


## Systematic Review and Meta-Analysis

# A SYSTEMATIC REVIEW AND META-ANALYSIS OF PARACERVICAL BLOCKS AS A PERIOPERATIVE STRATEGY IN REDUCING POSTOPERATIVE PAIN IN PATIENTS UNDERGOING LAPAROSCOPIC HYSTERECTOMY

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## ABSTRACT

**Introduction:** Perioperative strategies to reduce postoperative pain are important for enhancing patient satisfaction. However, further research and trials has sparked ongoing debates of various strategies regarding efficacy and safety. **Objective:** This study aims to improve evidence-based strategies regarding the effect of paracervical anaesthetic blocks in patients undergoing laparoscopic hysterectomy. **Methods:** A systematic literature search was conducted through PubMed, Google Scholar, and ScienceDirect for RCTs in laparoscopic hysterectomy patients administered paracervical blocks and those given placebos. The quantitative analysis of pooled relative risk and mean difference with a 95% confidence interval were performed using the Review Manager 5.4 software in the random-effects model or fixed-effects model forest plot. **Results:** Based on four RCTs included in the analysis, there were significant differences in overall postoperative pain scores assessed by VAS (Visual Analogue Scale) [MD = -0.82, 95%CI (-1.47 to -1.06), p = 0.01]. The subgroup analysis also showed significant differences in VAS pain scores at 30 min and 1 hour post-operation [MD = -2.13, 95% CI (-3.09 to -1.16), p = 0.0001] and [MD = -2.55, 95% CI (-4.29 to -0.81), p = 0.004]. However, there were insignificant results in adequate pain control [RR = 7.90, 95%CI (0.39 to 158.67), p = 0.18], length of hospital stay [MD = 0.01, 95%CI (-0.52 to 0.54), p = 0.96], additional analgesics requirement at 24 hours [RR = 0.88, 95% CI (0.55 to 1.39), p=0.58], and perioperative complications [RR = 0.90, 95%CI (0.56 to 1.47), p = 0.68]. **Conclusion:** This meta-analysis provides evidence that the administration of paracervical block in patients undergoing laparoscopic hysterectomy is associated with a reduction of postoperative VAS pain score but not associated with the length of hospital stay, adequate pain control, additional analgesics requirement at 24 hours, and perioperative complications.

**Keywords:** VAS; Paracervical Block; Laparoscopic; Hysterectomy; Meta-Analysis.

## ABSTRAK

**Pendahuluan:** Strategi perioperatif untuk mengurangi nyeri pasca operasi penting untuk meningkatkan kepuasan pasien. Namun, perdebatan yang sedang berlangsung tentang berbagai strategi mengenai efikasi dan keamanan muncul karena uji coba lebih lanjut telah dipublikasikan. **Tujuan:** Penelitian ini bertujuan untuk meningkatkan strategi bukti mengenai efek anestesi blok paraservikal pada pasien yang menjalani histerektomi laparoskopik. **Metode:** Pencarian literatur sistematis dilakukan pada PubMed, Google Scholar, dan ScienceDirect untuk studi RCT pada pasien histerektomi laparoskopik yang diberikan blok paraservikal dibandingkan dengan plasebo. Analisis kuantitatif risiko relatif gabungan dan perbedaan rata-rata dengan interval kepercayaan 95% dilakukan dengan menggunakan perangkat lunak *Review Manager 5.4* dalam model *random-effects* atau *fixed-effects forest plot*. **Hasil:** Berdasarkan empat studi RCT yang dimasukkan dalam analisis, terdapat perbedaan yang signifikan pada skor nyeri pasca operasi secara keseluruhan yang dinilai dengan VAS (*Visual Analogue Scale*) [MD = -0,82, 95%CI (-1,47 to -1,06), p=0,01]. Analisis subkelompok juga menunjukkan perbedaan signifikan pada skor nyeri VAS pada 30 menit dan 1 jam pasca operasi [MD = -2,13, 95%CI (-3,09 to -1,16), p=0,0001] dan [MD = -2,55, 95%CI (- 4,29 to -0,81), p=0,004]. Namun, terdapat hasil yang tidak signifikan pada kontrol nyeri yang adekuat [RR = 7,90, 95%CI (0,39 hingga 158,67), p=0,18], lama perawatan di rumah sakit [MD = 0,01, 95%CI (-0,52

hingga 0.54),  $p=0,96$ ], kebutuhan analgesik tambahan pada 24 jam [RR = 0,88, 95%CI (0,55 hingga 1,39),  $p=0,58$ ], dan komplikasi perioperatif [RR = 0,90, 95%CI (0,56 hingga 1,47),  $p=0,68$ ]. **Kesimpulan:** Meta-analisis ini memberikan bukti bahwa pemberian blok paraservikal pada pasien yang menjalani histerektomi laparoskopik berhubungan dengan penurunan skor nyeri VAS pasca operasi tetapi tidak berhubungan dengan lama tinggal di rumah sakit, kontrol nyeri yang adekuat, kebutuhan analgesik tambahan pada 24 jam, dan komplikasi perioperatif.

**Kata kunci:** VAS; Blok Paraservikal; Laparoskopik; Histerektomi; Meta-Analisis.

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## INTRODUCTION

Perioperative strategies under the control of anaesthesiologists, surgeons, or related physicians to reduce postoperative pain are important for enhancing patient satisfaction (1). Laparoscopic hysterectomy is a minimally invasive procedure for obstetrics and gynaecology surgery. It has more reported advantages than traditional abdominal hysterectomy, but its postoperative discomfort still requires attention (2,3). Postoperative pain after laparoscopic hysterectomy associated with incisional and visceral pain is most intense 30 min after surgery (2). Several strategies to reduce postoperative pain were researched, such as opioid use, transverse abdominis plane (TAP) blocks, intraperitoneal local anaesthetic, and port site infiltration (4). Visceral pain is a very intense, dull, or heavy inner pain caused by tissue manipulation during surgery. Although visceral pain dominates over incisional pain, it has often been neglected during postoperative pain management (2,4).

Sensitization of this painful stimulus is transmitted by the pelvic visceral nerve plexus, derived from the hypogastric plexus, due to the stimulation of the Lee-Frankenhauser plexus located within the uterosacral ligament. Local drug infiltration by paracervical block is a potentially promising strategy because it can block the pelvic afferent sensory nerve fibres (5,6). Moreover, infiltration drugs using bupivacaine were reported beneficial because

its onset action was 15 minutes, and its lasting effect was up to 9 hours (7).

However, current literature reported inconsistent results regarding the efficacy of paracervical block, and the available randomized trials (RCTs) could not answer whether the paracervical block is required for pain reduction after laparoscopic hysterectomy. Therefore, this study aims to improve the evidence-based strategies approach by conducting a systematic review and meta-analysis to provide the best answer regarding the clinical effects of administering paracervical blocks as a perioperative strategy in reducing postoperative pain in patients undergoing laparoscopic hysterectomy.

## MATERIAL AND METHOD

### Database Search and Study Selection

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guideline (8). A systematic literature search was performed through PubMed, Google Scholar, and ScienceDirect using the following keywords: paracervical block, hysterectomy, and laparoscopic hysterectomy. We only included articles that match our eligibility criteria based on PICOS: (i) Population: patients who underwent laparoscopic hysterectomy; (ii) Intervention: Paracervical block using bupivacaine; (iii) Comparator: Placebo; (iv) Outcomes: postoperative pain scores measured by the

visual analogue scale (VAS), length of hospital stay, adequate pain control, additional analgesics requirement at 24 hours, and perioperative complications; (v) Study design: Randomised controlled trials (RCTs).

The literature search was conducted in August 2022 without any year restrictions. All results from the electronic databases were stored in Rayyan.ai to undergo the selection process (9). Two independent reviewers performed the selection process based on title and abstract screening then the full-text selection was performed based on the eligibility criteria. Any conflicts during article selection were discussed with all authors.

### Data Extraction

All included studies underwent data extraction by two independent reviewers. The main outcome used in this study is postoperative pain scores measured by VAS. There were many secondary outcomes, such as length of hospital stay, adequate pain control, additional analgesics requirement at 24 hours, and perioperative complications. Other data extracted from the selected studies include the year of publication, country, surgical procedure approach, population, operating time, body mass index (BMI), intervention, and administration procedure of paracervical block. Any controversies between data extraction were discussed with other authors.

### Risk of Bias Assessment

We assessed the risk of bias for each study using the Cochrane Risk of Bias 2 (ROB 2) tool (10). This tool consists of several domains, such as randomization sequence generation, allocation concealment, performance bias, detection bias, attrition bias, reporting bias, and other sources of bias. Each

domain was graded as “low risk”, “unclear risk”, and “high risk” of bias. The risk of bias assessment was conducted by two reviewers independently. Any difference in grading was discussed with other authors.

### Data Synthesis and Analysis

The selected studies were analysed qualitatively and quantitatively using meta-analysis. We performed a meta-analysis using the Review Manager (RevMan) 5.4 software (Cochrane Collaboration, Oxford, UK) with 95% confidence intervals (CI). Pooled mean difference (MD) was performed to calculate postoperative pain scores and the secondary outcome of length of hospital stay. In addition, the pooled risk ratio was used to calculate other secondary outcomes, such as adequate pain control, additional analgesics requirement at 24 hours, and perioperative complications. The random effects model and fixed effects model forest plot were used based on heterogeneity. The random effects model was used when heterogeneity was high ( $I^2 \geq 50\%$ ), and the fixed effects model was used when heterogeneity was low ( $I^2 < 50\%$ )(11).

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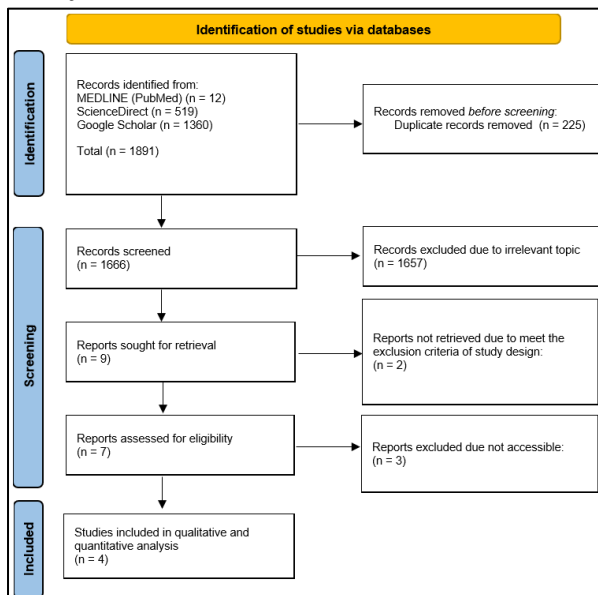
## RESULTS AND DISCUSSION

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### Study Selection

Based on our database search, we found 1891 articles from Google Scholar, ScienceDirect, and PubMed. We conducted the duplicate screening automatically using Rayyan.ai and then underwent title and abstract screening. A total of 7 articles were checked for full-text screening eligibility after the title and abstract screening. Quantitative analysis using meta-analysis was performed for four selected articles. [Figure 1](#) shows the PRISMA Flow Diagram.

### Study Characteristics and Risk of Bias



**Figure 1.** PRISMA Flow Diagram

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Grzesh et al., 2018	+	+	+	+	+	+	+
Lee et al., 2022	+	+	+	+	+	+	+
Noor et al., 2021	+	+	+	+	+	+	+
Radtke et al., 2019	+	+	+	+	+	+	+

**Figure 2.** Risk of Bias of Included Studies

[Table 1](#) summarises all the included RCT studies. The sample size varied between 41 to 132 samples. Two studies were conducted in the USA ([12,13](#)), one in India ([14](#)), and one in South Korea ([15](#)). The risk of bias assessment was conducted using the Cochrane ROB 2 tool,

and its result is presented in Figure 2. All included studies were found to have a low risk of bias. [Figure 2](#) shows the risk of bias assessment by the ROB 2 tool.

### Outcomes: Postoperative Pain Scores

Three studies reported that the overall postoperative pain scores assessed by VAS were significantly different between groups [pooled MD = -0.82, 95% CI (-1.47 to -1.06), p = 0.01]. Heterogeneity between studies was also high (I<sup>2</sup> = 80%). Moreover, the accordance results showed by subgroup analysis that paracervical block administration was statistically significant for reducing postoperative pain scores at 30-minutes [pooled MD = -2.13, 95% CI (-3.09 to -1.16), p < 0.0001] with low heterogeneity (I<sup>2</sup> = 0%). The subgroup analysis of VAS pain scores 1 hour after surgery showed a significant difference between groups [pooledMD = -2.55, 95% CI (-4.29 to -0.81), p = 0.004] and a high heterogeneity was observed (I<sup>2</sup> = 66%). [Figure 3](#) shows a forest plot for postoperative pain between the experimental and placebo groups.

### Outcomes: Length of Hospital Stay

Two studies observed length of hospital stay, and the results demonstrated no significant difference between the groups [pooled MD = 0.01, 95% CI (-0.52 to 0.54), p = 0.96] and low heterogeneity between the studies was observed (I<sup>2</sup> = 0%). [Figure 4](#) shows the forest plot for the length of hospital stay between the experimental and placebo groups.

### Outcomes: Adequate Pain Control

Two studies reported adequate pain control for patients with VAS scores ≤4 or ≤5, where 32/51 patients in the experimental group and 5/50 in the placebo groups showed improvement in pain control. However, this

analysis revealed that administering a paracervical block is not statistically significant for improving the number of patients with adequate pain control [pooled RR = 7.90, 95%CI (0.39 to 158.67), p = 0.18]. The

analysis also had considerable heterogeneity ( $I^2 = 78\%$ ). [Figure 5](#) shows the forest plot for postoperative pain between the experimental and placebo groups.

**Table 1.** Characteristics of included studies

Study (Country)	Surgical approach	Population	Operating time		BMI		Intervention	Administration of paracervical block
			Experimental	Control	Experimental	Control		
<b>Grzesh et al., 2018 (USA)</b>	Laparoscopic supracervical hysterectomy	132	89 (69–116) min	99 (73.5–117) min	27.2 ± 5.7	29.1 ± 6.9	20 ml 0.25% bupivacaine with 1:200,000 epinephrine	After intubation but before the first skin incision at 2, 5, 7, and 10 o'clock depth of 2 cm
<b>Radtke et al., 2019 (USA)</b>	Total laparoscopic Hysterectomy with GA	41	119.7 (15.5) min	132.5 (33.1) min	30.0 ± 9.8	32.7 ± 9.8	10 ml 0.5% bupivacaine with epinephrine	Injected into the cervical stroma at 3 and 9 o'clock with a depth of 2 to 3 cm
<b>Noor et al., 2021 (India)</b>	Total laparoscopic hysterectomy	60	4,038.0 ± 961.8 s	3,730.0 ± 483.6 s	26.9 ± 4.1	25.2 ± 1.9	10 mL of 0.5% bupivacaine	5 mL each at the 3 and 9 o'clock positions, with a depth of 2 cm
<b>Lee et al., 2022 (South Korea)</b>	Total laparoscopic hysterectomy with or without salpingo-oophorectomy	86	85.7 ± 20.6 min	83.5 ± 18.6 min	24.2 ± 4.2	24.4 ± 5.8	10 mL of 0.5% bupivacaine with 1:200,000 epinephrine vs 10 ml of normal saline	Injected into the cervical stroma at 3 and 9 o'clock with a depth of 1 to 2 cm after insertion but before fixation of the uterine manipulator

**Outcomes: Additional analgesics requirement at 24 hours**

Three studies reported additional analgesics requirements 24 hours after a laparoscopic hysterectomy, with 86/199 events in the experimental groups and 93/193 in the placebo groups. Overall, the paracervical block was not associated with a reduction in additional analgesics requirement at 24 hours in terms of opioid or narcotics and other pain medication [pooled RR = 0.88, 95%CI (0.55 to 1.39), p = 0.58] with high heterogeneity ( $I^2 = 75\%$ ). The subgroup analysis conducted for opioids or

narcotics and other pain medication showed no significant difference [pooled RR = 0.73, 95% CI (0.41 to 1.31), p=0.29 and RR = 1.57, 95% CI (0.80 to 3.09), p=0.19]. The heterogeneity was high for the opioids or narcotics subgroup ( $I^2 = 90\%$ ) and low for other pain medication ( $I^2 = 0\%$ ). [Figure 6](#) shows the forest plot for postoperative pain between the experimental and placebo group.

**Outcomes: Perioperative complications**

Two studies reported postoperative complications with 22/111 events in the



experimental groups and 23/107 events in the placebo groups. These results showed that the pooled estimates were not statistically significant [pooled RR = 0.90, 95% CI (0.56 to 1.47),  $p = 0.68$ ]. There was mild heterogeneity ( $I^2 = 0\%$ ). [Figure 7](#) shows the forest plot for postoperative pain between the experimental and placebo groups.

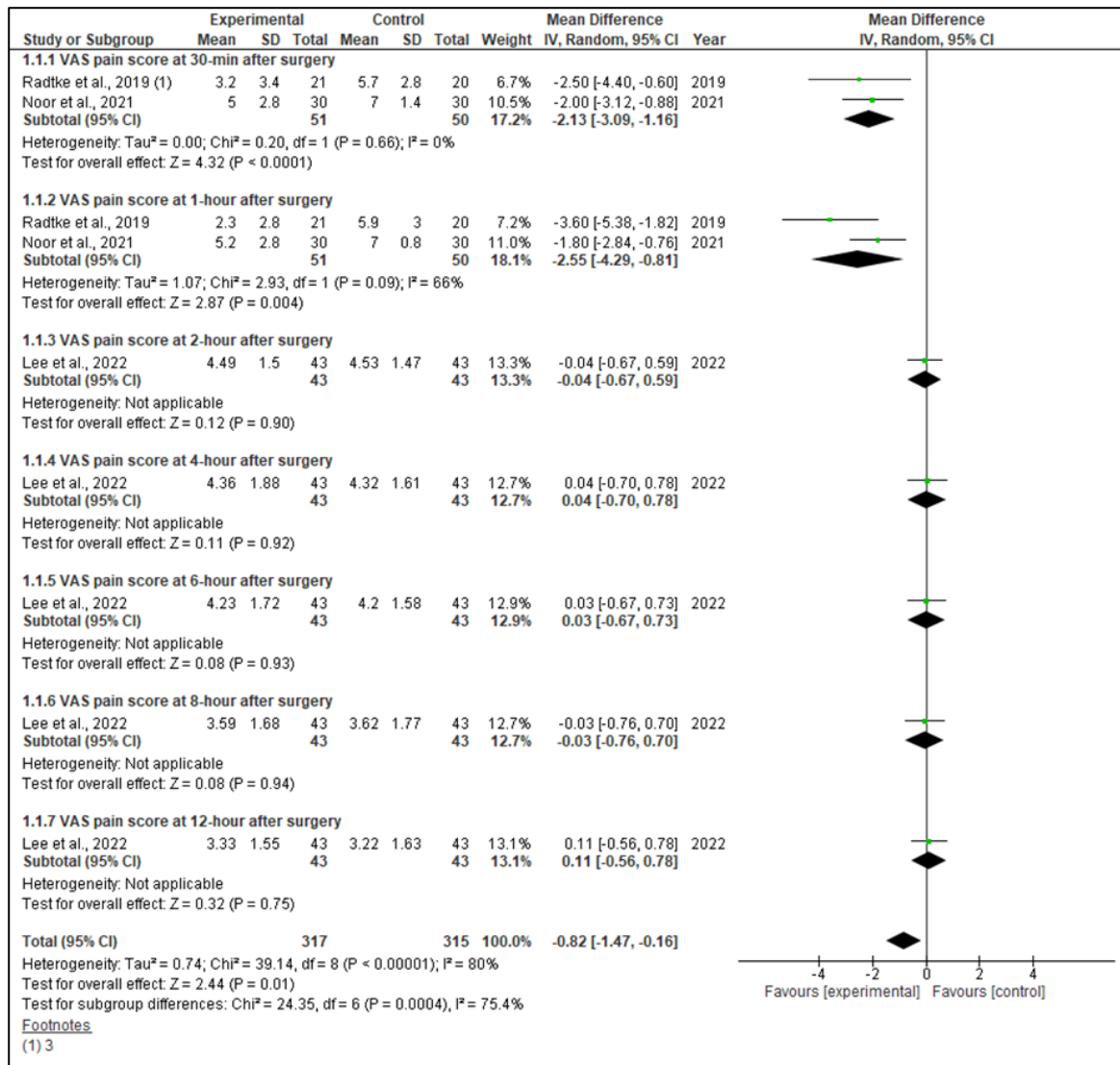
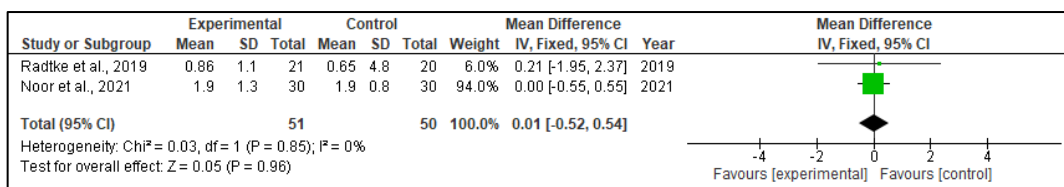
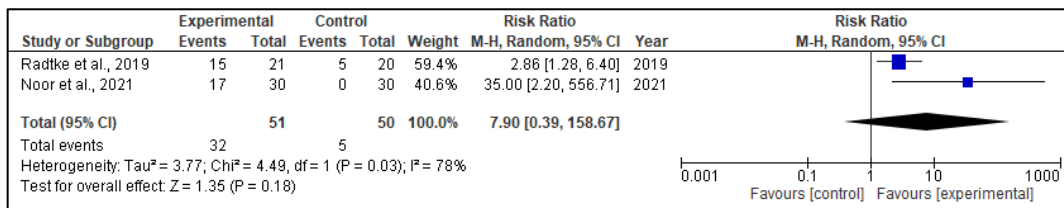
## Discussion

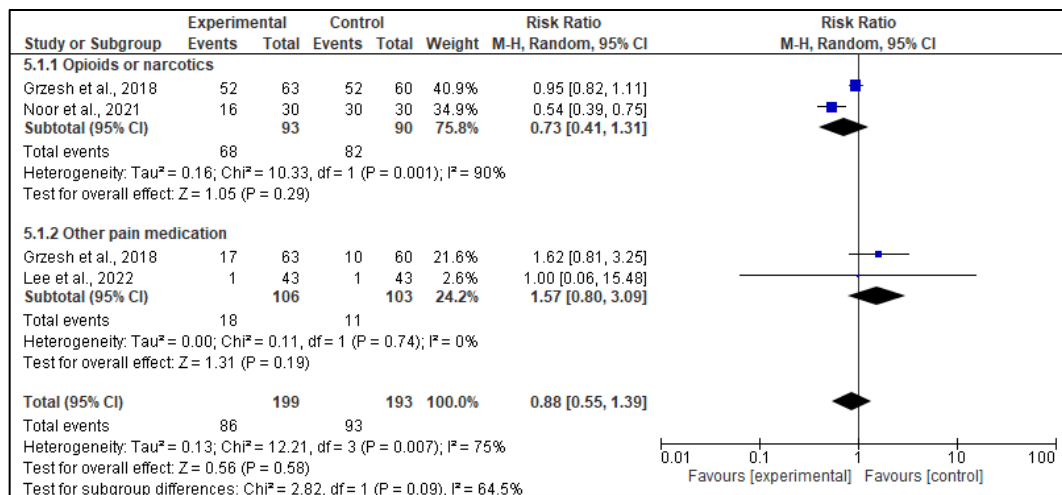
A meta-analysis of 4 RCTs involving 319 patients was conducted to provide evidence of the clinical effect of paracervical block in patients who underwent a laparoscopic hysterectomy. This study showed evidence of the benefit of administering paracervical block using bupivacaine compared to placebo to reduce postoperative pain scores, as assessed by VAS, for 30 minutes, 1 hour, and overall pain scores. Additionally, local anaesthetic preoperatively infiltrating the paracervical tissue is a potential pain control method because of tissue issues during a laparoscopic hysterectomy ([13](#)).

Paracervical block infiltration contributes to inhibiting the hypogastric plexus that is transmitted by the Lee-Frankenhauser stimulation in the uterosacral ligament. This inhibition is beneficial for reducing postoperative painful sensations ([5](#)). Although the results reported that paracervical block

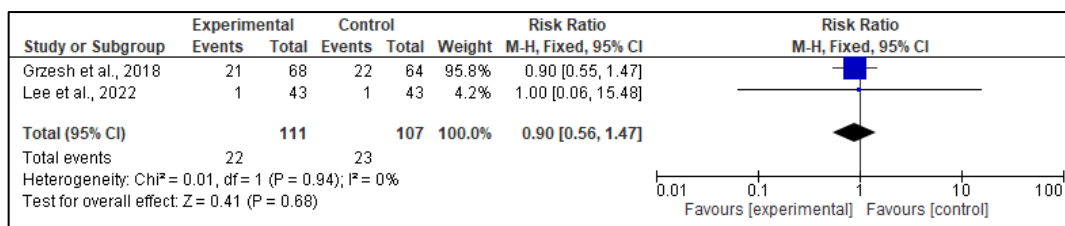
significantly reduces postoperative pain scores, it contradicts the outcome for the number of patients with adequate pain control. Radtke et al. reported successful pain control using criteria of an average pain score of 4 or less ([13](#)). Meanwhile, Noor et al. reported that adequate pain control was achieved when the mean VAS score was  $\leq 5$  ([14](#)).

Next, in this study, the length of hospital stay did not statistically differ between groups. Radtke et al. reported that it is important to understand that the majority of case decisions for hospitalization are not based on pain after surgery ([13](#)). Several patients who required additional analgesics at 24 hours were administered opioids and narcotics, and other pain medication. The analysis demonstrated no evidence for the benefit of paracervical blocks with overall additional analgesics requirements at 24 hours. These results align with the subgroup analysis for opioids, narcotics, and other pain medication. Grzesh et al. reported that even though the additional analgesics requirement was not significant at 24 hours, previous studies have demonstrated that the paracervical blocks resulted in a significant reduction in narcotics requirement for 7-days and 8-days post-operation and a significant reduction in other pain medication requirements for 6-days post-operation ([12](#)).


**Figure 3.** Forest Plot for Postoperative Pain Between the Experimental and Placebo Groups

**Figure 4.** Forest Plot for The Length of Hospital Stay Between the Experimental and Placebo Groups

**Figure 5.** Forest Plot for Adequate Pain Control Between the Experimental and Placebo Groups



**Figure 6.** Forest Plot for Additional Analgesics Requirement at 24 Hours Between the Experimental and Placebo Groups



**Figure 7.** Forest Plot for Perioperative Complications Between the Experimental and Placebo Groups

Noor et al. reported that the administration of paracervical blocks contributed to decreasing the need for additional opioid analgesic in the first 1 hour after surgery by 47% (14). Patients given paracervical blocks reported a higher ratio of perioperative complications despite the results showing no significant difference. Grzesh et al.'s study reported that patients experienced perioperative complications up to 6 weeks after surgery based on the Clavien-Dindo classification. Most of the recorded complications were Dindo grade 1 or 2, and there were no conversions to laparotomy (12). Additionally, Lee et al. reported that postoperative complications developed in each group, including an ileus in the experimental group and a vaginal cuff infection in the placebo group (15).

This systematic review and meta-analysis were conducted with the most up-to-date

literature search and used clinically important outcomes from RCT studies. The study selection process and appraisal of included studies were performed by two reviewers independently and showed a low risk of biased judgment.

Nevertheless, this study has some limitations. First, the quantitative analysis was conducted with a small sample size and limited studies. Second, there were different approaches in terms of the laparoscopic hysterectomy procedure. Third, postoperative pain assessed using pain scores is considered a subjective method for evaluation. Furthermore, multicentre RCTs with a large population and various outcomes are required to gain deeper insight.

## CONCLUSION

This meta-analysis provides evidence that the administration of paracervical blocks in



patients undergoing laparoscopic hysterectomies is effective in reducing postoperative pain measured by VAS but is not associated with perioperative complications, length of hospital stay, adequate pain control, and additional analgesics requirement at 24 hours.

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### Conflict of Interest

The authors declared that there is no conflict of interest in this study.

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### Authors' Contributor

All authors have contributed to several processes in this study.

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