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Epidural compared with non-epidural analgesia and cardiopulmonary complications after colectomy: A retrospective cohort study of 20,880 patients using a national quality database

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Abstract

Study Objective—Epidural analgesia may be associated with fewer postoperative complications and is associated with improved survival after colon cancer resection. This study used the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) to assess any association between epidural analgesia (versus non-epidural) and complications after colectomy.

Design—Retrospective cohort study.

Setting—603 hospitals in the United States reporting data to NSQIP.

Patients—From 2014–15 data, 4,176 patients undergoing colectomy with records indicating epidural analgesia were matched 1:4 via propensity scores to 16,704 patients without.

Interventions—None (observational study).

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Measurements—Primarily, we assessed the association between epidural analgesia and a composite of cardiopulmonary complications using an average relative effect generalized estimating equations model. Secondary outcomes included neurologic, renal, and surgical complications and length of hospitalization. Sensitivity analyses repeated the analyses on a subgroup of only open colectomies.

Main Results—We found no association between epidural analgesia and the primary outcome: average relative effect (95% CI) 0.87 (0.68, 1.11); P = 0.25. We found no significant associations with any secondary outcomes. In the 8,005 open colectomies, however, there was a significant association between epidural analgesia and fewer cardiopulmonary complications (average relative effect odds ratio [95% CI] of 0.58 [0.35, 0.95]; P = 0.03) and shortened hospital stay (HR for time to discharge [98.75% CI] of 1.10 [1.02, 1.18]; P<0.001).

Conclusions—We found no overall association between epidural analgesia and reduced complications after colectomy. In open colectomies, however, epidural analgesia was associated with fewer cardiopulmonary complications and shorter hospitalization. This may inform analgesic choice when planning open colectomy.

Keywords

Anesthesia; Epidural; Complication; Postoperative; Colectomy; Pain; Postoperative

1. Introduction

In recent years, there has been much interest in the potential effects of regional anesthesia or analgesia on outcomes after surgery. We previously used the linked Surveillance, Epidemiology, and End Results (SEER)-Medicare database to assess the impact of epidural analgesia use on recurrence and survival after colon cancer resection and found that epidural analgesia was associated with improved survival but not recurrence.[1]

Although our previous analysis was unable to find a difference in cancer recurrence, there was an early and persistent survival advantage among patients receiving epidural analgesia, even adjusting for multiple covariates. A decrease in perioperative adverse events could explain much of the observed mortality difference. Indeed, recent analysis of Cochrane Database systematic reviews suggests that epidural anesthesia may confer a mortality benefit in some patients.[2] There is also evidence showing epidural analgesia reduces postoperative pain and reduces a number of postoperative complications in various settings.[3–9] Our previous analysis, however, was unable to address the specific reasons for the mortality difference because the SEER-Medicare database has limited clinical detail to reliably capture many postoperative complications.

The American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) provides a rich, validated data source concerning perioperative care and postoperative complications from 603 participating hospitals (in 2015) in the United States, both academic and private (https://www.facs.org/quality-programs/acs-nsqip).[10] Each participating site has a trained Surgical Clinical Reviewer and a “Surgeon Champion” responsible for auditing cases to ensure data quality. Cases from each site are randomly

sampled on a risk-adjusted basis, so the NSQIP data only provide a sample of the overall case volume at each center. Starting in 2014, an additional variable was added to capture additional anesthetic techniques such as epidural analgesia, providing the ability to evaluate the impact of epidural analgesia on perioperative outcomes. We therefore used the 2014–15 ACS NSQIP Colectomy Procedure-Targeted and standard Participant Use Data Files (PUFs) to identify patients undergoing non-emergent colectomy and evaluate the primary hypothesis that patients with epidural analgesia (as defined below) would have a lower composite risk of 30-day mortality and cardiopulmonary complications than those without epidural analgesia. Secondary analyses tested the hypotheses that epidural analgesia is associated with fewer renal, neurologic, and surgical complications as well as shorter length of hospital stay than systemic analgesia. Because of the significant clinical differences between open and laparoscopic procedures, a subgroup analysis of only open colectomies was performed to evaluate whether the associations of epidural analgesia with the composite outcomes differ by procedure type.

2. Materials and Methods

This study using de-identified data was determined by the Cleveland Clinic Institutional Review Board to be exempt from review. We assessed the association between epidural analgesia around the time of colectomy (versus no epidural analgesia) on postoperative complications and hospital length of stay using the 2014 and 2015 NSQIP standard and colectomy procedure-targeted data. Patients undergoing colectomy for all indications were included. Patients were excluded from the analysis if they had emergency surgery, preoperative sepsis, disseminated cancer, or ventilator dependence. Further, patients with missing baseline, demographic, medical, or procedural characteristics were excluded.

Colectomy patients with epidural analgesia were compared descriptively to patients without epidural analgesia on baseline demographic, medical, and procedural characteristics defined in Table 1 using appropriate summary statistics (i.e., mean (standard deviation) for normally distributed data, median [interquartile range] for skewed data, or N (%) for categorical data). Epidural cases were defined as any colectomies with appropriate values for the “primary anesthesia” or “other anesthesia” variables. The primary anesthesia variable describes the main anesthetic technique used. The other anesthesia variable (introduced in 2014) aims to capture other techniques such as epidural analgesia or peripheral nerve blocks used in conjunction with general anesthesia.

To maximize statistical power, laparoscopic cases were included in the primary analysis because of the sizable number of such cases (2,725) with epidural analgesia. Because of the likely difference in clinical effects of epidural analgesia on laparoscopic versus open procedures, planned sensitivity analyses excluded laparoscopic cases to focus on open colectomy. Missing entries for the “other anesthesia” variable were interpreted as non-epidural cases if the primary anesthesia variable was not recorded as epidural.

We used propensity score matching to control for observed potential confounding.[11] Propensity scores (i.e., the probability of receiving epidural analgesia) were estimated using a multivariable logistic regression model of receiving epidural analgesia (versus non-

epidural) as a function of all of the potentially confounding variables listed in Table 1 (except for hematocrit, creatinine, and albumin due to missing data). Each epidural analgesia patient was matched to 4 patients who did not receive epidural analgesia using a greedy distance matching algorithm limiting distance to within 0.02 propensity score logit standard deviations of each other.[12]

Balance between groups on patient characteristics was assessed before and after propensity score matching using absolute standardized difference (ASD), defined as the absolute difference in means, mean ranks, or proportions divided by the pooled standard deviation. Variables with ASD > 0.10 were defined as imbalanced.[11]

2.1 Primary Analysis

We compared patients who received epidural analgesia to those who did not on a composite of cardiopulmonary complications including three components: cardiac complications, pulmonary complications, and 30-day mortality (defined in Table 2). Cardiac and pulmonary complications are each collapsed composites of various cardiac and pulmonary conditions (Table 2). A multivariate analysis was used to assess associations with the composite outcome, allowing capture of information about individual morbidities and the correlation between morbidities within each composite.

The association between epidural analgesia and the composite of cardiopulmonary complications was assessed using an average relative effect generalized estimating equations (GEE) model with an unstructured correlation structure.[13] This approach estimates the average association across components and therefore is not driven by components with higher incidence. This approach also accounts for correlation among components and allows assessment of the heterogeneity of the associations between epidural analgesia status and each outcome component. Heterogeneity of epidural analgesia use across the composite was assessed by testing for epidural-by-component interaction using a significance criterion of $P < 0.10$. We also assessed whether the association between epidural analgesia and the composite differed among patients with colectomy for colorectal cancer by testing for the colorectal cancer-by-epidural interaction using a significance criterion of $P < 0.10$.

2.2 Secondary Analyses

We assessed the associations between epidural analgesia (versus non-epidural) and separate composites of neurological, renal/urinary, and surgical complications using separate multivariable logistic regression models. The association between epidural analgesia and hospital length of stay was assessed using a Cox proportional hazard regression model adjusting for imbalanced baseline variables after matching. Patients who died before discharge were censored to the longest observed duration of hospitalization.

2.3 Sensitivity Analysis

To determine if the association between epidural analgesia and outcomes varied by surgical approach (laparoscopic versus open), the primary and secondary analyses were repeated using a subset of the cohort consisting only of patients undergoing open colectomy.

Procedures involving unplanned conversion from laparoscopic to open surgery were considered open.

Both the primary and secondary analyses were completed using an alpha of 0.05, with a significance criterion of 0.05 for the primary outcome and 0.0125 for each secondary outcome (i.e., 0.05/4). Analyses were completed using R version 3.3.2 (The R Foundation for Statistical Computing, Vienna, Austria) and SAS version 9.4 (SAS Institute, Carey, NC, USA).

2.4 Sample Size and Power

Empirical power was calculated based on the observed incidence of cardiopulmonary complications among patients who did not receive epidural analgesia (Table 2), a conservative correlation coefficient of 0.3 between outcomes, and the observed 4,176 patients who received epidural analgesia during colectomy. We estimated power using the MULTBINPOW SAS macro, which estimates power for average relative effect GEE models given varying correlations and sample sizes [Mascha EJ: Power Calculations for Tests on a Vector of Binary Outcomes (MULTBINPOW), Cleveland Clinic Statistical Software Series (http://www.lerner.ccf.org/qhs/software/multbinpow.php), 1.0 edition, Cleveland, Ohio 2011]. This SAS program uses simulations to compute and display comparative power of several parallel-group multivariate tests for treatment effect on a vector of binary events[14]. There was > 90% power at the 0.05 significance level to detect a 10% or greater relative difference in complications among epidural analgesia patients.

3. Results

The 2014 and 2015 NSQIP data included 56,569 colectomy cases. Among those, 4,329 colectomy patients who received epidural analgesia and 33,127 patients who did not were eligible for this analysis (Figure 1). 4,176 colectomy patients who received epidural analgesia were successfully matched 1:4 to 16,704 who did not (99% matched). Balance of groups on potentially confounding patient characteristics are presented before and after matching in Table 1. Virtually all patients received general anesthesia for their surgery, regardless of epidural analgesia use (4,136 of 4,176 epidural patients and 16,653 of 16,704 non-epidural patients). Groups were balanced on all patient characteristics after matching (i.e., ASD < 0.10 for all variables), so none were adjusted for in the primary or secondary analyses.

3.1 Primary analysis

The incidences of cardiopulmonary complications and each component of this composite are presented by treatment group in Table 2. There was no significant association between receiving epidural analgesia and the composite of cardiopulmonary complications, with an estimated average relative effect odds ratio (95% CI) of 0.87 (0.68, 1.11); P = 0.25 (Table 3).

There was no significant epidural-by-component interaction (P = 0.74), suggesting that the primary association is consistent across components of the composite. There was also no interaction between colorectal cancer and epidural analgesia during colectomy, suggesting

that the primary association is consistent regardless of whether the colectomy was performed to treat colorectal cancer (P = 0.50).

3.2 Secondary analysis

There was no association between epidural analgesia (versus non-epidural) and any of the secondary complications, with estimated odds ratios (98.75% CI) of 0.71 (0.23, 2.13) for stroke (P = 0.43), 1.01 (0.66, 1.55) for renal complications (P = 0.94), and 0.96 (0.85, 1.10) for surgical complications (P = 0.47); Table 3. Incidences of each complication are presented in Table 2.

There was no association between epidural analgesia and time to hospital discharge alive using Cox proportional hazards regression, with an estimated hazard ratio (98.75% CI) of 1.04 (0.99, 1.08); P = 0.04; Table 3. Median [Q1, Q3] time to hospital discharge was 5 [3, 7] days in each group (Table 2).

3.3 Sensitivity Analysis—Open Colectomy

Of the 20,880 patients included in the primary and secondary analyses, 8,005 (38%) underwent open surgery, including 1,611 epidural patients and 6,394 without epidural analgesia. Included in this subgroup are 1,860 cases involving unplanned conversion from laparoscopic to open, 314 of whom had epidural analgesia and 1,546 who did not. Assessment of absolute standardized difference between these subgroups indicated that covariates remained balanced (data not shown). Among the open surgery patients, epidural analgesia was significantly associated with a reduced composite of cardiopulmonary complications, with an average relative effect odds ratio (95% CI) of 0.58 (0.35, 0.95); P = 0.03 (Table 4). Epidural analgesia was also associated with a shorter duration of hospitalization in this subgroup, with a hazard ratio (98.75% CI) of 1.10 (1.02, 1.18) for time to discharge alive (P < 0.001). However, there was no difference between groups in terms of stroke, renal complications, or surgical complications.

4. Discussion

In this analysis, despite adequate *post-hoc* power, we found no overall significant association between epidural analgesia and the primary composite outcome. There was also no association with other complications or length of stay after colectomy. When looking specifically at open procedures, however, there was a significant association between epidural analgesia and a reduction in the primary composite outcome as well as shorter hospital length of stay.

There is ample reason to expect that epidural analgesia would improve patients' perioperative outcomes: epidural analgesia has been shown to reduce postoperative pain and pulmonary complications after major abdominal surgery,[3] to reduce the postoperative hypercoaguable state,[4] to hasten the return of bowel function and exercise capacity after colectomy,[5–7] to reduce cardiac and pulmonary complications after abdominal aortic surgery,[8] and to be associated with improved outcomes after esophagectomy.[9] In a recent meta-analysis of multiple types of surgery, epidural analgesia was associated with a reduction in multiple postoperative complications and mortality.[15] Of note, since the vast

majority of patients in our analysis also received general anesthesia, it will be difficult to separate any effects of epidural anesthesia from those of postoperative analgesia without detailed clinical information.

The NSQIP program provides a large, validated dataset covering over 600 institutions in the United States. This allows multicenter investigations at the national level without relying on often inaccurate administrative data.[16] Although it is a very large national database, the NSQIP program has been underutilized for anesthesiology research and holds great promise for further analyses. To our knowledge, this is the first study using NSQIP data to evaluate the association between epidural analgesia and outcomes after colectomy. Also using NSQIP data, Saied and colleagues demonstrated a reduction in several complications and hospital length of stay after a variety of procedures when comparing regional anesthesia to general anesthesia. Their analysis, however, utilized the primary anesthetic technique variable (for intraoperative care) and not the secondary anesthetic variable which would identify postoperative epidural analgesia. Notably, they did not find a reduction in myocardial infarction or mortality with regional anesthesia.[17]

The difference in results based on surgical approach (open versus laparoscopic) is consistent with prior work. Epidural analgesia is thought to be beneficial in general, but the specific context may be very important. Laparoscopic surgery is associated with less incisional pain, faster recovery and fewer postoperative complications than open procedures and is a key element of many enhanced recovery programs.[18] Instituting an enhanced recovery program including laparoscopic surgery may achieve many of the observed benefits of epidural analgesia. Indeed, within the context of an enhanced recovery protocol (that included laparoscopic surgery), epidural analgesia was not found to be advantageous other than providing slightly faster return of bowel function and improved pain scores.[19] It is also conceivable that some of the putative benefits of epidural or regional analgesia are due to systemic action of absorbed local anesthetic, as there can be significant systemic uptake.[20]

The finding of decreased length of stay among patients with epidural analgesia in the open colectomy group stands in contrast to the results of an analysis by the ERAS Compliance Group, who found an association between epidural analgesia and increased length of hospitalization in the context of an enhanced recovery program for colorectal cancer surgery.[18] Again, this may result from the enhanced recovery program favoring laparoscopic surgical approaches and utilizing other elements (transversus abdominis plane or other blocks, intravenous fluid minimization, early ambulation, and others) to hasten time to hospital discharge. There was also no detectable difference in the incidence of prolonged ileus, although the specific times to return of bowel function are not recorded and an undetected smaller difference may exist. Additionally, epidural analgesia is associated with complications (particularly hypotension and urinary retention) that may negatively affect the postoperative course.[15] Reassuringly, though, there were no differences detected in major complications between the groups.

As a retrospective cohort analysis, this study is limited by the available data and subject to confounding by unmeasured covariates. Although the NSQIP PUF is a rich data source, it

lacks many perioperative details including anesthetic and analgesic management and does not allow for identification of individual hospital sites. Thus, the database only indicates that epidural analgesia was used but does not provide information about clinical management or allow for stratified analysis. Finally, although it contains many records from over 600 institutions, the NSQIP PUF only provides a relatively small sample of the total surgical volume in the United States (estimated at 320,000 colectomy procedures annually[21]), which may limit generalizability.

Although it was adequately powered for the primary outcome, there are a number of limitations to this analysis. We planned this analysis to have 90% power at the 0.05 significance level to detect a 10% relative reduction in complications among epidural analgesia patients, so there is a small chance that we observed false negative primary findings. We expected 20% of colectomy patients would receive an epidural, but only observed an 11.5% incidence of epidural use. However, the “other anesthesia” record was not required to be filled out in the 2014 NSQIP data, likely leading to under-coding. Missing entries for this field were considered as non-epidural cases in this analysis, potentially causing misclassification bias towards a null result. Additionally, clinical details about the epidural analgesia (such as location, choice of medication, dosing regimen, and timing) were not available. For the sensitivity analyses, there were many laparoscopic colectomies identified with epidural analgesia. This limits the power of any subgroup analysis and may lead to not identifying a true association (should one exist) between epidural analgesia and other complications in open procedures. There were also numerous missing entries for cancer staging data, so cancer stage was not able to be used as a covariate. This is a potential confounder in the analysis, although all other covariates were balanced after propensity score matching.

Our analyses used listwise deletion, removing patients with missing baseline or procedural characteristics from the analysis, assuming that these were missing completely at random. If this assumption does not hold, listwise deletion could potentially bias our results. Our sensitivity analysis found that groups differed on key characteristics including colectomy for colon cancer, incidence of open surgery, and intraoperative epidural use. Most of the missing data occurred only due to unreported race, accounting for 14% of exclusions. Race, however, has been shown to have a significant impact on outcomes after colectomy[22, 23] and we therefore believe it is reasonable to exclude patients with missing race data from the analysis.

Finally, our primary analysis examined the association between epidural analgesia and a composite of cardiopulmonary complications and mortality. Traditionally, analyses of composite outcomes are difficult to interpret when using a collapsed composite approach (e.g., any versus no outcome) if the frequency, severity, or association with the exposure differs across components. We have avoided these challenges by choosing components with similar severity and performing a multivariate analysis. Instead of estimating the association between epidural use and the odds of having any component, we estimated the average association across individual components of the composite (e.g., “average relative effect” odds ratio). Therefore, results are not driven by components with the highest frequency. We verified that the association between epidural use and the composite was consistent across

components by assessing the epidural by component interaction. Thus, our analysis avoids many common limitations when using composite outcomes.

In conclusion, using 2014 and 2015 NSQIP colectomy data, we were unable to demonstrate an overall association between epidural analgesia and reduced complications after colectomy. For open procedures, however, epidural analgesia may be associated with fewer cardiopulmonary complications and decreased length of hospital stay. Our findings support a possible role for epidural analgesia in a multimodal analgesic regimen after open colectomy. Future prospective research should include an increased focus on functional outcomes (quality of recovery, discharge readiness, and others) as well as investigation into the systemic effect (if any) of epidurally-administered local anesthetics.

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Highlights

- Overall, epidural analgesia showed no difference in postoperative complications.
- In open colectomy, epidural analgesia is associated with fewer complications.
- Epidural analgesia may improve outcomes and speed recovery after open colectomy.

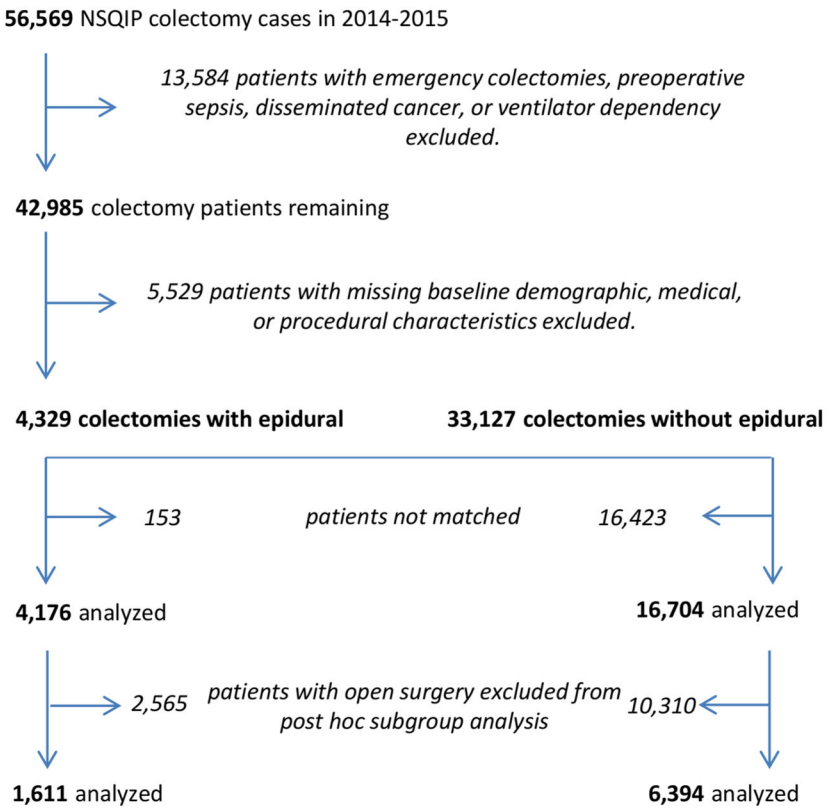

Figure 1.
Study flow diagram.

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Table 1

Balance of treatment groups on baseline demographic, medical, and procedural characteristics of the study population before and after propensity score matching.

Factor	Before matching Epidural (N = 4,329)	No Epidural (N = 33,127)	ASD*	After matching Epidural (N = 4,176)	No Epidural (N = 16,704)	ASD*
Demographics						
Age (years; range: 18–89 for all groups)	59 (15)	61 (15)	0.095	59 (15)	59 (15)	0.002
Female, n (%)	2,299 (53%)	17,475 (53%)	0.007	2,212 (53%)	8,878 (53%)	0.004
White, n (%)+	3,774 (87%)	28,421 (86%)	0.041	3,633 (87%)	14,479 (87%)	0.009
Body mass index (kg m^{-2})	27 [24, 32]	28 [24, 32]	0.046	27 [24, 32]	27 [24, 32]	0.002
Smoker, n (%)	709 (16%)	5,564 (17%)	0.011	678 (16%)	2,669 (16%)	0.007
ASA Status, n (%)			0.087			0.002
1	70 (2%)	767 (2%)		70 (2%)	277 (2%)	
2	1,906 (44%)	15,552 (47%)		1,879 (45%)	7,509 (45%)	
3	2,204 (51%)	15,589 (47%)		2,088 (50%)	8,366 (50%)	
≥4	149 (3%)	1,219 (4%)		139 (3%)	552 (3%)	
Partially/totally dependent functional status, n (%)	62 (1%)	676 (2%)	0.047	54 (1%)	247 (1%)	0.016
Medical History						
Steroid or immunosuppressant use, n (%)	497 (11%)	2,985 (9%)	0.082	462 (11%)	1,817 (11%)	0.006
Chemotherapy within 90 days of surgery, n (%)	287 (7%)	1,413 (4%)	0.104	248 (6%)	1,008 (6%)	0.004
Baseline hematocrit (%)+‡	38 (6)	38 (6)	0.019	38 (6)	38 (6)	0.024
Baseline creatinine (mmol L^{-1})+§	0.84 [0.70, 1.00]	0.85 [0.70, 1.00]	0.009	0.85 [0.70, 1.00]	0.83 [0.70, 1.00]	0.041
Baseline albumin (g L^{-1})+‖	3.8 (0.6)	3.8 (0.6)	0.049	3.8 (0.6)	3.8 (0.6)	0.019
Transfusion within 72 hours of surgery, n (%)	58 (1%)	621 (2%)	0.043	57 (1%)	199 (1%)	0.015
Acute renal failure prior to surgery, n (%)+	5 (0%)	49 (0%)	0.009	5 (0%)	19 (0%)	0.002
End stage renal disease on dialysis, n (%)	25 (1%)	217 (1%)	0.010	24 (1%)	98 (1%)	0.002
History of severe COPD, n (%)	188 (4%)	1,506 (5%)	0.010	176 (4%)	694 (4%)	0.003
History of congestive heart failure, n (%)	32 (1%)	287 (1%)	0.014	32 (1%)	127 (1%)	0.001
Presence of dyspnea, n (%)	280 (6%)	1,953 (6%)	0.024	259 (6%)	1,030 (6%)	0.001
Hypertension requiring medication, n (%)	1,938 (45%)	15,750 (48%)	0.056	1,877 (45%)	7,535 (45%)	0.003
Diabetes mellitus, n (%)			0.064			0.010

Factor	Before matching Epidural (N = 4,329)	No Epidural (N = 33,127)	ASD*	After matching Epidural (N = 4,176)	No Epidural (N = 16,704)	ASD*
Insulin-dependent	184 (4%)	1,719 (5%)		178 (4%)	718 (4%)	
Non-insulin dependent	369 (9%)	3,240 (10%)		363 (9%)	1,405 (8%)	
None	3,776 (87%)	28,168 (85%)		3,635 (87%)	14,581 (87%)	
Bleeding disorder or anticoagulant use, n (%)	104 (2%)	984 (3%)	0.035	101 (2%)	377 (2%)	0.011
Weight loss (>10%) in the last 6 months, n (%)	257 (6%)	1,317 (4%)	0.090	221 (5%)	853 (5%)	0.008
Presence of ascites, n (%)	18 (0.4%)	88 (0.2%)	0.026	14 (0.3%)	50 (0.3%)	0.006
Colectomy for colorectal cancer, n (%)	1,632 (38%)	12,595 (38%)	0.007	1,582 (38%)	6,357 (38%)	0.004
Procedural characteristics						
Estimated Probability of Morbidity (%)	12 [8, 17]	11 [8, 16]	0.149	12 [8, 17]	12 [8, 17]	0.020
Estimated Probability of Mortality (%)	0.3 [0.1, 0.8]	0.3 [0.1, 0.8]	0.069	0.3 [0.1, 0.8]	0.3 [0.1, 0.8]	0.001
Open surgery, n (%)	1,644 (38%)	12,977 (39%)	0.025	1,611 (39%)	6,394 (38%)	0.006
Duration of surgery (minutes)	181 [131, 248]	164 [118, 226]	0.202	178 [130, 242]	178 [126, 247]	0.006
Wound Class, n (%)			0.071			0.007
1-Clean	30 (1%)	296 (1%)		29 (1%)	111 (1%)	
2-Clean/contaminated	3,347 (77%)	26,401 (80%)		3,246 (78%)	13,028 (78%)	
3-Contaminated	576 (13%)	4,053 (12%)		549 (13%)	2,166 (13%)	
4-Dirty/infected	376 (9%)	2,377 (7%)		352 (8%)	1,399 (8%)	

Summary statistics are presented as mean (standard deviation), median [Q1, Q3], or n (%) as appropriate.

*Absolute standardized difference, defined as the absolute difference in means, mean ranks, or proportions divided by the pooled standard deviation. Variables with ASD > 0.1 are defined as imbalanced.

+Not included in the propensity score model due to missing data or very low incidence.

‡Hematocrit not measured for 324 epidural patients and 1,793 non-epidural patients before matching and 317 epidural and 850 non-epidural patients after matching.

§Creatinine not measured for 383 epidural patients and 2,741 non-epidural patients before matching and 373 epidural and 1,325 non-epidural patients after matching.

//Albumin not measured for 1,268 epidural patients and 10,330 non-epidural patients before matching and 1,247 epidural and 5,063 non-epidural patients after matching.

Table 2

Incidence of primary and secondary outcomes by treatment group among matched patients.

Primary outcome	Epidural (N = 4,176)	No Epidural (N = 16,704)
1. Cardiopulmonary complications and mortality *		
Cardiac complications	**28 (0.7)**	**123 (0.7)**
Intraoperative or postoperative myocardial infarction	21 (0.5)	77 (0.5)
Cardiac arrest requiring CPR	9 (0.2)	57 (0.3)
Pulmonary complications	**157 (4)**	**685 (4)**
Pneumonia	58 (1)	258 (2)
Unplanned tracheal intubation	49 (1)	192 (1)
Pulmonary embolism	28 (0.7)	94 (0.6)
Deep vein thrombosis/thrombophlebitis	53 (1)	191 (1)
Failure of weaning from ventilator (> 48 hours)	40 (1)	170 (1)
30-day mortality	**24 (0.6)**	**123 (0.7)**
Secondary outcomes +		
1. Stroke	**6 (0.1)**	**34 (0.2)**
2. Renal complications +	**43 (1.0)**	**170 (1.0)**
Progressive renal insufficiency without need for dialysis	30 (0.7)	121 (0.7)
Acute renal failure requiring new dialysis	13 (0.3)	50 (0.3)
3. Surgical complications +‡	**514 (12)**‡	**2,129 (13)**‡
Return to OR within 30 days	173 (4)	751 (5)
All-cause 30 day hospital readmission§	420 (10)§	1,687 (10)§
4. Days from operation to discharge//	**5 [3, 7]**	**5 [3, 7]**
Exploratory outcomes		
1. Infectious complications		
Superficial surgical site infection	206 (5)	740 (4)
Deep incisional surgical site infection	41 (1)	152 (1)
Organ space surgical site infection	151 (4)	731 (4)
Wound disruption	31 (0.7)	140 (0.8)
2. Sepsis		
Sepsis	102 (2)	546 (3)
Septic shock	41 (1)	204 (1)
3. Prolonged ileus¶	582 (14)	2,402 (14)

Summary statistics are presented as n (%) or median [Q1, Q3] as appropriate.

*The primary outcome is a composite consisting of 3 components: cardiac complications, pulmonary complications, and mortality. The 3 components were simultaneously analyzed using an average relative effect generalized estimating equations model using an unstructured covariance matrix.

+Renal complications and surgical complications are each collapsed composite analyzed using separate logistic regression models.

‡No data for 9 patients who received epidurals and 43 patients who did not.

§No readmission data for 9 patients who received epidurals and 44 patients who did not.

// Length of stay not reported for 9 patients who did not receive epidural analgesia.

¶ No data for 4 patients who received epidurals and 22 patients who did not.

Table 3

Association between epidural use and primary and secondary outcomes among matched patients.

Primary analysis	**Average relative effect odds ratio[*] (95% CI)[‡]**	**P-value[‡]**
Cardiopulmonary complications/mortality	0.87 (0.68, 1.11)	0.25
Secondary analyses	**Odds ratio[§] (98.75% CI)[//]**	**P-value[//]**
Stroke	0.71 (0.23, 2.13)	0.43
Renal complications	1.01 (0.66, 1.55)	0.94
Surgical complications[¶]	0.96 (0.85, 1.10)	0.47
	Hazard ratio[**] (98.75% CI)	
Time to discharge alive[a]	1.04 (0.99, 1.08)	0.04

[*] Odds ratio estimated using an average relative effect generalized estimating equations model using an unstructured covariance matrix.

[‡] Significance criterion of 0.05 was used for the primary analysis.

[§] Odds ratios estimated from separate logistic regression models.

[//] Significance criterion of 0.0125 used for each secondary analysis (i.e., 0.05/4, Bonferroni).

[¶] 52 patients removed from analysis due to missing surgical complications data.

[**] Hazard ratio estimated using Cox proportional hazards regression. Patients who died before discharge were censored to the longest observed hospital length of stay.

[a] 9 patients who did not receive an epidural excluded from analysis due to unreported hospital length of stay.

Table 4

The association between epidural use and primary and secondary outcomes among subset of matched patients who underwent open surgery (N = 8,005 patients, 1,611 of which had an epidural).

Primary analysis	**Average relative effect odds ratio[*] (95% CI)[‡]**	**P-value[‡]**
Cardiopulmonary complications/mortality	0.58 (0.35, 0.95)	0.03
Secondary analyses	**Odds ratio[§] (98.75% CI)[//]**	**P-value[//]**
Stroke	1.19 (0.23, 6.18)	0.80
Renal complications	0.47 (0.20, 1.15)	0.03
Surgical complications[¶]	0.96 (0.78, 1.19)	0.63
	Hazard ratio[**] (98.75% CI)	
Time to discharge alive[a]	1.10 (1.02, 1.18)	< 0.001

[*] Odds ratio estimated using an average relative effect generalized estimating equations model using an unstructured covariance matrix.

[‡] Significance criterion of 0.05 was used for the primary analysis.

[§] Odds ratios estimated from separate logistic regression models.

[//] Significance criterion of 0.0125 used for each secondary analysis (i.e., 0.05/4, Bonferroni).

[¶] 9 patients removed from analysis due to missing surgical complications data.

[**] Hazard ratio estimated using Cox proportional hazards regression. Patients who died before discharge were censored to the longest observed hospital length of stay.

[a] 10 patients who did not receive an epidural excluded from analysis due to unreported hospital length of stay.