29±0.04[b]	7.30±0.03[b]	7.31±0.02[b]	7.32±0.03[a]
$PaCO_2$ (mmHg)	R (*n*=10)	35±3	36±3	44±4[b]	45±5[b]	48±2[b]	53±6[b]	50±10[b]	47±5[b]	41±9[b]
	G (*n*=10)	36±2	37±2	44±4[b]	46±4[b]	48±3[b]	54±2[b]	48±7[b]	45±5[b]	49±3[b][c]
	H (*n*=10)	34±4	37±4	41±4[b]	44±5[b]	45±2[b]	45±8[b][e]	41±4[b][c]	41±5[b]	37±6[e]
HCO_3^- (mmol/L)	R (*n*=10)	21±1	22±1	25±2[b]	25±2[b]	25±1[b]	25±1[b]	25±2[b]	25±2[b]	23±1[a]
	G (*n*=10)	23±2	24±2	25±1[a]	25±2[a]	26±2[a]	26±1[a]	25±2[a]	25±1[a]	26±2[a][c]
	H (*n*=10)	21±3	20±2	23±2[a][c][e]	23±2[a][c][e]	24±2[b][e]	24±2[b]	23±2[a][c][e]	23±2[a]	23±1[a][e]
BE	R (*n*=10)	−3.0±1.9	−2.0±1.2[b]	−1.4±1.8[b]	−1.8±1.2[b]	−1.9±1.1[b]	−2.0±0.8[b]	−2.3±1.7	−2.0±2.0[b]	−3.0±2.0
	G (*n*=10)	−2.1±2.2	−0.9±2.3	−1.8±1.5	−1.9±2.2	−1.0±1.7	−1.8±1.5	−1.9±2.2	−1.8±1.4	−0.8±1.3
	H (*n*=10)	−2.9±2.7	−2.8±2.5	−3.0±2.4	−3.4±2.3	−2.9±2.4	−3.0±1.8	−3.6±2.0	−2.8±1.7	−3.2±2.1
Na^+ (mmol/L)	R (*n*=10)	139±3	138±3	138±3	138±3	137±3[a]	136±3[a]	137±3[a]	138±2	139±2
	G (*n*=10)	140±2	141±1	140±2	140±2	140±2	140±2[c]	139±1	139±1	140±1
	H (*n*=10)	139±4	151±3[b][d][f]	147±2[b][d][f]	146±2[b][d][f]	145±2[b][d][f]	143±2[a][d][e]	144±2[b][d][f]	143±2[a][d][f]	142±2
K^+ (mmol/L)	R (*n*=10)	3.6±0.5	3.3±0.4[b]	3.3±0.4[b]	3.5±0.5	3.6±0.6	3.5±0.3	3.9±0.5	3.9±0.5	3.4±0.4
	G (*n*=10)	3.6±0.5	3.2±0.6[b]	3.2±0.6[b]	3.3±0.6	3.5±0.5	3.4±0.2	3.5±0.5	3.4±0.6	3.4±0.2
	H (*n*=10)	3.4±0.4	3.1±0.3[b]	3.1±0.4[b]	3.2±0.4[a]	3.4±0.4	3.6±0.5	3.6±0.3	3.6±0.4	3.7±0.2
iCa^{2+} (mmol/L)	R (*n*=10)	1.22±0.03	1.20±0.04	1.21±0.05	1.22±0.05	1.20±0.04	1.21±0.03	1.20±0.05	1.20±0.03	1.21±0.05
	H (*n*=10)	1.21±0.04	1.12±0.05[b][d]	1.17±0.05[a]	1.16±0.03[b][c]	1.18±0.03	1.18±0.01	1.14±0.04[b][d]	1.13±0.04[b][d]	1.15±0.01[b]
	G (*n*=10)	1.22±0.04	1.19±0.03[f]	1.19±0.05[f]	1.19±0.05[f]	1.18±0.04[f]	1.19±0.01[f]	1.17±0.02[b]	1.18±0.02[f][e]	1.17±0.01[b]

Compared with the baseline value: [a] $P<0.05$, [b] $P<0.01$; compared with Group R: [c] $P<0.05$, [d] $P<0.01$; compared with Group G: [e] $P<0.05$, [f] $P<0.01$.

COP, Table 5: Compared with T_0, COP at T_{1-2} and T_{6-7} in group R decreased ($P<0.05$ or $P<0.01$). Compared with group R, COP at T_{1-2} in group G increased ($P<0.05$ or $P<0.01$).

Discussion

Numerous references [11–13] indicate that laparoscopy, to a certain extent, can affect the splanchnic perfusion. Patients who received laparoscopic colorectal surgery mostly had an insufficient blood volume before surgery [14,15]. However, elderly patients' cardiovascular reserve function is often reduced, and they mainly depend on increasing the end-diastolic volume to improve cardiac output [16]. Therefore, the right perioperative fluid treatment is one important means to maintain stable hemodynamics and the whole-body oxygen supply-demand balance in elderly patients undergoing laparoscopic colorectal surgery. So far, however, how to improve splanchnic perfusion in patients during laparoscopy with pneumoperitoneum is still under continuous exploration. Most intervention means used in clinical operation have mainly involved pneumoperitoneum and the operation conditions, such as reduced pneumoperitoneum pressure, slow inflation, shorter pneumoperitoneum duration, and avoiding extreme postures [17,18]. There are few studies on the application of volume management and its role.

Currently, the main hypervolemic fluids used in clinical practice are isotonic fluids, including crystalloid fluid and synthetic colloidal fluid.

Isotonic crystalloids are extracellular fluids, and have a temporary blood volume-increasing effect when used for acute hypervolemic fluid infusion at an early stage. However, most of fluids will soon leak out of blood vessels, and the use of a

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Table 5. Comparisons of Phi, P_gCO_2, $P_{g-a}CO_2$, and COP at different time points among the three groups ($\overline{\chi}\pm s$).

Index	Group	T_0	T_1	T_2	T_3	T_4	T_5	T_6	T_7	T_8
pHi	R (*n*=10)	7.38±0.07	7.36±0.07	7.36±0.06	7.34±0.04	7.32±0.06[b)]	7.27±0.03[b)]	7.28±0.09[b)]	7.31±0.06[b)]	7.29±0.03[b)]
	G (*n*=10)	7.40±0.09	7.38±0.06	7.37±0.05	7.34±0.03	7.33±0.02	7.33±0.01[a)c)]	7.33±0.04[a)]	7.33±0.04[a)]	7.33±0.01[a)c)]
	H (*n*=10)	7.42±0.08	7.37±0.08	7.34±0.08	7.34±0.03	7.34±0.03	7.30±0.03[b)]	7.29±0.03[b)]	7.30±0.02[b)]	7.29±0.02[b)e)]
P_gCO_2 (mmHg)	R (*n*=10)	39±5	40±4	47±7[b)]	52±6[b)]	55±4[b)]	60±3[b)]	58±12[b)]	54±6[b)]	47±1[b)]
	G (*n*=10)	40±8	39±7	46±3[a)]	51±4[b)]	53±3[b)]	59±2[b)]	53±3[b)]	50±4[b)]	43±2[b)]
	H (*n*=10)	38±8	39±9	46±9[b)]	50±6[b)]	51±5[b)]	53±6[b)c)]	49±5[b)]	49±3[b)]	47±3[b)]
$P_{g-a}CO_2$ (mmHg)	R (*n*=10)	4.0±1.3	3.3±0.6[a)]	3.2±0.3[a)]	6.5±1.7	6.8±1.5[a)]	7.1±1.9[a)]	7.5±1.9[a)]	6.6±1.5[a)]	5.1±1.4
	G (*n*=10)	4.0±1.3	1.5±0.5[a)]	1.2±0.5[a)c)]	4.3±0.9	4.8±1.8	4.5±1.0	4.9±1.5	4.3±1.4	4.1±1.4
	H (*n*=10)	4.1±1.9	1.8±0.8[a)]	1.5±0.4[a)]	5.1±1.0	5.2±1.8	7.3±1.5	7.6±1.3[a)]	6.8±1.4	5.3±1.6
COP	R (*n*=10)	21±4	19±3[b)]	20±3[a)]	21±3	21±2	20±3	20±3[a)]	20±3[a)]	21±3
	G (*n*=10)	21±3	23±2[d)]	22±1[c)]	23±2	21±2	21±2	21±2	21±2	20±1
	H (*n*=10)	21±2	21±2	21±2	21±2	22±1	20±2	20±2	20±2	20±1

Compared with the baseline value: [a)] $P<0.05$, [b)] $P<0.01$; compared with Group R: [c)] $P<0.05$, [d)] $P<0.01$; compared with Group G: [e)] $P<0.05$.

large amount is more likely to cause tissue edema. There are many types of synthetic colloidal fluids, and in recent years there are new products that are continuously developed with better compatibility with physiological conditions and a better blood volume increasing effect. Their clinical application has gradually improved. However, problems such as their impacts on coagulation function and the refractory tissue edema caused by leakage from the blood vessels still cannot be completely avoided. Altogether, isotonic solution can only passively expand blood volume, and cannot actively dredge the capillaries and improve microcirculation [19]. In contrast, hypertonic sodium chloride solution can quickly increase blood volume, correct hypoglycemia, improve organ blood flow and hemodynamics, and effectively increase myocardial contractility. As a new type of synthetic hypertonic colloidal solution, hypertonic sodium chloride hydroxyethyl starch 40 injection (HS) has been confirmed for its clinical safety and practicality in a large number of animal experiments and clinical observations of patients. However, its feasibility and effectiveness in the hypervolemic fluid infusion during induction of anesthesia is still under exploration.

The gastrointestinal mucosal blood supply system has physiological anatomical defects. The blood supply of the gastric mucosa is poor, and blood oxygen content is low; thus, not only is it very sensitive to ischemia and hypoxia changes, but its recovery is also slower than other organs [20]. It has been reported that the use of electrodes placed in the submucosal layer to directly determine the pH value is more sensitive and accurate than use of a gastric tonometer [21], but such an operation is invasive, and technically cannot be widely used for clinical monitoring. Laser Doppler flowmetry and tissue oxygen partial pressure (P_gO_2) detection seem to be useful, but the oxygen supply detection does not reflect the actual oxygen utilization of tissues [22]. Gastric tonometry is currently an easy-to-operate and reliable real-time monitoring approach that can reflect the oxygenation of gastric mucosa [23].

Currently, the gastric tonometer widely used in clinical practice is a multipurpose feeding tube with an airbag in the front end and a sampling tube connected at the distal end. Its placement method is the same as that of the traditional feeding tube (such as Tonocap™, Datex-Ohmeda, Helsinki, Finland). Once the arterial blood PCO_2 and pH values of patients are entered, the monitoring module will automatically calculate pHi and $P_{g-a}CO_2$, which are understood at a glance. Additionally, gastric tonometry requires a shorter balance time and is more accurate, with a lesser probability of errors and ability to identify mucosal acidosis at an early stage. Thus, it is currently a good noninvasive approach to assess splanchnic perfusion. Fiddian-Green et al. [24] substituted $PgCO_2$ into the Henderson-Hasselbalch formula, and obtained the pH (pHi) value of gastric mucosa as follows:

$$pHi=6.1+\log\{[HCO_3^-]/\alpha\times P_gCO_2\}$$

In the formula, 6.1 is the ionization equilibrium constant of carbonic acid, α is the solubility of CO_2 in plasma (≈0.03), $[HCO_3^-]$ is the bicarbonate ion concentration in the plasma, and pHi <7.32 is considered to be the evidence of gastric mucosal acidosis [25]. Many studies reported that it can suggest early postoperative complications and prognosis after large surgeries [26], and is more suitable for clinical applications.

pHi and $P_{g-a}CO_2$ are sensitive indicators of gastrointestinal mucosal ischemia and hypoxia. pHi> 7.32 and $P_{g-a}CO_2$ <1.1kPa are considered as the lowest thresholds for proper splanchnic perfusion [27]. In the present study, after pneumoperitoneum induction in patients of all three groups, pHa decreased, while $PaCO_2$ and $PgCO_2$ increased, and the two were positively correlated. This indicates that the increase in $PgCO_2$ is caused by hypercapnia, and that pHa, $PgCO_2$, and pHi calculated by Henderson-Hasselbalch formula mainly reflect the whole body's acid-base status, and they cannot accurately reflect the local mucosal perfusion. Since $P_{g-a}CO_2$ is not affected by whole-body acid-base status and $PaCO_2$, and can more accurately reflect the changes of splanchnic perfusion and oxygenation [28,29], in our study, $P_{g-a}CO_2$ and the correction formula pHi=7.40-log $PgCO_2/PaCO_2$ were used to evaluate splanchnic perfusion.

In the present study, CVP at T2 was significantly increased in all three groups (up to 20 cmH_2O), but significantly reduced at T_6, indicating that during laparoscopic colorectal cancer surgery, due to increased intra-abdominal pressure and postural changes, CVP is significantly influenced by the changes in intrapulmonary pressure, and cannot objectively and accurately reflect the actual volume status. After AHFI during the induction of anesthesia in patients of the three groups, $P_{g-a}CO_2$ was significantly lower than the baseline value, indicating that at early stage, the volume expansion effects of AHFI of 12 ml/kg balance solution, 12 ml/kg succinylated gelatin, and 3.5ml/kg hypertonic sodium chloride hydroxyethyl starch solution are similar, and early after the induction of pneumoperitoneum (30 min), they all can improve the splanchnic perfusion and oxygen supply. However, the $P_{g-a}CO2$ at T_2 in group G was significantly lower than that in group R, and with the lengthening of pneumoperitoneum, the $P_{g-a}CO_2$ values at time points from T_4 to T_7 in group R, and at T_6 in group H, were all higher than the baseline value. The pHi values of group R and group H were lower than 7.32 from T_5 to T_8, and the pHi values in group G were higher than 7.32 at all time points. These indicate that with the lengthening of pneumoperitoneum, the improving effects of the three solutions on splanchnic perfusion gradually become different. In this study, CI and ACI in the R group were significantly lower than the baseline at T_2 early (5 min) after the induction of pneumoperitoneum, but the values at T_6, the late stage after pneumoperitoneum, were significantly different from the values in groups G and H. The CVP in Group R at 5 minutes after the end of pneumoperitoneum (T_6) was significantly lower than those in groups G and H. These results indicate that, compared with the colloidal solution, the osmolarity of the balance solution was lower, the volume expansion effect was weaker and the effect duration was shorter [30]. Therefore, after a longer period of pneumoperitoneum (60 min), the perfusion in the gastric mucosa started to become low in group R, and low perfusion cannot be quickly improved even after the release of pneumoperitoneum. After AHFI of succinylated gelatin solution, the iCa^{2+} concentration in the plasma was significantly decreased, but was still within the normal range (iCa^{2+} normal value: 1.1–1.2 mmol/L). This is because succinylated gelatin can be retained in the blood vessels for 2 to 3 hours, and the calcium ion concentration is less than 0.4 mmol/L [31]. Although the hydroxyethyl starch solution does not contain Ca^{2+}, due to its small amount, the blood calcium concentration in group H was not significantly decreased.

Hypertonic sodium chloride hydroxyethyl starch solution can reduce the resistance of the systemic circulation and increase the negative charge on the surface of red blood cells, thereby maintaining the suspension stability of the blood and benefiting tissue perfusion [32]. However, the infusion of hypertonic sodium chloride hydroxyethyl starch solution can cause mild hypernatremia and hyperchloremia; thus, in the distal convoluted renal tubules, Na^+ is mostly reabsorbed by combining with Cl^-, leading to a reduction in Na^+-H^+ exchange and HCO_3^- reabsorption [33]. In this study, in the hydroxyethyl starch infusion group (group H), the compensatory increase of HCO_3^- was not as significant as those in groups R and G, and hyperchloremic acidosis had occurred. Therefore, although the volume extension effects of hypertonic sodium chloride hydroxyethyl starch and succinylated gelatin solution are comparable, under the conditions of laparoscopy-caused hypercapnia, the impact of hypertonic sodium chloride hydroxyethyl starch solution on the acid-base balance dilutes its improvement in splanchnic perfusion, while the succinylated gelatin was able to maintain good splanchnic perfusion over a longer period of pneumoperitoneum (60 min). Therefore, the difference among the three solutions in improving splanchnic perfusion is related to the differences in infusion effect and physicochemical properties.

Conclusions

AHFI during the induction of anesthesia can improve splanchnic perfusion in elderly patients undergoing laparoscopic colorectal surgery. Compared with the balance solution and hypertonic sodium chloride hydroxyethyl starch solution, succinylated gelatin solution can maintain good splanchnic perfusion, even after a long period of pneumoperitoneum (60 min). In this study, gastric mucosal pHi can better reflect the perfusion by splanchnic circulation in elderly patients undergoing laparoscopic surgery.

Conflict of interest

None.

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