Post-Pancreatoduodenectomy Outcomes and Epidural Analgesia: A 5-Year Single Institution Experience

Rachel E Simpson MD[a,f], Mitchell L Fennerty MD[a], Cameron L Colgate BS[c], E Molly Kilbane RN,[a] Eugene P Ceppa MD[a,f], Michael G House MD, FACS[a], Nicholas J Zyromski MD[a], Attila Nakeeb MD[a], C Max Schmidt MD, MBA, PhD, FACS[a,b,d-f]

Indiana University School of Medicine Departments of [a]Surgery, [b]Biochemistry/Molecular Biology, [c]Center for Outcomes Research in Surgery, Indianapolis, IN; [d]Walther Oncology Center, Indianapolis, IN; [e]Indiana University Simon Cancer Center, Indianapolis, IN; [f]Indiana University Health Pancreatic Cyst and Cancer Early Detection Center, Indianapolis, IN

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Corresponding Author:
C Max Schmidt, MD, PhD, MBA, FACS
Department of Surgery, Biochemistry & Molecular Biology
Indiana University School of Medicine
545 Barnhill Drive, Emerson Hall 129
Indianapolis, IN 46202
maxschmi@iupui.edu | www.pancyst.org
Office 317.948.8358 | Cell 317.372.9011 | Fax 317.274.0241

Brief Title: Epidural and Whipple Outcomes

ABSTRACT

Introduction: Optimal pain control post-pancreatoduodenectomy is a challenge. Epidural analgesia (EDA) is increasingly utilized despite inherent risks and unclear effects on outcomes.

Methods: All pancreatoduodenectomies (PD) performed from 1/2013-12/2017 were included. Clinical parameters were obtained from retrospective review of a prospective clinical database, the ACS NSQIP prospective institutional database and medical record review. Chi-Square/Fisher's Exact and Independent-Samples t-Tests were used for univariable analyses; multivariable regression (MVR) was performed.

Results: 671 consecutive PD from a single institution were included (429 EDA, 242 non-EDA). On univariable analysis, EDA patients experienced significantly less wound disruption (0.2% vs. 2.1%), unplanned intubation (3.0% vs. 7.9%), pulmonary embolism (0.5% vs. 2.5%), mechanical-ventilation >48hrs (2.1% vs. 7.9%), septic shock (2.6% vs. 5.8%), and lower pain scores. On MVR accounting for baseline group differences (gender, hypertension, pre-operative transfusion, labs, approach, pancreatic duct size), EDA was associated with less superficial wound infections (OR 0.34; CI 0.14-0.83; P=0.017), unplanned intubations (OR 0.36; CI 0.14-0.88; P=0.024), mechanical ventilation >48 hrs (OR 0.22; CI 0.08-0.62; P=0.004), and septic shock (OR 0.39; CI 0.15-1.00; P=0.050). EDA improved pain scores post-PD days 1-3 (P<0.001). No differences were seen in cardiac or renal complications; pancreatic fistula (B+C) or delayed gastric emptying; 30/90-day mortality; length of stay, readmission, discharge destination, or unplanned reoperation.

Conclusion: Based on the largest single institution series published to date, our data support the use of EDA for optimization of pain control. More importantly, our data document that EDA significantly improved infectious and pulmonary complications.

Keywords: Epidural analgesia, pancreatoduodenectomy, pain control, postoperative outcomes

Abbreviations:

Epidural Analgesia (EDA)

Non-Epidural Analgesia (non-EDA)

Pancreatoduodenectomy (PD)

Post-Operative Day (POD)

Enhanced Recovery After Surgery (ERAS)

Hepatopancreatobiliary (HPB)

American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP)

INTRODUCTION

The number of pancreatic resections in total and for benign pancreatic disease has steadily increased over the preceding decades.(1, 2) Despite this increasing incidence, the morbidity of pancreatic surgery, pancreatoduodenectomy (PD) in particular, has persisted around 45-50%.(3, 4) The development and implementation of Enhanced Recovery After Surgery (ERAS) programs serves as one strategy to try and mitigate such morbidity, by addressing postoperative stress and pain control, and through promotion of early oral feeding and mobility.(5) While ERAS programs have been established for nearly two decades in other surgical subspecialties, only recently has hepatopancreatobiliary (HPB) surgery adopted the concept.(6)

A key component to existing HPB-specific ERAS protocols is the use of regional analgesia, most commonly thoracic epidural-delivered analgesia. However, these guidelines are largely based on existing literature supporting the use of epidural analgesia (EDA) in non-HPB-specific patient populations. There is a large body of evidence to show that post-operative pain control is improved with EDA over other modalities across surgical subspecialties.(7-20) However, the association between EDA and reduced post-operative morbidity is less clear. A myriad of studies have shown reduction in mortality, infectious, pulmonary, renal, gastrointestinal, or cardiovascular complications with the use of EDA: but these results are based on heterogeneous cohorts ranging in breadth from inclusion of *all* surgical patients to highly specialized subpopulations for specific procedures.(7-9, 11, 12, 14, 15, 18, 20-31) Meanwhile, others have found conflicting results to suggest no benefit or worse outcomes with the use of EDA.(32-34) These differences in outcomes based on such diverse study populations suggests the true effect of EDA may vary by procedure type.(9) While several prospective studies exist

regarding the use of EDA in abdominal surgery, few are HPB- or pancreatectomy-specific.(35-37)

Far fewer studies have been dedicated to examining outcomes after pancreatectomy, particularly PD, and results are again mixed. Most agree that postoperative pain control after PD is improved with EDA(38-41) but argue that the rate of epidural failure is not worth this benefit.(38, 41) While there is some evidence to suggest improved postoperative outcomes with the use of EDA,(40, 42) others have reported the contrary.(38, 39) Many of these studies are restricted by very small numbers of patients, or are comprised of large datasets like the National Inpatient Sample with their unique and well-established set of limitations. Thus, larger single- or multi-institutional studies for the PD-specific population are warranted to further our knowledge of the effects of EDA on this specialized group of patients.

In this study, we aimed to perform the largest single-institution evaluation of post-operative outcomes for those with and without EDA after PD. A secondary aim was assessment of postoperative pain control in the EDA versus non-EDA subgroups, as pain control may have a direct link to certain postoperative outcomes as well as patient satisfaction and participation in rehabilitation.

METHODS

Patient Population

A retrospective review of our institution's prospectively maintained American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) database was performed to gather all recorded pancreatoduodenectomies (PD) performed from 1/2013-12/2017 (5-year period). The electronic medical record of each patient was reviewed to enhance existing data and to determine the analgesia modality utilized post-PD. Those with an epidural

(opioid and/or local anesthetic) placed in the immediate perioperative period were assigned to the Epidural Analgesia (EDA) group, whereas those without an epidural placed were assigned to the Non-Epidural Analgesia (Non-EDA) group. All postoperative pain scores for the first 72 hours after the time of case completion were reviewed and recorded. Acute Pain Service, General Surgery, and nursing notes were reviewed for immediate post-operative EDA complications (including hypotension, somnolence, dislodgment, etc.) and mitigation strategies that were employed. All data were collected and recorded according to the Indiana University Institutional Review Board guidelines.

Statistical Analysis

Univariable analysis was performed to compare EDA and Non-EDA subgroups at baseline, as well as postoperative outcomes. Chi-Square/Fisher's Exact test and the Independent-Samples t-test were used for categorical and continuous data respectively. To account for differences in the EDA and Non-EDA subgroups, multivariable analyses were performed using binary logistic and linear regression for categorical and continuous postoperative outcomes respectively. SPSS, Version 24 (IBM corp.) and SAS software were used for these analyses.

Variable Definitions

Several variables were included outside of the standard ACS-NSQIP database, or were redefined as follows:

1) Chronic Pancreatitis: patients were considered to have a primary indication for surgery of "Chronic Pancreatitis" when this was the primary indication for surgery listed in the operative report

2) Opioid User: patients were considered to be “Opioid Users” if opioids were prescribed and taken preoperatively for at least 1 week prior to surgery, based on the electronic medical record
3) Wound Classification: through thorough review of the operative reports and intraoperative cultures, only individuals with obvious purulence, purulent fluid or + fluid cultures, infected necrosis with documented + cultures, or gross contamination of gastrointestinal contents intraoperatively were included in the “Dirty/Infected” category. All other patients were grouped as “Other” which encompasses the standard Clean/Contaminated cases, as well as non-infectious Contaminated cases (ex: inflammatory changes, the presence alone of a biliary stent in the absence of purulent bile and + cultures).
4) Pathology Classification: patients were grouped into a Malignant or Benign/Non-Neoplastic pathology category based on individual diagnoses detailed in the Results section.
5) Clinically Significant Pancreatic Fistula: Included those graded B or C according to the International Study Group on Pancreatic Surgery(43)
6) Pain Scores: as reported by nursing at regular intervals (approximately every 1-4 hours depending on acuity of care), graded on a 0-10 scale by the patient

Perioperative Care

All PD were performed by surgeons well versed in the operation who regularly perform complex hepatobiliary operations. Over 95% of the PD performed in this series were by surgeons who completed over 100 PD throughout the 5-year period. The decision to pursue EDA or Non-EDA was dependent on the presence/absence of standard contraindications (i.e. infection at

insertion site, impaired coagulation)(20) patient and surgeon preference. Pain control for those with EDA is managed entirely by a specialized service of anesthesiologists, the Acute Pain Service until the time of epidural catheter removal. Patients without EDA are managed entirely by the surgical service.

RESULTS

Study Population

A total of 671 patients underwent PD over the 5-year period (January 2013-December 2017). For 429 (63.9%) patients, pain was controlled with EDA with or without alternative means, whereas pain was controlled with alternate methods only (non-EDA) for the other 242 (36.1%) patients. Though patients underwent PD for a wide variety of pathologies, there was a similar distribution of malignant pathology for EDA (n=281, 65.5%) and non-EDA (n=164, 67.8%) patients (P=0.551). The most common indication for PD was primary pancreatic malignancy, including ductal adenocarcinoma/acinar cell carcinoma (n=308, 45.9%). For benign pathology, the most frequent was chronic pancreatitis (n=104, 46.0%) which was equally distributed between EDA and non-EDA patients (15.6% vs 15.3%, P=1.000). The distribution of malignant and benign pathologies are summarized in **Figure 1a** and **Figure 1b** respectively.

Baseline demographics and comorbidities were similar with the exception of a higher proportion of males (57.4% vs. 46.4%, P=0.006), history of hypertension (61.2% vs. 51.0%, P=0.012), and preoperative transfusion requirements (2.5% vs. 0.2%, P=0.010) in non-EDA patients compared to EDA patients. There was a higher proportion of open PD performed (99.5% vs. 96.7%, P=0.006), and a higher incidence of small main pancreatic ducts defined as <3mm (21.5% vs. 13.8%, P=0.017) in the EDA group. These and other baseline features are summarized in **Table 1.**

Postoperative Outcomes

Patients with EDA revealed several significantly improved infectious, wound, and pulmonary outcomes above non-EDA patients on univariable and multivariable regression analyses. On univariable analysis, those with EDA had lower rates of septic shock (2.6% vs. 5.8%, P=0.034), wound disruption (0.2% vs. 2.1%, P=0.025), unplanned intubation (3.0% vs. 7.9%, P=0.005), prolonged ventilation (2.1% vs. 7.9%, P<0.001), and pulmonary embolism (0.5% vs. 2.5%, P=0.029). After multivariable regression controlling for significant group differences, several infectious and pulmonary outcomes were still improved with EDA. Namely, those with EDA were less likely to experience superficial wound infections (OR 0.34 [0.14-0.83], P=0.017), septic shock (OR 0.39 [0.15-1.00], P=0.050), unplanned intubation (OR 0.36 [0.14-088], P=0.024), and prolonged ventilation (OR 0.22 [0.08-0.62], P=0.004).

There was no significant difference in the rate of renal or cardiovascular complications, clinically significant postoperative pancreatic fistula (B+C) or delayed gastric emptying or length of stay between groups. The 30- and 90-day mortality, 30-day readmission rate, and incidence of unexpected return to the operating room within 30-days was also similar between patients with and without EDA. Outcomes are summarized in **Table 2.**

Pain Score Assessment

Postoperative pain scores were compared between EDA and non-EDA patients for the first 72-hours postoperatively at 24-hour intervals. On univariable analysis, postoperative pain scores were significantly lower for those with EDA compared to those without EDA on post-operative day (POD) 1, POD2, POD3, and on average over all 3 days. **(Figure 2).** On multivariable regression analysis, average pain scores remained significantly lower for those with EDA compared to those without EDA on POD 1 (B-coefficient -1.01[-1.42 to -.589]), POD

2 (B-coefficient -0.73[-1.09 to -0.36]), POD 3 (B-coefficient -0.79[-1.16 to -0.41]), and aggregate POD 1-3 (B-coefficient -0.91[-1.25 to -0.56]) (all P<0.001).

Epidural Complications

Complaints or complications potentially related to EDA were recorded for the first 24 hours postoperatively. One hundred and thirty-three of the 429 (31.0%) with an epidural had one or more issues within the first 24 hours. The most common occurrence was hypotension with/without somnolence or respiratory depression (n=68, 51.1%). Symptoms of opioid toxicity alone (somnolence, respiratory depression) were next most common (n=33, 24.8%), with the remaining patients experiencing a number of more rare complications. **(Figure 3a)** In general, these issues were mitigated with only minor adjustments necessary to the rate of infusion (n=50, 37.6%), medication mixture (n=55, 41.3%), or a combination of these two strategies (n=6, 4.5%). Only 18 patients (13.5%) required removal or replacement of the catheter for inadequate pain control secondary to suboptimal placement or accidental dislodgment. **(Figure 3b)**

DISCUSSION

ERAS programs for HPB surgery have recently been developed and implemented in an attempt to improve the seemingly stagnant and high rate of morbidity after pancreatic surgery. One important feature is the use of EDA to not only improve pain control, but surgical outcomes as well. However, pancreatectomy-specific literature is limited to very small series or large national databases with inherent limitations. To our knowledge, this is the largest single-institution series to date (671 patients) examining primarily surgical outcomes after PD with and without the use of EDA. While not the focus of the study, pain control was assessed as a secondary initiative.

In the present study, we report a lower rate of certain infectious complications with the use of EDA. Specifically, there was a lower unadjusted rate of septic shock for patients receiving EDA compared to non-EDA patients, which was borderline significant on multivariable regression analysis (P=0.050). We also found a significantly lower rate of superficial surgical site infections for patients with EDA after controlling for potential confounders. Notably, our institutional superficial surgical site infection rate for the entire cohort (3.3%) was much lower than expected for a clean-contaminated operation (exceeding 10%); this already low rate was further enhanced by the use of EDA. Results in the literature regarding infectious outcomes and EDA are conflicting and difficult to interpret due to differences in definitions for infectious complications. The majority of existing studies report decreased or similar rates of infectious complications including rates of pneumonia, urinary tract infection, sepsis/bacteremia, wound infection, or aggregates of these individual outcomes.(8, 9, 19, 24, 29, 39, 44-46) In examining liver and pancreatic resections specifically, Amini *et al.* revealed a lower rate of postoperative sepsis, but similar rate of wound infections between EDA and non-EDA patients.(45) In contrast, Pratt *et al*. examined PD specifically, and found an increased rate of *aggregate* infectious complications with EDA use. However, there was no significant difference in the rate of any individual component included in this aggregate analysis, including sepsis or wound infection.(38) Another study examining PD alone revealed a higher rate of overall wound complications with the use of EDA, defined as internal or external disruption; it is unclear if this definition includes wound infections, making comparison to the present study results difficult.(42) Mechanistically, there is support in the literature for a reduced rate of infectious complications with the use of EDA through dampening of the stress response to surgery and its associated attenuation of the immune system.(14, 23, 24) Thus, there is a logical explanation and

some prior evidence to validate our reduced rate of sepsis with EDA use, but our finding of reduced superficial wound infection in the EDA group is to our knowledge previously unreported for this population and warrants further evaluation.

Pulmonary complications are another heterogeneous category of morbidity cited in the EDA literature. It is known that upper abdominal surgery may have adverse effects on pulmonary function. In general, existing literature supports the claim that EDA reduces the rate of pulmonary complications, including respiratory failure, prolonged ventilation, and respiratory depression.(8, 9, 12, 15, 21, 22, 25, 31, 40, 45, 46) Though the minority, two studies regarding PD specifically have shown equal(39) or even increased(38) rates of pulmonary complications with EDA. Our results agree with the majority of the literature, as we found the rate of prolonged ventilation (>48 hours) and unplanned intubation was significantly lower in the EDA group compared to patients with non-EDA. Moraca *et al.* and Liu *et al.* propose this improvement in pulmonary function with the use of EDA is not only related to superior pain control, but also improvement in chest wall compliance, and modulation of inappropriate diaphragmatic reflex inhibition.(14, 23)

Many outcomes in the present study are in line with the existing PD-specific literature, including similar postoperative length of stay, mortality, readmission rates, and rate of delayed gastric emptying,(38, 39) yet some discrepancies remain. Pratt *et al.* reported a higher rate of POPF with the use of EDA that did not hold true in the present study.(38) Amini *et al.* reported a shorter postoperative length of stay in the EDA group on multivariable regression analysis, whereas we found this to be similar between EDA and non-EDA patients.(42)

The most consistently reported benefit of EDA over alternative means is superior pain control in the immediate postoperative period. While the existing literature for the surgical

population in general is expansive, studies pertaining to PD are fairly limited. Nonetheless, PD-specific studies that do address postoperative pain control are generally in agreement: EDA provides a postoperative analgesic benefit over other conventional methods of pain control. (38-40) Though not the primary aim of our study, we did include this metric in our analysis and validated these prior findings. In the present study, patients with EDA had significantly lower pain scores on POD1-3 compared to patients without EDA.

Despite the potential benefits, EDA holds inherent risk that cannot be ignored. These potential complications include sympathetic blockade resulting in hypotension, systemic opioid absorption with respiratory depression or somnolence/confusion, nausea/vomiting, pruritis, urinary retention, or the highly feared but exceedingly rare epidural hematoma or abscess that may cause permanent neurologic injury.(14, 18, 20, 40, 47) We examined the immediate (first 24-hours postoperatively) potential adverse effects associated with EDA in our patient population, and largely found relatively minor complications that were addressed with minimal changes in management. Most patients (69%) had no immediate complication associated with EDA. Because EDA requires close monitoring for complications and expertise in quickly mitigating such issues, Davies *et al.* supports the use of an Acute Pain Service—a group of specialized anesthesiologists familiar with EDA—to manage this modality of postoperative analgesia.(20) At our institution, this recommendation is followed.

This study has a few limitations. The first is in regard to the retrospective review of particular data points, namely those involving the use of EDA, immediate complications of EDA, and postoperative pain scores. We did our best to minimize missing retrospective data through a thorough review of the medical record, including nursing documentation of postoperative complications associated with the epidural and notification of house-staff. Secondly, the range of

EDA use was from 1-6 days (mean 3.6 days) in our patient cohort. Pain scores were tracked only through POD 3, to match with this average length of time the epidural catheter was in place. Though some patients had accidental dislodgment or required early removal of the epidural catheter before POD 3, this was the minority of cases (37 of 429 patients, 8.6%). Thus, we believe any skew in pain scores, or overall surgical outcomes, resulting from individuals utilizing EDA less than 3 days is minimal. Finally, the decision to utilize EDA at our institution is based partly on physician and patient preference, and may serve as a source of unaccountable selection bias. We tried to reduce this effect through controlling for all other recognized baseline group differences in multivariable analysis that may affect postoperative outcomes.

CONCLUSION

The use of EDA after pancreatoduodenectomy not only improved postoperative pain control, but reduced the rate of certain infectious and pulmonary complications. With proper patient selection and in the hands of experienced Acute Pain specialists, the use of EDA appears to be safe. The high rate of EDA use at our institution, as well as EDA recommendations included in the HPB-specific Enhanced Recovery protocols are justified.

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Table 1 Comparison of Baseline and Perioperative Characteristics for Patients with and without Epidural Analgesia

Characteristic	Epidural analgesia (N=429)		Non-epidural analgesia (N=242)		p Value
	Data	Missing, N	Data	Missing, N	
Preoperative demographic and comorbidity					
Age, y, mean (SD)	64.0 (12.9)	0	63.6 (12.4)	0	0.667
Sex, male, n (%)	199 (46.4)	0	139 (57.4)	0	0.006*
Race, Caucasian, n (%)	403 (94.2)	1	224 (94.1)	4	0.983
Preoperative opioid use, n (%)	176 (41.0)	0	99 (40.9)	0	0.976
BMI, kg/m², mean (SD)	27.5 (5.8)	0	27.6 (6.1)	0	0.721
Diabetes, n (%)	107 (24.9)	0	74 (30.6)	0	0.114
Tobacco use, n (%)	121 (28.2)	0	81 (33.5)	0	0.153
COPD, n (%)	34 (7.9)	0	22 (9.1)	0	0.600
CHF, n (%)	2 (0.5)	0	1 (0.4)	0	1.000
HTN, n (%)	219 (51.0)	0	148 (61.2)	0	0.012*
Steroid/immunesuppression, n (%)	9 (2.1)	0	5 (2.1)	0	0.978
Weight loss (>10% in 6 months), n (%)	91 (21)	0	53 (21.9)	0	0.779
Preoperative transfusion, n (%)	1 (0.2)	0	6 (2.5)	0	0.010*
SIRS/sepsis, n (%)	1 (0.2)	0	2 (0.8)	0	0.296
ASA Class, mean (SD)	3.0 (0.2)	0	3.0 (0.3)	0	0.552
Preoperative lab & pancreas-specific feature					
BUN, mg/dL, mean (SD)	15.8 (7.3)	3	15.7 (7.8)	8	0.862
Creatinine, mg/dL, mean (SD)	0.9 (0.3)	3	0.9 (0.4)	8	0.955
Albumin, g/dL, mean (SD)	3.9 (0.5)	5	3.7 (0.6)	12	<0.001*
White Cell Count (μL^{-1}), mean	8.0	7	8.0	14	0.968

(SD)	(3.1)		(3.8)		
Hematocrit, g/dL, mean (SD)	38.3 (5.1)	8	36.8 (6.1)	13	0.003*
INR, mean (SD)	1.1 (0.1)	48	1.1 (0.2)	48	0.009*
Preoperative jaundice, n (%)	160 (37.3)	0	82 (33.9)	0	0.377
Preoperative biliary stenting, n (%)	227 (52.9)	0	135 (55.8)	0	0.474
Preoperative chemotherapy, n (%)	61 (14.2)	0	38 (15.7)	0	0.603
Preoperative radiation, n (%)	11 (2.6)	0	8 (3.3)	0	0.578
Malignant pathology, n (%)	281 (65.5)	0	164 (67.8)	0	0.551
Primary diagnosis of pancreatitis, n (%)	62 (14.5)	0	29 (12.0)	0	0.370
Perioperative feature					
Wound class (Dirty/Infected)	8 (1.9)	0	6 (2.5)	0	0.593
Duration of operation, minutes, mean (SD)	292.4 (90.9)	0	297.0 (102.4)	0	0.562
Open operative approach, n (%)	427 (99.5)	0	234 (96.7)	0	0.006*
Small duct (< 3mm) , n (%)	88 (21.5)	19	32 (13.8)	10	0.017*
Soft gland, n (%)	178 (43.7)	22	100 (43.7)	13	0.987
Vascular reconstruction performed, n (%)	43 (10.0)	0	31 (12.8)	0	0.268

*Significant

CHF, congestive heart failure; HTN, hypertension; SIRS, Systemic Inflammatory Response Syndrome; ASA, American Society of Anesthesiologists; BUN, blood urea nitrogen; INR International Normalized Ratio

Table 2 Summary of Postoperative Outcomes for Patients with and without Epidural Analgesia

Outcome	Epidural analgesia (N=429)	Non-epidural analgesia (N=242)	Univariable analysis	Multivariable analysis*	
			p Value	p Value	B-Coefficient or odds ratio [95% CI]
Wound/infectious outcome, n (%)					
Superficial surgical infection	10 (2.3)	12 (5.0)	0.066	0.017†	0.34 [0.14-0.83]
Deep surgical infection	5 (1.2)	5 (2.1)	0.508	0.363	0.53 [0.14-2.08]
Organ space infection	33 (7.7)	27 (11.2)	0.131	0.287	0.71 [0.38-1.33]
Pneumonia	10 (2.3)	12 (5.0)	0.066	0.299	0.56 [0.19-1.70]
Urinary tract infection	11 (2.6)	9 (3.7)	0.398	0.555	0.71 [0.23-2.21]
C.Diff infection	5 (1.3)	2 (1.2)	1.000	0.524	1.80 [0.29-11.05]
Sepsis	17 (4.0)	18 (7.4)	0.052	0.066	0.47 [0.21-1.05]
Septic shock	11 (2.6)	14 (5.8)	0.034†	0.050†	0.39 [0.15-1.00]
Wound disruption	1 (0.2)	5 (2.1)	0.025†	0.071	0.13 [0.01-1.19]
Pulmonary outcome, n (%)					
Unplanned intubation	13 (3.0)	19 (7.9)	0.005†	0.024†	0.36 [0.14-0.88]
Pulmonary embolism	2 (0.5)	6 (2.5)	0.029†	0.107	0.15 [0.02-1.50]
Vent >48 hours	9 (2.1)	19 (7.9)	<0.001†	0.004†	0.22 [0.08-0.62]
Renal outcome, n (%)					
Progressive renal insufficiency	0 (0.0)	1 (0.4)	0.361	0.293	0.18 [0.01-4.36]
Acute renal failure	4 (0.9)	5 (2.1)	0.296	0.533	0.64 [0.15-2.65]
Cardiovascular outcome, n (%)					
Cerebrovascular accident	2 (0.5)	1 (0.4)	1.000	0.285	5.43 [0.01-107.67]
Cardiac arrest	4 (0.9)	3 (1.2)	0.707	0.664	1.77 [0.14-22.90]
Myocardial infarction	6 (1.4)	3 (1.2)	1.000	0.723	1.43 [0.20-10.21]
Transfusion w/in 72 hrs postop	113 (26.3)	65 (26.9)	0.884	0.157	1.39 [0.88-2.20]
Deep venous thrombosus	11 (2.6)	8 (3.3)	0.578	0.573	1.38 [0.44-4.40]
Pancreatectomy-specific outcome, n (%)					
Pancreatic fistula (B or C)	33 (7.7)	24 (9.9)	0.321	0.504	0.79 [0.40-1.58]
Delayed gastric emptying	72 (16.8)	40 (16.5)	0.932	0.684	0.90 [0.54-1.51]
Quality outcome					
Length of hospital stay, d, mean (SD)	10.5 (10.8)	11.1 (9.5)	0.460	0.776	-0.29 [-2.3 - 1.69]
Discharge to home, n (%)	358 (84.2)	187 (79.2)	0.106	0.341	0.78 [0.47-1.30]

30-day mortality, n (%)	10 (2.3)	5 (2.1)	0.824	0.493	1.59 [0.43-5.92]
90-day mortality, n (%)	10 (2.3)	7 (2.9)	0.657	0.928	0.95 [0.30-3.0]
≥ 1 readmission, n (%)	48 (13.5)	35 (14.5)	0.734	0.972	0.99 [0.58-1.69]
≥ 1 return to OR, n (%)	11 (2.6)	10 (4.1)	0.263	0.293	0.59 [0.22-1.58]

*Multivariable model included male sex, hypertension, preoperative transfusion, albumin, hematocrit, INR, operative approach, small duct

† Significant

OR, operating room

FIGURE LEGENDS

Figure 1. (A) Distribution of Malignant Pathology Amongst Pancreatoduodenectomy Cohort

(B) Distribution of Benign Pathology Amongst Pancreatoduodenectomy Cohort

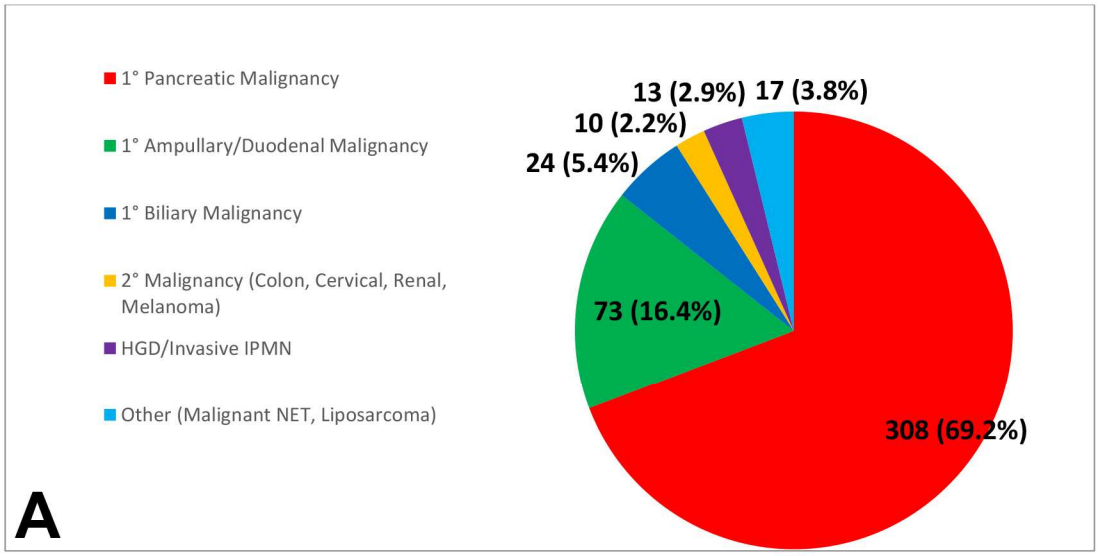
Figure 2. Univariable Analysis of Pain Scores (Postoperative Days 1-3 and Aggregate) for Patients With and Without Epidural Analgesia (Mean±Standard Deviation)

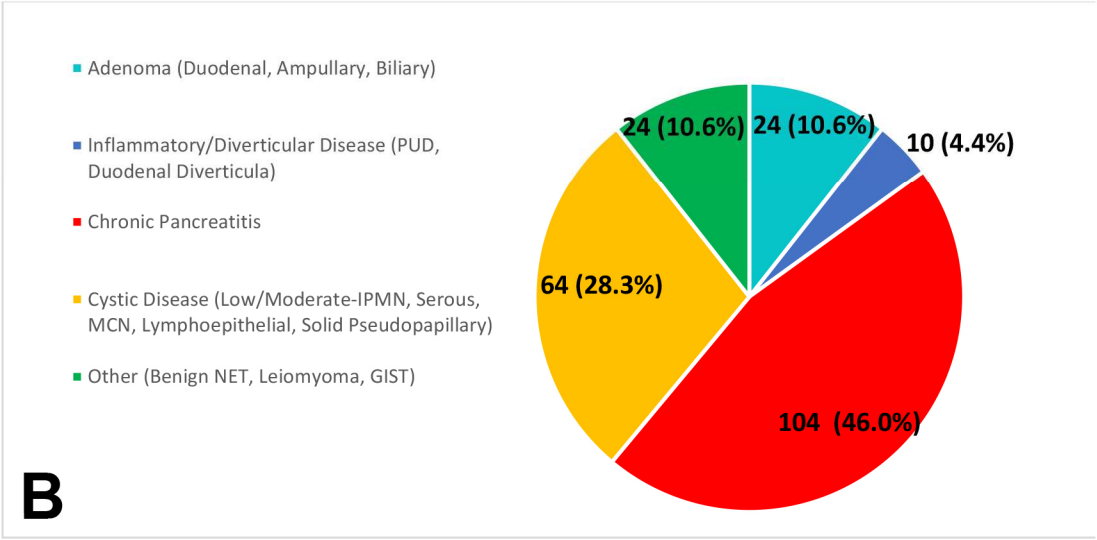
Figure 3. (A) Distribution of Potential Epidural Complications Within 24-Hours Postoperatively. *Other includes Nausea (2), Dizziness (1), Need for Anticoagulation (1), Concern for Medication-Related Heart Block (1), and Unstated Reason for Epidural Adjustment (4)

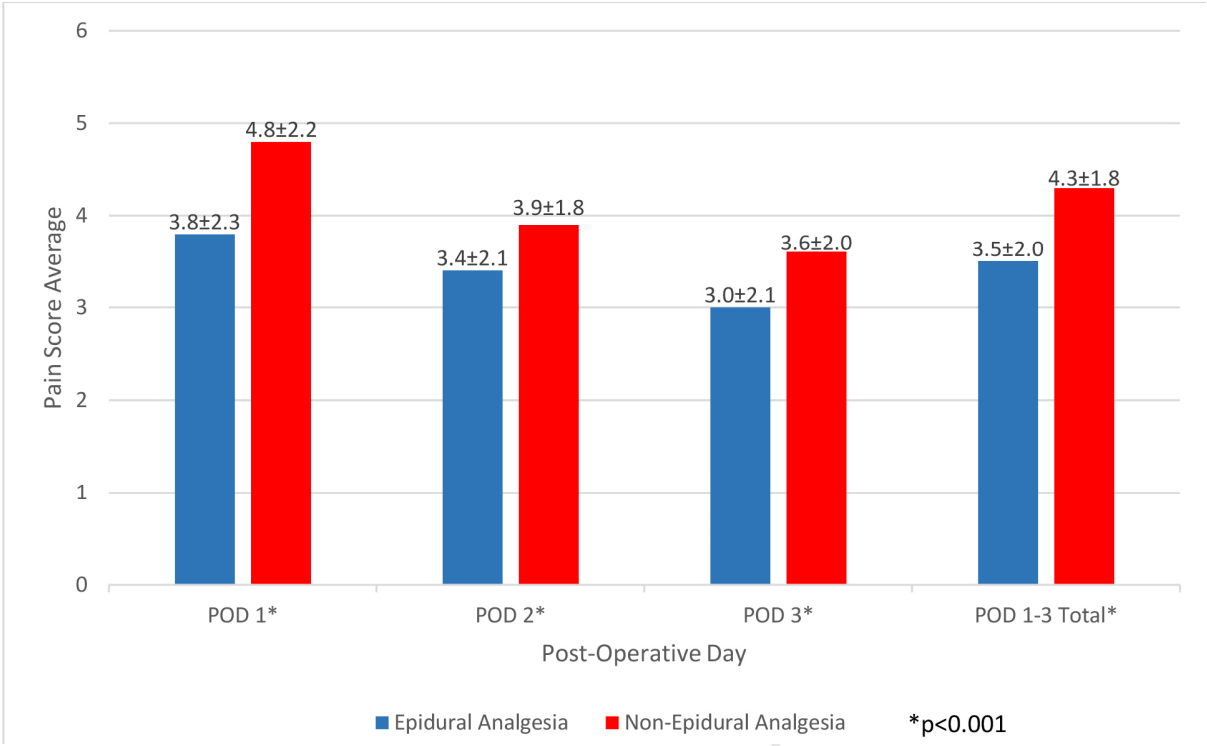
(B) Distribution of Mitigation Strategies for Potential Epidural Complications Within 24-Hours Postoperatively

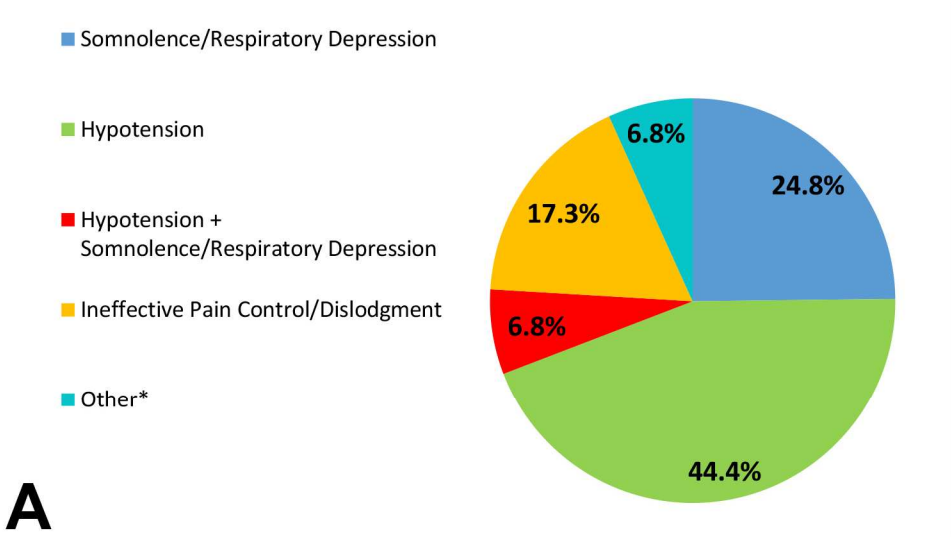
PRECIS

The use of epidural analgesia (EDA) after pancreatoduodenectomy not only improved postoperative pain control but also reduced the rate of certain infectious and pulmonary complications in this series. The recommendation for EDA use in hepatopancreatobiliary-specific enhanced recovery protocols may be justified.

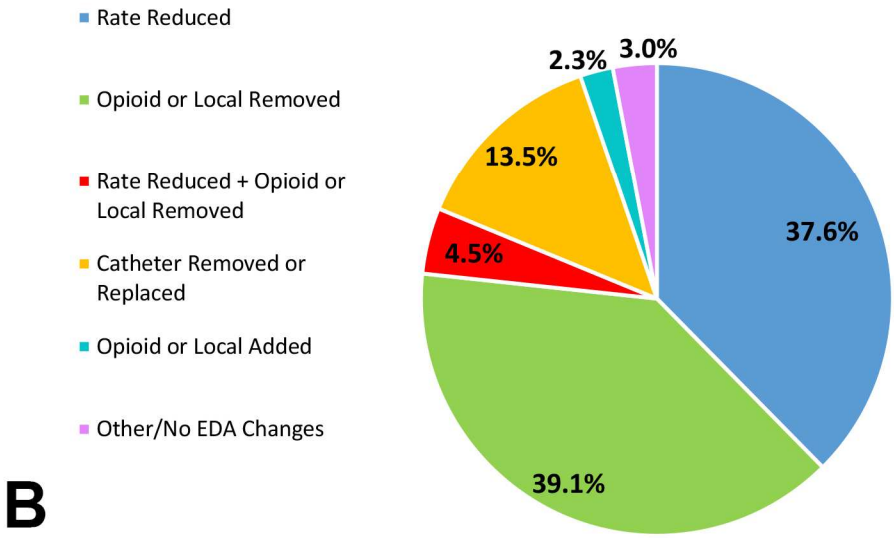

1° Pancreatic Malignancy
1° Ampullary/Duodenal Malignancy
1° Biliary Malignancy
2° Malignancy (Colon, Cervical, Renal, Melanoma)
HGD/Invasive IPMN
Other (Malignant NET, Liposarcoma)
13 (2.9%)
17 (3.8%)
10 (2.2%)
24 (5.4%)
73 (16.4%)
308 (69.2%)
A


Adenoma (Duodenal, Ampullary, Biliary)
Inflammatory/Diverticular Disease (PUD, Duodenal Diverticula)
Chronic Pancreatitis
Cystic Disease (Low/Moderate-IPMN, Serous, MCN, Lymphoepithelial, Solid Pseudopapillary)
Other (Benign NET, Leiomyoma, GIST)
24 (10.6%)
24 (10.6%)
10 (4.4%)
64 (28.3%)
104 (46.0%)
B





A



B