Enhanced recovery after urologic surgery: A VA Experience.

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Abstract

Background: Enhanced recovery after surgery (ERAS) protocols have become standard of care in perioperative management.

Methods: We retrospectively analyzed consecutive patients at our VA institution undergoing urologic surgery, namely nephrectomy and prostatectomy, with ERAS management over a six-month timeframe.

Findings: 62 patients underwent prostate (n=32) or kidney surgery (n=30) at our institution between September 2017 and February 2018. Median ERAS length of hospital stay for the prostatectomy group was 1.5 days and 3 days for the nephrectomy group (p=0.001). Intraoperatively, there was a trend towards increased median fluid administration for the ERAS nephrectomy group compared to the ERAS prostatectomy group (2275 vs 1990.5 ml; p=0.05), without a significant increase in estimated blood loss or total operative time. Patients in the ERAS prostate surgery group were out of bed one day sooner compared to patients in the ERAS kidney surgery group (median post op day 1 vs. median post op day 2, p=0.02). Minor complications were similar for both groups (36.7% for the ERAS nephrectomy group compared to 21.9% for the ERAS prostatectomy group; p=0.26), however there was a significant difference in major complications (26.7% for the ERAS nephrectomy group compared to 3.1% for the prostatectomy group; p=0.01). 30- and 90-day readmission rates were similar between the ERAS nephrectomy and ERAS prostatectomy groups (10% vs. 6.3%; p=0.67; and 6.7% vs. 0%; p=0.23). American Society of Anesthesia physical status classification (ASA) score was similar (median ASA 3 vs. 3; p=0.05) for both groups.

Conclusions: Despite ERAS based perioperative management for urologic procedures, there are significant differences in outcomes in this observational comparative study, possibly related to patient and or surgical factors.

Keywords: Nephrectomy, Prostatectomy, Perioperative care, Treatment outcome.

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Introduction

Due to rising health expenditures and transition to value based care, there has been an ongoing emphasis for finding new healthcare delivery paradigms to improve quality and safety while at the same time decreasing short-and long-term in-hospital costs [1,2]. Originally introduced in colon and rectal surgery after level 1 evidence from clinical trials, enhanced recovery after surgery (ERAS) protocols decrease gastrointestinal morbidity and the physiological stress response, along with decreasing hospital length of stay; resulting in cost savings and faster recovery [3-9]. ERAS protocols are intended to expand surgical care beyond the procedure itself, consisting of 24 components which have become standard of care within colorectal surgery which have replaced older practices such as mechanical bowel prep and NPO until first bowel movement [1,3,5,10].

In addition, use of traditional procedures such nasogastric tubes have also not been shown to prevent post-operative ileus to the degree of other alternatives such as maximizing non-narcotic analgesics [1,10]. After the introduction of ERAS in the 1990s, average length of stay for some colonic procedures decreased from 6 to 2 days along with a 50% reduction in complications [6,11]. Despite expanding since initial recommendations from the ERAS study group in 2001, identification of patient barriers, improving provider adherence, and standardization of pathways remain challenging for wider ERAS adoption by other surgical disciplines [1,6]. Significant variability in outcomes also remain for a variety of increasingly complex procedures standardized ERAS protocols may have a positive impact on patient counseling and education to decrease anxiety, speed recovery and improve wound healing after abdominal surgery [1-7]. Additional preoperative optimization measures which have shown benefit include smoking cessation several weeks prior to surgery as well as nutritional assessment [7-10].

Among high risk urologic surgery, complications of all types associated with radical cystectomy, lymph node dissection and urinary diversion or bladder reconstruction for the treatment of advanced bladder cancer (non-muscle invasive cT2) are reported to be greater than 50% with an associated mean length of stay of 10.5 days, compared to less than 2 days for robot-assisted laparoscopic radical prostatectomy [1,3-4,7-9,11]. More recent implementation of feasible ERAS based protocols for radical cystectomy have resulted in a decreased length of stay and cost reduction (up to $4488) per procedure with no additional complications or increased readmissions (approximately 30% at 90-days), as well as improved quality of life and return of bowel function [2-5,12-16] Expansion of ERAS management for radical prostatectomy has also been reported to decrease length of stay, blood loss, hospital cost, and improve return of bowel function for robot-assisted procedures [1]. Adoption of at least seven ERAS components has been found in meta-analysis to achieve consistent results [6].

Early resumption of enteral feeding, avoidance of nasogastric tubes and bowel preparation, along with ambulation, oral administration of a peripherally acting μ-opioid receptor antagonist (alvimopan), targeted intraoperative fluid balance, thermoregulation, and multimodal analgesia are common ERAS components with a high level evidence for promoting bowel motility, reducing postoperative nausea, and decreasing surgical stress response along with narcotic requirements [4-5,8-11,17]. Coordinated multidisciplinary preoperative education, nutritional assessment, optimization of comorbidities, promotion of carbohydrate loading, chewing gum, and intraoperative and postoperative deep vein thrombosis and surgical site infection prophylaxis are also beneficial aspects of ERAS, especially in older patients with more comorbidities who are predisposed to have longer lengths of hospital stay [1,4,6]. ERAS management is also associated with lower patient reported pain scores after urological surgery as well as improved quality of life and patient satisfaction [1,5].

Methods

Institutional review board approval was granted for a retrospective chart review of consecutive patients between September 2017 and February 2018 diagnosed with either a benign or malignant, renal or prostate mass requiring nephrectomy or prostatectomy. In the ERAS nephrectomy cohort, 43.3% were performed open, 43.3% performed with robotic-assistance, and 13.4% performed laparoscopic. In the ERAS prostatectomy cohort, 18.8% were performed open and 81.2% were done with a minimally invasive robotic approach.

All patients met with and were provided perioperative education and instructions by both anesthesia and urology providers prior to surgery. Optimization of chronic medical conditions such as anemia, hypertension, and diabetes were coordinated through a specialized preadmission clinic. Patients were continued on a regular diet until eight hours prior to surgery and allowed clear liquids, including carbohydrate-rich beverages if they were not diabetic up to two hours before surgery. No preoperative routine bowel prep was administered. Opioid sparing multimodal analgesia was utilized including scheduled IV acetaminophen, optional PO gabapentin and lyrica, IV ketorolac, intraoperative IV lidocaine infusion, and selected regional anesthesia with thoracic epidural analgesia (TEA) using local anesthetic only (0.2% ropivacaine) or transversus abdominis plane (TAP) blocks with infiltration of liposomal bupivacaine for most open procedures unless otherwise contraindicated.

Standardized IV antibiotics were given within one hour prior to skin incision and continued twenty-four hours post operatively. Intraoperatively, goal-directed fluid management was targeted to maintain euvolemia and restricted to replace surgical losses either with Lactated Ringers, Normal Saline, and or albumin. Vasopressors were used judiciously for the treatment of hypotension. Intraoperative normothermia was maintained with use of forced-air warming blankets. Nasogastric tubes were not routinely placed, and drains were minimized to the extent possible. Preemptive prophylaxis for nausea was administered in the presence of multiple factors. Multimodal analgesia was continued post-operatively. Diet was advanced to clear liquids starting post OP day 1 and advanced as tolerated to a regular diet starting post OP day 2. Additional multimodal agents were available for use post OP, including PO ultram, with opioids generally limited for breakthrough pain not otherwise controlled. Ambulation was encouraged starting post OP day 1. Discharge to home criteria included satisfactory pain control, adequate ambulation assessed by physical therapy on a case by case basis, tolerance of prescribed diet, and return of bowel function as demonstrated with flatus and or bowel movement.

Historical data was collected for both cohorts using retrospective chart review by trained abstractors on patient demographics and characteristics, disease pathology, perioperative hospital course, and associated complications and readmission rates between 30 to 90 days following hospital discharge. The ERAS nephrectomy cohort was compared to the ERAS prostatectomy cohort using SPSS 25 (IBM Corp, Armonk, NY, USA). Wilcoxon-Rank Sum Test was used to compare continuous variables and Pearson chi-squared (χ^2) or Fisher's exact tests were used to compare categorical variables with two-sided $P<0.05$ marking significance. Continuous variables are summarized with median values and interquartile ranges. Normally distributed variables are reported with mean and standard errors.

Results

30 consecutive patients at our institution underwent nephrectomy with ERAS based management between September 2017 and February 2018, meeting all criteria for inclusion in the ERAS nephrectomy historical cohort. Thirty-two consecutive patients at our institution also underwent prostatectomy with ERAS based management between September 2017 and February 2018 meeting all acceptable criteria for inclusion in the ERAS prostatectomy historical cohort. There were no differences among both groups with respect to age, gender, or BMI. There was however a significant difference in surgical modality, with greater use of robotic assisted laparoscopic approach for prostate surgery compared to kidney surgery (81.2% vs 13.4%; $P<0.001$) and greater use of laparoscopic only approach for kidney surgery compared to prostate surgery (43.3% vs

0%; $P<0.001$). Patients undergoing ERAS nephrectomy had a similar median American Society of Anesthesia physical status classification (ASA) score (3 vs 3; $p=0.05$). The median estimated blood loss was comparable between the nephrectomy and prostatectomy groups (135 vs 50 cc; $p=0.39$). Patients that underwent nephrectomy had a trend towards increased amount of fluid administration in comparison to patients that underwent prostatectomy (median 2275.0 vs 1990.5 cc; $p=0.05$). Total time of surgery from incision to closure was not significantly different between the two groups (median 147.5 vs 201.0 minutes; $p=0.10$) (Table 1).

Median length of hospital stays (LOS) was 3 (range 1-10) days in the ERAS nephrectomy group compared to 1.5 (range 1-6) days in the ERAS prostatectomy group ($P<0.001$). Apart from the rate of minor complications which was comparable in both groups (36.7% vs. 21.9%; $p=0.26$), there were a greater number of major complications in the kidney surgery group compared to the prostate surgery group (26.7% vs. 3.1%; $p=0.01$). In sub-analysis, among the most frequent minor complications in the ERAS nephrectomy group were blood transfusion (20%), followed by anastomotic urine leak (5%) or acute kidney injury (5%), and fever (1.15%), or ileus (1.15%). Among the most frequent major complications in the ERAS nephrectomy group were failure to thrive (2%), dehydration

***Table 1**. ERAS nephrectomy and ERAS prostatectomy patient characteristics.*

Variables	Nephrectomy	Prostatectomy	*P*-Value
Number of patients	n=30	n=32	--
Median Age (IQR)	67.0 (9.3)	63.5 (9.8)	0.06
Gender			
Male %	28 (93)	32 (100)	0.22
Female %	2 (7)	0 (0)	--
Median BMI (kg/m2) (IQR)	30.0 (9.1)	30.1 (5)	0.78
Median ASA (IQR)	3 (3-3)	3 (3-3)	0.05
Diagnosis (%)			
Renal Cell Carcinoma	22 (73.3)	--	--
Urothelial Carcinoma	3 (10)	--	--
Undifferentiated Carcinoma	1 (3.3)	--	--
Cyst Simple	1 (3.3)	--	--
Lipoma	1 (3.3)	--	--
Liposarcoma	1 (3.3)	--	--
Pseudotumor	1 (3.3)	--	--
Adenocarcinoma	--	28 (87.5)	--
BPH	--	4 (12.5)	--
Median Surgical Time (min) (IQR)	147.5 (125)	201 (84)	0.1
Approach %			
Open	13 (43.3)	6 (18.8)	0.05
Simple	--	3 (9.4)	
Radical with Ureterectomy	1 (3.1)	--	--
Cytoreductive	1 (3.1)	--	--
Partial	5 (15.6)	--	--
Radical	4 (12.5)	--	--
Radical w/ IVC Thrombectomy	1 (3.1)	3 (9.4)	--
Radical w/ Pancreatectomy	1 (3.1)	--	--
Laparoscopic	4 (13.4)	0 (0)	0.11
Radical	3 (9.4)	--	--
Radical w/ Ureterectomy	1 (3.1)	--	--
Robotic	13 (43.3)	26 (81.2)	0.007
Simple	--	1 (3.1)	--
Partial	9 (28.1)	--	--
Radical	3 (9.4)	25 (78.1)	--
Radical w/ Ureterectomy	1 (3.1)	--	--
Median IVF (ml) (IQR)	2275.0 (2753.0)	1990.5 (719.3)	0.05
Median EBL (ml) (IQR)	135 (250)	50 (213.75)	0.39
Median LOS (days) (Range)	3 (1-10)	1.5 (1-6)	0.001
Median Clear Diet (day) (Range)	1 (0-4)	1 (1-1)	0.09
Median Regular Diet (day) (Range)	2 (1-8)	2 (2-3)	0.08
Median Flatus (day) (Range)	2 (1-6)	2 (1-6)	0.59
Median Bowel Movement (day) (Range)	4 (1-10)	3 (2-4)	0.32
Median Out of Bed (day) (Range)	2 (1-7)	1 (1-3)	0.02
Regional Anaesthesia (%)	13 (43.3)	4 (12.5)	0.01
Transversus Abdominis Block	7 (23.3)	4 (12.5)	0.32
Thoracic Epidural	6 (20)	0 (0)	0.01

BMI: Body Mass Index; EBL: Estimated Blood Loss; ERAS: Enhanced Recovery After Surgery; IQR: Interquartile Range; IVF: Intravenous Fluid; LOS: Length of Stay; Min: Minutes

(2%), ileus with placement of nasogastric tube (2%), or Mallory Weiss injury (2%), followed by respiratory distress (1.67%), respiratory failure (1.67%), pulmonary embolism (1.67%), or hospital acquired pneumonia (1.67%). Among additional major complications in the ERAS nephrectomy group were acute kidney injury (3.3%), hemodynamic instability (1.15%), or sepsis (1.15%). In sub-analysis for the ERAS prostatectomy group, the most common minor complication was also blood transfusion (15.6%), followed by fever (3.15%), or clostridium difficile infection (3.15%). Among the most common major complications in the ERAS prostatectomy group were sepsis (1.55%) and pyelonephritis (1.55%). There was no significant difference in complications between the two groups by Clavien Classification (Table 2).

Readmission rates at both thirty– and 90-days were comparable between the ERAS nephrectomy and ERAS prostatectomy surgical groups (10 vs 6.3%; p=0.67, and 6.7 vs 0%; p=0.23). There were no significant differences in return of bowel function as measured by median resumption of clear diet (post op day 1 vs post op day 1, p=0.09), regular diet (post op day 2 vs post op day 2; p=0.08), first flatus (post op day 2 vs post op day 2; p=0.59) and first bowel movement (post op day 4 vs post op day 3; p=0.32) in both groups. Patients were mobilized later in the ERAS nephrectomy group compared to the ERAS prostatectomy group (post op day 2 vs. post op day 1; p=0.02) (Table 2). There were no significant differences in average median post OP day 1-7 visual pain scores (3.0 vs. 3.1; p=0.85) between the ERAS nephrectomy and ERAS prostatectomy groups. (Figure 1).

Discussion

Adoption of evidence-based ERAS protocols across surgical specialties, including urological practice, are associated with improved outcomes [3]. At our institution, ERAS based management for 2 different types of routine urologic surgeries showed a significant difference of one and a half days in length of stay (p=0.001). One recent related study of a prospective ERAS cohort using historical non-ERAS controls showed a median length of stay of 5 days for patients after radical cystectomy (with ERAS), which is 2-3.5 days more than we found for ERAS nephrectomy and prostatectomy patients at our VA institution [3]. We found no difference between nephrectomy and prostatectomy with ERAS in return of bowel function, with resumption of a clear liquid diet on median post day 1 and a regular diet on median post op day 2, postoperative flatus on post op day 2, and first bowel movement between post op day 3 and 4. One recent retrospective analysis of robot-assisted laparoscopic radical prostatectomy found a significant decrease in time to first defecation in patients managed with ERAS compared to a conventional non-ERAS group [18].

Our overall ERAS management includes no routine placement of NG tube, use of more liberal NPO guidelines, no bowel prep, early resumption of diet, opioid minimization along with use of regional anesthesia, and early post OP mobilization to reduce gastrointestinal complications, as well as meet discharge criteria and reduce hospitalization cost. Similar to other multimodal regimens, we employ epidural analgesia and peripheral nerve blocks by a dedicated pain service, recommend IV or PO acetaminophen, gabapentin, ketorolac, lyrica and ultram, antiemetics, ketamine and lidocaine to improve pain control, decrease opioid requirements, and reduce postoperative ileus. In both colorectal meta-analysis and urology prospective and retrospective cohorts, ERAS implementation resulted in an approximate cost savings of $2000-4500 per patient [3,10].

ERAS management is not associated with increased 30- and 90- day readmission or complication rates [3]. At our institution there were no differences observed in readmission rates among nephrectomy and prostate surgery. In a related urologic cohort study of 56 patients that underwent radical cystectomy, 30- and 90-day readmission rates were found to be 19 and 31% compared to 14.8 and 27.7% for 54 patients that underwent radical cystectomy with and without ERAS [3]. More gradual implementation of ERAS across our institution limited our study to assess the impact of ERAS among different types of surgery, instead of within the same surgery, as provided by a historical pre-ERAS control group, which has been shown already in most studies to result in improved outcomes [3]. No difference

Table 2. *Complications for ERAS nephrectomy and ERAS prostatectomy groups.*

Outcomes	ERAS Nephrectomy	ERAS Prostatectomy	P Value
Minor Complications (%)	36.7	21.9	0.26
Hematologic	20	15.6	0.75
Renal	10	0	0.1
Infectious	3.3	6.3	0.59
Gastrointestinal	3.3	0	0.59
Major Complications (%)	26.7	3.1	0.01
Gastrointestinal	10	0	0.11
Pulmonary	6.7	0	0.23
Renal	3.3	0	0.48
Infectious	3.3	3.1	0.96
Cardiovascular	3.3	0	0.48
Readmission (%)			
30 Day	10	6.3	0.67
90 Day	6.7	0	0.23
Clavien Classification (%)			
I	3.3	3.1	0.27
II	10	18.8	
III	6.7	0	
IV	13.3	3.1	

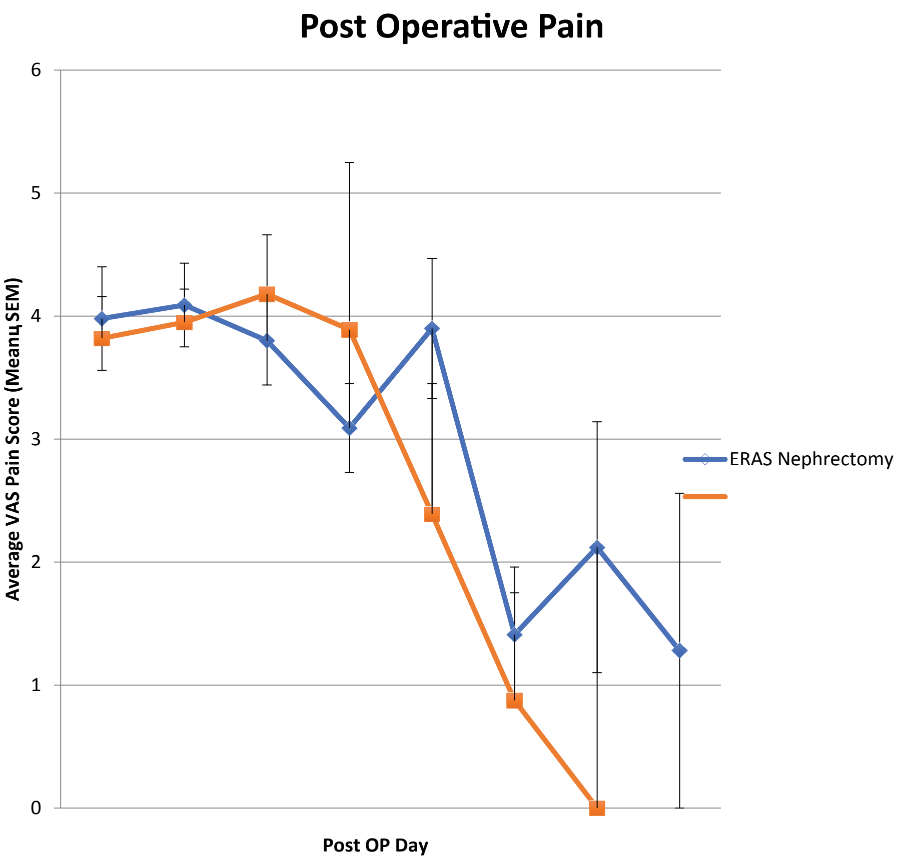

Figure 1. *Average median post OP day 1-7 visual pain scores between the ERAS nephrectomy and ERAS prostatectomy groups.*

was seen in rates of minor complications among patients that underwent nephrectomy compared to prostatectomy in our study, however there were differences in major complications (36.7 vs 21.9%; *p=0*.26 and 26.7 vs 3.1%; *p=0*.01) related possibly to differences in patient and or surgical factors.

In our cohort, there was a trend towards more use of an open surgical approach for nephrectomy compared to prostatectomy (43.3 vs 18.8%; *p=0*.05) and significantly less utilization of a robotic approach (43.3 vs 81.2%; *p=0*.007), comparable to the reported national average as of 2013 [19]. A recent meta-analysis of randomized control and observational studies along with a separate retrospective analysis found a learning curve with decreased minor and major complications, as well as decreased estimated blood loss with less need for transfusion, and decreased length of stay for partial nephrectomy using a robot-assisted approach compared to an open approach; which extended in a separate study to obese patients with BMI greater than 30 kg/m^2 with small renal masses [20-22]. A different retrospective study of 23, 753 patients between 2003 and 2015 found increased operative time which translated to higher mean 3month hospital cost associated with robotic-assisted radical nephrectomy compared to a conventional laparoscopic approach for the treatment of renal masses [19]. Albeit recent, our study is limited to retrospective data on a small cohort.

Conclusion

Urologic ERAS management at RICVAMC is a standardized multidisciplinary team approach to perioperative care for kidney, bladder and prostate procedures. Currently utilized ERAS components are evidence based and have been gradually introduced across the Veterans Health Administration surgical population, as reported in this single institution observational study. Despite adoption of quite specific ERAS care pathways, differences remain in outcomes, possibly related to inherent differences in disease process and or treatment.

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Competing and Conflicting Interests

The author declares that no competing interests exist.

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