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Prospective study of enhanced recovery after surgery protocol in children undergoing reconstructive operations

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Summary

Background
Enhanced recovery after surgery (ERAS) protocol is a set of peri-operative strategies to increase speed of recovery. ERAS is well established in adults but has not been well studied in children.

Objective
The purpose of the current study was to establish the safety and efficacy of an ERAS protocol in pediatric urology patients undergoing reconstructive operations. It was hypothesized that ERAS would reduce length of stay and decrease complications when compared with historical controls.

Study design
Institutional Review Board approval was obtained to prospectively enroll patients aged <18 years if they had undergone urologic reconstruction that included a bowel anastomosis. ERAS included: no bowel preparation, administration of pre-operative oral carbohydrate liquid, avoidance of opioids, regional anesthesia, laparoscopy when feasible, no postoperative nasogastric tube, early feeding, and early removal of intravenous fluids (IVF). Recent (2009—2014) historical controls were propensity matched in a 2:1 ratio on age, sex, ventriculoperitoneal shunt status and whether the patient was undergoing bladder augmentation. Outcomes were protocol adherence, length of stay (LOS), emergency department (ED) visits, re-admission within 30 days, re-operations and adverse events occurring within 90 days of surgery.

Results
A total of 26 historical and 13 ERAS patients were included. Median ages were 10.4 (IQR 8.0—12.4) and 9.9 years (IQR 9.1—11), respectively ($P = 0.94$) (see Summary Table). There were no significant between-group differences in prior abdominal surgery (38% vs 62%), rate of augmentation (88% vs 92%) or primary diagnosis of spina bifida (both 62%). ERAS significantly improved use of pre-operative liquid load ($P < 0.001$), avoidance of opioids ($P = 0.046$), early discontinuation of IVF ($P < 0.001$), and early feeding ($P < 0.001$). Protocol adherence improved from 8/16 (IQR 4—9) historically to 12/16 (IQR 11—12) after implementation of ERAS. LOS decreased from 8 days to 5.7 days ($P = 0.520$). Complications of any grade per patient decreased from 2.1 to 1.3 (OR 0.71, 95% CI 0.51—0.97). There were fewer complications per patient across all grades with ERAS. No differences were seen in emergency department (ED) visits, re-admissions and re-operations.

Discussion
Implementation improved consistency of care delivered. Tenets of ERAS that appeared to drive improvements included maintenance of euvolemia through avoidance of excess fluids, multimodal analgesia, and early feeding.

Conclusion
ERAS decreased length of stay and 90-day complications after pediatric reconstructive surgery without increased re-admissions, re-operations or ED visits. A multicenter study will be required to confirm the potential benefits of adopting ERAS.

Summary Table Pertinent findings regarding matched historical controls and patients who received care under an enhanced recovery after surgery protocol. Significant differences between groups with $P < 0.05$ are shown in bold.

	Matched		*P*-value
	Historical	ERAS	
Total patients	26 patients	13 patients	—
Median age, years (IQR)	10.4 (8.0—12.4)	9.9 (9.1—11.0)	0.940
Patients with spina bifida	16 (62%)	8 (62%)	1.000
Median protocol items per patient (IQR)	8 (4—9)	12 (11—12)	**<0.001**
Median length of stay,# midnights (IQR)	6 (5—7)	5 (3—6)	0.520
Total complications within 90 days	56 (2.1/patient)	17 (1.3/patient)	**0.035**
Re-admissions within 30 days	7 (0.27/patient)	1 (0.08/patient)	0.265
Re-operations within 90 days	8 (0.31/patient)	1 (0.08/patient)	0.235
ED visits within 90 days	17 (0.65/patient)	7 (0.54/patient)	0.570

ERAS, Enhanced recovery after surgery; ED, emergency department.

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Introduction

Fast track surgical principles were first described in the late 1990s by Henrik Kehlet, a Danish adult colorectal surgeon who published on a series of patients in which post-operative stay after open sigmoidectomy was reduced to 48 h versus traditional hospitalizations of 5–19 days [1]. Subsequently, there have been multiple studies examining and refining fast track surgical care, and evidence-based enhanced recovery guidelines have been established by the Enhanced Recovery After Surgery (ERAS) Society for adult colonic, pancreatic, rectal and pelvic surgery, and radical cystectomy patients [2–4].

The goals of ERAS are to maximize pain control, minimize peri-operative metabolic stress, optimize fluid balance, and decrease convalescence times. Although there was initially concern that these interventions might increase complication rates or re-admission to the hospital compared to more conservative/traditional peri-operative protocols, implementation of ERAS protocols in adult surgery patients has consistently demonstrated significant reductions in length of stay. ERAS protocols have also resulted in lower postoperative complication rates without a concomitant increase in hospital re-admissions [5].

Despite the growing evidence of benefits in adult surgical patients, there have been a handful of pediatric surgery reports of successful application of ERAS protocols and none in pediatric urology [6–8]. While these results are promising, the postoperative care of pediatric, adolescent and adult patients undergoing intra-abdominal urologic surgery at many centers often still involves routine use of nasogastric tubes and delay in resumption of enteric nutrition, potentially prolonging postoperative recovery.

The current study aimed to determine the safety and efficacy of an ERAS protocol in a pediatric population undergoing urologic reconstructive operations, with the aim to give pediatric urologists information regarding potential benefits. It was hypothesized that an ERAS protocol in these children will be safe, reduce length of stay, and decrease complications.

Methods

Study design

The study was a prospective, single-center, stage 2a development (i.e. investigative, pilot) trial of an ERAS protocol adapted for use in pediatric patients undergoing reconstructive operations that included a bowel anastomosis [9]. This study design was chosen to examine overall safety, efficacy and clinical outcomes of an ERAS care pathway. IRB approval was obtained in May 2014 (COMIRB 14-0203). Patients were approached for inclusion if they were aged <18 years at the time of surgery and they were undergoing urologic reconstruction that included a bowel anastomosis (bladder augmentation and/or continent ileovesicostomy). ERAS protocol was initially targeted to operations that included a bowel anastomosis, as these were felt to offer most potential for improvement given the metabolic stress of the operation and relatively long lengths of stay. All patients and families were consented for study inclusion pre-operatively.

ERAS protocol

Adult ERAS pathways were studied during the creation of this study protocol, and a multidisciplinary team including pediatric anesthesiology, nursing, and pediatric urology developed and adapted a formal protocol for this study. The care pathway used in this study includes elements that spanned pre-operative, intra-operative, and postoperative phases of care. In total, 16 items were defined and targeted for implementation in enrolled patients. Pre-operative protocol items included: (1) pre-operative counseling that discussed ERAS protocol and specific expectations regarding recovery, pain control and diet; (2) administration of a pre-operative clear liquid carbohydrate load (10 mL/kg up to a maximum of 300 mL 2–3 h prior to scheduled start time); (3) avoidance of hyperosmolar bowel preparation and instructions for patients on a bowel regimen to continue it up to the night before surgery; (4) guideline-appropriate antibiotics to be given within 60 min prior to incision. Intra-operative protocol items included: (1) use of regional anesthesia (epidural, caudal, transversus abdominis plane (TAP) blocks, or surgeon-placement of rectus sheath catheters delivering continuous local anesthetic postoperatively); (2) avoiding excess drains (no intraperitoneal or subcutaneous drains); (3) maintenance of euvolemia (total intravenous crystalloid fluid volume for case between 5 and 10 mL/kg/hour); (4) opioid-sparing anesthetic (no opioids); (5) use of minimally-invasive assistance [10]. Postoperative protocol items were: (1) avoidance of postoperative nasogastric (NG) tube on leaving the operating room; (2) nausea and vomiting pharmacologic prophylaxis (e.g. ondansetron); (3) early enteral feeding with clear liquid diet on the evening of surgery and regular diet on the day after surgery; (4) early mobilization (out of bed day after surgery); (5) use of non-opioid analgesics (acetaminophen, non-steroidal anti-inflammatories or NSAIDs); (6) discontinuation of maintenance intravenous fluids by postoperative day 2; (7) avoidance of oral or intravenous opioids postoperatively.

Patients who did not receive one or more protocol elements were still treated with the intention of ERAS and received as many other protocol elements as possible. While not a specific protocol element, patients with an antegrade continence enema (ACE) started flushes post-operative day 2 or 3, whereas historically this was started around day 4 after either flatus, spontaneous bowel movement or tolerating regular diet.

Information about ERAS was provided through teaching sessions to nursing staff, anesthesia care providers including the acute pain service, and urology attendings, residents and fellows. To maximize adherence, anesthesia developed a detailed intra-operative protocol to be followed during the case. Similarly, urology arranged pre-operative carbohydrate load and emphasized postoperative care plans at the end of the operative note and via direct discussions with the entire team. Planned criteria for discharge included: tolerating oral intake, pain controlled with oral medications, having bowel function, return to baseline mobility, and understanding of catheter-related instructions from a urology nurse.

Historical controls

To provide context and a comparison for the outcomes of interest, the current study retrospectively examined all patients in the 5 years prior to the implementation of the ERAS protocol (2009—2014) who were similarly <18 years of age and underwent an operation that included a bowel anastomosis. Data on age, sex, whether or not bladder augmentation was performed as part of their surgery, and ventriculoperitoneal (VP) shunt status was gathered for the purposes of matching.

Outcomes

Outcomes evaluated were adherence to ERAS protocol items and length of stay (LOS). A protocol score was calculated for all patients equal to the number of protocol items achieved (maximum of 16). Other outcomes included re-admission within 30 days, re-operation within 90 days, and number of 90-day complications by Clavien-Dindo classification [11]. Appendix Table 1 lists complications and associated grade that were tracked. All patients were examined for VP shunt infections. The following were recorded: demographic, medical co-morbidities, operation type, operation length, estimated blood loss, and fluid and opioid used intra-operatively and postoperatively. All opioids were recorded and converted to intravenous morphine equivalents.

Statistical analysis

Propensity-score matching was used to reduce confounding related to non-random assignment of the ERAS protocol. Historical controls were propensity matched 2:1 to ERAS protocol patients using exact matching. Groups were evaluated using standardized differences to enable comparison of covariate imbalance between the matched and unmatched cohorts [12]. A standard difference between −0.1 and 0.1 indicates the groups are well balanced (Appendix Table 2 and Appendix Fig. 1).

Descriptive analyses were performed, with measures reported as median and interquartile range, except where noted. Matched samples required special consideration for comparison [12]. Continuous variables were compared with logistic regression using the method of generalized estimating equations, and categorical variables were compared with Mantel—Haenszel test. Two-sided *P*-values were reported, with values <0.05 considered significant. Statistical analyses were performed using R 3.2.4 and MatchIt 2.4—22 (https://www.r-project.org).

Results

A total of 42 patients undergoing reconstructive operations were evaluated for inclusion in the prospective arm during the study period. Thirteen patients met study inclusion criteria and agreed to participate, with a median age of 9.9 years (IQR 9.1—11.0). Of the 29 who did not meet inclusion criteria, 26 underwent reconstructive operations that did not include a bowel anastomosis (all continent appendicovesicostomy) and three patients were ≥18 years of age. No patients who met inclusion criteria declined enrollment. No cases were canceled secondary to protocol problems or NPO violations in the ERAS group. There were no significant differences in age, sex, or underlying diagnoses between enrolled patients that received ERAS care and those excluded.

A total of 59 patients were identified as potential historical controls, and 26 were ultimately included in the analysis after propensity matching (2:1 ratio) to ERAS patients. Table 1 lists demographic information, comorbidities, and hospitalization data for matched controls and ERAS patients. Median ages were 10.4 (IQR 8.0—12.4) and 9.9 years (IQR 9.1—11), respectively ($P = 0.940$). Spina bifida was the primary underlying diagnosis in 62% of patients in both arms. There were no significant differences in prior abdominal surgery ($P = 0.221$), VP shunt status (58% vs 54%, $P = 0.823$), or ASA score ($P = 0.250$) between groups.

Bladder augmentation was the most common primary procedure performed (88% historical controls vs 92% ERAS patients), and three historic vs one ERAS patient underwent creation of a continent ileovesicostomy as the primary procedure. Secondary procedures commonly performed include continent appendicovesicostomy, continent ileovesicostomy, antegrade continence enema (ACE) channels and various bladder neck operations. Laparoscopic-assisted procedures were done in a minority of patients (23% vs 38%, $P = 0.346$), at the discretion of the primary surgeon when feasible [10].

All historical patients' charts were retrospectively examined to determine if they received ERAS care elements to compare protocol adherence (primary study outcome) after implementation (Table 2). Median protocol score was 8/16 (IQR 4—9) historically vs 12/16 (IQR 11—12) in the ERAS cohort. ERAS protocol significantly improved use of preoperative liquid load ($P < 0.001$), avoidance of intraoperative and postoperative opioids ($P = 0.046$), early discontinuation of IVF ($P < 0.001$), and early feeding ($P < 0.001$). Length of stay decreased from median of 6 days (mean 8.0, IQR 5—7) for historical patients to median of 5 days (mean 5.7, IQR 3—6) for ERAS patients. This difference was not significant. This compares favorably to recent national averages for pediatric bladder augmentation of mean 7—10 days [13]. There was an inverse correlation between protocol score and length of stay (Fig. 1).

The 90-day complications per patient decreased from 2.1 to 1.3 (OR 0.71, 95% CI 0.51—0.97). There were fewer complications per patient across all grades with implementation of the ERAS protocol. Most complications between the two study arms were Clavien-Dindo Grade I or II. Grades III and IV were less common with no Grade IV complications seen in the ERAS group (intensive care unit-level care). There were no Grade V injuries (death) seen in either historical or ERAS group. The ED visits were more common than expected with 0.65 visits/patient historically compared to 0.54 visits/patient in the ERAS cohort ($P = 0.570$). No differences were seen in re-admission within 30 days or re-operations within 90 days (Table 3).

Table 1 Operations performed, intra-operative characteristics, and hospital stay details.

	Matched		*P*-value
	Historical	ERAS	
Total patients	26 patients	13 patients	—
Median age, years (IQR)	10.4 (8.0–12.4)	9.9 (9.1–11.0)	0.940
Median follow-up, months (IQR)	57.9 (46.9–69.8)	23.4 (20.6–26.4)	**<0.001**
Sex			
Male	13 (50%)	7 (54%)	0.803
Female	13 (50%)	6 (46%)	
Medical comorbidities			
Prior VP shunt	15 (58%)	7 (54%)	0.823
Prior abdominal surgery	10 (38%)	8 (62%)	0.221
Undergoing augmentation	23 (88%)	12 (92%)	0.724
ASA score	3 (2–3)	2 (2–3)	0.250
Operations performed			
Bladder augmentation	23 (88%)	12 (92%)	0.724
Continent appendicovesicostomy (secondary)	7 (27%)	1 (8%)	0.307
Continent ileovesicostomy	12 (46%)	6 (46%)	1.000
Antegrade continence enema channel (secondary)	13 (50%)	4 (31%)	0.480
Bladder neck reconstruction	8 (31%)	3 (23%)	0.724
Bladder neck sling	6 (23%)	0 (0%)	0.157
Bladder neck closure	3 (12%)	1 (8%)	0.773
Operative details			
Skin-to-skin time, minutes (IQR)	270 (203–342)	277 (189–314)	0.380
EBL, mL (IQR)	50 (25–100)	75 (50–100)	0.307
Intraoperative IVF, mL/kg/hr (IQR)	8.6 (6.1–9.4)	6.4 (6.1–8.7)	0.750
Hospital details			
Start clear liquids, POD (IQR)	1 (1–2)	0 (0–0)	**<0.001**
Start regular diet, POD (IQR)	4 (2–5)	1 (1–1)	**0.002**
Return of bowel function, POD (IQR)	4 (3–5)	2 (1–3)	**0.002**
Mobilization, POD (IQR)	1 (1–1)	1 (1–1)	0.280
Removal of maintenance IVF, POD (IQR)	4 (4–5)	1 (1–3)	**<0.001**
Median length of stay,# midnights (IQR)	6 (5–7)	5 (3–6)	0.520
Mean length of stay,# midnights (S.D., min–max)	8.0 (7.3, 3–41)	5.7 (5.1, 2–22)	

Primary operations required a bowel anastomosis. Secondary operations are also listed. Ileovesicostomy was the primary operation in three historical patients and one ERAS patient. Percentages listed are the fraction of study arm population exposed.
$P < 0.05$ considered significant (shown in bold).
ACE, antegrade continence enema; ASA, American Society of Anesthesiologists; EBL, estimated blood loss; IQR, interquartile range; IVF, intravenous fluids; POD, postoperative day (day of surgery is POD #0); ERAS, enhanced recovery after surgery; VP, ventriculoperitoneal.
Matched continuous variables compared with logistic regression using the method of generalized estimating equations, and matched categorical variables compared with Mantel–Haenszel test.

A few outliers in the historical arm required intensive care unit care and had prolonged hospitalizations secondary to complications (deep space infection, ileus). One patient with six prior abdominal operations in the ERAS group required extensive lysis of adhesions, did well initially, but developed a prolonged ileus around postoperative day 6 requiring nasogastric (NG) tube placement and administration of total parental nutrition and 22 day LOS. This was classified as a Grade II complication. There were no VP shunt infections in the follow-up period for either group.

Discussion

Henrik Kehlet has long maintained that there should be no exclusion criteria for ERAS protocols: that all patients, regardless of age or comorbidity should be candidates [14]. Numerous studies have clarified the safety and value of individual principles in and of themselves [15–17]. The current study demonstrated that a comprehensive ERAS protocol in pediatric urology patients undergoing urologic reconstruction is feasible and safe.

As a quality improvement project, ERAS offered several benefits: it minimized provider and patient variation, and in this small initial experience, reduced overall complications. The first point cannot be overstated, as many providers likely overestimate the consistency of care delivered to their patients, which is usually determined by multiple specialties across multiple spaces within the hospital. This endeavor required interfacing with and engaging each of these areas in order to map out and implement the protocol. The historical group showed wider variation in protocol adherence (median protocol score 8/16, range 4–11) as compared to ERAS (median 12/16, range 10–14).

Table 2 Enhanced recovery after surgery protocol items achieved in historical and **e**nhanced recovery after surgery patient groups.

	Matched		*P*-value
	Historical	ERAS	
Total patients	26 patients	13 patients	—
Median number of protocol items achieved per patient (IQR)	8 (4–9)	12 (11–12)	**<0.001**
Pre-operative			
Counsel about ERAS protocol	0 (0%)	13 (100%)	**<0.001**
Oral clear-liquid carbohydrate load (10 mL/kg, 2–3 h prior start)	0 (0%)	10 (77%)	**<0.001**
No bowel preparation or extended clear liquid diet	21 (81%)	13 (100%)	0.1138
Antibiotic prophylaxis	26 (100%)	13 (100%)	1.0
Intra-operative			
Regional anesthesia	18 (69%)	12 (92%)	0.1336
Avoiding excess drains (pre-peritoneal or peritoneal spaces)	25 (96%)	13 (100%)	0.4795
Euvolemia, 5–10 mL/kg/hr IVF	19 (73%)	9 (69%)	0.8137
Minimizing opioids (none)	0 (0%)	2 (15%)	**0.0455**
Minimally-invasive (laparoscopy when feasible)	6 (23%)	5 (38%)	0.3458
Postoperative			
No nasogastric tube	25 (96%)	13 (100%)	0.4795
Nausea and vomiting prevention	25 (96%)	11 (85%)	0.2207
Early feeding (clear liquids POD#0, regular diet POD#1)	1 (4%)	12 (92%)	**<0.001**
Early mobilization (POD#1)	20 (77%)	10 (77%)	1.0
Adjunctive pain (NSAIDs $\pm$ acetaminophen)	26 (100%)	13 (100%)	1.0
Early removal of IVF (POD#2)	3 (12%)	9 (69%)	**<0.001**
Minimizing opioids (none)	0 (0%)	2 (15%)	**0.0455**

$P < 0.05$ considered significant (shown in bold).
ERAS, enhanced recovery after surgery; IVF, intravenous fluids; POD, post-operative day (day of surgery is POD #0); NSAIDS, non-steroidal anti-inflammatory drugs.

Based on the changes seen between historical practice and implementation of an ERAS protocol, the pillars of an effective ERAS pathway in this patient population appear to be maintenance of euvolemia through avoidance of excess intravenous fluids, avoidance of opioids through the implementation of multimodal analgesia and no routine NG tubes to allow for early feeding to stimulate the gastrointestinal tract.

Historically, the current group was not performing routine pre-operative bowel preparation (outside patients' normal bowel programs), so it was difficult to estimate the impact this might have had over routine use. Pre-operative, hyperosmolar, mechanical bowel preparation, long thought to reduce risk of infection from feces, may increase risk of surgical site infection, increase bowel wall edema, and in some cases, may increase the risk of bowel leak and anastomotic dehiscence [18]. Hyperosmolar bowel preparation contributes to patient dehydration and fluid shifts that may prolong recovery. Omission of formal bowel preparation prior to surgery in pediatric neurogenic bladder patients has been previously shown to be safe with regards to surgical site infection and more devastating VP shunt infections [19,20].

Despite this data, there is still a profound lack of high-quality pediatric-specific evidence in this area [21]. Providers have anecdotally expressed concern that neurogenic bowel patients are somehow 'different'. Neurogenic bowel is typically limited to rectum and sigmoid colon (hindgut), whereas most urology surgery, from current experience, harvest ileum for reconstruction purposes. In the absence of a motility disorder, the foregut and midgut (which extends to the splenic flexure) should be normal. At the current center, patients that have concomitant neurogenic bowel are evaluated and treated pre-operatively to avoid constipation and are encouraged to continue routine bowel regimen without changes (polyethylene glycol, retrograde enemas, etc) up to the night before surgery along with a regular diet regardless of intended bowel segment to be used. Patients avoid pre-admission (which adds to potential costs) and do not receive a pre-operative or post-operative NG tube, which mirrors trends seen in adult urology that involve bowel anastomoses [22,23]. Meta-analysis has shown this strategy to be safe, does not increase pulmonary complications, and reduces time to normal gastrointestinal function [24.].

The rationale for pre-operative clear liquid carbohydrate loading (e.g. ClearFast, Gatorade or Powerade) was less familiar to the current team prior to the study, but focuses on minimizing fasting time [25]. Many adult hospitals and anesthesiologists still adhere to the dogma of nil per os (NPO) after midnight, when the evidence against prolonged periods of fasting is quite substantive [26]. Surgery combined with fasting creates a metabolic and immune response that induces a catabolic state and impaired insulin resistance, which has been associated with increased morbidity [25]. Insulin resistance changes dramatically depending on the complexity and length of the operation, and is further influenced by an open (worse) or laparoscopic (better) approach [27]. Studies have demonstrated carbohydrate loading prior to surgery within acceptable timeframes with no increase in complications [28].

Table 3 Clinical outcomes for the study.

	Matched		OR (95% CI)	*P*-value
	Historical	ERAS		
Total patients	26 patients	13 patients	—	—
Re-admissions within 30 days	7 (0.27/patient)	1 (0.08/patient)	0.29 (0.03–2.54)	0.265
Re-operations within 90 days	8 (0.31/patient)	1 (0.08/patient)	0.31 (0.04–2.17)	0.235
ED visits within 90 days	17 (0.65/patient)	7 (0.54/patient)	0.88 (0.55–1.38)	0.570
Complications by grade				
Total complications within 90 days	56 (2.1/patient)	17 (1.3/patient)	**0.71 (0.51–0.97)**	**0.035**
Clavien-Dindo Grade I complications	20 (0.8/patient)	7 (0.5/patient)	0.67 (0.31–1.46)	0.316
Clavien-Dindo Grade II complications	22 (0.9/patient)	9 (0.7/patient)	**0.30 (0.11–0.82)**	**0.019**
Clavien-Dindo Grade III complications	10 (0.4/patient)	1 (0.08/patient)	—	NS
Clavien-Dindo Grade IV complications	4 (0.2/patient)	0	—	NS
Clavien-Dindo Grade V complications	0	0	—	NS
Complications by type				
1: Nausea/vomiting	10 (18%)	2 (12%)	—	0.058
1: Fever ≥38.0 ℃	4 (7%)	3 (18%)	—	0.564
1: Diarrhea	1 (2%)	1 (6%)	—	0.617
1: Wound dehiscence	2 (4%)	1 (6%)	—	1.000
1: Electrolyte disturbance	2 (4%)	0 (0%)	—	0.317
1: Incisional seroma	1 (2%)	0 (0%)	—	0.480
2: UTI, antibiotic ± fever	8 (14%)	2 (12%)	—	0.346
2: Urinary retention, catheter manipulation	6 (11%)	1 (6%)	—	0.248
2: Wound infection, drainage, antibiotic ± fever	3 (5%)	2 (12%)	—	0.752
2: Pyelonephritis, antibiotic ± fever	2 (4%)	3 (18%)	—	0.414
2: Ileus, nausea/vomiting, NG tube ± TPN	1 (2%)	1 (6%)	—	0.617
2: ACE issue, catheter manipulation	1 (2%)	0 (0%)	—	0.480
2: GI infection, antibiotic	1 (2%)	0 (0%)	—	0.480
3: Deep abscess requiring IR drainage, antibiotic	1 (2%)	0 (0%)	—	0.480
3: Mitrofanoff revision	1 (2%)	0 (0%)	—	0.480
3: Catheter malfunction/loss, replacement in OR	7 (13%)	1 (6%)	—	0.206
4: Respiratory failure requiring ventilation, ICU	1 (2%)	0 (0%)	—	0.480
4: Sepsis, septic shock, ICU	2 (4%)	0 (0%)	—	0.480
4: Multiorgan failure, ICU	1 (2%)	0 (0%)	—	0.480

Complication percentages represent fraction of total patients who had said complication.
Complications in ERAS group were limited to Clavien-Dindo Grades I, II, and III.
There were no serious complications (Clavien-Dindo Grades IV-V) in ERAS patients.
P-values <0.05 were considered significant (shown in bold).
ED, emergency department; NG, nasogastric; TPN, total parenteral nutrition; GI, gastrointestinal; ACE,; IR,; OR,; ICU, intensive care unit.

Reismann et al. demonstrated safe application of ERAS protocols in a wide variety of pediatric surgery procedures in Germany (including those with a bowel anastomosis), both of which demonstrated improvement in postoperative pain scores and reduced postoperative length of stay, with no increase in complication rates [6] West et al. compared a series of pediatric patients undergoing elective bowel resection for inflammatory bowel disease to a group of matched adult patients undergoing similar procedures on an ERAS protocol, and found the ERAS group had shorter hospitalizations and shorter time to starting solid diet [7]. As mentioned, there is relatively little experience in pediatric surgery populations with ERAS protocols as compared to the multitude of studies published over the last decade in adult patients [29].

Limitations of the current study were its single-center nature and limited number of patients. No randomization occurred by design, thus preventing any direct comparison or conclusions regarding the effects of the intervention studied on stated outcomes. The study focused on aggregate outcomes of a protocol, not individual elements, which have been studied and reported on elsewhere. It did not match patients on level of neurologic function, ambulatory status, or underlying diagnosis. The study was designed as a pilot study (stage 2a, development) and was not powered to detect a difference in LOS [30]. LOS is likely subject to the Hawthorne effect, due to inability to blind providers, but remains a simple and widely-used measure of recovery. The current study did not attempt to ascertain any patient-reported outcomes nor post-discharge functional status. Surgical quality is greatly impacted by surgeon skill and experience. Bowel segment choice may also have impact the complications. Three of 26 patients in the historical group used colon rather than ileum, but none had infectious complications. Future studies should control for bowel segment.

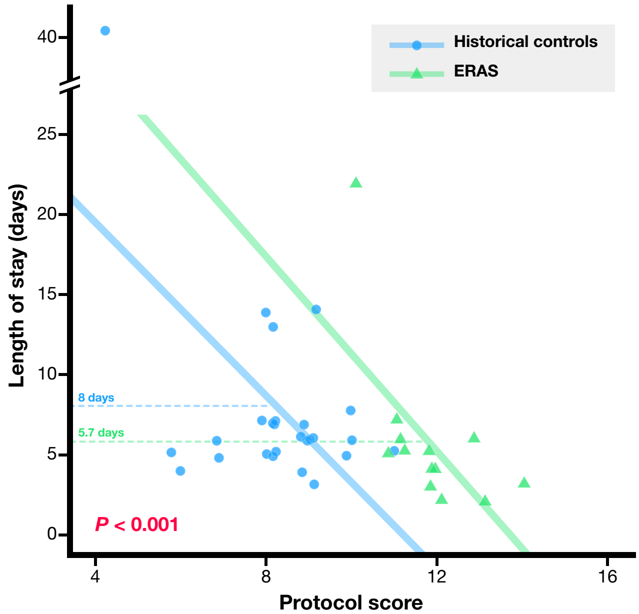


Figure 1 Protocol score for historical and ERAS patients plotted against length of stay. Increased scores were associated with decreased LOS. Solid lines represent linear regression models for each group. The two models were significantly different ($P < 0.001$). ERAS, enhanced recovery after surgery.

Increased adherence may be possible through use of a standardized ERAS order set. While many of these patients were seen in a multidisciplinary setting, some were from long distances and care received outside the current institution related to complications was possible, but less likely given the ample follow-up. Setting the bar at zero for intraoperative and postoperative opioids was perhaps overly restrictive. However, the data collected will be used to set opioid minimization thresholds in future studies. Future studies may look at specific elements to compare outcomes (e.g. laparoscopic-to non-laparoscopic-assisted cases), and ascertain specific reasons for non-compliance. Limiting the study to patients undergoing reconstruction with a bowel anastomosis was intentional to demonstrate overall feasibility of an ERAS protocol in patients undergoing more metabolically demanding operations, but consideration should be given to adapting it to other more common operations in the future.

Conclusion

ERAS can be safely applied in pediatric patients undergoing reconstructive operations requiring a bowel anastomosis, even in a population with a high prevalence of neurogenic bowel/bladder and VP shunt. A multi-center initiative has been started to study ERAS to determine if outcomes after surgery are improved and more cost-effective.

Conflicts of interest

None.

Funding

None.

Appendix Table 1 List of all tracked complications and associated Clavien-Dindo grade classification.

Grade I complications
Electrolyte disturbance
Fever (≥38 °C)
IV complication (infiltration)
Nausea/vomiting
Neuropraxia (positioning complication)
Transient elevation in serum creatinine
Wound dehiscence
Incisional seroma

Grade II complications
Blood transfusion
Catheter manipulation, ACE
Urinary catheter manipulation ± urinary retention
Ileus, nasogastric tube ± TPN ± nausea/vomiting
Bacteremia, antibiotics ± fever
Pyelonephritis, antibiotics ± fever
Wound infection, bedside drainage, antibiotics ± fever
UTI, antibiotics ± fever
GI infection, antibiotics ± fever ± diarrhea
Venous thromboembolism

Grade III complications
Abdominal abscess with IR/OR drainage, antibiotics
Bowel leak treated surgically in OR
Catheter malfunction/loss requiring placement in OR
Fascial dehiscence/evisceration treated in OR
Hemorrhage requiring embolization or OR
Small bowel obstruction treated surgically in OR
Urinoma requiring IR/OR drainage

Grade IV complications
Respiratory failure requiring ventilation, ICU
Renal failure, ICU
Multiorgan failure, ICU
Sepsis, septic shock, ICU

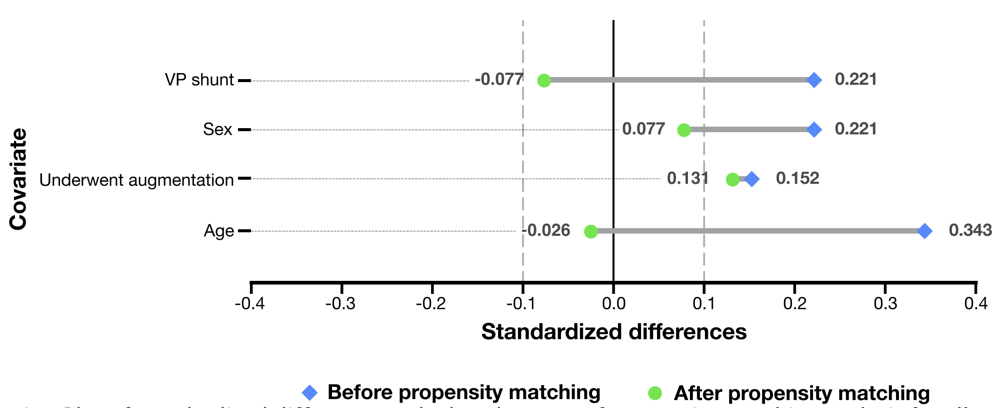
Grade V complications
Death

Although surgical fevers are classically felt to be important at ≥38.5 °C, the current study defined the threshold lower to capture as many events as possible, as many patients/families still become concerned.
ACE,; IR,; ICU, intensive care unit; GI, gastrointestinal; OR,; TPN, total parenteral nutrition

Appendix Table 2 Comparison of unmatched and propensity matched historical patients to prospective enhanced recovery after surgery patients.

	Unmatched		S.D.	*P*-value	Matched		S.D.	*P*-value
	Historical	ERAS			Historical	ERAS		
Total patients	59	13	—	—	26	13	—	—
Median age, years (IQR)[a]	8.9 (6.5–12.2)	9.9 (9.1–11)	0.343	0.257	10.4 (8.0–12.4)	9.9 (9.1–11.0)	−0.026	0.940
Sex[a]								
Male	26 (44%)	7 (54%)	0.221	0.539	13 (50%)	7 (54%)	0.077	0.803
Female	33 (56%)	6 (46%)			13 (50%)	6 (46%)		
Medical comorbidities								
Prior VP shunt[a]	24 (41%)	7 (54%)	0.221	0.538	15 (58%)	7 (54%)	−0.077	0.823
Undergoing augmentation[a]	51 (86%)	12 (92%)	0.152	1.000	23 (88%)	12 (92%)	0.131	0.724
Diagnoses								
Spina bifida	30 (51%)	8 (62%)	—	0.551	16 (62%)	8 (62%)	—	1.000
Imperforate anus	3 (5%)	2 (15%)	—	0.219	0 (0%)	2 (15%)	—	0.046
Spinal cord injury	4 (7%)	1 (8%)	—	1.000	1 (8%)	1 (8%)	—	0.617
Exstrophy	5 (8%)	0 (0%)	—	0.577	3 (23%)	0 (0%)	—	0.134
Sacral agenesis	4 (7%)	0 (0%)	—	1.000	2 (15%)	0 (0%)	—	0.317
VACTERL	3 (5%)	0 (0%)	—	1.000	1 (8%)	0 (0%)	—	0.480
Tethered cord	1 (2%)	1 (8%)	—	0.331	0 (0%)	1 (8%)	—	0.157
Cloacal exstrophy	1 (2%)	1 (8%)	—	0.331	0 (0%)	1 (8%)	—	0.157
Cerebral palsy	2 (3%)	0 (0%)	—	1.000	2 (15%)	0 (0%)	—	0.317
PUV	1 (2%)	0 (0%)	—	1.000	1 (8%)	0 (0%)	—	1.000
Non-neurogenic neurogenic bladder	1 (2%)	0 (0%)	—	1.000	0 (0%)	0 (0%)	—	—
Persistent UG sinus	1 (2%)	0 (0%)	—	1.000	0 (0%)	0 (0%)	—	—
Cloacal anomaly	1 (2%)	0 (0%)	—	1.000	0 (0%)	0 (0%)	—	—
BK cystitis, BMT	1 (2%)	0 (0%)	—	1.000	0 (0%)	0 (0%)	—	—
Rhabdomyosarcoma	1 (2%)	0 (0%)	—	1.000	0 (0%)	0 (0%)	—	—

Matching was not performed on underlying diagnoses, but these are listed for all groups for reference.
Standardized differences reported with propensity matching analysis that were between −0.1 and 0.1 were considered to be well balanced (all four variables improved after matching).
Unmatched continuous variables compared with Mann–Whitney U test, unmatched categorical variables tested with Fisher's exact test.
Matched continuous variables compared with logistic regression using the method of generalized estimating equations, and matched categorical variables compared with Mantel–Haenszel test.
ERAS, enhanced recovery after surgery; VP, ventriculoperitoneal; VACTERL; UG; BK; BMT,
[a] Covariates used for propensity matching.



Appendix Figure 1 Plot of standardized differences calculated as part of propensity matching analysis for all matched variables before and after matching historical controls to ERAS protocol patients. Covariates with a standardized difference > −0.1 or <0.1 are considered well balanced.

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