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REVIEW

Thoracic epidural analgesia (TEA) versus patient-controlled analgesia (PCA) in laparoscopic colectomy: a systematic review and meta-analysis

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Abstract

Purpose A meta-analysis of RCTs was designed to provide an up-to-date comparison of thoracic epidural analgesia (TEA) and patient-controlled analgesia (PCA) in laparoscopic colectomy.

Methods Our study was completed following the PRISMA guidelines and the Cochrane Handbook for Systematic Reviews of Interventions. A systematic literature screening was performed in MEDLINE and Web of Science. Fixed effects (FE) or random effects (RE) models were estimated based on the Cochran Q test result.

Results Totally, 8 studies were introduced in the present meta-analysis. Superiority of PCA in terms of length of hospital stay (LOS) (WMD 0.73, $p = 0.004$) and total complication rate (OR 1.57, $p = 0.02$) was found. TEA had a lower resting pain visual analogue scale (VAS) score at Day 1 (WMD −2.23, $p = 0.005$) and Day 2 (WMD −2.17, $p = 0.01$). TEA group had also a systematically lower walking VAS. Moreover, first bowel opened time (first defecation) (WMD − 0.88, $p < 0.00001$) was higher when PCA was applied.

Conclusions TEA was related to a lower first bowel opened time, walking, and resting pain levels at the first postoperative days. However, the overall complication rate and LOS were higher in the epidural analgesia group. Thus, for a safe conclusion to be drawn, further randomized controlled trials (RCTs) of a higher methodological and quality level are required.

Keywords TEA · PCA · Laparoscopic colectomy · Meta-analysis

Introduction

Colorectal surgery is one of the most commonly performed surgical operations, globally [1]. More specifically, in the USA alone, over 100,000 registered colorectal procedures have been recorded, over an 11-year period [1]. The overall morbidity rate of colorectal surgery can be as high as 24.6% [2], while in an emergency case setting, this rate ranges from 27.8 to 48.3% [3].

In order to achieve an optimum postoperative recovery, the introduction of the Enhanced Recovery after Surgery programs (ERAS) and the Enhanced Recovery Protocols (ERP) in colorectal surgery were proposed [4–6]. The establishment of the ERAS principles in colorectal procedures had as a consequence the reduction of the overall morbidity and the hospitalization duration, without increasing the readmission rate [2]. Furthermore, the combination of ERAS and minimal access principles, led to a synergistic positive effect on the overall postoperative outcome [4, 7, 8].

Efficient analgesia is of crucial importance during postoperative recovery and should be characterized by adequate pain relief, early mobilization, and return of bowel function and minimization of adverse events [4]. Following the introduction in open colorectal surgery, thoracic epidural analgesia (TEA) has been, similarly, proposed in laparoscopic colorectal procedures [4, 9]. Compared to conventional analgesia, or

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patient-controlled analgesia (PCA), TEA was associated with a superior analgesic effect, fewer cardiopulmonary complications, lesser postoperative nausea and vomiting (PONV), and shortened hospital stay [4, 10].

Although TEA is still considered useful in patients undergoing laparoscopic colectomy with respiratory diseases or at high risk of pulmonary complications, as well as in patients at high risk of conversion to laparotomy, based on the results of trials, where no superiority of TEA was documented, current guidelines do not recommend the routine application of this method in laparoscopic colorectal surgery [11]. Moreover, in a meta-analysis of ERAS randomized controlled trials (RCTs), TEA, when compared to PCA, displayed a longer length of hospital stay (LOS), with no difference in terms of complications or readmission rate [9]. However, studies that did not include the ERAS principles, reported an improved analgesic effect and a shorter return of bowel function [12–14].

Taking into consideration the above-mentioned facts, the present systematic review and meta-analysis of RCTs were designed and implemented, in order to provide an overall comparison between TEA and PCA in laparoscopic colorectal surgery, regarding their postoperative recovery effect, without confining in strict ERAS protocols.

Methods

Study protocol

The present meta-analysis was completed, following the guidelines proposed by the PRISMA study group [15] and the Cochrane Handbook for Systematic Reviews of Interventions.

Primary endpoint

As primary endpoint of this study was regarded the difference in the length of hospital stay (LOS) between the application of thoracic epidural analgesia and patient-controlled analgesia in patients submitted to laparoscopic colectomy for benign or malignant diseases.

Secondary endpoints

This meta-analysis included the following secondary endpoints: pooled visual analogue pain scores (VAS) at coughing, walking, or at rest, during the first postoperative days (first, second, and third postoperative day), time to first flatus, time to first bowel movement (first bowel sounds), time to first bowel opened (first defecation), time to tolerate diet, operation duration, and overall and specific (urinary retention, urinary tract infection, surgical site infection, anastomotic leak, ileus, vomiting, nausea) complication rate.

Eligibility criteria

Included studies were considered all human prospective randomized controlled trials (RCTs) comparing TEA and PCA in laparoscopic colorectal surgery for benign or malignant diseases of the colon and the rectum. Furthermore, the outcome data of the eligible studies should be retrievable and reported in English.

The exclusion criteria for this meta-analysis consisted of the following elements: (1) non-human studies, (2) no outcome of interest, (3) outcomes not reported in English, (4) irretrievable outcome data, (5) no comparison group, (6) duplicate trial data, (7) no RCT study design, (8) publications in the form of conference abstracts, letters to the editor, or expert opinions.

Literature search

In order to identify and retrieve the eligible studies, a systematic literature search was performed in electronic databases (MEDLINE and Web of Science). The last search date was 25/07/2018. The following search algorithm was applied: “analgesia” or “epidural” or “patient controlled” or “PCA” or “TEA” and “laparoscopic colectomy” or “laparoscopic colorectal”.

Study selection and data collection

After the removal of duplicate entries, studies were submitted to titles and abstracts screening. The identification and extraction of the eligible trials were completed, with the full text review, in order to assess the consistency with the inclusion criteria. It must be noted that all the database search, the study selection, the data extraction, and the methodological and quality evaluation of the included studies were performed in duplicate and blindly by two independent researchers (P.K. and S.C.). In case of a disagreement, the two reviewers implemented mutual revision and discussion in order to reach a consensus. If the discrepancy was not resolved successfully, the opinion of a third researcher (B.I.) was considered.

All eligible studies were submitted to rigorous quality and methodological assessment on the basis of the Cochrane’s risk of bias assessing tool [16]. This tool rates the included RCTs for the risk of introducing selection, performance, detection, attrition, and reporting bias in the trial methodology. The risk endpoints were appointed a color rating, with green, yellow, and red representing low, unclear, and high risk level, respectively. Cohen’s k statistic was calculated.

Statistical analysis

Statistical computations and data analyses were completed through the utilization of Cochrane Collaboration RevMan version 5.3 and IBM SPSS version 23. Dichotomous and continuous variables were reported in the form of odds ratio (OR) and weighted mean difference (WMD), respectively. The corresponding 95% confidence interval (95%CI) was provided for the analyses outcomes.

Regarding continuous variables, in case that the trial manuscript did not report the mean and the standard deviation (SD), they were estimated from the provided median and interquartile range (IR), on the basis of the formula described by Hozo et al. [17]. More specifically, if the sample size was > 25, then the mean was regarded as equal to the median. Furthermore, SD was calculated as IR/4 and IR/6 for sample sizes < 70 and > 70, respectively. Moreover, concerning the statistical method applied, the Mantel-Haenszel (MH) and the inverse variance (IV) were implemented in dichotomous and continuous variables, correspondingly. Both fixed effects (FE) and random effects (RE) models were calculated. The model that was finally estimated was based on the results of the Cochran Q test. In case of a statistically significant heterogeneity (Q test $p < 0.1$), then the RE model was provided. If the levels of heterogeneity were not significant (Q test $p > 0.1$), then FE model was reported. Further heterogeneity quantification included the estimation of I^2. Statistical significance was considered at the level of $p < 0.05$.

Risk of bias across studies

Visual inspection of the funnel plot of the primary outcome was performed, for the possible presence of publication bias to be determined. An Egger's test was, also, performed.

Results

Study selection

In total, 2804 studies were identified through electronic database search (Fig. 1). More specifically, the search algorithm applied retrieved 1070 and 1734 entries from MEDLINE and Web of Science, respectively. After the removal of 573 duplicate records, the titles and abstracts from 2231 trials were screened. As a result, in the first step, 2201 records were rejected. From the remaining 30 articles that underwent full text review, 8 studies did not incorporate an RCT design in their protocol and 15 studies were irrelevant and thus, they were excluded. Furthermore, through hand-searching of the related literature, one study was introduced. Therefore 8 studies [12–14, 18–22] were introduced in the present meta-analysis.

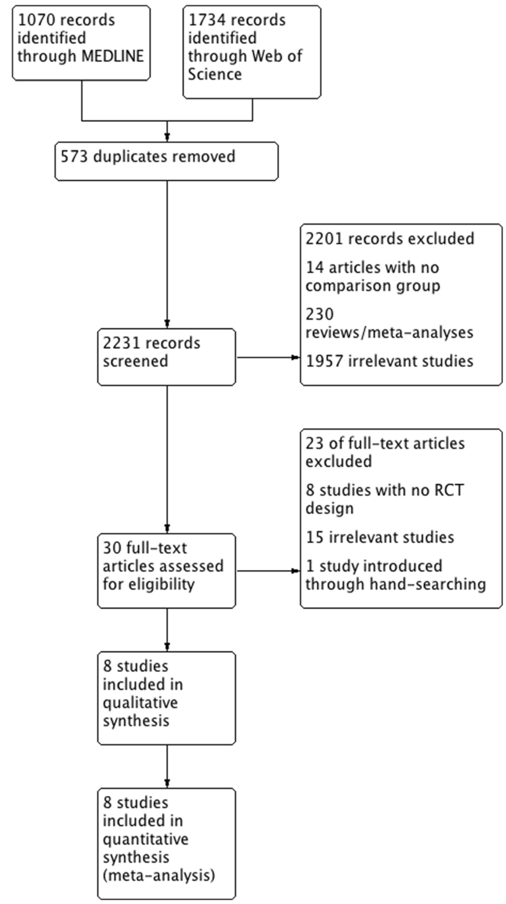

Fig. 1 Study flow diagram

Study characteristics

The characteristics of the included studies are shown in Table 1. In total, 492 patients were incorporated in this study.

As far as the underlying pathology of the patients was concerned, 222 malignancies and 231 benign diseases, such as diverticular and inflammatory bowel disease, were identified (Online resource, ESM Table 1). Moreover, regarding the procedure type, 107 laparoscopic right colectomies and 281 laparoscopic left colectomies and sigmoidectomies were recorded. Finally, a total of 58 laparoscopic low anterior resections and 6 abdominoperineal resections were reported.

The ASA score of the patients submitted to laparoscopic colectomy is summarized in ESM Table 2 (Online resource). ERAS protocol was implemented by 4 studies [18, 20–22]. Additionally, ESM Table 2 (Online resource), provides a summary of the analgesia protocol applied in each subgroup. Follow-up ranged from 14 days [20] to 1 month [12, 13, 22].

Risk of bias within studies

ESM Fig. 1 (Online resource) summarizes the quality assessment of the included studies. More specifically, although the majority of the eligible trials reported a random sequence

Table 1 Included studies characteristics

Author	Type of study	Operation	Group	Sample	Gender (M/F)	Age	BMI
Levy et al. [18]	RCT	Laparoscopic colectomy	TEA	30	16/14	68(11)	Weight: 75(14)
			PCA	30	16/14	66(12)	Weight: 82(15)
Neudecker et al. [19]	RCT	Laparoscopic colectomy	TEA	10	4/6	60(3.75)	24.8(1.325)
			PCA	10	2/8	65(8.5)	26.9(1.85)
Senagore et al. [12]	RCT	Laparoscopic colectomy	TEA	23	9/11	53(16)	Weight: 80.2(5.3)
			PCA	24	12/8	54(13)	Weight: 80(6.8)
Taqi et al. [13]	RCT	Laparoscopic colectomy	TEA	25	14/11	65(16.18)	Weight: 73.4(15.58)
			PCA	25	13/12	61.24(14.91)	Weight: 73.7(10.36)
Turunen et al. [20]	RCT	Laparoscopic colectomy	TEA	29	8/21	58.5(9.8)	27.1(4.2)
			PCA	29	10/19	55.8(12.7)	27.7(4.7)
Wongyingsinn et al. [21]	RCT	Laparoscopic colectomy	TEA	30	19/11	61(15)	26(4)
			PCA	30	19/11	58(16)	28(7)
Zingg et al. [14]	RCT	Laparoscopic colectomy	TEA	39	18/21	64.8(2)	n/a
			PCA	36	23/13	60.6(2.3)	
Hübner et al. [22]	RCT	Laparoscopic colectomy	TEA	65	37/28	63.1(15.1)	25.9(5.1)
			PCA	57	34/23	61.2(17.8)	25.5(4.2)

generation protocol [12, 18, 20–22], that was not the case for allocation concealment [18, 20, 21]. Furthermore, in all studies, the participants and the personnel were not blinded and in only two trials [13, 21], blinding of the outcome assessment was confirmed. Finally, high risk of attrition and reporting bias were identified in the study of Neudecker et al. [19]. Interrater agreement levels were estimated to be in satisfactory levels (Cohen's k statistic 88.8%, $p < 0.001$).

Primary endpoint

In total, 8 studies provided data regarding the length of hospital stay (Fig. 2). Meta-analysis of these data showed a statistically significant ($p = 0.004$) difference in favor of the PCA group (WMD 0.73; 95%CI 0.24, 1.23) in terms of LOS. Heterogeneity was significant between the studies (Q test $p < 0.00001$; $I^2 = 94\%$) and therefore, a RE model was applied.

Due to the high levels of heterogeneity that were observed, further analysis was performed. The graphical summary of the sensitivity analysis is displayed in ESM Fig. 2 (Online resource). Subgroup analysis regarding the analgesia protocol (bupivacaine and fentanyl versus morphine) did not reduce the overall heterogeneity level (WMD 0.23; 95%CI −0.06, 0.52; $p = 0.13$; Q test $p = 0.0001$; $I^2 = 85\%$). Pooled results of the studies implementing an ERAS protocol showed no statistically significant difference in terms of LOS ($p = 0.12$). Heterogeneity, though, was not reduced (Q test $p < 0.0001$; $I^2 = 96\%$). Since postoperative medications protocols were inconsistent and included a variety of treatments, subgroup analysis for this factor was not performed. Meta-regression for the variables of year ($p = 0.692$), sample size ($p = 0.97$), age ($p = 0.122$), BMI ($p = 0.022$), and follow-up duration ($p = 0.699$), concluded that only BMI was statistically correlated to the duration of the length of hospital stay. Further analysis in

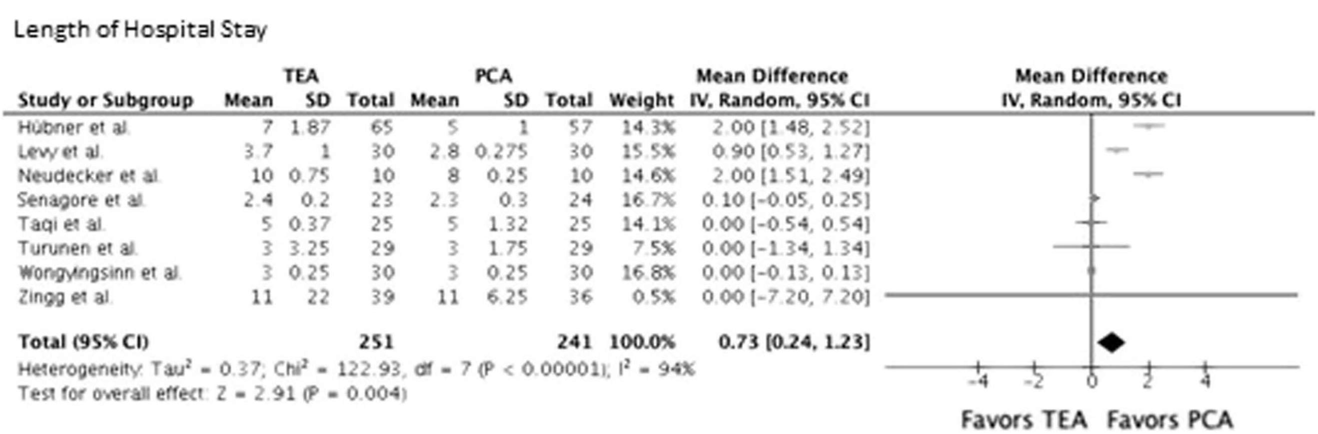

Fig. 2 Length of hospital stay

terms of other influencing factors was not performed due to the scarcity and inconsistency of the provided data.

Secondary endpoints

There was a statistically significant difference in favor of the TEA group (Fig. 3) in terms of overall VAS at Day 1 (WMD − 1.68; 95%CI − 2.27, − 1.10; $p < 0.00001$; heterogeneity Q test $p = 0.001$; $I^2 = 90\%$), but not in Day 3 (WMD − 0.26; 95%CI − 0.63, 0.12; $p = 0.18$; heterogeneity Q test $p = 0.1$; $I^2 = 63\%$). Data for Day 2 were unavailable.

Regarding VAS score at rest (Fig. 4), there was a statistically significant difference in favor of the TEA group at Day 1 (WMD − 2.23; 95%CI − 3.77, − 0.69; $p = 0.005$; heterogeneity Q test $p < 0.00001$; $I^2 = 97\%$) and Day 2 (WMD − 2.17; 95%CI − 3.84, − 0.51; $p = 0.01$; heterogeneity Q test $p < 0.00001$; $I^2 = 96\%$), but not in Day 3 (WMD − 0.97; 95%CI − 3.00, 1.06; $p = 0.35$; heterogeneity Q test $p < 0.00001$; $I^2 = 99\%$).

In terms of VAS score at coughing (Fig. 5), there was no statistically significant difference at Day 1 (WMD − 1.76; 95%CI − 6.17, 2.65; $p = 0.44$; heterogeneity Q test $p < 0.00001$; $I^2 = 100\%$), Day 2 (WMD − 1.76; 95%CI − 4.21, 0.69; $p = 0.06$; heterogeneity Q test $p < 0.00001$; $I^2 = 99\%$), and Day 3 (WMD 0.09; 95%CI − 1.74, 1.91; $p = 0.93$; heterogeneity Q test $p < 0.00001$; $I^2 = 97\%$).

As far as VAS score at walking was concerned (Fig. 6), there was a statistically significant difference in favor of the TEA group at Day 1 (WMD − 2.20; 95%CI − 3.77, − 0.64; $p = 0.006$; heterogeneity Q test $p < 0.00001$; $I^2 = 97\%$), Day 2 (WMD − 2.20; 95%CI − 3.77, − 0.64; $p = 0.006$; heterogeneity Q test $p < 0.00001$; $I^2 = 98\%$), and Day 3 (WMD − 0.97; 95%CI − 1.21, − 0.72; $p < 0.00001$; heterogeneity Q test $p = 0.64$; $I^2 = 0$).

Figure 7 summarizes the data regarding postoperative bowel function. Meta-analysis of these data showed a statistically significant difference in favor of the TEA group in terms of postoperative first bowel opened time (WMD − 0.88; 95%CI − 1.16, − 0.59; $p < 0.00001$; heterogeneity Q test $p = 0.09$; $I^2 = 58\%$), but not in postoperative first flatus (WMD − 0.43; 95%CI − 0.93, 0.07; $p = 0.09$; heterogeneity Q test $p < 0.00001$; $I^2 = 96\%$), first bowel movement (WMD − 0.33; 95%CI − 0.84, 0.18; $p = 0.20$; heterogeneity Q test $p = 0.002$; $I^2 = 80\%$), and first diet tolerance time (WMD 0.01; 95%CI − 0.58, 0.60; $p = 0.97$; heterogeneity Q test $p < 0.00001$; $I^2 = 97\%$)

There was a statistically significant difference in favor of the TEA group (WMD 5.05; 95%CI − 7.78, − 2.32; $p = 0.0003$; heterogeneity Q test $p = 0.26$; $I^2 = 21\%$) in terms of operation duration (Fig. 8).

Figure 9 summarizes the data regarding complications rate. Meta-analysis of these data showed a statistically significant difference in favor of the PCA group in terms of the overall complication rate (OR 1.57; 95%CI 1.07, 2.29; $p = 0.02$), but not in terms of urinary retention (OR 1.83; 95%CI 0.83, 4.03; $p = 0.13$), urinary tract infection (OR 0.31; 95%CI 0.03, 3.06; $p = 0.32$), SSI (OR 0.94; 95%CI 0.34, 2.59; $p = 0.91$), leak (OR 1.91; 95%CI 0.83, 4.43; $p = 0.13$), ileus (OR 1.22; 95%CI 0.58, 2.57; $p = 0.6$), vomiting (OR 1.75; 95%CI 0.97, 3.15; $p = 0.06$), and nausea (OR 1; 95%CI 0.48, 2.08; $p = 1$). Heterogeneity was not significant between the studies in most comparisons and therefore, a FE model was applied.

Risk of bias across studies

ESM Fig. 3 (Online resource) represents the funnel plot of the primary outcome. Visual inspection of the graphical representation leads to the conclusion that all eligible trials are symmetrically distributed and reside within the 95%CI limits. Similarly, Egger's test did not confirm the presence of a statistically significant publication bias ($p = 0.142$).

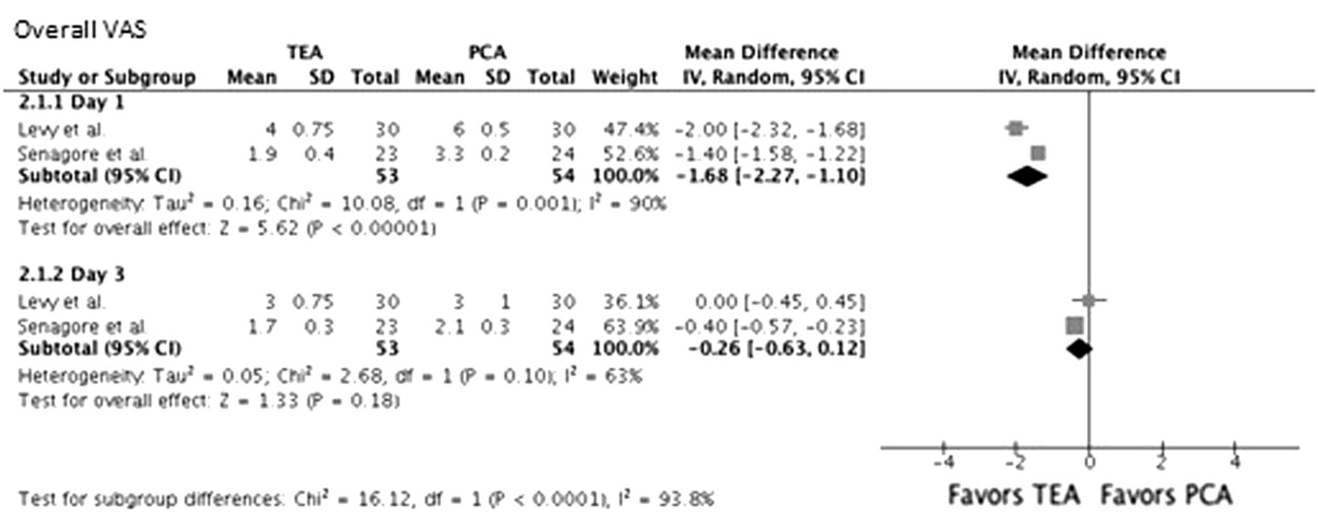

Fig. 3 Overall VAS

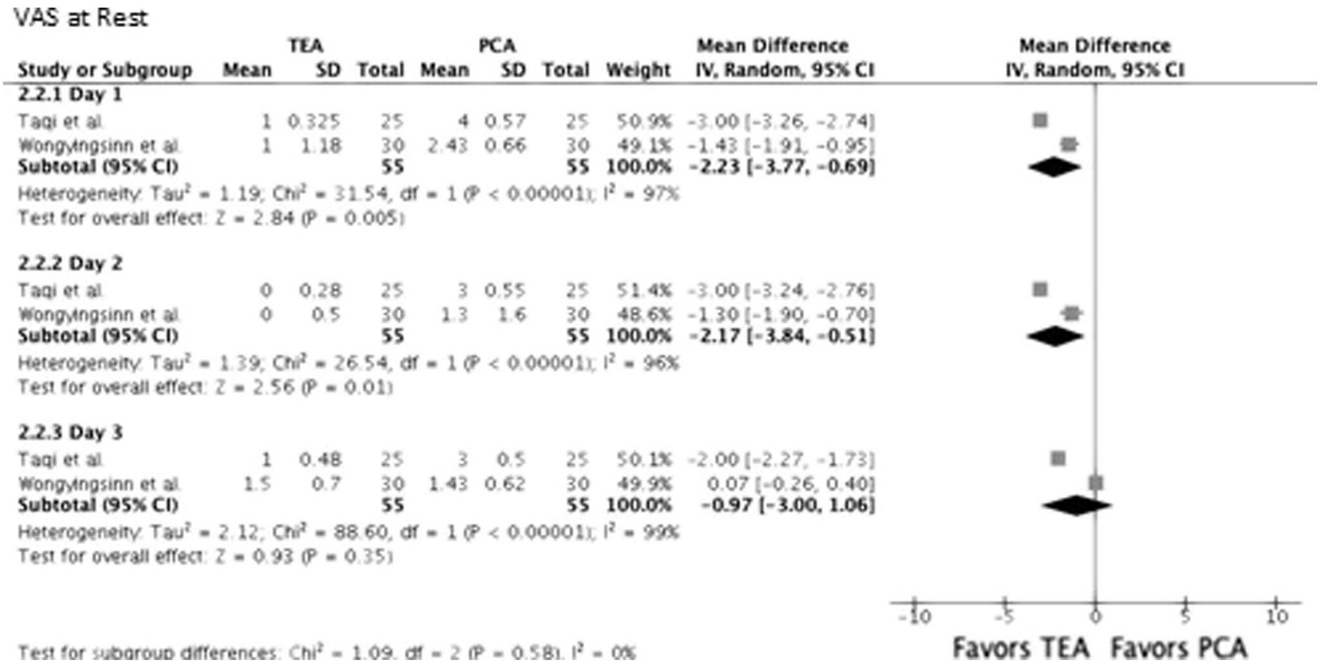

Fig. 4 VAS at rest

Discussion

Summary of evidence

Our meta-analysis results showed that TEA, compared to PCA was correlated with a longer hospital stay duration. However, our primary outcome suffered from a great heterogeneity level. Although inconsistency was noted in many study characteristics, only BMI was identified as a heterogeneity contributing factor. A possible explanation of this could be the higher overall complications rate in the TEA group. However, there was no difference between the two techniques considering specific complications, such as urinary retention and infection, nausea and vomiting, or operation-related adverse events, like SSI, leaks, and ileus. Operation duration was also lower when epidural analgesia was applied. As far as the postoperative recovery was concerned, the two techniques were equivalent in terms of first

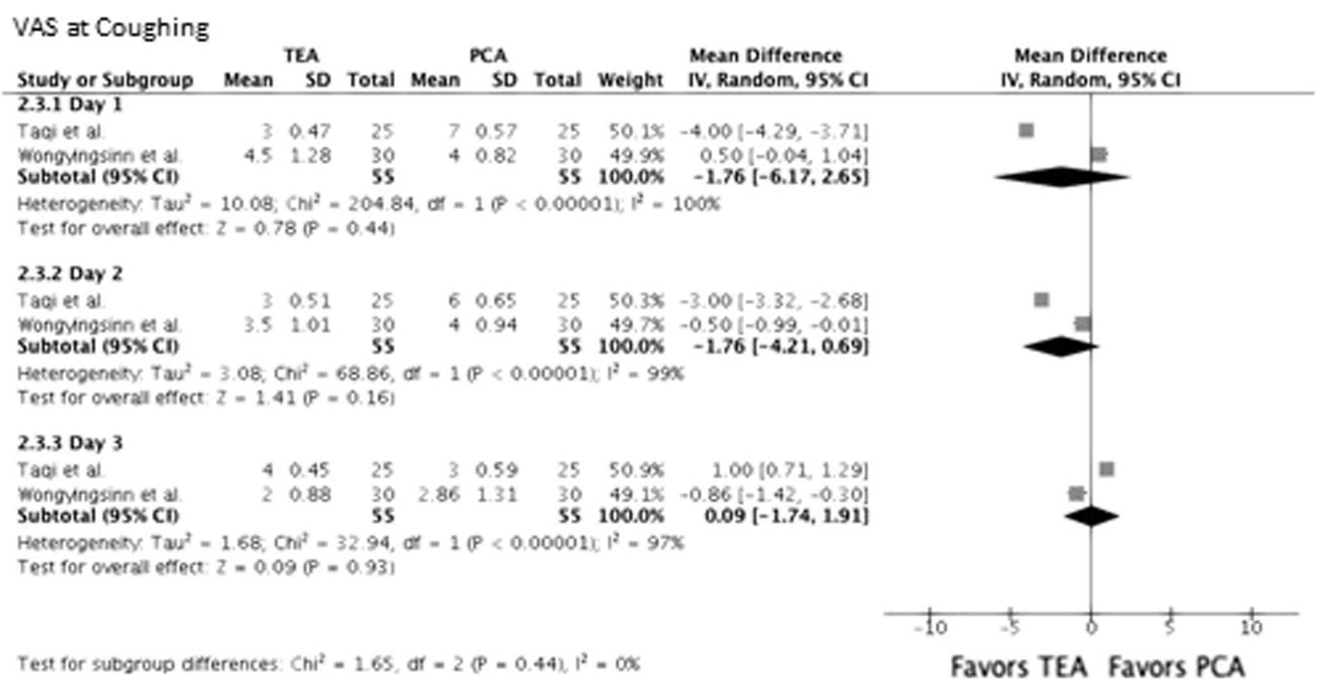

Fig. 5 VAS at coughing

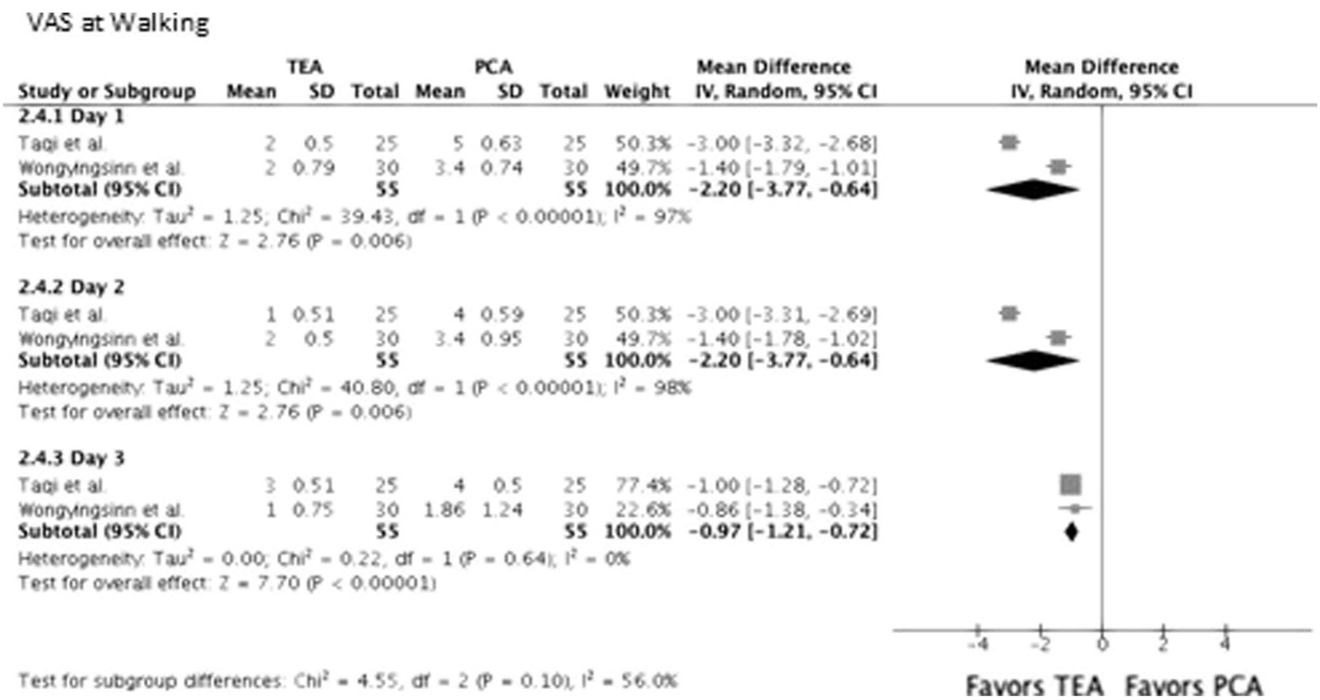

Fig. 6 VAS at walking

flatus, first bowel movement, and tolerate diet time. First bowel opened was significantly higher, in the PCA group. Regarding postoperative analgesia efficacy, TEA was superior at the first day in overall, resting, and walking measurements. Superiority at the second day was retained in resting and walking scales, while, only walking VAS scores were lower at the third day after surgery. Coughing VAS scores were equal between TEA and PCA.

ERAS and ERP programs entered clinical practice, almost two decades ago, having as a goal, the minimization of complications and the reduction of LOS [5, 6, 11, 23–27]. Taking into account the fact that postoperative enhanced recovery is a multifactorial issue, these protocols address various issues, such as operative stress, oral intake, mobilization, anesthesia, and analgesia technique [28, 29]. Despite being a crude measure of perioperative effectiveness, LOS, mainly due to its direct correlation with economic costs, is still utilized as a primary outcome in many studies [22, 30]. Extensive research has been performed for the effect of TEA in LOS [9, 31]. In a pioneering study, Bardram et al. estimated that when a laparoscopically assisted colectomy was combined with epidural analgesia, early per os nutrition, and mobilization, the LOS was reduced by 2 days [32]. Neudecker et al. and Senagore et al., in their respective RCTs, however, failed to validate these findings [12, 19]. Comparable hospitalization duration was, also, reported by Taqi et al. [13]. In a RCT by Levy et al., however, LOS was significantly higher when compared to PCA [19]. More specifically, mean hospital stay for TEA and PCA group was 3.7 and 2.8 days, respectively [19]. These results were attributed to the prolonged sympathetic inhibition and the slight motor blockade that averted early mobilization [19]. Similarly, cumulative analysis in our study showed that TEA, compared to PCA results in higher LOS. Although this outcome is susceptible to bias due to the high heterogeneity levels, the superiority of PCA in terms of hospital discharge was validated. This finding could possibly be correlated to the higher complication rate identified in TEA group.

Adequate pain relief is considered by many, as a quality index of postoperative recovery [33, 34]. Besides the physiological impact and the overall patient satisfaction levels, efficient postoperative analgesia enhances mobilization, shortens hospitalization duration, and reduces hospital costs [34]. Due to its effectiveness, TEA has been extensively used in abdominal surgery [10, 33–35]. In laparoscopic colectomy, when TEA was compared to PCA, VAS scales have also been lower [31, 36]. Comparative effectiveness of TEA, however, is confined only at the first postoperative days [14, 19–21]. Excluding the converted cases, Zingg et al. reported a significant effect of TEA during the first 7 days, while Levy et al. reduced this time range to the first postoperative day [14, 19]. In most protocols, the catheter is retained until the second day [4, 26, 27, 37]. However, in current literature, the epidural catheter removal time extends from 18 h up to 7 days [12, 14]. In our study, reported overall and resting pain in TEA group was lower during the first postoperative days. Exception to this was walking VAS, where TEA measurements were lower during all time endpoints. VAS difference during coughing did not seem to be affected by the analgesia modality.

Postoperative Bowel Function

Study or Subgroup	TEA Mean	TEA SD	TEA Total	PCA Mean	PCA SD	PCA Total	Weight	Mean Difference IV, Random, 95% CI
3.1.1 First Flatus								
Levy et al.	1.5	0.325	30	1.6	0.2	30	21.7%	-0.10 [-0.24, 0.04]
Taqi et al.	2	0.24	25	3	0.26	25	21.7%	-1.00 [-1.14, -0.86]
Turunen et al.	1	0.75	29	1	0.75	29	19.5%	0.00 [-0.39, 0.39]
Wongyingsinn et al.	1.01	0.48	30	1.13	0.56	30	20.8%	-0.12 [-0.38, 0.14]
Zingg et al.	1	1.5	39	2	1.25	36	16.4%	-1.00 [-1.62, -0.38]
Subtotal (95% CI)			**153**			**150**	**100.0%**	**-0.43 [-0.93, 0.07]**
Heterogeneity: Tau² = 0.30; Chi² = 99.50, df = 4 (P < 0.00001); I² = 96%								
Test for overall effect: Z = 1.67 (P = 0.09)								
3.1.2 First Bowel Movement								
Levy et al.	1	0.295	30	0.9	0.11	30	34.1%	0.10 [-0.01, 0.21]
Neudecker et al.	2.25	0.98	10	3.02	0.78	10	19.1%	-0.77 [-1.55, 0.01]
Taqi et al.	2.78	1.42	25	4.04	1.46	25	18.6%	-1.26 [-2.06, -0.46]
Wongyingsinn et al.	1.77	0.84	30	1.7	0.8	30	28.1%	0.07 [-0.35, 0.49]
Subtotal (95% CI)			**95**			**95**	**100.0%**	**-0.33 [-0.84, 0.18]**
Heterogeneity: Tau² = 0.19; Chi² = 15.38, df = 3 (P = 0.002); I² = 80%								
Test for overall effect: Z = 1.27 (P = 0.20)								
3.1.3 First Bowel Opened								
Levy et al.	3.1	0.625	30	4	0.53	30	37.3%	-0.90 [-1.19, -0.61]
Turunen et al.	2	2	29	2	1.5	29	8.4%	0.00 [-0.91, 0.91]
Zingg et al.	2.7	0.3	39	3.7	0.3	36	54.2%	-1.00 [-1.14, -0.86]
Subtotal (95% CI)			**98**			**95**	**100.0%**	**-0.88 [-1.16, -0.59]**
Heterogeneity: Tau² = 0.03; Chi² = 4.76, df = 2 (P = 0.09); I² = 58%								
Test for overall effect: Z = 6.06 (P < 0.00001)								
3.1.4 Tolerate Diet								
Hübner et al.	4	1	65	3	0.5	57	18.8%	1.00 [0.72, 1.28]
Levy et al.	2	0.82	30	1.43	0.375	30	18.5%	0.57 [0.25, 0.89]
Neudecker et al.	2	0.25	10	2.33	0.16	10	19.2%	-0.33 [-0.51, -0.15]
Taqi et al.	2	0.24	25	3	0.31	25	19.4%	-1.00 [-1.15, -0.85]
Wongyingsinn et al.	1.46	0.3	30	1.59	0.25	30	19.4%	-0.13 [-0.27, 0.01]
Zingg et al.	4	2.25	39	4	7	36	4.7%	0.00 [-2.39, 2.39]
Subtotal (95% CI)			**199**			**188**	**100.0%**	**0.01 [-0.58, 0.60]**
Heterogeneity: Tau² = 0.47; Chi² = 198.60, df = 5 (P < 0.00001); I² = 97%								
Test for overall effect: Z = 0.04 (P = 0.97)								
Test for subgroup differences: Chi² = 9.33, df = 3 (P = 0.03), I² = 67.8%								

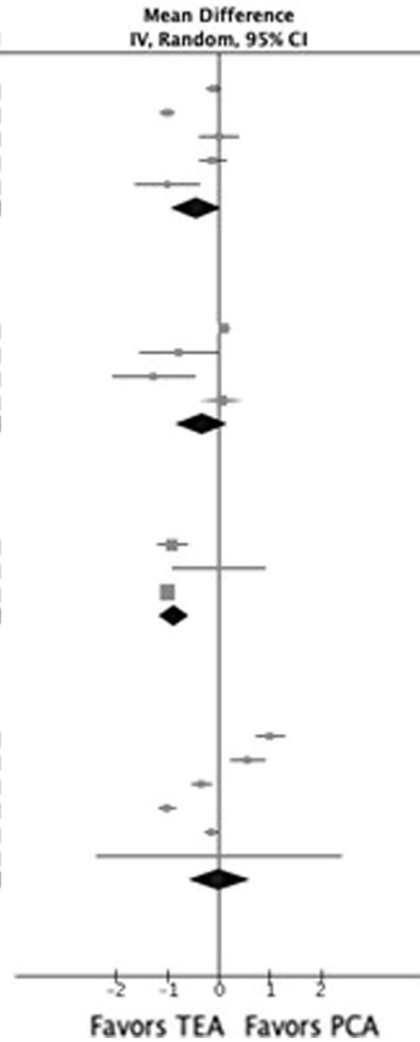

Fig. 7 Postoperative bowel function

Despite the fact that TEA is considered as a safe technique, it has been associated with various complications, such as urinary retention, epidural abscesses, hematomas, persistent neurological deficits, cardiac arrest, and catheter breakage [38, 39]. In a retrospective analysis of von Hosslin et al., the incidence of serious complications and long term adverse events was 0.1% and 0.014%, respectively [39]. On the contrary, PCA-related complications, such as nausea, vomiting,

Operation Duration

Study or Subgroup	TEA Mean	TEA SD	TEA Total	PCA Mean	PCA SD	PCA Total	Weight	Mean Difference IV, Fixed, 95% CI
Hübner et al.	239	107	65	235	104	57	0.5%	4.00 [-33.49, 41.49]
Levy et al.	105	28	30	97	23	30	4.4%	8.00 [-4.97, 20.97]
Neudecker et al.	193	25	10	205	20	10	1.9%	-12.00 [-31.84, 7.84]
Senagore et al.	100	42	23	104	29	24	1.7%	-4.00 [-24.72, 16.72]
Taqi et al.	190	11.6	25	200	10.9	25	19.2%	-10.00 [-16.24, -3.76]
Turunen et al.	120	36.25	29	135	26.25	29	2.8%	-15.00 [-31.29, 1.29]
Wongyingsinn et al.	213	90	30	220	78	30	0.4%	-7.00 [-49.62, 35.62]
Zingg et al.	176	7	39	180	7.5	36	69.0%	-4.00 [-7.29, -0.71]
Total (95% CI)			**251**			**241**	**100.0%**	**-5.05 [-7.78, -2.32]**
Heterogeneity: Chi² = 8.85, df = 7 (P = 0.26); I² = 21%								
Test for overall effect: Z = 3.62 (P = 0.0003)								

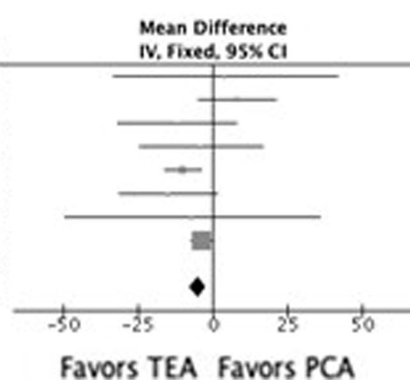

Fig. 8 Operation duration

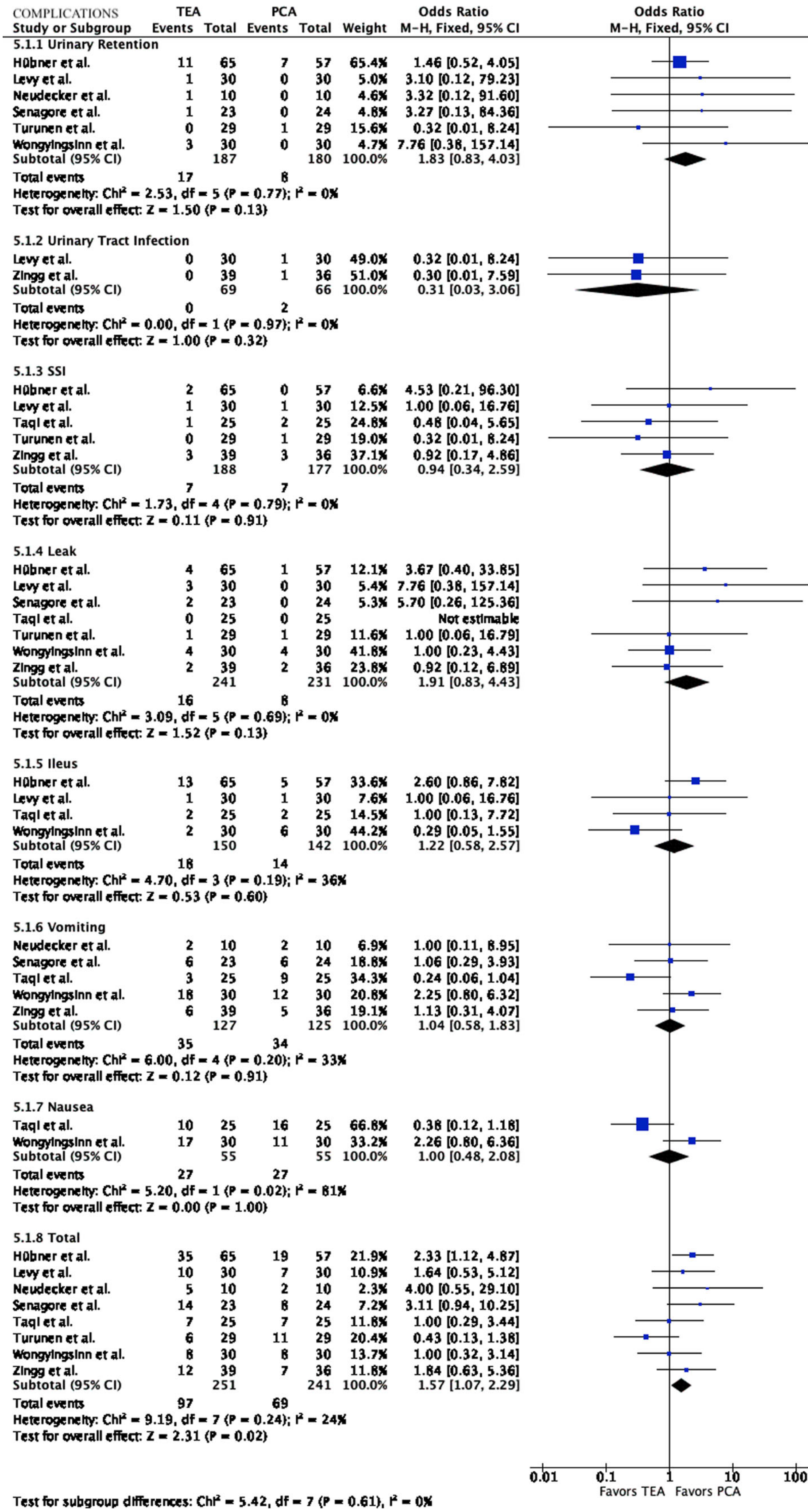

Fig. 9 Complications

and cardiopulmonary compromise, are associated to the systematic administration of opioids [40–42]. However, in a retrospective cohort study of 20,880 patients, the cardiopulmonary complication rate in laparoscopic colectomies was not reduced after the implementation of TEA [10]. Furthermore, according to recent studies, TEA postoperative PONV rates can reach the level of 26% in certain patient subgroups [43, 44]. Although primary pooled results in abdominal surgery displayed a higher complication rate for TEA group, subsequent meta-analyses in laparoscopic colectomies did not confirm that [9, 31, 45]. Our data analysis shows that despite the similar rates of postoperative nausea and vomiting, overall complications are higher in TEA.

Postoperative ileus is another important factor affecting recovery and the subsequent hospitalization cost, after a colorectal operation [2, 4, 6, 46]. This disturbed bowel motility is the result of a sympathetic reflex due to peritoneal trauma that is enhanced by prolonged intestine and mesentery handling [9]. In addition to this, the administration of opioids for adequate analgesia, through activation of the GI tract peripheral μ-opioid receptors, further aggravates postoperative ileus [47, 48]. In TEA, the administration of anesthetics in the thoracolumbar epidural area inhibits the sympathetic tone, allowing, thus, the promotion of intestine peristalsis [13]. Earlier return of bowel activity in combination with a superior analgesic effect established TEA as the gold standard regarding postoperative analgesia in open colectomy [4, 10, 11, 26]. Similarly, in laparoscopic colectomy, Taqi et al. supported a significant reduction in the postoperative ileus rates in TEA group [13]. This assumption was validated by a series of RCTs [14, 19]. Neudecker et al., however, in a small randomized series did not identify significant differences between TEA and PCA in terms of bowel function [19]. Furthermore, several other trials reported similar results [20, 21, 46]. Although overall pooled results imply a superiority of TEA, confinement in ERAS protocol studies contradicts these conclusions [9, 35]. Our meta-analysis suggests that implementation of TEA has as a result a shorter first bowel opened time, with no effect, though, on postoperative ileus rates.

Limitations

Several limitations should be considered, before appraising the results of this study. The main drawback of our meta-analysis was the high levels of heterogeneity identified not only in the primary, but also in the secondary endpoints. Etiological factors of this, between-studies, heterogeneity could possibly be the differences in the analgesia arms, the lack of uniformity in the postoperative medications administered and in the compliance to an ERAS protocol. Furthermore, patient stratification in terms of various factors, such as BMI, ASA, underlying pathology, and operation type, was inconsistent, and thus, this could be another source of bias. In addition to that, the small sample size of the included RCTs does not allow, safely, further sub-analyses to be performed and reduces the significance of our results. Moreover, a few numbers of studies were reported on postoperative pain levels and as a result, the level of evidence from these comparisons is not strong. Reporting of adverse events, in many eligible studies, was not categorized according to a classification system, and complications were not divided in analgesia or surgical related groups. This fact is considered as another important factor that could possibly result to misleading conclusions. Finally, reported methodological and quality flaws of the eligible trials also introduce a significant amount of bias.

Conclusions

Our study is a contemporary attempt to provide a pooled comparison of TEA with PCA regarding the postoperative recovery of the patients submitted to laparoscopic colectomy. When compared to PCA, TEA was associated with lower first bowel opened time, walking, and resting pain levels at the first postoperative days, validating thus the enhanced recovery related to TEA. However, overall complication rate and length of hospital stay were higher when epidural analgesia was performed. In order to draw a safe conclusion and since our findings do not comply with the previous reports of a shorter hospitalization duration using TEA, further RCTs with an adequate sample size and a higher methodological and quality level are required.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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