



# Do Laparoscopic Colorectal Procedures Need Fluid Optimization?

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## Abstract

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**BACKGROUND:** Goal-directed fluid therapy (GDFT) with hemodynamic monitoring may not be of benefit to all elective patients undergoing major abdominal surgery, particularly those managed in enhanced recovery after surgery protocols (ERAS) setting.

**AIMS:** We predicted different fluid and vasoactive drug consumption during the procedure and less complications in the group of patients, where invasive hemodynamic monitoring was used.

**METHODS:** Two groups of patients undergoing elective laparoscopic colorectal surgery were compared: A control group (CG), with standard hemodynamic monitoring, and a study group, (SG) with invasive hemodynamic monitoring and appropriate intraoperative interventions. We compared differences in intraoperative fluid consumption, length of hospital stay (LOS) and post-operative morbidity.

**RESULTS:** A group of 29 patients in SG had similar average intraoperative fluid balance (+438 mL) as 27 patients in CG (+345 mL)  $p = 0.432$ . Average LOS was 8 days ( $\pm 4$ ) in SG and 6 days ( $\pm 1$ ) in CG ( $p = 0.124$ ). Acute renal failure, anastomotic dehiscence, and indication for antibiotic treatment were predictors of statistically significant prolongation of hospital stay 3<sup>rd</sup> day after surgery, but independent of SG.

**CONCLUSION:** Since no differences between the groups were shown in overall fluid and vasoactive drug consumption, we conclude that GDFT is not needed in laparoscopic colorectal surgery, when ERAS is followed.

## Introduction

Oxygen delivery should be carefully managed to ensure good outcome in major abdominal surgery. Fluid optimization and adequate cardiac output are provided with fluid replacement therapy and vasoactive drugs [1], [2]. Goal-directed fluid therapy (GDFT) may not be useful to all elective patients undergoing major abdominal surgery, particularly those managed in (enhanced recovery after surgery [ERAS] protocols setting) [3]. Furthermore, for laparoscopic colorectal resections in ERAS protocol restrictive fluid replacement are used. Only the fluid that is lost during surgery is replaced [4].

Our study compared two groups of patients undergoing elective laparoscopic colorectal surgery: A control group (CG) with standard hemodynamic monitoring, and a study group (SG) with invasive hemodynamic monitoring.

We predicted different fluid and vasoactive drug consumption during the procedure and less complications due to inadequate oxygen delivery in the group of patients, where invasive hemodynamic monitoring was used.

## Materials and Methods

The study was approved by the National Medical Ethic Committee of the Republic of Slovenia (KME 127/05/12). Clinical trial ID NCT04719884.

The study was conducted in 2017 in Clinical department of anesthesiology and surgical intensive therapy, University Medical Centre Ljubljana.

Sixty patients, undergoing elective laparoscopic colorectal surgery, aged eighteen or older, American society of Anaesthesiologists (ASA) 2–3, were included in the study. Patients with cardiac arrhythmias were not included.

Informed consent and information were provided on the day before surgery by one of members of the research team. Preoperatively, patients were prepared in accordance with ERAS protocol.

Patients for SG (30 pts.) were included prospectively in 3 months period. Data for CG (30 pts.) were obtained from patient's records in consecutive order for 3 months before change in anesthetic technique with invasive hemodynamic monitoring.

Apart from this, anesthetic management did not differ between the groups.

After arrival to operating room an intravenous line was placed and patients were premedicated with midazolam (Dormicum, Roche Pharma AG, Germany) (1–2 mg i.v.).

SG patients received an arterial line into radial artery to record hemodynamic parameters observed by LIDCO Rapid monitor (LIDCO Ltd., United Kingdom).

For evaluation of the anesthesia depth, unilateral bispectral index monitor (BIS Vista, Coviden, Holland) was used.

In SG baseline values of nominal stroke index (SI), cardiac index (CI), mean arterial pressure (MAP), and regional oxygen saturation ( $rSO_2$ ) were recorded.

Before induction of anesthesia all patients received up to 200 mL of fluids, including antibiotics and other therapy.

Induction was conducted with a slow injection of fentanyl (Fentanyl Torrex, Chiesi, Austria) (3–5  $\mu\text{g}/\text{kg}$ ) or sufentanyl (sufentanil-hameln, Hameln pharma plus gmbh, Germany) (0.3–0.5  $\mu\text{g}/\text{kg}$ ), followed by a bolus of propofol (Propoven, Frasenius Kabi Austria, Austria) (1–2 mg/kg) or etomidate (Hypnomidate, GlaxoSmithKline, Italy) (0.2 mg/kg) and rocuronium (Esmeron, N. V. Organon, Holland) (0.6 mg/kg).

Patients were intubated, a nasogastric tube and a urine catheter were inserted.

Maintenance of general anesthesia was achieved using inhaled volatile agent - sevoflurane (Sevorane, AbbVie, Italy) in air/oxygen mixture ( $FiO_2$  0.04). The depth of anesthesia was titrated with sevoflurane to maintain BIS values between 40 and 55.

Muscle relaxation was monitored and rocuronium (10–20 mg) was supplemented according to term turnover frequency (TOF) values. All patients received an antiemetic (ondasetron [Setronon, Pliva Ljubljana, Slovenia] 4 mg and dexamethasone [Dexamethason Krka, Krka, Slovenia] 8 mg).

Lungs were ventilated with a tidal volume of  $\geq 8$  mL/kg ideal body weight. Normothermia (36–37°C) and normocapnia (5–5.5 kPa) were maintained.

An intravenous infusion of patient-controlled analgesia with piritramide (Piritramid-hameln, Hameln pharma plus Gmbh, Germany) was started at the beginning of laparotomy closure (infusion rate 1.5 mg/h, bolus 1.5 mg, lock out 30 min).

In both groups maintenance of fluid requirements was met by a basal infusion of balanced crystalloids (2 mL/kg/h) during the operation. Blood loss was supplemented with colloids and red blood cell transfusion.

In SG fluid optimization was performed before pneumoperitoneum and after abdominal desufflation with actions, described below, to achieved CI, MAP, and SI within 80% of baseline values.

In case of stroke volume variation (SVV)  $>10\%$  and SI and CI  $>10\%$  below the starting value, fluid challenge was performed with approximately 2 mL/kg of colloid over maximum of 5 min. The response was monitored.

If there was a fall in SVV and an increase in SI of  $>10\%$  and the SVV still  $>10\%$ , the second fluid challenge was performed.

If there was still a reduction in SVV after the second fluid challenge, but an increase in nSI  $<10\%$  and decrease in systemic vascular resistance, no additional fluids were given. Vasoactive drugs were used instead.

In CG hemodynamic were evaluated according to observed visible blood lost, invasive blood pressure measurement, measured hemoglobin values and urine output.

At the end of the operation, in both groups the muscle block was reversed with sugamadex (Bridion, N. V. Organon, Holland) (2–4 mg/kg) or neostigmin (Neostig 0.5 Carino, Carinopharm, Germany) (2.5 mg) and atropine (Atropina Solfato, Bioindustria, Italy) (1 mg), according to TOF values.

After the operation patients were transferred to postoperative recovery room and thereafter to Abdominal Surgery's high dependency unit.

Additional parameters were recorded in both groups, according to protocol. Intraoperatively we recorded: The duration of surgery, blood loss, fluid and blood consumption and urine output. Post-operative parameters were: The length of hospital stay (LOS), wound healing, reoperations, mortality and complications such as sepsis, pneumonia, acute respiratory infection, pleural effusion, myocardial infarction, lung embolism, cerebrovascular insult, dehiscence of gut anastomosis, intra-abdominal infection and urine infection. Parameters were recorded on the post-operative days 3, 5, and 8 and on hospital discharge.

### Statistical analysis

R, A language, and environment for statistical computing (R Foundation for Statistical Computing, Vienna, Austria. <http://www.R-project.org/>) were used to calculate general characteristics of included patients and intraoperative differences among groups. Chi-square tests and Mann–Whitney tests were used where appropriate. We calculated linear regression with length of stay as dependent variable and binomial logistic regression with intraoperative vasoactive support with noradrenaline (yes vs. no) as a dependent variable. Results with  $p < 0.05$  were considered statistically significant.

## Results

We have analyzed data of 29 patients in SG. One patient was omitted due to insufficient protocol adherence. Data of 27 patients in CG were analyzed. Three patients were transferred to oncology department for further treatment and their inclusion would distort LOS. General patients' characteristics, intraoperative fluid management, and LOS are displayed in Table 1. No

**Table 1: General patients' characteristics, intraoperative fluid management and LOS Mann-Whitney U test was used to compare the groups in selected variables**

Variable	Group	Mean value	SD	p-value
Patients' weight (kg)	SG	73	14	0.258
	CG	79	17	
Patients' height (cm)	SG	169	8	0.476
	CG	171	9	
Intraoperative crystalloids (mL)	SG	900	304	0.823
	CG	888	320	
Intraoperative colloids (mL)	SG	313	277	0.073
	CG	425	189	
Intraoperative fluid balance (+ or - mL)	SG	+1213	438	0.423
	CG	+1314	345	
Intraoperative diuresis (mL)	SG	219	265	0.238
	CG	247	234	
Intraoperative blood loss (mL)	SG	77	125	0.572
	CG	115	207	
Post-operative RBC infusion (mL)	SG	89	227	0.384
	CG	43	158	
LOS (days)	SG	8	4	0.124
	CG	6	1	

SG: Study group, CG: Control group, RBC: Red blood cell, LOS: Length of hospital stay.

significant differences were shown between the groups. Table 2 shows distribution of ASA status between the groups (There was no significant difference, Chi-square test,  $p = 0.711$ ) and Table 3 shows gender distribution with slight difference in number of male subjects (Chi-square,  $p = 0.048$ ).

**Table 2: ASA status distribution**

Group	ASA			Total
	1	2	3	
SG	2	18	9	29
CG	3	14	10	27
Total	5	32	19	56

ASA: American society of anesthesiologists, SG: Study group, CG: Control group.

Predictors for LOS are shown in results of linear regression in Table 4. Indication for antibiotic treatment 3<sup>rd</sup> day after surgery, acute renal failure and anastomotic dehiscence are predictors for statistically significant prolongation of LOS. Hemodynamic monitoring is insignificant predictor of duration of hospitalization. Binominal regression in Table 5 shows that patients who required intraoperative vasoactive support with noradrenaline were in both groups and have received similar amount of fluids.

**Table 3: Gender distribution**

Group	Gender		Total
	Male	Female	
SG	15	14	29
CG	7	20	27
Total	22	34	56

SG: Study group, CG: Control group.

**Table 4: Linear regression with length of stay (LOS) as dependent variable. Occurrence of anastomosis dehiscence and acute renal failure on 3<sup>rd</sup> day after surgery significantly increased LOS. Study group does not influence LOS**

Predictor	Estimate	SE	95% confidence interval		Significance	
			Lower	Upper	t	p
New ATB treatment 3 <sup>rd</sup> day after surgery						
Yes versus No	0.988	0.529	-0.0745	2.050	1.87	0.068
Acute renal failure 3 <sup>rd</sup> day						
Yes versus No	2.813	1.330	0.1422	5.484	2.11	0.039*
Anastomotic dehiscence 3 <sup>rd</sup> day						
Yes versus No	19.825	1.402	17.0096	22.641	14.14	<0.001*
Group						
SG-CG	-0.408	0.355	-1.1215	0.306	-1.15	0.257

\*Result is statistically significant. SG: Study group, CG: Control group.

## Discussion

Our research groups were homogenous regarding age, weight, height, and ASA status. Because our randomization process was only time based, difference in number of included male patients occurred, however subgroup analysis did not result in any significant differences. All patients underwent laparoscopic colorectal resection. No significant differences were shown between the groups regarding perioperative fluid administration, vasoactive drugs, and LOS. Major post-operative complications as infection (indication for post-operative antibiotic treatment), anastomotic dehiscence and acute renal failure were related to statistically significant prolongation of hospital stay. However, intraoperative fluid management did not affect this.

**Table 5: Binominal logistic regression with intraoperative vasoactive support with noradrenaline (yes vs. no) as a dependent variable. Study group does not influence the need for vasoactive support**

Predictor	p-value	Odds ratio	Lower	Upper
Group:				
CG-SG	0.189	2.172	0.683	6.91
Infused crystalloids	0.109	0.998	0.997	1.00
Infused colloids	0.697	1.000	0.998	1.00

SG: Study group, CG: Control group.

Because ERAS goals for perioperative fluid management include avoidance of hypovolemia and excessive fluid administration, we used restrictive fluid therapy in the CG to minimize fluid administration [4], [5], [6], [7]. Consequently, patients who required vasoactive support received similar amount of fluids. There are some guidelines, like NICE Guidance 12, that recommends the use of GDFT technology in patients undergoing major or high-risk surgery [3], [8]. Several meta-analyses of randomized control trials have shown that fluid optimization helps to lessen postoperative morbidity and LOS. This is most important for high-risk patients undergoing major surgery [9], [10], [11], [12]. Studies that compared GDFT to deliberate evidence-based fluid regimens did not show the same results [13], [14], [15]. Patients optimized with crystalloids received more fluids than patients optimized with colloids and postoperative complications or LOS were not significantly different, regardless the type of fluid chosen [16], [17].

The large multicenter randomized controlled study performed by Pearse *et al.* included 734

high-risk patients undergoing major abdominal surgery. It showed decrease of complications and mortality in GDFT patients, but the result was not significant [18]. It is supposed that GDFT may not be useful for all elective patients undergoing major abdominal surgery, especially when combined with ERAS protocol [3]. If pre-operative dehydration is avoided and early post-operative alimentation is emphasized as part of an ERAS protocol, then GDFT may be unnecessary because of the low risk of perioperative fluid imbalance [19], [20], [21]. An infusion of 1.5–2 mL/kg/h of balanced crystalloid solution provide adequate salt-water homeostasis during major abdominal surgery [22], [23]. On the other hand, not benefit was gained for patients undergone elective major abdominal surgery when GDFT was used within the setting of an ERAS protocol, compared with a fixed-volume regimen [3]. A randomized multicenter study of 150 elective colorectal surgery patients compared a zero-balance (restrictive) approach to GDFT. They could not find any differences between the groups [14].

Our study showed relevant data on days 3, 5, and 8. The differences between the groups were not significantly different in major complications such as acute myocardial infarction, dehiscence of anastomosis, pulmonary embolism, post-operative delirium, and cardiac arrhythmia. The same was observed in patients undergone brain tumor surgery [24].

Risk factors such as anemia, blood loss, transfusion, prolonged surgery, hypotension, use of vasoactive drugs, type of anesthesia, and inadequate fluid optimization that are important for incidence of gut anastomosis dehiscence were not significantly different in our study [25].

We found no differences between the groups in early mobilization. This is in line with the study of Bundgaard-Nielsen *et al.* who showed that fluid optimization improves functional hypovolemia, but not orthostatic intolerance which is presented in 50% of patients 6 h after major surgery [26].

## Conclusion

Our study showed that GDFT is probably unnecessary in laparoscopic colorectal surgery, if ERAS is followed. There were no significant differences between the groups regarding fluids and vasoactive drugs consumption and the incidence of complications.

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