Published in final edited form as:

Dis Colon Rectum. 2018 August ; 61(8): 946–954. doi:10.1097/DCR.0000000000001059.

Acute Kidney Injury in the Age of Enhanced Recovery Protocols

Taryn E. Hassinger, MD¹, George J. Stukenborg, PhD², Florence E. Turrentine, PhD¹, Robert H. Thiele, MD³, Bethany M. Sarosiek, MPH¹, Timothy L. McMurry, PhD², Charles M. Friel, MD¹, and Traci L. Hedrick, MD¹

¹Department of Surgery, University of Virginia Health System, Charlottesville, Virginia, USA

²School of Medicine, University of Virginia Health System, Charlottesville, Virginia, USA

³Department of Anesthesiology, University of Virginia Health System, Charlottesville, Virginia, USA

Abstract

BACKGROUND—Acute kidney injury is a prevalent complication after abdominal surgery. With increasing adoption of enhanced recovery protocols, concern exists for concomitant increase in acute kidney injury.

OBJECTIVE—This study evaluated effects of enhanced recovery on acute kidney injury through identification of risk factors.

DESIGN—Retrospective cohort study comparing acute kidney injury rates before and after implementation of enhanced recovery protocol.

SETTINGS—Large academic medical center.

PATIENTS—All patients undergoing elective colorectal surgery between 2010 and 2016, excluding patients with stage 5 chronic kidney disease.

MAIN OUTCOME MEASURES—Patients before and after enhanced recovery implementation were compared, with rate of acute kidney injury as the primary outcome. Acute kidney injury was defined as a rise in serum creatinine 1.5 times baseline within 30 days of surgery. Multivariable logistic regression identified risk factors for acute kidney injury.

RESULTS—A total of 900 cases were identified, including 461 prior to and 439 following enhanced recovery. 114 cases were complicated by acute kidney injury, with 11.93% of patients

Corresponding Author: Traci L. Hedrick, MD (Contact for Reprints), Department of Surgery, P.O. Box 800709, Charlottesville, VA, 22908, Telephone: (434) 243-2670 Fax: (434) 924-2520, th8q@hscmail.mcc.virginia.edu.

Disclaimers: The authors declare no conflicts of interest, use of off-label or unapproved drugs or products, or use of previously copyrighted material.

The authors declare no relevant financial relationships.

Presented as a poster presentation at the American Society of Colon and Rectal Surgeons Annual Scientific and Tripartite Meeting, Seattle, Washington, June 10–14, 2017.

Conception and design: TEH, RHT, CMF, TLH. Data acquisition: FET, BMS. Analysis and interpretation: TEH, GJS, TLH. Manuscript drafting and editing for important intellectual content: All Authors. Final approval: All Authors. Agreement to be accountable for all aspects of work: All Authors.

IF the manuscript is provisionally accepted, a VIDEO ABSTRACT will be required prior to final acceptance.

prior to and 13.44% after implementation of enhanced recovery ($p=0.50$). Five patients required hemodialysis, with two cases after protocol implementation. Multivariable logistic regression identified hypertension, functional status, ureteral stents, nonsteroidal anti-inflammatory drugs, operative time >200 minutes, and increased intravenous fluid administration on postoperative day 1 as predictors of acute kidney injury. Laparoscopic surgery decreased the risk of acute kidney injury. The enhanced recovery protocol was not independently associated with acute kidney injury.

LIMITATIONS—Retrospective and nonrandomized before-and-after design.

CONCLUSION—No difference in rates of acute kidney injury was detected before and after implementation of a colorectal enhanced recovery protocol. Independent predictors of acute kidney injury were identified and could be utilized to alter the protocol in high-risk patients. Future study is needed to determine if protocol modifications will further decrease rates of acute kidney injury in this population. See Video Abstract at <http://links.lww.com/DCR/Axxx>.

Keywords

Acute kidney injury; Colorectal surgery; Enhanced recovery; Risk factors

Acute kidney injury (AKI) is a frequently encountered postoperative complication following intra-abdominal surgery with rates approaching 15%.^{1, 2} It is identified by an acute decline in renal function ultimately accompanied by the disruption of fluid, electrolyte, and metabolic homeostasis. The severity of AKI ranges from mild changes in biochemical markers to profound kidney damage requiring temporary or permanent renal replacement therapy.³

The development of AKI is related to increased patient morbidity, including increased intensive care unit utilization and overall length of stay, increased rates of non-renal and additional renal complications, and the risk for permanent renal damage.^{1, 2, 4, 5} On a systems level, AKI also contributes to increased institutional expense based on the need for additional procedures and longer length of stay.³

The adoption of enhanced recovery protocols (ERP) has increased over the past several years, and many prospective and observational studies have highlighted their safety and ability to decrease length of stay, overall morbidity, and hospital costs.^{6–9} The focus on judicious intravenous fluid management, more liberal use of vasopressors to avoid excessive intraoperative fluid resuscitation, and administration of nonsteroidal anti-inflammatory drugs to limit narcotic use are fundamental to these protocols, with the overall goal of hastening return to bowel function.^{10–13} However, due to these basic tenants there is concern that the use of ERPs may result in an increased rate of postoperative AKI. In order to address this concern, we aimed to identify independent risk factors for AKI in our colorectal surgery population with the hypothesis that adoption of an ERP would be associated with an increased rate of postoperative AKI.

Materials & Methods

After obtaining institutional review board approval, a retrospective cohort study was conducted including all patients 18 years of age who underwent elective colorectal surgery

prior to (January 1, 2010 to August 5, 2013) and following (August 6, 2013 to January 31, 2016) implementation of an ERP. Patients were followed through 30 postoperative days. Readmissions were captured for each patient, but a readmission was not counted as a new patient.

All cases were performed at a single academic institution by 1 of 2 board certified colon and rectal surgeons. The primary outcome of AKI was defined as a rise in serum creatinine to a value 1.5 times the preoperative baseline value within 30 days of surgery (e.g. 1 mg/dL to 1.5 mg/dL) based on the most recent clinical practice guidelines from the Kidney Disease: Improving Global Outcomes (KDIGO) criteria.¹⁴

It is important to note that the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) defines *progressive renal insufficiency* as “the reduced capacity of the kidney to perform its function as evidenced by a rise in creatinine of >2 mg/dL from preoperative value (e.g. 1 mg/dL to 3 mg/dL), but with no requirement for dialysis within 30 days of the operation” and *acute renal failure* as “worsening of renal dysfunction postoperatively requiring hemodialysis, peritoneal dialysis, hemofiltration, hemodiafiltration, or ultrafiltration within 30 days of the operation in a patient who did not require dialysis preoperatively”. However, we elected to use the more liberal KDIGO definition of AKI, as defined above, as the primary outcome of this study given its greater sensitivity to capture more patients with less significant, yet likely clinically relevant, creatinine elevations in the postoperative period. Other secondary outcomes included postoperative complications based on NSQIP definitions (surgical site infection, wound disruption, postoperative pneumonia, unplanned intubation, pulmonary embolism, postoperative ventilator dependency for >48 hours, urinary tract infection, cerebrovascular accident, cardiac arrest, myocardial infection, postoperative transfusion within 72 hours, vein thrombosis requiring therapy, postoperative sepsis/septic shock, other postoperative occurrences), postoperative hemodialysis, length of stay, 30-day readmissions, and mortality.

Data Collection

Patients were identified from a prospectively collected database supplemented by data from the NSQIP database. NSQIP definitions for all demographics and outcome variables were used and can be found at https://www.facs.org/~media/files/quality%20programs/nsqip/nsqip_puf_user_guide_2015.ashx. Glomerular filtration rate was calculated, and patients were stratified into chronic kidney disease (CKD) stages 1 through 5. Chronic renal insufficiency was defined as stage 3 or 4 CKD. Patients with stage 5 CKD (GFR <15 mL/min or treatment by dialysis) were excluded.¹⁵

Enhanced Recovery Protocol Implementation

The preoperative and postoperative management strategies for the intervals prior to and following the implementation of the ERP have been previously described in detail.^{10–13} Prior to adoption of the protocol, patients were instructed to ingest only liquids the day prior to scheduled surgery, transitioning to taking nothing by mouth at midnight. Additionally, a mechanical bowel preparation was utilized on the day prior to surgery. In general, pain management strategies included a low thoracic epidural with intravenous (IV) opioids as

needed for open procedures and patient-controlled analgesia with IV opioids for laparoscopic procedures, prior to transition to oral opioids. Nonsteroidal anti-inflammatory drugs (NSAIDs) were also utilized; however, there was no standard protocol prior to ERP implementation, and thus these patients received NSAIDs sporadically. Intraoperative IV fluid management was dictated by the anesthesia team. Postoperative IV fluid was managed by the surgical team, and decisions regarding diet advancement were left to the discretion of the primary surgeon.⁸

Perioperative care was standardized on August 6, 2013 with the initiation of a colorectal surgery ERP. Patients were instructed to cease intake of solid foods at 6:00 PM on the evening prior to surgery. At this time, a mechanical bowel preparation was started. Intake of clear liquids was permitted until 2 hours prior to surgery, including a mandatory 20 ounces of Gatorade Thirst Quencher 2 hours prior to induction. Intraoperative anesthesia care was standardized as part of the protocol. For the first 6 months following ERP implementation, a dedicated group of 6 anesthesiologists and certified registered nurse anesthetists managed the anesthesia care. Following this time, care of ERP patients was opened to all anesthesia practitioners. Intraoperative fluid management was guided by a goal-directed fluid algorithm, with more liberal use of intraoperative vasopressors to maintain satisfactory hemodynamics.⁸ Postoperative IV fluids were continued at 40 cc/hr until the morning of postoperative day (POD) 1, at which time a soft diet was initiated. Regarding pain management, neuraxial analgesia was administered preoperatively with a single shot of intrathecal morphine, and IV ketamine as well as lidocaine were infused throughout the surgery. Postoperatively, patients received IV lidocaine, oral acetaminophen, and NSAIDs in addition to oral opioids for breakthrough pain.⁸ More specifically, patients received 200 mg of oral celecoxib in the surgical admissions suite. Postoperatively, patients were treated with 100 mg oral celecoxib twice daily. The only exceptions to celecoxib administration were a history of coronary artery disease or allergy to the medication. The patients were encouraged to take ibuprofen as needed following discharge but were not given a prescription.

Statistical Analysis

Separate univariate analyses were conducted to evaluate for differences in baseline characteristics between patients treated before and after ERP implementation as well as patients with and without AKI. Differences in outcomes were compared using the χ^2 test for categorical variables and Student's *t* test for continuous variables. Given an estimated baseline AKI rate of 12% in the pre-ERP population and a predicted increase in the AKI rate to 20% in the ERP group, 706 patients were required to achieve statistical power (1- β) of 0.80.

Finally, a multivariable logistic regression model was then created to identify risk factors for AKI. Dependent variables were chosen *a priori* based on clinical factors previously shown to affect AKI development. A *p* value of 0.05 was used for statistical significance. All of the statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC).

Results

Nine hundred patients were identified from the database between January 2010 and January 2016. Four hundred sixty-one patients (51.22%) underwent surgery prior to implementation of the ERP, and 439 patients (48.78%) underwent surgery after implementation. Demographic variables, procedural characteristics, and outcome variables for the 2 groups are reported in Table 1. The ERP group had a higher rate of laparoscopic procedures, longer operating room time, and less blood loss. Urine output was lower in the ERP group on POD 0 but not on POD 1. ERP implementation also resulted in less fluid administration on POD 0 (4104.39 mL $\pm$ 2255.67 mL vs. 1840.96 mL $\pm$ 1327.85 mL; $p < 0.0001$) and 1 (3623.66 mL $\pm$ 1338.29 mL vs. 2312.30 mL $\pm$ 2111.02 mL; $p < 0.0001$) as well as higher use of NSAIDs and intraoperative vasopressors. Overall complications, length of stay, and 30-day readmissions were all decreased in the ERP group. There was no difference in the rate of AKI between the groups ($p = 0.50$).

Acute Kidney Injury

One hundred fourteen cases were complicated by AKI, with 55 cases (11.93%) identified in the pre-ERP group and 59 cases (13.44%) in the ERP group. A histogram demonstrating the difference between preoperative and maximum postoperative creatinine values for each patient within 30 days of surgery for each time period is shown in Figure 1. Demographic variables, procedural characteristics, and outcome variables for patients with and without AKI are reported in Table 2. Patients diagnosed with AKI were older with a higher body mass index (BMI). Hypertension was more common in the AKI patients, but rates of diabetes and preoperative renal insufficiency did not differ between the groups. More patients with AKI underwent open surgery with longer operating room times and more blood loss. The presence of an ileostomy was also more common among patients with AKI. Use of NSAIDs was not more frequent in the AKI patients. The proportion of patients in the ERP group did not differ among those with and without AKI ($p = 0.50$). Importantly, patients with AKI had a longer length of stay and were more likely to experience a postoperative complication, including surgical site infection, 30-day readmission and mortality.

Finally, a multivariable logistic regression model was developed to identify risk factors for AKI (Table 3). Hypertension ($p = 0.001$), functional status ($p = 0.02$), ureteral stent ($p = 0.04$), NSAIDs ($p = 0.02$), operating time over 200 minutes ($p = 0.03$), and increased IV fluid administration on POD 1 ($p = 0.001$) were all associated with an increased risk of AKI. Open surgery was also associated with an increased risk of AKI ($p = 0.0008$). The ERP was not independently associated with AKI ($p = 0.09$). The C-statistic for the model was 0.84.

Discussion

The overall incidence of AKI in this study using the KDIGO guideline definition was 12.67%, with approximately the same percentage occurring both before and after implementation of an ERP.¹⁴ Contrary to our hypothesis, the implementation of a highly standardized ERP did not seem to be associated with an increased risk of AKI. However, we were able to identify multiple other risk factors for the development of AKI which could be used to alter management in these high-risk patients.

The incidence of AKI in our study is comparable to published rates of postoperative AKI following both major non-cardiac surgery and, more specifically, following major intraabdominal surgery.^{1, 2} The definition of AKI used in the current study (a rise in creatinine to a value 1.5 times the preoperative baseline value) was based on the most recent clinical practice guidelines from KDIGO which were intended to replace the Risk, Injury, Failure, Loss of kidney function, and End-stage renal failure (RIFLE) criteria. While this definition may seem quite liberal (e.g., identifying a patient with a creatinine that rose from 0.6 mg/dL to 0.9 mg/dL), recent data suggest that perioperative AKI is a frequently under-recognized condition.¹⁶ Studies in post-myocardial infarction and critically ill patient populations have shown that the KDIGO criteria is more sensitive in identifying clinically significant AKI and subsequent mortality when compared to other definitions such as the RIFLE criteria.^{17, 18} In the current study, there were very few patients with normal creatinine levels that met the definition for AKI (<10%). As demonstrated in Table 2, the average peak creatinine for the AKI group was 2.13 mg/dL, and the outcomes for patients with AKI were significantly worse (including mortality) compared to those without AKI, further demonstrating the clinical relevance of the KDIGO definition in this colorectal surgery population.

Multiple retrospective and prospective observational studies have sought to identify predictors for AKI, both in the generalized patient population as well as in postoperative patients. Many of the identified risk factors exhibit overlap in the previously published literature and with the current study including American Society of Anesthesiologists (ASA) classification and hypertension.^{2, 5, 19} In addition, our data identified associations between functional status, prolonged operating time (OR time >200 minutes), prophylactic ureteral stents, and NSAID use with AKI. Similar to ASA classification, functional status captures a measure of a patient's overall health and is therefore not a surprising finding. Open surgery was also found to be a risk factor for AKI. Patients undergoing both open and prolonged operations will experience larger insensible water losses when compared to laparoscopic or shorter duration procedures, which may at least partially explain this association.^{20, 21}

The multivariable logistic regression model also identified an association between increased IV fluid administration on POD 1 with postoperative AKI. It is impossible to discern a causal relationship between the increased volume of IV fluid on POD 1 and AKI in this retrospective study. More likely, the association between increasing IV fluid intake and AKI identified in this study reflects a reactive intervention to address the decreasing urine output signifying progression of renal injury rather than a true risk factor for AKI development.

Aggressive fluid resuscitation has nonetheless been the fundamental belief of many surgeons and anesthesiologists. However, emerging data suggest that too much fluid may, in fact, be harmful.^{22, 23} As such, reduction in IV fluids has become one of the fundamental concepts central to ERPs. Goal directed therapy (GDT), with the use of either invasive or non-invasive monitoring, is utilized in our ERP for intraoperative guidance of fluid and vasopressor management. Numerous randomized controlled trials have investigated renal outcomes following isolated GDT—outside of its use in enhanced recovery—with mixed results. Some studies have found a decrease in rates of postoperative AKI with the use of GDT, while others have found no superior renal outcomes with GDT as compared to standard

clinical care. Notably, there are no studies that indicate GDT leads to worse renal outcomes, which is also supported by the current analysis.^{24, 25}

Despite the existing evidence supporting the use of ERPs, there is a paucity of research on their potential effect on the development of AKI. In the United States, ERPs were first implemented in the colorectal surgery population and have gained in popularity after demonstrating improvements in clinical outcomes including substantial reductions in overall complications, length of stay, and healthcare expenditures.^{8, 26, 27} Guiding principles of enhanced recovery call for a reduction in administered volumes of IV fluid and the use of NSAIDs to spare opioid medications to expedite return of bowel function. As both of these individual components can lead to AKI via decreased renal perfusion, it is logical for there to be concern for increased rates of postoperative AKI with their use in ERPs.^{28, 29} Despite these concerns, this study would suggest that the implementation of a highly standardized colorectal ERP does not have a significant impact on AKI.

This study is the largest to date to evaluate the effect of enhanced recovery implementation on the development of AKI. Additionally, the definition of AKI utilized in this study is more restrictive than the NSQIP definition, enabling the identification of additional true AKI cases and making it more likely to detect an association between AKI and the protocol, if one existed.³⁰

Despite these strengths, there are several notable limitations to this study. AKI development commonly occurs secondary to other severe postoperative complications, such as sepsis from anastomotic leak, bleeding, or cardiac events. Because the implementation of the colorectal ERP also resulted in a significant decrease in the overall complication rate, it is possible that this diluted out any negative effect of the protocol on the overall rate of AKI.⁸ In order to further investigate the relationship between the development of complications and AKI, the diagnosis of AKI was removed from the definition of complication(s) and presented in Table 2. There was a complication rate of 30% in those without AKI versus 39% in those with AKI ($p=0.04$). A separate multivariable regression was performed replacing the ERP with overall complications to assess the possible relationship of complications (excluding AKI) and AKI. Complications were not significantly associated with AKI [OR 0.90 (0.54–1.49); $p=0.69$]. Additionally, AKI has been associated with many other factors including hyperglycemia, hypoalbuminemia, and hyperuricemia, which could not all be taken into account in the current study.³¹

The before-and-after study design predisposes toward the introduction of selection bias, though this is somewhat mitigated by the inclusion of potential confounders in the multivariable logistic regression model. In addition, all patients are put on the ERP despite medical comorbidities or extent of surgical procedure, further limiting the possibility for selection bias. Though the necessary sample size was exceeded to achieve statistical power of 0.80, the possibility of a type II error cannot be excluded to identify a smaller than expected effect on the development of AKI.

These results suggest that a well-organized and institutionally supported ERP can be implemented safely without an increase in AKI. This is, however, a single institution study.

As ERPs vary widely between institutions, caution must be taken in generalizing these results to other protocols. As such, further studies are warranted to validate our results.

Conclusion

This study identified similar rates of AKI before and after implementation of a highly standardized ERP in patients undergoing colorectal surgery. However, independent predictors of AKI were identified and could be utilized to alter the protocol in high-risk patients, including those with poor functional status, hypertension, or undergoing complex and prolonged open cases, particularly in the presence of a ureteral stent. Potential ERP modifications include avoidance of NSAIDs in all high-risk patients and implementation of renal protective strategies such as vigilant avoidance of hypotension in patients with a history of hypertension. Future prospective study is needed to determine if protocol modifications will further decrease rates of AKI in this patient population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding for this study was provided by National Institutes of Health surgical oncology grant T32 CA163177.

References

1. O'Connor ME, Kirwan CJ, Pearse RM, Prowle JR. Incidence and associations of acute kidney injury after major abdominal surgery. *Intensive Care Med.* 2016; 42:521–530. [PubMed: 26602784]
2. Romagnoli S, Zagli G, Tuccinardi G, et al. Postoperative acute kidney injury in high-risk patients undergoing major abdominal surgery. *J Crit Care.* 2016; 35:120–125. [PubMed: 27481746]
3. Rewa O, Bagshaw SM. Acute kidney injury-epidemiology, outcomes and economics. *Nat Rev Nephrol.* 2014; 10:193–207. [PubMed: 24445744]
4. O'Connor ME, Hewson RW, Kirwan CJ, Ackland GL, Pearse RM, Prowle JR. Acute kidney injury and mortality 1 year after major non-cardiac surgery. *Br J Surg.* 2017; 104:868–876. [PubMed: 28218392]
5. Abelha FJ, Botelho M, Fernandes V, Barros H. Determinants of postoperative acute kidney injury. *Crit Care.* 2009; 13:R79. [PubMed: 19463152]
6. Greco M, Capretti G, Beretta L, Gemma M, Pecorelli N, Braga M. Enhanced recovery program in colorectal surgery: a meta-analysis of randomized controlled trials. *World J Surg.* 2014; 38:1531–1541. [PubMed: 24368573]
7. Group EC. ERAS Compliance Group. The impact of enhanced recovery protocol compliance on elective colorectal cancer resection: results from an international registry. *Ann Surg.* 2015; 261:1153–1159. [PubMed: 25671587]
8. Thiele RH, Rea KM, Turrentine FE, et al. Standardization of care: impact of an enhanced recovery protocol on length of stay, complications, and direct costs after colorectal surgery. *J Am Coll Surg.* 2015; 220:430–443. [PubMed: 25797725]
9. Zhuang CL, Ye XZ, Zhang XD, Chen BC, Yu Z. Enhanced recovery after surgery programs versus traditional care for colorectal surgery: a meta-analysis of randomized controlled trials. *Dis Colon Rectum.* 2013; 56:667–678. [PubMed: 23575408]
10. Thiele RH, Raghunathan K, Brudney CS, et al. Perioperative Quality Initiative (POQI) I Workgroup. American Society for Enhanced Recovery (ASER) and Perioperative Quality Initiative

(POQI) joint consensus statement on perioperative fluid management within an enhanced recovery pathway for colorectal surgery. *Perioper Med (Lond)*. 2016; 5:24. [PubMed: 27660701]

11. Holubar SD, Hedrick T, Gupta R, et al. Perioperative Quality Initiative (POQI) I Workgroup. American Society for Enhanced Recovery (ASER) and Perioperative Quality Initiative (POQI) joint consensus statement on prevention of postoperative infection within an enhanced recovery pathway for elective colorectal surgery. *Perioper Med (Lond)*. 2017; 6:4. [PubMed: 28270910]
12. McEvoy MD, Scott MJ, Gordon DB, et al. Perioperative Quality Initiative (POQI) I Workgroup. American Society for Enhanced Recovery (ASER) and Perioperative Quality Initiative (POQI) joint consensus statement on optimal analgesia within an enhanced recovery pathway for colorectal surgery: part 1-from the preoperative period to PACU. *Perioper Med (Lond)*. 2017; 6:8. [PubMed: 28413629]
13. Scott MJ, McEvoy MD, Gordon DB, et al. Perioperative Quality Initiative ((POQI) I Workgroup. American Society for Enhanced Recovery (ASER) and Perioperative Quality Initiative (POQI) Joint Consensus Statement on Optimal Analgesia within an Enhanced Recovery Pathway for Colorectal Surgery: Part 2-From PACU to the Transition Home. *Perioper Med (Lond)*. 2017; 6:7. [PubMed: 28413628]
14. Section 2: Definition AKI. *Kidney Int Suppl*. 2011; 2:19–36. 2012.
15. Levey AS, Coresh J, Balk E, et al. National Kidney Foundation. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Ann Intern Med*. 2003; 139:137–147. [PubMed: 12859163]
16. Meersch M, Schmidt C, Zarbock A. Perioperative Acute kidney injury: an under-recognized problem. *Anesth Analg*. 2017; 125:1223–1232. [PubMed: 28787339]
17. Luo X, Jiang L, Du B, Wen Y, Wang M, Xi X. Beijing Acute Kidney Injury Trial (BAKIT) workgroup. A comparison of different diagnostic criteria of acute kidney injury in critically ill patients. *Crit Care*. 2014; 18:R144. [PubMed: 25005361]
18. Rodrigues FB, Bruetto RG, Torres US, Otaviano AP, Zanetta DM, Burdmann EA. Incidence and mortality of acute kidney injury after myocardial infarction: a comparison between KDIGO and RIFLE criteria. *PLoS One*. 2013; 8:e69998. [PubMed: 23894572]
19. Long TE, Helgason D, Helgadóttir S, et al. Acute Kidney Injury After Abdominal Surgery: Incidence, Risk Factors, and Outcome. *Anesth Analg*. 2016; 122:1912–1920. [PubMed: 27195635]
20. Lamke LO, Nilsson GE, Reithner HL. Water loss by evaporation from the abdominal cavity during surgery. *Acta Chir Scand*. 1977; 143:279–284. [PubMed: 596094]
21. Biegner AR, Anderson D, Olson RL, Vacchiano CA. Quantification of insensible water loss associated with insufflation of nonhumidified CO₂ in patients undergoing laparoscopic surgery. *J Laparoendosc. Adv Surg Tech A*. 1999; 9:325–329.
22. Brandstrup B, Tønnesen H, Beier-Holgersen R, et al. Danish Study Group on Perioperative Fluid Therapy. Effects of intravenous fluid restriction on postoperative complications: comparison of two perioperative fluid regimens: a randomized assessor-blinded multicenter trial. *Ann Surg*. 2003; 238:641–648. [PubMed: 14578723]
23. Thacker JK, Mountford WK, Ernst FR, Krukas MR, Mythen MM. Perioperative fluid utilization variability and association with outcomes: considerations for enhanced recovery efforts in sample US surgical populations. *Ann Surg*. 2016; 263:502–510. [PubMed: 26565138]
24. Prowle JR, Chua HR, Bagshaw SM, Bellomo R. Clinical review: volume of fluid resuscitation and the incidence of acute kidney injury - a systematic review. *Crit Care*. 2012; 16:230. [PubMed: 22866958]
25. Schmid S, Kapfer B, Heim M, et al. Algorithm-guided goal-directed haemodynamic therapy does not improve renal function after major abdominal surgery compared to good standard clinical care: a prospective randomised trial. *Crit Care*. 2016; 20:50. [PubMed: 26951105]
26. Miller TE, Thacker JK, White WD, et al. Enhanced Recovery Study Group. Reduced length of hospital stay in colorectal surgery after implementation of an enhanced recovery protocol. *Anesth Analg*. 2014; 118:1052–1061. [PubMed: 24781574]

27. Zhao JH, Sun JX, Gao P, et al. Fast-track surgery versus traditional perioperative care in laparoscopic colorectal cancer surgery: a meta-analysis. *BMC Cancer*. 2014; 14:607. [PubMed: 25148902]
28. Ungprasert P, Cheungpasitporn W, Crowson CS, Matteson EL. Individual non-steroidal anti-inflammatory drugs and risk of acute kidney injury: a systematic review and meta-analysis of observational studies. *Eur J Intern Med*. 2015; 26:285–291. [PubMed: 25862494]
29. Sarabu N, Rahman M. Nephrology update: acute kidney injury. *FP Essent*. 2016; 444:11–17. [PubMed: 27163760]
30. Bihorac A, Brennan M, Ozrazgat-Baslanti T, et al. National Surgical Quality Improvement Program underestimates the risk associated with mild and moderate postoperative acute kidney injury. *Crit Care Med*. 2013; 41:2570–2583. [PubMed: 23928835]
31. Nie S, Tang L, Zhang W, Feng Z, Chen X. Are there modifiable risk factors to improve AKI? *BioMed Res Int*. 2017; 2017:5605634. [PubMed: 28744467]

Figure 1.

Bar graph of change in creatinine between preoperative and maximum postoperative values for individual patients before (dark gray bars) and after (light gray bars) implementation of colorectal enhanced recovery protocol. Values >3 are grouped together as final measurement. Plot demonstrates no trend toward higher change in creatinine between the 2 groups.

Table 1

Patient Demographics, Procedure Characteristics, and Outcomes Before and After Implementation of an Enhanced Recovery Protocol

<i>Patient Factors</i>	Pre-Enhanced Recovery N = 461	Enhanced Recovery N = 439	p-value
Male	216	192	43.74% 0.35
Age (years)	57.26	+/- 15.74 58.17	+/- 16.09 0.39
Race			0.73
White	396	85.90% 381	86.79%
Asian	2	0.43% 2	0.46%
Black	57	12.36% 47	10.71%
Unknown	6	1.30% 9	2.05%
Hispanic	7	1.52% 6	1.37% 0.85
BMI (kg/m ²)	27.99	+/- 7.10 28.21	+/- 6.93 0.64
Current smoker	77	16.70% 89	20.27% 0.17
COPD	20	4.34% 29	6.61% 0.13
Diabetes	67	14.53% 59	13.44% 0.64
Hypertension	209	45.34% 182	41.46% 0.24
Preoperative creatinine	0.88	+/- 0.30 0.86	+/- 0.26 0.25
Renal insufficiency	62	13.45% 42	9.57% 0.07
Functional status			0.13
Independent	436	94.58% 427	97.27%
Partially dependent	21	4.56% 10	2.28%
Totally dependent	4	0.87% 2	0.46%
ASA classification			0.38

	Pre-Enhanced Recovery N = 461	Enhanced Recovery N = 439	p-value
ASA 1	2	2	0.46%
ASA 2	198	202	46.01%
ASA 3	246	228	51.94%
ASA 4	15	7	1.59%
Procedural Factors			
Surgical indication			0.77
Colonic neoplasia	138	132	22.34%
Rectal/anal neoplasia	103	104	23.69%
IBD	92	85	19.36%
Diverticular disease	56	61	13.90%
Other	72	57	12.98%
Open surgery	128	232	52.85%
Rectal procedure	108	88	20.05%
Ileostomy	136	135	30.75%
Wound class			<0.0001
Clean	3	1	0.23%
Clean/contaminated	364	396	90.21%
Contaminated	61	33	7.52%
Dirty/infected	33	9	2.05%
Ureteral stent	72	57	12.98%
NSAIDs	136	317	72.21%
Intraoperative hypotension	26	69	15.72%
Intraoperative vasopressor	311	340	77.45%
EBL >500 mL	103	49	11.16%

	Pre-Enhanced Recovery N = 461	Enhanced Recovery N = 439	p-value
OR time >200 minutes	200 43.38%	281 64.01%	<0.0001
IVF POD 0 (mL)	4104.39 +/- 2255.67	1840.96 +/- 1327.85	<0.0001
IVF POD 1 (mL)	3623.66 +/- 1338.29	2312.30 +/- 2111.02	<0.0001
UOP POD 0 (mL)	1019.20 +/- 729.80	592.07 +/- 502.61	<0.0001
UOP POD 1 (mL)	1846.78 +/- 1168.31	1937.30 +/- 1305.43	0.27
Outcomes			
Complication(s)*	183 39.70%	126 28.70%	0.001
Acute kidney injury	55 11.93%	59 13.44%	0.50
Highest creatinine	1.07 +/- 0.77	1.07 +/- 0.68	0.98
Postoperative hemodialysis	3 0.65%	2 0.46%	0.69
Length of stay (days)	8.47 +/- 7.63	6.59 +/- 7.75	<0.0001
30-day readmissions	88 19.10%	60 13.67%	0.03
Mortality	3 0.65%	4 0.91%	0.66

Categorical variables listed as N (%) and continuous variables listed as mean (standard deviation).

* Acute kidney injury is included in complication(s).

BMI=Body mass index; COPD=Chronic obstructive pulmonary disease; ASA Classification=American Society of Anesthesiologists Physical Status classification; NSAIDs=Nonsteroidal anti-inflammatory drugs; EBL=Estimated blood loss; OR=Operating room; IVF=Intravenous fluid; POD=Postoperative day; UOP=Urine output

Table 2
Patient Demographics and Procedure Characteristics in Patients with and without Acute Kidney Injury

<i>Patient Factors</i>	No AKI N = 786	AKI N = 114	p-value
Male	348	60	52.63% 0.09
Age (years)	57.02	62.46	+/- 13.74 0.001
Race			0.71
White	680	97	85.09%
Asian	4	0	0.00%
Black	90	14	12.28%
Unknown	12	3	2.63%
Hispanic	11	2	1.75% 0.77
BMI (kg/m ²)	27.84	29.88	+/- 8.24 0.004
Current smoker	138	28	24.56% 0.07
COPD	38	11	9.65% 0.03
Diabetes	108	18	15.79% 0.56
Hypertension	319	72	63.16% <0.0001
Preoperative creatinine	0.87	0.89	+/- 0.33 0.45
Renal insufficiency	88	16	14.04% 0.38
Functional status			0.002
Independent	760	103	90.35%
Partially dependent	23	8	7.02%
Totally dependent	3	3	2.63%
ASA classification			<0.0001

	No AKI N = 786	AKI N = 114	p-value
ASA 1	4	0	0.00%
ASA 2	365	35	30.70%
ASA 3	404	70	61.40%
ASA 4	13	9	7.89%
Procedural Factors			
Surgical indication			0.0003
Colonic neoplasia	246	24	21.05%
Rectal/anal neoplasia	174	33	28.95%
IBD	166	11	9.65%
Diverticular disease	93	24	21.05%
Other	107	22	19.30%
Open surgery	343	17	14.91%
Rectal procedure	169	27	23.68%
Ileostomy	225	46	40.35%
Wound class			0.001
Clean	4	0	0.00%
Clean/contaminated	677	83	72.81%
Contaminated	74	20	17.54%
Dirty/infected	31	11	9.65%
Ureteral stent	89	40	35.09%
Enhanced recovery protocol	380	59	51.75%
NSAID	388	65	57.02%
Intraoperative hypotension	79	16	14.04%
Intraoperative vasopressor	555	96	84.21%
EBL >500 mL	113	39	34.21%

	No AKI N = 786	AKI N = 114	p-value
OR time >200 minutes	397	84	73.68% <0.0001
IVF POD 0 (mL)	2896.62	3732.60	+/- 3048.74 <0.0001
IVF POD 1 (mL)	2837.46	3994.45	+/- 2682.83 <0.0001
UOP POD 0 (mL)	834.82	765.25	+/- 627.93 0.38
UOP POD 1 (mL)	1971.90	1534.88	+/- 1313.62 0.002
Outcomes			
Highest creatinine	0.92	2.13	+/- 1.47 <0.0001
Surgical site infection	89	26	22.81% 0.0006
Complication(s)*	235	45	39.47% 0.04
Length of stay (days)	6.79	12.78	+/- 10.68 <0.0001
30-day readmissions	118	30	26.32% 0.002
Mortality	1	6	5.26% <0.0001

Categorical variables listed as N (%) and continuous variables listed as mean (standard deviation).

* Complication(s) does not include acute kidney injury.

BMI=Body mass index; COPD=Chronic obstructive pulmonary disease; ASA Classification=American Society of Anesthesiologists Physical Status classification; NSAIDs=Nonsteroidal anti-inflammatory drugs; EBL=Estimated blood loss; OR=Operating room; IVF=Intravenous fluid; POD=Postoperative day; UOP=Urine output

Table 3

Multivariable Logistic Regression Results and Predictors of Acute Kidney Injury Following Colorectal Surgery

	Odds Ratio (95% CI)	p-value
<i>Patient Factors</i>		
Male	1.49 (0.92 – 2.40)	0.10
Age	1.20 (0.97 – 1.47)	0.09
Race (ref = White)		0.56
Asian	<0.01 (<0.01 – >99.99)	
Black	1.60 (0.78 – 3.28)	
Unknown	1.79 (0.38 – 8.53)	
BMI (kg/m ²)	1.01 (0.98 – 1.04)	0.60
Diabetes	0.77 (0.39 – 1.54)	0.47
Hypertension	2.53 (1.46 – 4.39)	0.001
Renal insufficiency	0.78 (0.38 – 1.63)	0.51
Functional status (ref = Independent)		0.02
Partially dependent	1.10 (0.38 – 3.14)	
Totally dependent	14.08 (2.11 – 93.91)	
ASA classification (ref = ASA 2)		0.12
ASA 1	<0.01 (<0.01 – >99.99)	
ASA 3	0.98 (0.58 – 1.64)	
ASA 4	4.03 (1.18 – 13.75)	
<i>Procedural Factors</i>		
Diverticular disease	1.32 (0.66 – 2.66)	0.43
Open surgery	3.15 (1.61 – 6.16)	0.0008
Ileostomy	1.36 (0.80 – 2.32)	0.26
Wound class (ref = Clean/contaminated)		0.51
Clean	<0.01 (<0.01 – >99.99)	
Contaminated	1.64 (0.85 – 3.15)	
Dirty/infected	1.38 (0.51 – 3.70)	
Procedure type (ref = Partial colectomy)		0.40
Total colectomy	2.16 (0.65 – 7.13)	
Proctocolectomy	0.50 (0.10 – 2.54)	
Rectal	1.19 (0.62 – 2.28)	

	Odds Ratio (95% CI)	p-value
Ureteral stent	1.89 (1.04 – 3.42)	0.04
Enhanced recovery protocol	1.82 (0.92 – 3.58)	0.09
NSAIDs	1.90 (1.09 – 3.31)	0.02
Intraoperative hypotension	1.96 (0.96 – 4.00)	0.07
Intraoperative vasopressor	1.00 (0.53 – 1.89)	1.00
EBL >500 mL	1.16 (0.64 – 2.10)	0.62
OR time >200 minutes	1.97 (1.08 – 3.60)	0.03
IVF POD 0 (mL)	1.06 (0.94 – 1.20)	0.32
IVF POD 1 (mL)	1.36 (1.13 – 1.62)	0.0009
UOP POD 0 (mL)	0.94 (0.64 – 1.39)	0.75
UOP POD 1 (mL)	0.81 (0.64 – 1.02)	0.08

C-statistic = 0.84

BMI=Body mass index; ASA Classification=American Society of Anesthesiologists Physical Status classification; NSAIDs=Nonsteroidal anti-inflammatory drugs; EBL=Estimated blood loss; OR=Operating room; IVF=Intravenous fluid; POD=Postoperative day; UOP=Urine output

Table 4

Supplemental Multivariable Logistic Regression Results and Predictors of Acute Kidney Injury Following Colorectal Surgery

	Odds Ratio (95% CI)	p-value
<i>Patient Factors</i>		
Male	1.51 (0.94 – 2.43)	0.09
Age (years)	1.21 (0.98 – 1.49)	0.08
Race (ref = White)		0.54
Asian	<0.01 (<0.01 – >99.99)	
Black	1.60 (0.78 – 3.30)	
Unknown	1.87 (0.39 – 8.94)	
BMI (kg/m ²)	1.01 (0.98 – 1.05)	0.51
Diabetes	0.78 (0.40 – 1.57)	0.50
Hypertension	2.47 (1.42 – 4.27)	0.001
Renal insufficiency	0.77 (0.37 – 1.61)	0.49
Functional status (ref = Independent)		0.03
Partially dependent	1.10 (0.38 – 3.14)	
Totally dependent	12.98 (1.98 – 85.19)	
ASA classification (ref = ASA 2)		0.10
ASA 1	<0.01 (<0.01 – >99.99)	
ASA 3	0.99 (0.59 – 1.67)	
ASA 4	4.25 (1.26 – 14.26)	
<i>Procedural Factors</i>		
Diverticular disease	1.29 (0.64 – 2.58)	0.48
Open surgery	2.99 (1.54 – 5.81)	0.001
Ileostomy	1.39 (0.82 – 2.37)	0.22
Wound class (ref = Clean/contaminated)		0.56
Clean	<0.01 (<0.01 – >99.99)	
Contaminated	1.60 (0.84 – 3.07)	
Dirty/infected	1.28 (0.48 – 3.39)	
Procedure type (ref = Partial colectomy)		0.39
Total colectomy	2.15 (0.66 – 6.95)	
Proctocolectomy	0.48 (0.10 – 2.46)	
Rectal	1.14 (0.59 – 2.19)	

	Odds Ratio (95% CI)	p-value
Ureteral stent	1.91 (1.05 – 3.45)	0.03
Complication(s)	0.90 (0.54 – 1.49)	0.69
NSAIDs	2.30 (1.38 – 3.83)	0.002
Intraoperative hypotension	2.18 (1.07 – 4.41)	0.03
Intraoperative vasopressor	1.12 (0.60 – 2.09)	0.71
EBL >500 mL	1.18 (0.65 – 2.13)	0.59
OR time >200 minutes	2.20 (1.22 – 3.98)	0.009
IVF POD 0 (mL)	1.03 (0.92 – 1.15)	0.59
IVF POD 1 (mL)	1.30 (1.10 – 1.54)	0.002
UOP POD 0 (mL)	0.88 (0.60 – 1.29)	0.51
UOP POD 1 (mL)	0.82 (0.64 – 1.03)	0.09

C-statistic = 0.84

* Complication(s) does not include acute kidney injury.

BMI=Body mass index; ASA Classification=American Society of Anesthesiologists Physical Status classification; NSAIDs=Nonsteroidal anti-inflammatory drugs; EBL=Estimated blood loss; OR=Operating room; IVF=Intravenous fluid; POD=Postoperative day; UOP=Urine output