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Continuous epidural infusion in gynecologic oncology patients undergoing exploratory laparotomy: The new standard for decreased postoperative pain and opioid use☆,☆☆

Sarah P. Huepenbecker [a], Sarah E. Cusworth [a], Lindsay M. Kuroki [b], Patricia Lu [c], Christelle D.K. Samen [c], Candice Woolfolk [a], Rosa Deterding [a], Leping Wan [a], Daniel L. Helsten [d], Michael Bottros [d], David G. Mutch [b], Matthew A. Powell [b], Leslie S. Massad [b], Premal H. Thaker [b,*]

[a] *Department of Obstetrics and Gynecology, Washington University, St. Louis, MO, United States of America*
[b] *Division of Gynecologic Oncology, Washington University, St. Louis, MO, United States of America*
[c] *Washington University School of Medicine, St. Louis, MO, United States of America*
[d] *Department of Anesthesiology, Washington University, St. Louis, MO, United States of America*

HIGHLIGHTS

- Perioperative epidurals decrease postoperative pain.
- Perioperative epidurals may decrease narcotic use and increase use of non-narcotic pain medications.
- Perioperative epidurals increase the risk of postoperative urinary retention and hypotension.
- Perioperative epidurals do not increase risk of venous thromboembolism.
- Perioperative epidurals may decrease incidence of postoperative wound infection.

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ABSTRACT

Objective. To compare the incidence of postoperative complications and opioid pain medication usage in gynecologic oncology patients who did and did not receive an epidural prior to undergoing exploratory laparotomy.

Methods. Retrospective cohort study of all patients undergoing exploratory laparotomy with the gynecologic oncology division at Washington University in St Louis between January 2012 and October 2015. Data on demographics, pathology, postoperative pain and opioid use, and incidence of postoperative complications were collected.

Results. Five hundred and sixty-one patients underwent laparotomy, 305 with an epidural and 256 without. Patients with an epidural used significantly less hydromorphone in the post-anesthesia care unit (PACU) ($p = 0.003$) and on postoperative day (POD)#1 ($p = 0.05$), less total opioids on POD#0 ($p < 0.01$), and more non-opioid pain medication on POD#1–3 ($p < 0.01$). Patients with an epidural had lower pain scores in the PACU ($p = 0.01$), on POD#0 ($p < 0.01$), POD#1 ($p < 0.01$), and POD#3 ($p = 0.03$). Patients with epidurals had shorter hospital length of stay ($p < 0.01$), no difference in hospital readmission or incidence of venous thromboembolism up to 90 days postoperatively, longer duration of Foley catheter (20.4 vs 10.3 h, $p = 0.02$) with no difference in postoperative urinary tract infection, higher incidence of postoperative hypotension (63% vs 36.3%, $p < 0.01$), and lower incidence of wound complications (5% vs 14.1%, $p < 0.01$).

Conclusions. Perioperative epidurals used in patients undergoing major abdominal surgery correlate with decreased postoperative opioid use, increased use of non-opioid pain medications, and improved pain relief postoperatively with acceptable postoperative risks and should be standard of care for these patients.

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* Corresponding author at: Washington University in St. Louis/Barnes Jewish Hospital, 660 South Euclid Avenue, Mail Stop 8064-37-905, St. Louis, MO 63110, United States of America.
E-mail address: thakerp@wustl.edu (P.H. Thaker).

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1. Introduction

In the United States, drug overdose deaths are a major public health concern. The dramatic rise in opioid prescribing in the United States is one driver of this epidemic [1], as postoperative opioid prescriptions contribute to new and prolonged opioid use [2,3]. There is good evidence that over-prescription has been commonplace, partially due to a lack of data regarding the appropriate dose of opioids to prescribe after common procedures [4]. After hysterectomy, a wide range of physician prescribing practices exists despite the fact that most patients use fewer than half of their prescribed opioid medications [5,6]. Newer studies have explored strategies to reduce the number and duration of postoperative opioids prescribed [7–9], but better strategies to improve non-opioid postoperative pain control are needed.

Perioperative epidural anesthesia has become an important aspect of enhanced recovery after surgery (ERAS) protocols based on studies in surgical literature demonstrating a significant decrease in postoperative pain in patients who received a perioperative epidural compared to those who relied on patient-controlled analgesia with intravenous opioids alone [10–14]. Although the data on epidural use and postoperative pain control in the gynecologic oncology population was initially mixed [15–17], it has more recently been shown to be an important intervention that can decrease postoperative opioid use in this population [18,19]. Because of this, perioperative epidural anesthesia has been proposed as a tool to address the opioid epidemic in gynecologic oncology patients [18,20,21].

Although epidural anesthesia provides excellent pain control for many operations, the side effects are not inconsequential, including risks of hypotension, urinary retention, and postoperative venous thromboembolism (VTE), with some studies suggesting that the postoperative risks may be higher in the gynecologic oncology cohort than in general surgery patients [18,22–26]. Given the conflicting data regarding pain control and risk of side effects with perioperative epidurals, this study's primary aim was to determine if there is an increased risk of VTE in patients with gynecologic cancer undergoing exploratory laparotomy who receive a perioperative epidural compared to those who do not have an epidural, and our secondary aims were to compare postoperative pain scores and opioid use in patients with and without epidurals. Our null hypothesis was that there would not be a change in VTE between groups, but that patients with an epidural would have lower immediate postoperative pain scores and opioid use.

2. Materials and methods

This was a retrospective chart review approved by the Institutional Review Board at Washington University in St Louis (ID#201602001). We included women who underwent laparotomy with the gynecologic oncology division for known or suspected malignancy between January 2012 and October 2015. This interval was selected to bracket the introduction of epidural anesthesia in 2013 and allowed assessment of two study cohorts with comparable numbers of patients in each group: cases operated in 2012–13 who did not have epidural catheters and those from 2013-15 who did. Patients were excluded if they had a history of deep vein thrombosis or pulmonary embolism (PE) or were <18 years old. No a priori or post hoc power calculation was performed given that the study was retrospective and all patients were included in analysis. Patient consent was waived given the retrospective nature of the study with low concern for patient harm.

All planned laparotomies were offered epidural analgesia after ERAS implementation in 2013. Pre-operative low thoracic level epidurals were placed by a dedicated anesthesia team. Our ERAS protocol mandated intraoperative fluid and glucose management but did not specify intraoperative anesthetics and data was not collected on intraoperative epidural use by the anesthesia team. Postoperatively, the epidural group received epidural 0.1% bupivacaine at an initial rate of 6 ml/hour through an indwelling catheter. The epidural was maintained postoperatively and managed primarily by the anesthesia acute pain service who saw the patient daily. The epidural was titrated to ensure adequate pain control and minimize side effects including hypotension. The anesthesia acute pain service determined the duration of the epidural therapy, which was stopped once adequate pain control had been be achieved with non-parenteral agents. All participants received standardized postoperative care according to a protocol for ERAS; deviations were recorded. Pneumatic compression devices were placed preoperatively and continued until discharge. Enoxaparin was begun once postoperative hemorrhage had been excluded unless comorbidities required an alternate anticoagulant and was continued for 14 days. Early ambulation and rapid diet advancement were encouraged. Until tolerating a regular diet, patients received on-demand intravenous hydromorphone via a patient-controlled analgesia (PCA) device, which was discontinued once patients tolerated oral medications. IV PCA was part of our pre-ERAS post-operative protocol and was kept in place because faculty were uncomfortable deferring PCA to patients who had failed oral analgesia until we became familiar with the success of the protocol. Patients also received 15–30 mg intravenous (IV) ketorolac every 8 h for the first two days postoperatively either PRN (prior to 2013) or scheduled (after implementation of ERAS protocol in 2013) followed by scheduled oral (PO) ibuprofen and gabapentin unless contraindicated by renal insufficiency, allergy, or other factors. These were supplemented by as needed acetaminophen (IV or PO), which was first line for pain, and oxycodone, which was second line for pain. Women with allergies to these medications received IV morphine, IV fentanyl, or PO hydrocodone as indicated. All patient received the same orders for post-operative pain medications and the same discharge prescriptions regardless of pain medication use while inpatient. Foley catheters were routinely removed on postoperative day 1 after surgery and replaced if the patient failed a void trial or had evidence of urinary retention based on ultrasound bladder scan.

Data was collected from the electronic medical record (Compass and MetaVision) and recorded in RedCap, a secure web application for building and managing online data. Data collection included demographic and clinical information including age, BMI, smoking status, medical comorbidities, American Society of Anesthesiologist (ASA) score as assigned by the surgical attending anesthesiologist, surgical pathology and surgical stage (if applicable). Data from the operation including procedures (hysterectomy, bilateral salpingectomy or salpingo-oophorectomy, lymph node dissection, omentectomy, bowel resection, and other tumor debulking), operative time, intraoperative hypotension requiring vasopressor administration by the anesthesia team, and incision type were collected. Post-anesthesia care unit (PACU) medication administration was obtained from MetaVision (iMDsoft, Wakefield, MA) for 549 patients and postoperative medication administration of PO acetaminophen, IV hydromorphone, PO ibuprofen, IV ketorolac, PO oxycodone, IV morphine, PO hydrocodone, and total opioid use by postoperative day was obtained from inpatient records for 558 patients. Total opioid use was calculated in PO morphine equivalents using conversion factors of 1.5× for PO hydrocodone, 20× for IV hydromorphone, 3× for IV morphine, and 1.5× for oxycodone, respectively, as defined by the Stanford Medicine Palliative Care Equivalency Table [27]. PACU and postoperative pain scores were assessed using a Likert scale of 0–10 as recorded in inpatient records. Postoperative outcomes collected included hypotension, Foley catheter duration in hours, urinary tract infection (UTI), venous thromboembolic events up to 90 days postoperatively, ileus, wound complications, hospital length of stay, and readmission within 30 days and between 30 and 90 days. The number of readmissions for each group was recorded, although reasons for readmission were not captured. Postoperative hypotension was defined as any systolic blood pressure <90 or diastolic blood pressure <50 during the patient's postoperative course, including after the epidural was removed. UTI was defined by symptoms with a positive urine culture. Venous thrombotic events included deep vein thrombosis as assessed via Doppler ultrasound and/or PE confirmed by radiography; superficial thrombi were not included. Wound complications were defined as cellulitis, wound infection, wound separation, necrotizing fasciitis, or fascial dehiscence.

Data analysis was performed using SAS software. Descriptive statistics were used to summarize demographic and clinical characteristics and to compare groups. Statistics for continuous variables were analyzed using either medians with interquartile ranges or means with standard deviations. Qualitative variables were summarized by counts and percentages. Bivariate analyses were conducted using Pearson's chi-square or Fisher's exact tests as appropriate. Student's t-tests or Mann-Whitney U tests were used for continuous variables as appropriate. No multi-variable analysis was performed, as there were no obvious confounders in our demographic and clinical data to adjust for. A p-value of ≤0.05 was considered significant.

3. Results

Of 561 women, 305 (54%) received perioperative epidural anesthesia and 256 (46%) did not. Of the 361 patients who underwent laparotomy after ERAS implementation in 2013, 62 (17%) declined preoperative thoracic epidural placement and were evaluated in the no epidural group, although their reasons for refusal were not documented. Patient demographics are presented in Table 1. The patients in the two groups did not differ significantly in age, race, BMI, medical comorbidities, prior abdominal surgery, smoking status, or ASA score. Women in the epidural group had significantly higher rates of ovarian and other/mixed cancer, while those in the non-epidural group had significantly higher rates of endometrial cancer and benign histology. The epidural group had a higher rate of stage III/IV cancer and a lower rate of stage I cancer compared to the no epidural group. There were no differences between patient groups in estimated blood loss or intraoperative IV crystalloid replacement, but patients who received an epidural had longer operative times and more intraoperative hypotension requiring vasopressor administration than patients without epidurals (75.7 vs 49.6%, $p < 0.01$).

Compared to those without epidurals, women who had epidurals had lower pain scores in PACU and on postoperative days 0, 1, and 3 (Table 2). Patients with epidurals used less hydromorphone in the PACU compared to patients without epidurals (1.3 vs 2.0 mg, $p < 0.01$). There were no differences in use of morphine, fentanyl, or meperidine, since these medications were uncommonly used; a subanalysis was not performed. Patients in the epidural group used less opioid analgesia on postoperative day 0 (10.0 vs 25.0 PO morphine equivalents, $p < 0.01$) and less hydromorphone on postoperative day 1 (3.8 vs 5.0 mg, $p = 0.05$) (Table 2). Patients with epidurals used more of selected non-opioid pain medications, including more acetaminophen on postoperative days 1–3 and more ibuprofen on postoperative day 3 (Table 2). There were no differences between groups in the use of IV ketorolac or PO oxycodone postoperatively. Too few patients received postoperative PO hydrocodone or IV morphine to compare across groups as a continuous variable.

Almost all patients (n = 489, 98.6%) received postoperative anticoagulation, with most given prophylactic enoxaparin (n = 475, 94.7%); there was no difference in use of anticoagulation between women who did and did not have epidurals (Table 3). Most began anticoagulation on either postoperative day 0 (46.6%) or postoperative day 1 (47.9%). In the epidural group, mean duration of epidural was 2.8 ± 1.4 days. Overall, 5.2% of our cohort developed a VTE within 30 days of operation. These included 2 patients with upper extremity DVTs, 9 with lower extremity DVTs, and 21 with PE. VTE was diagnosed in 4 women (0.7%) in our cohort between 30 and 90 days postoperatively including 1 patient with an upper extremity DVT, 1 with a lower extremity DVT, and 2 with PEs. There were no differences between groups in receipt of postoperative anticoagulation, development of VTE <30 days or 30–90 days postoperatively, or being readmitted to the hospital <30 days or between 30 and 90 days postoperatively (Table 3). Although patients who received epidurals kept Foley catheters longer than patients without epidurals (23 vs 22 h, $p = 0.03$) and had higher rate of Foley replacement (47 [15.4%] vs 29 [11.3%] patients, $p = 0.01$), there was no difference in the frequency of UTIs between groups, with UTIs in only 18 (6.3%) women postoperatively. Patients with epidurals had higher rates of postoperative hypotension than those without epidurals (192 [63%] vs 93 [36.3%] patients, $p < 0.01$). Rates of postoperative ileus did not differ between groups. The no epidural group had a higher rate of postoperative wound complications than the epidural group (14.1 vs 5%, $p < 0.01$). Patients in the epidural group had a shorter hospital length of stay ($p < 0.01$), and there was no difference in readmission rates within 30 days or between 30 and 90 days postoperatively (Table 3).

Table 1
Patient demographic and clinical characteristics.

	Epidural (N = 305)	No epidural (N = 256)	p-Value
Age, years (mean ± SD)	59.34 ± 13.3	58.84 ± 13.4	0.63
Race			0.38
White	240 (78.7)	211 (82.4)	
Non-white	65 (11.6)	45 (17.6)	
Black	54 (17.7)	40 (15.6)	
Other	11 (3.6)	5 (2.0)	
Body mass index (kg/m^2)[a]	29.1 (25.0–35.0)	31.0 (26.0–37.1)	0.11
Disease pathology[b]			**<0.01**
Ovarian/fallopian/peritoneal	144 (47.2)	90 (35.2)	**<0.01**
Endometrial cancer	112 (36.7)	117 (45.7)	**0.03**
Cervical cancer	15 (4.9)	14 (5.5)	0.77
Other/mixed	17 (5.6)	3 (1.2)	**<0.01**
Benign	21 (6.9)	35 (13.7)	**0.01**
None	1 (0.3)	1 (0.4)	0.90
Disease histology			0.91
Serous	88 (28.9)	52 (20.3)	
Mucinous	5 (1.6)	2 (0.8)	
Endometrioid	9 (3.0)	8 (3.1)	
Carcinosarcoma/MMMT	5 (1.6)	3 (1.2)	
Other/mixed	37 (12.1)	25 (9.8)	
Disease stage			**<0.01**
I	87 (28.5)	114 (44.5)	**<0.01**
II	18 (5.9)	20 (7.8)	0.37
III	106 (34.8)	62 (24.2)	**<0.01**
IV	53 (17.4)	27 (10.6)	**0.02**
Comorbidities			
Diabetes	65 (21.3)	56 (21.9)	0.87
Hypertension	154 (50.5)	133 (52.0)	0.73
Pulmonary disease	45 (14.8)	38 (14.8)	0.98
Congestive heart failure	27 (8.9)	14 (5.5)	0.13
Coronary artery disease	41 (13.4)	25 (9.8)	0.18
Thyroid disease	44 (14.4)	25 (9.8)	0.09
Chronic kidney disease	14 (4.6)	15 (5.9)	0.50
Prior abdominal surgery	199 (65.3)	175 (68.4)	0.45
Smoker			0.13
Current	46 (15.1)	35 (13.7)	
Former	83 (27.2)	53 (20.7)	
Never	176 (57.7)	168 (65.6)	
ASA score	2 (2–3)	2 (2–3)	0.64
Operative time (minutes)	167.0 (140.0–212.0)	159.0 (132.0–198.5)	**0.02**
Estimated blood loss (milliliters)	300.0 (200.0–500.0)	300.0 (200.0–500.0)	0.82
Intraoperative hypotension requiring pressors	231 (75.7)	127 (49.6)	**<0.01**
Intraoperative crystalloid (milliliters)	3611.0 (3010.0–4397.0)	3285.5 (2800.0–4205.0)	0.08

N = number of patients, overall percentage of patients unless otherwise specified.
SD = standard deviation, ASA = American Society of Anesthesiologists.
Bold values statistically significant result with p<0.05.
[a] Median, Range.
[b] Total number of patients = 310 in the epidural group and 260 in the no epidural group because 5 patients and 4 patients in each group, respectively, had concomitant cancers.

Table 2
Post-anesthesia care unit and postoperative pain medication use.

	Epidural (N = 305)	No epidural (N = 256)	p-Value
PACU opioid use			
Morphine use (mg)[a]	–	0.30 (±2.2)	–
Hydromorphone use (mg)	1.3 (0.8–2.1)	2.0 (1.4–2.6)	**<0.01**
Fentanyl use (mcg)	250.0 (250.0,-00.0)	250 (200.0–350.0)	0.51
Meperidine use (mg)[a]	12.5 (±0)	–	–
Acetaminophen use (mg)			
POD 0	1000.0 (1000.0–1000.0)	1000.0 (1000.0–1000.0)	0.22
POD 1	3000.0 (2000.0–3650.0)	1625.0 (975.0–2000.0)	**<0.01**
POD 2	2550.0 (1650.0–3000.0)	1950.0 (975.0–2600.0)	**<0.01**
POD 3	2000.0 (1300.0–3000.0)	1300.0 (650.0–2275.0)	**<0.01**
Hydromorphone use (mg)			
POD 0	1.5 (0.75–2.5)	1.8 (0.75–3.0)	0.22
POD 1	3.8 (2.0–6.8)	5.0 (2.0–8.5)	**0.05**
POD 2	3.0 (1.5–6.5)	3.3 (1.5–6.3)	0.90
POD 3	3.0 (1.0–5.8)	2.9 (1.3–6.6)	0.67
Ibuprofen use (mg)			
POD 0	–	–	–
POD 1	600.0 (600.0–600.0)	600.0 (600.0–800.0)	0.38
POD 2	1200.0 (600.0–1200.0)	1200.0 (600.0–1200.0)	0.55
POD 3	1200.0 (600.0–1200.0)	600.0 (600.0–1200.0)	**<0.01**
IV Ketorolac use (mg)			
POD 0	15.0 (15.0–30.0)	30.0 (15.0–30.0)	0.26
POD 1	45.0 (30.0–60.0)	45.0 (30.0–60.0)	0.72
POD 2	30.0 (15.0–60.0)	30.0 (30.0–60.0)	0.47
POD 3	30.0 (30.0–45.0)	30.0 (30.0–40.0)	0.54
PO Oxycodone use (mg)			
POD 0	–	–	–
POD 1	20.0 (10.0–30.0)	20.0 (10.0–30.0)	0.64
POD 2	30.0 (20.0–40.0)	25.0 (10.0–40.0)	0.34
POD 3	25.0 (10.0–40.0)	20.0 (10.0–30.0)	0.44
Total opioid use[b]			
POD 0	10.0 (0.0–35.0)	25.0 (10.0–55.0)	**<0.01**
POD 1	90.0 (50.0–155.0)	105.0 (50.0–180.0)	0.15
POD 2	60.0 (30.0–90.0)	52.5 (15.0–90.0)	0.16
POD 3	30.0 (6.3–60.0)	30.0 (0.0–60.0)	0.21

Median, IQR provided unless otherwise specified.
SD = standard deviation, PACU = post-anesthesia care unit, POD = postoperative day.
Bold values statistically significant result with p<0.05.
[a] Mean ± SD.
[b] In PO morphine equivalents (PO hydrocodone 1.5×, IV hydromorphone 20×, IV morphine 3× conversion, and PO oxycodone 1.5× conversion factor, respectively).

Table 3
Postoperative outcomes.

	Epidural (N = 305)	No epidural (N = 256)	p-Value
Duration of epidural (days)	3.0 (2.0–3.0)	–	–
PACU pain score	3.0 (0.0–5.0)	4.0 (1.0–5.0)	**<0.01**
POD 0 pain score[a]	3.0 (1.0–5.0)	4.0 (2.0–6.0)	**<0.01**
POD 1 pain score[a]	3.0 (2.0–4.0)	4.0 (2.0–5.0)	**<0.01**
POD 2 pain score[a]	3.0 (1.0–4.0)	3.0 (1.0–5.0)	0.13
POD 3 pain score[a]	3.0 (1.0–4.0)	3.0 (1.0–6.0)	**0.03**
Postoperative hypotension[d]	192 (63.0)	93 (36.3)	**<0.01**
Duration of Foley catheter (hours)[a]	23.0 (20.0–41.0)	22.0 (19.0–26.0)	**0.03**
Foley replaced postoperatively	47 (15.4)	29 (11.3)	**0.01**
Postoperative urinary tract infection[c]	13 (4.3)	5 (2.0)	0.12
Postoperative ileus	21/182 (11.5)	29/200 (14.5)	0.39
Postoperative wound complication	9/179 (5.0)	25/177 (14.1)	**<0.01**
Postoperative anticoagulation[a]	261 (85.6)	228 (89.1)	0.34
Enoxaparin	255 (83.6)	220 (85.9)	
Other (Heparin, Xarelto, other)	6 (2.0)	8 (3.1)	
Venous thromboembolism <30 days[b]	16 (5.3)	13 (5.6)	0.93
Upper extremity DVT	2 (0.7)	0 (0.0)	
Lower extremity DVT	4 (1.3)	5 (2.0)	
Pulmonary embolism	12 (3.9)	9 (3.5)	
Venous thromboembolism 30–90 days	3 (1.0)	1 (0.4)	0.64
Upper extremity DVT	0 (0.0)	0 (0.0)	
Lower extremity DVT	1 (0.3)	0 (0.0)	
Pulmonary embolism	2 (0.3)	1 (0.4)	
Length of hospital stay (days)	4.0 (3.0–5.0)	4.0 (3.0–6.0)	**<0.01**
Readmission within 30 days after surgery	39 (12.8)	35 (13.7)	0.52
Readmission 30–90 days after surgery	30 (9.8)	28 (10.9)	0.50

Median, IQR provided unless otherwise specified.
SD = standard deviation, PACU = post-anesthesia care unit, POD = postoperative day, DVT = deep vein thrombosis.
Bold values statistically significant result with p<0.05.
[a] Mean ± SD.
[b] Venous thromboembolism <30 days was reported per person.
[c] Postoperative urinary tract infection as defined by a positive urine culture.
[d] Postoperative hypotension was defined as systolic blood pressure <90 or diastolic blood pressure <50.

4. Discussion

While ERAS strategies can decrease postoperative pain and opioid use, our study is the largest to specifically demonstrate that perioperative epidural use as part of an ERAS protocol both improves postoperative pain control and decreases postoperative opioid use in a gynecologic oncology population. Introduction of perioperative epidural anesthesia as part of an ERAS protocol at our institution correlated with decreased immediate postoperative opioid use, increased use of non-opioid pain medications, and improved pain relief postoperatively with acceptable postoperative risks.

The use of thoracic epidurals can decrease the use of some postoperative opioids, which presents a potential solution to the widespread postoperative overuse and over-prescription of opioids in the United States. Bergstrom et al recently demonstrated that the implementation of a standardized ERAS protocol utilizing an epidural decreased opioid use without increasing postoperative pain control or complication rates in gynecologic oncology patients undergoing elective laparotomy by comparing 109 ERAS program participants to 158 historical controls in the pre-ERAS implementation period [19]. An earlier study by Modesitt et al also demonstrated a decrease in postoperative morphine use in gynecologic patients undergoing surgery by utilizing an ERAS protocol [28]. Our study demonstrated significantly reduced total opioid use on postoperative day 0 and hydromorphone use on postoperative day 1, despite the fact that both patient populations were ordered for the same pain regimen with opioid pain medications available for use. There was a non-significant increase in total opioid use on POD#2 which coincided with the most common day of epidural removal, suggesting that pain control worsened without the effect of the thoracic epidural. Although oral oxycodone use and overall opioid use did not decline in our population, our patients did demonstrate increased utilization of non-opioid pain medications including acetaminophen and NSAIDs for pain control. As the risks of opioids and their associated morbidity and mortality are increasingly recognized, a shift toward non-opioid pain medications has been advocated in postoperative pain control [29–31]. Recent studies have demonstrated that decreased postoperative opioid use can translate into less opioid prescriptions upon discharge and that discharge prescriptions can be tailored based on postoperative inpatient opioid use [7–9]. Our study did not evaluate opioid prescriptions upon discharge since our patients commonly receive standard discharge prescriptions, although future investigations at our institution will examine these questions.

Improved postoperative pain control has additional benefits beyond patient comfort in other postoperative settings, including decreased time to recovery milestones and decreased length of hospital stay, which our results support [29]. For example, the shorter length of stay in the epidural group could be explained by a faster return to ambulation and faster return of bowel function as demonstrated in other studies examining ERAS protocols. While these outcomes have been demonstrated in multiple surgical modalities and are generally accepted as part of ERAS protocols, the gynecologic oncology population may warrant special and different consideration. This is reflected in specialty-specific guidelines regarding pain management in gynecologic oncology patients, in both postoperative and long-term situations [21]. As Lindemann et al pointed out, ovarian cancer patients undergoing surgical intervention have a different scope of surgery, nutritional status, operating times, and perioperative fluid shifts compared to many other surgical populations, and thus the standard ERAS protocols may not strictly apply to them [32]. These concerns may transfer into a lack of thoracic epidural use in clinical situations. In a survey of gynecologic oncologists in Australia, only 15% of respondents used a thoracic epidural compared to 73% who predominantly used an opioid-based PCA for postoperative pain control [33]. Despite these concerns and a lack of data in our populations, ERAS protocols generally and thoracic epidurals specifically are now recommended by gynecologic oncology guidelines as part of multimodal postoperative anesthetic care [11,34].

Our results demonstrate risks from epidurals similar to those seen in other studies, including the risk of intraoperative and postoperative hypotension and postoperative urinary retention [22,23]. While these risks are salient, they appear to be of marginal clinical importance and were outweighed by the benefits of improved pain control. Likewise, the clinical impact of longer Foley duration and higher risk of Foley replacement in our population did not translate into an increased risk of urinary tract infections, although this was an uncommon event in both groups and may be subject to statistical fragility or a true lack of clinical association. Importantly, the suggestion of increased risk of VTE in gynecologic oncology patients with a patient-controlled epidural anesthesia found by Courtney-Brooks et al [24] was not duplicated in our study. The population examined by Courtney-Brooks was smaller than our cohort, and our results are in line with other studies in the general surgery and colorectal literature which do not suggest an increased risk of VTE in perioperative epidural usage [25,26]. One major difference between our studies is that our postoperative patients standardly receive PCAs with IV opioids in addition to epidural anesthesia, whereas the Courtney-Brooks et al cohort did not typically receive a PCA unless postoperative pain control was inadequate. This may help explain why our population did not have a reduction in overall opioid use past postoperative day 0.

Our retrospective study has limitations. It was conducted at a single institution and thus may not reflect postoperative practices at other institutions. Epidurals were introduced at the same time as a standard ERAS protocol and a protocol to reduce surgical site infections. For this reason, some associations with outcomes such as wound complications may reflect other components of standardized care rather than epidural use. It is not possible to say definitively that the change in pain medication use was due to the use of epidurals alone rather than other components of the ERAS protocol, although this was the most significant piece of the protocol that specifically addressed pain control. The only other differences in our protocol were scheduled postoperative IV ketorolac (which was not different between groups), early ambulation, POD#1 void trial, and rapid diet advancement. Other ERAS bundles that do not use epidurals, but do incorporate non-epidural pain adjuncts such as transversus abdominus plane blocks or intrathecal morphine, have also been shown to decrease post-operative opioid use [20]. In future studies, it may be interesting to compare a comparison between our epidural-containing ERAS protocol and another institution's non-epidural ERAS protocol to see what exact role the epidural played in post-operative pain control. During the period of introduction of protocols, division staff strove to adhere to standards, but not all patients received identical care and we did not obtain data on compliance to ERAS protocol implementation. We took measures to maximize compliance to the ERAS bundle but could not control for patient refusal, logistics prohibiting epidural placement, and error, which are all present in real world practice. In addition, our study examined a mixed cohort of patients who underwent laparotomy for known or suspected gynecologic malignancy, and 10% did not have a gynecologic malignancy upon surgical pathology review. We also grouped all surgical stages together, despite the fact that procedures may vary widely based on stage and pathology. Lastly, while our retrospective cohort study allowed us to compare epidurals as an intervention with defined pre-intervention and post-intervention populations, it did not allow us to adjust for the potential impact of a dedicated anesthesia acute pain service (which was an inherent component to epidural placement and postoperative care after 2013), nor other potential individual patient factors such as preoperative opioid use. We also did not examine or control for preoperative opioid use, which may have contributed to high pain medication requirements in the postoperative period. No multi-variable analysis was performed on our data, thus our results may have confounders that we did not account for.

A major strength of our study was the large cohort size and the focus on gynecologic oncology patients with pain scores and analgesia use collected prospectively in standard nursing documentation. It has more patients than most other retrospective reviews and prospective randomized controlled trials examining the effects of thoracic epidurals. Additionally, it represents the real world usage and effects of epidurals within the context of ERAS protocols. Additionally, our study included anesthesia PACU records with inpatient records and was thus able to examine postoperative pain and opioid use across multiple phases of postoperative care, whereas other studies have not.

Our hospital now uses perioperative thoracic epidurals as the standard of care for planned laparotomies in gynecologic oncology procedures. The results of this study have demonstrated that the benefits of perioperative epidurals outweigh the risks by decreasing postoperative opioid use, increasing non-opioid pain medication use, and improving pain relief after surgery, while not increasing the risk of postoperative VTE or other complications. In future initiatives, we will examine whether we can change our standard postoperative order set to specifically decrease opioid pain medication use in the postoperative period and decrease opioid prescriptions upon patient discharge, as well as whether the implementation of an outpatient clinic for patient-centered postoperative care will decrease long-term reliance on opioid medications, all of which will assist in our efforts to decrease opioid abuse.

Conflict of interest statement

Dr. Kuroki reports grants from Washington University Institute of Clinical and Translational Sciences (R25 STRENGTH) and grants from Washington University Institute of Clinical and Translational Sciences (KL2) during the conduct of the study. Dr. Mutch reports speaking for Clovis and Astra Zeneca. Dr. Powell reports personal fees from Roche Genentech, personal fees from Merck, personal fees from Tesaro, personal fees from Clovis Oncology, personal fees from AstraZeneca, outside the submitted work. Dr. Thaker reports personal fees from Celsion, personal fees from Tesaro, grants and personal fees from Merck, personal fees from Clovis Oncology, personal fees from Stryker, outside the submitted work.

Author contributions

Sarah Cusworth designed the study and wrote the initial IRB for the study. Sarah Cusworth, Patricia Lu, Christelle Samen, and Sarah Huepenbecker entered data for the study. Sarah Huepenbecker was involved in manuscript writing and editing. Candice Woolfolk, Leping Wan, and Rosa Deterding provided statistical oversight during study design and performed the statistical analysis for the study. Daniel Helsten and Michael Bottros contributed to study design, provided anesthesia data, and were involved in paper writing and editing. David Mutch, Matthew Powell, Lindsay Kuroki and Leslie Massad helped with study design and provided manuscript writing and editing oversight. Premal Thaker designed the study, provided guidance during data entry, and wrote and edited the final manuscript.

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