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ORIGINAL ARTICLE

Hemodynamic stability achievement by application of goal directed fluid therapy with different infusion solutions in colorectal surgery

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Summary

Purpose: *To determine whether there was a correlation between the type of administered infusion solutions intraoperatively with the quantity of administered infusion solutions, differences in values of cardiac output (CO) and cardiac index (CI) and need to use vasopressors and inotropes, between control and research groups.*

Methods: *This randomized prospective study included 55 patients with colorectal cancer. Subjects in the control group received only crystalloid solutions intraoperatively and postoperatively. The patients in the research group received a combination of colloid in dosage of 10mg/kg and crystalloid solutions. Patients in both groups were given goal directed fluid therapy.*

Results: *The control group received a significantly larger amount of crystalloid solution per kg of body weight during the entire surgical operation, in comparison with the volume of crystalloids in the research group (mean±SD 50.78±28.13 vs. 31.63±25.60 respectively, p=0.01). During the first hour of the surgery, the control group received a larger quantity of fluid in comparison with the research group (mean±SD 31.14±9.78 vs. 22.17±9.92 respectively, p=0.001). From the beginning of anesthesia until 6th postoperative hr the values of CI were significantly higher in the research group in comparison with the control group.*

Conclusions: *Goal directed fluid therapy with colloids, followed by crystalloids during surgery, decreased the total intraoperative fluid volumes, and provided higher values of CI intraoperatively which were also maintained postoperatively.*

Key words: *cardiac index, colorectal surgery, colloids, crystalloids, goal-directed fluid therapy, stroke volume*

Introduction

Hemodynamic stability during operative and postoperative periods is one of the important preconditions for a successful recovery of patients and for fewer complications [1]. Goal directed fluid therapy based on the optimization of stroke volume (SV), which is the amount of blood ejected from heart with each cardiac cycle, and cardiac output, which is the amount of blood ejected in one min, provides a favorable intraoperative hemodynamic stability and decreases the incidence of postoperative complications [2].

Sufficient tissue perfusion results from adequate cardiac output. Intravenous fluids are used to achieve optimal cardiac output. Mesenteric hypoperfusion due to inadequate fluid replacement can provoke postoperative ileus, anastomotic leakage and prolong the duration of hospital stay. Esophageal Doppler monitoring for goal directed

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fluid therapy (cardio Q) helps clinicians to administer optimal volume of intravenous fluids. Due to fewer postoperative complications, fewer days in intensive care and faster restoration of gastrointestinal functions, the use of esophageal Doppler is recommended in colorectal surgery [3-5].

Fluid replacement should be appropriate to the fluid losses during surgery. A lot of factors can have an influence on fluid losses from the body: vasodilatory effects of anesthesia, blood loss, hormonal response to surgery, insensible losses, increased capillary permeability and albumin escape rate. Loading the circulation system with excessive fluid volume should be avoided in abdominal surgery. Therefore, restrictive resuscitation of fluids is an advantage since it reduces the appearance of complications and hospital length of stay [6]. The most optimal resuscitation of the occurred loss is achieved by applying goal directed fluid therapy, since that way the patient receives the optimal amount of fluid necessary for good perfusion and tissue oxygenation.

The dilemmas on which fluid is a better choice during the postoperative period still exist: crystalloids versus colloids, since many studies suggest different solutions as a better choice. Supporters of colloid solutions in the perioperative period argue that smaller quantities of fluid are necessary in order to achieve a good hemodynamic response, in order for tissue edema to decrease and preserve the integrity of anastomosis [7]. By using HydroxyEtilStarch solution, with the application of goal directed fluid therapy according to hemodynamic algorithm for the optimization of SV, a better hemodynamic stability is achieved and intraoperative needs for fluid volume are decreased [8]. Feldheiser and colleagues and NICE study suggest that fluid resuscitation during surgery should be based on the hemodynamic algorithm for fluid resuscitation by monitoring SV after each bolus of solution (fluid challenge) [9,10].

Former studies usually compared crystalloid and colloid solutions. Fewer studies dealt with the effects of combined usage of crystalloids and smaller doses of colloids by means of goal directed fluid therapy. The idea of using a combination of HydroxyEthyl Starch with crystalloids in this study was based on the assumption that with an even lower total volume together with the administration of goal directed fluid therapy would achieve and maintain a better hemodynamic status of the patient, in comparison with goal directed fluid therapy only with crystalloids [6,11,12].

The aim of this research was to determine whether there was a correlation between the type of administered infusion solutions intraoperatively with the quantity of administered infusion solutions, differences in values of CO and CI and need to use vasopressors and inotropes, between control and research groups.

Methods

Study design

This randomized prospective pilot study included 55 patients with colorectal cancer, who were subjected to surgical treatment at the Oncology Clinic of the Institute for Oncology and Radiology of Serbia, Belgrade. The study was approved by the ethics committee of the School of Medicine of Belgrade University (Permission 29/VII-9). All subjects signed written consent to participate in this study.

The criteria for study inclusion were the following: patients with colon cancer, elective surgery, acceptance to participate in study, American Society of Anesthesiologists (ASA) class 1, 2 and 3, over 18 years old.

Patients who were not eligible for study inclusion: refusal to participate, age under 18, urgent operation, coagulopathies, ASA score over 3 and patients who wanted to withdraw from study and refused to participate regardless of the reason.

Patients

Randomization of patients into control or research group was performed before the induction of anesthesia. The patients were randomly assigned to either control or research group by randomization carried out by computer generated program package. Subjects belonging to control group received only crystalloid solutions (Solutio Hartman B Braun, Germany) both intraoperatively and postoperatively. Patients in the research group received a combination of colloid (6% Hydroxyethyl Starch 130/0.4 6g in 100mL, Fresenius Kabi, Norway) and crystalloid solutions (Solutio Hartman) in the following way: the therapy would begin with colloid solution administered in dosage of 10 mg/kg of patient's body weight until the assigned dose was spent, then crystalloid solution was administered until the end of the operation and during the postoperative period.

The patients from both groups were given goal directed fluid therapy based on the algorithm for the optimization of SV intraoperatively until 24 hrs from the end of the operation.

Goal directed fluid therapy

The fluid responsiveness of all patients was monitored by esophageal Doppler (CardioQ, Deltex Medical, England) System. The guidance parameter for fluid management was SV. Solution resuscitation during surgery was administered according to the following fluid resuscitation algorithm followed by SV after each fluid challenge [9,10].

Hemodynamic algorithm [9]:

- After initial bolus of 200ml of fluid (fluid challenge) SV was measured.

- If SV increase was less than 10% from the initial value, administration of fluid stopped.
- If the increase of SV was more than 10% from the initial value, additional boluses were administered and SVs were measured until the increase was less than 10%.
- If SV decreased more than 10% from the initial value, additional boluses were administered and SVs were measured until the decrease was less than 10%.
- In cases of hemodynamic instability or massive hemorrhage, bolus (fluid challenge) was increased to 400ml if Flow Time corrected (FTc) was under 300ms.

By following the stated hemodynamic algorithm we included vasopressors when mean arterial pressure decreased under 70 mm Hg, and inotropes if CI was under 2,5 L/min/m^2 and SV could not be increased by further administration of fluids. In the cases of intraoperative bradycardia (under 50 beats), we administered atropine, 0.5 mg IV.

The following vasopressors were used: 0.1% phenylephrine in dosage of 100-300mcg IV. Inotrope dobutamine was used continuously. A dose of dobutamine was titrated from 2.5-10 mcg/kg/min and after 15 min (sometimes more frequently in cases of significant hemodynamic changes or major blood loss) a reevaluation of the initial optimization was done. Infusion of dobutamine continued until reaching 2,5 L/min/m^2 CI values.

The value of hemoglobin of 7g/dL was the indication for transfusion of resuspended erythrocytes.

In this study, the range of referent values followed by hemodynamic parameters was as follows: Mean Arterial Pressure (MAP) 70-110 mmHg; Heart Rate (HR) 60-90 beats per minute; SV 60-100 ml; CO 4-8 L/min; Ftc 330-360ms; CI 2.5-4 L/min/m^2; Systemic Vascular Resistance (SVR) 800-1200; Oxygen Delivery (DO_2) 900-1150.

Despite the general acceptance of enhanced recovery after surgery (ERAS) [5] as a safe and cost-effective perioperative care bundle, a considerable percentage of colorectal units still advocate prolonged fasting prior to surgery without routine use of carbohydrate loading, as well as delaying resumption of oral intake postoperatively [13]. In the present study preoperative preparation for all patients started one day before the planned surgery and consisted of fasting without carbohydrate loading and application of crystalloids in order to resuscitate basal loss and other preoperative losses.

The patients were premedicated 30 min before the induction of anesthesia with 0.5mg of atropine and with midazolam in the dose of 0.07mg/kg im. Before the induction of anesthesia all patients were warmed for 15 min and received 500ml of crystalloid solution.

In all patients anesthesia technique was combined (regional and general endotracheal). Just before the anesthetic induction, epidural anesthesia puncture was performed in the mid-thoracic region (T8-T9 vertebral interspace) using the midline approach, for the purpose of perioperative analgesia, for which 0.25% chirocaine and fentanyl 150mcg were administered.

For induction of anesthesia propofol 2mg/kg was used. For facilitation of tracheal intubation we used rocuroniumin doses of 1mg/kg, and in order to maintain muscle relaxation the same was administered intermittently every 40 min at 0.6mg/kg dose. Anesthesia was maintained with sevofluran, end-tidal concentration of 0.8 minimal alveolar concentration (MAC) and the values of bispectral index (BIS) between 40 and 60, with a combination of gases *ana partes*: oxygen and air. Analgesia was maintained by continuous application of 0.25% chirocaine through infusion pump, with a speed of 5 to 8 ml/h and low doses of remifentanyl of 5ml/h through infusion pump. The patients were mechanically ventilated and the parameters of ventilation were adjusted so that the end tidal value of carbon dioxide ($ETCO_2$) was kept within a range from 35 to 40mmHg. Patients were warmed 30 min preoperatively and during surgery to a temperature of 37-39°C in order to maintain physiological central body temperature. A nasogastric probe, esophageal Doppler probe, temperature probe, central venous catheter and arterial line were applied in all patients.

Each patient from both groups received Hartman solution through one venous line which was administered at the speed of 5 ml/h, while on the other venous line fluid challenges were administered according to the stated algorithm for fluid resuscitation: in the control group only crystalloid solutions were used (Solutio Hartman), while in the research group we started with colloid boluses (6% Hydroxyethyl Starch). The assigned dose of colloids for fluid challenge was 10ml/kg, and when it was spent fluid challenge continued with boluses of Hartman solution until the end of the operation. Hemodynamic measuring was applied before and after fluid challenge, after each change in the mean artery pressure or heart frequency or every 15 min if no changes occurred.

Entries of the quantity of used fluid per kg of body weight, as well as hemodynamic and other measurings were done during the induction of anesthesia, intraoperatively every hour, before the reversion of neuromuscular block, and 6 and 24 hrs postoperatively.

Clavien-Dindo complication classification system was used to categorize complications by type and grade [14].

Statistics

Statistic software SPSS 23.0 was used for statistical data processing. From the methods of descriptive statistics the following methods were used: methods of central tendency (arithmetic mean value, median), variability measures (standard deviation, minimal and maximal value). Fisher exact and Pearson's chi-square test were used to examine the differences in the incidence of observed category characteristics between subjects in both observed groups with various ways of intraoperative fluid resuscitation. The selection of tests for numerically based characteristics depended on the type of data distribution. In the case of distribution different from normal and in comparing the two groups of subjects (with crystalloids and the combination of fluids)

Mann Whitney U test was used, and in the case of normal data distribution t-test was used. For the analysis of numerical characteristics observed and measured at various times in both analyzed groups, which behaved according to normal distribution type, we used two-way ANOVA with repeated measuring.

Results

There was no statistical difference between the two groups regarding age, sex, and body mass index (BMI), as well as regarding other variables (Table 1). There was no statistically significant difference between subjects from research and control groups in ASA score, present comorbidity: cardiological (HTA, AP, AIM,SPVA, VA, compensated heart insufficiency as well as in coronary interventions PCI, CABG), respiratory (HOBP), endocrine and metabolic disorders (DM type II, hypothyroidism), psychic disorders, nor in undergone chemotherapies, radiotherapies and reoperations (Table 1). In none of these two groups of patients were there any complications, rehospitalization, or death during the postoperative period until leaving the hospital (Table 1).

There was no statistically significant difference in the duration of anesthesia and surgery between the groups (Table 2). There was a statistically significant difference in the administered

Table 1. Patient characteristics at baseline

Characteristics	*Control group n (%)*	*Research group n (%)*	*Fisher exact test (p value)*
Gender			ns[2]
Male	18 (60)	11 (44)	
Female	12 (40)	14 (66)	
Age (years)			ns[1]
Mean (SD)	60 (13.79)	65.92 (8.35)	
BMI (kg/m²)			ns[1]
Mean (SD)	26.07(4.07)	25.83 (4.54)	
ASA status			ns
I	4 (13)	0 (0)	
II	15 (50)	18 (72)	
III	11 (37)	7 (28)	
Comorbidity (presence of types)	19 (63.3)	15 (60)	ns[2]
Cardiac comorbidity	15 (50)	14 (56)	ns[2]
Hypertension	14 (47.)	13 (52)	ns[2]
Angina	1 (3)	2 (8)	ns
Myocardial infarction	1 (3)	1 (4)	ns
Percutaneous coronary intervention	0 (0)	1 (4)	ns
Arrhythmia	1 (3)	2 (8)	ns
Cerebrovascular disease	1 (3)	2 (8)	ns
Compensated heart insufficiency	0 (0)	1 (4)	ns
Chronic obstructive pulmonary disease	3 (10)	3 (12)	ns
Endocrine and metabolic disease	7 (23)	3 (12)	ns
Diabetes mellitus II	5 (17)	3 (12)	ns
Hypothyroidism	2 (7)	1 (4)	ns
Hematological disease	1 (3)	1 (4)	ns
Psychiatric disease	3 (10)	3 (12)	ns
Therapy			
Chemotherapy	12 (40)	10 (40)	ns[2]
Radiotherapy	1 (3)	4 (16)	ns
Earlier operation	8 (27)	11 (44)	ns[2]
Complications			
Clavian-Dindo (grade 1-5)	0	0	-
Total patients	30 (100)	25 (100)	-

ns: not statistically significant, [1]t-test, [2]Pearson's chi-square test

intraoperative volume of crystalloid solution. The control group of patients received a significantly larger amount of crystalloid solution per kg of body weight during the entire operation, in comparison with the volume of crystalloids in the research group (p<0.05;Table 2), while during the postoperative period there was no statistically significant difference in the administered volumes of crystalloid solution between groups. During the first hour of surgery there was a statistically significant difference in the total volume of administered solution between the two groups: the control group received a larger quantity of fluid in comparison with the research group (mean±SD 31.14±9.78 *vs.* 22.17±9.92 respectively, p<0.01, Table 2). During the other hours of the operation and the final hour until the reversion of neuromuscular block there was no statistically significant difference in the quantity of administered fluids between the two groups of patients. There was no statistically significant difference in the dosage of administered erythrocytes per kg of body weight between the groups neither intra nor postoperatively. Fluid balance on the 0th day was statistically significantly higher in the control group (p<0.01, Table 2). No statistically significant difference was noted between the two groups of subjects in the application of vasopressors, after 6 and 24 hrs (Table 2), but during the first 6 hrs a larger number of patients received inotropes in the standard group although with no statistical significance (Table 2).

Statistically significant difference was noticed in the values of MAP-a, CVP-a, HR, SV and FTc during the times of measuring within each group, without statistically significant difference in the change of these parameters between groups over time (Table 3). While in the control group the value of MAP gradually increased until the end of anesthesia, in the research group MAP decreased during the first hr, and then increased until the end

Table 2. Perioperative use of fluids and medications

Characteristics	*Control group*		*Research group*		*p value*
	Mean (SD)	*Median*	*Mean (SD)*	*Median*	
Time (min)					
Anesthesia	150.83 (57.99)	135.00	130.60 (47.09)	120.00	0.167[a]
Surgery	128.00 (55.99)	112.50	110.60 (53.12)	95.00	0.245[a]
Crystalloids (ml/kg)					
intraoperatively	50.78 (28.13)	46.76	31.63 (25.60)	23.80	0.012[b]
6h postoperatively	22.49 (7.44)	21.05	25.42 (9.71)	28.13	0.216[b]
6-24h postoperatively	31.29 (21.61)	25.00	28.01 (17.55)	23.81	0.088[b]
Total fluids (ml/kg)					
in 1^{sth} of operation	31.14 (9.78)		7.17 (9.92)		0.001[a]
in 2^{ndh} of operation	11.13 (16.04	9.03	6.79 (8.93)	5.73	0.254[b]
in 3^{rdh} of operation	0.09 (5.53)	0.00	2.82 (14.08)	0.00	0.160[b]
till block reversion	6.29 (5.27)	5.97	6.62 (6.53)	3.99	0.916[b]
Transfusion of resuspended erythrocytes (ml/kg)					
intraoperatively	16.7 (61.53)	0.00	88.00 (235.56)	0.00	0.248[b]
in 6h postoperatively	96.87 (187.50)	0.00	127.52 (242.92)	0.00	0.877[b]
from 6h-24h postoperatively	37.76 (101.58)	0.00	9.60 (48.00)	0.00	0.234[b]
Fluid balance					
on 0th day	1581.00 (1317.73)	1375.00	440.52 (1467.24)	50	0.004[a]
on 1st postoperative day	-317.17 (1292.62)	-575.0	-485 (1032.49)	-480	0.602[a]
Drugs (n and %)					
Fenylefrine intraoperatively	9 (30.0)		8 (32.0)		0.873[c]
Dobutamine intraoperatively	3 (10.0)		1 (4.0)		0.617[d]
Fenylefrine 6h postoperatively	(0.0)		(0.0)		-
Dobutamine 6h postoperatively	4 (13.3)		0 (0.0)		0.117[d]
Fenylefrine 24h postoperatively	1 (3.3)		0 (0.0)		1.000[d]
Dobutamine 24h postoperatively	(0.0)		(0.0)		-
Total patients	30 (100)		25 (100)		-

[a]t-test, [b]Mann-Whitney U test, [c]Pearson chi-square, [d]Fisher exact test

of anesthesia, followed by increase in both groups until 6th postoperative hr (Table 3; Figure 1). The values of CVP increased until the first hr in both groups, and then decreased until the 24th postoperative hr in both groups (Table 3). The value of HR decreased gradually in both groups, and then increased gradually until 24th postoperative hr (Table 3). The SV value increased rapidly from the beginning and remained higher until the end of anesthesia and then decreased until the 24th postoperative hr (Table 3, Figure 2). The values of Ftc rapidly increased until the end of anesthesia and decreased in the same way until the 6th hr after surgery in both groups (Table 3).

Values of CO (Figure 3), DO_2, and SVR did not change significantly over time in either group, nor between the groups (Table 3). No statistically significant difference was noticed in CI in time within each group, but a statistically significant difference was noticed in the dynamics of change of CI value between groups (Table 3). From the beginning of anesthesia until the 6th postoperative hour the CI values were significantly higher in the research group in comparison with the control group. Twenty-four hours after surgery the CI values were still higher than in the control group (Figure 4). Statistically significant difference was noticed in the Hgb values between the groups during time (Figure 5). After the first hr of anesthesia the concentration of Hgb decreased in both groups and lower values of this parameter were measured in the research group ($p<0.05$; Table 3), until block reversion ($p<0.05$; Table 3).

No complications (Clavian-Dindo classification) during the postoperative period were noticed in either group (Table 1).

Table 3. Haemodynamic values intraoperatively and postoperatively

Characteristics	*Mean(SD)*		*Two way ANOVA*	
	Control group	*Research group*	*Factor time measure*	*Difference between groups*
MAP (mm Hg)			p=0.000	p=0.417
MAP 1 (anesthesia induction)	80.27(15.51)	80.28(14.07)		
MAP 2 (first operation hour)	82.90(23.38)	72.44(19.89)		
MAP 3 (till block reversion)	81.83(17.07)	85.28(17.71)		
MAP 4 (6^{th} postoperative hour)	90.89 (11.27)	90.32 (14.86)		
MAP 5 (24^{th} postoperative hour)	84.99 (15.14)	85.83(3.59)		
CVP (cm H_2O)			p=0.030	p=0.983
CVP 1 (anesthesia induction)	7.37 (3.08)	6.92 (2.77)		
CVP 2 (first operation hour)	8.40 (3.48)	7.72 (3.69)		
CVP 3 (till block reversion)	7.50 (3.03)	7.24 (3.09)		
CVP 4 (6^{th} postoperative hour)	6.58 (3.04)	6.12 (2.71)		
CVP 5 (24^{th} postoperative hour)	7.30 (3.47)	6.54 (2.87)		
HR (beats/min)			p=0.007	p=0.342
HR 1 (anesthesia induction)	74.77 (12.39)	73.24 (10.31)		
HR 2 (first operation hour)	73.23 (18.77)	71.60 (20.06)		
HR 3 (till block reversion)	73.37 (11.37)	77.64 (12.36		
HR 4 (6^{th} postoperative hour)	80.33 (13.26)	77.76 (14.04		
HR 5 (24^{th} postoperative hour)	83.57 (13.56)	80.96 (15.12		
SV (ml)			p=0.009	p=0.187
SV 1 (anesthesia induction)	80.07 (29.60)	74.60 (23.04		
SV 2 (first operative hour)	80.80 (25.63)	93.16 (34.11)		
SV 3 (till block reversion)	84.27 (27.44)	93.72 (18.53)		
SV 4 (6^{th} postoperative hour)	79.93 (18.68)	82.12 (14.35)		
SV 5 (24^{th} postoperative hour)	71.33 (20.98)	81.60 (16.27)		

MAP: Mean Arterial Pressure, CVP: Central Venous Pressure, HR: Heart Rate, SV: Stroke Volume, CO: Cardiac Output, CI: Cardiac Index, DO_2: Oxygen Tissue Delivery, SVR: Systemic Vascular Resistance, FTc: Flow Time corrected, Hgb: Hemoglobin concentration

Continued on the next page

Characteristics	*Mean(SD)*		*Two way ANOVA*	
	Control group	*Research group*	*Factor time measure*	*Difference between groups*
CO (L/min)			p=0.198	p=0.156
CO 1 (anesthesia induction)	5.91 (2.19)	5.46 (1.91)		
CO 2 (first operative hour)	6.09 (2.07)	6.75 (2.51)		
CO 3 (till block reversion)	6.07 (1.94)	6.91 (2.10)		
CO 4 (6th postoperative hour)	6.26 (1.79)	6.27 (1.57)		
CO 5 (24th postoperative hour)	5.82 (1.87)	6.45 (1.64)		
CI (L/min/m²)			p=0.147	p=0.043
CI 1 (anesthesia induction)	3.22 (1.21)	2.98 (1.04)		
CI 2 (first operative hour)	3.32 (1.18)	3.72 (1.41)		
CI 3 (till block reversion)	3.32 (1.09)	3.82 (1.27)		
CI4 (6th postoperative hour)	3.40 (0.92)	3.39 (0.75)		
CI 5 (24th postoperative hour)	3.22 (0.92)	3.83 (0.92)		
DO_2 (ml O2/min)			p=0.272	p=0.680
DO_2 1 (anesthesia induction)	899.07 (311.10)	880.48 (293.92)		
DO_2 2 (first operative hour)	902.87 (335.38)	954.48 (322.13)		
DO_2 3 (till block reversion)	934.00 (286.34)	1003.92 (338.08)		
DO_2 4 (6th postoperative hour)	942.20 (283.04)	1000.60 (334.68)		
DO_2 5 (24th postoperative hour)	871.30 (307.08)	977.48 (330.45)		
SVR (dyn-sec/cm^{-5})			p=0.368	p=0.453
SVR 1 (anesthesia induction)	1099.57 (463.74)	1044.74 (415.33)		
SVR 2 (first operative hour)	1140.83 (876.81)	819.04 (317.45)		
SVR 3 (till block reversion)	1110.83 (465.33)	965.67 (336.62)		
SVR 4 (6th postoperative hour)	1168.67 (438.57)	1089.35 (249.46)		
SVR 5 (24th postoperative hour)	1489.97 (1990.55)	1050.92 (323.20)		
FTc (ms)			p=0.000	p=0.155
FTc 1 (anesthesia induction)	346.00 (51.02)	328.12 (44.80)		
FTc 2 (first operative hour)	353.20 (74.99)	354.96 (83.81)		
FTc 3 (till block reversion)	363.63 (36.49)	381.96 (48.18)		
FTc 4 (6th postop hour)	337.73 (27.01)	352.24 (30.37)		
FTc 5 (24th postoperative hour)	339.40 (29.42)	351.64 (30.98)		
Hgb (mg/dl)			p=0.000	p=0.021
Hgb 1 (anesthesia induction)	11.87 (11.64)	11.68 (1.83)		
Hgb 2 (first operative hour)	10.78 (2.62)	9.75 (3.39)		
Hgb 3 (till block reversion)	11.60 (1.66)	10.50 (1.72)		
Hgb 4 (6th postoperative hour)	11.87 (1.67)	11.72 (1.48)		
Hgb 5 (24th postoperative hour)	11.53 (1.66)	11.63 (1.70)		
Total patients	30 (100)	25 (100)	-	-

MAP: Mean Arterial Pressure, CVP: Central Venous Pressure, HR: Heart Rate, SV: Stroke Volume, CO: Cardiac Output, CI: Cardiac Index, DO_2: Oxygen Tissue Delivery, SVR: Systemic Vascular Resistance, FTc: Flow Time corrected, Hgb: Hemoglobin concentration

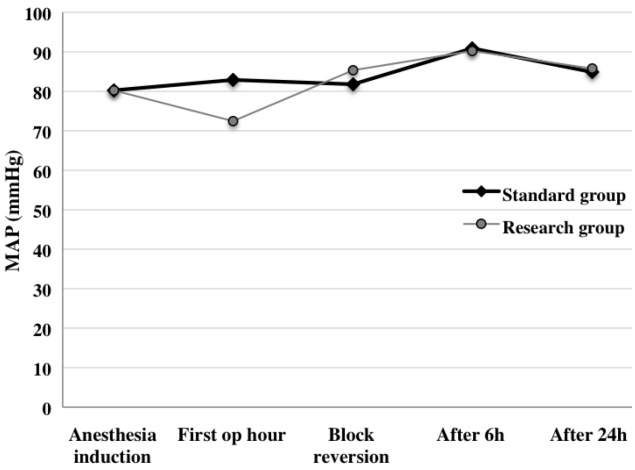

Figure 1. Mean Arterial Pressure changes within each group and between the groups (statistically significant intragroup difference: p=0.000; intergroup difference: p=0.417; Table 3).

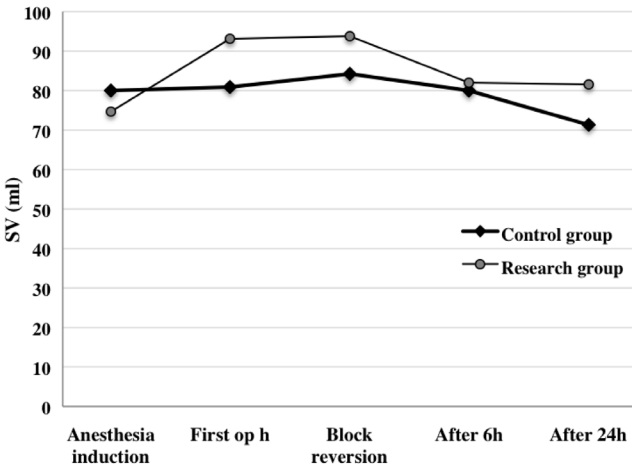

Figure 2. Stroke Volume changes within each group and between the groups (statistically significant intragroup difference: p=0.009; intergroup difference: p=0.187; Table 3).

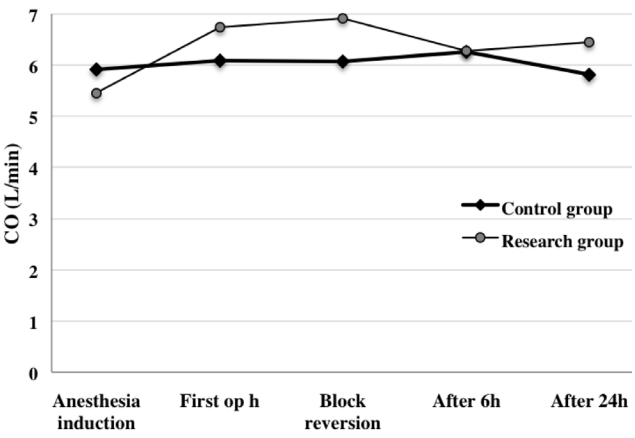

Figure 3. Cardiac Output changes within each group and between the groups (intragroup difference: p=0.198; intergroup difference: p=0.156; Table 3).

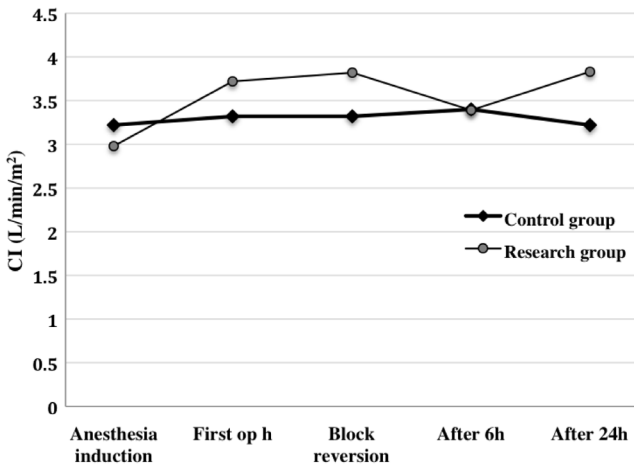

Figure 4. Cardiac Index changes within each group and between the groups (intragroup difference: p=0.147; statistically significant intergroup difference: p=0.043; Table 3).

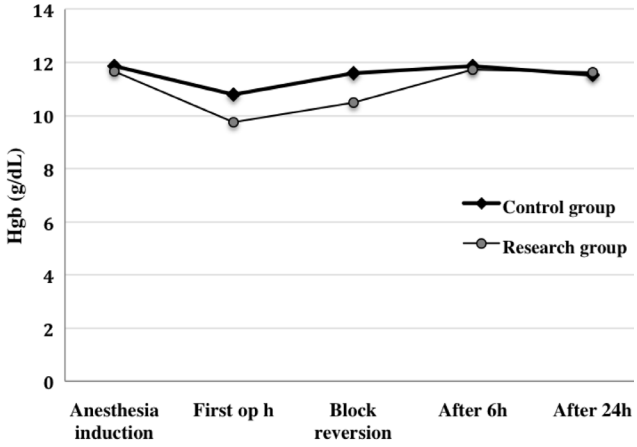

Figure 5. Hemoglobin concentration changes within each group and between the groups (statistically significant intragroup difference: p=0.000, statistically significant intergroup difference: p=0.021; Table 3).

Discussion

This is a study in which administration of crystalloids only was compared with the administration of combination of crystalloids and colloids at a dose of 10ml/kg TT, and the influence of these two therapy options on hemodynamic response of the patient both during and after colorectal surgery. Application of both kinds of solutions is usual during the perioperative period (day before surgery, day of surgery and 24hrs after surgery) and there is no firm evidence on the advantage of one group of solutions over the other [15,16]. Application of colloids was supported by the fact that colloids generally enlarge the intravascular space in smaller quantities and they remain longer in vascular bed when compared with crystalloids [17].

The results of our study showed that the values of CO between these two groups were not different, while there was a statistically significant difference between the values of CI. A significant increase of CI values occurred in the research group. The most significant changes in CI occur between the first hr until block reversion. These changes probably occurred in the research group due to the fact that patients received colloids first and only after that did they receive crystalloid solution. Due to already known and desirable characteristics of colloids to remain longer in intravascular space, CI values from the first hr grew and remained on higher level in the research group during the entire operation, even until the 24th postoperative hr. When comparing CO among patients, it is necessary to consider their body mass, height and patient surface. CI is a hemodynamic parameter in itself which connects CO of the left heart chamber per min, with body surface and thus it connects cardiac performance with the size of the patient's body. CI is therefore a good indicator of blood volume pumped by the heart according to one's body surface. CI is a significant clinical parameter which is used in the evaluation of patients with cardiac weakness, the critically ill and patients under anesthesia [18,19]. It could be said that according to the unit of body surface, higher values of CO were achieved in the research group of this study. Other monitored hemodynamic parameters did not show any significant difference between the two groups. In both groups there was a favorable hemodynamic stability. The study of Feldheiser and colleagues, who compared a combined administration of balanced colloids and balanced crystalloids in a 1:1 ratio with the group of unbalanced crystalloids also did not show the existence of differences in the hemodynamic stability of SV, CO, FTc and MAP values and the concentration of lactates between these two groups [9]. In the present study it can be seen that in the research group a favorable hemodynamic response was achieved since there was a significant decrease of MAP, HR and SVR and a simultaneous increase of SV and FTc as early as during the first hr, which indicates a faster loading of vascular space and the achievement of vasodilation. Delivering oxygen into tissues was not better in either group, but the values were satisfactory.

Patients in the research group of our study received fewer fluids per body mass unit during the first hr of surgery, while in other hrs and until the end of the operation there was no significant difference in the quantity of received fluid per unit of body mass. Also, the total quantity of crystalloids administered intraoperatively per body mass unit was lower in the research group. Patients in the research group received the minimal recommended dose of 6% hydroxyethyl starch with extra crystalloids, and we showed that the total quantity of administered fluid could be decreased for the same or better hemodynamic stability to be achieved as with larger amounts of fluids. In order to achieve the effect of better circulatory volume, colloids achieved better intraoperative circulatory flow when compared with crystalloids [11]. At the same time, smaller amount of fluid is administered and body overload is avoided. Perioperatively, an excessive amount of fluids is connected with increase of complications [20,31], and it was proved that restrictive resuscitation of fluids had better results in abdominal surgery [20] . Smaller amount of fluid in the research group of our study was probably the consequence of fluid remaining longer in the intravascular space and the ability of osmotic active molecules to draw fluids.

Patients in the research group received smaller volume of crystalloids intraoperatively in comparison with the control group. During the postoperative period, both groups of patients received the same amounts of fluid. After the 6th postoperative hr in one third of the patients in the control group inotrope dobutamine was administered. According to the algorithm, inotropes are included when values of CI fall under 2,5 L/min/m^2 and when SV cannot be increased by further administration of fluids [9]. The volume of circulating fluid in this period was insufficient to provide adequate blood preload into the heart in patients who received only crystalloids, and that was why inotropes were added. In the research group no patients had the need for administration of either inotropes or vasopressors. We suppose that maintaining favorable hemodynamics in this case was the consequence of the fact that colloids remained in the intravascular beds under 24 hrs.

The balance of fluids in the research group showed better in comparison with the control, crystalloid group, i.e. patients who received a combination of crystalloids and colloids intraoperatively received lower total amounts of fluid in order to achieve the same goal – to maintain good hemodynamics. Large positive intraoperative balance of fluids causes hemodilution, increases capillary permeability and increases the postoperative length of hospital stay [21]. Brandstrup et al. [20] and Nisanevich et al. [22] showed that there was a less favorable outcome in the postoperative period in patients who received larger quantities of fluids, especially crystalloids.

According to Hahn et al. [23], the initial fraction of crystalloids which remains in the intravascular space ranges from 50 to 70% in normovolemic pa-

tients and transfer of solution into the interstitium occurs within several min. This impression is also gained in our study, based on the changing of values of Hgb concentration intra and postoperatively. Intraoperatively and until 6th postoperative hr the concentration of Hgb in the research group was significantly lower due to hemodilution than in the control group which received only crystalloids. This could be explained by postponed transfer of fluid into the interstitium due to colloids remaining primarily in the intravascular space. As early as during the first postoperative day, differences in fluid balance were not significant since both groups were equalized, probably by elimination of colloid solutions from the body.

The occurrence of postoperative complications is associated with a variety of factors, such as age, comorbidity, physiological functional status, nutritional status, invasiveness of surgery, and cancer stage [24]. The Clavien-Dindo classification system [14] was used to assess the complications. There were no complications in either group of patients during the postoperative period.

Conclusion

Both ways of application of fluids by means of goal directed fluid therapy provide favorable hemodynamic stability both intraoperatively and postoperativaly. Yet, goal directed fluid therapy with colloids first, followed by crystalloids during surgery, decreases the total intraoperative fluid volumes, provides higher values of CI intraoperatively which are also maintained postoperatively, decreases the need for applying vasoactive medications and provides lower positive fluid balance.

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Conflict of interests

The authors declare no conflict of interests.

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