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Review

A network meta-analysis of updated haemostatic strategies for hysterectomy

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HIGHLIGHTS

- A comprehensive literature review and quantitative analysis were conducted.
- The best related hemostatic strategies for hysterectomy were determined.
- This article provided evidence-based suggestions for clinical decision-making.

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ABSTRACT

Objective: To determine the best haemostatic strategy for hysterectomy through a network meta-analysis.

Methods: We conducted a systematic literature search of the PubMed, Embase, and Cochrane Library databases and extracted data from randomized controlled trials comparing haemostatic strategies for hysterectomy. Direct comparisons and network meta-analyses were conducted in RevMan and ADDIS. Consistency models were established to identify the differences among different haemostatic strategies, and cumulative probability was used to rank the included strategies. Inconsistencies were also tested using node-splitting models.

Results: Twenty studies from 16 articles (2 articles contained 3 studies each) comprising 1392 patients were included. Direct meta-analysis showed that the LigaSure (SMD = −1.42 [−2.39, −0.44], P = 0.004), bipolar vessel sealing systems (BVSS) (SMD = −0.35 [−0.66, −0.03], P = 0.03), and pituitrin (SMD = −2.13 [−4.14, −0.13], P = 0.04) applications were effective haemostatic strategies. Based on the network meta-analysis and related subgroup analysis of different surgical procedures, the results showed that the application of pituitrin seemed to be the best haemostatic method for hysterectomy (Rank P = 0.64), especially for vaginal hysterectomy (Rank P = 0.72). The application of LigaSure was the best strategy for abdominal hysterectomy (Rank P = 0.54) but was not effective for laparoscopic hysterectomy (direct comparison with BVSS, MD = −31.39 [−146.61, 83.83], P = 0.59). The node-splitting models test revealed that no significant inconsistencies existed in this research.

Conclusions: Pituitrin application seemed to be the most effective haemostatic strategy for hysterectomy and was especially suitable for vaginal hysterectomy. The best method for reducing blood loss in abdominal hysterectomy was the application of LigaSure.

1. Introduction

Hysterectomy is one of the most common and effective surgical procedures to treat gynaecological disease and is performed on large numbers of women every year throughout the world [1]. The following three primary surgical hysterectomy procedures have been used for many years: abdominal, vaginal and laparoscopic hysterectomies. A previous Cochrane database review found that when compared with abdominal hysterectomy, vaginal hysterectomy is the preferred route for removing the uterus [2]. Meanwhile, laparoscopic hysterectomy is also favoured by many surgeons because of a faster return to normal activities, fewer wound infections and shorter hospital stays. However, for some large

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symptomatic leiomyomas of the uterus, abdominal hysterectomy may be used frequently thanks to its intrinsic advantages. In the early years, most hysterectomies were abdominal, with only 10–30% performed vaginally and less than 5% performed laparoscopically [3]. As surgical techniques have developed, each of these surgical procedures has become easier to use with any uterine condition in the appropriate circumstances.

As with any surgical treatment, complications affect the outcomes of hysterectomy. Haemorrhage, which is the most frequent and critical complication, often occurs during surgery. Therefore, adequate haemostatic techniques are essential during surgical procedures. Currently, surgical haemostasis can be secured by a variety of methods, including mechanical sutures (or clamping), electric coagulation, ultrasonically activated scalpel or drugs. Electrosurgical bipolar vessel sealing systems (BVSS) have been developed to seal large tissue bundles and blood vessels. This energy-based technology uses an alternative form of electrosurgery to denature collagen and elastin in vessel walls and subsequently reforms these proteins into a haemostatic seal. Currently, a new haemostatic system based on the combination of pressure and bipolar electrical energy, LigaSure (Valleylab, Boulder, CO, USA), is used to desiccate vascular tissues using a feedback-programmed amount of bipolar diathermy [4]. Most recently, LigaSure has been widely used in many surgical procedures. Its application in gynaecology is producing encouraging results both in laparoscopic and vaginal surgeries. Moreover, haemostatic medications are also used in gynaecological hysterectomy. Misoprostol, a synthetic analogue of prostaglandin E1, has been demonstrated to be applicable for the management of obstetric haemorrhage [5–7]. In addition, pituitrin, which is widely used in other gynaecological and obstetrical procedures, has been proven to elicit vasospasms and uterine contractions and was reported to reduce blood loss in hysteroscopic myomectomy [8,9]. Moreover, tranexamic acid, which inhibits fibrin degradation, is an antifibrinolytic agent that was approved for the treatment of haemorrhage many years ago [10].

Hence, as surgical techniques continue to improve, various haemostasis techniques are also becoming more refined. In the past two decades, many randomized controlled trials (RCTs) and systematic reviews have been reported. Certain haemostatic strategies were proved to be effective. However, among these haemostatic measures, the best strategy for hysterectomy remains uncertain. In the present study, we focus on previously reported RCTs that systematically compared haemostatic strategies based on comprehensive network meta-analysis to provide evidence-based suggestions for clinical decision-making.

2. Methods

2.1. Description of design

In recent years, many RCTs from different countries have been published. For inclusion in this study, the research had to have originated from studies that could be found in globally recognized databases. The studies were not limited to specific languages, although an English-language abstract had to be available for each study.

Various hemostatic measures from different studies, which reached basic consensuses or were demonstrated to be safe, were given full consideration for enrolment. Therefore, in this study, we only focused on types of haemostatic strategies, appropriate interventions and objective intraoperative blood loss. Data from the only primary endpoint, intraoperative haemorrhages, were compared based on comprehensive network meta-analysis.

Subgroup analyses of different surgical procedures were also performed in this study. For the record, if a comparison could not establish net connections (in the case of certain subgroup analysis, for example), direct comparison would also be used between specific studies for a more comprehensive evaluation.

2.2. Literature search and study selection

An electronic search was performed using PubMed, Embase, and Cochrane Library databases until June 2016. The search strings were based on MeSH terms, including “hysterectomy,” “metrectomy,” “metrosteresis,” “ureterectomy,” “hemorrhage,” “haemorrhage,” “hemostasis,” “hemostasia,” “hematischesis,” “blood loss,” and “randomized controlled trial.” Different combinations of these terms were used for the searches. We included all germane studies of human research, and missing details (including missing randomization, quantitative data and allocation methods) were manually searched or were requested from the authors. We did not apply any language or publication status restrictions.

The inclusion criteria included the following: (1) randomized controlled trials; (2) parameters of intraoperative blood loss should be provided in the studies; (3) raw data for haemorrhage should include the mean (and standard deviation) or medians (and ranges); (4) all data for meta-analysis must come from successful operations; and (5) each haemostasis method must be the only intervention performed.

The exclusion criteria eliminated studies with the following characteristics: (1) no control group, (2) incomplete raw data for the purpose of this research and the authors could not be reached for a response, (3) the study was limited to animals or cells, (4) data types were provided as neither mean ± SD nor medians (ranges), and (5) commentaries, review papers, and articles with missing or unavailable data.

2.3. Data extraction and quality assessment

The data extraction was independently accomplished by two authors (T. Guo and L. Ren). Disagreements were resolved without assumptions or simplifications by reaching consensus with the other authors (QX. Wang and K. Li). The Cochrane risk of bias assessment tool [11] was used to assess the methodological quality of individual studies. Studies were included if they met all of the following criteria: (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. All four investigators assessed the quality of the examined studies through discussion until reaching agreement.

2.4. Statistical analysis

In this research, we paid close attention to the haemostatic efficacy of different interventions. It was necessary to make comparisons between every haemostatic strategy via a comprehensive network meta-analysis based on the Bayesian theorem. This approach can be considered to be an extension of the traditional pair-wise meta-analysis, as it incorporates both direct and indirect information through a common comparator to obtain estimates of the relative interventional effects on multiple intervention comparisons [12,13]. We evaluated consistency by combining the quantitative estimates from direct and indirect comparisons according to the experimental design and primary outcomes of the included studies. If there was no evidence of relevant inconsistency, a consistency model could be used to draw conclusions about the relative effect of the included interventions. A relevant rank probability plot could present the best therapeutic measure. In addition, node-splitting analysis was also performed to prove that no