Combination of thoracic epidural analgesia with patient-controlled intravenous analgesia versus traditional thoracic epidural analgesia for postoperative analgesia and early recovery of laparotomy: a prospective single-centre, randomized controlled trial

Wenwen Xu
the First Affiliated Hospital of Sun Yat-Sen University
Youpei Li
the First Affiliated Hospital of Sun Yat-Sen University
Nanqi Li
the First Affiliated Hospital of Sun Yat-Sen University
Yu Sun
the First Affiliated Hospital of Sun Yat-Sen University
Chao Wang
the First Affiliated Hospital of Sun Yat-Sen University
Ke An (anke@mail.sysu.edu.cn)
the First Affiliated Hospital of Sun Yat-Sen University

Research Article

Keywords: Epidural analgesia, Patient-controlled intravenous analgesia, Postoperative analgesia, Enhanced recovery, Laparotomy

Posted Date: July 19th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1770872/v1

Abstract

Background*:* Thoracic epidural analgesia (TEA) always been the first choice for postoperative pain treatment, but associated complications and contraindications may limit its use. Our study put forward a new analgesic strategy that combines thoracic epidural analgesia (TEA) with patient controlled intravenous analgesia (PCIA) to optimized TEA.

Methods: Patients undergoing laparotomy were enrolled in this prospective randomized study. Patients were randomized to one of two groups: TEA/PCIA group and TEA group. Patients in TEA/PCIA group received TEA in the day of surgery and the first postoperative day and PCIA continued to use until the postoperative three days. Patients in TEA group received TEA during postoperative three days. A visual analogue scale (VSA) pain scores at rest and on movement at 6, 24,48,72h after surgery were recorded. In addition, we also compared the incidence of inadequate analgesia, adverse events, time to first mobilization, time to pass first flatus, time of oral intake recovery, time of urinary catheter removal, postoperative length of hospital stays, cumulative opioid consumption, and the overall cost in the two groups. We examined VAS pain scores using repeated measures analysis of variance; $p < 0.05$ was considered as statistically significant.

Results: Eighty-six patients were analysed (TEA/PCIA=44, TEA=42). The mean VAS pain scores at rest and on movement in TEA/PCIA group were lower than TEA group, with a significant difference on movement (P<0.05). TEA/PCIA group had lower pain scores on postoperative 3 days as compared with TEA group, with a significant difference at 48 h postoperatively (P<0.05). The time to first mobilization and pass first flatus were shorter in TEA/PCIA group (P<0.05). No significant difference between the two groups in terms of postoperative length of hospital stay, time of oral intake recovery, time of urinary catheter removal, cumulative opioid consumption, incidence of adverse events, incidence of inadequate analgesia, and overall cost.

Conclusions: The combination of TEA with PCIA for patients undergoing laparotomy, can enhance postoperative pain control and facilitate early recovery without increasing the incidence of adverse effects and overall cost of hospitalization.

Trial registration: ChiCTR1800020308 (China), 2018/12/23; registered at www.chictr.org.cn

1. Introduction

Initially introduced for colorectal surgeries, enhanced recovery after surgery (ERAS) has been expanded to other surgical specialties and largely facilitates postoperative recovery and attenuates peri-operative stress response and thus reduces complications and length of stay [1–3]. Adequate postoperative analgesia has always been considered as one of the key components for an ERAS program. Poor pain control would lead to delayed recovery and increased morbidity for patients and bring challenges to subsequent treatment. However, several analgesic techniques or drugs have been created and widely used for postoperative acute pain management within the past 20 years, the outcomes of acute pain

control are not always satisfactory. Correll et al. published a scientometric analysis pointed out that inappropriate use of new technologies and drugs impeded improvement on postoperative acute pain relief [4].

Thoracic epidural analgesia (TEA), as the cornerstone of postoperative pain relief in laparotomy, can provide better effective pain management compared with patient controlled intravenous analgesia (PCIA) [5]. Prior studies have supported that TEA could reduce the incidence of postoperative pulmonary complications and facilitate the recovery of gastrointestinal function [6, 7]. However, some problems still emerge in the application of TEA. For instance, postoperative hypotension, fluid overload, urinary retention, and motor block. Current guidelines for ERAS still emphasize the role of TEA in multimodal analgesia for postoperative pain control, thus, how to optimize TEA is important to laparotomy.

To our knowledge, laparotomy is often characterized by severe trauma, severe pain, and long recovery time. PCIA is not recommended for laparotomy because of its low efficacy and a higher rate of adverse events. However, combination of different classes of analgesics in PCIA, along with the advantage of rapid onset, may improve efficacy or minimize adverse effects. Therefore, under the concept of multimodal analgesia, our study put forward a new analgesic strategy that combines short-course TEA with PCIA on the first two postoperative days and apply PCIA alone afterwards in the subsequent two days (Fig. 1). This strategy could not only maximize effect of epidural analgesia, but also theoretically reduction of the adverse effects [8, 9]. The study attempted to take a multimodal analgesic approach to optimize postoperative analgesia and facilitate enhanced recovery. It is expected that the combination of TEA and PCIA would result in reduced pain scores, but it is uncertain that this approach could reduce pain scores without increasing costs or adverse effects, therefore, we conducted a prospective non-blinded randomised controlled trial to compare TEA/PCIA with TEA, to explore the feasibility of combination of TEA with PCIA in pain control and early recovery after laparotomy under the goal of ERAS.

2. Methods

This work was a single-centre prospective non-blinded randomised controlled trial. Ethical approval for this study (Ethical Committee No. [2018]265) was provided by the Ethics Committee of the First Affiliated Hospital of Sun Yat-Sen University (Chairperson Prof Churong Yan) on 24 October 2018. All methods were carried out in accordance with relevant guidelines and regulations (Declaration of Helsinki). The study was registered at www.chictr.org.cn (registration No. ChiCTR1800020308).

2.1. Participants

A total of 102 patients undergoing laparotomy in the First Affiliated Hospital of Sun Yat-Sen University between December 2018 and December 2019 were recruited. The patients aged 18–75 years, with an ASA I or II, and BMI ranging from 18 to 27 kg m^{-2}, who were undergoing laparotomy (hepatectomy, pancreaticoduodenectomy, gastrointestinal surgery, or colorectal surgery), were eligible for this study. Patients were randomly allocated to group TEA/PCIA or TEA according to a random number table using

the Social Sciences software version 20.0 (SPSS Inc, Chicago, IL, USA). All participants must be able to understand the research protocol and signed written informed consent. Exclusion criteria included contraindications to epidural analgesia and patients with a history of chronic pain and long-time medication with antidepressants, narcotic analgesics or nonsteroidal anti-inflammatory drug (NSAID) were also excluded.

Patients may discontinue participation in the trial at their own request, or be withdrawn if a surgery is not performed, or continuation of the trial may be detrimental to the patient's well-being in the investigator's opinion. Drop-out patients will be included in the final report to ensure complete transparency of the trial.

2.2. Preparations in the operation room before surgery

After establishing intravenous access and continuous monitoring in the operative room, the patients were placed in the lateral position to receive TEA prior to the induction of general anaesthesia. Insertion of an epidural catheter was performed between T8 and T10 in patients undergoing a right sided colonic resection or upper abdominal surgery (hepatectomy, pancreaticoduodenectomy, gastrointestinal open surgery), or between T10 and T11 in patients undergoing a left sided colonic resection. After identification of the correct epidural space using the loss of resistance technique with air, standard aseptic insertion procedure was performed. Injection of 3 ml of 2% lidocaine was carried out as a test dose. A sterile device was used to hold the catheter in place after excluding the spinal anaesthesia.

2.3. Standard general anaesthesia

All patients in the trial underwent a general anaesthesia. Anaesthesia was induced with sufentanil (0.3–0.5 mcg kg^{-1}), cisatracurium (0.2 mg kg^{-1}) or rocuronium (0.6mg kg^{-1}), propofol (2–3 mg kg^{-1}). Standard monitoring used in the surgery involved electrocardiogram, blood pressure, respiratory rate, oxygen saturation, end-tidal carbon dioxide, central venous pressure, temperature, and Narcotrend® (MonitorTechnik, Bad Bramstedt, Germany). Anaesthesia was maintained by propofol and sevoflurane, as the depth of anaesthesia showed as Narcotrend® value kept between 40 and 60.

2.4. Intervention in TEA/PCIA group

Half an hour before the completion of surgery, 0.4 mg of hydromorphone 2 ml and 5 ml of 0.25% ropivacaine were injected into the epidural space as a loading dose. All the patients were then connected with an epidural analgesic pump (Jiangsu REHN Medical Instruments Technology CO., ITD). As for analgesia regimen, 0.125% ropivacaine combined with hydrophilic opioids was used for TEA, with a background infusion rate of 2 ml h^{-1}. TEA was only applied in the day of surgery and the first postoperative day (about 36 hours). Hydromorphone combined with NSAID was used for PCIA until the postoperative three days. Removal time of an analgesia pump was recorded, and the cumulative opioid consumption was recorded in equivalents of oral morphine equivalents (OMEs) [10]. The types of medications and additional pain medication were documented in detail.

2.5. Intervention in TEA group

The patients in TEA group received epidural puncture and catheterization to establish epidural analgesia before anaesthesia induction. TEA was used until postoperative three days. The analgesia regimen for TEA was the same as that in TEA/PCIA group, with the analgesia pump settings of a background infusion rate of 2 ml h^{-1}. Similarly, detailed recording included removal time of an analgesia pump, cumulative opioid consumption, and additional pain medication.

2.6. Date collection

Patients' demographic information including age, sex, BMI, ASA grade, comorbidities, surgical type, incision type, and operation time was collected. Postoperative pain at rest and on movement was evaluated with visual analogue scale (VAS) pain score. The primary endpoints were mean VAS pain scores at rest and on movement postoperatively three days. The secondary endpoints included VAS pain scores at rest and on movement at 6, 24, 48 and 72 h postoperatively, incidence of inadequate analgesia, incidence of opioid-related adverse events, the time to first mobilization, the time to pass first flatus, the time of oral intake recovery, the time of the urinary catheter removal, postoperative length of hospital stay, cumulative opioid consumption, and overall cost.

2.7. Sample size

The mean VAS pain scores at rest and on movement postoperatively three days were the primary endpoints in our work. Kelly study showed that the minimum clinically significant VAS pain score in the management of severe pain was 1 cm [11]. Standard deviations varying between 1.4 and 1.8 cm have been reported, thus we estimated a standard deviation of 1.5 cm for the study. To achieve 90% power to detect a difference (1 cm) in the primary endpoints with a two-sided 5% level of significance, a sample size of 38 patients in each group of the study is needed. An additional four participants were recruited in each study arm to cover a maximum of 10% losses, thus the sample size required for each group was up to 42 subjects.

2.8. Statistical analysis

Statistical Package for the Social Sciences software version 20.0 (SPSS Inc, Chicago, IL, USA) was used for statistical analysis. All quantitative data were first examined for normality. Mean ± standard deviation was used for the statistical description of the quantitative data conforming to the normal distribution. *T*-test of independent samples was used for the comparison of the normally distributed data. The non-normally distributed data were represented by median and interquartile range and were compared by Mann-Whitney U test. In addition, this study compared the VAS pain scores of the two groups at different time points. These data were repeated quantitative measures data and received analysis through repeated measures analysis of variance. Frequency was used for statistical description of qualitative data, and chi-square test was used for the comparison of the frequencies. P values < 0.05 indicated statistically significant differences (the level of significance was bilateral).

3. Results

A total of 102 patients who met the inclusion criteria and signed the informed consent for participation in the study from November 2018 to November 2019 were recruited. Finally, 86 patients (44 patients in the TEA/PCIA group,42 patients in the TEA group) were included in the final statistical analysis, details of dropout reasons are given in Fig. 2. Baseline characteristics of the two groups are presented in Table 1(at the end of the manuscript). There was no significant difference in demographic characteristics, comorbidities, surgical type, and incision type between the two groups ($P > 0.05$). No significant differences were seen between the two groups in terms of operation time, intraoperative fluid intake, intraoperative blood loss, intraoperative sufentanil consumption, cumulative opioid consumption, as well as length of stay and complications in the post anaesthesia care unit (Table 2, at the end of the manuscript).

Table 1

Baseline characteristics of the included patients in the final statistical analysis.

	TEA/PCIA Group	TEA Group	*P*
Age (y)	56.1±11.1	54.6±13.0	0.569
Sex (Male: Female)	36:8	33:7	0.705
BMI (kg m^{-2})	21.7±2.8	22.2±3.0	0.491
ASA I-II, n (%)	44	42	0.924
ASA I, n (%)	7 (16)	7 (17)	—
ASA II, n (%)	37 (84)	35 (83)	—
Comorbidities, n (%)	13 (29.5)	13 (31.0)	0.887
Diabetes, n (%)	7	4	—
Hypertension, n (%)	4	8	—
Respiratory, n (%)	2	4	—
Surgical type, n (%)	44	42	0.833
Liver surgery, n (%)	21 (47)	21 (50)	—
Pancreaticoduodenectomy, n (%)	10 (23)	12 (28)	—
Gastrointestinal surgery, n (%)	7(16)	5(12)	—
Colorectal surgery, n (%)	6 (14)	4 (10)	—
Incision type, n (%)	44	42	0.657
Reversed L-shaped incision, n (%)	1 (2.3)	1 (2.4)	—
Roof incision, n (%)	19 (43.2)	20 (47.6)	—
Subcostal incision, n (%)	2 (4.5)	2 (4.8)	—
Midline incision, n (%)	15 (34.1)	17 (40.4)	—
Para-midline incision, n (%)	7 (15.9)	2 (4.8)	—

Data are expressed as Mean ± SD, number (%). TEA, thoracic epidural analgesia; PCIA, patient-controlled intravenous analgesia; BMI, body mass index; ASA, American Society of Anaesthesiologists.

Table 2

Operative characteristics, PACU variables and cumulative opioid consumption.

	TEA/PCIA Group	TEA Group	*P*
Operation time (min)	267 [211 to 334]	247 [195 to 348]	0.694
Intraoperative sufentanil consumption (ug)	28.5 ± 6.2	29.1 ± 8.4	0.716
Intraoperative fluid intake (mL)	3250 [2700 to 3700]	3250 [2475 to 5025]	0.955
Intraoperative blood loss (mL)	300 [112.5 to 475]	225 [100 to5 25]	0.705
Blood transfusion, n (%)	12 (27.3)	12 (28.6)	0.893
PACU length of stay (min)	97.9 ± 40.4	104.0 ± 34.8	0.513
PACU complications, n (%)	6 (13.6)	8 (19)	0.952
Pain, n (%)	2 (4.5)	2 (4.8)	—
Dysphoria, n (%)	1 (2.3)	1 (2.4)	—
Shiver, n (%)	3 (6.8)	3 (7.1)	—
Hypertension, n (%)	0 (0)	1 (2.4)	—
Pain and dysphoria, n (%)	0 (0)	1 (2.4)	—
Cumulative opioid Consumption (mg)	41.48 [26.34 to 66.85]	38.64 [29.19 to 42.00]	0.109

Data are expressed as Mean ± SD, median [IQR], number (%). TEA, thoracic epidural analgesia; PCIA, patient-controlled intravenous analgesia; PACU, post anaesthesia care unit.

The mean VAS pain scores during postoperative days 0–3 in TEA/PCIA group were lower both at rest (1.18 ± 0.46 vs 1.35 ± 0.50; $P > 0.05$) and on movement (2.45 ± 0.55 vs 2.68 ± 0.52; $P < 0.05$) as compared with TEA group (Table 3). The analgesic effects were excellent in both groups. TEA/PCIA group had lower VAS pain scores at rest and on movement at each time point as compared with TEA group, with a significant difference at 48 h postoperatively ($P < 0.05$).

Table 3

Mean VAS pain scores and VAS pain scores at various time points postoperatively.

	TEA/PCIA Group	TEA Group	*P*
Mean R-VAS	1.18 ± 0.46	1.35 ± 0.50	0.093
Mean M-VAS	2.45 ± 0.55	2.68 ± 0.52	0.046
6-h R-VAS	1.64 ± 0.75	1.88 ± 0.80	0.15
6-h M-VAS	2.95 ± 0.86	3.12 ± 0.83	0.37
24-h R-VAS	1.36 ± 0.49	1.38 ± 0.70	0.89
24-h M-VAS	2.61 ± 0.62	2.79 ± 0.68	0.22
48-h R-VAS	0.95 ± 0.57	1.21 ± 0.52	0.03
48-h M-VAS	2.23 ± 0.64	2.64 ± 0.66	0.004
72-h R-VAS	0.75 ± 0.62	0.93 ± 0.75	0.23
72-h M-VAS	1.98 ± 0.59	2.19 ± 0.77	0.153

Data are expressed as Mean ± SD. TEA, thoracic epidural analgesia; PCIA, patient-controlled intravenous analgesia; VAS, visual analogue scale; R-VAS, VAS score at rest; M-VAS, VAS score on movement.

No significant difference was found in the postoperative length of hospital stay, the time to urinary catheter removal, and the time of oral intake recovery between the two groups (Table 4). But TEA/PCIA group presented earlier mobilization and recovery of bowel function (shorter time to first pass flatus) ($P < 0.05$) (Table 4).

There was no significant difference in the incidence of opioid-related adverse events between the two groups (Table 5). Respiratory depression, local anaesthetic systemic toxicity, motor block, and catheter-related problems (dislodge, leakage, or blocking) were not found.

Table 4

Early postoperative recovery variables for the included patients.

	TEA/PCIA Group	TEA Group	*P*
Time to first mobilization (d)	2 [2 to 3]	3 [2 to 4]	0.015
Time to first pass flatus (d)	2 [2 to 3]	3 [2 to 3]	0.048
Time of oral intake recovery (d)	4 [2 to 5]	3 [2 to 6]	0.513
Time of urinary catheter removal (d)	3 [2 to 4.75]	3 [2 to 4]	0.832
PLOS(d)	9 [7 to 11.75]	9.5 [8 to 13]	0.345

Data are expressed as median [IQR]. TEA, epidural analgesia; PCIA, patient-controlled intravenous analgesia; PLOS, postoperative length of hospital stays.

Table 5

Incidences of inadequate analgesia and opioid-related adverse events.

	TEA/PCIA Group	TEA Group	*P*
Inadequate analgesia	9 (20.5)	13 (31.0)	0.265
Nausea/vomiting, n (%)	9 (20.5)	8 (19.0)	0.269
Mild	3 (7.0)	3 (7.1)	0.269
Moderate	5 (11.4)	5 (11.9)	0.269
Severe	1 (2.1)	0 (0.0)	0.269
Hypotension, n (%)	11 (25.0)	8 (19.0)	0.506
Dizziness, n (%)	3 (6.8)	4 (9.5)	0.646
Pruritus, n (%)	0 (0.0)	2 (4.8)	0.143
Urinary retention, n (%)	1 (2.3)	2 (4.8)	0.529
Others*, n (%)	0 (0.0)	0 (0.0)	—

Data are expressed as number (%). TEA, thoracic epidural analgesia; PCIA, patient-controlled intravenous analgesia; *: No respiratory depression, local anaesthetic intoxication, motor block, catheter prolapse were observed during the study. Patients with mean arterial pressure less than 65 mmHg were diagnosed with hypotension.

There was no significant difference between the two groups in the overall cost of hospitalization and the cost of anaesthesia (Table 6).

Table 6

Overall cost and cost of anaesthesia*.

	TEA/PCIA Group	TEA Group	*P*
Total cost (RMB)	75 011 [53 172 to 93 036]	75 773 [55 569 to 102 799]	0.777
Cost of anaesthesia (RMB)	5226 [4933 to 5740]	5171 [4658 to 5872]	0.412

Data are expressed as median [IQR]. *: A total of 82 patients were included in the statistical analysis, and four patients were excluded due to the special billing payment method in our hospital (three in TEA/PCIA group and one in TEA group). TEA, thoracic epidural analgesia; PCIA, patient-controlled intravenous analgesia.

4. Discussion

Our results showed that TEA/PCIA group received a significant reduction in VAS pain scores in the postoperative 0–3 days, with lower VAS pain scores at various time points postoperatively both in rest and on movement, it is consistent with our initial hypothesis. Epidural analgesia in short term not only maximized analgesic effect, but also reduce the adverse effects theoretically, such as urinary retention and motor block, which could cause by prolonged indwelling time of epidural analgesia [12, 13]. As the same time, opioids and NSAID were used for PCIA. Opioids can treat inadequate analgesia and reduce the regressed risk of sensory level of epidural analgesia, NSAID can effectively make up for the poor effect of TEA on inflammatory pain [14].

Adequate postoperative analgesia is important for early recovery. In this study, the time to first mobilization in TEA/PCIA group was earlier than that in TEA group, which may attribute to better pain control. Several previous studies have demonstrated that better pain control brings earlier mobilization, and thus contributes to recovery of gastrointestinal function and reduction of the risks of pulmonary complications and cardiovascular events [7, 15]. The time to first pass flatus in TEA/PCIA group was shorter than TEA group, early mobilization may be one reason, on the other hand epidural analgesia may promote a faster return in intestinal bowel motility via various mechanisms including decrease in opioid administration, blockade of the relevant sympathetic nerve, reduction of inflammatory reactions and a direct effect of systemic local anaesthetics.

In our study, the combination of TEA/PCIA required higher dosage of opioids compared with TEA alone. Thus, whether the risk of opioid-related adverse events in TEA/PCIA group would increase was also the focus of this study. Our results showed that no significant difference was seen in the incidences of opioid-related adverse events between the two groups. The incidence of postoperative nausea and vomiting was less frequent in both TEA/PCIA group (20.5%) and TEA group (19.0%), which is consistent with that incidence in our institution and lower than the generally reported incidence of 30–50% [16, 17].

Hypotension is a frequent unwanted side effect of epidural analgesia. TEA/PCIA group in our study did not show a lower incidence. Further analysis found that postoperative hypotension mainly occurred in the night of the first postoperative day. Postoperative hypotension of a major laparotomy is common and multifactorial. Due to the lack of a control group receiving PCIA alone, it is difficult to determine whether postoperative hypotension is attributable to epidural analgesia.

In the current study, nearly half of the patients underwent open hepatectomy, some studies considered epidural analgesia is not suitable for hepatectomy because it may be a risk factor for postoperative kidney failure due to hypotension. A published meta-analysis suggested that epidural analgesia in the presence of perioperative fluid restriction may lead to persistent hypotension and acute kidney injury after major hepatectomy [18]. However, the evidence for the association of TEA with postoperative acute kidney injury in abdominal surgery is controversial. In contrast, Popping et al. found that the patients receiving epidural analgesia did not have an increased risk of renal failure (OR: 0.78; 95% CI: 0.57–1.09) [19]. Recent controlled clinical trials and meta-analyses also supported that epidural analgesia is a safe and effective pain management option for hepatectomy [20, 21].

Postoperative acute kidney injury is a common occurrence after major open surgery. A recent study reported that its incidence after major open surgery ranged from 3.1–35.3% [22]. According to the diagnostic criteria of the Acute Kidney Injury Network (AKIN), its incidence after hepatectomy reported in relevant literature was in the range of 5.1–12.1% [18, 23–25]. With the same diagnostic criteria for acute kidney injury (AKI) [26], our study showed that the overall incidence of AKI was 4.9%, and all the AKI patients were mild and staged as AKIN Grade I. Subgroup analysis showed a low incidence of AKI after hepatectomy (2.4%). Among the four patients with renal injury, two had polycystic kidney detected by preoperative urologic ultrasound, two had hypertension and diabetes before surgery, and two received intraoperative blood transfusion. Postoperative AKI is multifactorial, and its association with epidural analgesia requires more clinical research.

4.1. Study limitations

There are several limitations in the current study. First, this study was performed in a unblinded fashion due to the difficulty in blinding the observers and patients to the assigned intervention. The second is the absence of a PCIA control group. In this study, it is difficult to analyse the effects of TEA itself when discussing the results, especially the adverse effects. In addition, the current study focused on patients undergoing major open surgery. Although the number of subjects included in the final analysis reached the requirement of sample size, the number of some subgroups was too small for further subgroup analysis. Next, we will pay more attention to hepatobiliary surgery.

5. Conclusion

In summary, the combination of TEA and PCIA for patients underwent major open abdominal surgery, can provide superior postoperative analgesia and facilitate early rehabilitation without increasing the

incidence rate of adverse effects and the overall cost of hospitalization.

Abbreviations

TEA
Thoracic epidural analgesia
PCIA
Patient controlled intravenous analgesia
VAS
Visual analogue scale
ERAS
Enhanced recovery after surgery
ASA
American Society of Anesthesiology
BMI
Body mass index
NSAID
Nonsteroidal anti-inflammatory drug
OMEs
Oral morphine equivalents
OR
Odds ratio
CI
Confidence interval
AKNI
Acute Kidney Injury Network
AKI
Acute kidney injury.

Declarations

Acknowledgments

Assistance with the study: We would like to acknowledge and express our deepest gratitude to the participants of this study.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data and materials

The full study protocol and raw data set can be obtained from the corresponding author (anke@mail.sysu.edu.cn).

Authors' contributions

#Wenwen Xu: designed the study and collected data, wrote the part of introduction, method, and discussion, and revised the paper. #**Youpei Li:** collected data, wrote the part of results, and made tables and figures. **#**: The two authors contribute to this work equally as co-first authors. **Nanqi Li:** data collection. **Yu Sun:** data collection. **Wang Chao:** data collection. **Ke An**: designed the study together with Wenwen Xu and revised the paper. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Ethical approval for this study (Ethical Committee No. [2018]265) was provided by the Ethics Committee of the First Affiliated Hospital of Sun Yat-Sen University (Chairperson Prof Churong Yan) on 24 October 2018. All methods were carried out in accordance with relevant guidelines and regulations (Declaration of Helsinki). Written informed consent was obtained from all participating subjects prior to enrollment.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. Br J Anaesth. 1997 May;78(5):606–17.
2. Greco M, Capretti G, Beretta L, et al. Enhanced recovery program in colorectal surgery: a meta-analysis of randomised controlled trials. World J Surg. 2014 Jun;38(6):1531–41.
3. Muller S, Zalunardo MP, Hubner M, et al. Zurich Fast Track Study Group. A fast-track program reduces complications and length of hospital stay after open colonic surgery. Gastroenterology. 2009 Mar;136(3):842–7.
4. Correll DJ, Vlassakov KV, Kissin I. No evidence of real progress in treatment of acute pain, 1993–2012: scientometric analysis. J Pain Res. 2014 Apr 11; 7:199–210.
5. Salicath JH, Yeoh EC, Bennett MH. Epidural analgesia versus patient-controlled intravenous analgesia for pain following intra-abdominal surgery in adults. Cochrane Database Syst Rev. 2018 Aug 30;8(8):CD010434.
6. Guay J, Nishimori M, Kopp S. Epidural local anaesthetics versus opioid-based analgesic regimens for postoperative gastrointestinal paralysis, vomiting and pain after abdominal surgery. Cochrane

Database Syst Rev. 2016 Jul 16;7(7):CD001893.

7. Pöpping DM, Elia N, Marret E, et al. Protective effects of epidural analgesia on pulmonary complications after abdominal and thoracic surgery: a meta-analysis. Arch Surg. 2008 Oct;143(10):990–9; discussion 1000.
8. Baldini G, Bagry H, Aprikian A, et al. Postoperative urinary retention: anesthetic and perioperative considerations. Anesthesiology. 2009 May;110(5):1139–57.
9. Wheatley RG, Schug SA, Watson D. Safety and efficacy of postoperative epidural analgesia. Br J Anaesth. 2001 Jul;87(1):47–61.
10. Nielsen S, Degenhardt L, Hoban B, et al. A synthesis of oral morphine equivalents (OME) for opioid utilisation studies. Pharmacoepidemiol Drug Saf. 2016 Jun;25(6):733–7.
11. Kelly AM. The minimum clinically significant difference in visual analogue scale pain score does not differ with severity of pain. Emerg Med J. 2001 May;18(3):205–7.
12. Baldini G, Bagry H, Aprikian A, et al. Postoperative urinary retention: anesthetic and perioperative considerations. Anesthesiology. 2009 May;**110**(5):1139–57.
13. Wheatley RG, Schug SA, Watson D. Safety and efficacy of postoperative epidural analgesia. Br J Anaesth. 2001 Jul;**87**(1):47–61.
14. Woolf CJ; American College of Physicians; American Physiological Society. Pain: moving from symptom control toward mechanism-specific pharmacologic management. Ann Intern Med. 2004 Mar 16;**140**(6):441–51.
15. Holte K, Kehlet H. Effect of postoperative epidural analgesia on surgical outcome. Minerva Anestesiol. 2002 Apr;68(4):157–61.
16. American Society of PeriAnesthesia Nurses PONV/PDNV Strategic Work Team. ASPAN'S evidence-based clinical practice guideline for the prevention and/or management of PONV/PDNV. J Perianesth Nurs. 2006 Aug;21(4):230–50.
17. Gan TJ, Diemunsch P, Habib AS, et al; Society for Ambulatory Anesthesia. Consensus guidelines for the management of postoperative nausea and vomiting. Anesth Analg. 2014 Jan;118(1):85–113.
18. Kambakamba P, Slankamenac K, Tschuor C, et al. Epidural analgesia and perioperative kidney function after major liver resection. Br J Surg. 2015 Jun;102(7):805–12.
19. 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 randomised controlled trials. Ann Surg. 2014 Jun;259(6):1056–67.
20. Ganapathi S, Roberts G, Mogford S, et al. Epidural analgesia provides effective pain relief in patients undergoing open liver surgery. Br J Pain. 2015 May;9(2):78–85.
21. Li J, Pourrahmat MM, Vasilyeva E, et al. Efficacy and Safety of Patient-controlled Analgesia Compared with Epidural Analgesia After Open Hepatic Resection: A Systematic Review and Meta-analysis. Ann Surg. 2019 Aug;270(2):200–208.

22. Gameiro J, Fonseca JA, Neves M, et al. Acute kidney injury in major abdominal surgery: incidence, risk factors, pathogenesis and outcomes. Ann Intensive Care. 2018 Feb 9;8(1):22.
23. Armstrong T, Welsh FK, Wells J, et al. The impact of pre-operative serum creatinine on short-term outcomes after liver resection. HPB (Oxford). 2009 Dec;11(8):622–8.
24. Cho E, Kim SC, Kim MG, et al. The incidence and risk factors of acute kidney injury after hepatobiliary surgery: a prospective observational study. BMC Nephrol. 2014 Oct 23; 15:169.
25. Tomozawa A, Ishikawa S, Shiota N, et al. Perioperative risk factors for acute kidney injury after liver resection surgery: an historical cohort study. Can J Anaesth. 2015 Jul;62(7):753–61.
26. Ricci Z, Cruz DN, Ronco C. Classification and staging of acute kidney injury: beyond the RIFLE and AKIN criteria. Nat Rev Nephrol. 2011 Apr;7(4):201–8.

Figures

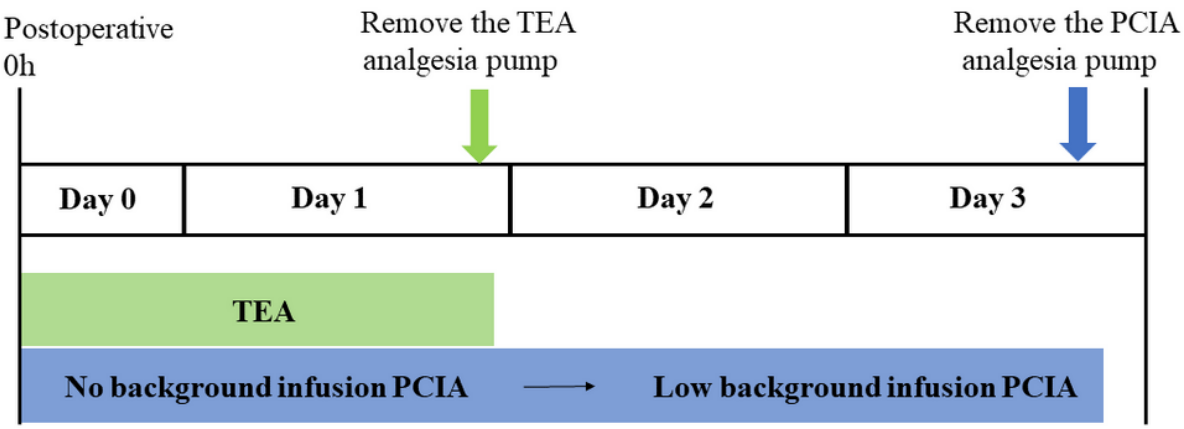

Figure 1

The protocol and flow diagram of the TEA/PCIA

Figure.2

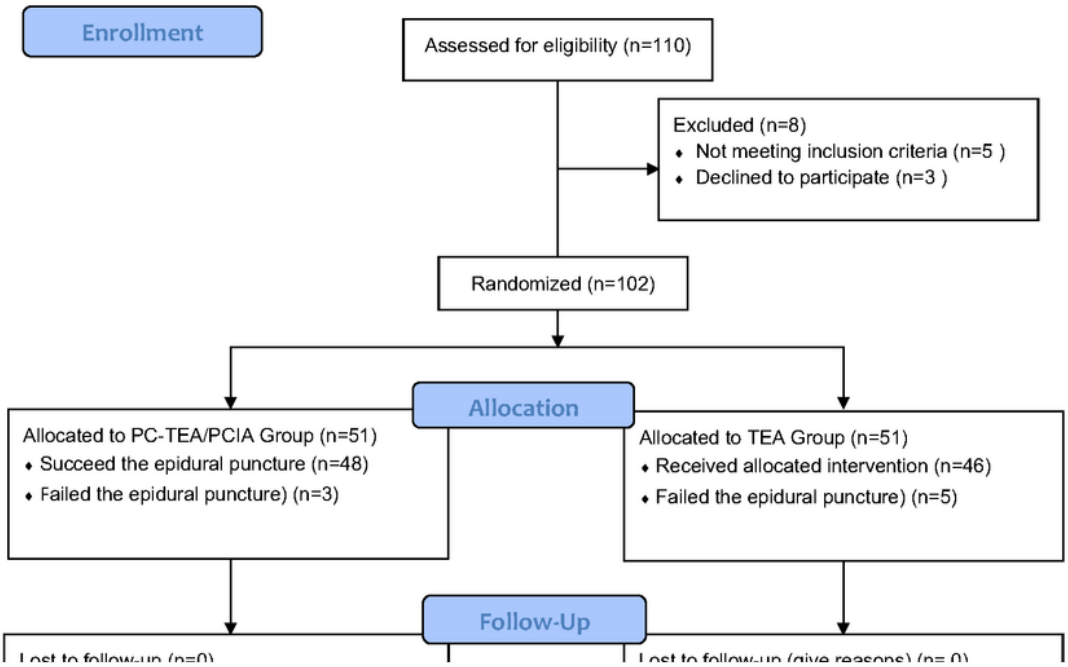

Figure 2

The CONSORT Flow Diagram In TEA/PCIA group, three patients failed to receive an epidural puncture, four patients withdraw from the research due to postoperative abdominal infection and haemorrhage. In TEA group, five patients failed to receive an epidural puncture, three were transferred to the ICU due to surgery complications, and one patient withdrew due to the changes in surgical protocols. TEA, thoracic epidural analgesia; PCIA, patient-controlled intravenous analgesia; ICU, intensive care unit.