OPEN

Thoracic Epidural Analgesia for Postoperative Pain Management in Liver Transplantation: A 10-year Study on 685 Liver Transplant Recipients

John Hausken, MD,[1] Håkon Haugaa, MD, PhD,[1,2] Morten Hagness, MD, PhD,[3] Pål-Dag Line, MD, PhD,[3,4] Espen Melum, MD, PhD,[4,5,6,7,8] and Tor Inge Tønnessen, MD, PhD[1,4]

Background. Thoracic epidural analgesia (TEA) is not widely used for postoperative pain management in liver transplantation due to hepatic coagulopathy-related increased risk of inducing an epidural hematoma. However, an increasing number of patients are transplanted for other indications than the end-stage liver disease and without coagulopathy allowing insertion of an epidural catheter. **Methods.** This study is a retrospective observational single-center study of all adult patients undergoing first-time liver transplantation at Oslo University Hospital between January 1, 2008, and December 31, 2017. Data regarding patient characteristics were obtained from the Nordic liver transplant registry, medical records, and pain registration forms. Patients without coagulopathy (international normalized ratio <1.5 and platelets >100 × 10^9/L) were eligible for TEA. **Results.** Out of 685 first-time liver transplantations in a 10-year period, 327 received TEA, and 358 did not. The median Model of End-stage Liver Disease score was lower in the TEA group than in the non-TEA-group (9 versus 17, $P < 0.001$), and fewer patients were hospitalized preoperatively (16 versus 127, $P < 0.001$). The median international normalized ratio (1.1 versus 1.6, $P < 0.001$) and platelet count (190 versus 78, $P < 0.001$) were different between the TEA and non-TEA groups. There were no serious complications related to insertion or removal of the TEA catheters. Patients in the TEA group had less pain with a mean numeric rating scale at postoperative days 0–5 of 1.4 versus 1.8 ($P = 0.008$). Nearly 50% of the patients were prescribed opioids when discharged from hospital (non-TEA 154 versus TEA 158, $P = 0.23$), and there was no difference after 1 year ($P = 0.718$). **Conclusions.** Our report revealed very good pain control with both TEA and the non-TEA modality. TEA was without any serious complications like epidural hematoma or infection/abscess in selected liver transplant recipients without severe coagulopathy. Opioid prescription at hospital discharge and by 1-year follow-up did not differ between the groups.

(*Transplantation Direct* 2021;7: e648; doi: 10.1097/TXD.0000000000001101. Published online 7 January, 2021.)

INTRODUCTION

Liver transplantation (LTx) is a life-saving procedure for acute liver failure and the only definite treatment for end-stage chronic liver disease and is increasingly also performed for primary liver cancer and in experimental protocols for metastases.[1] Pain after LTx is usually less severe compared with other major abdominal surgery procedures.[2,3] Nevertheless, good postoperative analgesia is essential for patient recovery and satisfaction also after LTx.[4,5] In the early era of our transplant program, opioids administered as nurse- or patient-controlled analgesia (PCA) was the basis of postoperative analgesia.[2]

Received 27 August 2020. Revision received 11 October 2020.

Accepted 1 November 2020.

[1] *Department of Anesthesiology, Division of Emergencies and Critical Care, Oslo University Hospital, Oslo, Norway.*

[2] *Department of MEVU, Lovisenberg University College, Oslo, Norway.*

[3] *Section for Transplantation Surgery, Department of Transplantation Medicine, Oslo University Hospital, Oslo, Norway.*

[4] *Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway.*

[5] *Norwegian PSC Research Center, Department of Transplantation Medicine, Division of Surgery, Inflammatory Diseases and Transplantation, Oslo University Hospital Rikshospitalet, Oslo, Norway.*

[6] *Research Institute of Internal Medicine, Division of Surgery, Inflammatory Diseases and Transplantation, Oslo University Hospital, Oslo, Norway.*

[7] *Section for Gastroenterology, Department of Transplantation Medicine, Division of Surgery, Inflammatory Diseases and Transplantation, Oslo University Hospital Rikshospitalet, Oslo, Norway.*

[8] *Hybrid Technology Hub-Centre of Excellence, Institute of Basic Medical Sciences, Faculty of Medicine, University of Oslo, Oslo, Norway.*

The authors declare no funding or conflicts of interest.

J.H. collected the data and drafted the manuscript. J.H., H.H., E.M., and T.I.T. contributed to the design and implementation of the research, to the analysis of the results, and to the writing of the manuscript. P.-D.L. and M.H. contributed to the analysis of the results and to the writing of the manuscript. All authors discussed the results and commented on the manuscript.

Correspondence: John Hausken, MD, Department of Anesthesiology, Division of Emergencies and Critical Care, Oslo University Hospital, 0027 Oslo, Norway. (jhausken@ous-hf.no).

ISSN: 2373-8731

DOI: 10.1097/TXD.0000000000001101

Administration of acetaminophen and NSAIDS to LTx recipients is restricted due to hepatotoxicity and high incidence of impaired renal function, respectively.[6]

Epidural analgesia is by many considered to be the optimal pain relief after major surgery and may improve perioperative outcomes when compared with general anesthesia.[7-9] Thoracic epidural analgesia (TEA) is an invasive procedure with risk of spinal cord injury due to epidural hematoma, infections, or direct puncture injuries.[10] It is also time consuming in the operating room (OR) and requires significant resources for observation during the first postoperative days (PODs), and a number of patients are also reluctant to this type of pain management.

In our LTx center, we have for nearly 2 decades offered TEA to patients without coagulopathy, defined as international normalized ratio (INR) >1.5 and platelets <100 × 10^9/L. In this study, we have explored data from all adult liver transplant recipients during the last 10 years focusing on safety and feasibility of TEA but also analyzed the effect of TEA versus non-TEA on postoperative pain scores and postoperative course as reflected by time until extubation and length of intensive care unit (ICU) stay.

MATERIALS AND METHODS

The study was approved by the South-Eastern Norwegian Research Ethic Committee for Medical and Health Research Ethics (REK no. 2018/2240), and the hospital Data Protection Officer. The study design was a retrospective observational single-center study, and all patients >18 years of age undergoing first-time LTx at Oslo University Hospital between January 1, 2008, and December 31, 2017, were eligible for inclusion. Data regarding patient characteristics were obtained from the Nordic liver transplant registry, medical records, and pain registration forms.

Selection Criteria for TEA

At the time of listing for LTx, all recipients received careful information about the choice of postoperative pain management. The decision to perform a TEA is mainly based on the coagulation profile; INR, platelets, and activated partial thromboplastin time (APTT) values and informed consent from the patient. Patients eligible for TEA are informed about the pros and cons; the vast majority of these prefer TEA. We do not consider recipients with a degree of liver failure requiring critical care treatment, renal replacement therapy, or mechanical ventilator support as candidates for TEA. For those patients with ongoing anticoagulant prescription pretransplant, a non-TEA strategy is chosen. Patients with earlier dissatisfaction with epidural analgesia or patients choosing non-TEA treatment are treated according to their choice. Premorbid psychiatric disorders, anxiety, and depression or patients on medication-assisted treatment for opioid use disorder are not considered contraindications to TEA.

Coagulation Profile

Laboratory tests included a complete blood count, biochemical and coagulation profile during the pretransplant work-up, at arrival in the hospital before transplantation and in the early posttransplant period before hospital discharge. Standard coagulation profile included platelet count, APTT, and INR.

Thoracic Epidural Analgesia

To minimize the risk of epidural hematoma and infections, we used the modified institutional protocols based on guidelines from New York School of Regional Anesthesia recommendations: an INR <1.5, APTT <45 s, a platelet count >100 × 10^9/L, and no signs of local skin infection. Before induction of general anesthesia the epidural catheter was inserted under sterile condition with a loss of resistance technique by an 18G needle at a mid-thoracic level (Th 7-10) to cover the dermatomes innervating the incision in the upper abdomen. The epidural infusion consisting of bupivacaine 1 mg/mL, fentanyl 2 μg/mL, and epinephrine 2 μg/mL was activated on the attending anesthesiologist's decision. Following the hospital protocols, the infusion rate was initiated at 5–10 mL/h, increased to maximum 15 mL/h if necessary, bolus dose of 5 mL was allowed every 30 minutes.

Non-TEA Pain Management

When leaving ICU, the patients were offered intravenous PCA with ketobemidone or oxycodone. The PCA pump was programmed to deliver 1 mg bolus of ketobemidone or oxycodone, with an 8-minute lockout interval and a maximum hourly dose of 7 mg. No baseline infusion was allowed. PCA was discontinued when the patients reported low pain scores and oral analgesics were considered appropriate. Patients not receiving PCA were administered intermittent boluses of analgesics.

Both the PCA with ketobemidone/oxycodone and TEA were administered with CADD-Legacy PCA Pump Model 6300 (SIMS Deltec, St. Paul, MN).

Anesthesia and Perioperative Care

All recipients received general anesthesia with thiopental or propofol, fentanyl, an inhalational anesthetic agent, and a nondepolarizing neuromuscular blocker.

A fast-track protocol together with early weaning from ventilator to minimize the use of intensive care resources is provided in our liver transplant unit whenever possible.

The surgical approach is an inversed L-shape or subcostal incision in the right upper abdomen, and the piggy-back technique with preservation of the recipient cava and a temporary portocaval shunt is routinely used. Single intraoperative unfractionated heparin of 2500–5000 units intravenously before the arterial vascularization is occasionally used, at least 120 minutes after the epidural catheter insertion. According to our center's protocol, all recipients received tacrolimus or sirolimus/everolimus, methylprednisolone, and mycophenolate mofetil. A bolus dose of 500–1000 mg methylprednisolone was administered before reperfusion of the liver graft according to the recipients immunological risk profile.

Our transplant center consists of dedicated specialists in the field of transplant medicine and surgery. All invasive procedures and anesthetic management were performed by experienced anesthesiologists in the liver transplant team.[11]

Postoperative Data Collection

Possible TEA-related complications like hematomas and infections, and overall pain intensity on PODs 0–5 were registered. The pain intensity was registered by nurses with an 11-point numeric rating scale (NRS) from 0 to 10, where 0 is no pain and 10 the most intense pain imaginable. When several ratings were registered on the same day, the mean value for that day was calculated.

Opioid use pretransplant, at discharge from the transplant center, and at 1-year follow-up was registered.

STATISTICAL ANALYSIS

Continuous variables are presented as median with 25 and 75 percentiles, and group comparisons were performed with the Mann–Whitney *U* test. Categorical variables are presented as numbers and percentages, and analyzed with Chi-square in contingency table analyses. IBM SPSS Statistics Version 25 was used for statistical analyses (IBM, Armonk, NY). *P* values <0.05 were regarded as statistically significant. GraphPad Prism 8 was used to provide the plot diagram in Figure 1.

RESULTS

A total of 705 primary liver transplants (LTX) were performed at our center in the study period. Twenty patients were excluded due to simultaneous transplantation of other solid organs or lack of data. Thus, 685 patients were available for final data analysis; out of these, 327 received TEA, and 358 were in the non-TEA group. The baseline characteristics are presented in Table 1. There were statistically significant differences between the TEA and non-TEA recipients with regards to model of end-stage liver disease score (9 versus 17), the American Society of Anesthesiologists (3 versus 4), and the number of patients that were hospitalized before transplantation (4.9% versus 35.5%).

In the TEA group, 310 out of 327 patients (95%) received TEA before LTX. In 6 patients, cannulation and insertion of an epidural catheter was not technically possible, and 3 patients received transfusion of platelets before insertion of the TEA catheter. There were no serious adverse events like epidural hematoma or epidural infection/abscess caused by insertion or removal of the epidural catheters. In 3 patients complaining of low back pain and numbness in the lower extremity, a magnetic resonance imaging of the spine was done, 2 had normal findings, and 1 patient had a not previously recognized spinal stenosis.

TABLE 1.

Baseline characteristics of 685 liver transplant recipients in the period January 1, 2008–December 31, 2017

	TEA	Non-TEA	*P*
Total	327 (48)	358 (52)	—
Male/female	200/127 (61/39)	211/147 (59/41)	0.55
Age (y)	55.1 (44.8–62.0)	55.2 (48.2–61.9)	0.52
BMI	24.1(21.8–27.0)	25.9 (22.7–29.3)	<0.001
Diagnosis			
Acute liver failure	1 (0)	21 (6)	<0.001
Chronic liver disease, nonmalignant	198 (61)	263 (74)	<0.001
Malignant liver disease[a]	128 (39)	74 (20)	<0.001
MELD score	9 (7–14)	17 (12–25)	<0.001
ASA score	3 (3–4)	4 (3–4)	<0.001
Cold ischemia time (min)	431 (337–517)	429 (341–521)	0.323
Donor age (y)	53 (41–65)	59 (43–69)	0.557
Waiting list time (d)	28 (12–65)	23 (6–57)	0.135
Dialysis	0 (0)	46 (13)	<0.001
Hospitalized before LTx	16 (4.9)	127 (35.5)	<0.001
ICU stay before LTx	2 (0.6)	53 (15)	<0.001
INR	1.1 (1.0–1.3)	1.6 (1.3–2.0)	<0.001
Platelet count ($\times 10^9$/L)	181 (128–264)	78 (57–105)	<0.001
APTT (s)	37 (34–41)	44 (38–53)	<0.001
Perioperative transfusion (mL)			
RBC	0 (0–750)	1000 (250–2000)	<0.001
Plasma	200 (0–800)	800 (400–1600)	<0.001
Platelets	0 (0–0)	350 (0–700)	<0.001

[a]Hepatocellular carcinoma (n = 139), secondary liver tumors from nonresectable cancer (n = 48), biliary tract carcinoma (n = 6), hepatic cholangiocarcinoma (n = 4), and other liver malignancies (n = 5).

Data are presented as n (%) or median (25–75 percentiles) and were analyzed with Chi-square- and Mann–Whitney U tests, respectively.

APTT, activated thromboplastin time; ASA, American society of anesthesiologist classification system; BMI, body mass index; ICU, intensive care unit; INR, international normalized ratio; LTx, liver transplantation; MELD, model of end-stage liver disease; non-TEA, not receiving thoracic epidural analgesia; RBC, red blood cells; TEA, thoracic epidural analgesia.

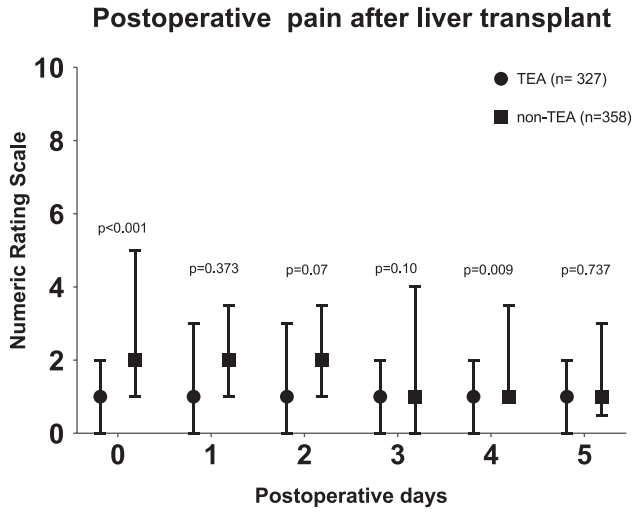

FIGURE 1. Numeric rating scale pain score during the first 5 postoperative days in 685 primary liver transplantation recipients (median and interquartile range). Numbers above the graphs are *P* values of compared postoperative pain scores in patients treated with TEA vs non-TEA, day-by-day (Mann–Whitney U test). non-TEA, pain management without thoracic epidural analgesia; TEA, thoracic epidural analgesia.

The overall pain intensity measured by NRS (0–10) during POD 0–5 revealed a significant difference between TEA and non-TEA, with 1.4 versus 1.8 ($P < 0.001$), respectively (Table 2). The day-to-day (0–5) median pain scores revealed NRS ≤2 in both groups. The highest NRS scores were registered during the first 3 PODs in the non-TEA group, whereas significant differences between the groups were only seen on days 0 and 4 (Figure 1). A total of 34 (4.9%) patients in this study reported moderate to severe pain on days 0–5 (NRS > 4), equally distributed in both the groups.

Lower extremity weakness/motoric block were reported in 37 patients (11.3%) in the TEA group, but the neurological symptoms did not persist in any patient after the removal of the epidural catheter. A total of 34 patients (10.4%) received a second epidural because of insufficient pain relief or inadvertent removal of the catheter. Sixteen patients initially treated with PCA received TEA in the late postoperative course for secondary interventions/re-operations, and in 35 patients, a supplementary PCA was used in combination with TEA or after TEA removal. A total of 225 (32.9%) recipients reported pruritus post-LTx, 54 (15.1%) in the non-TEA group and 171 (52.3%) in the TEA group ($P < 0.001$).

The TEA catheters were removed on median POD 7 (range 0–50 d). No patient required platelet transfusion or correction

TABLE 2.
Perioperative results

	TEA (n = 327)	Non-TEA (n = 358)	*P*
Opioids given intraoperatively, µg (median, IQR)	800 (650–950)	900 (750–1100)	0.004
NRS days 0–5 (median, IQR)	1.4 (0.3–2.2)	1.8 (0.6–2.7)	0.008
Discontinuation day of pain pumps, median (IQR)	7 (5–9)	5 (4–7)	<0.001
Discharged to home,[a] n (%)	249 (76)	174 (49)	<0.001
Discharge to local hospital, n (%)	76 (23)	175 (49)	<0.001
In-hospital mortality, n (%)	1 (0.3)	5 (1.4)	0.126
Pneumonia, n (%)	29 (9)	59 (17)	<0.001
Antibiotic treatment, n (%)	138 (42)	207 (58)	<0.001
LMWH > 5000 IU/24 h, n (%)	144 (44)	91 (25)	<0.001
Extubated in OR, n (%)	103 (32)	29 (8)	<0.001
ICU < 24 h, n (%)	199 (61)	123 (34)	<0.001
Ventilator hours (median, IQR)	3 (0.0–6.7)	9.3 (4.8–26.2)	<0.001
ICU hours (median, IQR)	19 (12–30)	30 (19–68)	<0.001
Days stayed on surgical ward (median, IQR)	11 (8.3–15)	11 (9–16)	0.45
Days stayed in transplant center (median, IQR)	22 (20–26.8)	23 (20–29)	0.003
Readmission to ICU, n (%)	18 (6)	54 (15)	<0.001
Required reintubation, n (%)	14 (4)	46 (13)	<0.001
Re-LTx, n (%)	25 (8)	30 (8)	0.724

[a]Hospital discharge data not available (n = 5).
The diagnosis of pneumonia is verified with radiograph and/or clinical examination.
ICU, intensive care unit; IQR, interquartile range; LMWH, low molecular weight heparin; LTx, liver transplantation; NRS, numeric rating scale; OR, operating room; TEA, thoracic epidural analgesia.

TABLE 3.
Opioid pain medications in 685 liver transplant recipients

	TEA (n = 327)	Non-TEA (n = 358)	*P*
Opioid use pre-Tx, n (%)	52 (16)	73 (21)	0.13
Discharge from hospital with opioids, n (%)	158 (48)	154 (43)	0.23
Still on opioids at 1-y follow-up, n (%)[a]	28 (9)	30 (8)	0.72

[a]Out of the patients that were discharged with opioids.
Non-TEA, pain management without thoracic epidural analgesia; TEA, thoracic epidural analgesia.

of INR before catheter removal; the median (interquartile range) platelet count was 182 × 10^9 (131–271)/L, APTT 32 (29–34) s, and INR 1.1 (1.0–1.2). One hundred three (32%) patients in the TEA group were extubated in the OR compared with 29 (8%) patients in the non-TEA group (Table 2).

Fifty-two (16%) recipients in the TEA group received opioids before transplantation versus 73 (21%) in the non-TEA group. When discharged from the transplant center approximately 3 weeks posttransplant, nearly half of the patients received an opioid prescription (Table 3). At 1-year follow-up, the opioid use still persisted in 28 (9%) in the TEA group versus 30 (8%) in the non-TEA group.

DISCUSSION

The present study revealed that TEA is feasible in selected LTx recipients without severe coagulopathy. None of the patients treated with TEA had serious complications like epidural hematoma or epidural infection/abscess. It provides less pain with median pain scores on NRS 1.4 [confidence interval (CI) 1.26-1.56] during the first 5 PODs as compared with a pain protocol without TEA with NRS 1.8 (CI 1.64-2.02). Thus, both groups had excellent pain relief. The non-TEA recipients had significantly higher model of end-stage liver disease and American Society of Anesthesiologists scores and were more frequently hospitalized before transplantation. In other words, the patients that did not receive a TEA had more advanced liver disease than the patients in the TEA group.

As opposed to the utilization of TEA in liver resection in patients without liver cirrhosis where TEA is considered safe due to the absence of coagulopathy,[12,13] the present study is to the best of our knowledge the first report on efficacy, safety, and pain score rating of TEA in liver transplant recipients. Importantly, because the pro- and anticoagulant factors are often simultaneously reduced in hepatic coagulopathy, an increased INR usually does not reflect an increased risk of bleeding in these patients,[14,15] probably making the epidural procedure safe to perform even with pathologically increased INR values, but that needs to be evaluated in future studies. Viscoelastic tests of coagulation (thromboelastography), a method to assess the coagulation status and the clot formation, may be a good alternative to conventional coagulation tests and an useful tool for the anesthesiologists in the assessment before the epidural insertion or removal.[16] Mallett et al[17] demonstrated that conventional tests, PT and INR, showed a hypocoagulable state, whereas the thromboelastography (TEG) was normal in patients with normal liver function undergoing surgical resection. Currently, no specific evidence-based recommendations exist from international guidelines about TEG and placement of epidural catheters in patients with co-existing liver disease undergoing LTx.[18-20]

Pain relief provided with central neuraxial and regional blocks may be superior compared with PCA with opioids,[21] but comparisons may be uncertain because reported pain scores vary widely between patients undergoing similar surgery.[22] In living donor hepatectomy, the use of epidural catheters seems safe, and removal of the epidural catheter is recommended at POD 5 if INR is below 1.5.[23-25] The indwelling TEA catheters were removed on POD 7 in our study with a median INR value of 1.1. Because our study population had a high proportion of recipients that received a liver graft because of malignancies with close to normal coagulation profile, a prophylactic higher dose of low molecular weight heparin was administered more frequently in the TEA group compared with the non-TEA group. These circumstances may have contributed to an approximate 24-hour delay of the TEA catheter removal due to safety reasons.[18]

We evaluated pain scores from the first 5 PODs. Although there were significant numerical differences in NRS scores, these differences hardly have any clinical significance because both groups had very good pain relief with median NRS ≤2. Only 4.9% of the patients reported moderate pain scores >4 on one or more occasions, which was equally distributed in both groups. The initial large doses of corticosteroids during the liver transplant procedure may have contributed to pain relief in both groups because steroids play an important role as co-analgesics in multimodal pain management protocols due to their anti-inflammatory activity.[26]

Preventing pneumonia and postoperative pulmonary failure appears to be in favor of the TEA group with 29 (9%) in the TEA group versus 59 (17%) in the non-TEA group, which is in line with previous reports.[27] However, in our study, a much larger percentage of the patients were hospitalized and

ICU-dependent before LTx in the non-TEA group, making it difficult to interpret the effect of TEA per se on these complications. Earlier studies have not shown any benefit of TEA compared with IV opioids in patients undergoing major abdominal high-risk surgery, except for preventing respiratory failure.[28,29]

Opioid use pre- and posttransplant affected patient and graft survival, and in an editorial in *Liver Transplantation*, the question is addressed if chronic pain is associated with patient survival and morbidity.[30,31] In our study, there was a nonsignificant difference in opioid use before LTx between the TEA (16%) and non-TEA (21%) group, which is consistent with previous observations in LTx recipients.[32] Despite low pain scores in the immediate posttransplant period, a considerable number of patients were discharged from our transplant center with opioid prescriptions, and receiving epidural analgesia did not have any opioid-reducing effect, although care should be taken interpreting these data because of the different patient populations (Table 3). In a study on opioid-naive patients undergoing abdominal surgery, the authors did not find any protective effect of epidural analgesia in the discharge prescription of opioids.[33] Preventing opioid use and chronic postsurgical pain should be an important focus area for future studies as this affects survival.[32] Achieving good pain control with noninvasive multimodal strategies and thereby avoiding indwelling epidural catheters may be a better option for the liver transplant recipient with coagulopathy disturbances and on immunosuppression therapy. A previous randomized controlled trial from our center revealed that postoperative pain in open liver surgery with a multimodal management was noninferior to TEA for the first 5 PODs and with significantly lower opioid use.[34] The multimodal treatment in the PCA group was paracetamol and ketorolac, but both drugs may be contraindicated in many of the liver transplant recipients due to liver and/or kidney failure. The use of nonopioid pain management has gained increased interest, and in a recently published review, Chadha et al[35] recommend the use of nonopioid pain strategies in the postoperative period, especially for recipients using opioids before LTX. The same authors do, however, not recommend neuraxial blocks.

The retrospective, single-center design is a limitation of our report. Another weakness is that the exact amount of opioid dosage/morphine equivalents could not be calculated. Electronic medical records with registration of opioids administered during the entire postoperative period have recently been implemented in our department and will, in the future, provide more exact calculation of the morphine equivalents.

Viscoelastic tests like TEG are used in the perioperative course to monitor and guide transfusion requirements and could have been used more frequently in addition to conventional coagulation parameters before epidural placement. The indication to use epidural is not very strict (eg, less pain/better comfort) because pain relief with non-TEA methods is effective, and we do not want to put the patients at risks for serious adverse events; therefore, safe margins for INR level and platelet count should be achieved. Future studies are warranted to clarify these aspects. The strength of our report is the high number of epidural procedures performed over a long time period using the same epidural technique and drug solution.

CONCLUSION

Our report revealed very good pain control with both TEA and the non-TEA modality. TEA was provided in selected liver transplant recipients without severe coagulopathy and was without any serious complications like epidural hematoma or infection/abscess. Opioid prescriptions at hospital discharge and at 1-year follow-up were equally distributed in both the groups. To determine if TEA or PCA is the better alternative for liver transplant recipients with no coagulopathies, a prospective, randomized controlled trial has to be performed.

ACKNOWLEDGMENTS

We are deeply grateful to the earlier staff members, Dr Robert Innes and Dr Svein Osnes, the pioneers in the liver transplant program, who introduced and carefully taught us the anesthetic management of the liver transplant recipient.

REFERENCES

1. European Association for the Study of the Liver. EASL clinical practice guidelines: liver transplantation. *J Hepatol*. 2016;64:433–485.
2. Milan Z. Analgesia after liver transplantation. *World J Hepatol.* 2015;7:2331–2335.
3. Moretti EW, Robertson KM, Tuttle-Newhall JE, et al. Orthotopic liver transplant patients require less postoperative morphine than do patients undergoing hepatic resection. *J Clin Anesth.* 2002;14:416–420.
4. Trzebicki J, Nicinska B, Blaszczyk B, et al. Thoracic epidural analgesia in anaesthesia for liver transplantation: the 10-year experience of a single centre. *Ann Transplant.* 2010;15:35–39.
5. Aniskevich S, Pai SL. Fast track anesthesia for liver transplantation: review of the current practice. *World J Hepatol.* 2015;7:2303–2308.
6. Feltracco P, Carollo C, Barbieri S, et al. Pain control after liver transplantation surgery. *Transplant Proc.* 2014;46:2300–2307.
7. Pöpping DM, Elia N, Van Aken HK, et al. Impact of epidural analgesia on mortality and morbidity after surgery: systematic review and meta-analysis of randomized controlled trials. *Ann Surg.* 2014;259:1056–1067.
8. Kooij FO, Schlack WS, Preckel B, et al. Does regional analgesia for major surgery improve outcome? Focus on epidural analgesia. *Anesth Analg.* 2014;119:740–744.
9. Smith LM, Cozowicz C, Uda Y, et al. Neuraxial and combined neuraxial/general anesthesia compared to general anesthesia for major truncal and lower limb surgery: a systematic review and meta-analysis. *Anesth Analg.* 2017;125:1931–1945.
10. Freise H, Van Aken HK. Risks and benefits of thoracic epidural anaesthesia. *Br J Anaesth.* 2011;107:859–868.
11. Hofer I, Spivack J, Yaport M, et al. Association between anesthesiologist experience and mortality after orthotopic liver transplantation. *Liver Transpl.* 2015;21:89–95.
12. Jacquenod P, Wallon G, Gazon M, et al. Incidence and risk factors of coagulation profile derangement after liver surgery: implications for the use of epidural analgesia-a retrospective cohort study. *Anesth Analg.* 2018;126:1142–1147.
13. Elterman KG, Xiong Z. Coagulation profile changes and safety of epidural analgesia after hepatectomy: a retrospective study. *J Anesth.* 2015;29:367–372.
14. Hartmann M, Szalai C, Saner FH. Hemostasis in liver transplantation: Pathophysiology, monitoring, and treatment. *World J Gastroenterol.* 2016;22:1541–1550.
15. Bezinover D, Dirkmann D, Findlay J, et al. Perioperative coagulation management in liver transplant recipients. *Transplantation.* 2018;102:578–592.
16. Ramsay MA, Trotter JF. The INR is only one side of the coagulation cascade: time to watch the clot. *Anaesthesia.* 2016;71:613–617.
17. Mallett SV, Sugavanam A, Krzanicki DA, et al. Alterations in coagulation following major liver resection. *Anaesthesia.* 2016;71:657–668.
18. Horlocker TT, Vandermeuelen E, Kopp SL, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Fourth Edition). *Reg Anesth Pain Med.* 2018;43:263–309.
19. Gogarten W, Vandermeulen E, Van Aken H, et al; European Scoeity of Anaesthesiology. Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology. *Eur J Anaesthesiol.* 2010;27:999–1015.

20. Breivik H, Norum H, Fenger-Eriksen C, et al. Reducing risk of spinal haematoma from spinal and epidural pain procedures. *Scand J Pain.* 2018;18:129–150.
21. Wu CL, Cohen SR, Richman JM, et al. Efficacy of postoperative patient-controlled and continuous infusion epidural analgesia versus intravenous patient-controlled analgesia with opioids: a meta-analysis. *Anesthesiology.* 2005;103:1079–1088. Quiz 1109.
22. van Boekel RL, Vissers KC, van de Vossenberg G, et al. Comparison of epidural or regional analgesia and patient-controlled analgesia: a critical analysis of patient data by the acute pain service in a university hospital. *Clin J Pain.* 2016;32:681–688.
23. Karna ST, Pandey CK, Sharma S, et al. Postoperative coagulopathy after live related donor hepatectomy: incidence, predictors and implications for safety of thoracic epidural catheter. *J Postgrad Med.* 2015;61:176–180.
24. Choi SJ, Gwak MS, Ko JS, et al. The changes in coagulation profile and epidural catheter safety for living liver donors: a report on 6 years of our experience. *Liver Transpl.* 2007;13:62–70.
25. Koul A, Pant D, Rudravaram S, et al. Thoracic epidural analgesia in donor hepatectomy: an analysis. *Liver Transpl.* 2018;24:214–221.
26. Romundstad L, Breivik H, Roald H, et al. Methylprednisolone reduces pain, emesis, and fatigue after breast augmentation surgery: a single-dose, randomized, parallel-group study with methylprednisolone 125 mg, parecoxib 40 mg, and placebo. *Anesth Analg.* 2006;102:418–425.
27. Odor PM, Bampoe S, Gilhooly D, et al. Perioperative interventions for prevention of postoperative pulmonary complications: systematic review and meta-analysis. *BMJ.* 2020;368:m540.
28. Rigg JR, Jamrozik K, Myles PS, et al; MASTER Anaethesia Trial Study Group. Epidural anaesthesia and analgesia and outcome of major surgery: a randomised trial. *Lancet.* 2002;359:1276–1282.
29. Peyton PJ, Myles PS, Silbert BS, et al. Perioperative epidural analgesia and outcome after major abdominal surgery in high-risk patients. *Anesth Analg.* 2003;96:548. Table of contents.
30. Randall HB, Alhamad T, Schnitzler MA, et al. Survival implications of opioid use before and after liver transplantation. *Liver Transpl.* 2017;23:305–314.
31. Rogal S, Dew MA, DiMartini A. High-dose opioid use and liver transplantation: an underestimated problem? *Liver Transpl.* 2017;23:285–287.
32. Fukazawa K, Rodriguez PJ, Fong CT, et al. Perioperative opioid use and chronic post-surgical pain after liver transplantation: a single center observational study. *J Cardiothorac Vasc Anesth.* 2020;34:1815–1821.
33. Ladha KS, Patorno E, Liu J, et al. Impact of perioperative epidural placement on postdischarge opioid use in patients undergoing abdominal surgery. *Anesthesiology.* 2016;124:396–403.
34. Hausken J, Fretland ÅA, Edwin B, et al. Intravenous patient-controlled analgesia versus thoracic epidural analgesia after open liver surgery: a prospective, randomized, controlled, noninferiority trial. *Ann Surg.* 2019;270:193–199.
35. Chadha R, Pai SL, Aniskevich S, et al. Nonopioid modalities for acute postoperative pain in abdominal transplant recipients. *Transplantation.* 2020;104:694–699.