

**Intraoperative Fluid management a modifiable risk factor for Surgical Quality - Improving Standardized Practice.**

**Short title:** Intraoperative fluid therapy.

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**Min Abstract**

We aimed to determine a safe zone of intraoperative fluid management associated with the lowest postoperative complication risk of acute kidney for elective colorectal surgery patients.

Total intraoperative ringer's lactate (RL)  $\geq 2.7$  L is independently associated with postoperative ileus and prolonged length of stay while the rate of intraoperative RL infusion (ml/Kg/hr) was less impactful in elective colorectal surgery patients.

## **Abstract:**

### **Background and objective:**

We aimed to determine a safe zone of intraoperative fluid management associated with the lowest postoperative complication rates without increased acute kidney injury (AKI) risk for elective colorectal surgery patients.

### **Patients, settings, and outcome measures:**

Elective colorectal surgeries between 2018 and 2020 were included. Unadjusted odds ratios for postoperative ileus, prolonged length of stay (LOS), and AKI were plotted against the rate of intraoperative ringer's lactate (RL) infusion (mL/kg/h) and total intraoperative volume. Binary logistic regression analysis, including fluid volumes as a confounder, was used to identify risk factors for postoperative complications.

### **Results:**

A total of 2,900 patients were identified. Of them, 503 (17.3%) patients had ileus, 772 (26.6%) patients had prolonged LOS, and 240 (8.3%) patients had AKI. The intraoperative fluid resuscitation rate (mg/kg/h) was less impactful on postoperative ileus, LOS, and AKI than the total amount of intraoperative fluid. A total fluid administration range between 300 mL and 2.7 L was associated with the lowest complication rate. Total intraoperative RL  $\geq 2.7$  L was independently associated with a higher risk of ileus (adjusted OR 1.465;95% CI 1.154-1.858) and prolonged LOS (adjusted OR 1.300;95% CI 1.047-1.613), but not AKI. Intraoperative RL  $\leq 300$  ml was not associated with an increased risk of AKI.

### **Conclusion:**

Total intraoperative RL  $\geq 2.7$  L was independently associated with postoperative ileus and prolonged LOS in elective colorectal surgery patients. A new potential standard for intraoperative fluids will require anesthesia case planning (complexity and duration) to ensure total fluid volume meets this new opportunity to improve care.

**Keywords:** Fluid therapy, ileus, perioperative care, colorectal surgery, acute kidney injury, enhanced recovery after surgery.

## Introduction:

Postoperative complications and extended length of stay (LOS) are critical determinants of surgical quality and undermine the goal of high quality and affordable care. Fluid management in the operating room is a complex issue that is a known determinant of surgical quality (1, 2). However, given the predictability of most elective operative procedures' duration and complexity, intraoperative fluid administration can be a modifiable factor. To date, standard practice within institutions, let alone national expectations related to fluid administration, are limited (3). This fact has perpetuated a quality gap.

The intraoperative fluid management debate has resulted from the heterogeneity in the definition between liberal and restrictive approaches (1, 4). Furthermore, the superiority of restrictive management over a liberal approach, in general, has been questioned due to the risk of postoperative acute kidney injury (AKI) (5). Simultaneously, fluid overload is a known risk for complications (6, 7). Therefore, one of the proposed methods to reduce complications and LOS includes balanced fluid management (2, 8).

We aimed to advance a well-established enhanced recovery pathway (ERP) (9-12) and define a fluid management strategy that would be simple to implement and improve quality. This study sheds new light on a "safe zone" of intraoperative fluid management to further enhance postoperative bowel recovery and minimize LOS while maintaining volume status.

## Materials and Methods:

This retrospective analysis included all consecutive adult patients who underwent elective colorectal inpatient surgery (colon, rectal, multivisceral resections and stoma-related procedures (Hartmann reversal and ileostomy/colostomy takedown) at Mayo Clinic, Rochester, Minnesota between May 5th, 2018 to June 8th, 2020. Patients coded as American Society of Anesthesiologists (ASA) class V, patients who underwent transanal, outpatient, wound debridement procedures, and patients with missing creatinine values pre- or post-operatively were excluded. Data were accessed from a prospectively maintained anesthesiologic database updated by dedicated staff. Ethical approval of the Institutional Review Board (IRB) was obtained.

## Cohorts:

Unadjusted odds ratios for postoperative ileus, LOS, and AKI were plotted against the total amount and rate (mL/kg/hr) of intraoperatively administered ringer's lactate (RL) volumes utilized to identify the optimal intraoperative fluid range (balanced fluids) associated with the least postoperative complications (**Figure 1**). Consequently, patients were divided into three cohorts based on fluid (RL) volume according to the values determined through **Figure 1** (cut-off values where the lower confidence interval crossed 1): balanced (300 mL to 2.7 L), liberal (> 2.7 L), and restrictive (< 300 mL). Ringer's lactate was used as a standard fluid resuscitation compound in our practice.

**Risk factors for complications:**

Demographics, anthropometrics, ASA class, preoperative comorbidities including diabetes mellitus, cardiac (myocardial infarction or congestive heart failure), respiratory (chronic obstructive pulmonary disease, interstitial lung disease or asthma), and renal diseases, smoking, home medications (including aspirin and anticoagulants), intraoperative hemodynamics (heart rate and blood pressure), need for blood products/albumin, the extent of resection (rectal, colon, multi-visceral resection), and operative approach were compared between patients who had complications versus patients without complications.

**Outcomes:**

Outcomes were postoperative ileus, AKI, and prolonged LOS. Ileus was defined as a need for postoperative nasogastric tube reinsertion or  $\geq 5$  postoperative days without bowel movement or flatus (13). The definition of AKI was based on the Kidney Disease Improving Global Outcomes (KDIGO) criteria (14): increase of postoperative serum creatinine  $\geq 0.3$  mg/dL compared to preoperative creatinine within 48 hours or  $\geq 1.5$  increase from the baseline which is known or presumed to have occurred within the previous seven days. Acute Kidney Injury (AKI) within 24 hours after the operation was reported as it is standard practice in our institution to check postoperative creatinine at this time and rarely required rechecking (15, 16). Of note, patients with lacking pre- or postoperative creatinine were excluded. Prolonged LOS was defined as LOS  $\geq 7$  days. Seven days was chosen as a cut-off as it represents the third quartile of LOS for the entire cohort.

**Enhanced Recovery Pathway (ERP):**

All patients were treated according to the previously and extensively described ERP protocol including combined bowel preparation (mechanical and oral antibiotics) for colorectal resections (9-12). As protocol compliance is very high in our institution, as previously reported (9), the protocol's adherence was not assessed in this study. In line with recent recommendations, invasive monitoring (goal-directed fluid therapy) in the setting of these elective procedures was not used outside high-risk patients or procedures (17). Low urinary output did not trigger fluid resuscitation if occurring in isolation (12). Hemodynamic drugs (i.e. noradrenaline) were preferred over i.v. fluids in order to adhere to a restrictive fluid regimen with a goal of zero fluid balance and euvolemia (18). Albumin was only occasionally used upon anesthetist's discretion to trigger urine output since it may be preferable over RL in some situations to allow for volume expansion and to prevent overhydration.

**Statistical analysis:**

Categorical variables were reported as frequencies and percentages, and continuous variables were reported as median (interquartile range: IQR). The differences between both groups were evaluated using the Chi-squared test or Fisher's exact test as appropriate for categorical

variables and Wilcoxon rank-sum test for continuous variables. A multivariable binary logistic regression model was used to assess the potential risk factors of ileus, AKI, and prolonged LOS. All tests were two-sided, and the significance level was 0.05. All analyses were conducted using the Statistical Package for Social Sciences (SPSS, version 25; SPSS, Inc., Armonk, NY, USA).

## Results:

A total of 2,900 patients were identified. Of them, 503 (17.3%) patients had ileus, 772 (26.6%) patients had prolonged LOS, and 240 (8.3%) patients had AKI. In patients presenting with postoperative ileus, 228 patients (45.3%) had an ileostomy, compared to 925 patients (38.6%) in patients without ileus ( $p=0.005$ ). The overall median operation time (skin to skin) was 3 hours (IQR 1.9 to 4.8).

As shown in **Figure 1**, the intraoperative fluid (RL) management rate (mL/kg/h) was less impactful on postoperative ileus, LOS, and AKI, than the total amount of intraoperative fluids (RL) was. A total RL level between 300 mL and 2.7 L was associated with the lowest complication rate.

Intraoperative RL administration  $> 2.7$  L was independently associated with higher rates of ileus and prolonged LOS but not AKI. Intraoperative RL administration  $< 300$  ml was not associated with higher rates of ileus, prolonged LOS, or AKI (**Tables 1, 2, and 3**).

As shown in **Table 1**, independent risk factors associated with a higher risk of postoperative ileus were male sex, ASA  $\geq 3$ , more extensive surgery (multi-visceral resections), need for blood transfusion, intraoperative albumin administration, and history of respiratory disease. Risk factors for prolonged LOS included age, ASA  $\geq 3$ , preoperative anticoagulation use, open surgery, more extensive surgery (multi-visceral resection), need for blood transfusion, intraoperative albumin or sodium chloride administration, and history of respiratory or renal disease (**Table 2**). Risk factors for AKI included male sex, ASA  $\geq 3$ , open surgery, need for intraoperative albumin administration and preoperative history of renal disease (**Table 3**).

## Discussion:

This retrospective analysis reinforces the literature's stance on the detrimental effect of excess intraoperative fluid. Delivery of greater than 2.7 L of intraoperative RL was independently associated with a higher risk of ileus and prolonged LOS. Restrictive intraoperative RL management (total ringer's lactate  $< 300$  ml) was not associated with a higher risk of AKI, ileus, or prolonged LOS.

Studies have shown perioperative fluid overload, inconsistently defined, was associated with higher rates of ileus, nausea and vomiting, length of stay, overall complications, and total cost (2, 19). Similarly, overly restrictive fluid management was associated with worse outcomes (2) and, more importantly, low tissue perfusion and a higher risk of AKI (5). The physiological ramifications of volume depletion lead to multiple changes within the human

body, including activation of the angiotensin-aldosterone system (20), changes to renal blood flow, glomerular filtration rate, and, ultimately, AKI (21). Volume expansion results in fluid accumulation in the interstitial space, leading to tissue edema (20). The subsequent hyperchloremic acidosis and tissue edema caused by these factors lead to tissue hypoxia and hypoperfusion (22). These factors collectively result in delayed anastomotic healing, wound healing, decreased pulmonary function, and postoperative ileus (6, 7, 19, 23, 24).

While risk factors for postoperative complications, including male sex, higher ASA class, comorbidities such as respiratory and renal diseases, and multi-visceral resections have been previously described (14, 31), they represent mostly unmodifiable factors. In sharp contrast, the modifiable risks of intraoperative fluid volume need to be strongly considered to modernize standard pathways to improve patient care. The optimal fluid volume at which perioperative complications are decreased without increasing AKI is challenging to identify due to non-standardized definitions between studies (1). In 2009, Varadhan and Lobo conducted a meta-analysis of randomized controlled trials after choosing the description of balanced fluid therapy for patients who received a total amount of isotonic sodium chloride between 1.75 L/day and 2.75L/day. Interestingly, they found a decrease in postoperative complications and shorter length of stay in the balanced fluid group (1.75 L/day to 2.75 L/day) compared to the unbalanced groups (< 1.75 L/ day or > 2.75 L/day) (8). However, they could not answer the question about the impact on kidney function nor intraoperative management. In contrast to our present study, they excluded studies that used ringer's lactate. Theoretically, the use of sodium chloride is considered to be inferior to buffered fluids such as RL or Hartmann's solution mainly due to the potential risk of hyperchloremic metabolic acidosis, retention time in the interstitial compartment, and the potential harm on the cellular level (25-28). Moreover, our analysis represents a distinct group of colorectal surgeries that follows a fully implemented enhanced recovery pathway.

In the RELIEF trial, AKI rates were significantly higher in the restrictive group (5 mL/kg/hr) compared to the liberal (8 mL/kg/hr) group (8.6% vs. 5%; respectively) (5). However, the trial's pragmatic design, i.e., different practice protocols among the participating institutions, has put its results into question regarding the conclusion's generalizability. The rate per kilogram per hour of intraoperative RL was not impactful on postoperative complications in our series, but the total amount of RL was. This is not surprising given that the operative time in a teaching institution can reflect more than case complexity. Moreover, operative time predictions (based on the last five similar cases on an individual surgeon basis) in our institution are known and afford systematic opportunity to plan for intraoperative fluid rates per hour to achieve the total target volume. Operation time was not included in the regression model due to high colinearity with total amount of RL infused (29, 30). Instead, more representative surrogates for complex procedures, in particular, intraoperative factors (i.e. need for another type of fluid infusion (eg albumin), need for blood transfusion, intraoperative hemodynamics) were investigated. This may explain i.e. the association of administered blood products and postoperative ileus. Operative time is largely unmodifiable and unspecific in the setting of a teaching hospital, as are patient-related comorbidities.

Therefore, the focus of our paper was on modifiable opportunities such as intra-operative fluids.

Based on our previous publications from different timelines and the present study's results, a critical value of 2.7 L – 3 L might be considered (8, 16, 19) as a potential new standard to advance perioperative care.

The limitations of this series include the retrospective analysis and the risk of selection bias. Moreover, our institutional intraoperative monitoring was traditional (static) versus an invasive (dynamic) approach, often used in goal-directed therapy. Nevertheless, a recent meta-analysis found no difference between restrictive fluid management and goal-directed methods (31). It is also essential to consider that colloid use, especially albumin, has a high amount of sodium chloride, potentially leading to high complication rates, explaining the higher adjusted risk of complications in our study regarding albumin infusion. As an institutional standard, colloid transfusion is reserved for prolonged operations and given after infusion of higher RL volumes. At this point, the answer to the efficacy of preemptive colloids versus goal-directed therapy for more prolonged operations needing > 2.7 L of RL cannot be obtained from our present study, and further investigations are required based on our findings. The subjective measure “estimated blood loss” was not used as a parameter for the present analysis, despite an undeniable correlation with intravenous fluid replacement. Instead, We decided to use more objective measures such as intraoperative blood transfusion or hemodynamics. Finally, the increased use of additional blood products (red blood cells, albumin) in patients presenting with postoperative ileus may be explained by the complexity of the procedure rather than a cause-effect relationship. As a consequence, these patients undergoing more extended procedures were also prone to postoperative complications including ileus.

### **Conclusion:**

Intraoperative ringer's lactate > 2.7 L was associated with a higher adjusted odds of ileus and prolonged LOS in elective colorectal patients. These findings open the possibility to standardize our institutional This research did not receive any specific grant from funding agencies in the public, commercial, or non-profit sectors. This original study has not been published, presented, or submitted to any other journal.

**Conflict of interest:** Authors have no conflict of interest to disclose approach to intraoperative fluid management, which is a modifiable risk factor for surgical quality. potential new standard for intraoperative fluids will require anesthesia case planning (complexity and duration) to ensure total fluid volume meets this opportunity to improve care.

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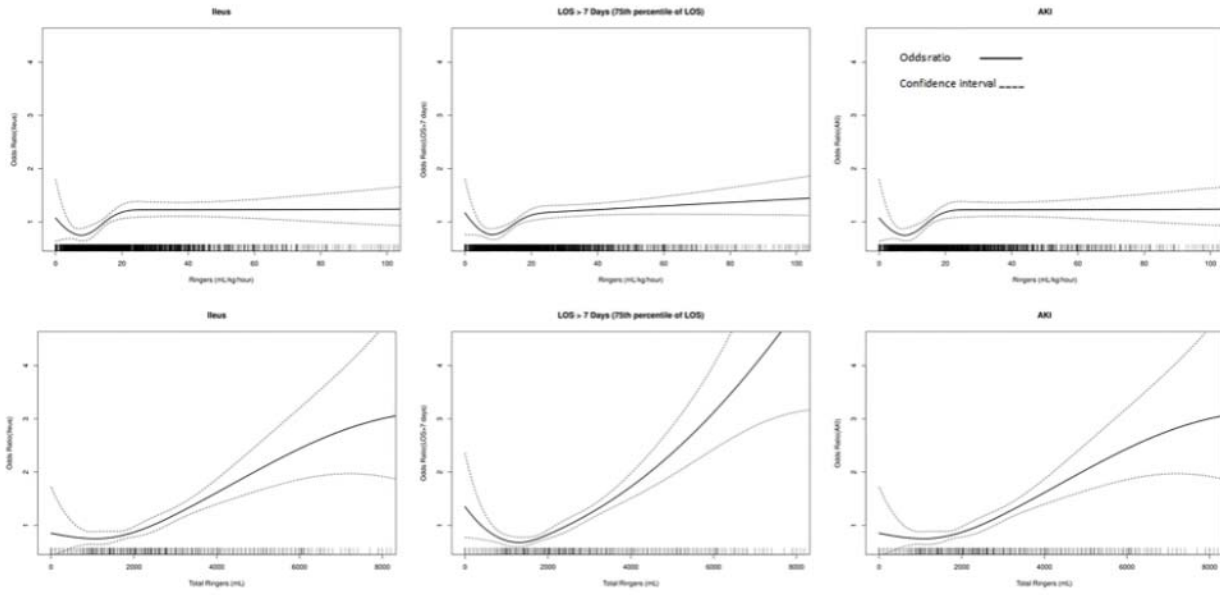


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**Figure 1:** Intraoperative fluid management and postoperative complications.



Plotted are the unadjusted odds ratios with their confidence intervals against rates (top) and total (lower) of lactated ringer infusion.

AKI: acute kidney injury, LOS: length of stay.

**Table 1:** Risk factors for Ileus

	<b>Ileus</b>		<b>Univariable P-value</b>	<b>Multivariable model Odds ratio (95% CI)</b>
	No (N=2397)	Yes (N=503)		
<b>Age, years</b>			0.2682	
Mean (SD)	55.0 (16.9)	55.9 (16.4)		
Median	57.0	58.0		
Q1, Q3	42.0, 68.0	43.0, 69.0		
Range	(19.0-96.0)	(20.0-92.0)		
<b>Sex; Male</b>			<.0001	<b>1.673 (1.366 - 2.048)</b>
	1150 (48%)	303 (60.2%)		
<b>BMI; kg/m<sup>2</sup></b>			0.9160	
Mean (SD)	27.7 (6.5)	27.7 (6.2)		
Median	27.0	27.2		
Q1, Q3	23.0, 31.2	23.6, 31.2		
Range	(13.7-66.0)	(14.5-56.2)		
<b>Smoking</b>			0.098	
Missing	5	2		
Non/Former	2212 (92.5%)	452 (90.2%)		
Current	180 (7.5%)	49 (9.8%)		
<b>ASA; ≥ 3</b>			<.0001	<b>1.266 (1.026 - 1.563)</b>
	1019 (42.5%)	275 (54.7%)		
<b>Comorbidities</b>				
CVS			0.0029	1.339 (0.917 - 1.953)
	134 (5.6%)	46 (9.1%)		
Respiratory			0.0083	<b>1.366 (1.039 - 1.797)</b>
	312 (13.0%)	88 (17.5%)		
D.M.	84 (3.5%)	19 (3.8%)	0.7302	
Renal	163 (6.8%)	44 (8.7%)	0.1240	
Cancer	725 (30.2%)	170 (33.8%)	0.1172	
<b>Preoperative medication use</b>				
Aspirin	4 (0.2%)	0 (0.0%)	>0.99	
Anticoagulant	115 (4.8%)	34 (6.8%)	0.0714	
<b>Intraoperative hemodynamics</b>				
Highest HR during the operation; ≥ 120			0.6159	
	416 (17.4%)	92 (18.3%)		
Minimum MAP			0.0633	
N	2397	503		

Mean (SD)	54.1 (11.3)	53.1 (11.9)		
Median	54.0	53.0		
Q1, Q3	47.0, 61.0	46.0, 60.0		
Range	(25.0-169.0)	(30.0-167.0)		
<b>Intraoperative transfusions</b>				
Any blood product	85 (3.5%)	52 (10.3%)	<.0001	<b>1.823 (1.108 - 3.001)</b>
Albumin	433 (18.1%)	166 (33.0%)	<.0001	<b>1.570 (1.212 - 2.032)</b>
NaCL 0.9%	92 (3.8%)	39 (7.8%)	0.0002	0.956 (0.564 - 1.618)
Total Lactated Ringer			< 0.0001	
Balanced ( 300 mL to 2.7L)	1697 (70.8%)	283 (56.3%)		Reference
<300 mL	39 (1.6%)	6 (1.2%)		0.690 (0.284 - 1.676)
>2.7L	661 (27.6%)	214 (42.5%)		<b>1.465 (1.154 - 1.858)</b>
<b>Surgical approach; MIS</b>	1157 (48.3%)	193 (38.4%)	<.0001	0.786 (0.613 - 1.009)
<b>Extent of resection</b>			<.0001	
Colon Resection	789 (32.9%)	136 (27.0%)		Reference
Rectal Resection	558 (23.3%)	130 (25.8%)		1.061 (0.798 - 1.411)
Multi-visceral resection	200 (8.3%)	75 (14.9%)		<b>1.474 (1.003 - 2.168)</b>
Stoma related procedure	850 (35.5%)	162 (32.2%)		1.077 (0.799 - 1.451)

N: number, SD: standard deviation, Q1: first quartile, Q3: third quartile, BMI: body mass index, Kg: Kilogram, m: meter, ASA: American Society of Anesthesiologists, CVS: cardiovascular system, D.M.: diabetes mellitus, HR: heart rate, MAP: mean arterial pressure, MIS: minimally invasive surgery, CI: confidence interval

**Table 2:** Risk factors for a prolonged length of stay (LOS)

	LOS		Univariable P-value	Multivariable model Odds ratio (95% CI)
	≤ 7 Days (N=2128)	>7 Days (N=772)		
<b>Age; per ten years</b>			<.0001	1.034 (0.975 - 1.098)
Mean (SD)	54.4 (16.8)	57.4 (16.8)		
Median	56.0	60.0		
Q1, Q3	41.0, 67.0	46.0, 70.0		
Range	(19.0-96.0)	(20.0-95.0)		
<b>Sex; Male</b>	1055 (49.6%)	398 (55.1%)	0.3466	
<b>BMI</b>			0.5236	
N	2128	772		
Mean (SD)	27.6 (6.3)	27.8 (6.9)		
Median	27.0	26.9		
Q1, Q3	23.1, 31.1	23.0, 31.7		
Range	(13.7-66.0)	(14.5-65.7)		
<b>Smoking</b>			0.0209	
Missing	7	0		
Non/Former	1968 (92.8%)	696 (90.2%)		Reference
Current	153 (7.2%)	76 (9.8%)		1.313 (0.961 - 1.793)
<b>ASA; ≥ 3</b>	832 (39.1%)	462 (59.8%)	<.0001	<b>1.633 (1.340 - 1.989)</b>
<b>Comorbidities</b>				
CVS	104 (4.9%)	76 (9.8%)	<.0001	1.274 (0.897 - 1.811)
Respiratory	265 (12.5%)	135 (17.5%)	0.0005	<b>1.303 (1.015 - 1.672)</b>
D.M.	66 (3.1%)	37 (4.8%)	0.0006	0.892 (0.563 - 1.413)
Renal	119 (5.6%)	88 (11.4%)	<.0001	<b>1.416 (1.017 - 1.972)</b>
Cancer	640 (30.1%)	255 (33.0%)	0.1279	
<b>Preoperative medication use</b>				
Aspirin	1 (0.0%)	3 (0.4%)	0.06	
Anticoagulant	74 (3.5%)	75 (9.7%)	<.0001	<b>2.500 (1.742 - 3.587)</b>

<b>Intraoperative hemodynamics</b>				
<b>Highest HR during the operation; <math>\geq 120</math></b>	351 (16.5%)	157 (20.3%)	0.0163	1.230 (0.970 - 1.560)
<b>Minimum MAP</b>			<.0001	0.991 (0.982 - 0.999)
N	2128	772		
Mean (SD)	54.7 (11.2)	51.9 (11.5)		
Median	55.0	52.0		
Q1, Q3	48.0, 61.0	44.0, 59.0		
Range	(25.0-169.0)	(30.0-167.0)		
<b>Intraoperative transfusions</b>				
Any blood product	45 (2.1%)	92 (11.9%)	<.0001	<b>1.796 (1.112 - 2.898)</b>
Albumin	329 (15.5%)	270 (35.0%)	<.0001	<b>1.795 (1.421 - 2.266)</b>
NaCL 0.9%	50 (2.3%)	81 (10.5%)	<.0001	<b>1.833 (1.141 - 2.946)</b>
Total Ringer			<.0001	
Balanced ( 300 mL to 2.7L)	1539 (72.3%)	441 (57.1%)		Reference
<300 mL	29 (1.4%)	16 (2.1%)		1.112 (0.565 - 2.189)
>2.7L	560 (26.3%)	315 (40.8%)		<b>1.300 (1.047 - 1.613)</b>
<b>Surgical approach; MIS</b>	1059 (49.8%)	291 (37.7%)	<.0001	<b>0.749 (0.602 - 0.931)</b>
<b>Extent Of Resection</b>			<.0001	
Colon Resection	708 (33.3%)	217 (28.1%)		Reference
Rectal Resection	497 (23.4%)	191 (24.7%)		1.047 (0.813 - 1.347)
Multi-visceral resection	142 (6.7%)	133 (17.2%)		<b>1.834 (1.293 - 2.602)</b>
Stoma related procedure	781 (36.7%)	231 (29.9%)		0.992 (0.763 - 1.290)

LOS: length of stay, N: number, SD: standard deviation, Q1: first quartile, Q3: third quartile, BMI: body mass index, Kg: Kilogram, m: meter, ASA: American Society of Anesthesiologists, CVS: cardiovascular system, D.M.: diabetes mellitus, HR: heart rate, MAP: mean arterial pressure, MIS: minimally invasive surgery, CI: confidence interval.

**Table 3:** Risk factors for acute kidney injury (AKI)

	AKI		Univariable P-value	Multivariable model Odds ratio (95%CI)
	No (N=2660)	Yes (N=240)		
<b>Age; per ten years</b>			<.0001	1.082 (0.985 - 1.188)
Mean (SD)	54.8 (16.9)	59.4 (16.0)		
Median	57.0	62.0		
Q1, Q3	42.0, 68.0	51.0, 71.0		
Range	(19.0-96.0)	(20.0-93.0)		
<b>Sex; Male</b>			<.0001	<b>1.898 (1.427 - 2.524)</b>
	1299 (49%)	154 (64.2%)		
<b>BMI; per one unite</b>			0.0005	1.019 (0.998 - 1.040)
Mean (SD)	27.5 (6.4)	29.1 (6.9)		
Median	26.8	28.8		
Q1, Q3	22.9, 31.1	24.7, 32.8		
Range	(14.0-66.0)	(13.7-53.9)		
<b>Smoking</b>			0.2131	
Missing	7	0		
Non/Former	2448 (92.3%)	216 (90.0%)		
Current	205 (7.7%)	24 (10.0%)		
<b>ASA; ≥ 3</b>			<.0001	1.438 (1.045 - 1.977)
	1142 (42.9%)	152 (63.3%)		
<b>Comorbidities</b>				
CVS	152 (5.7%)	28 (11.7%)	0.0003	1.259 (0.779 - 2.037)
Respiratory	353 (13.3%)	47 (19.6%)	0.0070	1.393 (0.970 - 2.000)
D.M.	91 (3.4%)	12 (5.0%)	0.0163	0.890 (0.595 - 1.332)
Renal	170 (6.4%)	37 (15.4%)	<.0001	<b>1.817 (1.186 - 2.784)</b>
Cancer	809 (30.4%)	86 (35.8%)	0.0823	
<b>Preoperative medication use</b>				
Aspirin	4 (0.2%)	0 (0.0%)	>0.99	
Anticoagulant	141	8 (3.3%)	0.1903	



	(5.3%)			
<b>Intraoperative hemodynamics</b>				
Highest HR during the operation; $\geq 120$	465 (17.5%)	43 (17.9%)	0.8650	
Minimum MAP; per one unite			0.0190	0.997 (0.984 - 1.010)
Mean (SD)	54.1 (11.4)	52.3 (11.0)		
Median	54.0	53.0		
Q1, Q3	47.0, 61.0	44.0, 59.0		
Range	(25.0-169.0)	(30.0-92.0)		
<b>Intraoperative transfusions</b>				
Any blood product	110 (4.1%)	27 (11.3%)	<.0001	1.484 (0.801 - 2.751)
Albumin	515 (19.4%)	84 (35.0%)	<.0001	<b>1.454 (1.027 - 2.057)</b>
NaCL 0.9%	110 (4.1%)	21 (8.8%)	0.0013	0.988 (0.516 - 1.894)
Total Ringer			<.0001	
Balanced ( 300 mL to 2.7L)	1851 (69.6%)	129 (53.8%)		Reference
<300 mL	38 (1.4%)	7 (2.9%)		1.331 (0.491 - 3.604)
>2.7L	771 (29.0%)	104 (43.3%)		1.391 (0.983 - 1.967)
<b>Surgical approach; MIS</b>	1262 (47.4%)	88 (36.7%)	0.0014	<b>0.706 (0.501 - 0.996)</b>
<b>Extent Of Resection</b>			0.0003	
Colon Resection	858 (32.3%)	67 (27.9%)		Reference
Rectal Resection	624 (23.5%)	64 (26.7%)		1.109 (0.748 - 1.645)
Multi-visceral resection	235 (8.8%)	40 (16.7%)		1.408 (0.849 - 2.336)
Stoma related procedure	943 (35.5%)	69 (28.7%)		0.908 (0.597 - 1.380)

AKI: acute kidney injury, N: number, SD: standard deviation, Q1: first quartile, Q3: third quartile, BMI: body mass index, Kg: Kilogram, m: meter, ASA: American Society of Anesthesiologists, CVS: cardiovascular system, D.M.: diabetes mellitus, HR: heart rate, MAP: mean arterial pressure, MIS: minimally invasive surgery, CI: confidence interval