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Authors

Hanna, Mark H Jafari, Mehraneh D Jafari, Fariba <u>et al.</u>

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Randomized Clinical Trial of Epidural Compared with Conventional Analgesia after Minimally Invasive Colorectal Surgery

CrossMark

Mark H Hanna, MD, Mehraneh D Jafari, MD, Fariba Jafari, MD, Michael J Phelan, PhD, Joseph Rinehart, MD, Coral Sun, MD, Joseph C Carmichael, MD, FACS, Steven D Mills, MD, FACS, Michael J Stamos, MD, FACS, Alessio Pigazzi, MD, PhD, FACS

| BACKGROUND: | The effectiveness of thoracic epidural analgesia (EA) vs conventional IV analgesia (IA) after |
|---------------|--|
| | minimally invasive surgery is still unproven. We designed a randomized controlled trial |
| | comparing EA with IA after minimally invasive colorectal surgery. |
| | A total of 87 patients who underwent minimally invasive colorectal procedures at a single |
| STUDT DESIGN. | |
| | institution between 2011 and 2014 were enrolled. Eight patients were excluded and 38 |
| | were randomized to EA and 41 to IA. Pain was assessed with the Visual Analogue Scale |
| | and quality of life with the Overall Benefit of Analgesia Score daily until discharge. |
| RESULTS: | Mean age was 57 ± 14 years, 43% of patients were female, and mean BMI was 28.6 ± 6 kg/m ² . |
| | The 2 groups were similar in demographic characteristics and distribution of diagnoses and |
| | procedures. Epidural analgesia had a higher incidence of hypotensive systolic blood pressure |
| | (<90 mmHg) episodes (9 vs 2; $p < 0.05$) and a trend toward longer Foley catheter duration |
| | (3 \pm 2 days vs 2 \pm 4 days; p > 0.05). Epidural and IA had equivalent mean lengths of stay (4 |
| | \pm 3 days vs 4 \pm 3 days), daily Visual Analogue Scale scores (2.4 \pm 2.0 vs 3.0 \pm 2.0), and |
| | Overall Benefit of Analgesia Scores (3.2 ± 2.0 vs 3.2 ± 2.0), and similar time to start oral diet |
| | $(2.8 \pm 2 \text{ days vs } 2.2 \pm 1 \text{ days})$. Epidural analgesia patients used a higher total dose of nar- |
| | |
| | cotics (147.5 \pm 192.0 mg vs 98.1 \pm 112.0 mg; p > 0.05). Epidural and IV analgesia had |
| | equivalent total hospital charges ($144,991 \pm 67,636$ vs $141,339 \pm 75,579$; p > 0.05). |
| CONCLUSIONS: | This study indicates that EA has no added clinical benefit in patients undergoing minimally |
| | invasive colorectal surgery. A trend toward higher total narcotics use and complications with |
| | EA was demonstrated. (J Am Coll Surg 2017;225:622-630. © 2017 by the American Col- |
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Enhanced recovery after surgery (ERAS) pathways were developed to optimize and standardize perioperative care to improve outcomes, reduce complications, and shorten length of stay (LOS) after colorectal operations.¹ One of the tenets of some ERAS protocols is optimizing postoperative pain control with thoracic epidural analgesia (EA) to circumvent the need for IV narcotics.²⁻⁴ Recent randomized trials have suggested fluid management, minimally invasive surgery, and EA as the key elements of the ERAS principles.⁵⁻⁷

However, there is ongoing controversy about the true benefit of EA when combined with minimally invasive colorectal surgery (MIS CRS).⁸⁻¹² Centers with high laparoscopic expertise have reported excellent outcomes without the use of EA.¹³⁻¹⁵ In addition, recent prospective studies have even suggested a slower postoperative

From the Departments of Surgery (Hanna, MD Jafari, F Jafari, Carmichael, Mills, Stamos, Pigazzi) and Anesthesia (Rinehart, Sun), School of Medicine, and Department of Statistics (Phelan), University of California, Irvine, CA. Correspondence address: Alessio Pigazzi, MD, PhD, FACS, Department of Surgery, School of Medicine, University of California, Irvine, 333 City Blvd West, Suite 850, Orange, CA 92868. email: apigazzi@uci.edu

| EA | = epidural analgesia |
|---------|---|
| ERAS | = enhanced recovery after surgery |
| IA | = IV analgesia |
| LOS | = length of stay |
| MIS CRS | = minimally invasive colorectal surgery |
| OBAS | = Overall Benefit of Analgesia Score |
| PCA | = patient-controlled anesthesia |
| PO | = per os |
| VAS | = Visual Analogue Scale |

recovery when EA was used with MIS CRS.⁷ The advent of novel and more sophisticated pain-control regimens and modalities have shrouded the true benefit of EA.^{14,15} This obvious contradiction in the currently available recommendations, evidence, and current practice patterns has created a need for more prospective data to help elucidate the true benefit, if any, of EA in the realm of MIS CRS.

The goals of this randomized controlled trial were, therefore, to compare the use of EA with conventional IV analgesia (IA) after MIS CRS and determine its effects on postoperative LOS, outcomes, and complications in a prospective fashion.

METHODS

The study was designed as a single-center, prospective, parallel-group, non-inferiority study comparing the effects of EA vs IA on postoperative recovery after MIS CRS. From January 2011 to December 2014, patients undergoing elective MIS CRS were assessed for eligibility for inclusion in the study. Eligible patients were then randomized in a balanced fashion (1:1) to receive EA or IA analgesia in conjunction with their elective MIS CRS. All patients underwent operations at the University of California, Irvine Medical Center, which were performed by 4 colorectal surgeons. The study was given full approval by the IRB committee of University of California, Irvine and all patients were provided informed consent in their native language before enrollment. The trial was registered at ClinicalTrials.gov (NCT02086123).

Inclusion and exclusion criteria

The inclusion criteria were specified as follows: age 18 years or older, subjects undergoing laparoscopic large bowel resection or rectal resection with anastomosis, University of California, Irvine inpatients and outpatients scheduled for elective surgery for both benign and malignant conditions. Patients were not eligible for the study if

they were undergoing emergent procedures; had a history of allergy to EA or IA; had documented history of chronic pain or chronic narcotic use; were pregnant patients or nursing females; and had a history of severe cardiovascular, pulmonary, renal, hepatic, hematologic, or systemic disease.

Enrollment, interventions, and monitoring

Study details were explained to the subjects during their first consultation visit by the operating surgeon once patient eligibility was established. Subjects were given time until their preoperative visit to decide whether they would like to participate in the study. On the preoperative visit, informed consent was obtained from subjects who decided to participate in the study. Random envelopes designating EA vs IA were made. An envelope was then picked randomly by a member of the surgical team at the time of the preoperative visit in the clinic. This allowed time to coordinate with anesthesia to prepare for EA in those subjects who were enrolled into this arm. For medical and logistic reasons, blinding was not considered for this trial.

Subjects in the EA group received EA in the operating room before induction of anesthesia. The anesthesiologist in charge of the case inserted the epidural catheter in the T10-T11 space before the operation. At the end of the operation, a solution of bupivacaine (0.1%) and fentanyl $(2 \ \mu g/mL)$ was initiated in the epidural group at a rate of 6 to 10 mL/h (target: Visual Analogue Scale [VAS] score <4) with bolus of 3 mL of the solution allowed every 40 minutes (patient-controlled EA). The epidural catheter was typically left in place until the 3rd postoperative day, which was the standard practice in our hospital. Patients randomized to the IA cohort were started on a hydromorphone IV patient-controlled anesthesia (PCA) with a loading dose of 0.5 mg. A bolus of 0.3 mg was allowed every 10 minutes up to a maximal dose of 1.8 mg every hour.

Alvimopan 12 mg per os (PO) was given once preoperatively to both intervention groups and was continued postoperatively until patients had adequate return of bowel function, as demonstrated by having a bowel movement, or continued up to postoperative day 7 if no bowel movement, as advised by the drug manufacturer. A Foley catheter was placed in the operating room for bladder drainage and was kept in place until after epidural removal. In cases of suboptimal pain control or patient discomfort, a bolus was given through the epidural and the rate of infusion of the epidural PCA or standard IV PCA was increased per institutional protocol. Toradol IV and acetaminophen PO or per rectal were available for additional pain control if needed. Low-molecular-weight heparin was used for deep venous thrombosis prophylaxis. Both intervention groups were treated according to ERAS principles postoperatively, this required the fulfillment of the following criteria: preoperative counseling, active prevention of hypothermia, no routine use of postoperative nasogastric tubes or drains, enforced early postoperative mobilization, fluid restriction, and early removal of urinary catheters. Despite the fact that no standard ERAS protocol was available during the study period, all cases included in the study were done at a single site (University of California, Irvine Medical Center) and done by 4 colorectal surgeons who all adhered to ERAS principles and postoperative management of patients was mostly homogenous.

Patients in both arms underwent only MIS CRS without the need for open or hand-assisted techniques. This was done in a purely laparoscopic/robotic fashion, which meant the patients required only small trocar incisions and a small extraction incision (approximately 5 cm Pfannensteil incision was used for the majority of cases).

Subjects in both groups were followed daily by members of the research team and they had their laboratory results and vital signs monitored per standard postoperative protocol.

End points and pain assessment

Postoperative pain was assessed using the validated VAS.¹⁶ Side effects and quality of life were measured using the Opioid Related Symptom Distress Scale, which assesses 12 common opioid-related symptoms, including nausea and vomiting, by 3 ordinal measures: frequency, severity, and bothersomeness. Another assessment tool used was the Overall Benefit of Analgesia Score (OBAS),17 which is a simple, multidimensional quality-assessment instrument to measure subjects benefit from postoperative pain therapy. We used the recent International Consensus definition to determine readiness for hospital discharge after CRS for patients enrolled in the study.¹⁸ Patients who achieved the following criteria were deemed safe and ready for discharge from inpatient care: tolerance of oral intake, recovery of lower gastrointestinal function, adequate pain control with oral analgesia, ability to mobilize and self-care, and no evidence of complications or untreated medical problems. Once these criteria were achieved, discharge would take place as soon as the patient had adequate post-discharge support and was willing to leave the hospital. If a stoma was constructed, the patient or the patient's family received training on stoma care before discharge was completed.

Statistical analysis

The primary end point was to estimate the mean difference in hospital LOS for the control arm (IA) and the treatment arm (EA). The null hypothesis was defined as the means are equal, and the alternative hypothesis was defined that EA resulted in a shorter hospital stay of 1 less day on average compared with IA. Our trial was designed as a superiority trial, with EA being presumed to have a superior and shorter hospital LOS compared with IA. Adopting a power of 80%, a 2-sided type I error (α) of 0.05 and an anticipated dropout rate of 10%, the calculated sample size was 120 patients per group. This was determined with power analysis using a 2-tailed t-test and differences between 2 independent means was performed and indicated that enrollment of 120 subjects per group would provide the study with 80% power to detect a decrease of 1 day in LOS. This was calculated based on the difference between 6-day LOS for IA and presumed 5-day LOS for the EA group. This calculation was based on the average LOS for our laparoscopic CRS patients at University of California, Irvine.

Data collected included age, sex, American Society of Anesthesiologists grade, weight, type of colectomy, indication for operation, amount of analgesic administered, complications, pain scores, hospital LOS, and Charlson Age Comorbidity Score.¹⁹ Descriptive statistics were reported as absolute or relative frequencies for categorical variables and as median (range or interquartile range) or mean \pm SD for continuous variables as appropriate. Fisher's exact test was used to analyze categorical variables. The Student's t-test and the Mann-Whitney U test were used to compare normal and non-normal continuous variables, respectively. Data were analyzed by use of the Statistical Package for the Social Sciences (version 21.0, IBM Corp). The trial was conducted and the results are presented according to the CONSORT (Consolidated Standards of Reporting Trials) guidelines.²⁰ A p value < 0.05was considered statistically significant. Outcomes were analyzed according to the intention-to-treat principles.

RESULTS

During the course of 3 years, 87 consecutive patients were assessed for eligibility, of which 8 were excluded (Fig. 1). Of those patients that were excluded after assessment, 4 did not meet inclusion criteria, 2 refused to participate, and 2 were excluded for other reasons. A total of 79 patients were randomized; 38 patients to the EA cohort and 41 patients to the IA cohort. There was excellent follow-up in each group; no patients were lost to follow-up or required cessation of their respective interventions. Seven patients in the EA arm crossed over to the IA arm and 1 patient in the IA arm crossed over to the EA arm.

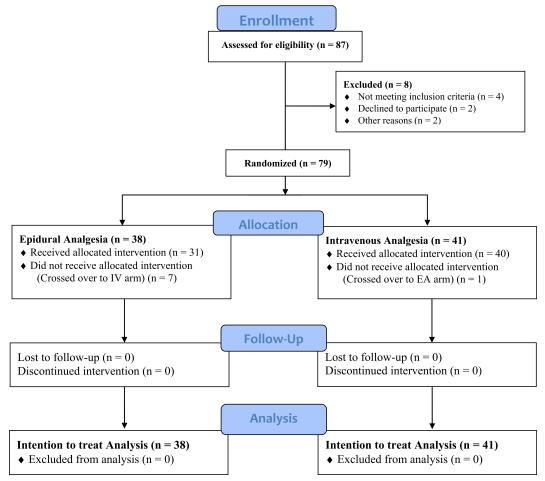


Figure 1. Study flowchart. CONSORT (Consolidated Standards of Reporting Trials) diagram. Randomized controlled trial comparing epidural analgesia (EA) vs IV analgesia in patients undergoing minimally invasive colorectal surgery.

The recruitment process spanned 3 years, during which 87 patients were assessed and a total of 79 were randomized. Yearly interval analysis was conducted with intention-to-treat principles of the evolving comparison groups. The difference in the median LOS remained negligible between the 2 groups (4 ± 3 days vs 4 ± 3 days; p > 0.05), with no trends toward a true divergence, which allowed recruitment to terminate early and before the initially anticipated target sample sizes was reached for each cohort. Due to these findings and the fact that recruitment was slower than anticipated, we decided to terminate the study early at 87 patients enrolled.

Patient demographic data

The demographic data are shown in Table 1. Median age was 54 ± 12 years, 43% of patients were female, and mean BMI was 28.6 ± 6 kg/m². There was no significant difference in age, sex, BMI, diagnosis, or type of procedure between the 2 groups. American Society of Anesthesiologists class distribution was found to be significantly higher in the IA cohort (p = 0.01). Charlson Age Comorbidity Scores were similar between the 2 cohorts. Size of the largest incision (extraction site) was measured in both groups among the majority of patients. Mean length of the largest incision was 3.30 ± 3.09 cm in the EA group and 2.70 ± 3.3 cm in the IA group (p = 0.16). However, because not all patients that were randomized had their incisions measured in a standardized fashion, this parameter was excluded from our analysis. No conversions to open surgical technique occurred in either group.

Complications

The incidence of surgical and postoperative complications is summarized in Table 2. There was no difference in the overall rate of postoperative complications between the 2 groups, however, EA had a higher incidence of hypotensive systolic blood pressure (<90 mmHg) episodes (9 vs 2 episodes;

| Table 1. | Characteristics, | Diagnoses, | and Procedure | e Details of Patient | s Receiving Epidural | vs IV Analgesia after Minimally |
|-----------------------------|------------------|------------|---------------|----------------------|----------------------|---------------------------------|
| Invasive Colorectal Surgery | | | | | | |

| Variable | Epidural analgesia (n $=$ 38) | IV analgesia (n $=$ 41) | p Value |
|--|-------------------------------|-------------------------|---------|
| Age, y, median \pm SD | 60 ± 12 | 53 ± 14 | 0.50 |
| Sex, male/female | 20/18 | 26/15 | 0.51 |
| BMI, kg/m ² , median \pm SD | 29.4 ± 6.0 | 26.6 ± 6.0 | 0.07 |
| American Society of Anesthesiologists class, n (%) | | | 0.01* |
| II | 11 (29) | 29 (71) | |
| III | 27 (71) | 8 (20) | |
| IV | 0 (0) | 4 (9) | |
| Drain present, n (%) | 20 (53) | 24 (59) | 0.65 |
| Ostomy present, n (%) | 18 (47) | 13 (32) | 0.17 |
| Charlson Age Comorbidity Score, mean \pm SD | 2.2 ± 2.0 | 1.8 ± 1.6 | 0.51 |
| Diagnosis, n (%) | | | 0.96 |
| Colon cancer | 9 (24) | 12 (29) | |
| Rectal cancer | 15 (39) | 14 (34) | |
| Inflammatory bowel disease | 4 (11) | 4 (9) | |
| Diverticulitis | 8 (21) | 11 (27) | |
| Benign disease | 2 (5) | 0 (0) | |
| Procedure, n (%) | | | 0.50 |
| Right colectomy/ileocecal resection | 8 (21) | 8 (20) | |
| Left colectomy/sigmoid resection | 11 (29) | 11 (27) | |
| Low anterior resection/proctectomy | 13 (34) | 20 (49) | |
| Total/subtotal colectomy | 3 (8) | 1 (3) | |
| Abdominoperineal resection | 3 (8) | 1 (3) | |
| *6 : : 1 : : : : : : : : : : : : : : : : | | | |

*Statistical significance, p < 0.05.

p < 0.05) compared with the IA cohort. There was a total of 12 epidural complications, these included 10 episodes of failed epidural catheter insertion and 2 episodes of epidural catheter malpositioning, all of which were resolved with a second attempt at epidural catheter insertion.

Outcomes

Primary end point and postoperative outcomes are summarized in Table 3. EA and IA had an equivalent median LOS (EA: 4 ± 3 days vs IA: 4 ± 3 days; p > 0.05), median daily VAS score (EA: 2.4 ± 2.0 vs IA: 3.0 ± 2.0 ;

| Table 2. | Complications of Patient | s Receiving Epidural vs l | V Analgesia after | ^r Minimally Invasive | Colorectal Surgery |
|----------|--------------------------|---------------------------|-------------------|---------------------------------|--------------------|
|----------|--------------------------|---------------------------|-------------------|---------------------------------|--------------------|

| Complication | Epidural analgesia, n (%) (n = 38) | IV analgesia, n (%) (n = 41) | p Value |
|-----------------------------------|---------------------------------------|---------------------------------|---------|
| Surgical complications | 6 (16) | 3 (7) | 0.24 |
| Total postoperative complications | 16 (42) | 15 (37) | 0.62 |
| Ileus | 1 (3) | 3 (7) | 0.34 |
| Anastomotic leak | 1 (3) | 0 (0) | NA |
| Urinary tract infection | 0 (0) | 1 (2) | NA |
| Urinary retention | 4 (11) | 2 (5) | 0.34 |
| Paraplegia | 0 (0) | 0 (0) | NA |
| Headache | 5 (13) | 4 (10) | 0.63 |
| Wound infection | 1 (3) | 0 (0) | NA |
| Other | 1 (3) | 4 (10) | 0.19 |
| Readmission within 30 d | 3 (8) | 2 (5) | 0.58 |
| Hypotensive episodes | 9 (24) | 2 (5) | 0.02* |
| Epidural complications | 12 (32) | NA | NA |
| | | | |

*Statistical significance, p < 0.05.

NA, not applicable.

| Outcomes | Epidural analgesia (n $=$ 38) | IV analgesia (n = 41) | p Value* |
|--|-------------------------------|-----------------------|----------|
| Length of stay, d, median \pm SD | 4.0 ± 3.0 | 4.0 ± 3.0 | 0.37 |
| Visual Analogue Scale, median \pm SD | 2.4 ± 2.0 | 3.0 ± 2.0 | 0.56 |
| Overall Benefit of Analgesia Score, median \pm SD | 3.2 ± 2.0 | 3.2 ± 2.0 | 0.50 |
| Total narcotics (IV equivalent of morphine, mg), mean \pm SD | 147.5 ± 192.0 | 98.1 ± 112.0 | 0.16 |
| Postoperative recovery, d, median \pm SD | | | |
| Start of ambulation | 2.0 ± 1.0 | 2.0 ± 2.0 | 0.71 |
| Foley removal | 3.0 ± 2.0 | 2.0 ± 4.0 | 0.97 |
| Nasogastric tube removal | 1.0 ± 1.0 | 0.5 ± 1.0 | 0.90 |
| Flatus | 2.0 ± 1.0 | 2.0 ± 1.0 | 0.96 |
| Bowel movement | 2.0 ± 1.0 | 3.0 ± 2.0 | 0.62 |
| Oral diet | 2.0 ± 2.0 | 2.0 ± 1.0 | 0.17 |
| Start of per os pain medication | 2.0 ± 1.0 | 2.0 ± 1.0 | 0.30 |
| EA removal | 2.0 ± 1.0 | NA | NA |

Table 3. Postoperative Outcomes of Patients Receiving Epidural vs IV Analgesia after Minimally Invasive Colorectal Surgery

*Statistical significance, p < 0.05.

EA, epidural analgesia; NA, not applicable.

p > 0.05), median daily OBAS (EA: 3.2 ± 2.0 vs IA: 3.2 ± 2.0 ; p > 0.05), and an equivalent time to start PO diet (EA: 2.0 ± 2.0 days vs IA: 2.0 ± 1.0 days; p > 0.05). Pain was well controlled by both modalities, although there was a nonsignificant trend toward higher quality of life OBAS in the epidural group when it was continued beyond postoperative day 2 (Fig. 2). There was no significant difference between the 2 groups when comparing time of postoperative ambulation, time to Foley or nasogastric tube removal, and return of bowel function. The EA patients had a trend toward a higher total dose of narcotics (147.5 \pm 192.0 mg vs 98.1 \pm 112 mg; p > 0.05).

Table 4 summarizes the rate of postoperative side effects and costs of each treatment arm. There was no significant difference in the overall incidence of nausea/ vomiting, itching, sweating, chills, or dizziness between the EA and IA cohorts. Total hospital charges were prospectively tracked for each patient enrolled in the study. Total charges were stratified into pharmacy costs (which included opioid and medication costs) and operation and recovery costs (which included procedural costs). The EA and IA cohorts had equivalent total hospital charges (\$144,991 vs \$141,338; p > 0.05). There was a trend toward higher pharmacy costs in the group of patients that received EA intervention (\$16,458 vs \$13,782; p > 0.05).

DISCUSSION

Optimal pain control after CRS is crucial in reducing perioperative stress and enhancing postoperative recovery of patients. Prolonged neuronal blockade provided by EA has several recognized benefits, including a reduction in pain scores and faster return of bowel function after open colorectal resection.⁷ This benefit is not as clearly defined after MIS CRS. In fact, in this single-center, prospective, randomized controlled trial, we found no significant differences in LOS, pain scores, or patient quality of life with the use of EA compared with IA after MIS CRS. We also did not find any significant differences in postoperative outcomes and most postoperative complications. Finally, our analysis revealed a significant increase in hypotensive adverse events related to epidural use and a nonsignificant trend toward higher overall narcotic use and higher pharmacy costs with EA compared with IA. Our findings suggest that EA does not add any appreciable clinical benefits to MIS CRS done under ERAS principles.

We did not find any significant difference in our primary end point, LOS, between the EA and IA groups. This is in agreement with multiple earlier randomized trials.^{12,13,21} Those studies, however, were limited by their small sample size. Levy and colleagues²¹ reported a median hospital LOS of 3.7 days after epidural analgesia, significantly longer than that of PCA (2.8 days) (p <0.001). In addition, several other small randomized trials did not find any difference in LOS between EA vs IA.8,9 The EA benefits are proven in patients undergoing open procedures with large midline incisions where EA helps provide superior pain relief and reduction of cardiopulmonary complications.⁷ These benefits become less apparent in MIS CRS, where incisions are smaller and patients are less dependent on the efficacy of their pain control to facilitate their postoperative recovery. The effects of EA on LOS have also been studied outside of ERAS programs in 2 studies. A randomized trial of EA in laparoscopic CRS without an ERAS program revealed no difference in LOS and a second retrospective study based on

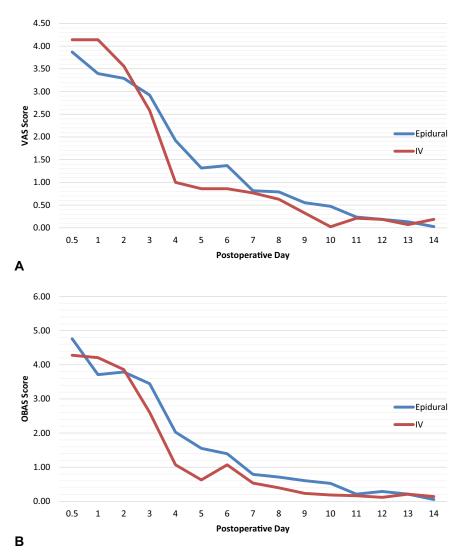


Figure 2. Postoperative pain and quality of life scores for epidural analgesia patients (blue line) and IV analgesia patients (red line), respectively, undergoing minimally invasive colorectal surgery. (A) Postoperative pain and (B) quality of life were assessed by the use of a Visual Analogue Scale (VAS) and Overall Benefit of Analgesia Score (OBAS) before operation, the evening after operation, and daily thereafter.

a trial database also revealed that laparoscopy was an independent predictive factor of early recovery, but that EA was not.^{22,23}

Our study found no difference in the efficacy of pain control with the use of EA in MIS CRS, median daily VAS score (EA: 2.4 ± 2.0 vs IA: 3.0 ± 2.0 ; p > 0.05), and median daily OBAS (EA: 3.2 ± 2.0 vs IA: 3.2 ± 2.0 ; p > 0.05). Some studies have suggested better pain control with the use of EA in MIS CRS,²² but other randomized trials have not.^{24,25} Most of these studies were limited by small samples and their results are hard to reconcile. There was no difference in the overall rate of postoperative complications between the 2 groups, however, EA had a higher incidence of hypotensive systolic blood pressure (<90 mmHg) episodes (9 vs 2 episodes; p < 0.05) compared with the IA cohort. This can be explained by the transitory hemodynamic instability due to sympathetic blockage experienced in EA patients.⁸ The higher incidence of hypotensive episodes seen in our study with EA suggest that the use of EA in MIS CRS patients might actually offset some of the inherent advantages of an MIS resection by requiring more hemodynamic monitoring and possibly longer ICU stays.^{5,7,12}

| Outcomes | Epidural analgesia (n = 38) | IV analgesia (n $=$ 41) | p Value* |
|-------------------------|-----------------------------|-------------------------|----------|
| Side effects, n (%) | | | |
| Nausea/vomiting | 12 (32) | 15 (36) | 0.81 |
| Itching | 19 (50) | 17 (41) | 0.50 |
| Sweating | 9 (24) | 10 (24) | 1.00 |
| Chills | 12 (32) | 13 (31) | 1.00 |
| Dizziness | 15 (40) | 18 (43) | 0.82 |
| Cost, \$, mean \pm SD | | | |
| Operation/recovery cost | $61,945 \pm 19,036$ | $62,149.12 \pm 18,870$ | 0.45 |
| Pharmacy cost | $16,458 \pm 12,521$ | $13,783 \pm 7,173$ | 0.27 |
| Total charges | $144,991 \pm 67,636$ | $141,339 \pm 75,579$ | 0.56 |

Table 4. Side Effects and Cost of Patients Receiving Epidural vs IV Analgesia after Minimally Invasive Colorectal Surgery

*Statistical significance, p < 0.05.

Our analysis is the first of its kind to compare the costeffectiveness of EA vs IA after MIS CRS. We found a trend with EA toward a higher total dose of narcotics $(147.5 \pm 192 \text{ mg vs } 98.1 \pm 112 \text{ mg; } p > 0.05)$ and higher pharmacy costs (\$16,458 vs \$13,782; p > 0.05). Similar findings were seen in a cost analysis by Tilleul and colleagues,²⁶ which revealed continuous wound analgesia and IV PCA to be significantly more cost-effective techniques of postoperative analgesia compared with EA after open abdominal operation. These findings again suggest that although EA was traditionally described as an essential component of an ERAS, it might not be as cost-effective as initially anticipated, especially in patients undergoing MIS CRS. In fact, these findings suggest other principles of ERAS (such as early PO intake, early mobility, and multimodal analgesia) are more essential after MIS CRS, and that forgoing EA can lead to a more cost-effective postsurgical recovery.²⁷⁻²⁹

Our study has several limitations. Randomization allowed both the EA and IA cohorts to be well-matched in terms of demographic characteristics and comorbidities. However, we failed to reach our recruitment targets, which were outlined previously in our power analysis. There might be some underlying differences in outcomes and complications that would have been better illustrated with a larger sample size. Despite this limitation, our patient cohort remains one of the largest randomized controlled trials evaluating EA conducted to date in MIS CRS. It is also important to concede that there is an inherent heterogeneity to the way EA is administered. Any varying combination of thoracic levels and combination and concentrations of medications can be used. This means that although EA administration was standardized in this trial, the findings of this type of EA intervention cannot be extrapolated to the heterogeneous nature of EA intervention out in nationwide clinic practice.

CONCLUSIONS

Our analysis suggests that EA has no added clinical benefit in patients after MIS CRS. We found a significant increase in hypotension events, and no significant benefit in LOS, effectiveness of pain control, or patient quality of life in patients who received EA. In addition, a trend toward higher total narcotics and costs with EA was seen that was not statistically significant. These findings suggest that EA is not an essential component of contemporary ERAS pathways in MIS CRS. Future research should focus on alternative methods, such as transverse abdominus fascial blocks, wound infiltration, systemic steroids, and systemic lidocaine,^{14,15} which might be more clinically beneficial and cost-effective.

Author Contributions

- Study conception and design: Rinehart, Sun, Carmichael, Mills, Stamos, Pigazzi
- Acquisition of data: Hanna, F Jafari, Phelan, Rinehart, Sun, Carmichael, Mills, Stamos, Pigazzi
- Analysis and interpretation of data: Hanna, MD Jafari, Phelan, Rinehart, Sun, Carmichael, Mills, Stamos, Pigazzi
- Drafting of manuscript: Hanna, MD Jafari, Phelan, Rinehart, Sun, Carmichael, Mills, Stamos, Pigazzi
- Critical revision: Hanna, MD Jafari, Phelan, Rinehart, Sun, Carmichael, Mills, Stamos, Pigazzi

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