Published in final edited form as:

Ann Surg. 2017 September ; 266(3): 545–554. doi:10.1097/SLA.0000000000002386.

A Randomized Controlled Trial of Postoperative Thoracic Epidural Analgesia Versus Intravenous Patient Controlled Analgesia after Major Hepatopancreatobiliary Surgery

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Abstract

Objectives—The primary objective of this randomized trial was to compare thoracic epidural analgesia (TEA) to intravenous patient controlled analgesia (IV-PCA) for pain control over the first 48 hours after hepatopancreatobiliary (HPB) surgery. Secondary endpoints were patient-reported outcomes, total narcotic utilization and complications.

Summary of Background Data—Although adequate postoperative pain control is critical to patient and surgeon success, the optimal analgesia regimen in HPB surgery remains controversial.

Methods—Using a 2.5:1 randomization strategy, 140 patients were randomized to TEA (N=106) or IV-PCA (N=34). Patient-reported pain was measured on a Likert scale (0–10) at standard time intervals. Cumulative pain area under the curve (AUC) was determined using the trapezoidal method.

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Financial Disclosures: None

National Meeting Presentation: These data were presented at the 2017 137th Annual American Surgical Association Annual Meeting

Results—Between the study groups key demographic, comorbidity, clinical and operative variables were equivalently distributed. The median AUC of the postoperative time 0 to 48 hour pain scores was lower in the TEA group (78.6 vs 105.2 pain-hours, $p=0.032$) with a 35% reduction in patients experiencing 7/10 pain (43% vs 66%, $p=0.05$). Patient-reported outcomes and total opiate use further supported the benefit of TEA on patient experience. Anesthesia related events requiring change in analgesic therapy were comparable (12.2% vs. 2.9%, respectively, $p=0.187$). Grade 3 surgical complications, median length of stay (6 days vs 6 days), readmission (1.9% vs 3.1%), and return to the OR (0.9 vs 3.1%) were similar (all $p>0.05$). There were no mortalities in either group.

Conclusions—In major HPB surgery, TEA provides a superior patient experience through improved pain control and less narcotic use, without increased length of stay or complications.

Keywords

hepatectomy; pain management; pancreaticoduodenectomy; patient reported outcomes (PROs); quality of life

INTRODUCTION

As the safety of hepatopancreaticobiliary surgery has significantly improved, the practice has grown in cases and complexity.[1–14] Compared to traditional open surgical procedures, minimally invasive laparoscopic surgery has led to decreased postoperative pain.[15–17] However, in the majority of hepatic and pancreatic resections, a minimally invasive approach is not technically feasible; and postoperative pain continues to be poorly controlled despite high narcotic doses, with adverse impact on patient experience and patient outcomes.[18]

Inadequate pain control after open abdominal procedures may have both primary and secondary impacts on patient outcomes. In the initial postoperative period, inadequate pain control contributes to the neuroendocrine stress response, increased complications and prolonged length of stay.[19,20] These adverse initial outcomes can delay overall recovery, limiting the patient's ability to return to normal levels of function, and in the case of cancer patients, the ability to return to intended oncologic therapy (RIOT).[21] This is particularly relevant in hepatopancreatobiliary surgery, where procedures can be disabling and most patients undergo oncologic resection. Effective pain control is, therefore, imperative in these patients. Yet, the best modality for pain control after hepatopancreaticobiliary resection remains unclear.

Two of the most common analgesic modalities used after inpatient abdominal surgery are thoracic epidural analgesia (TEA) using local anesthetic agents and/or narcotics, and intravenous patient controlled analgesia (IV-PCA) using narcotics. Multiple non-randomized comparisons have been reported, however, relatively few level 1 data from randomized trials are available.[22–28] Currently, the advantages and disadvantages between these two strategies continue to be debated, and the most effective strategy has not been determined. The objective of this randomized control trial (RCT) was to compare the efficacy of pain control and safety between TEA and IV-PCA.

METHODS

Patients

This study was conducted between February 2012 and September 2016 at the University of Texas MD Anderson Cancer Center. The Ethical Committee on Clinical Investigation approved this RCT and it was registered in accordance with [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT01438476) (NCT01438476). A written informed consent was obtained before surgery from all participating patients.

Eligible patients were 18 years of age or older undergoing liver or pancreatic resection for malignancy. Both minor and major hepatectomies were included in the RCT. Major hepatectomy was defined by the Brisbane 2000 terminology as resection of 3 or more Couinaud segments.[29–32]

All patients were required to have adequate coagulation function within 30 days of surgery, defined as platelet count $\geq 100,000/\text{mL}$, INR ≤ 1.5 , and partial thromboplastin time (PTT) ≤ 40 seconds. Patients with fever, evidence of infection, or other coexisting medical conditions that would preclude epidural placement were excluded. Other exclusions included: history of chronic pain, long-term narcotic use, history of anaphylaxis to local anesthetics or narcotics, previous or current neurologic disease affecting the hemithorax or below, bleeding diathesis or coagulopathy, major open abdominal/thoracic surgery in the previous 30 days under general anesthesia (except total intravenous anesthesia), ongoing use or planned perioperative use of anticoagulants (not including deep vein thrombosis prophylaxis). Patients with educational, psychiatric (untreated or poorly controlled schizophrenia, major depression, or bipolar disorder), or communication (language) barriers that would preclude accurate assessment of postoperative pain and/or ability to answer questions about pain were not eligible.

Randomization

After providing written informed consent, patients undergoing resection were randomly assigned on the morning of surgery to the TEA or IV-PCA group with a 2:1 TEA: IV-PCA randomization strategy.

Analgesic Regimens

All patients randomized to TEA had a thoracic epidural catheter placed preoperatively in the holding area or the operating room. Epidural catheters were placed between the 5th and 10th thoracic interspinous levels using standard technique according to institutional practices. After a negative test dose, a bolus of 10 mcg/kg of epidural hydromorphone (maximum of 1 mg) was administered prior to securing the catheter. All epidural catheters were tested for correct placement and level of block was documented. Prior to surgical incision, 3–10 mL of 2% lidocaine was administered incrementally through the epidural catheter to establish a block. Continuous analgesia was subsequently achieved with an epidural infusion of bupivacaine 0.075% and hydromorphone 5 mcg/mL at 5–8 mL/hr. Secondary alternatives to hydromorphone were fentanyl and bupivacaine. Infusion rates on the surgical floor were 5–8 mL/hr with an added patient controlled epidural analgesia dose of 3 mL every 10 minutes

as needed (not to exceed 6 mL/hr). Infusions and catheters were discontinued when patients were successfully tolerating a diet (or tube feeds) and could be safely transitioned to oral/enteral analgesics.

For patients randomized to the IV-PCA group, intraoperative intravenous narcotics were titrated by the Anesthesia team until the patient was awake and alert in the post-anesthesia care unit, and then IV-PCA infusion was initiated. Hydromorphone was the opioid of choice unless the patient had allergic reaction or other contraindications. Secondary alternatives included fentanyl or morphine. The initial recommended starting dose settings included: no basal rate, 0.2 mg every 10 minutes of demand dosing, and a 0.5 mg nursing bolus every 1 hour as needed for additional pain control.

Adjunctive oral, rectal, or intravenous non-narcotic analgesics (ie. Acetaminophen or non-steroidal) were utilized at the discretion of the Acute Pain Service and/or primary surgical team for both the TEA and IV-PCA groups. In cases with inadequate pain control, cross-over between arms was permitted, although all patient outcomes were assessed within randomized groups on an intention-to-treat basis.

Study Endpoints

The primary endpoint was the area under the curve (AUC) pain score during the first 48 hours after surgery. Patient-reported pain scores were assessed in both groups with a numeric/visual pain scale (0–10) at multiple time points per day that started immediately in the post-operative care unit and concluded after post-operative day (POD) 5. With pain scores collected at specific time points, an Area Under the Curve for pain was calculated for the first 48 hours after surgery (AUC 48) using the trapezoidal method. Additionally, episodes of severe pain, defined as any pain score response of 7 or greater, were recorded. Secondary study endpoints included patient-reported functional outcomes, narcotic use over the first 5 post-operative days, surgical complications, analgesic related complications and length of stay.

To calculate total narcotic use, all medication doses were converted into oral morphine equivalents (OME) using previously reported conversions.[33] When calculating OME, narcotics dosed through the TEA were considered equivalent (1:1) to IV narcotic dosing administered either through intravenous line or IV-PCA.

Surgical and analgesic complication data were collected in real time and retrospectively graded with the Modified Accordion Severity Grading System (MAGS).[34] Each complication was categorized into its appropriate system: neurology, cardiovascular, pulmonary, gastrointestinal, renal, wound, sepsis, and other. In addition, post-operative bile leak and liver failure was specifically included for analysis using standard definitions.[35,36] Severe complications were defined as a MAGS 3–5. All complications were reviewed by two surgical oncology department staff members. Intraoperative and postoperative administration of packed red blood cells was considered a transfusion. The postoperative transfusion period included any time after the operation until hospital discharge. For patients with TEA, the Acute Pain Service monitored the epidural site daily for evidence of hematoma, cellulitis, abscess, cerebrospinal fluid leak, and malfunction. Analgesic

complication was defined as any event that required a discontinuation of the analgesic modality being utilized.

Several validated patient-reported outcome tools were administered to further measure pain, satisfaction with pain control, quality of life and recovery of function. The Short Form (SF)-8 health survey [37–39] and SF-36 [40–42] were both administered preoperatively. Approximately 24 hours following surgery, the SF-8 was repeated, while the SF-36 was administered near day of hospital discharge. Quality of recovery and patient satisfaction were measured with the Health Outcomes Recovery Survey (HORS) [43] with daily administration on the first 5 post-operative inpatient days. In this survey, patients were asked “how satisfied or unsatisfied are you with overall performance of your pain medication?” This patient satisfaction score was measured on a scale from 1–7: 1. Very satisfied, 2. Somewhat satisfied, 3. Slightly satisfied, 4. Neither satisfied nor unsatisfied, 5. Slightly unsatisfied, 6. Somewhat unsatisfied, 7. Very unsatisfied.

Data Collection

For all patients, data was prospectively collected in real-time. Variables collected included patient demographics, pain scores, perioperative clinical information, and complications. Patient-reported pain assessment began in the post anesthesia care unit (PACU) by the nursing staff approximately every hour until the patient was transferred to their designated inpatient care units. In the overnight recovery suite and general floor, pain was assessed by nursing staff approximately every 4 hours; while in the surgical intensive care unit (SICU), pain was assessed by the nursing staff every hour.

Statistical Analysis

The distribution of each continuous variable was summarized by its mean $\pm$ standard deviation and/or median with range (R)/interquartile range (IQR). The distribution of each categorical variable was summarized in terms of its frequency and percentage. Continuous variables were compared between treatment groups by Wilcoxon rank sum tests, and for the categorical variables, the comparison between treatments was conducted with Fisher’s Exact tests. To assess the relative impact of patient, surgical and analgesia variables on study endpoints, univariate and multivariate regression models were developed. Backward step-wise model selection was used to obtain the final regression model for the primary endpoint of AUC48. Piecewise polynomial regression was used to characterize mean pain score trends over time with 95% confidence bands representing interval estimators that characterize the extent of uncertainty at significance level 0.05 over the follow-up time domain observed in our study population. AdaptFitOS version 0.62 package was utilized in R version 3.1.3 to compute the confidence bands. Other statistical analyses were performed using SPSS Statistics 21 (IBM, Armonk, NY). All tests were two-sided.

RESULTS

During the study period, 178 screened patients were initially eligible for inclusion to the RCT. A Consort flow diagram of this RCT is shown in Figure 1.[44] Among the 178 eligible patients, 38 patients were excluded due to withdrawal of consent, development of exclusion

criteria and/or the finding of unresectable disease at surgery. The study concluded with 140 patients eligible for analysis, with 106 patients allocated to the TEA group and 34 patients allocated to the IV-PCA group.

Patient Characteristics

Table 1 reports the distribution of patient characteristics, preoperative and perioperative variables between the TEA and IV-PCA groups. 136 patients had a liver resection and 4 patients had a major pancreas resection (3 pancreaticoduodenectomies and 1 total pancreatectomy). Oncologic indications for resection included colorectal liver metastases (88, 62.9%), cholangiocarcinoma (13, 9.3%), hepatocellular carcinoma (9, 6.4%), gallbladder adenocarcinoma (7, 5%), neuroendocrine tumor (5, 3.6%), and other histologies (17, 12.1%). There were no differences observed in preoperative clinical or perioperative features between TEA and IV-PCA groups.

Primary Endpoint: Postoperative Pain Experience

The median length of time on the study pain control modality was similar between randomized groups (TEA: 4 days, IQR 3–4 days vs. IV-PCA: 4 days, IQR 3–5 days, $p=0.597$). For all patients, the overall median AUC 48 was 86.4 pain-hours (Range: 0–267.3). The median AUC 48 was less in patients who had TEA (78.6, R: 0–228.5) vs. IV-PCA (105.2, R: 33.9–267.3), $p=0.0322$. Additionally, fewer patients in the TEA (42.5%) group experienced inadequate pain control compared to those in the IV-PCA (61.8%) group, $p = 0.0747$. Figure 2 graphically depicts the pain experience in the TEA group when compared to IV-PCA. After adjustment of preoperative clinical features and perioperative factors, multivariate regression identified older age (Coefficient: 1.18, Standard Error 0.42, $p=0.006$) and use of TEA (coefficient: 25.8, Standard Error: 10.38, $p=0.0142$) to be independently associated with a lower AUC 48.

Postoperative Surgical and Analgesic Related Complications

Among 140 patients, 50 (35.7%) patients experienced a surgical complication, with 10 (7.1%) of these patients experiencing a severe complication. Collectively, there were 1 neurologic, 8 cardiac, 3 respiratory, 5 renal, 14 gastrointestinal, 8 wound, and 7 other complications. For liver related complications, there were 5 (3.6%) patients with bile leak and 1 (0.7%) patient who had liver failure. There were zero symptomatic deep vein thrombosis (DVT) events, but two patients were diagnosed with pulmonary embolism in the absence of DVT. Comparing TEA and IV-PCA groups, severe surgical complication rates were similar (37.7% vs. 31.3%, respectively, $p=0.705$). The median peak postoperative bilirubin was 1.4 (R: 0.3 mg/dL to 11.8 mg/dL), and the median peak postoperative creatinine was 0.9 (R: 0.1 mg/dL–2.3 mg/dL), with no differences in these values between the study groups. Overall, 2 (1.4%) patients returned to the operating room, and 3 (2.1%) required readmission. The median length of stay was the same between TEA (6 days, IQR: 5–7 days) and IV-PCA (6 days, IQR: 5–7 days), $p=0.957$. There were no 90-day mortalities.

Twelve patients experienced an analgesic related complication that required discontinuation of the original pain control modality. For analgesic related complications, there was no difference between TEA and IV-PCA (12.2% vs. 2.9%, respectively, $p=0.187$), and all were

less than MAG 3. Two patients with TEA required replacement of the epidural catheter due to catheter migration or malfunction and two TEA group patients required change of pain management modality to IV-PCA due to inadequate pain control. In 15 patients, TEA had to be placed on hold for a median time of 2 hours (IQR: 1–3.25 hours) due to hypotension. Among these patients who experienced hypotension with TEA in place, the median peak creatinine was 0.67 mg/dL (IQR: 0.6 mg/dL–0.84 mg/dL) with only one patient developing a peak creatinine above 1.5 mg/dL during hospitalization.

Postoperative Narcotic Utilization

The median cumulative OME over the first 5 postoperative days was markedly less in the TEA (155.3 mg, R: 53.43–2747.3 mg) group when compared to IV-PCA (429.8 mg, R: 69.8–1787.5 mg), $p<0.001$. Additionally, patients in the TEA group required less daily OME for the majority of postoperative days (POD 0–3, all $p<0.001$; Figure 3). The use of traditional adjuvant agents, such as acetaminophen and ketorolac, was equally distributed between groups.

Patient-reported Outcomes

The vast majority of patients completed the SF-8 before (TEA: 99.1%; IV-PCA 100%) and after (TEA: 90.1%; IV-PCA 94.1%) surgery. Using this tool, TEA and IV-PCA patients were found to have similar levels of baseline (preoperative) pain (Table 2), $p=0.468$; in contrast, postoperatively, a significantly larger number of patients in the TEA (62.5%) group reported having less than mild pain when compared to the IV-PCA (40.6%) group, $p=0.03$.

The SF-36 was answered by 85.8% of TEA and 79.4% of IV-PCA patients. While average calculated preoperative freedom from pain scores from the SF-36 were similar between TEA (90.69 ± 15.96) vs. IV-PCA (85.38 ± 19.62) $p=0.159$, postoperative freedom from pain scores were higher in patients with TEA (37.11 ± 24.64) than patients with IV-PCA (25.93 ± 16.74), $p=0.010$. After adjustment of preoperative clinical features and perioperative factors, multivariate regression identified TEA (Coefficient: -12.92, Standard Error 5.41, $p=0.019$) to be the sole factor associated with less negative change in pain score between preoperative evaluation and discharge.

Likewise, SF-36 negative change in average fatigue/energy scores was less in the TEA (21.91 ± 15.70) group when compared to the IV-PCA (32.93 ± 17.01) group, $p=0.002$. Multivariate linear regression analysis for factors independently associated with less negative change in fatigue identified patients with TEA (Coefficient: -8.98, Standard Error 3.14, $p=0.005$) and patients with a resection less than a major hepatectomy (Coefficient: -9.09, Standard Error 2.71, $p=0.001$).

The HORS instrument was answered by the majority of patients on each post-operative day (POD 1: 91.4%, POD 2: 88.6%, POD 3 86.4%, POD 4: 82.4%, POD 5 83.3%). This instrument identified greater patient satisfaction with pain control in the TEA group compared to the IV-PCA group ($p=0.022$, Figure 4). Further analysis with a mixed effects model to control for covariates identified a strong association between TEA and patient satisfaction with pain control, $p=0.035$.

DISCUSSION

As short-term hepatobiliary surgical outcomes have improved, focus is shifting to patient experience and oncologic outcomes. Regarding the important aspect of optimization of perioperative analgesia, the hepatobiliary surgical literature includes a number of non-randomized studies suggesting that TEA is a more complex analgesic regimen that, when inadequately supported at the bedside, can be associated with safety concerns including hypotension and a need for excessive fluid and blood product administration.[22–28] The efficacy of the pain control associated with this modality has been observed to be as good or better than intravenous narcotics. One small randomized trial, comparing TEA to IV-PCA, demonstrated superior pain control in the epidural arm but with a longer time to fulfill discharge criteria. Furthermore, analgesia in the PCA arm was augmented with continuous infiltration of local anesthetic using wound catheters and patient recovery beyond length of stay was not measured.[45] Given the lack of randomized data on this important topic, it is clear that further investigation was warranted.

In the current study a patient cohort, treated mainly with open liver resection, was randomized to TEA vs. IV-PCA with a primary endpoint of pain score AUC over the first 48 hours after surgery, and secondary endpoints of narcotic usage and patient-reported satisfaction, pain control and function. TEA-treated patients experienced similar rates of complications, length of stay and mortality with no statistically or clinically significant increase in hypotensive episodes, transfusion, or renal insufficiency events. Moreover, the pain control experience associated with TEA was superior, particularly during the first 48 hours after surgery. Although not specifically addressing pain level at rest in comparison to during activity, this methodology did include simultaneous evaluation of pain level and function. Ultimately, the primary endpoint was confirmed on four scales, including AUC of pain scores, severe pain event rates, total narcotic usage and patient-reported outcomes of satisfaction with pain control and function.

Several areas of the study require specific commentary. First, the randomization strategy was 2.5 TEA to 1 IV-PCA entrant. The rationale for this methodology was to simultaneously have the statistical power to comment on the primary endpoint of AUC 48, as well as, to comment on potential TEA-related anesthetic complications, including hypotension, transfusion and renal insufficiency. By weighting the accrual toward the TEA group the study was able to determine that the TEA was both effective and safe.

Second, with specific regard to the TEA regimen, the study utilized a strict protocol for drug concentration, infusion, and boluses. The concentration of local anesthetic was 0.075% bupivacaine, a concentration that is lower than typically reported. Using this lower concentration and a regimented rescue bolus regimen, study patients achieved excellent pain control, while avoiding hypotension and other commonly reported anesthetic complications that have been associated with TEA catheters. The data, therefore, support a reevaluation of prior studies that found excessive rates of hypotension and/or fluid resuscitation in the absence of reporting epidural concentration data, variability in concentration and drug choice, or higher concentrations of local anesthetic.[28]

Third, within the literature on this topic this study uniquely included patient-reported outcomes data in addition to patient-reported pain scores. These data are important because they confirm that the patient satisfaction and experience associated with improved pain scores was superior in the TEA group. Furthermore, the patient function in the TEA group was superior to the IV-PCA group. This finding is related not only to lower pain levels and less concomitant anxiety, but also to the almost 3-fold reduction in narcotic usage in the TEA group.

This reduction in IV and enteral narcotics is important, as the United States grapples with a significant narcotic dependence that is frequently initiated during a procedure or surgery.[46] Furthermore, in oncologic care there is emerging data that many cancers have high levels of *mu* opioid receptor expression, [47,48] that when activated by opiate narcotics could potentially mediate tumor growth and spread.[49,50] As more is learned about the interaction between these receptors and perioperative narcotics, it may become imperative that oncologic surgeons seek alternative methods to reduce perioperative opioid delivery. This trial supports that TEA is a safe and effective tool for limiting opiate narcotic dosing.

Fourth, like any randomized trial, global progress in the field does not wait for published results. During the course of this study, enhanced recovery and transversus abdominus plane (TAP) block have emerged as advances in multiple areas of surgical care. Although this study was pathway driven with a modern protocol containing several progressive elements common to enhanced recovery (eg. minimization of tubes and drains), specific oral non-opioid analgesic agents common to many enhanced recovery pathways were not given. Regarding, more traditional adjuvant agents, such as acetaminophen and ketorolac, the distribution of use was equivalent in each group.

Lastly, it is clear that minimally invasive approaches provide pain and experience advantages to patients. However, a recent national audit of 2015–2016 activity found that the vast majority of liver resections (84%) continue to be done through open approaches, with a higher penetrance of minimally invasive approaches in minor liver resection (78%), compared to major liver resection (95%) (unpublished ACS-NSQIP HPB collaborative data courtesy of Dr. Henry Pitt). Although each of these recent trends was not included in this trial, the results validate the shared concepts of the trial, which focused on the still most common (open) surgical approach and established that regional block is superior to IV-PCA based analgesic strategies. The TEA-based strategy now forms a standard-of-care for subsequent randomized trial comparison to other regional blocks, such as TAP, with enhanced recovery adjuvants in both arms. Preferably such a trial would be performed in a multi-center fashion, however the use of multiple metrics of patient experience with pain control, including patient reported outcomes, facilitates the detection of substantial differences between modalities, obviating the need for large (ie. thousands of patients) cohorts.

In summary, this randomized trial, which focused mainly on liver surgery patients, finds that TEA provides a superior pain control experience, with no deficit in surgical complications, anesthetic complications, length of stay, or mortality.

Acknowledgments

The authors would like to recognize the significant contributions of Ms. Ruth Haynes (administrative support), Ms. Theresa Honey, BS (Senior Research Data Coordinator), Ms. Rose Joan D Erfe, BS CCRC (Research Coordinator Clinical Studies), Wei Qiao MS PhD (analyst in Department of Biostatistics.), and the MD Anderson Department of Anesthesiology and Perioperative Medicine Acute Pain Service.

Funding Sources: Dr. Bradford Kim is supported by National Institutes of Health grant T32CA009599; Patient Reported Outcomes analysis was supported by NIH/NCI, R01CA205146 to Dr. Xin Shelley Wang

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Figure 1.
Consort Flow Diagram

Figure 2. Pain Scores Over Time in Thoracic Epidural Analgesia (TEA) vs. Intravenous Patient Controlled Analgesia (IV-PCA). The depicted 95% confidence bands represent interval estimators that characterize the extent of uncertainty for mean estimation of pain score at significance level 0.05 over the 48-hour follow-up time.

Figure 3.
Median Oral Morphine Equivalent (with Interquartile Range) Used on Each Postoperative Day in Thoracic Epidural Analgesia (TEA) vs. Intravenous Patient Controlled Analgesia (IV-PCA)

Figure 4. Patient Satisfaction with Thoracic Epidural Analgesia (TEA) vs. Intravenous Patient Controlled Analgesia (IV-PCA) measured by the Health Outcomes Recovery Survey (HORS): Lower score indicates better patient reported pain satisfaction.

Table 1

Patient Characteristics, Preoperative, Perioperative Features, and Pain Experience

Clinical Features	TEA	% or IQR	IV-PCA	% or IQR	p
n	106	75.7	34	24.3	
Age, median years	56.3	48.9–62.8	57.4	51.6–63.8	0.487
Male	63	59.4	15	44.1	0.164
ASA = 3	97	91.5	31	91.2	1.000
BMI, median kg/m ²	27.3	22.3–30.8	26.5	23.5–29.9	0.312
Preoperative Chemotherapy	72	67.9	18	52.9	0.150
Portal Vein Embolization	12	11.3	3	8.8	1.000
Liver Resection	103	97.2	33	97.1	1.000
Major Hepatectomy	70	66.0	20	58.8	0.538
Pancreas Resection	3	2.8	1	2.9	1.000
Intraoperative					
Midline Incision	29	27.4	12	37.5	0.376
L or J Incision	71	67.0	20	58.8	0.413
Subcostal or Chevron Incision	5	4.7	1	2.9	1.000
Minimally Invasive	1	0.9	1	2.9	1.000
EBL, median mL	200	100–300	200	100–431.25	0.429
OR Time, median minutes	263	210.25–324.25	276	196–395.25	0.594
Air Leak Test	47	44.3	15	44.1	1.000
Intraoperative Drain	32	30.2	10	29.4	0.845
Intraoperative Transfusion	2	1.9	1	2.9	0.569
Postoperative					
Postoperative Transfusion	4	3.8	3	8.8	0.361
Positive Margin	14	13.2	6	17.6	0.575
Any Complication	40	37.7	10	31.3	0.418
Severe Complication	7	6.6	3	9.4	0.705
Peak Bilirubin, median mg/dL	1.4	1–2	1.4	0.98–2.13	0.840
Peak Creatinine, median mg/dL	0.87	0.68–1.0	0.81	0.65–0.97	0.541
Liver Failure	1	0.9	0	0.0	1.000

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Clinical Features	TEA	% or IQR	IV-PCA	% or IQR	p
Bile Leak	3	2.8	2	5.9	0.595
Return to OR	1	0.9	1	3.1	0.428
Length of Stay, median days	6	5–7	6	5–7	0.957
Readmission	2	1.9	1	3.1	0.569
90 Day Mortality	0	0.0	0	0.0	1.000
Any Analgesia Related Complication	13	12.2	1	2.9	0.187
Ileus	8	7.5	2	5.9	1.000
Inadequate Pain Control in First 48 Hours	45	42.5	21	65.6	0.075
AUC 48, median	78.6	49.6–115.3	105.2	64.2–144.2	0.032

Abbreviations: ASA, American Society of Anesthesiologist; AUC 48, Area Under the Curve in first 48 hours; BMI, Body Mass Index, EBL, dL, deciliters; Estimated Blood Loss, mg, milligrams; IV-PCA, Intravenous Patient Controlled Analgesia; OR, Operating Room; TEA, Thoracic Epidural Analgesia.

Table 2

Patient-reported pain from SF-8 before and after surgery.

	TEA	%	IV-PCA	%
<u>Preoperative Pain</u>				
None	64	61.0	16	47.1
Very Mild	25	23.8	9	26.5
Mild	8	7.6	6	17.7
Moderate	5	4.8	2	5.9
Severe	3	2.9	1	2.9
Very Severe	0	0.0	0	0.0
<u>POD 1 Pain</u>				
None	33	34.4	10	31.3
Very Mild	27	28.1	3	9.4
Mild	13	13.5	5	15.6
Moderate	15	15.6	6	18.8
Severe	6	6.3	5	15.6
Very Severe	2	2.1	3	9.4

Abbreviations: IV-PCA, Intravenous Patient Controlled Analgesia; TEA, Thoracic Epidural Analgesia; POD, Post-operative

SF-36 Health Domains Preoperatively and at Discharge (Higher score represents less dysfunction)

Table 3

	TEA		IV-PCA		p
	Mean	SD	Mean	SD	
Preoperative					
Physical	87.9	15.6	79.6	23.7	0.098
Role/Physical	92.7	13.6	85.0	24.9	0.136
Role/Emotional	93.6	10.9	91.7	18.3	0.526
Fatigue/Energy	65.4	13.9	70.1	12.9	0.123
Emotional	71.1	12.5	71.5	12.6	0.877
Social	89.2	17.9	91.2	15.0	0.589
Pain	90.7	16.0	85.4	19.6	0.159
Mental Health	76.4	15.7	78.3	15.9	0.565
At Discharge					
Physical	33.0	25.1	23.5	28.1	0.097
Role/Physical	79.3	31.0	84.1	32.6	0.490
Role/Emotional	89.2	21.7	86.3	28.5	0.564
Fatigue/Energy	43.8	15.0	38.7	14.8	0.126
Emotional	65.8	13.6	63.5	13.7	0.456
Social	44.0	32.5	50.5	34.1	0.368
Pain	37.1	24.6	25.9	16.7	0.010
Mental Health	68.5	19.3	69.8	17.3	0.750

Abbreviations: IV-PCA, Intravenous Patient Controlled Analgesia; SD, Standard Deviation; TEA, Thoracic Epidural Analgesia

Scale: 0–100; 0: Worst Possible Score, 100: Best Possible Score