

Different minimally invasive surgical methods to hysterectomy for benign gynecological disease: A systematic review and network meta-analysis

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Abstract

Background and Aims: This network meta-analysis aimed to compare the perioperative efficacy of various minimally invasive hysterectomy procedures for treating benign gynecological diseases and to assess whether vaginal natural orifice transluminal endoscopic hysterectomy (VNOTEH), a recently emerging procedure, is inferior to traditional laparoscopy.

Methods: We searched PubMed, Cochrane Library, Embase, China National Knowledge Infrastructure (CNKI), China Biology Medicine disc (CBM), Wanfang Data, and China VIP Database from inception to August 2022 and updated in June 2023. We included randomized controlled trials (RCTs) comparing different minimally invasive hysterectomy techniques in patients with benign gynecological conditions. The intervention measures included nine minimally invasive hysterectomies. The two researchers used the Cochrane risk-of-bias assessment tool for study appraisal. All statistical analyses and drawings were performed using STATA 17.0 and R 4.4.1. A network meta-analysis (NMA) was conducted to compare the effectiveness of minimally invasive hysterectomy and rank its relative impact probabilistically.

Results: A total of 78 RCTs involving 7640 patients and nine minimally invasive hysterectomy methods with 16 intervention combinations were included in this study. Among these, 2, 63, and 13 studies were deemed to have a low, medium, and high risk of bias, respectively. Based on the Surface Under the Cumulative Ranking (SUCRA) probability ranking results of NMA, laparoendoscopic single-site surgery-laparoscopic-assisted vaginal hysterectomy (LESS-LAVH) demonstrated superior outcomes in terms of complications, infections, and 24-h postoperative pain scores. LAVH exhibited better performance in injuries and hospital stays, total laparoscopic hysterectomy showed the least blood loss, and vaginal hysterectomy had the shortest operation time.

REGISTRATION: This research has been prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) (CRD 42023397507).

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Conclusion: LESS-LAVH and LAVH are recommended options, if feasible. Meanwhile, VNOTEH can achieve comparable results to traditional laparoscopy but requires careful attention to the risk of injury and infection. Future research should aim to broaden the search scope by including high-quality, large-scale, multicenter RCTs.

KEYWORDS

gynecology, hysterectomy, minimally invasive surgery, network meta-analysis, systematic review

1 | INTRODUCTION

Patients with benign gynecological diseases of the uterus or cervix often undergo hysterectomy for indications such as uterine fibroids, endometriosis, hyperplasia, abnormal uterine bleeding, pelvic pain, uterine prolapse, and cervical intraepithelial neoplasia.¹ According to incomplete statistics, millions of patients worldwide undergo hysterectomies annually. Approximately 600,000 patients undergo hysterectomies annually.² According to statistics from 2016 in China, approximately 2.8 million patients underwent hysterectomy in various hospitals at all levels.³

Various approaches to hysterectomy mainly include the following three methods: laparotomy, laparoscopy, and vaginal hysterectomy.⁴ In recent years, robotic laparoscopy, single-port laparoscopy, and transvaginal natural orifice transluminal endoscopic surgery (VNOTES) have gradually emerged and have been used in gynecology to provide patients with more options for hysterectomy. Among these, vaginal, laparoscopic, and VNOTES are considered to be minimally invasive surgeries and are mainly used for patients with benign gynecological conditions.⁴

The different surgical approaches for hysterectomy are the most important factors causing postoperative morbidity.⁵ The advantages of minimally invasive surgery over open surgery have been confirmed.⁶ However, regardless of the minor trauma of minimally invasive surgery, it may also result in new problems, such as an increased incidence of pneumoperitone-related complications. The highest incidence of urinary system injury occur in patients who underwent laparoscopic hysterectomy. Bladder injuries are more common in patients undergoing vaginal hysterectomy. Injuries to the ureter and intestine are also more likely to occur, and the surgical risk should not be underestimated.⁷

Determining which minimally invasive surgical method is safer and more effective for hysterectomy requires further exploration; in particular, VNOTES, which has emerged in recent years, lacks sufficient evidence-based medicine to prove whether it has the same or even greater advantages as classic minimally invasive surgery. Baekelandt⁸ published a systematic review of laparoscopy-assisted vaginal hysterectomy (LAVH), which included only two retrospective cohort studies and no randomized controlled trials (RCTs), whereas the recently updated study by Housmans et al.,⁹

which compared laparoscopic and traditional vaginal approaches, only included one RCT. These factors are worthy of attention. Healthcare professionals also serve as holistic care practitioners. Therefore, it is imperative to carefully consider the advantages and disadvantages of various surgical methods to provide essential advice and assistance to patients during the decision-making processes.

Although studies have reported the advantages and disadvantages of different hysterectomy procedures for benign diseases, issues remain, including the incomplete coverage of surgical methods and inconsistent results from multiple studies. This review summarizes the existing evidence from all published RCTs on minimally invasive hysterectomy for benign diseases, focusing on all types and covering almost all categories of minimally invasive surgery, and is therefore comprehensive. Subsequently, a network meta-analysis (NMA) and systematic review of different minimally invasive hysterectomy procedures were conducted to examine their effectiveness and safety. We chose to conduct an NMA because it provides a comprehensive comparative framework that allows us to simultaneously evaluate multiple interventions and address the inconsistencies in existing studies.

2 | METHODS AND ANALYSIS

2.1 | Protocol and registration

This study was prospectively registered in PROSPERO (CRD 42023397507) and conducted according to the PRISMA guidelines (Appendix 1).

2.2 | Eligibility criteria

The inclusion criteria were as follows: (1) research type: RCTs in which one minimally invasive hysterectomy was compared with another; (2) participants: patients who had undergone minimally invasive hysterectomy due to benign gynecological conditions; and (3) outcomes: at least one of the following outcome measures was assessed: (1) primary outcome: perioperative complications,

intraoperative injuries, and postoperative infections; and (2) secondary outcome: intraoperative blood loss, 24-h postoperative pain scores, hospital stays, and operation times.

The exclusion criteria were as follows: (1) studies in languages other than Chinese or English, (2) data with contradictions or inconsistencies, (3) conference papers/abstracts/protocols without research results, and (4) duplicate publications.

2.3 | Search strategy

A comprehensive electronic systematic literature search of seven databases (PubMed, Cochrane Library, Embase, CNKI, CBM, Wanfang Data, and China VIP Database) was conducted from database inception to August 2022 for RCTs published publicly in Chinese and English (the literature search was updated in June 2023); the PubMed database search strategy is shown in Appendix 2. We also searched for relevant studies outside these databases.

2.4 | Study selection and data extraction

Two research personnel (GMJ and LH) who had received training in evidence-based methodology independently completed the literature screening and data extraction based on the eligibility criteria of the study. The inclusion of studies with discrepancies found at the title/abstract review stage was decided by reviewing the full text, and in case of any disagreements at the full-text stage, a third review author was consulted for discussion and decision-making. Finally, self-made data extraction tables were used to extract the research characteristics and results, including basic research information, general characteristics of the research subjects, intervention measures, outcome indicators, and the surgical experience of the surgeons.

The surgeries investigated included vaginal hysterectomy (VH), laparoscopic hysterectomy (LH), laparoscopic-assisted VH (LAVH), laparoendoscopic single-site surgery-LH (LESS-LH), laparoendoscopic single-site surgery-laparoscopic assisted VH (LESS-LAVH), laparoendoscopic single-site surgery-total LH (LESS-TLH), vaginal natural orifice transluminal endoscopic hysterectomy (VNOTEH), and robot-assisted LH (RALH).

2.5 | Quality evaluation

Two researchers (GMJ and LH) used the Cochrane risk-of-bias assessment tool¹⁰ for quality assessments. The tool included seven evaluation fields: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome measures, incomplete outcome data, selective reporting, and other biases.

The risk of bias for each RCT was judged as “low” (random sequence generation uses computer-generated random number

tables; allocation of hidden variables uses sealed envelopes; blinding is properly implemented; data are complete, with no researcher dropouts or loss to follow-up exceeding 5%; all expected outcomes are fully reported; and no other obvious sources of bias are present), “unclear” (the methods for generating random sequences lack clear description; the allocation of hidden variables remains unreported; the implementation of blind methods is ambiguous; the integrity of the result data is unknown; the completeness of the outcome data is unknown; the report incompletely presents the anticipated results; and inadequate information exists to evaluate other potential biases), or “high” (the generation of machine sequences utilizes inappropriate methods; allocation of hidden variables is unclear or not used; blinding is either not implemented or insufficient; important outcome data is lost or the proportion of lost or unavailable data exceeds 5%; selective reporting of results; or other obvious signs of bias).

The determination of the overall bias risk is based on the assessment results in various fields. If all field scores are “Low,” the overall bias risk assessment is also “Low,” indicating a low bias risk. If at least one field yields a result of “Some concerns” and no field has a score of “High risk,” the overall bias risk assessment is categorized as “Some concerns,” signifying a moderate bias risk. If at least one field evaluation result indicates “High risk,” then the overall bias risk assessment is classified as “High risk,” suggesting a high level of bias in the RCT. Discrepancies were resolved through deliberation until consensus was reached.

2.6 | Statistics

STATA 17.0 and R 4.4.1 were employed to summarize and analyze the NMA using Markov chain Monte Carlo simulations in a Bayesian-based framework. Summary of mean differences (MDs, Cohen's *d*) and 95% confidence intervals (CIs) for continuous outcomes and odds ratios (ORs) with CI for dichotomous outcomes.

2.6.1 | Model fitting and testing

The random-effects model was selected, as we expected that studies would differ both methodologically and clinically (between-study heterogeneity).¹¹ The node-splitting method was employed to assess the consistency of direct and indirect comparisons when a closed loop was present, and a $p > 0.05$ indicated no significant inconsistency between direct and indirect comparisons. Transitivity was evaluated for each treatment comparison by examining study features and patient population characteristics. The Brooks-Gelman-Rubin diagnostic plot was used to evaluate model convergence. Based on the curve distribution, if the median value and 97.5% quantile of the PSRF were close to 1 and achieved stability, it suggested satisfactory convergence.¹²

2.6.2 | Network diagrams

Network diagrams were generated to illustrate the network geometry. The width of the lines is proportional to the number of trials comparing every pair of treatments, and the size of each circle is proportional to the number of randomly assigned participants.

2.6.3 | Forest plots

Forest plots were generated to present the effect size estimates and CIs as well as to combine the effect size estimates.

2.6.4 | Surface under the cumulative ranking (SUCRA)

The study presented SUCRA values, which represent the likelihood of a specific treatment ranking first for a particular outcome, expressed as percentages, with scores closer to 100% indicating a greater probability of the treatment being the most effective among all treatments examined for that outcome.

2.6.5 | League tables

A league table was created with the treatments ranked from worst to best along the leading diagonal.

2.6.6 | Additional analyses

Reporting bias was evaluated by drawing funnel plots when 10 studies were included in the analysis.

Sensitivity analysis was conducted on the primary outcome measures to assess the robustness of the NMA findings. This study was conducted after excluding trials judged to have a high risk of bias.

Subgroup analysis was performed to evaluate the impact of various subgroups based on the uterine weight, uterine size, and race reported in the trials.

Missing data were excluded from the meta-analysis after accounting for the number of women lost to follow-up or who dropped out.

3 | RESULTS

3.1 | Study selection

A total of 15,376 articles were retrieved. EndnoteX9.0 was utilized for deduplication. After screening the titles and abstracts according to the eligibility criteria and further reading the full text, a final total of 78 RCTs involving 7640 patients and evaluating nine

minimally invasive hysterectomy methods with 16 intervention combinations were included in this study (Wang, 2013).¹³⁻⁹⁰ The process flow diagram for document screening is shown in Figure 1. The characteristics of the included studies are summarized in Appendix 3.

3.2 | Quality evaluation

The overall risk of bias in the 78 RCTs included in the NMA was moderate. Among them, only two studies were deemed to have a low risk of bias, 63 studies had a medium risk of bias, and 13 had a high risk of bias.

A summary of the risk of bias for each trial is presented in Appendix 4. Of the included studies, 41 provided detailed descriptions of the random sequence generation, and their randomization methods were accurate; 20 provided detailed instructions on implementing allocation concealment; nine studies did not implement patient blinding; and seven studies did not carry out researcher blinding, indicating a high risk of bias. In terms of the presence of incomplete outcome data, six studies exhibited a loss to follow-up rate $\geq 10\%$; with regard to selective reporting, 54 studies were deemed to have an unclear risk due to undefined primary and secondary outcomes; in other bias domains, 54 studies had an unclear risk due to inadequate reporting on surgeon experience, while one study was classified as high risk.

3.3 | Findings from network meta-analysis

For all outcome indicators, the node analysis showed no inconsistencies between the direct and indirect results of the intervention measures ($p > 0.05$). The convergence assessment results demonstrated that the PSRF values were 1 or close to 1, indicating an excellent model convergence and high reliability of the analysis results. The model constructed in this study can effectively predict the data.

3.3.1 | Primary outcomes

Complications

Results of the NMA revealed that LESS-TLH had a higher complication rate than LESS-LAVH (OR = 5.69, 95% CI [1.12, 28.86]). Based on the cumulative ranking plot, SUCRA value, and NMA results, the ranking of complications from least to most was LESS-LAVH > LAVH > VNOTEH > TLH > LESS-LH > LH > VH > RALH > LESS-TLH (Figure 2, Table 1A).

Injuries

The NMA results revealed that the VH group had a higher intraoperative injury rate than the LAVH group (OR = 2.66, 95% CI [1.51, 4.68]) and the LH group exhibited a higher injury rate than the LAVH

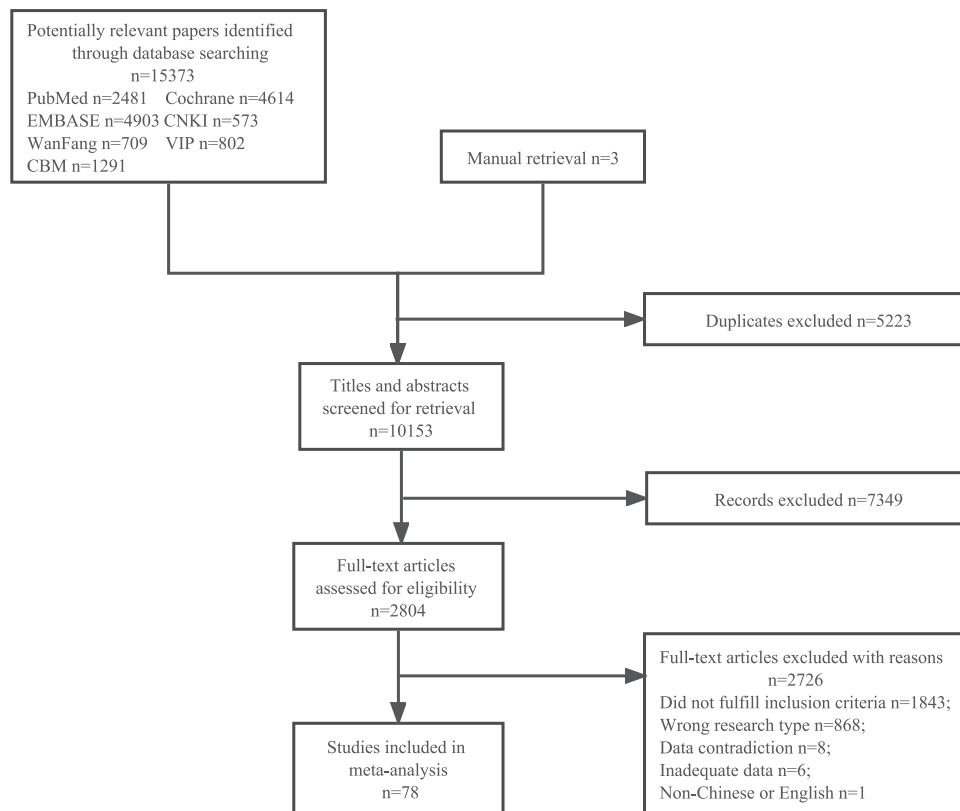


FIGURE 1 The process flowchart for document screening.

group (OR = 3.59, 95% CI [1.18, 10.90]). Based on the cumulative ranking plot, SUCRA value, and NMA results, the ranking of injuries from least to most was LAVH > RALH > LESS-LAVH > LESS-LH > TLH > LESS-TLH > VH > LH > VNOTEH (Figure 3, Table 1B).

Infections

The NMA results revealed no significant differences between the intervention and control groups. Based on the cumulative ranking plot, SUCRA value, and NMA results, the ranking of infection incidences from lowest to highest was LESS-LAVH > LAVH > LESS-LH > VH > RALH > LESS-TLH > TLH > VNOTEH (Figure 4, Table 1C).

3.3.2 | Secondary outcomes

Blood loss

As the LH and LESS-LH interventions were not interconnected with other interventions, the network effects of LH and LESS-LH were analyzed separately, and the results showed no significant statistical difference between LH and LESS-LH (MD = 11.5, 95% CI [-1.90, 25.00]); however, it is noteworthy that the sorting result of LH (sucrose value = 95.2%) outperformed that of LESS-LH (sucrose value = 4.8%), while the NMA of other interventions did not differ significantly among interventions. The ranking of blood loss was as follows: TLH > LAVH > LESS-LAVH > RALH > VNOTEH > LESS-TLH > VH.

Pain scores at 24 h postoperatively (24-h pain)

Results of the NMA revealed that patients who underwent LESS-LAVH (MD = -1.79, 95% CI [-3.06, -0.52]), LAVH (MD = -1.72, 95% CI [-2.79, 0.65]), and TLH (MD = -1.40, 95% CI [-2.33, -0.46]) exhibited lower pain scores at 24 h postoperatively than those who underwent VH. The ranking of pain scores at 24 h postoperatively from lowest to highest was as follows: LESS-LAVH > LAVH > VNOTEH > TLH > LESS-TLH > VH.

Hospital stays

LAVH resulted in a shorter hospital stay than VH (MD = -1.91, 95%CI [-2.70, -1.12]) and TLH (MD = -2.02, 95% CI [-3.28, -0.77]). The ranking of hospital stay from shortest to longest was as follows: LAVH > LESS-LAVH > LESS-LH > VNOTEH > LH > VH > TLH > LESS-TLH > RALH.

Operation time

The NMA results revealed that, in comparison to TLH (MD = -22.45, 95% CI [-26.41, -8.49]), LH (MD = -37.70, 95% CI [-67.90, -7.49]), LESS-TLH (MD = -36.74, 95% CI [-62.60, -10.88]), RALH (MD = -55.63, 95% CI [-93.78, -17.49]), and LESS-LH (MD = -71.80, 95% CI [-120.94, -22.69]), VH required a shorter operation time; in contrast to TLH (MD = -14.81, 95% CI [-29.08, -0.55]), LESS-TLH (MD = -29.11, 95% CI [-55.22, -2.99]), RALH (MD = -48.00, 95% CI [-86.48, -9.52]), and LESS-LH (MD = -64.18, 95% CI [-113.82, -14.53]),

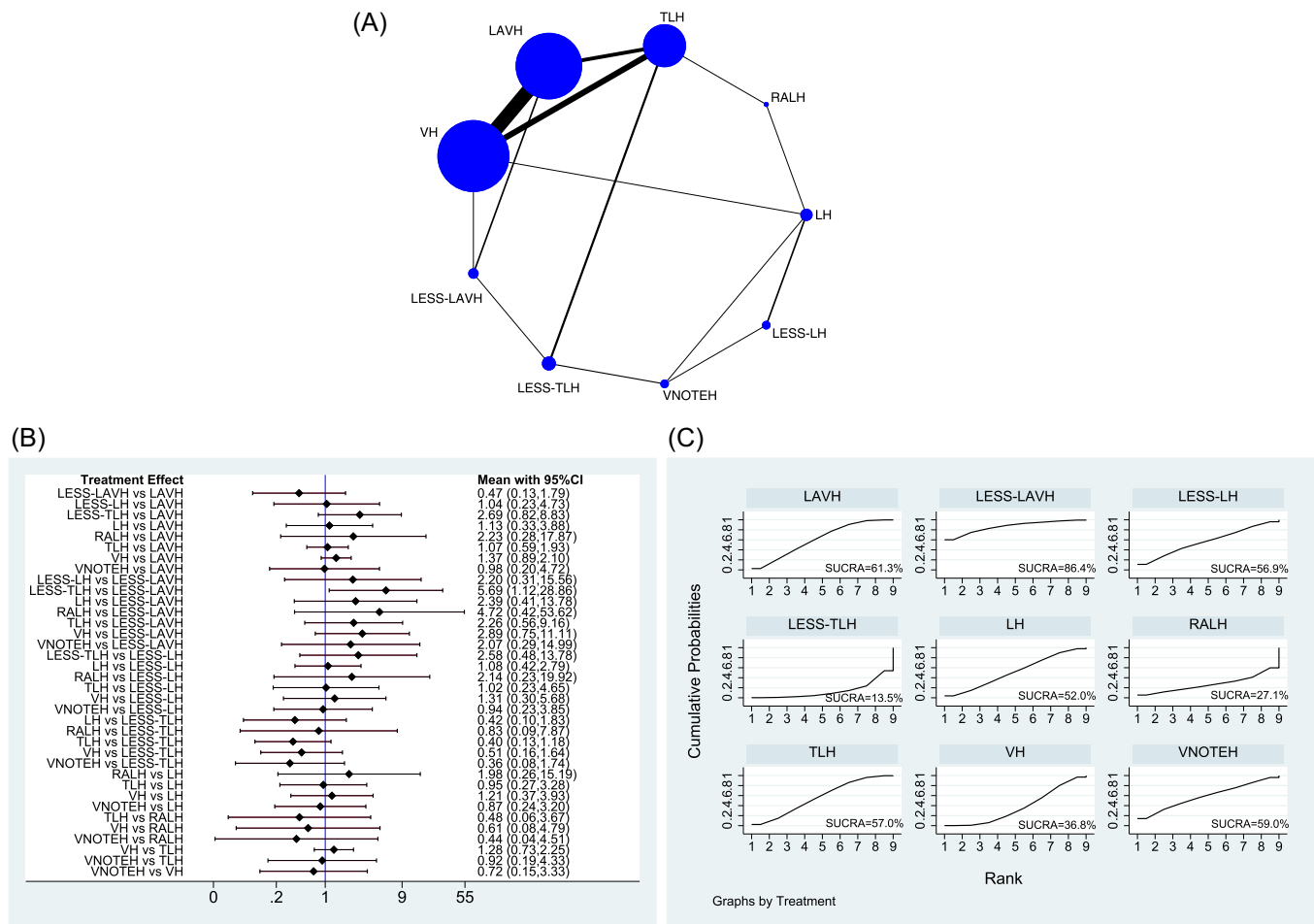


FIGURE 2 Specific details regarding the complications' network meta-analysis: (A) Network diagram for all treatment comparisons of complications. (B) Forest plot of complications. (C) Probability ranking of complications. LAVH, multi-port laparoscopic-assisted vaginal hysterectomy; LESS-LAVH, laparoendoscopic single-site surgery-laparoscopic-assisted vaginal hysterectomy; LESS-LH, laparoendoscopic single-site surgery-laparoscopic hysterectomy; LESS-TLH, laparo-endoscopic single-site surgery-total laparoscopic hysterectomy; LH, multiport laparoscopic hysterectomy with three or four abdominal incisions; RALH, robot-assisted multi-port laparoscopic hysterectomy with three or four abdominal incisions; TLH, multiport total laparoscopic hysterectomy with three or four abdominal incisions; VH, vaginal hysterectomy; VNOTEH, trans-vaginal natural orifice transluminal endoscopic hysterectomy.

LAVH had a shorter operation time; and the operation time of VNOTEH was comparatively shorter than that of LESS-LH (MD = -53.76, 95% CI [-106.74, -0.77]). The operation times were ranked from shortest to longest as follows: VH > LAVH > LESS-LAVH > VNOTEH > TLH > LH > LESS-TLH > RALH > LESS-LH.

3.4 | Publication bias

3.4.1 | Complications

Most of the studies included in the analysis exhibited a symmetrical distribution on both sides of the funnel plot, whereas five studies were outside the 95% CI of the funnel plot (Appendix 5), indicating a possible publication bias or small sample effect. After thorough analysis, it was determined that the bias could not be attributed to any of the experimental or statistical methods.

3.4.2 | Injuries and infections

The studies included in the analysis exhibited a symmetrical distribution on both sides of the funnel plot (Appendices 6 and 7), indicating a low likelihood of publication bias.

3.5 | Sensitivity analysis

The main outcome indicators were subjected to a sensitivity analysis by excluding RCTs deemed to have a high risk of bias.

3.5.1 | Complications

After excluding RCTs with a high risk of bias, the original nine groups of interventions were reduced to eight, owing to insufficient studies

TABLE 1 League tables showing the results of the network meta-analyses comparing the effects of all minimally invasive hysterectomy methods (odds ratios with 95% confidence intervals) on complications (A), injuries (B), and infections (C).

(A) NMA of complications									
LESS-TLH									
1.20 (0.13,11.42)									
	RALH								
1.97 (0.61,6.33)	1.63 (0.21,12.79)	VH							
2.38 (0.55,10.39)	1.98 (0.26,15.19)	1.21 (0.37,3.93)	LH						
2.58 (0.48,13.78)	2.14 (0.23,19.92)	1.31 (0.30,5.68)	1.08 (0.42,2.79)	LESS-LH					
2.52 (0.85,7.48)	2.09 (0.27,16.07)	1.28 (0.73,2.25)	1.06 (0.30,3.66)	0.98 (0.22,4.44)	TLH				
2.75 (0.58,13.08)	2.28 (0.22,23.47)	1.40 (0.30,6.49)	1.15 (0.31,4.24)	1.06 (0.26,4.36)	1.09 (0.23,5.15)	VNOTEH			
2.69 (0.82,8.83)	2.23 (0.28,17.87)	1.37 (0.89,2.10)	1.13 (0.33,3.88)	1.04 (0.23,4.73)	1.07 (0.59,1.93)	0.98 (0.20,4.72)	LAVH		
5.69 (1.12,28.86)	4.72 (0.42,53.62)	2.89 (0.75,11.11)	2.39 (0.41,13.78)	2.20 (0.31,15.56)	2.26 (0.56,9.16)	2.07 (0.29,14.99)	2.11 (0.56,7.99)	LESS-LAVH	
(B) NMA for injuries									
VNOTEH									
2.09 (0.11,38.10)	LH								
2.82 (0.18,43.73)	1.35 (0.52,3.52)	VH							
2.04 (0.14,28.67)	0.98 (0.05,17.81)	0.72 (0.05,11.22)	LESS-TLH						
4.69 (0.33,65.92)	2.25 (0.67,7.49)	1.66 (0.80,3.46)	2.30 (0.16,32.42)	TLH					
6.27 (0.08,475.19)	3.00 (0.12,74.35)	2.22 (0.08,63.33)	3.08 (0.04,233.54)	1.33 (0.04,41.16)	LESS-LH				
8.99 (0.25,324.86)	4.30 (0.35,52.64)	3.19 (0.32,32.24)	4.41 (0.12,159.68)	1.91 (0.17,21.68)	1.43 (0.02,84.11)	LESS-LAVH			
9.58 (0.26,347.91)	4.59 (0.30,69.29)	3.40 (0.27,43.12)	4.71 (0.13,171.01)	2.04 (0.18,23.27)	1.53 (0.02,102.42)	1.07 (0.03,33.14)	RALH		
0.13 (0.01,2.08)	3.59(1.18,10.90)	2.66 (1.51,4.68)	3.68 (0.24,57.51)	1.60 (0.75,3.40)	1.20 (0.04,35.72)	0.83 (0.08,9.02)	0.78 (0.06,9.99)	LAVH	
(C) NMA of infections									
VNOTEH									
2.08 (0.03,150.65)	TLH								
1.78 (0.20,16.09)	0.86 (0.02,33.75)	LESS-TLH							
2.08 (0.01,346.86)	1.00 (0.06,16.44)	1.17 (0.01,118.50)	RALH						
2.95 (0.04,205.54)	1.42 (0.62,3.27)	1.66 (0.04,62.40)	1.42 (0.08,26.39)	VH					
3.24 (0.12,87.13)	1.56 (0.01,345.76)	1.82 (0.03,95.55)	1.56 (0.00,684.21)	1.10 (0.01,235.64)	LESS-LH				

(Continues)

TABLE 1 (Continued)

(C) NMA of infections									
3.24 (0.05,223.96)	1.56 (0.76,3.22)	1.82 (0.05,67.91)	1.56 (0.09,28.13)	1.10 (0.56,2.13)	1.00 (0.00,213.68)	LAVH			
5.48 (0.11,273.39)	2.64 (0.46,15.16)	3.08 (0.12,77.94)	2.64 (0.10,71.59)	1.86 (0.36,9.64)	1.69 (0.01,280.42)	LESS-LAVH			

Note: Treatments are ranked from worst to best along the diagonal, starting from the top left, and bold font indicates a statistically significant difference between the two treatments.

Abbreviations: LAVH, multi-port laparoscopic-assisted vaginal hysterectomy; LESS-LAVH, laparoscopic single-site surgery-laparoscopic-assisted vaginal hysterectomy; LESS-LH, laparoscopic single-site surgery-laparoscopic hysterectomy; LESS-TLH, laparoscopic single-site surgery-total laparoscopic hysterectomy; LH, multiport laparoscopic hysterectomy with three or four abdominal incisions; RALH, robot-assisted multi-port laparoscopic hysterectomy with three or four abdominal incisions; TLH, multiport total laparoscopic hysterectomy with three or four abdominal incisions; VH, vaginal hysterectomy; VNOTEH, trans-vaginal natural orifice transluminal endoscopic hysterectomy.

(Appendix 8). The results showed no statistical differences between the interventions (see Appendix 9), with minimal changes in ranking. LESS-LAVH remained ranked first, VNOTEH outperformed LAVH, and LH outperformed LESS-LH (Appendix 10).

3.5.2 | Injuries

After excluding RCTs with a high risk of bias, the original nine groups of interventions were reduced to six, owing to insufficient studies (Appendix 11). The findings revealed a statistically significant difference between the VH and LAVH groups (OR = 3.10, 95% CI [1.64, 5.85]); however, no significant difference was observed between the other intervention controls (Appendix 12). The ranking remained relatively stable, with LAVH maintaining its top position, and LESS-TLH outperforming VH (Appendix 13).

3.5.3 | Infections

After excluding RCTs with a high risk of bias, the original eight groups of interventions were reduced to six, owing to insufficient studies (Appendix 14). In cases where LESS-TLH and VNOTEH failed to establish network connections with other interventions, the network effects of "LAVH, LESS-LAVH, VH, TLH" and "LESS-TLH, VNOTEH" were analyzed independently. The outcomes indicated a statistically significant difference between TLH and LAVH (OR = 2.67, 95% CI [1.11, 6.41]); however, no significant difference was observed between the other intervention controls (Appendix 15). The ranking remained relatively stable, and LESS-LAVH achieved an optimal result (Appendix 16). No significant difference was observed between the VNOTEH and LESS-TLH groups (OR = 1.68, 95% CI [0.07, 37.85]), and the ranking remained consistent with previous findings, indicating that LESS-TLH outperformed VNOTEH.

3.6 | Subgroup analysis

Due to the small number of studies involved in some intervention schemes, a subgroup analysis of all outcome indicators was not possible. During the literature review, it was noted that factors such as uterine weight, uterine size, and ethnicity might have influenced the results. Therefore, subgroup analyses were performed based on these three factors. However, as 28 studies did not report uterine weight, and some studies lacked clear distinctions between the number of weeks of uterine size, insufficient data were available. Consequently, no such analysis was performed. Consequently, only race-based subgroup analyses were performed for the three primary outcome indicators (complications, injuries, and infections) to compare the VH, TLH, and LAVH groups.

We conducted a subgroup analysis to compare the outcomes between the VH and TLH groups and found no significant differences in complications (Appendix 17) ($I^2 = 0\%$, $p = 0.475$, OR = 0.79, 95% CI [0.50, 1.25]), injuries (Appendix 18) ($I^2 = 0\%$, $p = 0.867$, OR = 0.59,

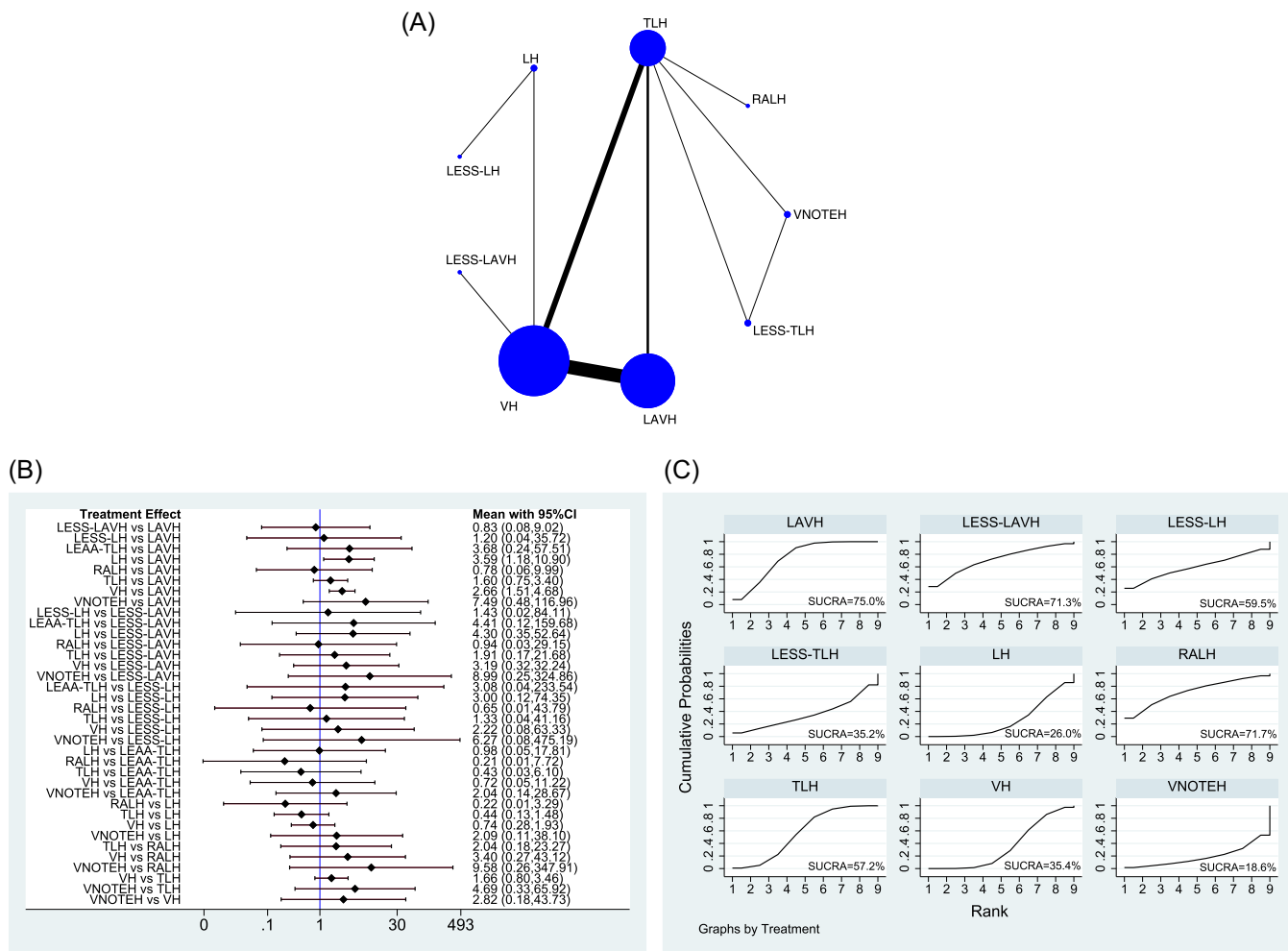


FIGURE 3 Specific details regarding the injuries' network meta-analysis: (A) Network diagram for all injury treatments. (B) Forest plot of injuries. (C) Probability ranking of injuries. LAVH, multi-port laparoscopic-assisted vaginal hysterectomy; LESS-LAVH, laparoendoscopic single-site surgery-laparoscopic-assisted vaginal hysterectomy; LESS-LH, laparoendoscopic single-site surgery-laparoscopic hysterectomy; LESS-TLH, laparo-endoscopic single-site surgery-total laparoscopic hysterectomy; LH, multiport laparoscopic hysterectomy with three or four abdominal incisions; RALH, robot-assisted multi-port laparoscopic hysterectomy with three or four abdominal incisions; TLH, multiport total laparoscopic hysterectomy with three or four abdominal incisions; VH, vaginal hysterectomy; VNOTEH, trans-vaginal natural orifice transluminal endoscopic hysterectomy.

95% CI [0.24, 1.44]), or infections (Appendix 19) ($I^2 = 0\%$, $p = 0.791$, OR = 2.45, 95% CI [0.77, 7.81]). Furthermore, no notable heterogeneity was observed within the intra- or inter-subgroup combinations, indicating that race did not contribute to this variability.

We conducted a subgroup analysis to compare outcomes between the VH and LAVH groups. The results showed that for complications (Appendix 20), the intragroup heterogeneity of the domestic and foreign groups was minimal and not statistically significant, whereas a statistical difference was observed between the two groups ($I^2 = 38.3\%$, $p = 0.026$, OR = 0.86, 95% CI [0.53, 1.38]). This increased heterogeneity may be attributed to race. However, there were no significant differences in the incidences of injuries (Appendix 21) ($I^2 = 0\%$, $p = 0.826$, OR = 0.40, 95% CI [0.21, 0.74]) or infections (Appendix 22) ($I^2 = 0\%$, $p = 0.591$, OR = 0.81, 95% CI [0.38, 1.74]).

We conducted a subgroup analysis to compare the outcomes between the TLH and LAVH groups and found no significant differences in complications (Appendix 23) ($I^2 = 0\%$, $p = 0.758$, OR = 0.80,

95% CI [0.46, 1.37]) or infections (Appendix 24) ($I^2 = 0\%$, $p = 0.462$, OR = 0.76, 95% CI [0.32, 1.78]). Furthermore, no notable heterogeneity was observed within the intra- or inter-subgroup combinations, indicating that race did not contribute to this variability.

4 | DISCUSSION

4.1 | The application status of minimally invasive hysterectomy in benign gynecological diseases

Minimally invasive hysterectomy, characterized by minimal trauma and rapid recovery, has been widely applied in the treatment of benign gynecological diseases, such as uterine fibroids, adenomyosis, abnormal uterine bleeding, and pelvic organ prolapse. It has demonstrated favorable outcomes compared with traditional open surgery in terms of surgical trauma, infection rates, blood loss, pain levels, hospital stay,

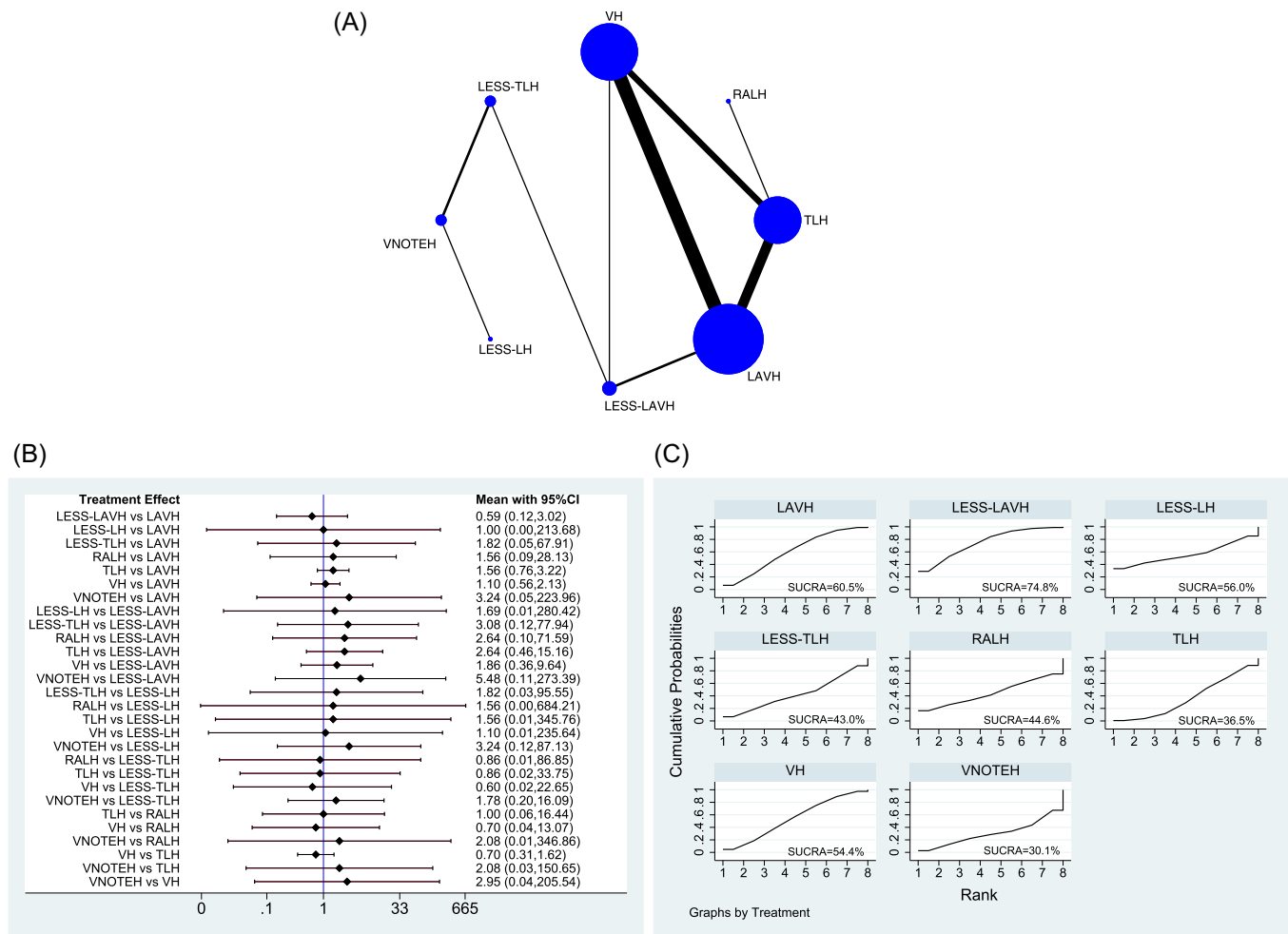


FIGURE 4 Specific details regarding the infections' network meta-analysis: (A) Network diagram for all treatments for infections. (B) Forest plot of infection rates. (C) Probability ranking of infections. LAVH, multi-port laparoscopic-assisted vaginal hysterectomy; LESS-LAVH, laparoendoscopic single-site surgery-laparoscopic-assisted vaginal hysterectomy; LESS-LH, laparoendoscopic single-site surgery-laparoscopic hysterectomy; LESS-TLH, laparo-endoscopic single-site surgery-total laparoscopic hysterectomy; LH, multiport laparoscopic hysterectomy with three or four abdominal incisions; RALH, robot-assisted multi-port laparoscopic hysterectomy with three or four abdominal incisions; TLH, multiport total laparoscopic hysterectomy with three or four abdominal incisions; VH, vaginal hysterectomy; VNOTEH, trans-vaginal natural orifice transluminal endoscopic hysterectomy.

and medical costs.⁹¹⁻⁹³ Minimally invasive hysterectomies include VH and LH. These minimally invasive surgical approaches have specific indications for different clinical situations.⁹⁴ With ongoing technological advancements, the range of indications for minimally invasive hysterectomy continues to expand.^{92,93,95} Furthermore, emerging techniques such as RALH, LESS, and VNOTEH are continuously evolving to provide patients with more options.⁹⁵⁻⁹⁷

4.2 | Evolution and improvement of minimally invasive hysterectomy techniques

4.2.1 | Innovations in surgical instruments and equipment

In recent years, with the advancement of medical technology, the instruments and equipment used in minimally invasive hysterectomy

have been continuously optimized and improved, with higher flexibility and precision, making the operation more delicate and safe and providing the surgeon with better operative experience.⁹⁸ Second, the introduction of 3D laparoscopic systems has significantly enhanced the clarity and perception of the surgical field.⁹⁹ Additionally, the application of robot-assisted surgery systems has introduced new possibilities for minimally invasive hysterectomies. Particularly in managing complex cases, such as large uteri, these systems have demonstrated unique advantages.^{99,100}

4.2.2 | Innovations in surgical approaches

The development of LESS and the emergence of new minimally invasive techniques such as VNOTE have provided new options for minimally invasive hysterectomy. VNOTES technology has shown significant advantages in terms of aesthetic satisfaction and rapid

recovery, making it a promising direction for future developments in minimally invasive surgeries.¹⁰¹

4.2.3 | Optimization and standardization of surgical techniques

Optimization and standardization of surgical techniques are crucial for improving surgical quality and safety. Training and learning curve management are important for optimizing surgical techniques.¹⁰² Standardizing surgical procedures helps reduce surgical complications and improves surgical efficiency, effectively reducing surgical risk.¹⁰³ Furthermore, the potential applications of imaging guidance technology, artificial intelligence, and virtual reality technology in minimally invasive hysterectomy are promising.^{104–106}

4.3 | Challenges and controversies in minimally invasive hysterectomy

The first challenge is the steep learning curve, which requires surgeons to undergo systematic training and long-term practice to achieve proficiency.¹⁰⁷ The second is the high equipment costs, which may limit its widespread adoption in certain medical institutions. Additionally, for specific scenarios such as severe adhesions or large uterine tumors, traditional open surgery may still be considered a safer choice.¹⁰⁸ Nevertheless, the role of minimally invasive hysterectomy in the treatment of benign gynecological diseases has been widely acknowledged. With ongoing technological advancements and accumulated experience, the indication range for minimally invasive hysterectomy is expected to expand.

4.4 | Analysis of outcomes of minimally invasive hysterectomy

However, there are also differences between different types of minimally invasive surgeries. This can be observed in the NMA results.

4.4.1 | LESS-LAVH and LAVH are ranked among the top three

From the perspective of the three primary and four secondary outcome indicators, LESS-LAVH and LAVH ranked among the top three in terms of SUCRA for each outcome indicator, indicating their overall superiority as surgical methods. After conducting sensitivity analysis of the main outcome indicators and excluding high-risk articles, LAVH surpassed LESS-LAVH as the top-ranking procedure for infection indicators. However, the overall rankings of both procedures remained unchanged. This may be attributed to the combined advantages of laparoscopic and vaginal surgeries, which provide a clear surgical field of view with minimal invasion and damage.³³

Nevertheless, LESS-LAVH and LAVH have distinct advantages in terms of various outcome indicators, each with its own strengths. Therefore, the benefits of single-port surgery are not particularly prominent, possibly due to the lack of measurement of other factors, such as aesthetic effect and satisfaction, or a lack of direct comparison studies between the two procedures (only three RCTs). This limits the advantages of single-port surgery. However, in clinical practice, an increasing number of younger women prefer single-port surgeries.

4.4.2 | VH exhibits the shortest operation time, and TLH manifests the least blood loss

Additionally, as previously mentioned, VH had the shortest operation time, which may be attributed to the gynecologist's extensive experience in vaginal surgery and the reduced number of laparoscopic perforation steps, resulting in a reduced operation time. Numerous studies have indicated that transvaginal hysterectomy should be prioritized for suitable patients, where feasible.^{1,7,109} However, the limitations of this operation due to insufficient exposure may obscure the advantages of VH in surgeries beyond optimal indications, such as those involving excessively large uteri and intrauterine or extra-uterine diseases.

These findings also indicate that blood loss during TLH surgery was minimal, although this remains controversial. The analysis revealed significant variability in reported blood loss across studies, which was potentially attributable to differences in measurement methodologies, suggesting a potential bias and warranting further investigation.

4.4.3 | Ranking of VNOTEH

However, the latest single-port laparoscopic VNOTEH that caught our attention exhibited above-average outcomes in terms of various indicators such as complications, blood loss, pain scores at 24 h post-operatively, hospital stay, and operation time. It ranked the lowest in terms of injury and infection. This finding is consistent with that of the meta-analysis of Housman et al., which compared VNOTES with conventional laparoscopy.⁹

This is related to the inherent characteristics of the VNOTES. In the third era of the surgical revolution, after open and endoscopic surgeries, VNOTES holds great promise and vast potential for development. However, as an emerging technology, VNOTES is still in the initial stages of exploration. The limitations of surgical instruments, inexperience of surgeons, immaturity of techniques, and chopstick effect contribute to increased difficulty and injury risk during surgery.¹¹⁰ Additionally, owing to the posterior fornix approach used in VNOTES, some disruption may occur in the vaginal microecological balance, leading to inflammation, and postoperative vaginal bleeding can increase the likelihood of an incision infection.¹¹¹ However, a limited number of RCTs have

investigated VNOTEH, which may have affected the interpretation of the results.

Nonetheless, VNOTES demonstrated efficacy comparable to that of conventional laparoscopic surgery for uterine removal, although medical practitioners require extensive clinical practice to improve their surgical skills and proficiency. Furthermore, RCTs on VNOTES should be expanded to identify the least invasive, most expeditious, and optimal approach for patients.

4.4.4 | Other worst-ranked surgical procedures

The LESS-TLH group exhibited the highest incidence of complications. This may be attributed to the inherent difficulty of the LESS-TLH procedure and its prolonged duration, which increases the likelihood of intraoperative complications. Similarly, in terms of operation time, LESS-LH required the longest operation duration, which may be due to the inherent complexity of the procedure itself.¹

In terms of blood loss and pain scores 24 h postoperatively, VH was ranked last. As stated previously, VH is a suitable surgical option for the treatment of benign uterine diseases. However, when the size of the uterus exceeds the recommended range for VH, the advantages become less apparent and it may even exacerbate bleeding and pain.^{1,27} Unfortunately, owing to insufficient information regarding uterine size in some literature sources, a subgroup analysis based on this factor could not be conducted and requires further investigation.

The RALH group had the longest hospitalization duration. Although RALH ranked low-middle overall, it demonstrated a significant advantage in terms of injury indicators (ranking second). This may be due to the ability of RALH to enlarge the tissue up to 5–10 times under a high-definition field of view during surgery, allowing for better identification of small blood vessels and lymph nodes and facilitating fine operations while reducing intraoperative injuries.¹¹²

For women, the uterus is not just a reproductive organ; it is also considered an emotional hub with strong psychological effects that can lead to changes in sexual function and psychological well-being, thereby leading to a non-negligible risk of posttraumatic stress.^{101,113} Therefore, a hysterectomy can be a difficult choice for women who are highly concerned about the safety and efficacy of the chosen surgical approach. Results of the NMA on different minimally invasive hysterectomy procedures partially answered this question to some extent; considering feasibility and safety, LAVH or LESS-LAVH should be given priority. Therefore, the potential of VNOTES and RALH warrants further investigation. However, it is also important to note that the choice of surgical approach should be comprehensively evaluated based on the patient's clinical condition (e.g., disease severity, uterine and vaginal structural conditions, presence of extrauterine diseases, and effectiveness of conservative treatment), patient-specific factors (such as age, fertility requirements, preferences, and economic status), and institutional considerations (e.g., equipment availability and technical expertise).

5 | ADVANTAGES AND LIMITATIONS

This study assessed the perioperative outcomes of various minimally invasive hysterectomies in patients with benign gynecological conditions. The analysis of the outcome indicators and RCTs included in this review was more comprehensive than that of previous studies. Additionally, for the first time, the latest minimally invasive surgery, VNOTEH, was incorporated into the NMA to compare its advantages and disadvantages with other surgical methods, thereby evaluating the effectiveness of VNOTEH. Finally, various outcome indicators were used to analyze and categorize the benefits and drawbacks of all minimally invasive surgical methods, thereby providing clinical practitioners with valuable reference points and areas of focus.

This study has some limitations. For instance, despite the inclusion of numerous literature sources, there was a dearth of large-scale studies and the overall quality was suboptimal. Specifically, the descriptions and allocations of the blinding methods were inadequate, which may have resulted in methodological heterogeneity. The presence of clinical heterogeneity may be attributed to various factors, including uterine size, BMI, age, and physician experience. However, due to the absence of specific descriptions in the original studies or ambiguous data boundaries, it was not possible to categorize the studies accordingly. Additionally, limited direct comparative evidence is available for certain results owing to the scarcity of studies, particularly those involving innovative minimally invasive procedures. Consequently, subgroup analysis could not be conducted to further investigate the sources of heterogeneity. Although subgroup analyses were conducted on certain outcomes, heterogeneity could not be completely eliminated. Moreover, this study solely focused on perioperative outcome indicators, neglecting long-term outcome measures, such as recovery time to return to normal activities, quality of life, and long-term complications. Additionally, patient-reported outcome measures and objective economic evaluation indicators were not assessed, potentially affecting the generalizability of the findings.

6 | CONCLUSIONS

This study included 78 RCTs involving 7640 patients and evaluated the efficacy of nine minimally invasive hysterectomy procedures compared with 16 control methods. Based on the SUCRA probability ranking results of the NMA, LESS-LAVH demonstrated superior outcomes in terms of complications, infections and 24-h postoperative pain scores; LAVH exhibited better performance in terms of injuries and hospital stays; TLH showed the least blood loss; and VH had the shortest operation time. Considering all outcome indicators, LESS-LAVH and LAVH are the recommended first options, if feasible. Meanwhile, VNOTEH can achieve comparable results to traditional laparoscopy but requires careful attention to the risk of injury and infection. It is important to acknowledge the limitations of this study and exercise caution when extrapolating its results. Future research should aim to broaden the search scope by including

high-quality, large-scale, multicenter RCTs, particularly those involving innovative, minimally invasive surgical procedures. This will enhance the stability of the results and evidence-based credibility to make the best choice for women who require hysterectomy for the treatment of benign diseases.

AUTHOR CONTRIBUTIONS

Meijun Guan: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; software; validation; writing—original draft; writing—review and editing. **Hui Li:** Data curation; investigation; methodology; validation; writing—review and editing. **Tian Tian:** Project administration; resources; software; supervision. **Jirong Peng:** Resources; supervision. **Yan Huang:** Methodology; resources. **Li He:** Formal analysis; project administration; resources; supervision; writing—review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

TRANSPARENCY STATEMENT

The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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