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ORIGINAL ARTICLE

Postoperative pain control using continuous i.m. bupivacaine infusion plus patient-controlled analgesia compared with epidural analgesia after major hepatectomy

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Abstract

Objectives: There is debate concerning the best mode of delivery of analgesia following liver resection, with continuous i.m. infusion of bupivacaine (CIB) plus patient-controlled i.v. analgesia (PCA) suggested as an alternative to continuous epidural analgesia (CEA). This study compares these two modalities.

Methods: A total of 498 patients undergoing major hepatectomy between July 2004 and July 2011 were included. Group 1 received CIB + PCA ($n = 429$) and Group 2 received CEA ($n = 69$). Groups were analysed on baseline patient and surgical characteristics. Primary endpoints were pain severity scores and total opioid consumption. Secondary endpoints were pain management failures, need for rescue medication, postoperative (opioid-related) morbidity and hospital length of stay (LoS).

Results: In both groups pain was well controlled and >70% of patients had no or minimal pain on PoDs 1 and 2. The numbers of patients experiencing severe pain were similar in both groups: PoD 1 at rest: 0.3% in Group 1 and 0% in Group 2 ($P = 1.000$); PoD 1 on movement: 8% in Group 1 and 2% in Group 2 ($P = 0.338$); PoD 2 at rest: 0% in Group 1 and 2% in Group 2 ($P = 0.126$), and PoD 2 on movement: 5% in Group 1 and 5% in Group 2 ($P = 1.000$). Although the CIB + PCA group required more opioid rescue medication on PoD 0 (53% versus 22%; $P < 0.001$), they used less opioids on PoDs 0–3 ($P \leq 0.001$), had lower morbidity (26% versus 39%; $P = 0.018$), and a shorter LoS (7 days versus 8 days; $P = 0.005$).

Conclusions: The combination of CIB + PCA provides pain control similar to that provided by CEA, but facilitates lower opioid consumption after major hepatectomy. It has the potential to replace epidural analgesia, thereby avoiding the occurrence of rare but serious complications.

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Introduction

The upper abdominal wall incision is a major contributor to postoperative pain after liver resection.[1,2] Given the continuing increases in both the volume and extent of liver surgery, along with the introduction of enhanced recovery programmes,[3–7] there is debate about the optimal method of delivering postoperative analgesia. Effective postoperative pain control will reduce the incidence of numerous postoperative complications, can facilitate early mobilization and may result in earlier recovery.[8,9] Pain control is usually achieved by the administration of opioids, which may cause side-effects, such as sedation, respiratory depression, pruritus, hallucinations and postoperative nausea and vomiting (PONV).

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Epidural analgesia has been considered superior to i.v. patient-controlled analgesia (PCA) for postoperative pain relief in patients recovering from major upper abdominal operations,[10,11] although patient satisfaction with i.v. PCA is higher.[11] However, the use of epidural analgesia after hepatectomy is still subject to debate. Because epidural analgesia can lead to serious complications, such as epidural abscess or haematoma,[12] it may be contraindicated when postoperative coagulopathy is expected.[13,14] In addition, epidural methods take time to induce anaesthesia and may not function adequately in up to 30% of patients.[15]

An alternative analgesic modality for the control of postoperative pain is the continuous infiltration of local anaesthetic using wound catheters placed in the abdominal wall.[16–18] It is nearly a decade since this method of postoperative pain management was introduced in liver surgery and it has shown promising results.[19,20] In other fields of surgery, the use of continuous wound infiltration has suggested a reduction in costs.[21–23] The most recent study, a randomized controlled trial (RCT) performed by Revie *et al.* in 2012, demonstrated that local wound infiltration combined with i.v. PCA, compared with continuous epidural analgesia (CEA), reduced the time required to fulfil criteria for discharge from hospital, but provided inferior analgesia.[24]

This retrospective study provides insights into the postoperative analgesic merits of i.m. continuous infusion of bupivacaine (CIB) combined with i.v. PCA, compared with mid-thoracic CEA alone after major hepatic surgery.

Materials and methods

Patients

All open major hepatectomies (n = 545) performed in the Hepatobiliary Unit of the North Hampshire Hospital in Basingstoke, UK, between July 2004 and July 2011 were included for screening. Data were prospectively collected and stored in a dedicated database by research staff blinded to the type of postoperative analgesia. Data on postoperative milestones, such as day of first oral intake and day of independent mobilization, were retrospectively added to the database after all available documentation for both living and deceased patients had been reviewed. Primary study endpoints were pain severity scores at rest and on movement during the first 48 h postoperatively, and total opioid requirements during the first 72 h postoperatively. Secondary endpoints were pain management failures, need for rescue medication, opioid-related morbidity and hospital length of stay (LoS).

Surgery

General anaesthesia was induced with i.v. propofol (1.5–2.0 mg/kg) and fentanyl (1–2 mcg/kg), with maintenance using volatile anaesthetics (iso-, des- or sevoflurane) in oxygen and air. For this study, major hepatectomy was defined as resection of at least three liver segments according to Couinaud's classification.[25] Hepatectomies were performed by four liver surgeons (MR, FKSW, TGJ and ABC), of whom only one (TGJ) used epidural catheters as the preferred method of providing postoperative analgesia. Standard transection techniques were used for liver resection under total or selective hepatic vascular exclusion, as described previously.[26,27] Unfavourable intraoperative incidents were graded according to the Satava system for the evaluation of surgical error, adapted for liver surgery.[28] Postoperative morbidity was classified and analysed using the Accordion system for grading surgical complications (with Clavien–Dindo modifications), as described by Strasberg *et al.*[29,30] Operating time was defined as the time between the first induction of anaesthesia and the patient's departure from the theatre. All patients received antibiotic, and nausea and vomitus (PONV) prophylaxis preoperatively. In the CIB + PCA group, PONV prophylaxis (cyclizine or dexamethason on induction, ondansetron postoperatively) was continued until PCA was removed.

Incision, wound closure and catheter placement

Access to the abdominal cavity was achieved with a right subcostal incision[31,32] extended to the bed of the right 12th rib laterally and through the upper midline to the level of the xiphoid superiorly ('L' incision). The skin incision was made by knife; diathermy was used through subcutaneous tissue and muscles. Wound closure and catheter placement techniques were also standardized and have been previously described by Basu *et al.*[19]

Delivery of analgesic drugs

Immediately after wound closure, the i.m. catheters were flushed with a 10-ml bolus of 0.25% bupivacaine, and continuous i.m. catheter infusions of 0.25% bupivacaine were commenced at a rate of 3 ml/h by syringe pump. This was continued for 72 h postoperatively. Patient-controlled analgesia using morphine (1 mg bolus with a 5-min lockout) or a fentanyl infusion (20 mcg bolus with a 5-min lockout) was set up. In the CEA group, an epidural catheter was sited before surgery in the thoracic T5–T12 region. This epidural catheter was also used to provide analgesia during surgery (20 ml bupivacaine 0.25%). During emergence from anaesthesia, the patient was transferred to the recovery area, in which the PCA + CIB or CEA was started. The epidural infusion of bupivacaine 0.1% with 2 mcg/ml fentanyl was set at 5–15 ml/h. A dedicated pain team unaware of the type of hepatic resection or any concomitant surgical procedure(s) assessed and scored the patients daily until the i.v. or epidural analgesia could be stopped. Pain intensity was scored using a verbal rating scale (VRS) ranging from 0 (no pain) to 4 (worst imaginable pain). The level of sedation was also measured on a 5-point scale (0 = awake, 1 = dosing intermittently, 2 = sleeping and easy to wake, 3 = sleeping and difficult to wake, 4 = unarousable). Wound and urinary catheters were removed at the discretion of the operating surgeon, but usually after 72 h [midnight on postoperative day (PoD) 3]. Pain management failures in both groups were defined as the need for rescue medication or a switch to a different opioid. The need for rescue medication was defined as any additional epidural, i.v., i.m. or oral administration of an opioid. A switch to a different analgesic protocol was defined as any change in analgesic medication, concentration or infusion rate. In the event of the technical failure

of the epidural catheter, the patient was commenced on PCA with morphine or fentanyl. Oral analgesia [acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs) and opioids] was available in a standard manner to all patients. No standardized enhanced recovery after surgery (ERAS) programme was implemented during this study period.

Statistics

To facilitate comparisons between the two patient groups and the different opioids, all opioids required were converted to an i.v. morphine equivalent (Table 1). Comparisons between groups were performed using Pearson's chi-squared or Fisher's exact test for non-normally distributed categorical variables, as appropriate, and the Mann–Whitney *U*-test or Kruskal–Wallis test for continuous variables. All statistical tests were two-sided. A *P*-value of < 0.05 was considered to indicate statistical significance. Statistical analysis was performed using IBM SPSS Statistics for Windows Version 19.0 (IBM Corp., Armonk, NY, USA).

Table 1 Opioid conversion ratios

	Conversion ratio	References
Intravenous administration		
Morphine	1:1	
Fentanyl, mcg/ml	1:10	[36–38]
Epidural administration		
Fentanyl, mcg/ml	3:10	[39]
Oral administration		
Oxycodone	2:1	[36]
Morphine	3:1	[36,38,40]
Tramadol	15:1	[36]

Opioid conversion ratios lead to an i.v. morphine (mg/ml) equivalent.

Results

General and surgical characteristics

Of 545 patients identified in the database for the study period, a total of 498 patients (CIB + PCA, $n = 429$; CEA, $n = 69$) underwent major liver resection and were included in this study. For 41 of the 47 patients excluded, no data on opioid requirements could be retrieved. This was mostly the result of either admission with sedation to the intensive care unit (ICU) or the absence of fluid balance/opioid infusion charts. Of the remaining six excluded patients, four received PCA without CIB, and one received epidural analgesia combined with CIB. No data at all could be retrieved for the final patient. General patient characteristics are shown in Table 2 and surgical characteristics in Table 3.

Table 2 General characteristics of patients undergoing major hepatectomy in the present series

	Epidural group ($n = 69$)	CIB + PCA group ($n = 429$)	*P*-value
Age, years, median (range)	63 (29–84)	63 (21–86)	0.695
Male sex, *n* (%)	42 (60.9%)	269 (62.7%)	0.770
BMI, kg/m^2, median (range)	24.0 (20.0–33.5)	26.0 (16.0–44.0)	0.126
ASA physical status, *n* (%)			
Class 1	2 (2.9%)	10 (2.3%)	0.673
Class 2	51 (73.9%)	320 (74.6%)	0.924
Class 3–5	13 (18.8%)	87 (20.3%)	0.828
Number of comorbidities, *n* (%)			
0	37 (53.6%)	196 (45.7%)	0.240
1	19 (27.5%)	136 (31.7%)	0.466
2	6 (8.7%)	61 (14.2%)	0.190
≥3	7 (10.1%)	33 (7.7%)	0.498
Indication for surgery, *n* (%)			
Colorectal metastases	56 (81.2%)	369 (86.0%)	0.290
Hepatocellular carcinoma	1 (1.4%)	4 (0.9%)	0.529
Cholangiocarcinoma (intrahepatic and hilar)	1 (1.4%)	12 (2.8%)	1.000
Other malignancies[a]	3 (5.8%)	32 (7.4%)	0.453
Benign disease[b]	8 (10.1%)	12 (2.6%)	**0.003**
Previous abdominal surgery	59 (85.5%)	376 (87.6%)	0.324

CIB + PCA, i.m. continuous infusion of bupivacaine plus i.v. patient-controlled analgesia; BMI, body mass index; ASA, American Society of Anesthesiologists.
A *P*-value of < 0.05 was considered to indicate statistical significance.
[a]Other malignancies include metastases of carcinoid, breast cancer, melanoma, neuroendocrine tumour, appendix carcinoma, ovarian carcinoma, squamous cell carcinoma of the vagina, renal cell carcinoma, lymphoma, endometrial carcinoma, gastrointestinal stromal tumour, mixed type hepatocellular carcinoma/cholangiocarcinoma, lymphoma and keratinizing squamous cell carcinoma.
[b]Benign diseases include cyst(s), adenoma, focal nodular hyperplasia, haemangioma and angiomyolipoma.

Table 3 Operative characteristics of patients undergoing major hepatectomy in the present series

	Epidural group (*n* = 69)	CIB + PCA group (*n* = 429)	*P*-value
Operating time, min, median (range)	260 (150–475)	260 (28–480)	0.356
Blood loss, ml, median (range)	295 (55–844)	369 (30–5344)	**0.020**
Incision, *n* (%)			
Right subcostal	67 (97.1%)	425 (99.1%)	0.165
Other[a]	2 (2.9%)	4 (0.9%)	0.196
Segmental distribution of hepatectomies, *n* (%)			
3 segments	8 (11.6%)	65 (15.2%)	0.438
3 segments + wedge	3 (4.3%)	26 (6.1%)	0.783
3 segments + multiple wedge	1 (1.4%)	9 (2.1%)	1.000
4 segments	40 (58.0%)	163 (38.0%)	**0.002**
4 segments + wedge	5 (7.2%)	70 (16.3%)	0.051
4 segments + multiple wedge	3 (4.3%)	25 (5.8%)	0.783
5 segments	5 (7.2%)	49 (11.4%)	0.301
5 segments + wedge	3 (4.3%)	13 (3.0%)	0.475
5 segments + multiple wedge	1 (1.4%)	6 (1.4%)	1.000
6 segments	0	3 (0.7%)	1.000
Additional procedures, *n* (%)			
Cholecystectomy	13 (18.8%)	66 (15.4%)	0.478
Lymph node sampling	0	12 (2.8%)	0.387
Diaphragmatic resection	3 (4.3%)	18 (4.2%)	1.000
Roux-en-Y reconstruction	1 (1.4%)	3 (0.7%)	0.450
Right colectomy	1 (1.4%)	2 (0.5%)	0.361
Incisional hernia repair	0	3 (0.7%)	1.000
Ablation	0	6 (0.7%)	1.000
Other[b]	2 (2.9%)	45 (11.2%)	**0.046**
Satava classification, *n* (%)			
Grade I	0	17 (4.0%)	0.147
Grade II	0	2 (0.5%)	1.000
Grade III	0	1 (0.2%)	1.000

CIB + PCA, i.m. continuous infusion of bupivacaine plus i.v. patient-controlled analgesia.
A *P*-value of < 0.05 was considered to indicate statistical significance.
[a]Other incisions include abdominal longitudinal incision, Mercedes Benz incision and laparoscopic converted to open surgery.
[b]See Appendix 1 for details.

Primary endpoints

The total median opioid consumption in milligrams (i.v. morphine equivalent) was markedly lower in the CIB + PCA group (for all time-points: $P \leq 0.001$). However, postoperative pain was equally well controlled in both groups (Table 4). The maximum percentages of pain scores missing for the complete group of included patients were 27.7% and 28.3% on PoDs 1 and 2, respectively.

Secondary endpoints

Intramuscular catheters were removed at a median of PoD 3 (range: PoD 2–5). Data on pain management failures, need for rescue medication and technical failures are shown in Table 4. Overall morbidity was higher in the epidural group (39.1%) than in the CIB + PCA group (26.1%) ($P = 0.030$). Complication grades rated on the Accordion system (with Clavien–Dindo modifications), length of hospital stay and readmissions are displayed in Table 5. One death occurred in the epidural group (1.4%) and two (0.5%) occurred in the CIB + PCA group ($P = 0.361$). The patient in the epidural group died from myocardial infarction. In the catheter group, one patient died from liver failure and the other from multi-organ failure caused by severe sepsis after endoscopic retrograde cholangiopancreatography (ERCP) for a bile leak. Specific complications per group are shown in Table 6. No instances of respiratory depression were observed. There were no reported cases of epidural hematoma, abscess formation or paralysis in the group that received an epidural catheter.

Table 4 Postoperative analgesia in patients undergoing major hepatectomy in the present series

	Epidural group (*n* = 69)	CIB + PCA group (*n* = 429)	*P*-value
Time to discontinuation, days, median (range)	3 (1–5)	4 (1–8)	**0.001**
Cumulative opioid consumption[a], mg, median (range)			
12 h	29.1 (0.0–266.0)	17.5 (0.0–1015.0)	< **0.001**
24 h	91.2 (5.0–1546.4)	43.0 (0.0–1225.0)	**<0.001**
48 h	148.4 (6.0–1952.8)	58.0 (0.0–1625.0)	**<0.001**
72 h	186.1 (4.0–1952.8)	61.0 (0.0–1650.0)	**<0.001**
VRS score at rest PoD 1, *n* (%)			
0	41 (89.1%)	234 (73.8%)	**0.024**
1	4 (8.7%)	69 (21.8%)	**0.047**
2	1 (2.2%)	13 (4.1%)	1.000
3	0	1 (0.3%)	1.000
4	0	0	
VRS score on movement PoD 1, *n* (%)			
0	29 (65.9%)	92 (29.4%)	**<0.001**
1	11 (19.4%)	148 (46.8%)	**0.006**
2	3 (6.8%)	52 (16.4%)	0.118
3	1 (2.3%)	20 (6.3%)	0.491
4	0	4 (1.3%)	1.000
VRS score at rest PoD 2, *n* (%)			
0	42 (93.3%)	273 (87.5%)	0.256
1	2 (4.4%)	32 (10.3%)	0.284
2	0	7 (2.2%)	0.603
3	1 (2.2%)	0	0.126
4	0	0	
VRS score on movement PoD 2, *n* (%)			
0	26 (59.1%)	134 (42.8%)	**0.042**
1	15 (34.1%)	118 (37.7%)	0.632
2	1 (2.3%)	45 (14.4%)	**0.027**
3	1 (2.3%)	16 (5.1%)	0.706
4	1 (2.3%)	0	0.124
Pain management failures, PoD 0–3[b], *n* (%)	22 (31.9%)	231 (53.8%)	**0.001**
Opioid rescue medication[c], *n* (%)			
PoD 0	15 (21.7%)	228 (53.1%)	**<0.001**
PoD 1	3 (4.3%)	8 (1.9%)	0.185
PoD 2	5 (7.2%)	6 (1.4%)	**0.010**
PoD 3	6 (8.7%)	5 (1.2%)	**0.002**
Switch to different analgesic protocol[d], *n* (%)	14 (20.3%)	6 (1.4%)	**<0.001**
Technical failure	14 (20.3%)	114 (26.6%)	0.268
Dislocation	7 (10.9%)	4 (0.9%)	
Leakage	4 (6.3%)	1 (0.2%)	
Occlusion	3 (4.7%%)	109 (25.8%)	

CIB + PCA, i.m. continuous infusion of bupivacaine plus i.v. patient-controlled analgesia; PoD, postoperative day; VRS, verbal rating scale (0–4). A *P*-value of < 0.05 was considered to indicate statistical significance.
[a]Expressed as i.v. morphine equivalent (any route).
[b]Pain management failure: need for rescue medication or switch to different opioid.
[c]Rescue medication: any additional intravenous, epidural, intramuscular or oral opioid.
[d]Switch to different analgesic protocol: change of drug, concentration or infusion rate.

Table 5 Postoperative outcomes in patients undergoing major hepatectomy in the present series

	Epidural group (n = 69)	CIB + PCA group (n = 429)	P-value
Complications (Accordion Classification), n (%)			
Grade I	3 (4.3%)	16 (3.7%)	0.737
Grade II	10 (14.5%)	31 (7.2%)	0.057
Grade III	0	14 (3.3%)	0.235
Grade IV	11 (15.9%)	40 (9.3%)	0.130
Grade V	2 (2.9%)	7 (1.6%)	0.361
Grade VI (death)	1 (1.4%)	2 (0.5%)	0.361
Length of stay, days, median (range)	8 (3–80)	7 (3–95)	**0.005**
Readmissions (<30 days), n (%)	2 (2.9%)	15 (3.5%)	1.000

CIB + PCA, i.m. continuous infusion of bupivacaine plus i.v. patient-controlled analgesia.
A P-value of < 0.05 was considered to indicate statistical significance.

Discussion

This study compared the analgesic value of CEA with that of CIB + PCA following major hepatectomy. Data for this large, retrospective cohort show that CIB + PCA provided analgesic control equivalent to that of CEA. No significant differences in the numbers of patients experiencing severe pain were observed between the two groups and the majority of patients in both groups had no or minimal pain during the first 48 h postoperatively. Strikingly, the CIB + PCA group consumed significantly lower total volumes of opioids, had lower postoperative morbidity and a decreased hospital LoS.

The present findings would appear to indicate that postoperative pain was well controlled in both groups and that very few patients experienced severe pain on PoDs 1 and 2. In addition, most patients (>70%) in both groups had zero or minimal pain at rest or on movement. There is little practical difference between level 0 and level 1 pain, but 'no pain' and 'severe pain' lie at either end of any pain intensity scale and thus it seems safe to conclude that the present findings are reliable. The use of CIB + PCA also led to a substantial decrease in opioid consumption without compromising pain control. The decrease in opioid consumption was expected and can be explained by two factors. Unlike those in the CIB + PCA group, patients with epidurals were not able to control their opioid administration. In addition, the local analgesic effect of bupivacaine reduces the need for i.v. opioid infusion. Interestingly, patients with wound catheters were discharged 1 day earlier than those in the epidural group, at a median of 7 days rather than 8 days ($P = 0.005$).

An increased need for rescue medication in the CIB + PCA group was observed. In most patients rescue medication was given on the day of surgery (PoD 0), but this was countered by an increased need for rescue medication and a switch to i.v. opioids in the CEA group on PoDs 1–3. In addition, CIB + PCA was continued for 1 day longer than epidural analgesia. This mainly reflects the practicalities of managing epidurals as it is part of postoperative practice to remove the catheter after 72 h unless otherwise clinically indicated. The high percentage (53.1%) of patients requiring rescue medication may be explained by the possibility that the local analgesic effect of the bupivacaine infusion may have been suboptimal directly after surgery. The epidural analgesia was started prior to the incision, whereas the wound catheters were commenced immediately after wound closure. It may take time for bupivacaine to reach all adjacent tissue and associated nerve endings. Unlike a correctly functioning epidural analgesic, which provides a complete block, bupivacaine infusion exhibits only a local effect and additional opioids may be required.

Another important result refers to the finding that when one of the catheters was dislodged or occluded (often by a faulty connector or by the faulty insertion of the catheter into the connector), pain control was adequately maintained by just one catheter. This is supported by the stagnant opioid consumption on PoDs 2 and 3 with adequate maintenance of pain control. This implies that a single infusing catheter combined with PCA may be sufficient to control postoperative pain.

The findings of this study are in keeping with those of earlier reports on the beneficial results of this technique with regard to pain control, opioid consumption and recovery.[16,19,24,33] It has been claimed that epidural analgesia is superior to PCA for postoperative pain relief in patients recovering from major upper abdominal operations.[10,11] However, the present study shows that when PCA is combined with CIB via i.m. catheters, equivalent pain control can be achieved. As Khorgami *et al.*[34] demonstrated in a recent RCT, the technique of local interfascial analgesia is also feasible for midline incisions.

The present results confirm the clinical applicability of wound catheters. Not only does this analgesic approach provide equivalent pain control with reduced opioid intake, but it also represents a quicker and very likely cheaper method of doing so. Abandoning the use of epidural analgesia eliminates the risk for epidural-related complications (haematoma, abscess and nerve damage) and may improve cost-effectiveness as anaesthetic time may be shortened

Table 6 Morbidity in patients undergoing major hepatectomy in the present series

	Epidural group (n = 69)	CIB + PCA group (n = 429)	P-value
Overall morbidity, n (%)	27 (39.1%)	112 (26.1%)	**0.030**
Complications, n (%)			
Bile leak	2 (2.9%)	16 (3.7%)	
Liver failure	13 (18.8%)	43 (10.0%)	
Sepsis	0	5 (1.2%)	
Abdominal abscess	1 (1.4%)	4 (0.9%)	
Ileus	0	5 (1.2%)	
Pneumonia	3 (4.3%)	11 (2.6%)	
Pleural effusion	1 (1.4%)	4 (0.9%)	
Myocardial infarction	1 (1.4%)	2 (0.5%)	
Wound infection	1 (1.4%)	11 (2.6%)	
Renal failure	2 (2.9%)	7 (1.6%)	
Postoperative haemorrhage	0	4 (0.9%)	
Peritonitis	0	2 (0.5%)	
Ascites	1 (1.4%)	8 (1.9%)	
Biliary stricture/stenosis	0	4 (0.9%)	
Multi-organ failure	1 (1.4%)	4 (0.9%)	
Pneumothorax	0	2 (0.5%)	
Urinary tract infection	2 (2.9%)	6 (1.4%)	
Atrial fibrillation	3 (4.3%)	2 (0.5%)	
Other	2 (2.9%)	12 (2.8%)	
Analgesia-related morbidity (all), n (%)	29 (45.3%)	169 (41.4%)	0.558
Pruritus	14 (20.3%)	92 (21.4%)	
Hallucinations	7 (10.1%)	80 (18.6%)	
Dizziness	4 (5.8%)	32 (7.5%)	
Hypotension requiring treatment	5 (7.2%)	0	
Acute confused episode	3 (4.3%)	4 (0.9%)	
Wound infection	1 (1.4%)	11 (2.6%)	
Urinary retention	0	3 (0.7%)	
Sedation score PoD 1			
0	37 (82.2%)	215 (59.9%)	**0.004**
1	8 (17.8%)	129 (35.9%)	**0.015**
≥2	0	15 (4.2%)	0.392

CIB + PCA, i.m. continuous infusion of bupivacaine plus i.v. patient-controlled analgesia; PoD, postoperative day.
A P-value of < 0.05 was considered to indicate statistical significance.
Other complications include: haematoma at resection area (n = 1), transient ischaemic attack (n = 1), Horner's syndrome (n = 1), pulmonary embolism (n = 1), respiratory failure (n = 1), alcohol withdrawal (n = 1), deep vein thrombosis (n = 1), infected line (n = 1), allergic reaction (n = 1), sacral pressure sore (n = 1), cellulites (n = 1), partial portal vein thrombosis (n = 1), axillary nerve palsy (n = 1) and cerebral infarct (n = 1).

and the CIB + PCA combination does not require specialist supervision on the ward. The lower total opiate dose received may also reduce opiate-associated side-effects. In patients in whom experts aim to achieve faster postoperative recovery within the context of an ERAS programme, the use of CIB + PCA may result in a further reduction in the time required to meet recovery criteria.

The partly retrospective design of this study resulted in the incomplete availability of pain scores. The complete availability of pain data might have altered the comparability of the groups and might have implied an increased superiority or inferiority of either of the two analgesic modalities. In addition, an inherent bias of surgeon preference influencing outcomes cannot be excluded. The strengths of this study include its use of a large and uninterrupted cohort of patients submitted to major liver resection in an expert centre, whereas other prospective series are considerably smaller. The patients investigated in this study represent

a population at risk for postoperative coagulopathy and the development of epidural hematoma.

It would be interesting for future research to compare patient-controlled epidural analgesia with CIB + PCA and to look into the number and location of wound catheters needed to achieve the optimal local analgesic effect. Lastly, it would be interesting to compare the local wound infusion technique with that of the transversus abdominis plane block,[35] which can also be regarded as safe and effective after abdominal surgery.

Conclusions

Continuous i.m. bupivacaine infusion with i.v. PCA provides equivalent pain control and a lower level of opioid consumption compared with CEA following major hepatectomy. The CIB + PCA technique could replace that of epidural analgesia with the potential for greater safety, improved postoperative outcomes and a reduced hospital LoS.

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Conflicts of interest

None declared.

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Appendix 1

The following (combined) procedures were performed only twice in the study cohort: Cholecystectomy + biliodigestive anastomosis, skeletonization of the hepatoduodenal ligament, closure of ileostomy, block dissection of the hepatoduodenal ligament, cava resection, node block dissection of the lesser sac, diaphragm + peritoneal nodule resection, cholecystectomy + hepatoduodenal ligament biopsy, deroofing of a liver cyst and excision of peritoneal deposits not in the lesser sac.

The following (combined) procedures were performed only once in the study cohort: En bloc gastric resection + cholecystectomy, block dissection of the hepatoduodenal ligament + diathermy ablation, excision of aortocaval lymph node + peritoneal deposit resection, skeletonization of the hepatoduodenal ligament + Roux loop biliary reconstruction + cholecystectomy, block dissection of the lesser sac + excision of the common bile duct + Roux loop reconstruction, colon excision + cholecystectomy, reconstruction of the v. cava, right hemicolectomy + diathermy ablation, sleeve resection of the duodenum, posterior pelvic extenteration, en bloc total mesorectal excision + appendicectomy + excision of a mesenteric mass, diaphragm resection and repair of two incisional hernias, cholecystectomy + excision of the greater omentum, exploration of common bile duct + removal of a stone, splenectomy, insertion of terminal ileostomy, gastroduodenal ligament + cholecystectomy, vascular reconstructions, nephrectomy + adrenalectomy, block dissection of the lesser sac + excision of common bile duct + Roux loop reconstruction + repair of an incisional hernia, reconstruction of the bile duct, small bowel resection, small bowel biopsy and resection of part of the diaphragm and lung.