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Research Article

Evidence -Based Guideline on Post-Operative Pain Management after Open Liver Surgery for Resource Constrained Area: A Systematic Review Article

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Abstract

Background: Sufficient pain treatment is essential for a more successful recovery following liver resection surgery. The management of pain during perioperative recovery from open liver surgery is difficult because of the risks involved, including intra operative blood loss, hypotension, coagulopathy, pulmonary problems, and damage of the liver and kidney. Effective care of pain following surgery is essential for reducing complications, length of stay in the hospital, and expenses. As a result, creating the best possible pain management guidelines for open liver surgery in a region with limited resources is essential.

Objective: To develop evidence-based guidelines for postoperative pain management after open liver surgery in resource constrained area.

Methods: A search was conducted using inclusion and exclusion criteria to retrieve published material from 2013 to 2023 from PubMed, Google Scholar, and the Cochrane database. Key words, phrases, and topic headings such as "liver OR hepatic" AND "liver resection" OR "hepatic resection" OR "hepatectomy") AND "postoperative pain" AND "pain management" OR "epidural" OR "neuraxial" OR "intrathecal" OR "spinal" OR "infiltration" OR "nerve block" OR "paravertebral block" OR "transversus abdominis plane block" OR "NSAID" OR "opioid" OR "ketamine" based on demographic data, results, and methodological quality, filters were applied. In conclusion, this review encompassed 1 meta-analysis, 1 systematic review, 8 randomized controlled trial studies, 1 observational cohort study, and 2 cross-sectional investigations.

Conclusion: Continuous wound infiltration with local anesthetic drugs is the most effective way to alleviate postoperative pain following liver surgery. In the absence of contraindications, it is recommended to utilize bilateral sub costal TAP blocks or TEA. Systemic opioids should be kept as emergency analgesics during the post-operative recovery period.

Keywords: Liver surgery; Liver resection; Hepatectomy; Postoperative pain

Abbreviations

OPL: Open Liver Resection; HUCSH: Hawassa University Comprehensive Specialized Hospital; ITM: Intrathecal Morphine; RCT: Randomized Controlled Clinical Trials; IVPCA: Intra Venous Patient Controlled Analgesia; TPVB: Thoracic Paravertebral Block; TAPB: Transversus Abdominis Plane Block; TEA: Thoracic Epidural Analgesia; CWI: Continuous Wound Infiltration; ESPB: Erector Spinae Plane Block; NSAID: Non-Steroidal Anti-Inflammatory Drug

Introduction

"Liver surgery" is a term used to describe a group of surgical procedures used to treat various liver disorders, such as alcohol-related liver disease, cirrhosis, liver cancer, and hepatitis B and C. The most common type of liver surgery is hepatectomy, which involves removing the liver whole or in part [1,2]. The control of post-operative pain has always been the main focus in order to deliver more effective results for perioperative care. Effective pain management lowers the risk of cardio-respiratory problems, promotes bowel function, makes early mobilization, and speed recovery. Pain-control techniques believed to improve subjective comfort also block trauma-induced nociceptive impulses, which lower autonomic and somatic reflex responses to pain [3,4].

Following open liver surgery, a number of methods were employed to alleviate postoperative pain, including epidural, intrathecal; local wound infiltration, patient-controlled analgesia, and peripheral nerve blocks. The major objective of postoperative pain management is to maximize pain relief while minimizing side effects associated with different analgesic classes. On the other hand, because open liver surgery is connected to intra operative blood loss, hypotension, coagulation abnormalities, pulmonary issues, and liver damage, it offers complications for perioperative pain management [5]. The "gold standard" in open thoracic and abdominal surgery is Thoracic Epidural Analgesia (TEA). Complementary issues could result in issues including post-operative hypotension and delayed catheter removal due to possible coagulopathy, which could hinder healing and make it harder to move around [6,7]. Despite the effectiveness of systemic intravenous administration of analgesics (including opioids and non-steroidal anti-inflammatory drugs), this method is limited in its use because the metabolism and elimination of opioids depends on liver and kidney function. Additionally, this method is associated with potentially dangerous side effects, such as respiratory depression, nausea and vomiting, pruritus, and gastrointestinal bleeding [8,9].

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Sufficient preoperative planning and postoperative pain treatment improve the outcome of patients undergoing liver surgery. Research on managing pain following liver resection has been conducted in the past, but guidelines for minimizing problems, prolonged hospital stays, and expenses have not yet been created. Patients with liver pathology undergoing both elective and emergency surgery will find guidance for post-operative pain management in this guideline. Furthermore, it will lessen the likelihood of respiratory adverse outcomes following surgery, such as cardiac arrest and death, which could occur from untreated extreme pain. Thus, the creation of guidelines for the treatment of pain following liver surgery will serve as a knowledge base for medical professionals. The main objective of this review article is to develop guidelines about perioperative pain management for open liver surgery in resource constrained area.

Scope of the guideline

Target audience of this guideline includes group of health care providers who give health care for patients who had undergone open liver surgery, including doctors and anesthetists as well as other health care professionals contributing to a multidisciplinary approach. All patients who have undergoing open liver surgery were the target population of this guideline.

Materials and Methods

Protocol

Preferred Reporting of Systematic Review and Meta-Analysis (PRISMA) is the method used for reporting this review.

Eligibility criteria for this review

Studies included in this review: Studies published in English from 2013-2023 on Post-operative Pain Management after Open liver Surgery.

Studies excluded from these studies: Studies on laparoscopic liver surgery, studies contain Title and abstract only, research released by non-English-language, were excluded.

Search strategy

This review began with the search for articles related to analgesia for post -operative pain of liver surgery. Searching engines such as Google Scholar, Pub Med, Cochrane library and manual searching published in English were systematically searched from 2013-2023. The search was done by using keywords, phrases, and specific subject headings. The searching strategies were done in accordance with different electronic databases strategies. Articles were searched as (("liver OR hepatic") AND ("liver resection" OR "hepatic resection" OR "hepatectomy") AND ("postoperative pain") AND ("pain management" OR "epidural" OR "neuraxial" OR "Intrathecal" OR "spinal" OR "infiltration" OR "nerve block" OR "paravertebral block" OR "transversus abdominis plane block" OR "NSAID" OR "opioid" OR "ketamine")) after keywords were extracted. Each keyword is connected via a Boolean operator “AND” or “OR”. The selections of the studies were after screened of the studies based on title, abstract and finally after carefully reading the full text.

The quality of the evidence was evaluated by the principles of the Grading of Recommendations Assessment, Development and Evaluation (GRADE1) system to assess the quality of evidence. Articles unrelated to postoperative pain management for open liver surgery and anesthesia, manuscripts with unavailable full text were rejected. After removing the duplicates with end note's reference manager, all 12 retrieved studies were evaluated for inclusion in the systematic literature review based on the inclusion and exclusion criteria. After examining the abstract and title of each article, citations that were merely abstracts or didn't meet the inclusion criteria were eliminated. The whole texts of the remaining citations were obtained and looked at. The PRISMA flowchart (Figure 1 and 2) shows a summary of the search strategy findings (Table 1).

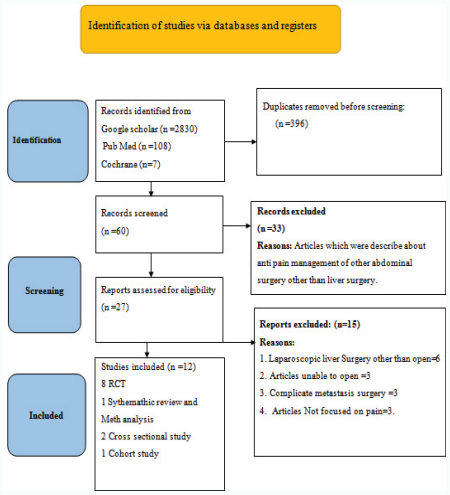

Figure 1: PRISMA flow diagram.

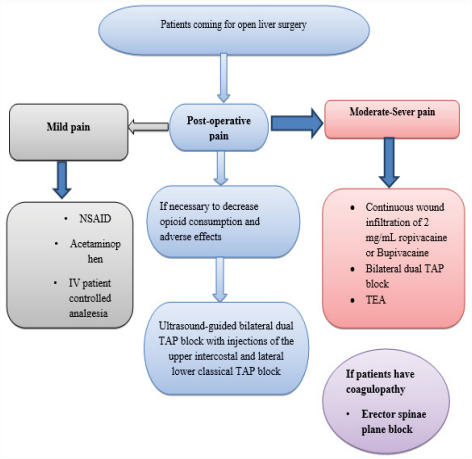

Figure 2: Management algorithm flow chart.

Table 1: Grade of Recommendations and level of evidences.

Grade of Recommendations	Level of Evidences	Type of Study
A	1a	Systematic review of (homogeneous) randomized controlled trials
A	1b	Individual randomized controlled trials (with narrow confidence intervals)
B	1c	All or none randomized controlled trials
B	2a	Systematic review of (homogeneous) cohort studies of "exposed" and "unexposed" subjects including low quality RCT
B	2b	Individual cohort study / low-quality randomized control studies
B	3a	Systematic review of (homogeneous) case-control studies
B	3b	Individual case-control studies
C	4	Case series, low-quality cohort or case-control studies

Implementation plan

These guidelines are intended for use by anesthetist and other individuals who give health care service for surgical patients, especially those who are involved during preoperative optimization and postoperative handover. These guidelines also intended to apply to all pain management and anesthetic care delivered in patients with liver pathology coming for open liver surgery. This guideline can be applied both in local setting and international level. The only problem to apply all finding in local setting is shortage of medications and equipment; beyond this it doesn't have negative effect on patient management and outcome.

Discussion

The post-operative management of pain in patients with liver surgery is not standardized, and specific conclusions are not yet drawn, even though different clinical trials, systematic reviews, and different evidences were developed at different times. The goal of this guideline was to compile data regarding pain control following open liver surgery.

Literature findings

A comprehensive review and meta-analysis were carried out in 2017 to examine the safety and effectiveness of patient-controlled analgesia against epidural analgesia after open hepatic resection. Two hundred seventy eight (278) patients were included in four RCTs. In patients undergoing open hepatic resection, epidural analgesia was found to be more effective at controlling pain than PCA, without any significant difference in the length of hospital stay, any adverse events, or blood transfusion requirements. Therefore, in this patient population, neuraxial analgesia should be the first choice for the treatment of postoperative pain [10]. (Level of evidence 1a: grade of recommendation A).

A quality improvement initiative was done in Parkland on 50 patients who had open liver surgery to compare epidural analgesia and ultrasound-guided erector spine plane block for pain management. In patients undergoing open hepatic resection, this study showed that TEA provided a better analgesic effect than right-sided ESPB block, as determined by opioid intake and pain ratings during rest and deep inhalation. While in patients with a high risk of coagulopathy, ESPB may be a safer option to TEA, but it may not be as effective in reducing visceral discomfort brought on by open liver surgery [11]. (Level of evidence 1b and grade of recommendation A).

Patients who have cirrhosis can benefit from Opioid-Free Anaesthesia (OFA) since they are more vulnerable to the negative effects of opioids than other patients. OFA is a multimodal procedure designed to enhance patient satisfaction and anesthetic quality by combining non-opioid drugs with regional anesthetic procedures [12,13].

Bilateral ESP block with OFA is a successful method for postoperative analgesia in cirrhotic patients undergoing liver resection, according to a study conducted in Egypt on forty patients who were randomly assigned to the block group (n=20) of OFA with ESPB and the conventional group (n=20) of conventional balanced anaesthesia with opioid (OFA associated non-opioid drugs [dexmedetomidine, magnesium sulphate, xylocaine, and acetaminophen] and ESPB) and ESPB [14]. (Level of evidence 1b and grade of recommendation A).

Although Thoracic Epidural Analgesia (TEA) has a relatively high failure rate (9% to 20%), the most recent ERAS Society guidelines for patients undergoing liver resection surgery did not recommend using it, even though epidural analgesia has been thought to be superior to IV analgesics [15]. Postoperative coagulopathy poses a risk to safety after epidural catheter removal, as it might result in hypotension and severe renal damage. The following two drug groups were used in the study. Group 2 (control): ITM (0.25 mg preservative free) with two exceptions, as two patients included in the study had an ITM dose of 0.5 mg. Group 1 (BUPI) drugs are ITM (0.25 mg preservative free)+Intrathecal local anaesthetic (11.25 mg (1.5 mL of 0.75% bupivacaine)) ± Intrathecal fentanyl (25 mcg). The addition of hyperbaric bupivacaine to intrathecal [16]. (Level of evidence 1c and grade of recommendation B).

An open-label, randomized, controlled, non-inferiority trial was conducted in Fujian Provincial Hospital at china to compare the postoperative analgesic efficacy of VC-ESPB (VC-ESPB group) and conventional intravenous opioid-based pain management with 106 patients' undergone open major hepatectomy.

A separate randomised control experiment was carried out to investigate if continuous ropivacaine wound infiltration lowers the need for analgesics following liver resection. The study included all patients (over the age of 18) listed for open liver metastases resection, with tumours confirmed by histology, ≥ 3 weeks between chemotherapy and the planned resection, ASA Physical Status ≤ 3, and liver and renal function tests within predetermined ranges. In light of these RCTs, the postoperative period following an open hepatectomy saw a continuous infiltration of 2 mg/mL ropivacaine into the wound, which resulted in a complete decrease in morphine consumption of 0.5 mg/kg and sped up recovery and discharge [17,18]. (Level of evidence 1b and grade of recommendation A).

In order to determine if intravenous, multimodal, Patient-Controlled Analgesia (IV-PCA) could be non-inferior to multimodal Thoracic Epidural Analgesia (TEA) in patients undergoing open liver surgery, another prospective, randomised, controlled, non-inferiority experiment was conducted. Random assignment was used to allocate patients who underwent open liver resection surgery between February 2012 and February 2016. The mean pain score on the numeric rating scale, which was the primary endpoint, was 1.7 in the IV-PCA group and 1.6 in the TEA group, indicating non-inferiority. On postoperative days 0 and 1, the TEA group's pain levels were lower; however, on days 2 and 5, they were either higher or equal. Patients in the IV-PCA group had a noticeably shorter postoperative hospital stay. When it came to treating postoperative pain in patients having open liver resection, IV-PCA and TEA were shown to be equally effective overall [19]. (Level of evidence 1b and grade of recommendation A).

Different studies have confirmed that an ultrasound-guided bilateral dual TAP block, which involves injecting the upper intercostal and lateral lower classical TAP compartments to anaesthetize the upper (Th6-Th9) and lower (Th10-L1) abdominal wall, can improve the severity of pain after major abdominal surgery, reduce the need for opioids, and promote early mobilization. Bilateral dual TAP block is a promising regional analgesic technique [20]. Following a laparoscopic hepatectomy, efficient postoperative analgesia is achieved with ultrasound-guided bilateral dual TAP block. Additionally, the study demonstrates that plasma ropivacaine concentrations linked to neurotoxicity are rarely obtained after laparoscopic hepatectomy using ultrasound-guided bilateral dual TAP blocks with 3 mg/kg ropivacaine [21]. (Level of evidence 1b and grade of recommendation A).

In order for patients to recuperate and feel satisfied after abdominal procedures, adequate pain management is essential. Due to their common presentation of much comorbidity and the huge incisions left after typical open hepatic-biliary procedures, patients are more susceptible to discomfort from the wound [22]. Patients frequently find it difficult to deep breathe, cough, eat, or move normally due to the excruciating postoperative pain across their right upper abdomen. All of these increase the risk of unfavorable sequalae such as pneumonia, urine retention, and a delayed resumption of bowel movement. Therefore, for patients undergoing open liver resections, intravenous patient-controlled analgesia with ultrasound-guided abdominal nerve block could be an effective analgesic technique for preventing such problems by reducing severe postoperative pain [23]. (Level of evidence 1c and grade of recommendation B).

Combining TAP and IVPCA led to improved postoperative pain management, a reduction in fentanyl consumption, and a reduced length of stay in critical care. A well-rounded, multimodal postoperative pain treatment can include TAP block [24]. (Level of evidence 1b and grade of recommendation A).

Large surgical wounds, lengthy incisions, and extensive tissue damage are the results of open surgery used to remove hepatocellular carcinoma tumours, and these complications can cause excruciating immediate postoperative pain. Sixty patients (60) who had scheduled hepatectomy procedures between January 2014 and January 2016 were subjected to RCT. The patients were randomly assigned to one of three groups: intravenous Patient-Controlled Analgesia (PCA) group, which received fentanyl intravenous analgesia postoperatively; Local Incision Analgesia (LIA) group, which received local infiltration with ropivacaine combined with a postoperative analgesia pump; and the control group, which received tramadol hydrochloride injection. This study proved that a safe and efficient way to control postoperative pain after a hepatectomy is by local incision analgesia [25]. (Level of evidence 1b and grade of recommendation A).

For patients recovering from significant upper abdominal surgeries, epidural analgesia has been shown to be more effective than IV patient-controlled analgesia in terms of postoperative pain reduction. Between July 2004 and July 2011, 498 patients had major hepatectomy; a Randomized Controlled Trial (RCT) was used to compare epidural analgesia with continuous intravenous bupivacaine infusion plus patient-directed analgesia for postoperative pain management. When combined with IV PCA, continuous intramuscular bupivacaine infusion results in comparable pain management and less opioid intake than when CEA is used. Epidural analgesia may be replaced with the CIB+PCA approach, which has the potential to increase safety, enhance postoperative results, and shorten hospital stays [26]. (Level of evidence 1b and grade of recommendation A).

It has been stated that epidural analgesia is preferable to over the course of six years, a retrospective case-control study was carried out to assess the effectiveness of morphine and fentanyl PCA in liver resection patients with respect to pain management, opioid consumption, and adverse effects. While pain management was adequate for all groups, the morphine group experienced faster pain relief with a lower morphine equivalent dose. Patients on fentanyl, however, were less sedated; both medications require careful observation in the early postoperative phase because of their potential for respiratory depression and the requirement for naloxone administration. To find the optimal dose with the fewest negative effects, more research on the PCA settings' dosage is necessary [27]. (Level of evidence is 3b and grade of recommendation B).

An RCT trial that involved 80 individuals who had hepatectomy appointments and ran from October 2013 to August 2014. Patients were randomly assigned to one of two groups, consisting of 40 patients each, and were given either a placebo or 40 mg of parecoxibsodium. Following the procedure, 48 hours of postoperative Patient-Controlled Intravenous Analgesia (PCIA) with fentanyl 40 mg every 12 hours was administered to two groups. Parecoxib sodium used in conjunction with PCA fentanyl analgesia was evaluated clinically for its effects on postoperative pain. The results showed that postoperative pain control might be improved with parecoxib sodium perioperative medication, without increasing the risk of side events [28]. (Level of evidence 1b and grade of recommendation A) (Table 2).

Strength

This guideline included recent studies focused on treatment of postoperative pain of open liver surgery and which enables the clinical to use it and give good post-operative pain management care for patients underwent open liver surgery.

Limitations

This study has some limitations. First only English-language and full text articles were included in the review.

The guideline focuses only on open liver surgery and it misses laparoscopic liver surgery.

Conclusion

For the best pain control following open liver resection, this evidence-based guideline selected an analgesic regimen. If NSAIDs are not contraindicated, we advise using them in the postoperative pain control of liver resection patients. The most effective method for treating postoperative pain after liver surgery is continuous wound infiltration. It is advised to use either TEA or bilateral sub costal TAP blocks if there are no contraindications. During the recovery phase following surgery, systemic opioid should be reserved as rescue analgesics.

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Table 2: The Results of the Studies incorporated in the development of this Evidence-Based Guideline.

S.No	Author	Study on Risk stratification for post-operative	Study Design	Main Finding	Quality / Level of study
1	Li et al. [10]	Efficacy and Safety of patient-controlled analgesia compared with epidural analgesia after Open hepatic resection august 2019	Systematic Review and Meth analysis	Epidural analgesia was observed to be superior to patient-controlled analgesia for pain control in patient undergoing open hepatic resection	1a
2	Stewart et al. [11]	Pain Management After Open Liver Resection: Epidural Analgesia Versus Ultrasound-Guided Erector Spine Plane Block	RCT	Thoracic epidural analgesia provides superior pain relief than Erectus spine plane block after open liver resection.	1a
3	Abdel-Kader et.al. [16]	Evaluation of the addition of bupivacaine to intrathecal morphine for intraoperative and postoperative pain management in open liver resections	RCT	The addition of bupivacaine to inthrathecal morphine for patients Undergoing hepatectomy led to lower intraoperative opioid usage with equivalent postoperative opioid usage and without worrisome outcomes of hemodynamic instability or acute renal failure. Further, there was also an improvement in bowel function in the bupivacaine group as compared to the ITM group	1a
4	Elshafietal al. [14]	Erector Spine Block with Opioid Free Anesthesia in Cirrhotic Patients Undergoing Hepatic Resection	RCT	Bilateral erector spine block with opioid free anesthesia is an effective approach for intra- and postoperative analgesia in cirrhotic patients undergoing liver resection than convectional group	1a
5	Revie et al. [15]	Effectiveness of epidural analgesia following open liver resection	Cross sectional retrospective study	Epidural analgesia provided inadequate postoperative pain relief in approximately 20% of liver resection patients and was associated with the administration of significantly greater volumes of i.v. colloid solution	2c
6	Peres-bechelot et al. [17]	A 96-hour continuous wound infiltration with ropivacaine reduces analgesic consumption after liver resection	RCT	Preperitoneal continuous wound infiltration of 2 mg/mL with ropivacaine significantly reduces intravenous morphine consumption during the 96 postoperative hours resulting in an absolute reduction of 0.5 mg/kg.	1b
7	Xin et al. [18]	Efficacy of Postoperative Continuous Wound Infiltration with Local Anesthesia After Open Hepatectomy	RCT	Surgical wound infusion with ropivacaine after hepatectomy can improve pain relief at rest and accelerate recovery and discharge.	1b
8	Hausken et al. [19]	Intravenous patient-controlled Analgesia versus thoracic epidural analgesia after open liver surgery	RCT	Intravenous patient-controlled analgesia was inferior compared to epidural analgesia after open liver surgery	1b
9	Tsai et al. [23]	A Retrospective Comparison of Three Patient-Controlled Analgesic Strategies: Intravenous Opioid Analgesia Plus Abdominal Wall Nerve Blocks versus Epidural Analgesia versus Intravenous Opioid Analgesia Alone in Open Liver Surgery	Cros section Retrospective study	For postoperative pain management, it is expected that the TEA group required the least amount of opioid; however, IV-PCA + NBs and TEA demonstrated comparable postoperative outcomes, namely, the time to remove nasogastric tube/urinary Catheter, to start the diet, and the length of hospital stay. IV-PCA with NBs could thus be a reliable analgesic modality for patients undergoing open liver resections.	2c
10	Wu et al. [25]	Postoperative local incision analgesia for acute pain treatment in patients with hepatocellular carcinoma	Cohort study	Local incision analgesia improves the analgesic effect, causes fewer adverse reactions and increases postoperative survival time. Our study demonstrated that local incision analgesia is a safe and effective method of postoperative pain management following hepatectomy.	1c
11	Wong-Lun-Hing et al. [26]	Postoperative pain control using continuous i.m. bupivacaine infusion plus patient-controlled analgesia compared with epidural analgesia after major hepatectomy	RCT	The combination of continuous i.m bupivacaine + patient-controlled analgesia provides pain control similar to that provided by epidural analgesia, but facilitates lower opioid It has the potential to replace epidural analgesia, thereby avoiding the occurrence of rare but serious complications.	1b
12	Wang et al. [28]	Perioperative analgesia with parecoxib sodium improves postoperative pain and immune function in patient undergoing hepatoctectomy for hepatocellular carcinoma	RCT	Perioperative analgesia with parecoxib sodium combined with patient-controlled analgesia improves postoperative pain with better enhancement of analgesic efficacy	1B

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