



Case Report

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Epidural Analgesia after Gynecologic Oncology Surgery in the Era of Enhanced Recovery



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Abstract

Objective: To compare pain scores, opioid use, and frequency of complications in gynecologic oncology patients who received epidural analgesia versus those who did not.

Methods: Two hundred fifty-four patients who underwent laparotomy between 2011 and 2013 were included in this retrospective study. We compared demographics, details of surgery, length of hospitalization, complications, pain scores, and total systemic opioids used between the epidural and no epidural groups. Opioid use was reported in intravenous (IV) morphine equivalents.

Results: Demographic data were similar between the two groups. One hundred seventy-eight patients (70%) received an epidural. Reported mean pain scores were slightly lower during the first 24 hours for those with an epidural compared to those without (2.6+1.7 vs. 3.1+2.1, P=.0558). Patients with an epidural used significantly less systemic opioids in the first 24 hours after surgery (47.1+ 22.8 mg vs. 87.1+ 65.6 mg; P<.001). There were no differences in thirty-day complications (epidural group 39.9%, no-epidural group 35.5%; p=0.513), venous thrombo embolism (VTE) (3.0% vs 1.0%; P=.53) or length of hospital stay (5.7+ 4.4 vs. 6.3+ 5.9 days; P=.42).

Conclusion: Patients undergoing laparotomy in gynecologic oncology who received an epidural used half the amount of systemic opioids in the first 24 hours. There was no difference in post-operative complications, thrombo embolic events or hospital stay between the two groups. Pain scores were similar. Decreased systemic opioid use in the first 24 hours after surgery without an increase in complications may be an important step to facilitate goal attainment in enhanced surgical recovery pathways.

Keywords: Surgery; Epidural; Opioids; Enhanced Recovery

Introduction

Multiple peer-reviewed publications address the topic of postoperative pain control in gynecologic oncology surgery [1-7]. Because many of these surgeries require large laparotomy incisions, patients frequently receive intravenous opioids for pain control. Patient-controlled analgesia, or PCAs, are often used as the mechanism of delivery as they allow patients to deliver pain medications based on their perceived needs [4,5,8]. Intravenous opioids are associated with undesired side effects, including nausea, pruritus, hallucinations, and delay in return of bowel function, which may ultimately lead to prolonged hospitalization and extended recovery times.

Alternatively, epidural analgesia is a commonly used and well-studied method for pain control after major abdominal surgeries [2,4,9]. Epidural analgesia is administered by placing

a small gauge flexible catheter into the epidural space to provide continuous dosing of pain medications. The catheters are typically placed pre-operatively but not utilized until the surgery is completed. Occasionally, epidural catheters are placed post-operatively, if the laparotomy was unexpected or when post-operative pain control is sub-optimal. Medications introduced via the catheter into the epidural space may include a local anesthetic, an opioid, or both. Analgesia can then be optimized while balancing adverse effects, allowing for decreased sedation compared to intravenous opioids [3,5].

To date, studies evaluating epidural analgesia for postoperative pain in gynecologic surgery have shown inconsistent results. There are studies demonstrating the efficacy of epidural use during abdominal and pelvic surgery [4,9-11]. While one publication demonstrated that the analgesic

effect may be poor for women undergoing gynecologic surgery specifically [5]. In the latter study, those with an epidural were more likely to require supplemental IV opioids to achieve adequate pain control. A separate concern is the potential for reduced mobility when the epidural catheter is in place. Some patients experience a temporary decrease in lower extremity sensation after epidural placement, which could interfere with post-operative ambulation.

Reduced mobility is associated with an increased risk of venous thromboembolism (VTE) and may result in protracted urinary catheterization, with a subsequent increase in urinary tract infections (UTI) [2,4,12,13]. Prolonged catheterization, in particular, has become a quality metric and many hospitals emphasize early removal to reduce infection risk. There are other potential drawbacks to epidural analgesia specific to our patient population. It has known side effects that can be of particular concern in more complicated gynecologic oncology surgeries. For example, hypotension is a common side effect of epidural placement, and can be of serious consequence following bowel resection and reanastomosis [13,14].

“Hypotension can result in hypoperfusion to newly created staple lines..”, resulting in breakdown of these vulnerable areas. Although no published data report an increase in bowel leaks in patients who receive epidural analgesia; “...anecdotally, this is a common concern...” among gynecologic oncologists. The use of epidural analgesia varies from institution to institution and surgeon to surgeon. Currently, there are no standardized recommendations for the use of epidural analgesia in gynecologic oncology surgery, and its use is typically determined by surgeon’s preferences and hospital culture. In our institution, patients are almost uniformly offered epidurals for gynecologic oncology surgery, but many decline due to fear of additional needle sticks, nerve injury, or previous negative experiences with regional anesthesia.

This retrospective cohort study hopes to shed further light on the use of epidural analgesia for postoperative pain following gynecologic oncology surgery, particularly in the era of enhanced recovery pathways. Enhanced recovery pathways are quickly gaining traction in gynecologic oncology [15,16], but the role of epidural analgesia as part of these pathways is unknown. We hypothesize that patients receiving epidural analgesia used less systemic opioids compared to patients not receiving epidural analgesia. We evaluated retrospectively collected data collected on patients that underwent gynecologic oncology surgeries and had or did not have an epidural placed for postoperative pain control at a single institution between 2011 and 2013.

Materials and Methods

This retrospective cohort study was approved by the University of Wisconsin Institutional Review Board. All patients over the age of 18 who underwent laparotomy performed by a gynecologic oncologist between October 2011 and February

2013 were included in the initial chart review. Pfannenstiel and midline vertical skin incisions were included. Vaginal, laparoscopic, robotic or single port surgeries were excluded, unless these surgeries were converted to open laparotomies. Eligible patients were identified using ICD 9 codes for the most common gynecologic oncology procedures performed at our institution (including exploratory laparotomy, total abdominal hysterectomy, lymphadenectomy, bowel resection, omentectomy and bowel resection). Demographics, details of surgery, body mass index (BMI), length of hospital stay, complication rates, pain scores, and systemic opioid use were compared between the epidural and no-epidural groups.

Three investigators reviewed the data independently to ensure data integrity. Surgeries were labeled “extensive” if they included a bowel resection, splenectomy, or lymph node dissection. All opioid dosages were converted into intravenous (IV) morphine equivalents. Total opioid use included medications administered in the operating room, PACU, and during the patients’ post-operative hospital admission. Opioids given via the epidural catheter were included. Pain scores were collected using a Visual Analog Scale (VAS) and Brief Pain Inventory (BPI) pain scores, recorded three times a day and averaged over a 24-hour period. Charts were reviewed for a history of pre-existing pain syndromes, such as fibromyalgia, chronic back pain, endometriosis, or any chronic opioid use, which the investigators felt may be relevant to post-operative opioid use. All covariates were identified a priori. Postoperative complications were recorded, including hospital readmission within the first 30 days after surgery, wound complications, UTIs and postoperative VTE (including both DVT and pulmonary embolism (PE)).

Differences in the frequency distributions of baseline covariates by epidural usage were compared via Chi-square test for categorical variables and a t-test for continuous variables. Covariates considered for all statistical approaches included age, body mass index (BMI), diagnosis, length of hospital stay, complications, pain score, day of discharge and epidural usage. The frequency of complication rates between patients who used epidurals were compared to those patients who declined or were ineligible for epidural placement. The outcome variable was total dosage of systemic opioids used in the first twenty-four hours (reported in IV morphine equivalents) and our main predictor of interest was epidural use.

A multivariable linear regression was performed to determine if any of the covariates were associated with the total opioid equivalents used in the first 24 hours. The analytic strategy for selecting the final model was to investigate each predictor to the outcome through a univariate analysis process. After gaining some inferences from the univariate analysis, interactions among the predictors were checked before proceeding to fit a full model. Since the interaction terms were not significant, our main effect model was used as our final model. In addition, the variables that failed to reach significance

at the alpha level of 0.05 were left out of the main effect model. Data analysis was performed using the Stata Statistical Software: Release 14 (College Station, TX: Stata Corp LP).

Results

Three hundred fifty charts were reviewed based on ICD-9 codes. Two hundred fifty four patients ultimately met our inclusion criteria and had post-operative data available for analysis. Demographic data are presented in Table 1. One hundred seventy-eight patients (70%) received an epidural. The epidural remained in place for an average of 1.6 days. There were no significant differences between patients in the epidural and non-epidural groups with respect to age, BMI, cancer diagnosis and complexity of surgery. The mean age of all subjects included in this study was 58.3 years (range 18-90). The mean BMI was 31.6 mg/kg² (range 16.3-61.9). The majority of surgeries (247/254) were performed using a midline vertical incision, the remaining were Pfannenstiel incisions. One hundred eighty-nine patients (74.4%) ultimately had a cancer diagnosis on final pathology. One hundred and nineteen patients (46.9%) underwent an extensive surgery, as described in the methods section. No deaths were reported during the study period, and no patients were lost to follow-up in the 30 days following hospital admission.

Table 1: Patient Characteristics.

Factor	Epidural N=178	No Epidural N=76	P-value
Age (mean)	58	58.9	0.62
BMI (mean)	31.8	31	0.49
Type of Incision			
Midline Vertical	173	74	0.94
Pfannenstiel	5	2	0.23
Diagnosis			
Benign	47	18	0.65
Malignant	131	58	0.14
Chronic Pain Syndrome			
Yes:	31	9	0.32
No:	140	61	
Anxiety or Depression			
Yes:	50	17	0.44
No:	121	53	

Pain was measured both by patient’s subjective experience and total systemic opioid use. In the first 24 hours, reported mean pain scores were slightly lower for those with an epidural compared to no epidural (2.6+1.7 vs. 3.1+2.1, P=.0558) (Figure 1). Mean pain scores were not significantly different in the last 24 hours of hospitalization (2.2+1.53 vs 2.3+2.0, P=.69). The difference in mean pain scores from their first 24 hours and last 24 hours also demonstrated no statistical significance

(0.39+2.0x vs 0.77+2.1, P=.17). Patients in the epidural group used nearly half the amount of systemic opioids in the first 24 hours after surgery compared to patients who did not have an epidural (47.1+22.8 mg vs. 87.1+ 65.6 mg; P<.001) (Figure 2).

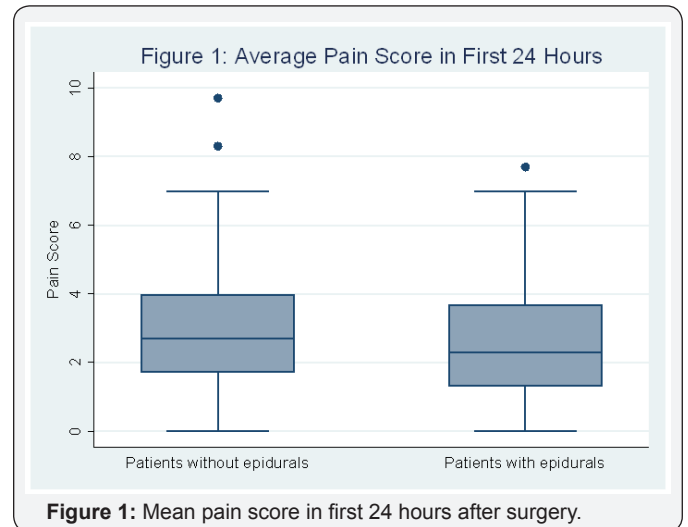


Figure 1: Mean pain score in first 24 hours after surgery.

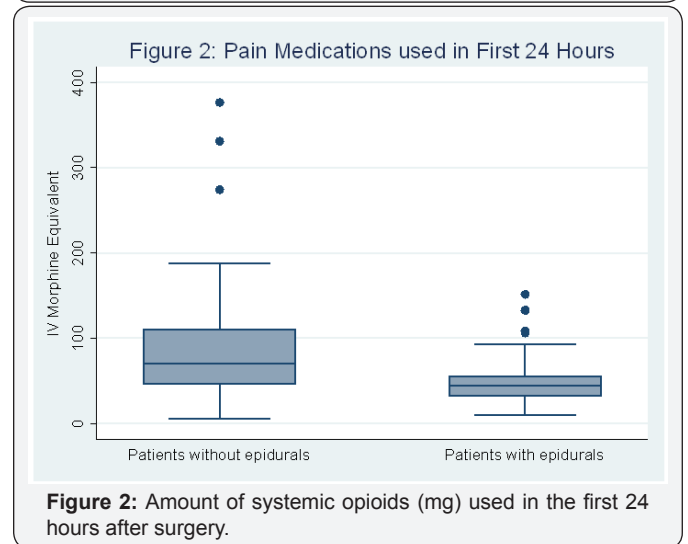


Figure 2: Amount of systemic opioids (mg) used in the first 24 hours after surgery.

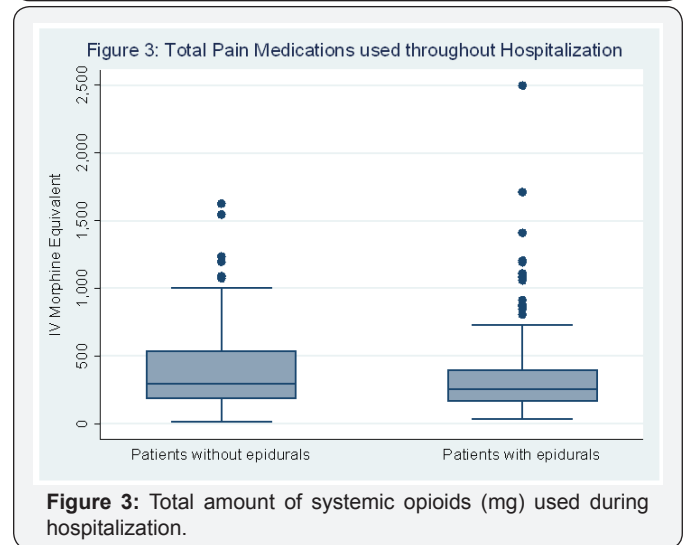
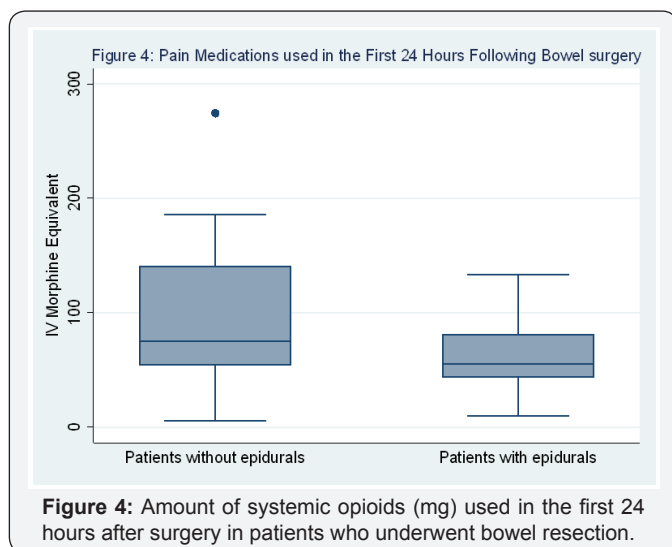


Figure 3: Total amount of systemic opioids (mg) used during hospitalization.



Over the course of their hospitalization, there was no statistical difference in total systemic opioid use in the two groups (343+308.3 mg vs 408+349.9 mg, $P=.14$) (Figure 3). Epidural catheters were left in place an average of 1.6 days. Twenty-eight patients underwent bowel resection with either reanastomosis or ostomy formation and had an epidural for postoperative pain, compared to 12 patients who underwent bowel surgery without an epidural. Use of epidural analgesia significantly reduced use of systemic opioids used in the first 24 hours in this subgroup (61.6+29.5 mg vs 98.6+75.5 mg, $P=.03$) (Figure 4). There was no increase in complications in patients who underwent bowel surgery and had an epidural placed. Although this subgroup is too small to make useful comparisons, no bowel leaks or anastomotic breakdowns were reported in the epidural group.

The presence of a pre-existing pain syndrome did not affect systemic opioid use in the first 24 hours in either group. Patients with a pain syndrome used a mean of 57.6 mg of IV morphine equivalents compared to those without a pain syndrome who used a mean of 58.2 mg ($P=.94$). However, those using an epidural who had a pain syndrome used less systemic opioids throughout the hospitalization (343.4+308.3 mg vs 408.2+349.9 mg, $P=.14$), although this difference was not statistically significant. There was no difference in mean length of hospital stay between those in the epidural group and no-epidural group (5.7+4.4 vs 6.25+5.9 days, $P=.42$). There were no differences in postoperative complications (epidural group 39.9%, no-epidural group 35.5%; $P=.51$). Rates of VTE were examined separately and were similar in both groups (epidural group, 3%; no-epidural group, 1%, $P=.53$).

Discussion

We found that patients who received an epidural used fewer opioids, reported similar pain scores and did not have an increase in post-operative complications. These results would be

generalizable to adult populations undergoing laparotomy that includes complicated pelvic and upper abdominal procedures. Patients receiving epidural analgesia did not have delays in ambulation, but were more likely to experience episodes of hypotension, resulting in fluid boluses. "Euvolemia is a critical part of enhanced recovery pathways, and it appears that epidural anesthesia may Post-operative pain control in gynecologic oncology..." has evolved considerably in the last several years. Enhanced Recovery After Surgery (ERAS) pathways have been widely embraced, largely due to excellent data in the colorectal surgery literature [13,17,18].

ERAS focuses on early ambulation, Foley catheter removal, and limited intravenous opioids. The role of epidural analgesia within enhanced recovery pathways is poorly understood. We are attempting to examine the potential benefits of epidural analgesia when used in combination with ERAS with a prospective randomized controlled trial currently accruing at our institution (NCT02423876). In this study, all patients participate in ERAS after gynecologic surgery. Subjects are randomized to either receive an epidural or not, in addition to standard ERAS. Our primary outcome is mean pain score in the first 24 hours after surgery.

Until the role of epidural analgesia as part of ERAS is clarified, one must consider the known benefits of epidurals, particularly in reducing opioid needs in the first 24 hours after surgery. Fewer opioids translate into less nausea and vomiting and earlier return of bowel function, which has been confirmed in multiple publications both in the gynecology and colorectal literature [6,10,11,15]. Improved pain control also leads to early, sustained ambulation. We believe that epidural analgesia may add additional benefit to ERAS. The complications of epidural analgesia most commonly feared based on anecdotal evidence, specifically an increase in infection rates, VTE, and extended hospital stay, were not seen in this retrospective review.

Additional benefits of regional analgesia and anesthesia have been studied in non-gynecologic cancers. The breast cancer literature has numerous publications supporting that neuro-axial blockade (most commonly, para-vertebral blocks) improves cancer outcomes [19,20]. The mechanisms behind this are not fully understood, but may be related to a decrease in inflammation and/or decreased systemic opioid use. Many neoplasms contain opioid receptors [21-23]. Intuitively, decreasing opioids may be beneficial from a cancer standpoint. The benefits of epidural analgesia may ultimately extend far beyond improved pain control.

The strengths of our study are the inclusiveness of a variety of gynecologic surgeries, including extensive oncologic resections, performed primarily through midline vertical skin incisions. A total of six surgeons were involved in the procedures described and the data were abstracted and reviewed by three independent parties. The weaknesses of our study are its retrospective design and relatively homogenous patient population. Also,

the medications given to both groups of patients were in no way standardized. The use of non-opioid pain relievers (non-steroidal anti-inflammatory agents, acetaminophen) was not reported nor standardized between the two groups. Patients who did not receive an epidural either were ineligible due to medical contraindications, declined to have one placed, or the surgeon was opposed to epidural placement. This introduces potential selection bias in the epidural group.

Conclusion

In conclusion, patients undergoing laparotomy for gynecologic oncology indications who received an epidural used less systemic opioids in the first 24 hours after surgery. Patients who received epidurals had similar rates of postoperative complications, thromboembolic events, and length of hospital stay when compared with those who did not. Pain scores were similar in both groups. Decreased systemic opioid use in the first 24 hours after surgery without an increase in complications may be an important step in facilitating goal attainment in enhanced surgical recovery pathways.

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