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The Impact of Perioperative Epidural Placement on Post-Discharge Opioid Use in Patients Undergoing Abdominal Surgery

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Abstract

Introduction—Opioids play a crucial role in providing analgesia throughout the perioperative period, however patients may become persistent users of these medications months after surgery. Epidurals have been posited to prevent the development of persistent pain, but there is little data on the effect of epidurals on persistent opioid use.

Methods—This study was conducted using a claims database of a large, nationwide commercial health insurer. We identified opioid naïve patients who underwent open abdominal surgery from January 2004 through December 2013. Propensity scores for epidural placement were calculated accounting for demographic characteristics, resource utilization, and comorbid conditions (including medical, psychiatric, and pain conditions). Time-to-event analysis was used with the primary outcome defined as thirty days without filling an opioid prescription after discharge. Additionally, total morphine equivalents dispensed within ninety days of discharge was also calculated for each patient.

Results—A total of 6,432 patients were included in the final propensity score matched cohort. The cox proportional hazards ratio was 0.96 (95% CI:0.91–1.01, p-value:0.0910) for the relationship between epidural placement and time till a 30 day gap without filling an opioid prescription. There was no difference in the total morphine equivalents dispensed within 90 days of discharge between the groups (p=0.7670).

Conclusions—Epidural placement was not protective against persistent opioid use in a large cohort of opioid naïve patients undergoing abdominal surgery. This finding does not detract from

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the other potential benefits of epidural placement. More research is needed to understand the mechanism of persistent opioid use after surgery and its prevention.

Introduction

There have been multiple campaigns to increase awareness amongst both patients and physicians about the importance of appropriate pain relief.^{1,2} The success of these efforts are reflected by the fact that opioids are now amongst the most commonly prescribed medications in the United States.³ These initiatives, while in many aspects laudable, have been accompanied by a concurrent increase in the rate of opioid related deaths.⁴

The perioperative period presents a unique circumstance that highlights the tension between these two major public health concerns of providing pain relief with a potentially addictive substance. Patients undergoing surgery are subjected to an acute insult that generates a tremendous amount of pain and opioids play a crucial role in providing analgesia throughout the perioperative period.⁵ At the same time prior studies have shown that there is a risk of long-term opioid use postoperatively in opioid naïve patients with rates ranging from 3.1% – 7.7%.^{6,7}

Epidurals represent a potential intervention that can be used by anesthesiologists to provide effective pain relief with limited side effects. It has been posited that by providing preventive analgesia, epidurals can prevent central sensitization and stop the transition from acute to chronic pain.⁸ While clinical data demonstrating this effect is limited, epidurals may prevent persistent postoperative pain in some patients undergoing thoracotomy and abdominal surgery.⁹ It is also plausible that limiting the exposure to potentially addictive opioids perioperatively through the use of an epidural would translate into decreased opioid use after discharge.

To our knowledge, there are no prior studies examining the relationship between epidural placement and post-discharge opioid consumption. The hypothesis of this study is that epidurals will reduce the amount of opioids consumed after discharge and prevent persistent use of these medications.

Methods

Study Design and Setting

Data for the study were obtained from a de-identified research database called InVision for Data Mart, a product of OptumInsight Life Sciences (Eden Prairie, MN). The database collects information regarding membership and reimbursement transactions of a large, nationwide commercial health insurer. Transactions captured by the database include pharmacy dispensing, inpatient and outpatient services and procedures. The study examined members and their dependents who were enrolled in a health plan from January 2004 through December 2013.

The database represents an open cohort with a cross sectional size that was approximately 14 million persons depending on the study year. Demographics of individuals in the database are similar for all those under 65 living in the United States with the exception of

geographical distribution, which is a function of the market share of the insurer rather than underlying population density. The use of these de-identified data for research was approved by the Partners Institutional Review Board (Boston, MA).

Study Population

Patients 18 years or older undergoing one of the following open surgical procedures during the study time period were included in the analysis: colectomy, pancreatectomy/Whipple procedure, nephrectomy, splenectomy, cystectomy and adrenalectomy. Procedures were identified using current procedural terminology (CPT) codes present during an inpatient admission. These surgeries were selected based on the fact that they are all abdominal procedures, for which anesthesiologists may place an epidural. Furthermore these procedures either had separate codes for a laparoscopic and open version of the procedure, or were unlikely to be performed laparoscopically. This study only considered open procedures, as the risk/benefit of using epidurals in minimally invasive procedures is a debated topic that should be studied separately. Patients were excluded if they had a CPT or International Classification of Disease 9th Edition (ICD-9) code indicating that a laparoscopic procedure was performed during the index surgical admission. To further decrease the likelihood of misclassifying the type of surgery, patients with an ICD-9 code for laparoscopy (54.21) during the index admission were excluded. A list of CPT and ICD-9 codes used to define surgical procedures can be found in table S1.

To be included in the study, a patient must have had at least six months of a baseline period of enrollment in the health plan prior to the index operation. If a patient filled a prescription for an opioid during the baseline period then he or she was eliminated from the study, as were patients with ICD-9 codes for opioid abuse or dependence, in order to obtain a cohort of opioid naïve patients. Patients with metastatic cancer or a previous palliative care visit were identified using ICD-9 codes and were excluded from the analysis, as opioids are appropriately used in this setting for chronic cancer related pain. Finally patients discharged to a location other than home were excluded from the analysis, as opioid consumption could not be tracked during a stay at a rehabilitation or acute care facility.

Definition of Exposure and Outcome

Epidural placement was assessed by the presence of one or more of the following CPT codes: 62318, 62319.^{10,11} The primary outcome of the study was time to discontinuation of opioids. This was defined as a period of thirty days without filling a prescription for an opioid after discharge from the hospital.

Covariates

Covariates were identified using pharmacy billing, ICD-9 and CPT codes present during the six-month baseline period. Covariates were selected based on identified predictors of persistent postoperative pain and opioid use^{6,12}, as well as biologic plausibility. There were three groups of potential confounders that were extracted from the database: demographic characteristics, resource utilization, and comorbid conditions (including medical, psychiatric, and pain conditions). The demographic variables included were age, sex, year of procedure and surgery type. Resource utilization during the baseline period was accounted

for by including variables such as the number of prescriptions filled for distinct medications, number of hospitalizations and days spent in the hospital. These measures serve as markers of the severity of comorbidity of an individual patient and may be related to epidural use and postoperative prescribing patterns.

We adjusted for medical comorbidities including coronary artery disease, heart failure, chronic pulmonary disease, diabetes, chronic renal failure and malignancy. As a summary measure of a patient's comorbid conditions, we calculated the Gagne comorbidity score as a covariate.¹³ We also included several pain related and psychiatric disorders including fibromyalgia, back pain, a history of substance abuse and anxiety disorder. Given that the database has robust pharmacy transactions, the models incorporated covariates based on prescriptions filled for various medications, which may be markers of comorbid pain, medical, or psychiatric conditions or their severity. These included possible analgesics such as muscle relaxants, anti-depressants, anti-convulsants, benzodiazepines, non-steroidal anti-inflammatories and gabapentinoids. To further define medical covariates, we also determined whether patients filled a prescription for a beta-blocker, angiotensin converting enzyme inhibitors, nitroglycerin, statins, albuterol, tiotropium and several other cardiac and pulmonary medications. A complete list of ICD-9 and CPT codes used to generate covariates can be found in table S2.

Statistical Analysis

A propensity score (PS) was calculated to predict the probability of receiving an epidural based on the predictors mentioned using a logistic regression model. All covariates were included in the model without further selection. Age was divided into categories and included in the model as a categorical variable. All other continuous variables were divided into tertiles and included as categorical variables to account for non-linear associations. Each patient who received an epidural was propensity score matched (PS-matched) to two patients who did not receive an epidural. This ratio was selected after examining the number of exposed and unexposed subjects in order to maximize the number of matched patients and ensure the most efficient use of the data. This step was undertaken prior to any analysis of the data. Matching was achieved using pairwise nearest neighbor matching with a maximum caliper size of 0.05 using a publically available algorithm.^{14,15} Balance of covariates amongst the exposure groups in the matched cohort was assessed using standardized difference, with a difference of 10% to signify imbalance between groups.¹⁶

We then performed a time-to-event analysis on the matched cohort with follow-up beginning on the day of discharge from the hospital. Patients were censored at death, disenrollment from the health plan, a subsequent hospitalization, or a study event. The time to event was defined as thirty days after the last opioid prescription filled or after hospital discharge if no opioid prescription was filled within thirty days of discharge. To determine association, we calculated cox-proportional hazards ratios to determine if the groups had different hazards of persistent opioid use.

Sensitivity analyses

Given that opioids are often used as needed, we sought to explore whether our effect estimate would be sensitive to changes in outcome definition. As a sensitivity analysis we re-defined the outcome as a 15-day gap of not filling an opioid prescription. We also performed an additional analysis where we incorporated the days supply of the opioid prescription listed in the database and defined the time to event as thirty days after the last day supply of the previous opioid prescription or the thirtieth day after hospital discharge if no opioid prescription was filled within thirty days of discharge.

The primary analysis used several different surgery types. To ensure that the heterogeneity in surgical procedures did not account for the findings, we limited the cohort to only patients undergoing colectomies and repeated the primary analysis.

We used non-survival analytic techniques to determine if there was any association between epidurals and persistent opioid use within the propensity score matched cohort. We estimated the proportion of patients who received more than two opioid prescriptions within ninety days after discharge. Also, the proportion of patients who filled an opioid prescription between ninety days and one hundred and eighty days of discharge was also calculated. These proportions were then compared with a chi-square test to determine if the difference was statistically significant. In an alternative approach, we assessed the total amount of opioid dispensed. To facilitate comparison across opioid classes, all opioid prescriptions were converted to morphine equivalents^{17,18} and the total amount of opioids dispensed within 3 months of discharge was calculated. These values were then compared with a t-test.

All analyses were performed in SAS (version 9.3; SAS, Carey, NC), with significance defined as a two-tailed p-value of 0.05. Additionally, we felt that a hazard ratio of 0.8 would represent a clinically meaningful difference for the primary analysis.

Results

Primary Analysis

A total of 11,537 patients met all inclusion criteria in the study, of which 2,220 received an epidural (19%). The number of patients excluded for each criterion is displayed in figure 1. A greater proportion of patients with an epidural had a diagnosis of cancer, liver disease and renal disease. They were less likely to have a hemostatic disorder or have filled a prescription for oral anti-coagulants. A complete description of the cohort characteristics can be found in table 1 and table S3.

A propensity score for receiving an epidural was calculated based on all covariates and patients who received an epidural were matched to those who did not in a 1:2 ratio. Of the 2,220 patients who received an epidural, 2,144 were matched to two patients who did not receive an epidural (97%). Characteristics were similar between the two groups after matching and the maximum absolute standardized difference was less than 2.6% across all covariates. Characteristics of the propensity score matched cohort are displayed in table 2 and table S4.

The crude cox proportional hazards ratio (HR) associated with epidural placement was 0.99 (95% CI: 0.94–1.04, p-value: 0.6295) when examining time till a 30-day gap without filling an opioid prescription in the entire cohort before PS-matching. The result was similar when performing the analysis in the PS-matched cohort. The cox-proportional hazards ratio was 0.96 (95% CI:0.91–1.01, p-value:0.0910) for the relationship between epidural placement and time till a 30 day gap without filling an opioid prescription after propensity score matching. Time-to-event curves were plotted and were similar between the two groups in the PS-matched cohort (figure 2). A summary of all the results is displayed in table 3.

Sensitivity Analyses

Additional analyses were performed within the propensity-matched cohort to see if the effect estimate was sensitive to outcome measurement. When changing the time to event to 15 days without filling an opioid prescription, there was still no difference between the groups (HR: 0.96, 95% CI:0.91–1.01, p-value:0.1401). When incorporating days supply, there was no difference in the rate of discontinuation of opioids 30 days after the supply ended (HR: 0.97, 95% CI:0.92–1.02, p-value:0.2095). The primary analysis was repeated in the sub-group of patients who received colectomies and there remained no difference between the groups (HR:0.97, 95% CI:0.92–1.03, p-value:0.3725).

There was no difference in the total morphine equivalents dispensed within 90 days of discharge between the groups (mean 606 vs 651, $p=0.7670$). A larger proportion of patients who had an epidural filled two or more opioid prescriptions within ninety days of discharge compared to those who did not receive an epidural (30.4% vs 27.5%, $p=0.0138$). There was no difference in the proportion of patients who filled a single opioid prescription between ninety and one hundred and eighty days after discharge between the groups (11.6% for patients who received an epidural vs 11.5% for patients who did not receive an epidural, $p=0.9120$). The results of the sensitivity analyses are displayed in table 4.

Discussion

In a large cohort of opioid-naïve patients undergoing abdominal surgeries, epidural placement was not protective against persistent opioid use. The results were robust to several sensitivity analyses performed. While previous studies have investigated the association between epidural placement and chronic pain, this is the first study to our knowledge to examine the impact of epidurals on persistent opioid use.

The incidence of chronic pain following surgery has been estimated to be 5–65% depending on the type of procedure and population studied.¹² Furthermore, prior studies have shown that there is a risk of long-term opioid use postoperatively in opioid naïve patients with rates ranging from 3.1% – 7.7%.^{6,7} In our study more than a quarter of patients filled at least two opioid prescriptions within ninety days and eleven percent filled a prescription between ninety to one hundred and eighty days after discharge.

The mechanism by which acute postsurgical pain transforms to chronic pain has not been elucidated and is likely multifactorial. It has been hypothesized that by providing preventive analgesia, epidurals can prevent central sensitization and stop this transition.⁸ Additionally,

effective treatment of acute pain has been shown to decrease the risk of chronic post-surgical pain¹⁹ and it has been demonstrated that epidurals provide superior analgesia in the perioperative period compared to intravenous patient controlled analgesia.²⁰ The ability of epidurals to decrease persistent pain has been demonstrated in patients undergoing abdominal surgery and thoracotomy.^{9,21–23} However the results have not been unequivocal. A study of patients who underwent laparotomy showed no difference in pain outcome six months after surgery between patients who did and did not receive an epidural.²⁴ In another study of patients undergoing prostatectomy, epidurals were associated with a difference in pain scores at 9.5 weeks but not at 3.5 and 5.5 weeks after surgery.²⁵

We had no method of assessing postoperative pain and thus this measure was not included in the analysis as an outcome. However the use of a claims database allowed for a much larger cohort than other prior studies examining persistent pain after surgery. Persistent opioid consumption can potentially be considered as a surrogate measure of persistent pain²⁶ and may indicate even greater functional impairment. The lack of an association found in our study may mean that the difference in the amount of persistent pain between groups is not sufficient enough to manifest as a difference in opioid consumption.

We did note a small increase in the proportion of patients filling a second prescription for an opioid within ninety days of discharge in patients who received an epidural. The difference was small and likely reached statistical significance due to the large sample size of the study. In light of all of the other findings of this study, this single result is unlikely to have any clinical relevance.

The conclusions of this study are supported by the fact that we had detailed information on all filled prescriptions, as well as potential confounders that were present prior to the surgical admission. Additionally this is one of the largest databases of its kind that allowed us to follow patients longitudinally and capture information both pre and post-surgery. The size of the database allowed us to place several restrictions on the cohort in order to facilitate the interpretability of the analysis while still retaining a sample size large enough from which to make inferences.

However, when interpreting the results of the study it is important to consider the limitations of our data. Despite the fact that this study utilizes a rich and robust dataset, unmeasured confounding is a concern. One main source of potential confounding not accounted for is the size of the incision. While the models are able to adjust for type of surgery, this may not capture the true extent of surgery. Therefore epidural placement could be a marker for a larger incision, which would be more painful in the postoperative period. This association could potentially mask a protective effect. That said, given the surgical procedures that were selected for the study, we would generally not expect significant variation in the approach or incision size.

This cohort was limited to patients with commercial insurance and we imposed several exclusion criteria in order to create a study population that was opioid naïve. This was to ensure that we captured opioid use that was related to surgery rather than due to chronic dependence or use. Therefore the results might not be generalizable to all patients

undergoing surgery and there could be a sub-group of patients in whom epidurals could prevent persistent opioid consumption.

Despite its limitations, our study provides strong evidence that in a large nationwide cohort of opioid naïve patients undergoing abdominal surgery, epidural placement was not protective against prolonged opioid use after surgery. This finding obviously does not detract from the benefits of epidurals including superior perioperative analgesia and a potential reduction of certain perioperative complications.²⁷ Indeed, we believe that epidurals should continue to be a mainstay in the provision of perioperative analgesia for patients undergoing abdominal surgery. However, more research is needed to better understand the mechanism of persistent opioid use after surgery and its prevention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Pizzo PA, Clark NM. Alleviating suffering 101--pain relief in the United States. *N Engl J Med*. 2012; 366:197–9. [PubMed: 22256802]
2. Lanser P, Gesell S. Pain management: the fifth vital sign. *Healthc Benchmarks*. 2001; 8:68–70. 62. [PubMed: 11474948]
3. Kuehn BM. Opioid Prescriptions Soar. *JAMA*. 2007; 297:249–51. [PubMed: 17227967]
4. Paulozzi LJ. Prescription drug overdoses: A review. *Journal of Safety Research*. 2012; 43:283–9. [PubMed: 23127678]
5. American Society of Anesthesiologists Task Force on Acute Pain Management. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. 2012; 116:248–73.
6. Clarke H, Soneji N, Ko DT, Yun L, Wijesundera DN. Rates and risk factors for prolonged opioid use after major surgery: population based cohort study. *BMJ*. 2014; 348:g1251. [PubMed: 24519537]
7. Alam A, Gomes T, Zheng H, Mamdani MM, Juurlink DN, Bell CM. Long-term analgesic use after low-risk surgery: a retrospective cohort study. *Arch Intern Med*. 2012; 172:425–30. [PubMed: 22412106]
8. Katz J, Clarke H, Seltzer Z. Preventive Analgesia: Quo Vadimus? *Anesth. Analg*. 2011; 113:1242–53.
9. Andrae MH, Andrae DA. Regional anaesthesia to prevent chronic pain after surgery: a Cochrane systematic review and meta-analysis. *British Journal of Anaesthesia*. 2013; 111:711–20. [PubMed: 23811426]
10. Wu CL, Anderson GF, Herbert R, Lietman SA, Fleisher LA. Effect of postoperative epidural analgesia on morbidity and mortality after total hip replacement surgery in medicare patients. *Reg Anesth Pain Med*. 2003; 28:271–8. [PubMed: 12945019]
11. Cummings KC, Xu F, Cummings LC, Cooper GS. A comparison of epidural analgesia and traditional pain management effects on survival and cancer recurrence after colectomy: a population-based study. *Anesthesiology*. 2012; 116:797–806. [PubMed: 22273991]

12. Macrae WA. Chronic post-surgical pain: 10 years on. *British Journal of Anaesthesia*. 2008; 101:77–86. [PubMed: 18434337]
13. Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. *J Clin Epidemiol*. 2011; 64:749–59. [PubMed: 21208778]
14. Rassen, JA.; Shelat, AA.; Myers, J.; Glynn, RJ.; Rothman, KJ.; Schneeweiss, S. One-to-many propensity score matching in cohort studies. In: Schneeweiss, S.; Smith, SR., editors. *Pharmacoepidemiol Drug Saf*. Vol. 21. 2012. p. 69-80.
15. Rassen, JA.; Doherty, M.; Huang, W.; Schneeweiss, S. *Pharmacoepidemiology toolbox*. Boston, MA: <http://www.hdp-harmacoepi.org> [Last Accessed: October 17, 2015]
16. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med*. 2009; 28:3083–107. [PubMed: 19757444]
17. Korff MV, Saunders K, Thomas Ray G, Boudreau D, Campbell C, Merrill J, Sullivan MD, Rutter CM, Silverberg MJ, Banta-Green C, Weisner C. De Facto Long-term Opioid Therapy for Noncancer Pain. *The Clinical Journal of Pain*. 2008; 24:521–7. [PubMed: 18574361]
18. Mercadante S, Porzio G, Aielli F, Adile C, Verna L, Ficorella C, Giarratano A, Casuccio A. Opioid switching from and to tapentadol extended release in cancer patients: conversion ratio with other opioids. *Curr Med Res Opin*. 2013; 29:661–6. [PubMed: 23540512]
19. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. *The Lancet*. 2006; 367:1618–25.
20. Wu CL, Cohen SR, Richman JM, Rowlingson AJ, Courpas GE, Cheung K, Lin EE, Liu SS. Efficacy of postoperative patient-controlled and continuous infusion epidural analgesia versus intravenous patient-controlled analgesia with opioids: a meta-analysis. *Anesthesiology*. 2005; 103:1079–88. quiz 1109–10. [PubMed: 16249683]
21. Sentürk M, Ozcan PE, Talu GK, Kiyan E, Camci E, Ozyalçin S, Dilege S, Pembeci K. The Effects of Three Different Analgesia Techniques on Long-Term Postthoracotomy Pain. *Anesth Analg*. 2002; 94:11–5. [PubMed: 11772793]
22. Obata H, Saito S, Fujita N, Fuse Y, Ishizaki K, Goto F. Epidural block with mepivacaine before surgery reduces long-term post-thoracotomy pain. *Can J Anaesth*. 1999; 46:1127–32. [PubMed: 10608205]
23. Lavand'homme P, De Kock M, Waterloos H. Intraoperative epidural analgesia combined with ketamine provides effective preventive analgesia in patients undergoing major digestive surgery. *Anesthesiology*. 2005; 103:813–20. [PubMed: 16192774]
24. Katz J, Cohen L. Preventive analgesia is associated with reduced pain disability 3 weeks but not 6 months after major gynecologic surgery by laparotomy. *Anesthesiology*. 2004; 101:169–74. [PubMed: 15220787]
25. Gottschalk A, Smith DS, Jobes DR, Kennedy SK, Lally SE, Noble VE, Grugan KF, Seifert HA, Cheung A, Malkowicz SB, Gutsche BB, Wein AJ. Preemptive epidural analgesia and recovery from radical prostatectomy: a randomized controlled trial. *JAMA*. 1998; 279:1076–82. [PubMed: 9546566]
26. Aubrun F, Langeron O, Quesnel C, Coriat P, Riou B. Relationships between measurement of pain using visual analog score and morphine requirements during postoperative intravenous morphine titration. *Anesthesiology*. 2003; 98:1415–21. [PubMed: 12766651]
27. Freise H, Van Aken HK. Risks and benefits of thoracic epidural anaesthesia. *British Journal of Anaesthesia*. 2011; 107:859–68. [PubMed: 22058144]

Box Summary**What we already know about this topic**

- Opioid exposure to treat early postoperative pain may go on to persistent opioid use and abuse
- Whether improved acute pain analgesia and opioid sparing from epidural analgesia during hospitalization could affect the incidence of persistent opioid use is unknown

What this article tells us that is new

- In a review of over 6,400 patients who underwent open abdominal surgery, propensity matched analysis showed no effect of use of epidural analgesia on time to discontinuation of opioids after hospital discharge or dose of opioids administered in the first 90 days after discharge

Figure 1.
Flow chart of patient selection

Figure 2.

Time-to-event curves displaying the proportion of patients in each group who had a thirty day period without filling a prescription for an opioid after discharge

Table 1

Selected baseline patient characteristics of cohort, stratified by whether the patient received an epidural, N(%) or mean, (standard deviation)

	Total	Epidural Placed	No Epidural Placed
Total, n	11537	2220	9317
<u>Surgical Procedure</u>			
Adrenalectomy	200(1.7)	58(2.6)	142(1.5)
Cystectomy	196(1.7)	47(2.1)	149(1.6)
Colectomy	7714(66.9)	1316(59.3)	6398(68.7)
Nephrectomy	2301(19.9)	610(27.5)	1691(18.2)
Pancreatectomy	367(3.2)	148(6.7)	219(2.4)
Splenectomy	849(7.4)	63(2.8)	786(8.4)
<u>Gender</u>			
Female	5209(45.2)	1007(45.4)	4202(45.1)
<u>Age</u>			
18–39	1225(10.6)	167(7.5)	1058(11.4)
40–54	3577(31.0)	690(31.1)	2887(31.0)
55–64	4188(36.3)	837(37.7)	3351(36.0)
65–74	1614(14.0)	323(14.6)	1291(13.9)
75 and older	933(8.1)	203(9.1)	730(7.8)
<u>Resource Utilization</u>			
Length of Stay during Surgical Admission (days), mean (std dev)	8.35(7.5)	8.02(4.9)	8.43 (8.0)
Hospitalization in the 30 days prior to Surgical Admission	1776(15.4)	343(15.5)	1433(15.4)
<u>Comorbidities</u>			
Gagne Comorbidity Score	0.83(1.5)	0.85(1.4)	0.83(1.5)
Alcohol or Drug Abuse/Dependence	153(1.3)	27(1.2)	126(1.4)
Asthma	559(4.9)	114(5.1)	445(4.8)
Back Pain	1760(15.3)	369(16.6)	1391(14.9)
Chronic Obstructive Pulmonary Disease	707(6.1)	150(6.8)	557(6.0)
Cancer	6235(54.0)	1419(63.9)	4816(51.7)
Chronic Pain	39(0.3)	7(0.3)	32(0.3)
Fibromyalgia	268(2.3)	63(2.8)	205(2.2)
Hemostatic Disorder	375(3.3)	57(2.6)	318(3.4)
Liver Disease	1531(13.3)	362(16.3)	1169(12.6)
Renal Disease	2964(25.7)	727(32.8)	2237(24.0)
<u>Medications Used During Baseline Period</u>			
Beta-Blocker	2043(17.7)	422(19.0)	1621(17.4)
COX-2 Inhibitor	182(1.6)	43(1.9)	139(1.5)
Heparin or LMWH	117(1.0)	16(0.7)	101(1.1)
Muscle Relaxants	342(3.0)	57(2.6)	285(3.1)

	Total	Epidural Placed	No Epidural Placed
Non-Selective NSAIDs	785(6.8)	127(5.7)	658(7.1)
Oral Anti-Coagulants	353(3.1)	48(2.2)	305(3.3)

Values are displayed as N (%), unless otherwise stated, other covariates included in the study are listed in table S3

Abbreviations:

std dev – standard deviation

COX-2 – cyclooxygenase-2

LMWH – low molecular weight heparin

NSAID – non-steroidal anti-inflammatory drug

Table 2

Selected baseline patient characteristics of cohort, stratified by whether the patient received an epidural, after propensity score matching

	Epidural Placed	No Epidural Placed	Standardized Difference (%)
Total, n	2144	4288	
<u>Surgical Procedure</u>			
Adrenalectomy	57(2.6)	97(2.3)	2.6
Cystectomy	45(2.1)	83(1.9)	1.1
Colectomy	1315(61.3)	2664(62.1)	−1.7
Nephrectomy	595(27.8)	1204(28.1)	−0.7
Pancreatectomy	89(4.2)	158(3.7)	2.4
Splenectomy	63(2.9)	114(2.7)	1.7
<u>Gender</u>			
Female	963(44.9)	1941(45.3)	−0.7
<u>Age</u>			
18–39	166(7.7)	335(7.8)	−0.3
40–54	676(31.5)	1305(30.4)	2.4
55–64	803(37.5)	1631(38.0)	−1.2
65–74	306(14.3)	631(14.7)	−1.3
75 and older	193(9.0)	386(9.0)	0.0
<u>Resource Utilization</u>			
Length of Stay (days) during Surgical Admission, mean (std dev)	7.91(4.9)	7.79(6.0)	0.0
Hospitalization in the 30 days prior to Surgical Admission	320(14.9)	642(15.0)	−0.1
<u>Comorbidities</u>			
Gagne Comorbidity Score	0.85(1.4)	0.88(1.4)	0.0
Alcohol or Drug Abuse/Dependence	26(1.2)	53(1.2)	−0.3
Asthma	108(5.0)	224(5.2)	−0.8
Back Pain	352(16.4)	706(16.5)	−0.1
Chronic Obstructive Pulmonary Disease	139(6.5)	302(7.0)	−2.2
Cancer	1347(62.8)	2718(63.4)	−1.2
Chronic Pain	7(0.3)	15(0.4)	−0.3
Fibromyalgia	60(2.8)	113(2.6)	1.0
Hemostatic Disorder	55 (2.6)	114 (2.7)	−0.6
Liver Disease	319(14.9)	614(14.3)	1.6
Renal Disease	699(32.6)	1408(32.8)	−0.5
<u>Medications Used During Baseline Period</u>			
Beta-Blocker	399(18.6)	834(19.5)	−2.1
COX-2 Inhibitor	39(1.8)	83(1.9)	−0.9
Heparin or LMWH	16(0.8)	33(0.8)	−0.2

	Epidural Placed	No Epidural Placed	Standardized Difference (%)
Muscle Relaxants	55(2.6)	111(2.6)	-0.1
Non-Selective NSAIDs	126(5.9)	246(5.7)	0.6
Oral Anti-Coagulants	48 (2.2)	90 (2.1)	1.0

Values are displayed as N (%), unless otherwise stated, other covariates included in the propensity score were year, number of office visits, distinct medications filled, hospitalizations and days spent in the hospital during the baseline period. Additional comorbidities included were diabetes, cerebrovascular disease, migraines, mood disorder, obesity, osteoarthritis, oxygen dependent, psychosis, rheumatoid arthritis, congestive heart failure, delirium, dementia, inflammatory bowel disease, seizure disorder, ischemic heart disease, liver disease, renal disease, history of smoking, cardiac dysrhythmia. Additional medications included were angiotensin converting enzyme-inhibitor, angiotensin II receptor blockers, anti-psychotics, anxiolytics, corticosteroids, digoxin, diuretics, hypoglycemic, insulin, statins calcium channel blockers, chronic respiratory therapy, anti-arrhythmics, anti-consultants, anti-depressants, and anti-platelet agents. The distribution of these covariates in the propensity score matched cohort are shown in table S4

Abbreviations:

std dev – standard deviation

COX-2 – cyclooxygenase-2

LMWH – low molecular weight heparin

NSAID – non-steroidal anti-inflammatory drug

Table 3

Association Between Epidural Placement and Persistent Opioid Use

	No Epidural	Epidural*	p-value
<i>Time Since Last Opioid Prescription Filled</i>			
Primary analysis			
30 Day Gap - Crude	ref	0.99(0.94–1.04)	0.6295
30 Day Gap – Propensity Matched	ref	0.96 (0.91–1.01)	0.0910

Results represent hazard ratios with 95% confidence intervals in parentheses

Abbreviations:

ref – reference category

Table 4

Results from the Sensitivity Analyses

	No Epidural	Epidural*	p-value
<i>Time Since Last Opioid Prescription Filled</i>			
15 Day Gap	ref	0.96 (0.91–1.01)	0.1401
30 Day Gap Accounting Day Supply	ref	0.97 (0.92–1.02)	0.2095
Colectomy only cohort--30 Day Gap	ref	0.97 (0.92–1.03)	0.3725
<i>Non-Survival Analysis</i>			
Total morphine equivalents dispensed within 90 days of discharge, mean (sd)	606 (5288)	651 (6566)	0.7670
Proportion of patients filling 2 or more opioid prescriptions within ninety days of discharge, n (%)	1178/4288 (27.5%)	652/2144 (30.4%)	0.0138
Proportion of patients filling a single opioid prescription between ninety to one hundred and eighty days of discharge, n (%)	492/4288 (11.5%)	248/2144 (11.6%)	0.9120

* Results represent hazard ratios with 95% confidence intervals in parentheses, except where noted.

Abbreviations:

ref – reference category

sd – standard deviation