Title

Failed epidural after upper abdominal laparotomy in chronic pain patients with opioid use — a retrospective case control study

Journal

Scandinavian Journal of Pain, 26(1)

ISSN

1877-8860

Authors

Andersen, Johnny Dohn Holmgren
Khridina, Iryna
Kristensen, Danja Lykke
et al.

Publication Date

2026

DOI

10.1515/sjpain-2026-0017

Peer reviewed

Observational Studies

Johnny Dohn Holmgren Andersen, Iryna Khridina, Danja Lykke Kristensen, Christine Puck Holler, Michael Rowbotham and Eske Kvanner Aasvang*

Failed epidural after upper abdominal laparotomy in chronic pain patients with opioid use – a retrospective case control study

https://doi.org/10.1515/sjpain-2026-0017
Received February 9, 2026; accepted May 30, 2026;
published online July 23, 2026

Abstract

Objectives: Opioid therapy for chronic pain complicates post-operative pain management. This study evaluated the incidence of failed epidural analgesia, defined as epidural catheter replacement, in opioid-treated chronic pain patients vs. pain-free opioid-naïve controls undergoing elective upper laparotomy.

Methods: We conducted a retrospective case–control cohort study of adult patients undergoing elective upper laparotomy with epidural anesthesia (EA) for postoperative pain management. The intervention group comprised chronic pain patients, defined as pain lasting >3 months with stable daily opioid use. Controls were pain-free opioid-naïve patients. Patients with known illegal opioid use were excluded. A sample size of 75 chronic opioid-treated pain patients and 75 pain-free patients would allow for detection of a 15 % between group difference in epidural catheter replacement at a 0.05 significance level.

Results: Seventy-five chronic pain patients and 75 pain-free opioid-naïve controls were included. Chronic pain patients were more often female, had more co-morbidities, and more frequently underwent pancreatic resections; liver resections were more common among controls. The median preoperative daily oral morphine equivalent use among chronic pain patients was 45 mg (IQR, 20–80). Epidural analgesia failure occurred four times more often in chronic pain patients compared with controls (41.3 % vs. 10.7 %; p<0.01).

Conclusions: Chronic preoperative opioid use for pain significantly increased the rate of postoperative epidural catheter replacement. The findings were not explained by external preoperative, technical or surgical factors, supporting further pathophysiological investigations to tailor mechanism based interventions.

Keywords: opioids; postoperative pain; chronic pain; failed epidural

Introduction

Chronic pain is often associated with altered pain perception [1, 2]. Tolerance develops with long-term opioid therapy and may require increased doses to maintain an equianalgesic effect [3–9]. These pathophysiological changes may elevate pain intensity and reduce pain thresholds during the perioperative period. Higher opioid doses may be required to adequately control acute pain during and after surgery [6, 8, 10]. Higher postoperative opioid doses are associated with prolonged hospital stays and increased healthcare costs [11, 12]. Increased opioid doses in the early postoperative phase, may persist after hospital discharge, especially when opioid stewardship by providers is inadequate. Higher daily opioid doses are associated with increased morbidity and mortality [13, 14].

Analgesic tolerance is clinically accompanied by respiratory tolerance to opioids when doses are stable. However, studies suggest that similar to pain-free opioid-naïve patients, a proportion of chronic pain and opioid treated patients experience unpredictable opioid-related adverse effects such as respiratory depression when as-needed doses of opioid are added to the usual opioid dosage in an effort to manage increased pain, including postoperative pain [8, 9, 15].

***Corresponding author: Eske Kvanner Aasvang**, Department of Anesthesiology, Center for Cancer and Organ Diseases, Rigshospitalet, University of Copenhagen, Blegdamsvej 9, 2200, Copenhagen, Denmark; and Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark, E-mail: eske.kvanner.aasvang.01@regionh.dk
Johnny Dohn Holmgren Andersen, Iryna Khridina, Danja Lykke Kristensen and Christine Puck Holler, Department of Anesthesiology, Center for Cancer and Organ Diseases, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark
Michael Rowbotham, Department of Anesthesia, University of California San Francisco, San Francisco, USA

Consequently, opioid titration in this patient population is particularly challenging, as clinicians must balance the need for adequate analgesia against a heightened risk of complications [15]. These concerns underscore the importance of opioid-sparing strategies in perioperative pain management, particularly in patients with chronic pain. Epidural analgesia (EA) is a widely recommended component of multimodal analgesic protocols for major abdominal surgery and plays a crucial role in enhancing postoperative outcomes in this vulnerable population [12, 16–18].

Epidural failure, when defined as the clinical decision to remove and reinsert the epidural catheter due to ineffective analgesia, despite increased drug local dosage, ranges from 14-30 % without any evident differences between thoracic or lumbar placement [19]. Imaging studies suggest the underlying cause can be attributed to incorrect catheter placement/displacement in 50 % of cases [20]. The remaining half are suggested to be related to suboptimal dosages of local anesthesia (bupivacaine, ropivacaine, etc.). There are few epidural dosage studies that include chronic pain and opioid users despite the possibility of altered nociception in patients with chronic pain and from long-term opioid use itself [6, 21, 22]. A retrospective study comparing epidural dosages in chronic pain and opioid users (n=17) with opioid naïve patients (n=99) undergoing surgery, suggested that adequate analgesia required threefold higher dosages and longer treatment durations in chronic pain and opioid treated patients [23]. Nonetheless, current clinical standards may follow a 'one-size fits all' approach and do not distinguish between opioid users and opioid naïve patients.

The underlying pathophysiological mechanisms may include central sensitization and/or opioid-induced alterations in local anesthetic efficacy [24]. Indeed, studies in both animal models and humans with opioid tolerance have shown reduced sensitivity to local anesthetics administered intrathecally or topically [25–28]. That opioid tolerance results in a need for increased opioid dosage has been well described regarding oral and intravenous opioid administration [29] but not for epidural administration.

The current study aimed to investigate the incidence and related factors for failed thoracic epidural analgesia after major abdominal surgery, in chronic pain patients on chronic opioid therapy compared with opioid-naïve patients without chronic pain. Ultimately, this may aid the development of evidence-based stratified analgesic strategies for improved analgesia in opioid treated patients. We hypothesized that failed epidural analgesia would be more frequent in patients with chronic pain and preoperative opioid use compared to opioid-naïve patients without chronic pain.

Methods

Study design and population

This retrospective, case-control cohort study was approved by the Legal Department at Rigshospitalet, Copenhagen University Hospital (ID: WZ.22042433), after requirements for written and oral information were waived by the regional ethical committee due to the retrospective design. The study was registered at ClinicalTrials.gov (NCT05662566) before data collection commenced.

Inclusion criteria for all study patients were: age ≥18 years; elective upper laparotomy including pancreatic, liver, gastric, colonic, small bowel, explorative laparotomy, or any combination thereof; planned thoracic epidural analgesia; and no contraindications to procedure-specific standard multimodal analgesia (including high-dose glucocorticoid, paracetamol, and wound infiltration with local anesthetics). For the chronic pain and opioid group, the following criteria were adopted: >3 months pain and daily scheduled opioid use regardless of dosage, and not only as per needed. The pain-free opioid-naïve group were patients without chronic pain, from here on termed pain-free opioid-naïve patients, with the following specific exclusion criteria: no chronic pain, no daily use of opioids or other drugs with potential analgesic effects (e.g., gabapentinoids, tricyclic antidepressants, benzodiazepines, or medical cannabinoids). Daily use of acetaminophen or NSAIDs was accepted. Exclusion criteria (all patients): substance abuse.

Study definitions

The primary study outcome was failed epidural, defined as epidural catheter replacement postoperatively within the first three postoperative days, and after a standardized departmental algorithm for optimization had been followed. The optimization algorithm includes sensory block testing with ice to map the sensory blockade, aiming to cover the surgical wound area. If the block is inadequate, optimization is attempted in the form of 3 to 5 ml 0.5 % bupivacaine (patient height dependent), catheter adjustment in the form of retraction aiming for a minimum of 3 cm epidural-space catheter length (30).

Secondary outcomes included: length of stay in the post-anaesthesia care unit (PACU), total length of hospital stay, daily and cumulative epidural opioid administration, and as-needed systemic opioid administration, and daily and cumulative epidural local analgesic dosage (bupivacaine).

Demographic, pharmacologic, surgical and epidural procedural parameters were recorded (see Table 1). Preoperative and postoperative opioids were converted into oral morphine equivalents (OMEQ) to facilitate comparison.

Table 1: Demographic details of chronic opioid and pain-free opioid-naïve patients.

		Chronic opioid (n=75)	Pain-free opioid naive (n=75)
Age, years	Median (IQR)	68 (58–75)	68 (60–74)
Height, cm	Median (IQR)	170 (164–175)	173 (165–181)
Weight, kg	Median (IQR)	73 (63–87)	73 (67–92)
BMI kg/m^2	Median (IQR)	26 (23–30)	25 (23–28)
Sex	Female, %	48 (64)	30 (40)
ASA class, %			
	1	0	1 (1.3)
	2	18 (24.0)	44 (58.7)
	3	56 (76.0)	30 (40.0)
Comorbidities, %			
Heart disease		18 (24.0)	12 (16)
Lung disease		18 (24.0)	6 (8.0)
Diabetes		24 (32.0)	11 (15)
Bowel disease		18 (24.0)	6 (8.8)
Prior bowel surgery		25 (33.3)	16 (21)
Low back pain		25 (33.3)	1 (1.3)
Prior spine surgery		9 (12.0)	0
Psychiatric diagnosis		2 (2.7)	0
Renal insufficiency		4 (5.3)	1 (1.3)
Liver cirrhosis		1 (1.3)	3 (4.0)
Surgical procedure			
Liver		15 (27 %)	35 (46.7 %)
Pancreas		40 (53.3 %)	24 (32.0 %)
Bowel		20 (26.7 %)	16 (21.3 %)
Anesthetist experience			
Trainee		25 (33.8)	21 (29.2)
Specialist registrar		49 (66.2)	51 (70.8)
Opioids (OMEQ) median (IQR)		45 (20–80)	0
Other preop. analgesics, %			
Gabapentinoids		20 (26.7)	0
TCA		3 (4.0)	0
SNRI		6 (8.0)	0
Paracetamol		31 (41.3)	0
NSAID		1 (1.3)	0
Cannabis (medical)		2 (2.7)	0

IQR, inter quartile range; ASA, American society of anaesthesiology; BMI, body mass index; OMEQ, oral morphine equivalents. Data on anesthetist experience level was missing in 4 cases.

Epidural analgesia protocol

Epidural catheters are part of the multimodal analgesia protocol within the integrated Enhanced recovery after Surgery (ERAS) regimen at our institution. As a tertiary hospital, all epidural procedures were performed by specialists or trainees with more than 2 years of anaesthesia training including in regional anaesthesia. The department performs >1,000 thoracic epidurals annually. Epidural placement was per standard performed preoperatively primarily via a paramedian (lateral) approach, subsequently via the median (midline) access. For the procedures related to this study, the catheter was inserted at the thoracic level (Th8 to Th11) corresponding to the planned surgical incision site, using the loss-of-resistance-to-saline technique. Subsequently, if no fluid could be aspired via the catheter, 3 mL lidocaine 2 mg/mL with epinephrine 5 µg/mL was injected to rule out accidental intrathecal or vascular placement. Two boluses of bupivacaine 0.5 % (3 mL) were then administered 15 min apart. A continuous bupivacaine/opioid infusion of 5 mL/h was started with either bupivacaine 2.5 mg/mL + morphine 0.05 mg/mL, or bupivacaine 2.5 mg/mL + sufentanil 1 µg/mL (in cases where morphine was contraindicated, e.g., renal insufficiency). Intraoperatively, additional boluses of bupivacaine 0.5 % (3 mL) were administered hourly.

General anaesthesia

General anaesthesia consisted of total intravenous anesthesia consisted of propofol and remifentanil is standard at our facility. Inhalation anaesthesia with Sevoflurane may be indicated in cases of severe liver failure or major liver resections and always in the combination with Remifentanil.

As a port of the multimodal strategy all patients are given acetaminophen 1 g and Dexamethasone. Additional opioid is not standard but only given as a rescue.

Post-operatively, the epidural blockade spread was assessed using ice to define the sensory blockade by asking the patient if they sense cold or warmth. Motor function was assessed using the Bromage scoring system. Per standard, epidural infusion was set at 5 mL/h but could range from 3 to 8 ml/h dependent on clinical assessment. Patients were discharged from the PACU once sufficient motor function was

regained to allow standing by the side of the bed, and that the epidural analgesia covered the surgical incision.

After PACU discharge, daily follow-up was performed by PACU nursing staff to confirm catheter function and analgesia quality, available 24/7 all weekdays. Nurses on the ward could administer supplemental boluses of the bupivacaine/opioid mixture (5 mL via the infusion pump, 60-min lockout). In case of inadequate epidural analgesia, the PACU-staff were contacted and If needed, an attending physician evaluated the patient for further epidural optimization or catheter replacement. This optimization was performed at any time when needed.

Sample size

Based upon the existing literature of 14–30 % epidural catheter replacement due to analgesic failure, we assumed a 20 % failure rate in the chronic pain group vs. a 5 % failure rate in the pain-free opioid naïve group. A sample size of 2 × 73 (total n=146) patients, rounded to 2 × 75 (total n=150) would have 80 % power at a 5 % significance level to detect a minimum absolute difference of 15 % (25 % relative difference) in epidural analgesia failure between groups.

Data analysis

Descriptive statistics were used to present demographic and baseline characteristics including medians with interquartile ranges or means with 95 % confidence intervals, where appropriate. The primary outcome was compared between groups using the Chi-square test. Secondary outcomes were compared using Student's *t*-test or Wilcoxon's rank-sum test, depending on data distribution. Data were entered into the regional approved REDCap database system (REDCap, Texas, USA) and analyzed using SPSS statistics v.29.0.1.0 (171) (IBM, NY, USA).

Results

To identify 75 chronic pain patients that fulfilled the inclusion criteria, a total of 1,278 patient charts were screened, covering the 2.3-year period from November 2020 to February 2023 (Figure 1). Of 299 patient charts showing preoperative pain, the most common reasons for exclusion were preoperative pain lasting shorter than 3 months (n=79), acute laparotomy (n=64), or patient specification that their data could not be used for research (n=32) (Figure 1). After screening 104 charts of pain-free opioid naïve patients, the pre-specified target of 75 pain-free opioid naïve patients without exclusion criteria was met and the remaining 904 charts were not further considered.

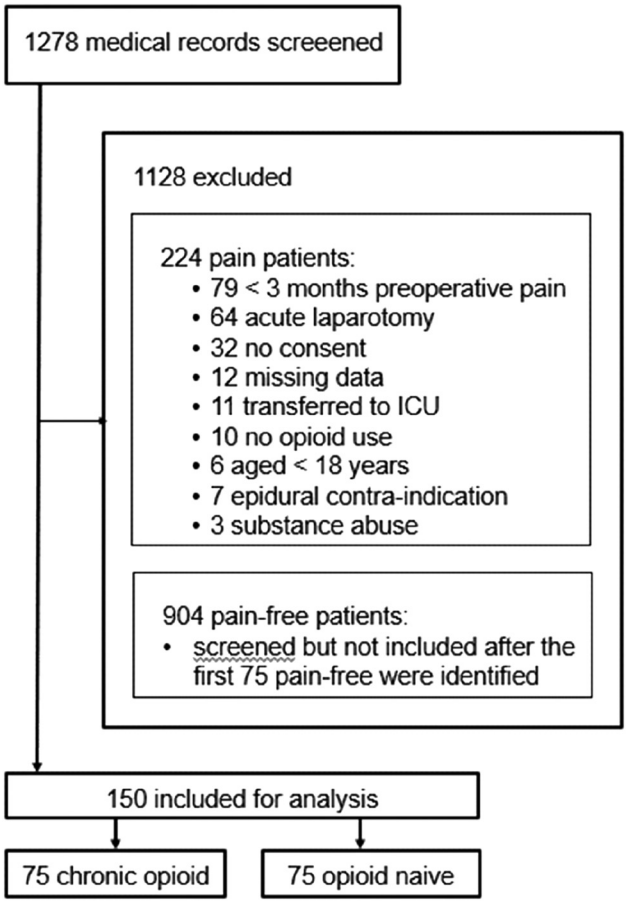

Figure 1: Patient identification flow-chart. Identification process of 2 × 75 patients with or without preoperative chronic opioid use.

Demographic and clinical baseline data are summarized in Table 1. Chronic pain and opioid patients had a higher incidence of individual co-morbidities, reflected in their higher ASA-class distribution, (p<0.001). Pain -free opioid-naïve patients did not have a daily use of any analgesics besides paracetamol and NSAIDs. Chronic pain patients had a median daily OMEQ of 45 mg (IQR 20–80). Concomitant gabapentinoid treatment was present in 26.7 % and 41.3 % used paracetamol daily.

Primary outcome

A total of 39 patients (26.0 %, 95 % CI 19.6–33.6) had an epidural catheter replacement. There was a significantly higher incidence of epidural catheter replacement in the chronic pain and opioid group of 41.3 % (95 % CI 30.1–53.3,

n=31) compared to 10.7 % (95 % CI 4.7–19.9, n=8) in the pain-free opioid naïve patients, p<0.001 (Table 1).

Secondary outcomes

Explanatory variables

Concomitant gabapentinoid use did not significantly alter the risk of epidural catheter replacement, 32 % vs. 45 % replacement in gabapentinoid vs. no-gabapentinoid patients, (p=0.23).

When comparing the pain-patients with epidural catheter replacement to pain-patients without replacement, no significant differences were found regarding age, sex or BMI. There was a non-significant inverse relation between epidural catheter replacement and preoperative OMEQ where pain patients with epidural catheter replacement had a mean OMEQ of 45.1 (95 % CI 32.2–58.9) vs. 67.5 (95 % CI 49.0–86.0) for pain patients without epidural catheter replacement (p=0.49; Table 2).

Surgical procedure distribution differed significantly between groups. Pancreatic surgery was more frequent in the chronic pain and opioid group (55 % vs. 31 %), while liver surgery was more common in the pain-free opioid-naïve group (47 % vs. 20 %) (p=0.02). However, as seen in Figure 2, the replacement incidence was the same across the three surgical procedure groups with minor variations.

Details regarding the primary epidural placement are presented in Table 3. No systematic differences were found related to number of attempts, access technique (air, saline, median, paramedian), level of placement, depth of the epidural catheter or the anesthetist experience between the chronic pain and opioid vs. pain-free opioid naïve groups.

The time between PACU arrival and epidural catheter replacement was 7 h (IQR 1–24) in chronic pain and opioid patients and 1.5 h (IQR 0–4.5 h) in pain-free opioid naïvepatients.

In those patients needing a replacement catheter, the median depth of the epidural catheter within the epidural space was 7 cm with 25 % of cases being 8 cm or more, by far exceeding the recommended maximum depth of 5 cm to avoid migration into the lateral recesses traversed by the nerve roots, distal displacements, or erroneous segmental level of epidural injection [30]. The two patient groups did not differ significantly on this aspect of catheter placement.

Insufficient analgesia was the predominant reason for catheter replacement in the pain group (n=30, 96.8 %) but not in the pain-free opioid naïve group where prolonged motor blockade (n=3, 37.5 %) or accidental epidural catheter removal during mobilization (n=2, 25.0 %) were the main reasons.

Intra-operative opioid dosage was significantly higher in chronic pain and opioid patients (26 OMEQ, 95 % CI 16–32) vs. pain-free opioid naïve (6 OMEQ, 95 % CI 3–9, p<0.001). The difference in intraoperative bupivacaine approached significance when comparing chronic pain and opioid (88 mg, 95 % CI 83–94) vs. pain-free opioid naïve (81 mg, 95 % CI 74–87), p 0.083.

In the PACU, chronic pain patients received significantly more systemic opioid (54 OMEQ (95 % CI 34–73)) than pain-free opioid naïve (9 OMEQ (95 % CI 4–14), p=0.002). In both patient groups, those with subsequent epidural catheter replacement received more opioids than those who didn't have catheter replacement (65 OMEQ (95 % CI 37–94) vs. 15 OMEQ (95 % CI 0–206), chronic pain and opioid vs. pain-free opioid naïve, respectively, p=NS).

Bupivacaine dosage in the PACU was significantly higher in pain patients 25 mg (95 % CI 17–31) vs. pain-free opioid naïve 8 mg (95 % CI 4–12), p<0.001. In patients with catheter replacement the dosage was 35 mg (95 % CI 22–49) in chronic pain and opioid patients vs. 8 (95 % CI 0–21) in pain-free opioid naïve.

Table 2: Comparison of demographic factors in pain patients with or without failed epidural.

	Failed ED (n=31)	Not failed ED (n=44)
Pre-op OMEQ (mean, 95 % CI)	45.1 (32.2–58.9)	67.5 (49.0–86.0)
Pre-op OMEQ/kg (mean, 95 % CI)	0.6 (0.4–0.8)	1.0 (0.7–1.3)
Age (mean, 95 % CI)	66.4 (62.5–70.2)	67.9 (64.7–71.1)
Sex, female, %	35.5 %	36.4 %
BMI (mean, 95 % CI)	26.9 (24.6–29.1)	26.2 (24.6–27.8)
ASA median (25th–75th IQR)	3 (2–3)	3 (2–3)
Low-back-pain, %	41.9 %	27.3 %
Gabapentinoids, %	19.4 %	29.5 %

ED, epidural; BMI, body mass index; OMEQ, oral morphine equivalents; CI, confidence interval; IQR: inter quartile range.

Length of stay (LOS)

A notable difference in hospital stay was observed, with chronic pain and opioid patients staying a median of 3 days longer than pain-free opioid naïve patients (9.6 vs. 6.6 days). PACU stay was also prolonged in the chronic pain and opioid group (10.1 vs. 5.1 h). Among all patients, an epidural catheter replacement was associated with approximately 3 additional hours in the PACU, irrespective of group assignment.

Post-PACU analgesic requirements

Opioid requirements (excluding pre-, intraoperative and PACU dosage) during the first 4 days after PACU discharge was 167 OMEQ (95 % CI 113–220) in chronic pain and opioid patients vs. 39 OMEQ (95 % CI 30–49) in pain-free opioid

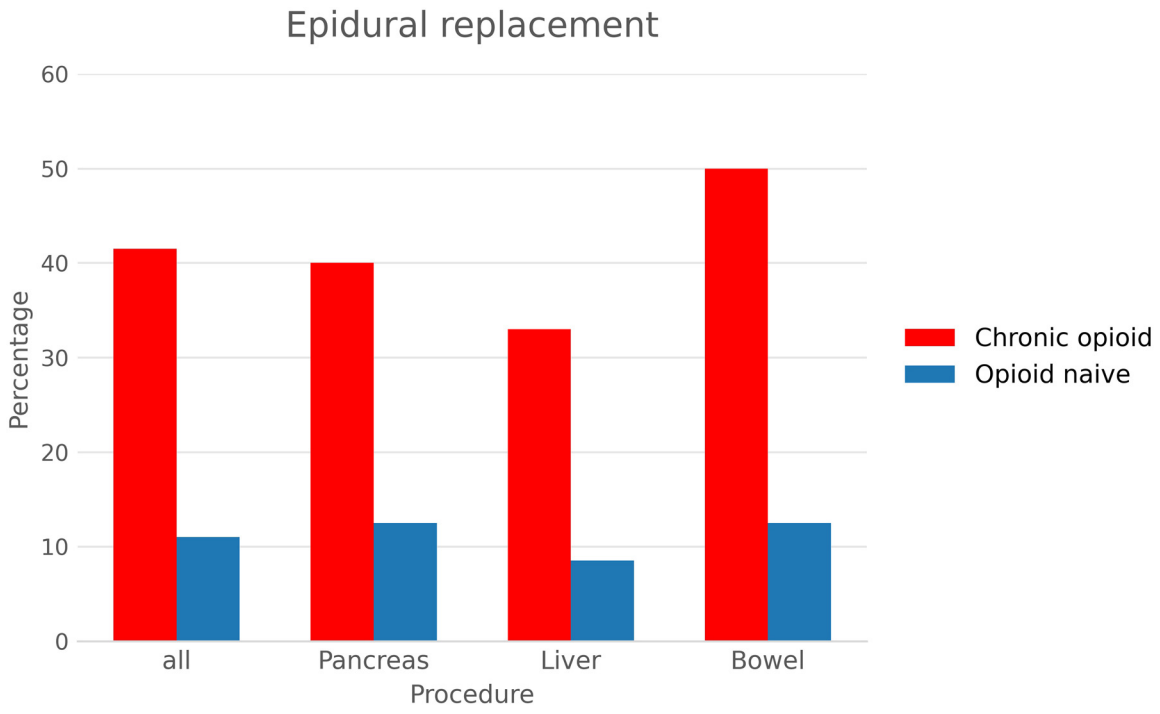

Figure 2: Procedure specific epidural catheter replacement incidence after abdominal laparotomy in chronic pain and opioid use vs. pain-free opioid naïve patients. Chronic pain patients all had preoperative opioid use.

naïve. Of the entire group of patients, only 20 (13.3 %) did not require additional opioid during their first 5 post-PACU days.

The day after epidural removal, 35 (47 %) of chronic pain and opioid users and 15 (20 %) of pain-free opioid naïve had an increased opioid demand compared to the day before.

Discussion

The present study supports the hypothesis that chronic pain patients on opioids have a significantly higher risk of epidural analgesia failure after abdominal laparotomy than pain-free opioid-naïve patients. The difference in epidural analgesia failure rate between patients on chronic preoperative opioids for managing longstanding pain (42.3 % of compared to 10.7 % in pain-free opioid-naïve patients) is highly significant ($p<0.001$). In the entire group of 150 patients, the overall 26 % (95 % CI 19.6–33.6 %) incidence of epidural catheter replacement is consistent with previous reports [20], and further highlights the marked difference between chronic pain and opioid and pain-free opioid naïve patients. One might assume that higher preoperative opioid dosages would increase the risk of postoperative epidural failure, but we did not find such a correlation supporting the individual variation in opioid effects, and that preoperative opioids alone increased the risk for epidural catheter replacement.

One key issue in the study design should be addressed, namely the interaction between opioid treatment for pain and pain therapy using only non-opioid analgesics. Ideally, having two chronic pain patient groups, one with and one without opioids would allow us to investigate the relative contribution of opioids to the risk of failed epidural. However, after screening 299 charts of patients with pain, we found only 10 chronic pain patients who were not treated with opioids. The following discussion should therefore be seen in the light of the most prevalent pain population in Denmark, namely chronic pain patients being treated with opioids. In the USA and some other countries, management of chronic pain with opioids is much less common, potentially due to the experiences from the US opioid epidemic.

Besides pre-operative opioid use and pain, we found no other preoperative demographic factors to explain the observed difference in epidural analgesia failure rate. Thus, despite differences in surgical procedure distribution with more pancreatic resections in chronic pain and opioid patients and more liver resection in pain-free opioid naïve, the replacement distribution when stratified within procedures was the same as the overall finding. The different procedures have differences in the surgical incision localization and length, so we deliberately chose to compare upper laparotomies to minimize procedure differences. Different organs have different innervation and inflammatory responses to surgery, both of which could affect pain perception, but we

Table 3: Epidural procedure and optimization data in chronic vs. pain-free opioid naïve patients.

	Chronic opioid			Pain-free opioid-naïve		
	All	ED-failure	No ED-failure	All	ED-failure	No ED-failure
		31 (41.3)	44 (58.7)		8 (10.7)	67 (89.3)
Preoperative placements attempts n, %						
1	46 (61.3)	17 (37.0)	29 (63.0)	49 (65.3)	4 (8.2)	45 (91.8)
2	16 (21.3)	7 (43.8)	9 (56.3)	13 (17.3)	3 (23.1)	10 (76.9)
3 or more	13 (17.4)	7 (53.8)	6 (46.2)	13 (17.4)	1 (7.7)	12 (92.3)
Access technique, %						
Median	2 (2.7)	0	2	2 (2.7)	0	2 (100)
Paramedian	70 (93.3)	30 (40.0)	40 (60.0)	66 (88.0)	8 (12.1)	58 (91.9)
Missing	3 (4.0)	1 (33.3)	2 (66.7)	7 (9.3)	0	7 (100)
LOR-air	28 (37.3)	10 (35.7)	18 (64.3)	28 (37.3)	3 (10.7)	25 (89.3)
LOR-saline	44 (58.7)	19 (43.2)	25 (56.8)	40 (53.4)	3 (7.5)	37 (92.5)
Missing	3 (4.0)	2 (66.7)	1 (33.3)	7 (9.3)	2 (28.6)	5 (71.4)
Placement level, %						
Th7-8	3 (4.0)	1 (33.3)	2 (66.7)	4 (5.3)	0	4 (100)
Th8-9	39 (52.0)	16 (41.0)	23 (59.0)	39 (52.0)	3 (7.7)	36 (92.3)
Th9-10	26 (34.7)	11 (42.3)	15 (57.7)	27 (36.0)	4 (14.8)	23 (85.2)
Th10-11	5 (6.7)	2 (40.0)	3 (60.0)	3 (4.0)	1 (33.3)	2 (66.7)
Missing	2 (2.7)	1 (50.0)	1 (50.0)	2 (2.7)	0	2 (100)
LOR depth (cm), median (IQR)	6.0 (5.0–7.0)	6.0 (5.0–6.5)	6.0 (5.0–7.0)	6.0 (5.0–6.5)	5.0 (5.0–6.5)	6.0 (5.0–7.0)
Epidural catheter length in the epidural space (cm), median (IQR)	7.0 (6.5–7.5)	7.0 (6.0–7.5)	7.0 (6.5–7.5)	7.0 (6.5–8.0)	7 (5.5–8.5)	7.0 (6.5–8.0)
Anesthetist experience						
Trainee	49 (66.4)	18 (36.7)	31 (63.3)	51 (68.0)	7 (13.7)	44 (86.3)
Registrar	25 (33.3)	12 (48.0)	13 (52.0)	21 (28.0)	1 (4.8)	20 (95.2)
Missing	1 (1.3)	1 (100)	0	3 (4.0)	0	3 (100)

ED, epidural; LOR, loss of resistance; Th, thoracic; **Epidural catheter length in the epidural space**: calculated as the length of the epidural catheter at the skin minus the length of LOR.

did not find differences to support this regarding risk for epidural catheter replacement.

Similarly, we did not find a lower dosage of opioids or local anesthetics administered during surgery or during the PACU-stay to chronic pain and opioid patients that could explain the higher occurrence of epidural catheter replacement. Chronic pain and opioid users received significantly higher opioid administration, in line with the recommended increased dosage in chronic pain and opioid users [31]. The consequences of replacing an epidural are discomfort to the patient, a new risk of dural puncture and the more rare but important epidural hematoma and infection (risk of procedural complications) [32]. Significantly higher opioid demands before replacement increase the risk for opioid related side-effects including the feared respiratory depression and related mortality [33].

From an organizational point of view, the current study shows a prolonged median length of PACU stay of 3 h which may cause delays in the OR patient flow, as the PACU is a bottle neck for operating theater efficacy and may ultimately result in cancelled procedures. Thus, a strategy to pursue early identification and interventions to improve function of suboptimal epidurals would be beneficial.

The current study also shows that the current clinical standard epidural regimen does not relieve the chronic pain and opioid patient from needing additional opioids during the hospital stay. Thus, 95 % of chronic pain and opioid pain patients required additional opioids after PACU discharge. In contrast, 27 % of pain-free opioid naïvepatients were able to have their postoperative pain managed without supplemental opioids and when opioids were required, the dosages were lower.

It is known that higher ASA class is associated with a longer length of stay, and overall, the chronic pain and opioid group had more patients in ASA class 3. However, the observed 3 day longer LOS in chronic pain and opioid users is greater than reported in the literature, and opioid use may be the explanation. Future studies that match the patient groups on ASA class would help resolve this issue.

External factors do not fully explain the significant difference in risk for epidural catheter replacement. Therefore, a focus on altered nociception from chronic pain and opioid use is justified. Chronic pain is associated with increased central facilitation of nociceptive input, clinically resulting in hyperalgesia and allodynia. Chronic pain and opioid use

for pain results in analgesic tolerance development, resulting in a need for increased opioid dosages to achieve the same analgesic effect. Until recently it has been argued that opioid themselves may result in hyperalgesia, but this has largely been disproven as a clinical problem [3, 7, 34]. However, animal and to some extent human, studies suggest that the analgesic tolerance is not as strongly linked to tolerance towards opioid induced respiratory depression (OIRD). In a study of monkeys, the animals became tolerant during prolonged opioid treatment, but with each increase in dosage the risk for OIRD increased. This may explain why chronic pain and opioid treated patients tolerate their usual dosage well, but exposure to additional as-needed opioid doses may result in OIRD in this group as well as in pain-free opioid naïvepatients. In addition to opioid tolerance development, opioids have also been reported to result in tachyphylaxis to local anesthetics, resulting in lower efficacy than in pain-free opioid naïve, but the clinical impact and the underlying mechanisms are still under debate [24].

As with all studies, ours has limitations. The main limitation is the retrospective nature, resulting in less control over collected variables. However, the electronic healthcare records allowed for structured collection of the primary outcome and related variables with a high completeness. A key factor that should be included in future prospective studies are more detailed descriptions of the actual nociception and the impact of opioids, surgical procedure and pain levels before surgery. This could allow for a more detailed and individualized pathophysiological understanding of risk factors. As with all studies, we could have had a larger sample size to assess risk factors, especially for the non-opioid group. Finally, our findings should be confirmed by other studies. We believe that our stratified approach of looking into the risk of preoperative opioids for epidural catheter replacement is a strength, especially in the setting of a thorough attempt to improve the initial epidural as evidenced by the increased use of local anesthetics in the PACU. Finally, our detailed inclusion of external risk factors to rule out other causes than opioids for the increased risk of replacement is a strength of the current study.

Combining our results and the current evidence, we suggest that trials be initiated investigating the efficacy and safety of increased epidural opioid dosing, and potentially also local anesthetic volume, in chronic pain and opioid treated pain patients. Whether this should be one-size-fits-all chronic pain and opioid users, or tailored to the specific chronic dosage should also be investigated.

In conclusion, chronic preoperative opioid use resulted in a four-fold risk for need for epidural catheter replacement. The findings were not explained by external preoperative, technical or surgical factors, suggesting The findings were not explained by external preoperative, technical or surgical factors, supporting further pathophysiological investigations to tailor mechanism based interventions.

Research ethics: The study was conducted in accordance with the 2013 Helsinki Declaration.
Informed consent: Not applicable.
Author contributions: The author(s) have (has) accepted responsibility for the entire content of this manuscript and approved its submission.
Use of Large Language Models, AI and Machine Learning Tools: Not applicable.
Conflict of interest: None.
Research funding: None.
Data availability: The raw data can be obtained on request from the corresponding author.

References

1. Latremoliere A, Woolf CJ. Central sensitization: a generator of pain hypersensitivity by central neural plasticity. J Pain 2009;10:895–926.
2. Richebé P, Capdevila X, Rivat C. Persistent postsurgical pain: pathophysiology and preventative pharmacologic considerations. Anesthesiology 2018;129:590–607.
3. Chu LF, D'Arcy N, Brady C, Zamora AK, Young CA, Kim JE, et al. Analgesic tolerance without demonstrable opioid-induced hyperalgesia: a double-blinded, randomized, placebo-controlled trial of sustained-release morphine for treatment of chronic nonradicular low-back pain. Pain 2012;153:1583–92.
4. Hina N, Fletcher D, Poindessous-Jazat F, Martinez V. Hyperalgesia induced by low-dose opioid treatment before orthopaedic surgery. Eur J Anaesthesiol 2015;32:255–61.
5. Sampaio-Cunha TJ, Martins I. Knowing the enemy is halfway towards victory: a scoping review on opioid-induced hyperalgesia. J Clin Med 2022;11. https://doi.org/10.3390/JCM11206161.
6. Chapman CR, Davis J, Donaldson GW, Naylor J, Winchester D. Postoperative pain trajectories in chronic pain patients undergoing surgery: the effects of chronic opioid pharmacotherapy on acute pain. J Pain 2011;12:1240–6.
7. Svensson CK. Opioid-induced hyperalgesia: is it a clinically relevant phenomenon. Int J Pharm Pract 2022;30:479–83.
8. Hayhurst CJ, Durieux ME. Differential opioid tolerance and opioid-induced hyperalgesia: a clinical reality. Anesthesiology 2016;124:483–8.
9. Paul AK, Smith CM, Rahmatullah M, Nissapatorn V, Wilairatana P, Spetea M, et al. Opioid analgesia and opioid-induced adverse effects: a review. Pharmaceuticals 2021;14. https://doi.org/10.3390/PH14111091.
10. Aasvang EK, Lunn TH, Hansen TB, Kristensen PW, Solgaard S, Kehlet H. Chronic pre-operative opioid use and acute pain after fast-track total knee arthroplasty. Acta Anaesthesiol Scand 2016;60:529–36.

11. Gan TJ, Robinson SB, Oderda GM, Scranton R, Pepin J, Ramamoorthy S. Impact of postsurgical opioid use and ileus on economic outcomes in gastrointestinal surgeries. Curr Med Res Opin 2015;31:677–86.
12. Guay J, Nishimori M, Kopp S. Epidural local anaesthetics versus opioid-based analgesic regimens for postoperative gastrointestinal paralysis, vomiting and pain after abdominal surgery. Cochrane Database Syst Rev 2016;7:CD001893.
13. Jørgensen CC, Petersen M, Kehlet H, Aasvang E. Analgesic consumption trajectories in 8975 patients 1 year after fast-track total hip or knee arthroplasty. Eur J Pain 2018;22:1428–38.
14. Kunkel ST, Gregory JJ, Sabatino MJ, Borsinger TM, Fillingham YA, Jevsevar DS, et al. Does preoperative opioid consumption increase the risk of chronic postoperative opioid use after total joint arthroplasty? Arthroplast Today 2021;10:46–50.
15. Pattullo GG. Clinical implications of opioid-induced ventilatory impairment. Anaesth Intensive Care 2022;50:52–67.
16. Huxtable CA, Roberts LJ, Somogyi AA, Macintyre PE. Acute pain management in opioid-tolerant patients: a growing challenge. Anaesth Intensive Care 2011;39:804–23.
17. Chou R, Gordon DB, De Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, et al. Management of postoperative pain: a clinical practice guideline from the American pain society, the American society of regional anesthesia and pain medicine, and the American society of anesthesiologists' committee on regional anesthesia, executive committee, and administrative council. J Pain 2016;17:131–57.
18. Kumar K, Kirksey MA, Duong S, Wu CL. A review of opioid-sparing modalities in perioperative pain management: methods to decrease opioid use postoperatively. Anesth Analg 2017;125:1749–60.
19. Hermanides J, Hollmann MW, Stevens MF, Lirk P. Failed epidural: causes and management. Br J Anaesth 2012;109:144–54.
20. Motamed C, Farhat F, Rémérand F, Stéphanazzi J, Laplanche A, Jayr C. An analysis of postoperative epidural analgesia failure by computed tomography epidurography. Anesth Analg 2006;103: 1026–32.
21. Costa AR, Tavares I, Martins I. How do opioids control pain circuits in the brainstem during opioid-induced disorders and in chronic pain? Implications for the treatment of chronic pain. Pain 2024;165:324–36.
22. Rodríguez-Lagos L, Fernández-Carnero J, Laguarta-Val S, Serrano-García B, Martín-Vera D, Runge N, et al. Conditioned pain modulation and temporal summation in patients with knee osteoarthritis: a systematic review and meta-analysis. J Pain 2025: 105464. https://doi.org/10.1016/j.jpain.2025.105464.
23. De Leon-Casasola OA, Parker BM, Lema MJ. Epidural analgesia versus intravenous patient-controlled analgesia: differences in the postoperative course of cancer patients. Reg Anesth 1994;19:307–15.
24. Kongsgaard UE, Werner MU. Tachyphylaxis to local anaesthetics. What is the clinical evidence? A systematic review. Acta Anaesthesiol Scand 2016;60:6–14.
25. Liu Q, Gold MS. Opioid-induced loss of local anesthetic potency in the rat sciatic nerve. Anesthesiology 2016;125:755–64.
26. Brennan TJ, Lennertz RC, Kang S. Are opioid-tolerant patients resistant to local anesthetic nerve blockade? Anesthesiology 2016;125:625–6.
27. Vosoughian M, Dabbagh A, Rajaei S, Maftuh H. The duration of spinal anesthesia with 5 % lidocaine in chronic opium abusers compared with nonabusers. Anesth Analg 2007;105:531–3.
28. Karbasy SH, Derakhshan P. Effects of opium addiction on level of sensory block in spinal anesthesia with bupivacaine for lower abdomen and limb surgery: a case-control study. Anesth Pain Med 2014;4. https://doi.org/10.5812/AAPM.21571.
29. Sjøgren P, Jonsson T, Jensen NH, Drenck NE. Hyperalgesia and myoclonus in terminal cancer patients treated with continuous intravenous morphine. Pain 1993;55:93–7.
30. Afshan G, Chohan U, Khan FA, Chaudhry N, Khan ZE. Appropriate length of epidural catheter in the epidural space for postoperative analgesia: evaluation by epidurography. Anaesthesia 2011;66:913–18.
31. Ryan M, Moynihan TJ, Loprinzi CL. As-needed morphine: yes, but at what dose and at what interval? J Clin Oncol 2005;23:3849–52.
32. Cameron CM, Scott DA, McDonald WM, Davies M. A review of neuraxial epidural morbidity: experience of more than 8,000 cases at a single teaching hospital. Anesthesiology 2007;106:997–1002.
33. Khanna AK, Bergese SD, Jungquist CR, Morimatsu H, Uezono S, Lee S, et al. Prediction of opioid-induced respiratory depression on inpatient wards using continuous capnography and oximetry: an international prospective, observational trial. Anesth Analg 2020;131:1012–24.
34. Rowbotham MC, Wallace M. Evolution of analgesic tolerance and opioid-induced hyperalgesia over 6 months: double-blind randomized trial incorporating experimental pain models. J Pain 2020;21:1031–46.