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4 **Reduced Length of Hospital Stay in Colorectal Surgery after Implementation**
5 **of an Enhanced Recovery Protocol.**
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3
4 **Abstract**

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7 Background

8
9 Enhanced Recovery After Surgery (ERAS) is a multimodal approach to
10 perioperative care that combines a range of interventions in order to enable early
11 mobilization and feeding after surgery. We investigated the feasibility, clinical
12 effectiveness and cost savings of an ERAS program at a major US teaching hospital.
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21 Methods

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23 Data were collected from consecutive patients undergoing open or laparoscopic
24 colorectal surgery during two time periods, before and after implementation of an
25 ERAS protocol. Data collected included patient demographics, operative, and
26 perioperative surgical and anesthesia data, need for analgesics, complications,
27 inpatient medical costs, and 30-day readmission rates.
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39 Results

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41 There were 99 patients in the traditional care group, and 142 in the ERAS group.
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43 The median length of stay (LOS) was 5 days in the ERAS group compared with 7
44 days in the traditional group ($p < 0.001$). The reduction in LOS was significant for
45 both open procedures (median 6 days vs. 7 days, $p = 0.01$), and laparoscopic
46 procedures (4 days vs. 6 days, $p < 0.0001$). ERAS patients had fewer urinary tract
47 infections (13% vs. 24%, $p = 0.03$). Re-admission rates were lower in ERAS patients
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Discussion

Implementation of an Enhanced Recovery protocol for colorectal surgery at a tertiary medical center was associated with a significantly reduced LOS and incidence of urinary tract infection. This is consistent with other studies in the literature and suggests that Enhanced Recovery programs could be implemented successfully and should be considered in US hospitals.

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4 **Introduction**
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9 Evidence-based medicine has been arguably the biggest driver for the change in
10 practice and improvement in outcomes seen over the last twenty years, yet much
11 routine perioperative care in colorectal surgery is not evidence-based. Despite lack
12 of evidence for preoperative bowel preparation in colorectal surgery, routine use of
13 nasogastric tubes, and nil by mouth instructions until bowel sounds are heard
14 postoperatively, all three are still widely practiced.¹⁻³
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26 With traditional perioperative care, factors such as pain, stress, immobilization and
27 postoperative ileus can lead to a length of stay (LOS) of greater than 10 days and
28 complication rates of 45–48% after major elective open colorectal surgery.^{4,5} If a
29 complication occurs this has been shown to be a primary determinant of long-term
30 survival.⁶ Khuri et al analyzed data from over 100,000 patients undergoing major
31 surgery and demonstrated that the occurrence of any one of the 22 types of
32 complications collected in the National Surgical Quality Improvement Program
33 (NSQIP) database reduced median patient survival over the following 10 years by
34 69%.⁶ Caring for patients with complications is also expensive, with the average
35 cost of a surgical complication estimated at \$10,000.⁷
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53 Enhanced Recovery After Surgery (ERAS) is a multidisciplinary perioperative care
54 pathway that aims to standardize perioperative care, and apply evidence-based
55 medicine to all aspects of a patient’s operative journey.⁸ ERAS pathways also aim
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4 to reduce the stress response to surgery; and have been shown to reduce
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6 complications, and LOS after major surgery, with the added benefit of reducing
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8 healthcare costs.^{2,9,10}
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14 Although Enhanced Recovery has been described for some time¹¹, implementation
15
16 is not widespread. There are many barriers to implementation that need to be
17
18 overcome to achieve success. As a result, within the United States few major
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20 centers have reported adoption of an ERAS program. However, as we move toward
21
22 a new era in the delivery of healthcare, a program that can improve quality yet
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24 reduce healthcare costs is of significant interest. The purpose of this study was to
25
26 assess the clinical effectiveness and cost savings of an ERAS protocol for colorectal
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28 surgery at a tertiary medical center. We hypothesized that adoption of an ERAS
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30 protocol reduces length of hospital stay, complications, and medical costs when
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32 compared with traditional care.
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4 **Methods**
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8 After approval from Duke University Medical Center IRB (ref. no. Pro00028555,
9 approved 2/16/2011), we compared data from consecutive patients undergoing
10 open or laparoscopic colorectal surgery within the ERAS protocol with a previous
11 cohort of patients before introduction of the ERAS protocol. Three colorectal
12 surgeons at Duke University Medical Center performed all of the procedures.
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23 **Study design**
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25 We conducted a quantitative observational comparative effectiveness study.
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27 The study consisted of three phases.
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30 1. Retrospective analysis of perioperative data from patients undergoing
31 surgery according to traditional practices from January to June 2009. After
32 this time practice changes gradually occurred in anticipation of
33 implementation of the full ERAS protocol in 2010.
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- 40 2. Implementation phase: the ERAS protocol was implemented in March 2010
41 after training of staff members. A three-month implementation period
42 allowed all staff to become familiar with the protocol.
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- 48 3. Post-implementation phase: between June and December 2010,
49 perioperative data were collected prospectively from patients undergoing
50 surgery within the ERAS protocol.
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4 Data collected included patient demographics, operative, and perioperative
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6 surgical and anesthesia data, need for analgesics, complications, inpatient medical
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8 costs, and 30-day readmission rates. All patients who underwent an elective colon
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10 or rectal resection by one of the three colorectal surgeons within the pre- and post-
11
12 implementation periods were included in this analysis. There were significant
13
14 differences in patient management before and after introduction of the ERAS
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17 protocol.
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24 **Pre-Intervention Management**

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26 Before introduction of the ERAS pathway, there was little standardization of care.
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28 Patients were fasted from midnight on the day of surgery, and all patients received
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30 bowel preparation. All other patient management was at the discretion of the
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32 surgical and anesthesia providers. Placement of thoracic epidurals was rare due to
33
34 surgical preference for enoxaparin to be given 2 hours preoperatively (see
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36 RESULTS). Intraoperative fluid administration was based on changes in
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38 hemodynamics (BP and HR) and urine output. Early mobilization and feeding were
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40 not undertaken
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49 **Post-implementation Management: ERAS protocol**

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51 After implementation of the ERAS pathway, care was standardized using a pathway
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53 that was adapted from the evidence described in the ERAS consensus statement
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55 (Supplementary Tables 1 and 2).² Patients in the ERAS group were educated in the
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57 preoperative surgical clinic about the ERAS pathway and were encouraged to ask
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4 questions. Routine bowel preparation was not performed for colonic procedures,
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6 and patients were allowed to drink clear fluids until 3 hours preoperatively.
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9 Patients also were given 240 mL of an oral preoperative drink (Gatorade™,
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11 PepsiCo, Purchase, NY), which they were told to drink 3 hours preoperatively.
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16 In all patients without contraindications an epidural catheter was placed at the T8-
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18 T10 level, while in the preoperative holding area. Small doses of midazolam and
19
20 fentanyl were given to facilitate epidural insertion and maintain patient comfort.
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24 After placement of the epidural and before skin incision patients received
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26 thromboprophylaxis with heparin 5000 i.u. subcutaneously, and perioperative
27
28 antibiotics were administered before surgical incision.
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33 All patients received general anesthesia with an oral endotracheal tube.
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36 Intraoperative analgesia was provided using a single epidural dose of
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38 hydromorphone at induction (0.4-0.8 mg based on body weight) followed by an
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40 infusion of bupivacaine (2.5 mg/mL at 3-6 mL/h). No intraoperative intravenous
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42 opioids were given after induction of anesthesia without discussion with the
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44 attending anesthesiologist.
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50 Intravenous (IV) crystalloid (Lactated Ringers) 1 L was given during induction of
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52 anesthesia. An infusion of Lactated Ringers was then started and maintained
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54 throughout the procedure using a dedicated infusion pump (set at 3 mL/kg/h for
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56 laparoscopic colectomy, and 5 mL/kg/h for open colectomy, based on lean body
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4 weight). All patients received intraoperative Goal-Directed Fluid Therapy (GDFT)
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6 with a minimally invasive cardiac output monitor. Boluses of IV colloid were given
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8 to optimize stroke volume (SV) using a 10% algorithm (see Supplementary Table
9
10 2). The monitor used was normally the Esophageal Doppler (EDM™ Deltex Medical,
11
12 Inc., Irving, TX). The LiDCORapid™ (LiDCO Ltd., Cambridge, UK) was used as an
13
14 alternative when invasive blood pressure monitoring was performed. The need for
15
16 an arterial line was based on the clinical judgment of the anesthesiologist.
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19 Orogastic tubes, placed following the induction of anesthesia, were removed at the
20
21 end of the procedure. Surgical drains were not routinely used.
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29 Postoperatively patient's urinary catheter was removed on the day after surgery.
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31 Postoperative analgesia was provided using an epidural local anesthetic/opioid
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33 infusion (bupivacaine 0.125% and hydromorphone 10 mcg/mL) for up to 72 hours.
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35 Regular adjunctive analgesia with acetaminophen and NSAIDS was used whenever
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37 possible, and patients were transitioned to oral opioids after removal of the
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39 epidural catheter. Patients were encouraged to drink liquids immediately after
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41 surgery. IV fluid administration was discontinued once adequate oral intake was
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43 achieved, usually on the first morning after surgery. All preoperative medications
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45 were recommenced when patients tolerated oral intake.
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54 Patients were cared for in an environment that encouraged early mobilization.
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56 They were encouraged to be out of bed on the day of surgery, and for at least six
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58 hours on every subsequent day.
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4 **Cost Analysis**
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6 Patient bills for the index hospitalization period were obtained from the Duke
7 University Medical Center (DUMC) patient data repository. Medical costs were
8 estimated by multiplying hospital department charges on study subject bills by
9 their associated ratios of cost to charge from DUMC's Medicare Cost Reports. For
10 reporting purposes, Medicare Cost Report departments were aggregated into
11 clinically meaningful units. Results are presented as unadjusted mean values by
12 treatment strategy with estimated differences and 95% confidence intervals before
13 and after adjusting for age, sex, and procedure type. Unadjusted and adjusted non-
14 parametric bootstrap analyses were used to estimate the variability of cost
15 estimates and to develop a cost acceptability curve that showed the percent of
16 bootstrap samples for which use of the ERAS protocol would be cost saving versus
17 the traditional protocol.^{12,13}
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40 **Statistical Analysis**
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42 A sample size analysis showed that a Mann-Whitney rank-sum test based on a
43 symmetric distribution with expected mean difference of 2 days in LOS and a
44 standard deviation of 5 would have 80% power with 106 patients per group. If the
45 group distributions of LOS are skewed, 100 patients per group provides 95%
46 power assuming a 65% probability of a shorter LOS in the ERAS group. All relevant
47 patient characteristics, operative and postoperative data were summarized with
48 descriptive statistics and compared between the pre- and post- implementation
49 groups with t-tests, rank-sum tests, or chi-squared tests as appropriate. The
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4 primary clinical outcome was postoperative hospital LOS. LOS was defined as
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6 postoperative number of nights in the hospital. Secondary outcomes were days to
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8 first stool, estimated blood loss, postoperative pain scores (measured twice a day),
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10 postoperative IV morphine equivalents¹⁴, surgical site infection (SSI, includes
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12 superficial incisional infection, deep incisional infection, organ space infection and
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14 wound disruption), urinary tract infection (UTI), readmission rate, and death. Pain
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16 was assessed using a 0-10 verbal response scale (VRS), where “0” represents no
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18 pain and “10” represents worst possible pain twice a day as part of the standard of
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20 care nursing protocol. The highest pain reported each day was recorded from the
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22 day of surgery until discharge or the fifth day post-op. Then the set of maximum
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24 pain scores were averaged for each patient to give each patient an average
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26 maximum pain score. Pain scores were compared between therapy groups using a
27
28 rank-sum test. SSI and UTI were diagnosed according to criteria from the American
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30 College Of Surgeons National Surgical Quality Improvement Program.¹⁵
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41 Because of its skewed distribution, LOS was initially compared between groups
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43 with an unadjusted rank-sum test. For covariable-adjusted testing, a parametric
44
45 multivariable regression tested the effect of ERAS on a log-transformation of LOS,
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47 adjusting for surgical approach (laparoscopic or open) and patient characteristics
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49 including ASA class, age, gender, BMI, surgical duration, and pelvic procedure. The
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51 interactions of effects of ERAS and all these co-variables were also tested. Because
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53 a laparoscopic approach has a significant effect on LOS, and was also more frequent
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55 after ERAS implementation, special attention was given to distinguishing between
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4 these two effects. The interaction was tested in the multivariable model, and as a
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6 follow-up the ERAS effect was tested in open and laparoscopic groups separately,
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8 both with unadjusted rank sum tests and with multivariable regression. The log
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10 transformation of LOS did not attain Kolmogorov-Smirnoff test standards for
11
12 normality, but it greatly reduced the test statistics as well as skewness and
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14 kurtosis. These indicators, along with the consistency between the rank-sum test
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16 and a t-test with the log-transformed values, gave us confidence that the
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18 distribution was not unduly influencing the results of the parametric adjusted
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20 regression. All secondary clinical outcomes were compared with t-tests, rank-sum
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22 tests, or chi-square tests without co-variable adjustment. All comparisons were
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24 made at a significance level of 0.05, and all analyses were performed with SAS®
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26 version 9.3 (SAS Institute, Cary, NC).
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Results

There were 99 patients in the traditional care group, and 142 in the ERAS group.

The relevant patient characteristics and surgical details are included in Table 1.

There was no significant difference in age, sex, BMI, or ASA status between the two groups. Operations did not differ statistically in terms of length of surgery (median 300 min in the traditional group and 270 min in the ERAS group, $p=0.11$), however significantly more patients in the ERAS group underwent a laparoscopic rather than an open surgical approach (56.3% vs. 40.4%, $p = 0.01$).

The median LOS was 5 days (interquartile range (IQR) = 3-7) in the ERAS group compared with 7 days (IQR = 5-8) in the traditional group. The p -values for the effect of ERAS on LOS were $p < 0.0001$ in both the unadjusted rank-sum test and in the adjusted covariate model. The reduction in median LOS was significant for open procedures (6 days vs. 7 days, $p = 0.01$), and laparoscopic procedures (4 days vs. 6 days, $p < 0.0001$, rank-sum tests) (Table 2). While surgical approach had a significant effect on LOS ($p < 0.0001$ in both the unadjusted rank-sum test and in the adjusted covariate model), the effect of ERAS was statistically consistent regardless of approach. That is, in the model adjusting for approach and other covariables, the interaction between ERAS and approach was non-significant ($p=0.5398$, Table 2b). In addition to surgical approach, the other significant covariables in our model were female gender (shorter stay, $p=0.0016$) and shorter duration of surgery (shorter stay, $p=0.0032$). There was also a significant reduction

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4 in re-admission rates within 30 days in ERAS patients compared to patients in the
5
6 traditional group (9.8% vs. 20.2%, unadjusted chi-square $p = 0.02$).
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11 Thoracic epidural analgesia (TEA) was used in 92% of patients in the ERAS group
12 compared to 18% of patients in the traditional group ($p < 0.0001$). This resulted in a
13
14 significant reduction in the intraoperative and postoperative morphine
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16 requirements in the ERAS patients compared to the traditional group (Table 3).
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19 Pain scores were significantly lower in the ERAS group compared to controls
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21 (Table 3).
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29 GDFT was used in all patients in the ERAS group. ERAS patients received less
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31 crystalloid (mean 2261 mL vs. 3170 mL, $p < 0.0001$) and more colloid (mean
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33 1072mL vs. 716 mL, $p < 0.0001$) than patients in the traditional group, resulting in
34
35 an overall reduction in the amount of intraoperative IV fluid administered in ERAS
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37 patients. There was no significant difference in intraoperative urine output
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39 between the two groups.
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46 In the ERAS group, 74% (105/142) of patients began clear fluids on the day of
47 surgery, compared to 15% (15/99) in the traditional group ($p < 0.0001$). Early
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49 mobilization was accomplished in 70% (99/142) of patients in the ERAS group
50
51 ambulating on postoperative day (POD) 1. There was a significant reduction in the
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53 duration of ileus in the ERAS patients compared with traditional care (mean time to
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55 first stool 2.4 days vs. 3.4 days, $p = 0.0001$).
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7 There was a significant reduction in urinary tract infection in ERAS patients (13%
8 vs. 24%, $p = 0.03$), presumably related to the earlier removal of Foley catheters.

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11 There was a lower percentage of surgical site infection (28% vs. 37% $p = 0.15$) in
12 ERAS patients that did not reach statistical significance.
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19 Patients undergoing laparoscopic surgery in the traditional group received more
20 opioids and experienced more pain (Table 4). Intraoperative and postoperative
21 opioid use, the average postoperative pain score, and the highest postoperative
22 pain score, were all significantly reduced in the ERAS group.
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32 Overall there was no statistically significant difference in unadjusted total medical
33 costs for patients in the ERAS pathway and traditional care groups (\$18,377 vs.
34 \$20,537; difference, -\$2161; 95% CI, -\$6352 to \$2030; $p=0.31$) (Table 5A). **Similar**
35 **results for the ERAS pathway versus traditional care were observed after**
36 **adjustment for age, sex, and procedure type (difference, -\$1854; 95% CI, -\$6072 to**
37 **\$2363; $p=0.39$) (Table 5B). While the use of open surgery was more costly than**
38 **laparoscopic surgery, this difference also was not significant after adjustment**
39 **(difference, \$2849; 95% CI, -\$1315 to \$7012; $p=0.18$). Use of the ERAS protocol**
40 **was associated with reductions in room-related costs and an increase in medical**
41 **and surgical supply costs before and after adjustment.**
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The net reduction in medical costs achieved with the ERAS protocol was approximately 10% of traditional care medical costs before and after adjustment. These results were confirmed in bootstrap analyses in which use of the ERAS pathway versus traditional care would be expected to achieve some degree of cost saving in 85% of unadjusted and 82% of adjusted medical cost samples (Figures 1 and 2).

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4 **Discussion**
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7 Implementation of an Enhanced Recovery protocol for colorectal surgery at a
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9 tertiary medical center was associated with a significantly reduced LOS, incidence
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11 of urinary tract infection, and readmission rates. The reduction in LOS was similar
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14 to other studies in the literature from diverse centers around the world in open
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17 colorectal surgery.^{4,5,16}
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22 For patients without complications, LOS is largely determined by the duration of
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24 postoperative ileus. Once the ileus has resolved most patients are discharged home
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26 within 1-2 days. Several perioperative factors including preoperative fasting and
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28 bowel preparation, analgesic and anesthetic techniques, and perioperative fluid
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30 management influence the duration of ileus.¹⁷ Enhanced recovery programs aim to
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32 minimize ileus to facilitate immediate feeding and mobilization on the day of
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37 surgery.
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42 Our study showed a greater reduction in LOS for laparoscopic surgery than for
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44 open surgery. This was surprising and could possibly be due to the fact that there
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46 was a greater change in practice from baseline in the laparoscopic procedures. Only
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48 7.5% of patients undergoing laparoscopic surgery in the traditional group received
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50 epidural anesthesia compared to 92.5% in the ERAS group. This resulted in a large
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52 reduction in opioid use and pain scores in patients undergoing laparoscopic
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57 colectomy within the ERAS program.
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4 Compared with traditional care the re-admission rate was also reduced in patients
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6 following the ERAS protocol, demonstrating that patients were physiologically
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8 ready to leave hospital earlier with the ERAS pathway.
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14 The ERAS pathway can be divided into three components – preoperative,
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16 intraoperative, and postoperative. The key principals of the preoperative
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18 component are to prepare the patient (and the relatives) psychologically for the
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20 care program, managing expectation and to prevent a prolonged fasting state. This
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22 is achieved through a combination of nutritional supplements, the avoidance of
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24 routine bowel preparation, allowing clear fluids until 2 hours before induction of
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26 anesthesia, and use of a preoperative carbohydrate drink. These interventions are
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28 evidence-based, and improve subjective well-being, primarily by reducing thirst.¹⁸
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36 Intraoperative elements are the key to successful ERAS pathways, and lay the
37
38 groundwork to enable early mobilization and feeding. Minimally invasive surgery is
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40 an important component.^{8,19} The two major anesthetic factors are fluid
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42 management optimization and the minimization of intravenous opioids, which can
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44 delay the return of normal bowel function.²⁰
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51 The first goal of intraoperative fluid management should be avoidance of fluid
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53 excess, which has shown to be associated with adverse outcomes.^{21,22} The amount
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55 of intraoperative crystalloid given in our study was significantly reduced compared
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57 to similar surgeries ten years ago when it was not unusual to receive greater than 6
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4 liters of intraoperative crystalloid.^{23,24} Only 20% of an intravenous crystalloid
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6 bolus remains in the circulation after 1 hour,²⁵ with the rest distributed in the
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8 extravascular space and contributing to perioperative weight gain, bowel wall
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10 edema, and prolonged ileus.²¹ In a recent analysis of the different elements of an
11
12 ERAS protocol, avoidance of fluid excess was the single most important factor.²⁶
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14 In addition, GDFT with a minimally invasive cardiac output monitor can optimize
15
16 stroke volume. Multiple studies have shown that GDFT reduces hospital LOS and
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18 complications after major surgery.²⁷ These two goals of fluid therapy are not
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20 mutually exclusive and can be achieved with a background crystalloid infusion
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22 supplemented by colloid boluses to maximize stroke volume. However, there is
23
24 currently a lack of information on the role of GDFT within an ERAS program.
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34 Thoracic epidural anesthesia is well established as the analgesic technique of
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36 choice in open major abdominal surgery, with studies showing consistently
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38 superior analgesia to intravenous opioids in the first 72 hours after surgery.²⁸ TEA
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40 is also highly effective at reducing postoperative ileus compared to intravenous
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42 opioids, with a reduction in the duration of ileus after open colectomy of
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44 approximately 36 hours.²⁰
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51 The choice of analgesic technique for laparoscopic surgery is more controversial,
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53 and many centers use alternative multimodal regimes incorporating transversus
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55 abdominis plane (TAP) blocks²⁹ or spinal anesthesia.³⁰ We chose to administer
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57 epidural anesthesia for all patients in our ERAS program, including those
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4 undergoing laparoscopic surgery, because our institution is a tertiary referral
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6 center where a significant proportion of the laparoscopic procedures are complex
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8 operations involving rectal resection, pouch formation, inflammatory bowel
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10 disease patients, or redo operations. In our patient population, patients undergoing
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12 laparoscopic surgery seemed to benefit from epidural analgesia with a dramatic
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14 reduction in pain scores and postoperative opioid use that was as significant for
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16 laparoscopic surgery as open procedures.
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24 Other centers have shown that epidurals can impair discharge after laparoscopic
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26 colectomy by reducing mobility and complicating fluid management.³⁰ Why is this
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28 so different to our results? Different patient populations may play a role and
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30 certainly laparoscopic surgeries cannot all be considered equal. Very few of our
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32 patients had simple colectomies without rectal work or stoma formation, where
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34 discharge can often be achieved within 2-3 days, and therefore epidural analgesia
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36 may not be beneficial. Further studies are needed to evaluate different regional
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38 techniques in different types of laparoscopic colorectal surgery.
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46 Successful implementation of the preoperative and intraoperative elements of an
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48 ERAS pathway enables mobilization and feeding to occur on the day of surgery.
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50 Patients are encouraged to sit out of bed for at least 6 hours on every postoperative
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52 day; and with only evidence-based use of surgical drains, catheters, or nasogastric
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54 tubes.³¹ .
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4 The percentage of patients having a surgical site infection (SSI) in our study was
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6 high. SSIs are the most common complication after colorectal surgery, and although
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8 some centers have reported SSI rates less than 10%,³² the incidence of SSIs after
9
10 colorectal surgery has been reported to be as great as 25-30% in several large,
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12 observational studies.³³⁻³⁵ Our SSI rate decreased after introduction of the ERAS
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14 program but remains high and we are currently evaluating a bundle of care
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16 measures to reduce bacterial contamination of the surgical site. Future strategies
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18 should also concentrate on timely recognition and management of complications
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20 when they occur, which is an important determinant of postoperative
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22 mortality.^{36,37}
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32 There was a trend towards lower medical costs in the ERAS group that did not
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34 reach statistical significance. However, cost data typically are skewed and require a
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36 larger sample than was available in the present study to detect significant
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38 differences. **Therefore bootstrap analysis was used to look at the distribution of the**
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40 **difference in mean values of the two samples, and showed that the ERAS protocol**
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42 **would be expected to cost less than control in 85% of unadjusted and 82% of**
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44 **adjusted medical cost samples.** This was mainly related to the reduction in LOS in
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46 the ERAS group.
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53 The main limitation of our study is that it was not a blinded randomized controlled
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55 trial (RCT). Furthermore, all of the elements of the ERAS protocol were introduced
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57 simultaneously. Thus, it is impossible to determine which elements may be
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4 responsible for the observed outcome differences. Unfortunately, it is practically
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6 impossible to blind a bundle of care with so many different interventions.
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9 Additionally the complexity in implementing ERAS programs would make a
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11 randomized controlled trial (RCT) to assess their clinical effectiveness technically
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13 challenging. Implementation programs can take several months and involves
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15 education and training for all perioperative care providers. It is therefore difficult
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17 and may indeed be confusing and potentially unsafe for patients to be randomized
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19 to traditional or ERAS care as would occur in a RCT. However, in our study there
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21 were no significant differences in the baseline characteristics between the patients
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23 during the control and the intervention periods, and the magnitude of the change in
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25 LOS was substantial.
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34 Another limitation is that non-clinical confounders, such as the availability of the
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36 surgical team to make discharge decisions can affect the time of discharge from
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38 hospital. Whilst no practice changes occurred in discharge planning during the
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40 study the change in organizational workflows after the introduction of the ERAS
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42 pathway may have improved the discharge process in the ERAS group compared to
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44 the traditional group.
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51 It is possible that the observed benefits could be due to a laparoscopic approach
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53 and the use of epidural analgesia. It is also possible that it is not the epidural per se
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55 that causes the observed benefits but the early feeding and mobilization that the
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57 epidural facilitated. In other words, if the patient undergoing traditional care has a
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4 good working epidural but is still fasted and undergoing bed rest, the benefits of
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6 the epidural in aiding recovery may not be realized.
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11 Finally, it is also possible that all elements of the protocol are important with the
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13 reduction in LOS and complications proportional to the number of elements
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15 implemented.²⁶ As the enhanced recovery process develops, further research will
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17 aim to identify crucial elements of the protocol. Some interventions may turn out
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19 to be more important than others, and some may be nonessential. However,
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21 current evidence suggests that adherence to the ERAS protocol as a whole is the
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23 best approach.²⁶
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32 In conclusion, we showed a significant reduction in LOS after implementation of an
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34 enhanced recovery program for colorectal surgery. The reduction in LOS was
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36 significant for patients undergoing open and laparoscopic colorectal resection. Our
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38 data support the evidence that enhanced recovery programs should be considered
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40 as the new standard of care for patients undergoing elective colorectal resection.
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Table 1. Patient demographics, anthropometrics, and clinical characteristics

	Traditional N=99	ERAS N=142	P-Value
Age (year)	56 ± 15	58 ± 15	0.54
Male/female	43/56	69/73	0.43
Height (cm)	171 ± 10	172 ± 10	0.41
Weight (Kg)	81 ± 20	83 ± 20	0.47
BMI	27.7 ± 5	28.5 ± 7	0.78
ASA Physical Status			
I	3	0	0.0715
II	39	53	
III	53	87	
IV	4	2	
Type of surgery			
Colon	54 (55%)	75 (53%)	0.79
Pelvic	45 (45%)	67 (47%)	
Laparoscopic approach (%)	40.4 %	56.3 %	0.01
Duration of surgery (min)*	300 ± 136	270 ± 126	0.11

Data are expressed as mean ± SD or n (%)

*** Incision to end of surgery**

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4 **Table 2a. Length of stay**
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	Mean \pm SD		Median (IQR)		Diff (95% CI)*	P- Value**
	Traditional	ERAS	Traditional	ERAS		
All procedures (days)	8.3 \pm 8.1	6 \pm 4.2	7 (5, 8)	5 (3, 7)	2 (1 - 2)	<0.0001
Open procedures (days)	9.3 \pm 6.6	7.1 \pm 3.9	7 (6, 9)	6 (5, 8)	1 (0 - 2)	0.0133
Laparoscopic procedures (days)	6.9 \pm 5	5.2 \pm 4.2	6 (4.5, 7.5)	4 (3, 5.5)	2 (1 - 2)	<0.0001

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* Difference between medians, and estimated 95% Confidence limits for the difference.

** P-values in this table are from unadjusted rank-sum tests comparing therapy groups.

Table 2b. Multivariable linear regression on log-transformed LOS

Factor	Beta Coefficient	P-Value
Laparoscopic approach	-0.218	0.0001
ERAS protocol	-0.253	<0.0001
ASA 3-4	0.128	0.0516
Duration of surgery (minutes)	0.0007	0.0033
Female gender	-0.200	0.0019
Interaction: Laparoscopic surgery and ERAS protocol	-0.080	0.5398

Duration of surgery is the number of minutes from incision to end of surgery. No transformation of this number was necessary, as none provided meaningful improvement in the correlation with log(LOS)

Table 3: Patient Outcomes

	Traditional	ERAS	P-Value
POD to first oral liquid	1.8 ± 1.9	0.5 ± 1	<0.0001
POD to first stool	3.4 ± 1.7	2.4 ± 1.6	0.0001
OR crystalloid	3170 ± 1621	2261 ± 1282	<0.0001
OR colloid	716 ± 519	1072 ± 530	<0.0001
OR blood	83 ± 321	80 ± 474	0.142
OR FFP	20 ± 128	33 ± 209	0.9408
OR estimated blood loss	319 ± 314	246 ± 430	0.0003
OR urine output	460 ± 349	490 ± 318	0.2799
Highest postoperative pain score	6.8 ± 2.3	5.6 ± 2.7	0.0004
Average pain score Days 0-5	4.9 ± 2.1	3.3 ± 1.9	<0.0001
Total intraoperative morphine equivalents (mg)	53.1 ± 28	20.8 ± 23.5	<0.0001
Total postoperative morphine equivalents (mg)			
Median (IQR)	120 (69 - 267)	29.8 (10 - 85)	<0.0001
Mean	196 ± 191	85 ± 175	
Surgical Site Infection (%)	37.3%	28.8%	0.16
Urinary Tract Infection (%)	24.2%	13.4%	0.03
Readmission (%)	20.2%	9.8%	0.02
Death (%)	1%	0%	0.41

POD = Postoperative day; OR=Operating room

Table 4: Pain scores and opioid consumption by surgical approach

		Median (IQR)		Mean ± SD		P-Value
		Traditional	ERAS	Traditional	ERAS	
Highest postoperative pain score	Open	7 (5, 9)	6.5 (5, 8)	6.6 ± 1.7	6.3 ± 2.3	0.36
	Lap	7.5 (6, 8)	5 (3, 7)	7.1 ± 1.8	5 ± 2.9	<0.0001
Average pain score Days 0-5	Open	4.5 (3.4, 6.5)	3.5 (2.2, 4.8)	4.9 ± 2.3	3.7 ± 1.9	0.0020
	Lap	4.6 (3.9, 6)	3 (1.3, 4.6)	4.8 ± 1.7	3.1 ± 1.9	<0.0001
Total intraoperative morphine equivalents (mg)	Open	56.7 (33.4, 70.1)	15 (10, 25)	56.9 ± 32.3	25.8 ± 33.1	<0.0001
	Lap	43.2 (35.1, 60.2)	15 (10, 20)	47.5 ± 19.1	16.9 ± 10.4	<0.0001
Total postoperative morphine equivalents (mg)	Open	171 (63.4, 351)	40 (16.5, 134)	220 ± 196	123 ± 242	<0.0001
	Lap	110.1 (71.8, 162)	20 (6.7, 61.7)	159 ± 179	53.7 ± 74.5	<0.0001

Table 5A: Medical Costs (US \$)

Hospital Department Groups	Medical costs		Unadjusted Difference (ERAS - traditional)	Lower CI (95%)	Upper CI (95%)	Unadjusted P-Value
	Traditional (n=99)	ERAS (n=142)				
Non-ICU	3121	2551	-570	-1074	-66	0.027
ICU	3251	2019	-1232	-2979	516	0.17
Pharmacy	1350	853	-497	-946	-47	0.03
Medical and Surgical Supplies	6380	7186	806	-283	1896	0.15
Lab & ECG	1343	1018	-325	-671	21	0.07
Radiology	411	404	-7	-282	269	0.96
OR + PACU	3403	3383	-19	-260	222	0.88
Anesthesia	248	234	-14	-32	5	0.14
Blood related	251	139	-112	-270	47	0.17
Dialysis	0	0	0			
Other	776	579	-197	-743	350	0.48
Total	20,537	18,377	-2161	-6352	2030	0.31

Table 5B: Adjusted Medical Costs (\$, US)

Hospital Department Groups	Adjusted Difference (ERAS - traditional)	Lower CI (95%)	Upper CI (95%)	Adjusted P-Value
Non-ICU	-509	-1013	-6	0.047
ICU	-1072	-2834	691	0.23
Pharmacy	-463	-914	-12	0.044
Medical and Surgical Supplies	684	-410	1778	0.22
Lab & ECG	-265	-612	82	0.13
Radiology	16	-263	295	0.91
OR + PACU	20	-220	261	0.87
Anesthesia	-12	-30	7	0.21
Blood related	-89	-249	71	0.27
Dialysis	-167	-722	387	0.55
Other				
Total	-1854	-6072	2363	0.39

*Estimated differences and 95% confidence intervals were adjusted for age, sex, and procedure type.

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Legend

Figure 1: Unadjusted cost savings

Cumulative distribution chart depicting the percent of bootstrap sample iterations in which the ERAS treatment strategy would be expected to be cost saving versus control using unadjusted values.

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4 **Supplementary Table 1.**
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6 **Duke University Colorectal Surgery ERAS Protocol Summary**
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PHASE OF CARE, LOCATION	INTERVENTION
SURGICAL PLANNING, SURGICAL CLINIC	Identify elective surgery patients who can benefit from participation Educate patients about the track and our expectations Reinforce with a written copy of our plan and expectations Screen for malnutrition, tobacco abuse, and diabetes (H&P, labs)
PREOPERATIVE ASSESSMENT, PREOPERATIVE ASSESSMENT CLINIC	Routine preoperative screening, specific attention to known risk factors Distribute <ul style="list-style-type: none">• Nutritional supplements if serum albumin <3.5• Smoking cessation info• Chlorhexidine sponges for 2 preoperative showers• Carbohydrate drink for morning of surgery (Gatorade™) Reinforce with written instructions
DAY OF OPERATION, PREOPERATIVE HOLDING AREA	Identify ERAS patients and initiate protocol Epidural anesthesia placement – T8-12 region Thromboprophylaxis with heparin 5000U sc after placement of epidural
INTRAOPERATIVE, OPERATING ROOM	Antibiotic prophylaxis before incision Sequential compression devices placed before induction of anesthesia Use epidural throughout case without any intravenous opioids Goal-directed intravenous fluid therapy Orogastric tube removed before leaving OR Foley discontinued in OR, except for pelvic operations
POSTOPERATIVE CARE, SURGICAL WARD	Diet begins night of surgery Ambulation begins night of surgery Head of bed at 30 degrees at all times Continue epidural for up to 72 hours postoperatively

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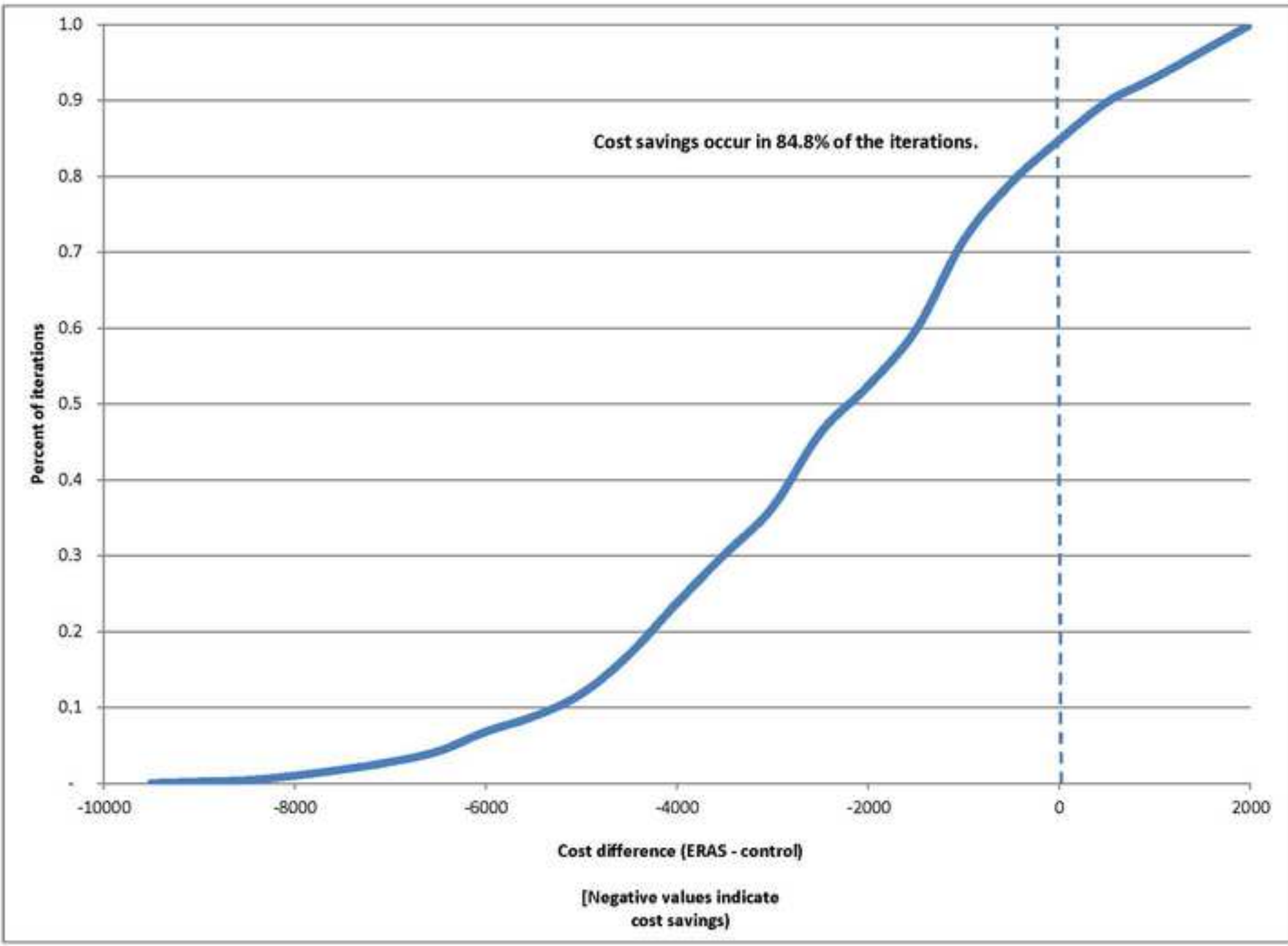
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6 **Supplementary Table 2.**
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8 **Anesthesia colorectal enhanced recovery guidelines**
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INTVENTION	PROTOCOL
THORACIC EPIDURAL	T 8-12 region 5000U subcutaneous heparin can be given after placement Hydromorphone 0.4mg-0.6mg before induction of anesthesia Lidocaine 2% bolus at least 10 minutes pre-incision (40-100mg) Run infusion of 0.25% bupivacaine throughout case (3-6 ml/hr.) No intraoperative iv opioids after induction without discussion with the Attending Anesthesiologist Switch to bupivacaine 0.125%/hydromorphone 10mcg/ml in epidural pump before leaving for PACU at end of case. <ul style="list-style-type: none">Settings: Infusion 4-6 ml/hour; 2ml bolus every 30 minutes
GOAL-DIRECTED FLUID THERAPY	1000 ml LR bolus – commenced in preoperative holding area to be infused during induction and then finished. LR infusion for rest of case based on LEAN BODY WEIGHT (max 80Kg) <ul style="list-style-type: none">5ml/Kg/hr. for open cases (max 400ml/hr.)3ml/Kg/hr. for laparoscopic cases (max 240ml/hr.) Esophageal Doppler placed after induction. Record initial Stroke Volume (SV). After incision (after pneumoperitoneum for laparoscopic cases) give a 250ml colloid bolus over <15 min (suggest five 50ml syringe pushes). <ul style="list-style-type: none">If SV increases by >10 % repeat bolus.If SV increases by < 10% patient does not require a further bolus.Record peak value achieved.If still hypotensive consider phenylephrine infusion.Give a further colloid bolus when SV drops 10% from peak value.Repeat cycle. Max Voluven™ dose 50 ml/Kg Reduce LR to 2ml/Kg/hr. before transfer to PACU.

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Cost difference (ERAS - control)
[Negative values indicate cost savings]