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Duration of the thoracic epidural catheter in a fast-track recovery protocol may decrease the length of stay after a major hepatectomy: A case control study

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ABSTRACT

Background: Fast-track recovery protocols are applied to major surgeries, including hepatectomies. The optimal duration of thoracic epidural catheter has not yet been defined.
Objective: To determine the ideal time to remove the epidural catheter after major hepatectomy.
Patients–methods: Forty-eight consecutive patients who underwent major hepatectomy over 4 years were studied. The data from laparoscopic hepatectomy were not included. Patients who underwent hepaticojejunostomy were included. A modified protocol of rapid postoperative recovery was implemented. In the first 24 patients, an epidural catheter was maintained for 4 days (group A), while in the next 24, the catheter was maintained for 2 days (group B). The length of hospital stay, time of functional recovery, and use of opioids and laxatives were recorded.
Results: There was no postoperative mortality. The average length of hospital stay was 6.92 ± 1.79 and 6.09 ± 2.08 days for groups A and B, respectively. The mean functional recovery was 5.46 ± 0.3 and 5.26 ± 0.91 days for groups A and B, respectively. However, in group B, more opioid analgesics by 50% and more laxatives by 17% were used.
Conclusions: After major hepatectomy, a reduction from 4 to 2 days' duration of the epidural catheter may lead to a reduction in the length of hospital stay.

1. Introduction

Fast track (FT) or enhanced recovery after surgery (ERAS) programs are often applied to major surgeries, including hepatectomy.[1] It is well established that improper pain management, enteric dysfunction and immobilization of the patient increases the duration of the hospital stay after colorectal surgery.[2] Hepatic resections and elective colorectal surgeries are procedures that involve high stress, and convalescence may sometimes be slow.

Despite recent developments in the perioperative and postoperative care of these patients, the optimal duration of the thoracic epidural catheter is not yet defined. Many FT protocols have been introduced over the years with many variations in the management of postoperative epidural analgesia.[3,4]

According to our center's FT original protocol, a thoracic epidural catheter was utilized for 4 days, and the use of a urinary bladder catheter 4 days followed. The aim of this study was to define whether the reduction from 4 to 2 days of using an epidural catheter led to a reduction in the length of hospital stay after a major hepatectomy.

2. Materials and methods

This study is a retrospective analysis of the prospectively recorded data of 48 consecutive patients who underwent operations from June 2008 to June 2012. In the first 24 patients, the epidural catheter was maintained for 4 days (control group), while in the next 24 patients, it was maintained for 2 days only (study group). The data from patients who underwent laparoscopic hepatectomy were not included, while the data from patients with hepatectomy and hepatojejunostomy were included.

The preoperative evaluation and preparation for anesthesia and surgery consisted of standard plasma liver function tests, preoperative radiological evaluations with triple phase contrast-enhanced computed tomography (CT) and/or selective magnetic resonance imaging (MRI), with or without CT-positron emission tomography (CT-PET). Decisions on the patients' treatment strategies were multidisciplinary. Patients' demographics, ASA grades, diagnoses, preoperative chemotherapy regimens, operative procedures, blood loss, complications, duration of hospital stay and total length of stay with readmission were recorded. The Brisbane terminology was used for the description of the resections.[5] The FT protocol in our center

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consisted of 9 major points: 1) high thoracic epidural catheter, 2) no drain placement unless the hepatectomy is non-anatomical,[6] 3) immediate extubation, 4) unrestricted diet from the first postoperative day, 5) mobilization as much as possible from the first postoperative day, 6) systematic administration of 4 g of paracetamol, 7) systematic administration of 2 g of magnesium, 8) maintaining central vein pressure $<$ 5 cm H_2O during hepatectomy and the first 48 h[7] and 9) glucose clamping.[8] The number of deaths, number of postoperative complications/readmissions, time of functional recovery, time of hospital stay, number of readmissions, use of opioids analgesics and use of laxatives were studied too.

Functional recovery was achieved when patients fulfilled the following criteria: tolerance of oral diet, full mobilization (as prior to surgery), pain control with only oral analgesics (not opioids), passage of flatus and normalization of liver biochemical tests. When all five criteria were met, the patient was discharged.

Any complication occurred within 90 days of surgery was considered postoperative. Major complications, as defined by the International Study Group of Liver Surgery (ISGLS), included the following: 1) hepatic failure,[9] 2) bile leakage[10] and 3) hemorrhage.[11] The Dindo and Clavien classification was used for the determination of the severity of complications.[12]

2.1. Surgical technique

A typical bilateral subcostal "chevron" incision with possible midline extension ("Mercedes-Benz" incision) was performed. A routine intraoperative ultrasonography was performed at the beginning of the operation to confirm the number and size of the lesions in relation to the vascular structures of the liver. The inflow maneuver (Pringle's technique) was not used.

Once the hepatic capsule was marked, the first 2 cm of the parenchyma transection was performed using ultrasonic vibration (Harmonic Focus Long Curved Shears, Ethicon, Norderstedt, Germany). Deeper transaction was performed by pressurized jet of water (Hydro-Jet, Erbe, Tubingen, Germany) and stapler devices (Echelon Flex Endopath Stapler, Ethicon, Norderstedt, Germany). Drains were placed selectively, and the abdomen was closed according to the standard surgical fashion.

2.2. Anesthesia and postoperative management

All patients were managed with thoracic epidural anesthesia, with the catheter inserted immediately before the beginning of the operation. After i.v. administration of a bolus dose of 500 ml of colloids at 60 mg/ml (Venofudin, B. Braun, Melsungen, Germany), the catheter were introduced at the T6-T7 (or T5-T6) intervertebral space. A test dose of 3 ml ropivacaine 7.5 mg/ml (Naropeine, AstraZeneca, Athens, Greece) was administered to exclude intrathecal end/or intravascular placement of the catheter. After a negative test dose, a single dose bolus of 6 ml ropivacaine 7.5 mg/ml was administered to achieve a T4 level of sensory block. The procedure was performed under general anesthesia involving tracheal intubation and control ventilation. The induction was achieved by intravenous propofol 2 mg/kg (Propofol-®Lipuro 1%, B. Braun, Melsungen, Germany) and fentanyl 3–5 μg/kg (Fentanyl, Janssen-Cilag, Athens, Greece). Neuromuscular blockade was achieved with vecuronium bromide 0.1 mg/kg (Norcuron 1 mg/ml, N.V. Organon, Oss, Netherlands). All patients were monitored intraoperatively with a triple lumen central venous catheter, which was introduced in the right or left internal jugular vein. Invasive arterial lines introduced in the right or the left radial arteries were also utilized. A nasogastric tube, a urinary catheter, core temperature monitoring, forced warm air blankets and the use of sequential calf compression devices were all employed. Patients at the induction also received intravenous dexamethasone 8 mg (Dexaton 4 mg/ml Vianex, Athens, Greece) ondansetron 4 mg (Vefron 8 mg/4 ml, Opus-Materia, Paleo Faliro, Greece) and/or metoclopramide 10 mg (Primperan, Sanofi-Aventis, Athens, Greece) as prophylaxis against postoperative nausea and vomiting (PONV).

At the end of the procedure, all patients were transferred, intubated, and admitted to the ICU to tightly control their hemodynamic parameters (BP, CVP, HR) for possible hemorrhagic diathesis, diuresis and temperature. The extubation was performed upon arrival to the ICU along with the removal of the nasogastric tube. The epidural catheter was maintained either 48 or 96 h after its insertion (depending on the duration of the stay). Postoperatively, patients received a standard continuous infusion of ropivacaine 2 mg/ml in a dose of 15–25 mg/h, titrated to effect (VAS score $\leq$ 3).[13] At the same time, all the patients received intravenous paracetamol (Apotel 1 g, Uni-Pharma, Athens, Greece) in a dose of 2 g in 4 divided doses during the first day, which was increased to 4 g in 4 divided doses from the second day of their stay in the ICU.

Epidural catheters were removed on postoperative day 5 in group A and on day 3 in group B. The practice was to remove the catheter if the INR was $<$1.6. If it was prolonged, FFPs were given before removal of the epidural catheter.

3. Statistical analysis

Continuous data were described as medians (range) and analyzed with Student's t test. Categorical data were described as numbers and percentages and analyzed with the x^2 test. A p value of less than 0.05 was considered statistically significant. Statistical analysis was performed using SPSS for Mac, version 20.0.0 (SPSS Inc., Chicago, IL, USA).

4. Results

The demographics and clinical details are reported in Table 1. The mean duration of surgery in group A was 296 min (range 174–510), and in group B, 290 min (range 156–410), $p > 0.05$. The mean blood loss was 166.7 ml (range 0–500) in group A and 173.9 ml (range 0–500) in group B, $p > 0.05$. Other details of the hepatic resections are reported in Table 2. Hemihepatectomy was the most common type of operation in both groups (7/24 in group A & 16/24 in group B), followed by extended hemihepatectomy (5/24 in group A & 5/24 in group B). The types of hepatectomies are presented in Table 3.

The oral fluid intake for group A was 39.8 h (range 38–42), and for group B, 41.9 h (range 38–57), $p = 0.129$. Eleven patients (45%) received opioids in group A, and 22 (91.6%), in group B. Discontinuation of opioids was achieved after 2 days for group A and 3.95 days for group B, $p = 0.001$. Laxatives were used in 17 patients (70.8%) in group A and in 21 (87.5%) in group B. The time to functional recovery was 5.5 days (range 4–7) in group A and 5.3 days (range 4–8) in group B, $p = 0.467$ (Table 4).

No perioperative mortality was recorded (90 days). Major complications occurred in four patients in group A and in four patients in group B (Table 5). The length of stay was 6.9 days (range 5–13) in group A and 6.1 days (range 5–12) in group B, $p = 0.152$. One patient was readmitted in group A, and two, in group B. The total length of stay was 7.1 days (range 5–13) in group A and 6.4 days (range 5–12) in group B, $p = 0.250$.

5. Discussion

In this study, we investigated the impact of reducing the duration of the epidural catheter in major hepatic resections from 4 to 2 days. Although several studies have been published in the literature regarding ERAS programs of liver resection, the optimal duration of epidural analgesia has not been standardized.[3,4,14–17]

Not long ago, liver resection moved from a high-risk procedure with significant mortality (over 5%) and morbidity to a safe, routine surgery.[18–20] The adoption of hepatic parenchyma transection devices with the advances in the perioperative anesthesiologic management resulted in the reduction of bleeding and parenchyma resection time.[21] With the introduction of ERAS protocols, the benefits of advances in the technique and anesthesia are increasing. Although in various studies, the methodology of the protocols is not

Table 1
Patient demographics and diagnoses.

Groups	A ($n = 24$)	B ($n = 24$)	p-Value
Age (range)	48.8 (31–75)	57.8 (32–73)	n/s
Sex (M:F)	18:6	16:8	n/s
ASA grade			
1	0	0	
2	5	3	
3	19	21	
Pre-op chemotherapy	8	13	
Diagnosis			
Colorectal mets	8	12	
Neuroendocrine mets	2	3	
Cholangiocarcinoma	7	3	
HCC	2	3	
Benign tumors	5	3	

*n/s denotes absence of statistical significance ($p > 0.05$).

Table 2
Summary of operative and postoperative details.

Groups	A ($n = 24$)	B ($n = 24$)	p-Value
Operation time (min)	296 (174–510)	290 (156–410)	0.809
Blood loss (mL)	166.7 (0–500)	173.9 (0–500)	0.861
Drain (n)	16 (75%)	21 (87.5%)	
Drain removal (days)	4 (3–7)	4.2 (3–10)	0.097
Max CVP (cmH_2O)	5.5 (4–8)	5.5 (4–8)	0.873
Max Glu (mg/dL)	132.6 (99–208)	132 (98–202)	0.952
Min Glu (mg/dL)	74.4 (55–96)	74.5(57–98)	0.982

Table 4
Primary and secondary outcomes.

Groups	A ($n = 24$)	B ($n = 24$)	p-Value
LoS (days)	6.9 (5–13)	6.1 (5–12)	0.152
Readmissions, (n)	1	2	
Total LoS (days)	7.1 (5–13)	6.4 (5–12)	0.250
Oral fluid intake (hours)	39.8 (38–42)	41.9 (38–57)	0.129
Functional recovery (days)	5.5 (4–7)	5.3 (4–8)	0.467
Opioid use (n)	11 (45.8%)	22 (91.6%)	
Opioid duration (days)	2 (1–5)	3.95 (2–7)	0.001
Laxatives use (n)	17 (70.8%)	21 (97.5%)	0.160

the same, the principal end points, such as the hospital LoS and the number of readmissions, are improved compared with the preceding era.[4,16] The other two important points, morbidity and mortality, although variable among the different studies (38–45%), show no important differences with ERAS programmes.[9,19] However, not all the referred complications have been graded according to the Dindo-Clavien Classification System, which makes it difficult to draw definitive conclusions.

ERAS studies dealing with open liver surgery are emerging very fast in the literature. According to the review article of Coolsen et al.,[16] the most influential are three case control studies,[7,22,23] two randomized systematic trials (RCT)[3,11] and one retrospective case series.[24] None of these studies dealt with the optimal duration of postoperative analgesia using an epidural catheter. In the RCT study of Koea et al., in which a comparison between epidural and intrathecal analgesia was performed, both types of analgesia remained for 3 days.[3] In another study performed by Connor et al., again using both types of postoperative analgesia, the epidural catheter remained for 6 days (range 5–10), while the intrathecal catheter stayed for 3 (range 2–24).[4]

Stamenkovic et al. studied the optimal time of epidural catheter removal but outside of the ERAS programs. The aim of this study was to identify the "safe" time to remove the epidural catheter using as criteria the coagulopathy perspective and not the LoS. In the 123 patients who underwent liver resection, the catheter was removed on day 5 (1–11) without any epidural or spinal hematoma.[17]

In our study, patients who maintained the epidural catheter for 4 days had comparable functional recoveries with those who kept it for only 2 days ($p = 0.467$). LoS and total LoS, although not significantly different ($p = 0.152$ & $p = 0.250$) show a reduction in the duration of hospitalization for group B. This is most likely due to a type II error (false negative) because the number of patients in each group was relatively small.

Both patient groups had similar operative and postoperative data; therefore these parameters could not have any effect on the outcomes of our FT program. However, since all hepatectomies in the control group were performed earlier (year-wise) than hepatectomies in the study group, potential selection bias in regards with surgeons' operative experience could not be eliminated.

An important observation is that the group of patients who were managed with 2 days of the epidural catheter had an increased need for analgesic opioids and laxatives. Notably, the number of patients who received opioids in group B was the double the number in group A. Not only did more patients need opioids but the duration of their use also doubled. Laxatives, although not directly correlated with the duration of hospitalization, as shown by Hendry et al.,[8] were used in almost all patients who had the epidural catheter for only 2 days, most likely because these patients used significantly more opioids, but laxative use was not permitted to compromise the primary end point, the hospital LoS.

Major complications included three bile leakages in each group (all managed by CT guided drainage) and one case of hemorrhage in each group (managed with blood transfusion alone). Bile leakage was the cause of the three readmissions in each group. No mortality or any other major complication was recorded. In all the groups, oral food intake was achieved early, with no significant differences among the groups.

In conclusion, the removal of the epidural catheter on postoperative day 3 may lead to a decrease in the LoS without an impact on morbidity, mortality or readmission rates. However, its removal certainly increased the need for opioid analgesia. In view of our results, and although the number of patients in the two groups was limited, a compromise should be reached between the two time points of epidural catheter removal. Therefore, the optimal duration of the epidural catheter might be 3 days. Naturally, more studies with a larger number of patients are warranted to confirm our suggestion.

Ethical approval

Ethical Approval was obtained by the IRB of "Euromedica Geniki Kliniki" General Hospital (ref.: 2-008/42).

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Author contribution

Ntinas: Design, manuscript, revisions.
Kardassis: Data collection, manuscript, revisions.
Konstantinopoulos: Procedures, data collection, manuscript.

Table 3
Types of hepatectomy.

Groups	A	B
Hemihepatectomy	7	16
Hemihepatectomy plus $\geq$ 1 metastasectomies	2	0
Extended hemihepatectomy	5	5
Multiple segmentectomy ($\geq$2 segments)	2	2
Central hepatectomy	3	1
Repeat hepatectomy	3	0

Table 5
Postoperative complications.

Groups	A	B
Major		
Bile leakage	3	3
Hemorrhage	1	1
Minor		
Pneumonia	2	2
Urinary tract infection	5	3
Dindo-Clavien classification		
Grade I	7	5
Grade II	1	1
Grade III	3	3
Grade IV	0	0
Grade V	0	0

Kottos: Procedures, data collection, manuscript.
Manias: Procedures, data collection, manuscript.
Kyritsi: Procedures, data collection, manuscript.
Zilianaki: Procedures, data collection, manuscript.
Vrochides: Idea, manuscript, revisions.

Conflict of interest

There are no conflicts of interest.

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