



## Review

## Identifying the superior surgical procedure for endometrial polypectomy: A network meta-analysis

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## ABSTRACT

**Objective:** To identify the superior surgical procedure for endometrial polypectomy based on network meta-analysis.**Method:** Literature retrieval was conducted in globally recognized databases, namely, MEDLINE, EMBASE and Cochrane Central, to address relative randomized controlled trials (RCTs) investigating the clinical effects of respective surgical procedure for endometrial polypectomy. Surgical parametric data, including operative time, success rates and complications, were quantitatively pooled and estimated based on the Bayesian theorem. The values of surface under the cumulative ranking (SUCRA) probabilities regarding each parameter were calculated and ranked by various procedures. Node-splitting analysis was performed to test the inconsistency of the main results and publication bias was assessed by examining funnel-plot symmetry.**Results:** After a detailed review, 8 RCTs containing 5 different procedures were finally included for network meta-analysis. The results indicated that hysteroscopic morcellation possessed the highest possibility of revealing best clinical effects on operative time (SUCRA, 0.49), success rate (SUCRA, 0.90) and complications (SUCRA, 0.50). Moreover, node-splitting analysis and funnel-plot symmetries illustrated no inconsistency or obvious publication bias in the current study.**Conclusions:** Current evidence demonstrated that hysteroscopic morcellation showed optimal potential superior clinical effects for endometrial polypectomy compared to other procedures. However, high-quality large sample trials are still expected, and new investigations on other relative procedures in this field should be included in the future.

## 1. Introduction

Endometrial polyps are hyperplastic overgrowths of endometrial glands that project above the uterine surface. They have a common pathology and have a high prevalence rate among middle-aged and elderly women and are usually asymptomatic and discovered as an incidental finding [1,2]. Endometrial polyps are usually diagnosed in regular physical examinations by ultrasound. In symptomatic patients, they may present in the form of abnormal uterine bleeding [3]. Generally, endometrial polyps are benign and exhibit low malignancy rates [4,5]. However, known risk of malignancy can be highly variable depending on the patients' risk factors, such as menopause, symptoms of

dysfunctional uterine bleeding, a history of endometrial hyperplasia, and large polyps [3,6]. Moreover, endometrial polyps may associate with some other disease, such as infertility [7]. Therefore, clinical intervention is accepted even in the absence of symptoms.

For endometrial polyp therapy, surgical removal is commonly applied and its clinical feasibility has been demonstrated [8]. With the advent of hysteroscopy, hysteroscopic resection has been widely used and has gained increasing acceptance in the diagnosis and treatment of endometrial polyps. It can provide direct view and exhibits the possibility of converting the procedure from diagnostic to operative. At the same time, the development of other electronic or energy devices also provide extra options for endometrial polypectomy. For instance,

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monopolar or bipolar electrode based on an electronic system has been commonly used since the last century [9]. Moreover, mechanical or energy systems also provoke other procedures for endometrial polypectomy, such as laser resection or hysteroscopic morcellation [10]. These innovative procedures present multiple clinical surgical options for the management of endometrial polypectomy, and it is possible that endometrial polypectomy could be completely performed in outpatient settings. However, among all the current clinical procedures, the superior one for endometrial polypectomy still remains unknown. Thus, it is necessary to conduct a comprehensive quantitative comparison to evaluate the clinical efficacy of different surgical procedures based on network meta-analysis to provide objective evidence for clinical decision-making.

## 2. Methods

### 2.1. Literature search and retrieval

This study was conducted in strict accordance with the previously established PRISMA guidelines [11], and this work has been reported in line with Assessing the Methodological Quality of Systematic Reviews (AMSTAR). We initiated literature retrieval only in globally recognized electronic databases to ensure the authority of raw data. Thereby, the literature search was performed in MEDLINE, EMBASE and Cochrane Central. Different combinations of relevant mesh terms were used to address relative trials (an example of a search strategy is presented in [Supplementary Table S1](#)). Moreover, we did not apply any restrictions on publication status, but full English abstracts and texts of each trial were identified.

### 2.2. Inclusion and exclusion criteria

The inclusion criteria were (1) randomized controlled trials (RCTs); (2) trials focused on surgical procedure for endometrial polypectomy; (3) different applications of surgical procedures; and (4) both experimental and control groups received the same basic treatments.

The following items were defined as exclusion criteria: (1) non-RCTs; (2) no control group, or summarized experiences; (3) reviews, comments, case reports or study protocols; (4) experimental studies based on basic science; (5) trials with insufficient raw data; and (6) vague comparisons or mixed diseases.

### 2.3. Raw data extraction and quality assessment

General information (e.g., author name, publication data and region) and intervention-related characteristics (e.g., sample size and reported parameters) were abstracted using a predesigned form. In our current study, we aimed to evaluate the merits and drawbacks of different surgical procedures, thus surgical-relative data was selected as parametric data for quantitative comparisons. Considering the completeness and relevance of published raw data, we addressed 3 parameters, namely, operative time, success rate and complications to make comprehensive pooled estimates about the clinical effects of different procedures.

Moreover, the included trials were assessed by the Cochrane Risk of Bias assessment tool [12] to clarify the relative bias risk of individual studies with the following requirements: 1) free of selection bias; 2) free of performance bias; 3) free of detection bias; 4) free of attrition bias; 5) free of reporting bias; and 6) free of other bias. Relative graphics of bias risks for all included trials and the judgement for each trial were rated by Review Manager software (version 5.3).

The raw data extraction and bias risk assessment were independently conducted by two investigators. Any disagreements were resolved by group discussion with all team members.

### 2.4. Statistical analysis

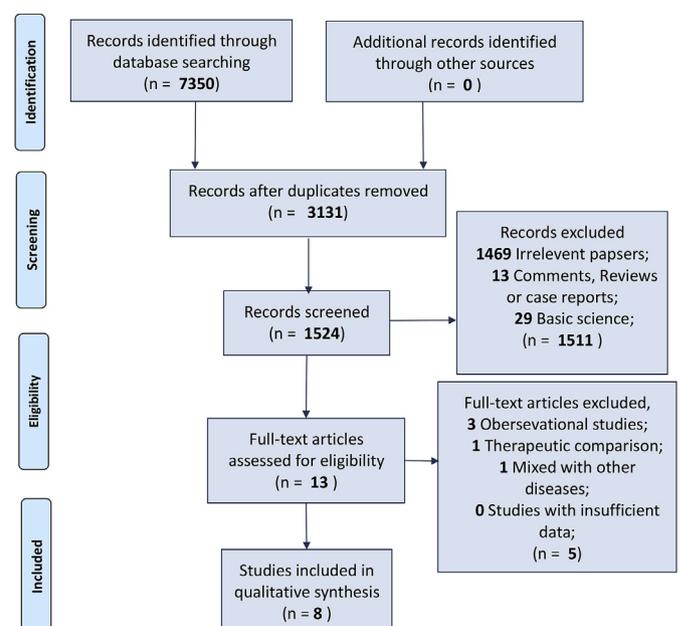
To establish comprehensive pooled estimates of the clinical effects of different procedures for endometrial polypectomy, we performed a quantitative meta-analysis regarding respective parameters based on the Bayesian theorem. This statistical procedure incorporates both direct and indirect information through a common comparator to obtain estimates of the relative interventional effects on multiple intervention comparisons [13,14]. The values of surface under the cumulative ranking (SUCRA) probabilities were calculated to reveal the pros and cons of different surgical procedures. The highest SUCRA values represented the probability of achieving the best clinical effects regarding each parameter [15,16]. Odds ratios (ORs) and relative credible intervals (CIs) derived from network meta-analysis were calculated to exhibit the comparison of different procedures. Both consistency and inconsistency model approaches were used to detect reliability of main results. Node-splitting analysis was conducted for closed loop calculation and no statistical inconsistency was shown if  $P > 0.05$  [17]. Potential Scale Reduction Factor (PSRF) values were set and limited to 1 to complete the calculation, and publication bias was assessed by examining funnel-plot symmetry.

Notably, for studies presenting median and range values, the raw data were converted to mean plus standard deviation by Luo and Wan formulas [18,19]. Data manipulation and statistical analyses of network meta-analysis were conducted using the Stata software package (version 12.0).

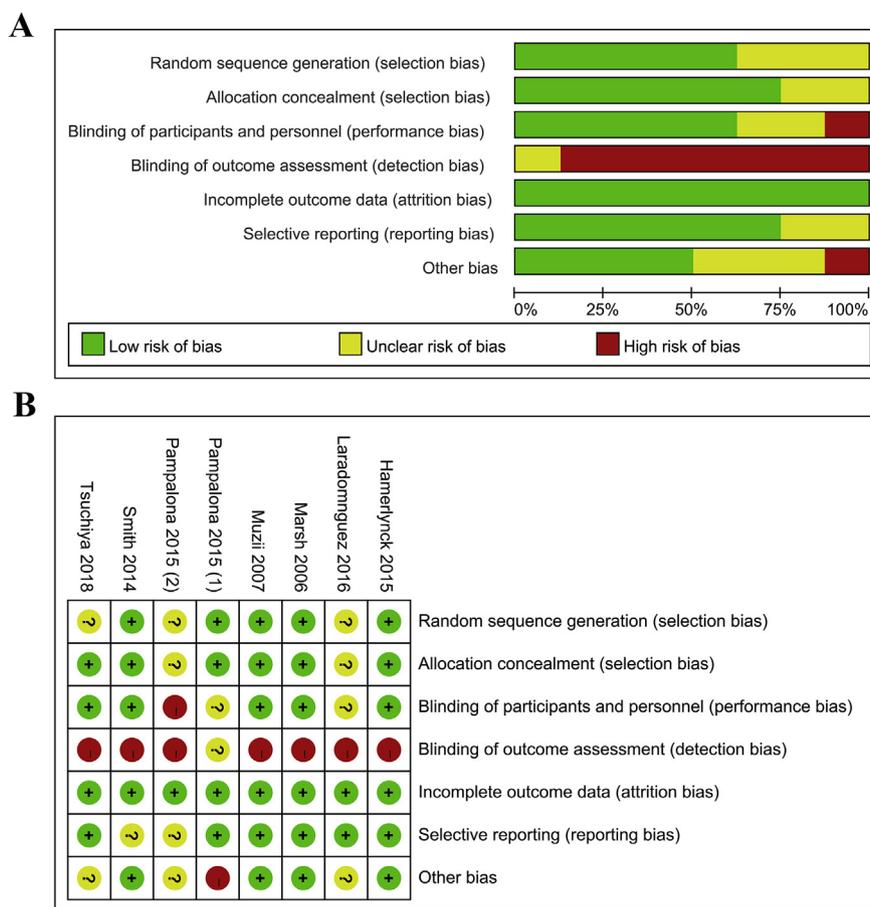
## 3. RESULTS

### 3.1. Study characteristics and quality assessment

With detailed reviewing titles, abstracts and full texts, we identified 8 RCTs containing 722 patients for the final pooled estimates ([Fig. 1](#)) [20–27]. For quality assessment, random generation and concealed allocation were reported in most included trials, but the double-blind process was barely detected (details in [Fig. 2](#)). These trials were published from 5 different countries and 5 different surgical procedures, namely, hysteroscopic morcellation, bipolar electrode, diode laser, monopolar electrode and traditional resectoscopy; were investigated; and were established with network connections for the comparisons



**Fig. 1.** Flow diagram of the process of selecting studies for this network meta-analysis.



**Fig. 2.** Bias assessment for included trials. (A) Risk of bias graph presented as percentages across all of the included studies; (B) judgements regarding each risk of bias item for each included study.

(Table 1) (Fig. 3).

### 3.2. Results of the network meta-analysis

As mentioned above, to comprehensively evaluate the clinical effects of 5 different surgical procedures, 3 relative parameters, namely, operative time, success rates and complications, were used for quantitative pooled estimates.

For operative time, 5 RCTs containing 466 patients provided relative raw data (Supplementary Fig. S1). After quantitative pooled estimates, we discovered that hysteroscopic morcellation seemed to be the best surgical procedure achieving the shortest operative time (SUCRA, 0.49) (Supplementary Table S2) (Fig. 4).

There were 7 RCTs comparing 4 procedures, which reported the success rates (Supplementary Fig. S2). The objective results, according to network meta-analysis, revealed that hysteroscopic morcellation was the superior procedure achieving the highest success rate compared to

others (SUCRA, 0.90) (Supplementary Table S2) (Fig. 4).

For safety evaluation, 6 trials containing 488 patients reported postoperative complication rates for the assessment (Supplementary Fig. S3). The results of pooled estimates showed that hysteroscopic morcellation had the lowest complication rates compared to other surgical procedures (SUCRA, 0.50) (Supplementary Table S2) (Fig. 4).

Therefore, after quantitatively comparing the respective parameters, based on network meta-analysis, we noticed that hysteroscopic morcellation demonstrated the shortest operative time, the highest success rate and the least complications. Thus, current evidence suggests that hysteroscopic morcellation is the superior surgical procedure for endometrial polypectomy.

### 3.3. Data consistency and publication bias

To test the steadiness and reliability of the main results in the current network meta-analysis, we performed quantitative analysis based

**Table 1**  
Characteristics of included studies.

Author	Year	Country	Interventional procedures	Sample size	Available parameter
Hamerlyncx	2015	Belgium	Hysteroscopic Morcellation vs. Bipolar Electrode	84	Operative time; Successful rate; Complication rate;
Lara-Domnguez	2016	Spain	Diode Laser vs. Bipolar Electrode	102	Operative time; Successful rate; Complication rate;
Marsh	2006	UK	Monopolar Electrode vs. Bipolar Electrode	40	Successful rate; Complication rate;
Muzii	2007	Italy	Traditional Resectoscopy vs. Bipolar Electrode	100	Operative time; Complication rate;
Pampalona (1)	2015	Spain	Hysteroscopic Morcellation vs. Bipolar Electrode	81	Operative time; Successful rate
Pampalona (2)	2015	Spain	Hysteroscopic Morcellation vs. Bipolar Electrode	127	Successful rate;
Smith	2014	UK	Hysteroscopic Morcellation vs. Bipolar Electrode	121	Successful rate; Complication rate;
Tsuchiya	2018	Japan	Hysteroscopic Morcellation vs. Monopolar Electrode	67	Operative time; Successful rate; Complication rate;

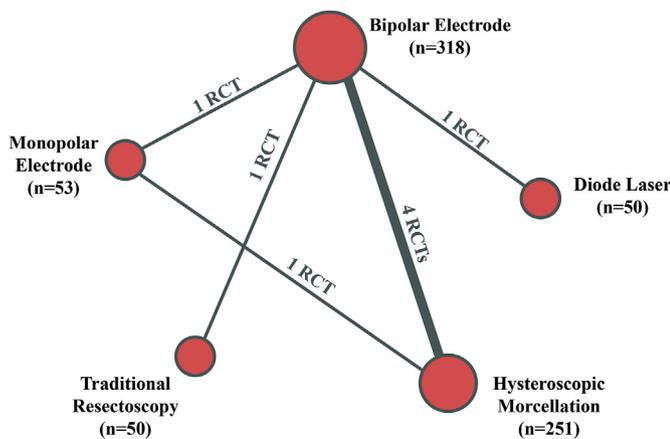


Fig. 3. Network connections of all of the included trials. The numbers on the line indicate the quality of studies compared with every pair of procedures, which are also represented by the width of the lines. Additionally, the sizes of the areas of the circles indicate the respective sample sizes.

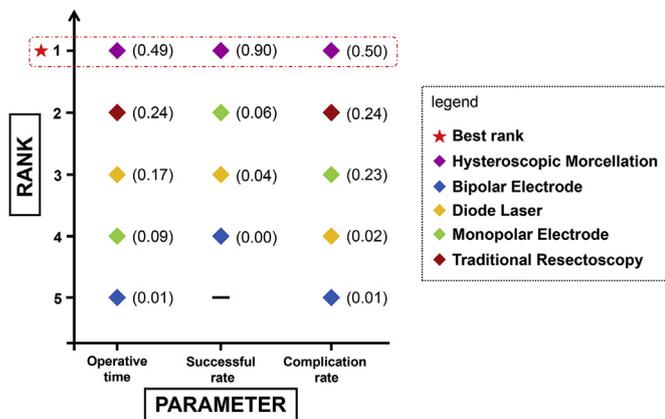


Fig. 4. Plot of surface under the cumulative ranking curve values of respective procedures regarding different parameters.

on the model mentioned above. If the condition of PSRF was limited to 1 in each data operator, we then noticed that relative ORs and credible intervals were similar with the data of the consistency model (Supplementary Table S2- 3). Furthermore, closed loop was observed regarding success and complication rates (Supplementary Figure S2- 3), thus we performed node-splitting analysis to detect the data consistency. The results indicated that all  $P > 0.05$ ; thereby, no potential inconsistent risk existed (Supplementary Table S4). On the other hand, funnel-plot symmetries regarding operative time (Supplementary Fig. S4), success rate (Supplementary Fig. S5) and complication rate (Supplementary Fig. S6) were observed, which demonstrated no obvious publication bias existed in our current study.

#### 4. Discussion

The current study aimed to make comprehensive evaluation of clinical effects of different procedures for endometrial polypectomy based on quantitative meta-analysis. After conducting the literature retrieval in 3 globally recognized databases, we identified 8 relevant RCTs with 722 in the sample size. Among these trials, 5 different surgical procedures were quantitatively compared based on the Bayesian theorem regarding 3 regular surgical parameters. The results indicated that hysteroscopic morcellation exhibited the superior clinical effects by achieving the shortest operative time, highest success rate and lowest complication rate. Node-splitting analysis demonstrated that no potential inconsistency existed in our main results and funnel-plot

symmetries implied no obvious bias was detected. Therefore, we concluded that hysteroscopic morcellation seemed to be the best surgical procedure for endometrial polypectomy based on current evidence.

Although removal of polyps obviously are easier than removal of myomas, different clinical parametric data still illustrated that different procedures reveal various effects. Hysteroscopic morcellation has been clinically applied since a decade ago [10]. Two previous meta-analyses demonstrated that hysteroscopic morcellation revealed better clinical efficacy than resectoscopic operations for endometrial lesions [28,29]. However, these 2 studies ignored the details of the procedures and made comparisons on different diseases. Thus, it could not provide adequate evidence for endometrial polypectomy. To the best of our knowledge, our current study is the first comprehensive, precise estimate of various procedures based on quantitative analysis. It clarified that hysteroscopic morcellation was superior to other procedures by revealing shorter operative time, higher success rates and fewer complications. Before hysteroscopic morcellation, the standard technique to remove endometrial polyps was resectoscopy with monopolar electrical current [10]. Since then, a disposable miniature bipolar electro-surgical system has been developed to be used with standard operating hysteroscopes to cut away polyps, with safety, accessibility, and feasibility [8,9,30]. However, retrieval of the detached polyp tissue from within the uterine cavity requires additional instrumentation, which may prolong the operative time of procedure. Thus, polypectomy under visual control with the resectoscope with an electro-surgical system seemed to be an effective way, but it takes more steps, which are tiring in the long run, and inconvenient to perform. By contrast, hysteroscopic morcellation makes tissue fragments easily removable and collected for subsequent histological analysis. Therefore, this procedure allows simultaneous tissue cutting and extraction from the uterine cavity under direct hysteroscopic view, reducing time from repeated insertion and removal of the hysteroscope to extract material through the endocervix during resectoscopy. Additionally, it was claimed that application of hysteroscopic morcellation showed shorter learning curves and was easier to use [31,32]. These may be the reasons why hysteroscopic morcellation takes shorter operative time than other procedures. For the success rate, it usually means the rate of complete removal of all polyps [33]. Previous studies claimed that electrodes reveal incomplete or partial resection of endometrial lesions whereas they exhibited impossibility of completely extracting the resected material, especially large lesions [9,25]. Moreover, electrical heating fluids may generate more steam bubbles and make the procedure more laborious, which usually results in increased failure rates. In contrast, hysteroscopic morcellation makes it possible to simultaneously cut and aspirate, resulting in better visualization and facilitating the complete removal of all lesion tissue. More importantly, the procedure is associated with a minimum risk of bubble-related embolism. These facts lead it to present higher success rates. Thus, we elucidated that hysteroscopic morcellation avoids the need for additional instrumentation within the uterine cavity, and reduces bubble formation or the accumulation of excised tissue fragments. These can improve visualization and safety during the procedure. More importantly, shorter operative time makes the procedure with hysteroscopic morcellation promote greater tolerance. Based on these theoretical foundations, we reckoned that hysteroscopic morcellation has more potential factors to bring fewer complications.

In summary, we performed quantitative analysis and made comprehensive explanations regarding relative parameters and demonstrated that hysteroscopic morcellation revealed superior clinical benefits compared to other procedures. In addition, some potential directions for future investigations based on our current study were also raised. Hysteroscopic morcellation and electrode seem to be followed with interest in this field. However, some other procedures, such as laser resection, or devices were barely focused on. Procedures with laser systems were newly applied and demonstrated effectiveness and safety [21,34]. They enable the surgeon to respect surgical planes and to tackle diseases in locations not easily accessible. This made it exhibit

more advantages and possible to replace electrode for polypectomy [21]. Although, hysteroscopic morcellation seemed to reveal more benefits than laser systems in this current meta-analysis, according to indirect comparison. However, the relative data was inadequate and no evidence of direct comparison or pairwise meta-analysis focused on this. This may be a new clinical research direction in the future. Additionally, our current study illustrated that hysteroscopic morcellation possessed the highest probability to achieve the best clinical effects regarding multiple parameters. However, more direct evidence with significant differences was still in need, especially the evidence for complications due to its low recurrence rate [35]. Thereby, we encourage large sample studies to be performed in the future. In addition, we must admit some inevitable drawbacks existed in our current study. First, this was a medium sample study and only 8 RCTs were included and basically reported from Europe. Thus, some potential local or other bias may contribute to our conclusions. Second, we compared only 3 parameters for quantitative analysis and some parameters such as long-term efficacy and cost-effectiveness could not be evaluated due to data insufficiency. Lastly, commonly in meta-analysis, quality of the original data may have inevitable effects on our final conclusions.

On the basis of current evidence, our study determined hysteroscopic morcellation revealed optimal potential to result in shorter operative time, higher success rates and fewer complications. This procedure should be recommended for endometrial polypectomy. In addition, inadequate data of some parameters were still in need to support our conclusions, whereas more high-quality large sample trials are expected in the future.

#### Ethical approval

None.

#### Sources of funding

None.

#### Author contribution

Tao Guo and Zhen Li designed the research; Tao Guo, Hui Zhou, Jian Yang, Ping Wu, Pengpeng Liu and Zhisu Liu performed the research and data collection; Tao Guo, Hui Zhou and Jian Yang contributed analytic tools and data analysis; Tao Guo and Zhen Li wrote the paper.

#### Conflicts of interest

The authors have no conflicts of interest to disclose.

#### Research registration number

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Zhen Li.

#### Provenance and peer review

Not commissioned, externally peer-reviewed.

#### Data statement

We declare that our manuscript involved complete data and no additional data are available for current submission. Moreover, new data may be added if our manuscript needs to be revised.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijso.2019.01.003>.

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