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Review Article

Epidural vs. transversus abdominis plane block for abdominal surgery – a systematic review, meta-analysis and trial sequential analysis

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Summary

Traditionally, pain relief for abdominal surgery has centred on epidural analgesia, but transversus abdominis plane block is increasingly being used. Our aim was to compare the analgesic efficacy and the side-effect profile of transversus abdominis plane block with epidural analgesia in a systematic review with meta-analysis and trial sequential analysis. After a systematic search of the electronic databases, we identified 18 randomised controlled trials with 1220 patients. Confirmed by trial sequential analysis, our first co-primary outcome, postoperative pain score at rest at 12 h, was decreased by a mean difference (95%CI) of 0.69 (0.12–1.27; p = 0.02) with epidural analgesia compared with transversus abdominis plane block, with the quality of evidence graded as low. No difference was found for the second co-primary outcome, postoperative pain score at rest at 24 h, with the quality of evidence rated as very low. Relative to transversus abdominis plane block, epidural analgesia further reduced the need for intravenous morphine-equivalent consumption during the 0–24 h interval by a mean difference (95%CI) of 5.91 mg (2.34–9.49; p = 0.001) at the expense of an increased incidence of hypotension at 72 h, with a risk ratio (95%CI) of 5.88 (2.08–16.67; p < 0.001). Our meta-analysis was limited by detection and performance bias, significant statistical heterogeneity and publication bias. In view of the minimal clinically important difference in postoperative pain scores, epidural analgesia was interpreted to not be clinically different to transversus abdominis plane block after abdominal surgery. With transversus abdominis plane block, the increase in intravenous morphine-equivalent consumption at 24 h should be balanced against the decreased risk of hypotension at 72 h. In choosing between epidural analgesia and transversus abdominis plane block, potential benefits should be balanced against the reported risk of harm, although the confidence in the evidence varied, underlining the uncertainty in our estimates.

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Introduction

In the past, pain relief for abdominal surgery has centred on epidural analgesia, a widely advocated regional technique [1]. Enthusiasm for this, however, has decreased with the appreciation of the possible technical difficulties in insertion, a relatively high incidence of block failure, and the risk of neuraxial complications such as hypotension, abscess and haematoma [2]. Further, the growing focus on elements of enhanced recovery, including minimally invasive laparoscopic surgical approaches, postoperative anticoagulation practices, and early ambulation, as well as physiotherapy [3], has influenced the increasing use of

alternative and less invasive analgesic strategies such as transversus abdominis plane (TAP) block.

First described in 2001 by Rafi et al. as a landmark-guided approach [4], the aim of the TAP block was to anaesthetise the seventh to the twelfth thoracic spinal nerves, and the iliohypogastric and the ilioinguinal nerves. Numerous modifications of the TAP block technique, including the use of ultrasound, have now been described. Hence, TAP block is a term for a heterogenous group of approaches that differ in the site of needle insertion and injection, but share the common endpoint of injection of local anaesthetic into the fascial plane between the internal oblique and the transversus abdominis muscles [1]. Compared with placebo, TAP block has been associated with a decrease in pain scores and a reduction in opioid consumption in the postoperative period [5].

In the evaluation of the efficacy and the utility of the TAP block relative to epidural analgesia in abdominal surgery, two previous meta-analyses have found no evidence of a difference in pain scores as well as a lower incidence of hypotension and a shorter hospital stay with the TAP block [6, 7]. These meta-analyses, nevertheless, have been limited by the modest number of source studies, and the possibility of a type-2 statistical error cannot be excluded. In light of this, the uncertainty surrounding the role of the TAP block for abdominal surgery continues. Moreover, since these systematic reviews have been performed, further trials have been published, potentially adding weight to the available evidence base.

Our aim was to conduct a systematic review and meta-analysis to compare the analgesic efficacy, side-effects and the functional outcomes of TAP block with epidural analgesia in patients undergoing abdominal surgery. In order to control for the risk of false negative and false positive findings, we used trial sequential analysis with the objective of increasing the validity of our results.

Methods

We followed the recommendations from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [8]. In order to find relevant trials for this and a related meta-analysis, we performed a systematic search of the electronic databases, Central, CINAHL, Embase, Global Health, LILACS, MEDLINE, Scopus and Web of Science, from inception to 11 December 2019. Controlled vocabulary terms and text words, relating to the main components of the review were chosen, including 'epidural', 'neuraxial' or 'caudal' analgesia and 'TAP' or 'nerve block'. Further details of the search strategy are provided in the Supporting Information (Appendix S1).

All of the retrieved article citations were entered into a reference management software program, Rayyan (Qatar Computing Research Institute, 2016, Doha, Qatar), where the duplicates were removed and the remainder were screened for eligibility. Only randomised controlled trials that included adult patients undergoing abdominal surgery with TAP block as the intervention and epidural analgesia as the comparator, and which had been published in the English language, were considered for inclusion. Search results were independently screened by two authors (ND and KE) using the title and the abstract. The full texts of potentially eligible articles were subsequently evaluated for inclusion. Discrepancies were resolved by discussion until consensus was reached or, if needed, involvement of the third author (EA). We then manually reviewed the reference lists of all included articles for additional studies, and queried Google Scholar for relevant trials not already identified using the previously described search strategy.

Once all studies to be included in the present meta-analysis had been identified, the same two authors independently performed an assessment of the risk of bias in each trial and extracted data from the trials. Discrepancies were resolved by discussion until consensus was reached or, if required, by involvement of the third author. The Cochrane Collaboration's tool can be applied to evaluate for the presence of different types of bias, to include selection (randomised sequence generation and allocation concealment), performance and detection (blinding), attrition (incomplete outcome data), and reporting (selective reporting) bias, and thus facilitates the examination of the methodological quality of studies [9]. Continuous outcomes were extracted as means and standard deviations. If the mean and the standard deviation had not been reported, we followed the recommendations from the Cochrane Collaboration, approximating the mean to be equivalent to the median, and estimating the standard deviation to be the interquartile range/1.35 or the range/4 [10]. Dichotomous outcomes were converted to the overall numbers of incidence. Data presented in only graphical format were extracted with a plot digitising software program, Plot Digitizer (Version 2.1, Free Software Foundation, 2015, Boston, USA). In the event that we needed to clarify the details of their methodology or request missing data, we attempted to contact the authors of the respective articles, up to three times in total.

Data extracted from the trials included the following: the sample size and number of patients in each study arm;

nature of surgery; main mode of anaesthesia; approach, method of localisation and technique of injection for TAP block; local anaesthetic bolus and infusion protocol for TAP block and epidural techniques; and the postoperative analgesia regimen. Our co-primary outcomes were the postoperative pain score at rest at 12 h and 24 h. Secondary outcomes included: the postoperative pain score at rest at 0–2 h, 48 h and 72 h; postoperative pain score on movement at 0–2 h, 8–12 h, 24 h, 48 h and 72 h; interval intravenous (i.v.) morphine-equivalent consumption at 0–24 h, 24–48 h and 48–72 h; rate of failure of both blocks; incidence of postoperative hypotension, nausea and vomiting, pruritus and urinary retention at 24 h, 48 h and 72 h; rate of wound infection; time to first flatus and bowel sounds; time to ambulation; quality of recovery; and hospital length of stay.

Data were entered from a standardised form in Microsoft® Excel (Microsoft Corp, Redmond, WA, USA) to Review Manager (Version 5.3, The Nordic Cochrane Centre, 2014, Copenhagen, Denmark) by one author (ND), the accuracy of which was confirmed by another author (EA). It was our intention to conduct meta-analysis for an outcome solely if it was reported by two or more randomised controlled trials. Statistical heterogeneity, I^2, consequent to clinical or methodological diversity, was calculated for each outcome with predetermined thresholds for low (25–49%), moderate (50–74%) and high (≥ 75%) levels [11]. If low heterogeneity was found, it was assumed that the true effect of the intervention was the same in every included trial, and a fixed effect model was chosen to represent the best estimate of the intervention effect. In the event that moderate or high heterogeneity was present, it was assumed that the effect of the intervention was not the same in every included trial but followed some distribution, and the DerSimonian and Laird random effects model was chosen to represent the average intervention effect. For continuous outcomes, data were subjected to the inverse-variance method, where the weight allocated to each trial is selected to be the inverse of the variance of the effect estimate, resulting in the calculation of a weighted mean difference (95%CI). For dichotomous outcomes, data were subjected to the Mantel-Haenzel method, resulting in the calculation of a risk ratio (95%CI). All tests were two-tailed and performed at the 5% statistical significance level. In order to investigate statistical heterogeneity for our co-primary outcomes, prespecified sub-group analyses were undertaken for: the nature of surgery (open, laparoscopic or combination of open, laparoscopic and robotic or otherwise unspecified); the approach of the TAP block (lateral, subcostal or combined); and the technique of injection for the TAP block (single-shot or continuous catheter).

To evaluate the risk of publication bias in relation to all outcomes, a funnel plot was drawn and visually examined. On the y-axis, the standard error of the mean difference of the outcome of interest (measure of trial size) was plotted as a function, on the x-axis, of the mean difference of the outcome. Our results were verified with the performance of Duval and Tweedie's trim and fill test, in which the smaller studies producing funnel plot asymmetry are removed and the omitted trials and their missing counterparts are replaced, and Egger's linear regression test using Comprehensive Meta-Analysis (Version 3.3, Biostat, 2014, New Jersey, USA). The quality of evidence for each outcome was rated for risk of bias, inconsistency, indirectness, imprecision and publication bias, and an overall grading of the quality of evidence for all outcomes was produced, with reference to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system [12].

Last, we performed a trial sequential analysis with TSA Viewer (Version 0.9.5.10 Beta, Copenhagen Trial Unit, 2016, Copenhagen, Denmark). The Sidik Jonkman random effects model, that is less likely to underestimate the heterogeneity between trials, was chosen to calculate the Z-statistic, which is equal to the meta-analysed intervention effect divided by its standard error. In cumulative meta-analysis, adjusted significance testing has two objectives: first, to measure and account for the strength of the available evidence; and second, to control for the risk of type-1 and type-2 statistical errors occurring when repeated significance testing on accumulating data is performed [13]. The strength of the available evidence can be considered by determining the required information size for a conclusive and reliable meta-analysis. It can be derived from the risk of type-1 and type-2 statistical errors, which we set at 5% and 20%, respectively, resulting in a power of 80%. In order to control for the risk of type 1 error, the Lan and DeMets alpha-spending function was used to adjust the threshold for statistical significance to account for the elevated risk of random error before the meta-analysis has surpassed its required information size. In order to control for the risk of type-2 error, an extension of the Lan and DeMets alpha-spending function was used to adjust the threshold for non-inferiority or non-superiority, or no difference, representing what is referred to as futility boundaries before the meta-analysis has surpassed its required information size.

Results

Of the initial 3213 unique article citations identified by the search strategy, 18 randomised controlled trials fulfilled the

inclusion criteria [14–31]. Details of the screening process are illustrated in Fig. 1 and the results of the risk of bias assessment are presented in Fig. 2. None of the trials described measures to blind participants, personnel and outcome assessors, placing them at risk of performance and detection biases. In the 14 instances where we needed to clarify details of trial methodology or request missing data, three authors responded with the required information [17, 21, 25].

Overall, the number of patients included in each trial ranged from 40 to 93, with the exception of one trial that had 179 [24]. The included trials comprised a total of 1220 patients, 614 of whom received TAP block and 606 of whom received epidural analgesia. Characteristics of the trials are detailed in Table 1. In 13 trials, the abdominal surgery was open [14, 16, 17, 19, 20, 22, 23, 25, 26, 28–30]; in one trial it was laparoscopic [31]; and in four trials it was combination of open, laparoscopic and robotic or otherwise undefined [18, 21, 24, 27]. The main mode of anaesthesia was general in most trials [14, 16–26, 28–31] and neuraxial in two trials [15, 27]. Transverse abdominis plane block was performed under ultrasound guidance in all of the trials but three, where it was either inserted using the landmark technique [29] or surgically

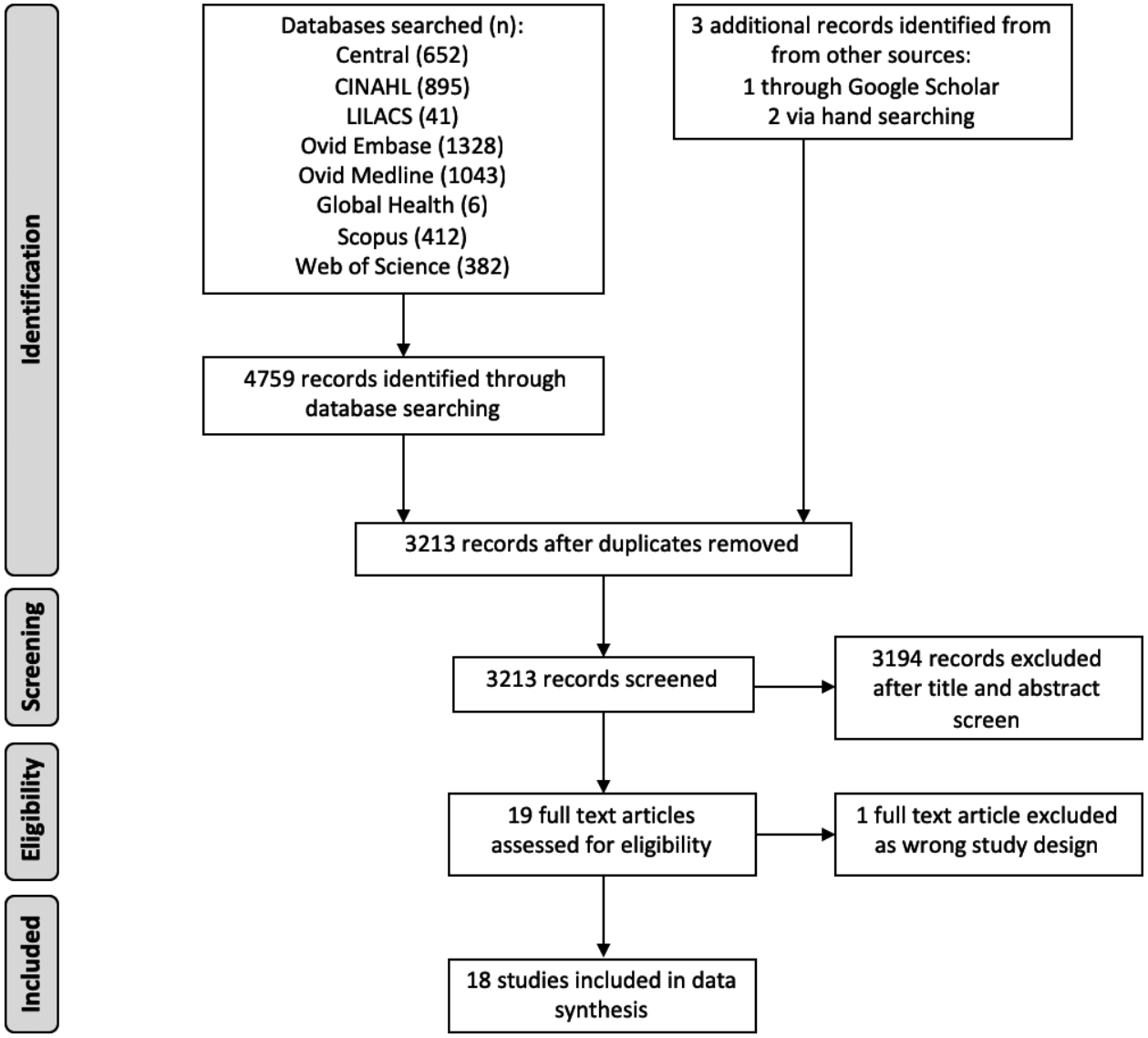

Figure 1 PRISMA flow diagram summarising the retrieved, included and the excluded randomised controlled trials. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

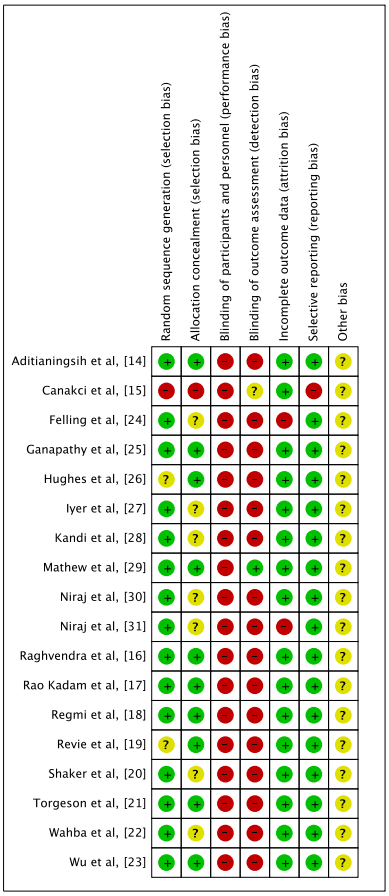

Figure 2 Risk of bias assessment of included trials using the Cochrane's Collaboration's tool. ?, unclear risk; -, high risk; + low risk.

placed [19, 26]. In nine trials, the approach of the TAP block was lateral [15, 16, 18, 19, 24, 26–29], whereas it was subcostal in four trials [21–23, 30] and combined or either lateral or subcostal in five trials [14, 17, 20, 25, 31]. The TAP block consisted of a single-shot injection in eight trials [14–16, 20, 23, 24, 28, 29] with the use of a continuous catheter in 10 trials [17–19, 21, 22, 25–27, 30, 31]. The failure rate of TAP block and epidural analgesia varied, respectively, from 0–37% to 0–30%. Moreover, two trials included an intra-operative injection of local anaesthetic through an epidural catheter in order to provide surgical analgesia in the TAP group [29, 30], while two trials involved the additional surgical placement of a rectus sheath block in the TAP group [19, 26].

Our first co-primary outcome, the postoperative pain score at rest at 12 h, was reported by 11 trials from 747 patients [14, 16, 18, 19, 22, 25, 26, 28–31]. It was decreased by a mean difference (95%CI) of 0.69 (0.12–1.27; p = 0.02, I^2 = 94%) with epidural analgesia compared with TAP block (Fig. 3). In the leave-one-out sensitivity analysis, the mean difference (95%CI) varied from 0.55 (0.04–1.06) with the omission of Raghvendra et al. [16] to 0.77 (0.16–1.37) with the omission of one of Aditianingsih et al., Hughes et al., Ganapathy et al. or Kandi et al. [14, 25, 26, 28]. If the three trials that contributed the most weight to the meta-analysis of the postoperative pain score at rest at 12 h were excluded [16, 19, 28], then no difference was found between TAP block and epidural analgesia, with a mean difference (95%CI) of 0.54 (−0.10 to 1.18; p = 0.10, I^2 = 88%). The high level of statistical heterogeneity was not explained by the type of surgery (p = 0.14), or the approach (p = 0.33) or the technique of injection (p = 0.91) for the TAP block. Other than a superiority of epidural analgesia relative to TAP block using the continuous catheter technique, where there was a mean difference (95%CI) of 0.67 (0.03–1.31, I^2 = 89%), further sub-group differences were not demonstrated. Both the Duval and Tweedie's trim and fill test and the Egger's test suggested the presence of publication bias. In the former test, two missing trials were imputed to the right of the mean difference. In the trial sequential analysis, the required information size of 648 patients was reached and the Z-curve crossed the trial sequential monitoring boundary, suggesting firm evidence for the superiority of epidural analgesia compared with TAP block for this particular outcome (Fig. 4).

Our second co-primary outcome, the postoperative pain score at rest at 24 h, was reported by 13 trials in 650 patients [14, 16–19, 22, 23, 25, 26, 28–31]. No difference was demonstrated between TAP block and epidural analgesia (Fig. 5). In the leave-one-out sensitivity analysis, the mean difference (95%CI) varied from 0.30 (−0.14 to 0.73) with the omission of Raghvendra et al. [16] to 0.73 (−0.05 to 1.50) with the omission of Mathew et al. [29]. Our results did not change if the trials that contributed the most weight to the meta-analysis of the postoperative pain score at rest at 24 h were excluded [19, 28]. The high level of statistical heterogeneity was not explained by the type of surgery (p = 0.16), the approach (p = 0.57) or the technique of injection (p = 0.64) for the TAP block. Other than a superiority of epidural analgesia relative to TAP block in laparoscopic surgery, where there was a mean difference of 0.96 (95%CI 0.24–1.69), further sub-group differences were not demonstrated. Only the Duval and Tweedie's trim and fill test and not the Egger's test suggested the presence of publication bias. In the former test, four missing trials were imputed to the right of the mean difference. In the trial sequential analysis, the required information size of 1255 patients was not reached, and the Z-curve had not crossed either the trial sequential or futility boundaries, suggesting

Table 1 Characteristics of the included trials.

Trial	Group (n)	Surgery	TAP block technique	Local anaesthetic for TAP block	Local anaesthetic for epidural	Anaesthesia	Postoperative analgesia
Aditianingsih et al. [14]	TAP block (25) Epidural analgesia (25)	Laparoscopic donor nephrectomy with a Pfannenstiel incision	USG, bilateral lateral and unilateral subcostal approach, single-shot injection	20 ml bupivacaine 0.25% for each injection	Continuous postoperative infusion of bupivacaine 0.125% at a rate of 6 $ml.h^{-1}$	General anaesthesia	i.v. morphine PCA
Canakci et al. [15]	TAP block (40) Epidural analgesia (40)	Caesarean section	USG, bilateral lateral approach, single-shot injection	20 ml bupivacaine 0.25% on each side	Single bolus of 16 ml bupivacaine 0.5%, fentanyl 50 μg and morphine 3 mg	Neuraxial anaesthesia	Dexketoprofen PRN
Felling et al. [24]	TAP block (92) Epidural analgesia (87)	Open, laparoscopic and robotic abdominal surgery	USG, bilateral lateral approach, single-shot injection	20 ml liposomal bupivacaine 133 mg on each side	Continuous infusion of bupivacaine 0.0625% and fentanyl of unspecified concentration at a rate of 6–8 $ml.h^{-1}$	General anaesthesia	Regular paracetamol and NSAIDs gabapentin in the latter part of the study, opioids PRN
Ganapathy et al. [25]	TAP block (26) Epidural analgesia (24)	Laparotomy	USG, bilateral lateral and subcostal approach, continuous block	Lateral TAP: 10 ml ropivacaine 0.5% bolus injection on each side Subcostal TAP: 20 ml ropivacaine 0.5% bolus injection on each side Single lateral and subcostal TAP injections followed by a combined continuous infusion of ropivacaine 0.35% at a rate of 4–5 $ml.h^{-1}$ on each side for 72 h	5 ml bupivacaine 0.25% ± additional 3 ml bupivacaine 0.25% boluses followed by a continuous postoperative infusion of bupivacaine 0.1% and hydromorphone 10 $\mu g.ml^{-1}$ at a rate of 8 $ml.h^{-1}$ for 72 h	General anaesthesia	Regular paracetamol, naproxen and gabapentin
Hughes et al. [26]	TAP block (49) Epidural analgesia (44)	Open liver surgery	Surgical placement under direct vision, unilateral lateral and rectus sheath approaches, continuous block	40 ml levobupivacaine 0.125% bolus injection in total followed by a combined continuous infusion of levobupivacaine 0.375% at a rate of 4 $ml.h^{-1}$ for 48 h	10 ml levobupivacaine of unspecified concentration followed by a continuous infusion of levobupivacaine 0.1% at an unspecified rate	General anaesthesia	i.v. morphine PCA

(continued)

Table 1 (*continued*)

Trial	Group (n)	Surgery	TAP block technique	Local anaesthetic for TAP block	Local anaesthetic for epidural	Anaesthesia	Postoperative analgesia
Iyer et al. [27]	TAP block (33) Epidural analgesia (36)	Lower abdominal surgery	USG, bilateral lateral approach, continuous block	20 ml bupivacaine 0.125% boluses every 8 h through each catheter for 48 h	10 ml bupivacaine 0.125% boluses every 8 h for 48 h	Neuraxial anaesthesia	Paracetamol and tramadol PRN
Kandi et al. [28]	TAP block (30) Epidural analgesia (30)	Laparotomy	USG, bilateral lateral approach, single-shot injection	20 ml bupivacaine 0.125% on each side	Continuous infusion of bupivacaine 0.125% at a rate of 4–8 $ml.h^{-1}$ for 48 h unless still needed for pain relief	General anaesthesia	Paracetamol and morphine PRN
Mathew et al. [29]	TAP block (20) Epidural analgesia (20)	Total abdominal hysterectomy with a Pfannenstiel incision	Landmark guided, bilateral lateral approach, single-shot injection	15 ml bupivacaine 0.25% on each side	Intra-operative: 6–8 ml lidocaine 2% with adrenaline 5 μg ml^{-1} every 90 min Postoperative: 8 ml bupivacaine 0.125% every 6 h for 24 h	General anaesthesia	Morphine PRN
Niraj et al. [30]	TAP block (27) Epidural analgesia (31)	Laparotomy	USG, bilateral subcostal approach, continuous block	1 $mg.kg^{-1}$ bupivacaine 0.375% boluses every 8 h through each catheter for 72 h	20 ml bupivacaine 0.25% followed by a continuous postoperative infusion of bupivacaine 0.125% and fentanyl 2 $\mu g.ml^{-1}$ at a rate of 6–12 $ml.h^{-1}$ and a bolus of 2 ml with a lock out period of 30 min for 72 h	General anaesthesia	Regular paracetamol and i.v. tramadol, epidural analgesia if TAP block failed and i.v. morphine PCA if epidural failed
Niraj et al. [31]	TAP block (30) Epidural analgesia (31)	Laparoscopic abdominal surgery	USG, bilateral lateral approach, continuous block and bilateral subcostal approach, single-shot injection	2.5 $mg.kg^{-1}$ levobupivacaine 0.375% in total for all four quadrant blocks followed by a continuous infusion of levobupivacaine 0.25% through both catheters at a rate of 8–10 $ml.h^{-1}$ for 48 h	20 ml bupivacaine 0.25% followed by a continuous infusion of bupivacaine 0.125% and fentanyl 2 $\mu g.ml^{-1}$ at a rate of 8–12 $ml.h^{-1}$ and a bolus of 2 ml with a lock out period of 30 min	General anaesthesia	Regular paracetamol and diclofenac with tramadol PRN

(continued)

Table 1 (*continued*)

Trial	Group (n)	Surgery	TAP block technique	Local anaesthetic for TAP block	Local anaesthetic for epidural	Anaesthesia	Postoperative analgesia
Raghvendra et al. [16]	TAP block (30) Epidural analgesia (30)	Total abdominal hysterectomy	USG, bilateral lateral approach, single-shot injection	1.5 mg.kg^{-1} ropivacaine 0.75% at a maximum dose of 150 mg on each side	10–15 ml ropivacaine 0.5% ± additional 5 ml ropivacaine 0.5% bolus to reach a sensory block up to T8 followed by a continuous postoperative infusion of ropivacaine 0.2% at a rate of 10 ml.h^{-1}	General anaesthesia	i.v. tramadol PCA
Rao Kadam et al. [17]	TAP block (22) Epidural analgesia (19)	Laparotomy	USG, bilateral lateral or subcostal approach depending on the surgery, continuous block	20 ml ropivacaine 0.375% bolus injection on each side followed by a continuous infusion of ropivacaine 0.2% at a rate of 8 ml.h^{-1} through each catheter for 72 h	8–15 ml ropivacaine 0.2% followed by a continuous postoperative infusion of ropivacaine 0.2% at a rate of 5–15 ml.h^{-1} for 72 h	General anaesthesia	Regular paracetamol and i.v. fentanyl PCA
Regmi et al. [18]	TAP block (35) Epidural analgesia (35)	Lower abdominal surgery	USG, bilateral lateral approach, continuous block	0.4 ml kg^{-1} bupivacaine 0.25% at a maximum dose of 2 mg kg^{-1} on each side followed by a continuous infusion of bupivacaine 0.125% at a rate of 5 ml h^{-1} through each catheter for 24 h	15 ml bupivacaine 0.25% followed by a continuous postoperative infusion of bupivacaine 0.125% at a rate of 5–12 ml h^{-1} for 24 h	General anaesthesia	i.v. morphine PCA
Revie et al. [19]	TAP block (49) Epidural analgesia (44)	Open liver surgery	Surgical placement under direct vision, unilateral lateral and rectus sheath approaches, continuous block	20 ml levobupivacaine 0.25% bolus injection, unspecified whether per catheter or in total, followed by a combined continuous infusion of levobupivacaine 0.375% at a rate of 4 ml.h^{-1} for 48 h	Continuous infusion of bupivacaine 0.1% and fentanyl 2 μg.ml^{-1} at a rate of 7–10 ml.h^{-1}	General anaesthesia	Regular paracetamol for all patients and unspecified opiate PCA in TAP group
Shaker et al. [20]	TAP block (32) Epidural	Laparotomy	USG, bilateral lateral and subcostal	10 ml liposomal bupivacaine and 20 ml	Bupivacaine 0.125% and fentanyl 2	General anaesthesia	Paracetamol, ketorolac, gabapentin

(continued)

Table 1 (*continued*)

Trial	Group (n)	Surgery	TAP block technique	Local anaesthetic for TAP block	Local anaesthetic for epidural	Anaesthesia	Postoperative analgesia
	analgesia (35)		approaches, single-shot injection	bupivacaine 0.5% on each side	mcg.ml^{-1} at an unspecified rate		and opioid PRN
Torgeson et al. [21]	TAP block (41) Epidural analgesia (37)	Laparoscopic or open colorectal surgery	USG, bilateral, subcostal approach, single-shot injection	40 ml liposomal bupivacaine 133 mg on each side	Boluses of bupivacaine 0.0625% and fentanyl 2 μg.ml^{-1} intra-operatively followed by a continuous postoperative infusion at a rate of 6 ml.h^{-1} and a bolus of 2 ml with a lock out period of 30 min for 48 h	General anaesthesia	Regular paracetamol and ketorolac
Wahba et al. [22]	TAP block (22) Epidural analgesia (22)	Laparotomy	USG, bilateral subcostal approach, continuous block	20 ml bupivacaine 0.25% on each side followed by boluses of 15 ml bupivacaine 0.25% every 8 h through each catheter	10 ml bupivacaine 0.125% followed by a continuous postoperative infusion of bupivacaine 0.125% at a rate of 6–8 ml.h^{-1}	General anaesthesia	i.v. morphine PCA
Wu et al. [23]	TAP block (27) Epidural analgesia (29)	Laparotomy	USG, bilateral subcostal approach, single-shot injection	20 ml ropivacaine 0.375% on each side	Before induction of anaesthesia: 8 ml ropivacaine 0.25% Intra-operative: Continuous infusion of ropivacaine 0.25% at a rate of 5 ml.h^{-1} Postoperative: Continuous infusion of bupivacaine 0.125% and morphine 8 μg.ml^{-1} at a rate of 5 ml.h^{-1} for 72 h	General anaesthesia	i.v. morphine PCA

PCA, patient-controlled analgesia; PRN, pro re nata; TAP, transversus abdominis plane; USG, ultrasound guided.

that an adequate information size has not been reached for this outcome (Fig. 6).

In regard to the secondary outcomes, the results of the meta-analyses are presented in Table 2. The quality of evidence evaluated with the GRADE system for each primary and secondary outcome is detailed in Table 3. Of the other outcomes, differences in the method of reporting data and insufficient data precluded the meta-analysis of: the incidence of hypotension and postoperative nausea and vomiting at other time-points; the rate of pruritus and wound infection; the time to first bowel sounds; and the quality of recovery. In the one trial which examined the rate of pruritus, no difference was found between epidural analgesia and TAP block [23]. The rate of wound infection

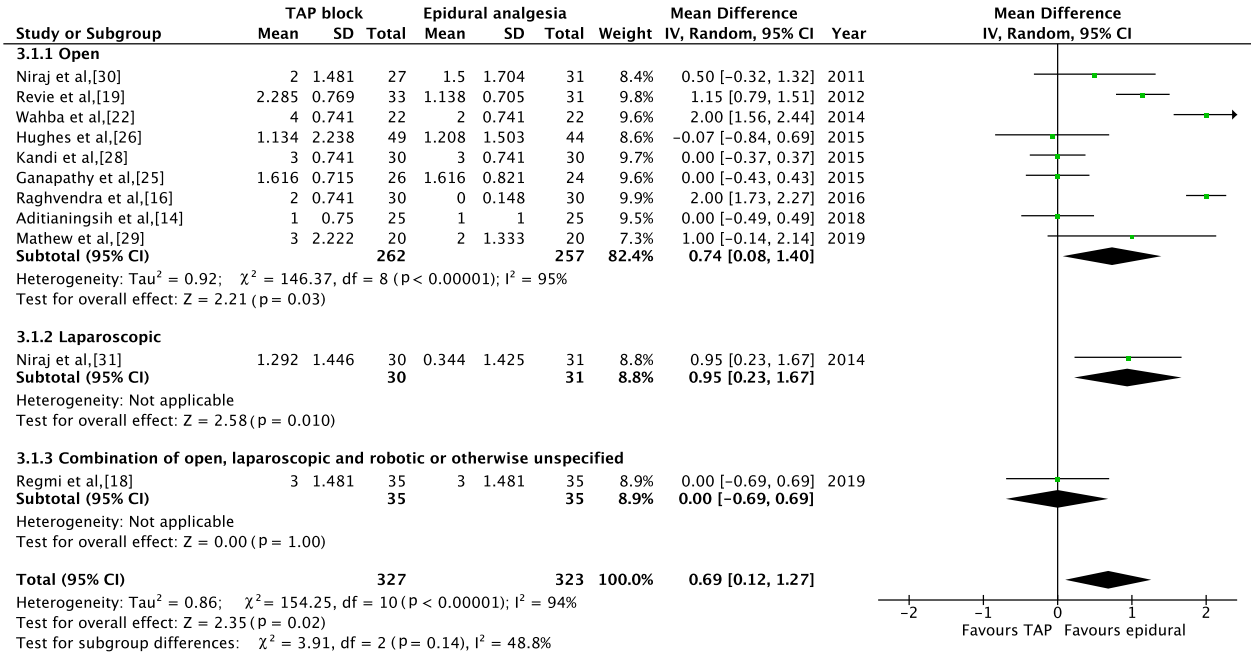

Figure 3 Forest plot of the pain score at rest at 12 h according to the type of surgery. TAP, transversus abdominis plane.

and the time to first bowel sounds were not revealed to be different between TAP block and epidural analgesia in two trials [25, 26] and one trial, respectively [25]. In terms of the quality of recovery, no difference was shown between epidural analgesia and TAP [29]. None of the trials reported the incidence of urinary retention.

Discussion

Our meta-analysis demonstrated that epidural analgesia in comparison with TAP block decreased the postoperative pain score at rest at 12 h and 48 h by a mean difference of 0.7 and 0.8 units, respectively, and on movement at 0-2 h and 48 h by a mean difference of 0.9 and 0.6 units,

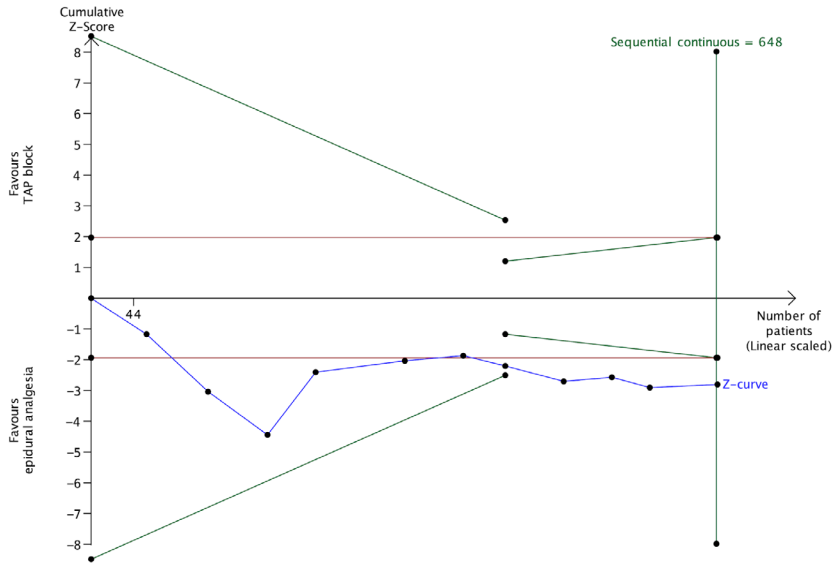

Figure 4 Trial sequential analysis for the pain score at rest at 12 h. The red line depicts the conventional threshold for statistical significance at p = 0.05 and the outer and the inner angled green lines, respectively, represent the adjusted threshold for statistical significance and the futility boundaries. The blue line depicts the Z-curve and the vertical green line is the required information size.

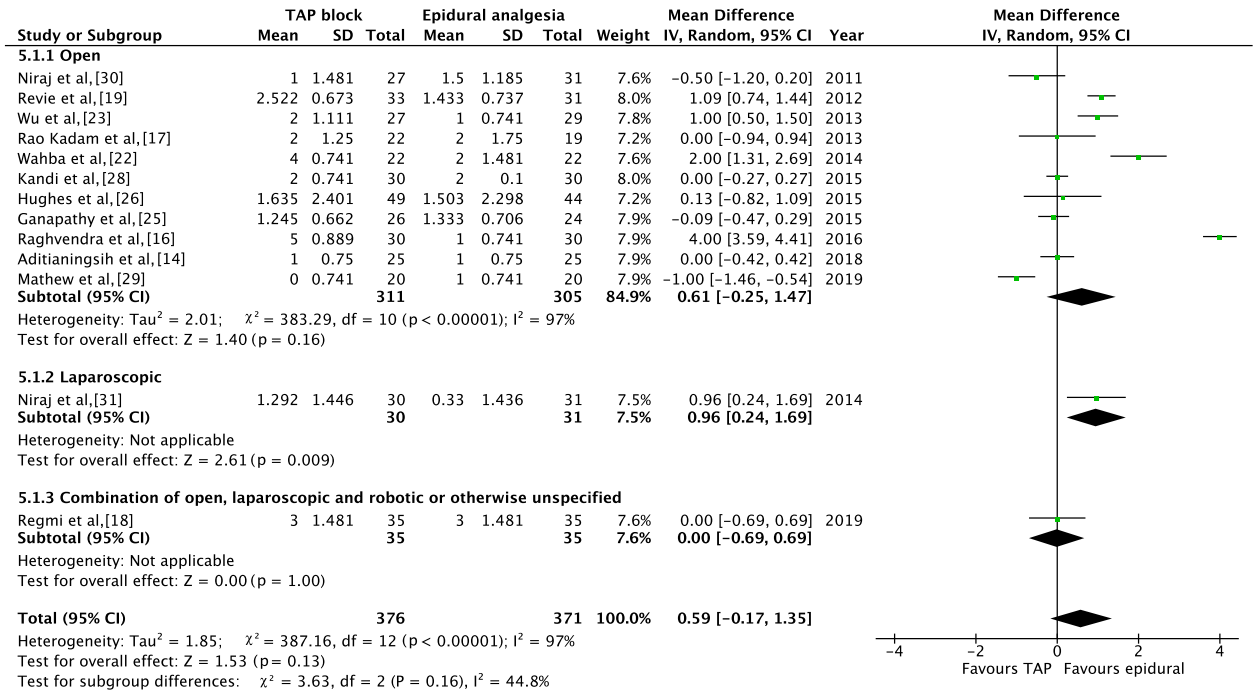

Figure 5 Forest plot of the pain score at rest at 24 h according to the type of surgery. TAP, transversus abdominis plane.

respectively. The quality of evidence was rated to be low and very low, respectively, for the co-primary outcomes of the postoperative pain score at rest at 12 h and 24 h. Relative to TAP block, epidural analgesia further reduced the need for i.v. morphine-equivalent consumption at the 0–24 h interval by a mean difference of 6 mg at the expense of an increased incidence of hypotension at 72 h, with no significant effect on functional outcomes.

It is likely that these findings could be due to the epidural delivering somatic and visceral analgesia and the

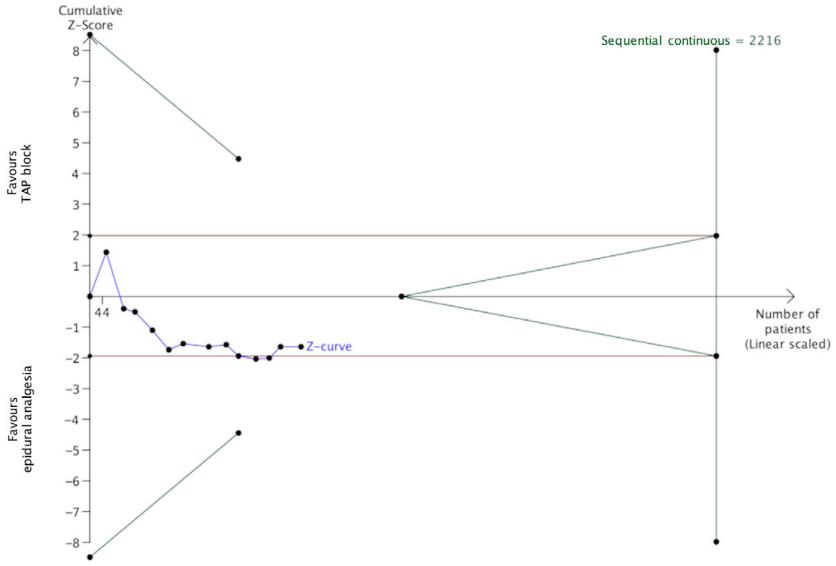

Figure 6 Trial sequential analysis for the pain score at rest at 24 h. The red line depicts the conventional threshold for statistical significance at p = 0.05 and the outer and the inner angled green lines, respectively, represent the adjusted threshold for statistical significance and the futility boundaries. The blue line depicts the Z-curve and the vertical green line is the required information size.

Table 2 Meta-analysis of the secondary outcomes. Values are mean difference or risk ratio.

Outcomes	Number of trials	Number of patients		Effect size (95%CI)	I^2 (%)	p value
		TAP	Epidural			
Pain score at rest						
0–2 h [14, 16–19, 22, 23, 26, 28, 29, 31]	11	323	316	0.52 (−0.26 to 1.31)	96	0.190
48 h [17, 19, 20, 22, 23, 25, 26, 30, 31]	9	268	266	0.75 (0.18 to 1.32)	87	0.010
72 h [17, 23, 25, 26, 30]	5	151	147	0.11 (−0.08 to 0.31)	31	0.270
Pain score on movement						
0–2 h [14–19, 22, 23, 26, 31]	10	273	266	0.88 (0.1 to 1.65)	88	0.030
12 h [14–16, 18, 19, 22, 25, 26, 30, 31]	10	277	273	0.67 (−0.13 to 1.48)	91	0.100
24 h [14–19, 22, 23, 25, 26, 30, 31]	12	326	321	0.87 (−0.62 to 2.36)	99	0.250
48 h [17, 19, 22, 23, 25, 26, 30, 31]	8	210	207	0.59 (0.03 to 1.14)	79	0.040
72 h [17, 23, 25, 26, 30]	5	151	147	0.00 (−0.74 to 0.73)	77	0.990
Interval i.v. morphine-equivalent consumption						
0–24 h (mg) [14, 16–18, 22–24, 26, 29]	9	322	311	5.91 (2.34 to 9.49)	95	0.001
24–48 h (mg) [17, 22–24, 26]	5	212	201	3.38 (−2.22 to 8.97)	84	0.240
48–72 h (mg) [17, 23, 24, 26]	4	190	179	−0.22 (−5.76 to 5.31)	82	0.940
Failure and side-effects						
Failure rate [15,17,18,21,23,25,27,30,31]	9	289	289	0.97 (0.60 to 1.56)	0	0.890
Incidence of postoperative nausea and vomiting at 24 h [28, 29]	2	17	21	0.81 (0.49 to 1.35)	0	0.410
Incidence of hypotension at 24 h [17, 18]	2	57	54	0.19 (0.03 to 1.02)	0	0.050
Incidence of hypotension at 72 h [23, 25, 26]	3	102	97	0.17 (0.06 to 0.48)	0	< 0.001
Functional outcomes						
Time to first flatus (h) [21–26, 31]	7	287	274	4.82 (−1.23 to 10.87)	71	0.120
Time to ambulation (h) [22,26,31]	3	101	97	−8.13 (−16.19 to −0.07)	74	0.050
Hospital length of stay (days) [17,21,24,28,31]	5	215	204	−0.07 (−0.27 to 0.13)	31	0.490

TAP, transversus abdominis plane.

TAP block producing somatic analgesia, that is just to the skin, muscles and aponeuroses, transversalis fascia, and the parietal peritoneum of the abdominal wall [1]. In the interpretation of these differences in pain scores with epidural analgesia and TAP block, it must be remembered that a decrease in the pain score may not equate to a clinically important reduction in pain or an improvement in the patient's postoperative experience. Studies have indicated that a change in the pain score on the visual analogue scale of 10–20 out of 100 mm or 33% should indicate a clinically important difference in the intensity of pain [32–34]. Notably, this difference between epidural analgesia and TAP block in the postoperative pain score at rest at 12 h did not persist if the three most influential trials were excluded from the meta-analysis. It is possible that their methodology inherently favoured epidural analgesia over TAP block, either because the epidural approach consisted of a continuous infusion unlike the single-shot injection of TAP block, or the TAP block involved a unilateral rather than bilateral technique insufficient to cover the surgical site. No differences were revealed between epidural analgesia and TAP block in the postoperative pain score or the need for i.v. morphine-equivalent consumption at 72 h. Such results could be explained by the use of a continuous TAP catheter in half of the included trials and a decreasing visceral contribution to pain over time.

Our results are similar to those reported in two previous meta-analyses [6, 7]. In a meta-analysis of 10 trials by Baeriswyl et al., that included children and adults, no differences were demonstrated between epidural analgesia

Table 3 GRADE quality of evidence assessment for each outcome.

Outcome	Limitations	Inconsistency	Indirectness	Imprecision	Publication bias	Number of patients/ trials	Conclusion	Quality of evidence
Pain score at rest								
0–2 h	Serious limitations[a]	Serious inconsistency[c]	No serious indirectness	No serious imprecision	Serious publication bias[g]	639/11	No difference between epidural analgesia and TAP block	Very low quality (⊕)
12 h	Serious limitations[a]	Moderate inconsistency[d]	No serious indirectness	No serious imprecision	Serious publication bias[g]	650/11	Decreased pain score with epidural analgesia	Low quality (⊕⊕)
24 h	Serious limitations[a]	Serious inconsistency[c]	No serious indirectness	Serious imprecision[e]	Serious publication bias[g]	747/13	No difference between epidural analgesia and TAP block	Very low quality (⊕)
48 h	Serious limitations[a]	Moderate inconsistency[d]	No serious indirectness	No serious imprecision	Serious publication bias[g]	534/9	Decreased pain score with epidural analgesia	Low quality (⊕⊕)
72 h	Serious limitations[a]	No serious inconsistency	No serious indirectness	No serious imprecision	Serious publication bias[g]	298/5	No difference between epidural analgesia and TAP block	Low quality (⊕⊕)
Pain score on movement								
0–2 h	Serious limitations[a]	Moderate inconsistency[d]	No serious indirectness	No serious imprecision	Serious publication bias[g]	539/10	Decreased pain score with epidural analgesia	Low quality (⊕⊕)
12 h	Serious limitations[a]	Serious inconsistency[c]	No serious indirectness	No serious imprecision	No serious publication bias	550/10	No difference between epidural analgesia and TAP block	Low quality (⊕⊕)
24 h	Serious limitations[a]	Serious inconsistency[c]	No serious indirectness	No serious imprecision	Serious publication bias[g]	647/12	No difference between epidural analgesia and TAP block	Very low quality (⊕)
48 h	Serious limitations[a]	Serious inconsistency[c]	No serious indirectness	No serious imprecision	No serious publication bias	417/8	Decreased pain score with epidural analgesia	Low quality (⊕⊕)
72 h	Serious limitations[a]	Moderate inconsistency[d]	No serious indirectness	No serious imprecision	No serious publication bias	298/5	No difference between epidural analgesia	Moderate quality (⊕⊕⊕)

(continued)

Table 3 (*continued*)

Outcome	Limitations	Inconsistency	Indirectness	Imprecision	Publication bias	Number of patients/ trials	Conclusion	Quality of evidence
							and TAP block	
Interval i.v. morphine-equivalent consumption								
0–24 h	Serious limitations[a]	Serious inconsistency[c]	No serious indirectness	No serious imprecision	No serious publication bias	633/9	Decreased morphine-equivalent consumption with epidural analgesia	Low quality (⊕⊕)
24–48 h	Serious limitations[a]	Serious inconsistency[c]	No serious indirectness	No serious imprecision	No serious publication bias	413/5	No difference between epidural analgesia and TAP block	Low quality (⊕⊕)
48–72 h	Serious limitations[a]	Serious inconsistency[c]	No serious indirectness	Serious imprecision[e]	Serious publication bias[g]	369/4	No difference between epidural analgesia and TAP block	Very low quality (⊕)
Failure and side-effects								
Failure rate	Serious limitations[a]	No serious inconsistency	No serious indirectness	No serious imprecision	No serious publication bias	9/578	No difference between epidural analgesia and TAP block	Moderate quality (⊕⊕⊕)
Rate of postoperative nausea and vomiting at 24 h	Moderate limitations[b]	No serious inconsistency	No serious indirectness	Serious imprecision[f]	Too few studies to assess	38/2	No difference between epidural analgesia and TAP block	Moderate quality (⊕⊕⊕)
Rate of hypotension at 24 h	Serious limitations[a]	No serious inconsistency	No serious indirectness	No serious imprecision	Too few studies to assess	111/2	No difference between epidural analgesia and TAP block	Moderate quality (⊕⊕⊕)
Rate of hypotension at 72 h	Serious limitations[a]	No serious inconsistency	No serious indirectness	No serious imprecision	Serious risk of publication bias[f]	199/3	Decreased rate of hypotension with TAP block	Low quality (⊕⊕)
Functional outcomes								
Time to first flatus	Serious limitations[a]	Serious inconsistency[c]	No serious indirectness	No serious imprecision	No serious publication bias	561/7	No difference between epidural analgesia and TAP block	Low quality (⊕⊕)

(continued)

Table 3 (*continued*)

Outcome	Limitations	Inconsistency	Indirectness	Imprecision	Publication bias	Number of patients/ trials	Conclusion	Quality of evidence
Time to ambulation	Serious limitations[a]	Moderate inconsistency[d]	No serious indirectness	No serious imprecision	No serious publication bias	198/3	No difference between epidural analgesia and TAP block	Moderate quality (⊕⊕⊕)
Hospital length of stay	Serious limitations[a]	No serious inconsistency	No serious indirectness	No serious imprecision	No serious publication bias	419/5	No difference between epidural analgesia and TAP block	Moderate quality (⊕⊕⊕)

TAP, transversus abdominis plane; GRADE, Grading of Recommendations Assessment, Development and Evaluation.
[a]In most studies, participants, personnel and outcome assessors were not blinded. Final decision to rate down quality of evidence by one level for risk of bias.
[b]Only two studies reported this outcome, of which one had and one had not blinded participants, personnel and outcome assessors. Final decision to not rate down quality of evidence for moderate limitations.
[c]I^2 was above 50% with wide variance of point estimates across studies. Final decision to rate down quality of evidence by one level for serious inconsistency.
[d]Even though the I^2 was above 50%, the point estimates did not vary widely between studies. Final decision to not rate down quality of evidence for moderate inconsistency.
[e]Confidence interval included null effect as well as appreciable benefit and/or harm. Final decision to rate down quality of evidence by one level for serious imprecision.
[f]Sample size was small and confidence interval included null effect as well as appreciable benefit and/or harm. Final decision to rate down quality of evidence by one level for serious imprecision.
[g]Final decision to rate down quality of evidence by one level for serious publication bias.

and TAP block in either the postoperative pain score at rest at 12 h or the i.v. morphine-equivalent consumption at the 0–24 h interval [6]. Further, they found the i.v. morphine-equivalent consumption at the 24–48 h interval to be decreased by a mean difference (95%CI) of 3.2 mg (0.6–5.8) in favour of epidural analgesia and the hospital stay to be reduced by a mean difference (95%CI) of 0.6 days (−0.9 to −0.3) in support of TAP block. In the present meta-analysis, we used a similar methodology to that by Baeriswyl et al., yet the greater number of included trials and the inclusion of only adults is likely to be responsible for the increased robustness of results. In the meta-analysis of four trials by Zhang et al., that included only adults, the cumulative morphine-equivalent consumption at 72 h, which we did not report, was shown to be no different between epidural analgesia and TAP block [7].

Epidural analgesia has been a widely advocated regional technique for pain relief in abdominal surgery. Our findings continue to challenge this paradigm. In previous studies and meta-analyses comparing the analgesic benefit of epidural analgesia vs. i.v. morphine, the mean difference in the pain score at rest at 24 h varied from less than 0.7–0.9 on a 10-point scale [35–37]. It may be that the effectiveness of epidural analgesia is diminished by the increasing adoption of minimally invasive laparoscopic surgical approaches, its relatively high failure rate of 13–47% [38] and the use of multimodal analgesia. On the other hand, TAP block decreased the pain score at rest at 24 h by a mean difference of 0.5 relative to systemic opioids [5]. In light of the clinically important difference in the intensity of pain and the rare but serious risks associated with epidural analgesia, such as fatal cardiovascular collapse, meningitis, spinal cord ischaemia and vertebral canal abscess or haematoma [2], TAP block might represent an alternative to epidural analgesia.

This meta-analysis has several limitations. First, most included trials were at risk of detection and performance bias because the involved participants, personnel and outcome assessors were not blinded to the analgesic intervention. Second, a few outcomes such as hypotension were not defined in a consistent manner between the different trials. Third, the results were characterised by significant heterogeneity which was not explained by the type of surgery, the approach or the

technique of injection for the TAP block. The extent of clinical and methodological diversity in the included trials, however, probably reflects that present in clinical practice. Fourth, the meta-analysis of some outcomes such as postoperative nausea and vomiting included fewer than four trials and/or less than 200 patients. Fifth, our primary outcomes were subject to publication bias in favour of TAP block and might have been, at least in part, to the restriction of included trials to the English language. Fifth, many of the included trials did not report the outcomes related to side-effects or functional outcomes, precluding the meta-analysis of several of these.

In conclusion, epidural analgesia was statistically superior to TAP block in the postoperative pain score at rest at 12 h and the need for i.v. morphine-equivalent consumption at the 0–24 h interval, but these differences were not clinically important. In choosing between epidural analgesia and TAP block, potential benefits should be balanced against the reported risk of harm, although the confidence in the evidence varied from very low to moderate, underlining the uncertainty in our estimates. Transversus abdominis plane block might represent a reasonable and relatively non-invasive alternative to epidural analgesia in abdominal surgery. Future trials should focus on the side-effects and the functional outcomes related to epidural analgesia and TAP block. Last, the relative utility of thoracic paravertebral block and novel fascial plane techniques such as quadratus lumborum block should be explored.

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Supporting Information

Additional supporting information may be found online via the journal website.

Appendix S1 Database(s): Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to April 08, 2019.