



## Review

## Surgical and clinical safety and effectiveness of robot-assisted laparoscopic hysterectomy compared to conventional laparoscopy and laparotomy for cervical cancer: A systematic review and meta-analysis

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### Abstract

**Aim:** This study aimed to evaluate the surgical safety and clinical effectiveness of RH versus LH and laparotomy for cervical cancer.

**Methods:** We searched Ovid-Medline, Ovid-EMBASE, and the Cochrane library through May 2015, and checked references of relevant studies. We selected the comparative studies reported the surgical safety (overall; peri-operative; and post-operative complications; death within 30 days; and specific morbidities), and clinical effectiveness (survival; recurrence; length of stay [LOS]; estimated blood loss [EBL]; operative time [OT]) and patient-reported outcomes.

**Results:** Fifteen studies comparing RH with OH and 11 comparing RH with LH were identified. No significant differences were found in survival outcomes. The LOS was shorter and transfusion rate was lower with RH compared to OH or LH. EBL was significantly reduced with RH compared to OH. Compared to OH, overall complications, urinary infection, wound infection, and fever were significantly less frequent with RH. The overall, peri-operative, and post-operative complications were similar in other comparisons. Several patient-reported outcomes were improved with RH, though each outcome was reported in only one study.

**Conclusions:** RH appears to have a positive effect in reducing overall complications, individual adverse events including wound infection, fever, urinary tract infection, transfusion, LOS, EBL, and time to diet than OH for cervical cancer patients. Compared to LH, the current evidence is not enough to clearly determine its clinical safety and effectiveness. Further rigorous prospective studies with long-term follow-up that overcome the many limitations of the current evidence are needed.

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**Keywords:** Cervical cancer; Robotic hysterectomy; Radical hysterectomy; Open hysterectomy; Laparoscopic hysterectomy

### Introduction

Robot-assisted laparoscopic hysterectomy (RH) has been developed as a minimally invasive treatment approach for gynecological diseases.<sup>1</sup> Robotic surgery has technical advantages over conventional laparoscopy or laparotomy, including three-dimensional viewing, more accurate instrument control, and a shorter learning process.<sup>2,3</sup> However, the robotic surgical system lacks tactile feedback.<sup>4</sup>

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Although several systematic reviews evaluated the safety and effectiveness of RH compared to conventional surgical techniques for gynecological diseases,<sup>5–9</sup> previous studies for cervical cancer are limited. Most previous reviews showed that RH reduced the operative time (OT), length of stay (LOS), rate of transfusion, and incidence of complications compared to open hysterectomy (OH) and decreased the LOS and estimated blood loss (EBL) compared to laparoscopic hysterectomy (LH).<sup>6,8–11</sup> However, these studies are limited due to the low quality of the primary studies included, small sample sizes, and short-term follow-up periods. Therefore, the clinical safety and effectiveness of RH compared to conventional surgical techniques remain uncertain. Recently, several primary studies reported benefits in patient-centered outcomes as well as surgical outcomes, with RH.<sup>12–14</sup>

We performed a systematic review and meta-analysis to evaluate the surgical and clinical benefits and risks of RH compared to LH or OH for cervical cancer patients.

## Materials and methods

The methods for this study were specified a priori based on the recommendations in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.<sup>15</sup>

### Search strategy

We searched for studies comparing RH with LH or OH for the treatment of cervical cancer using Ovid-Medline, Ovid-EMBASE, and the Cochrane Library databases, along with five domestic databases (KoreaMed, KMBase, KISS, RISS, and KisTi) without restriction of language or publication year. Search terms combined MESH-terms (uterine neoplasms) and the related terms “cervical cancer,” “uterine cancer,” “gynecologic cancer,” “Robotics,” “Computer-assisted surgery,” “telerobot,” “remote operation,” “remote surgery,” “Da Vinci,” and “Zeus.” We also reviewed the bibliographies of relevant articles to identify additional publications and examined the references from Intuitive Surgical Korea Ltd.

### Study selection

Two authors independently evaluated the eligibility to determine whether they met all of the inclusion criteria. Disagreements were resolved by discussion or consultation with third author. The inclusion criteria specified (1) studies that focused on patients with cervical cancer, (2) comparative studies between RH and OH or LH, (3) studies that reported at least one outcome of interest, and (4) published original, peer-reviewed articles. Non-original studies, animal tests or preclinical trials, abstract-only publications, reports in a language other than English or Korean, and duplicates were excluded.

### Data extraction and quality assessment

The quality of studies was assessed using the risk of bias for non-randomized studies (ROBANS ver 2.0) developed based on the Cochrane risk of bias. The quality assessments were performed by two independent researchers (DAP and JEY). Disagreements were resolved by consensus of all authors. Two reviewers independently extracted the safety and effectiveness indexes into a prespecified data extraction form and double checked them. Especially complication outcomes consisted of the overall, intra-operative and post-operative complications, and individual adverse events including major complications, such as injury to the bladder and ureter, cystotomy, vaginal complications, thromboembolism, ileus/bowel obstruction, and wound infection, and minor complications such as post-operative fever and urinary tract infection.

### Statistical analysis

The meta-analyses were conducted using Review Manager 5.3 (RevMan, The Cochrane Collaboration, Oxford, UK) and Comprehensive meta-analysis 2.0 (CMA). The Cochrane-Q statistic and the  $I^2$  statistic were used to assess statistical heterogeneity. The weighted mean difference (WMD) and 95% confidence intervals (CI) were used as the summary variables for continuous outcomes and the relative risk (RR) and 95% CI for dichotomous variables. Heterogeneity was analyzed using a chi-squared test and a P value < 0.10 was used to establish statistical significance with the  $I^2$  test.<sup>16</sup>  $I^2$  values > 50% were considered substantial evidence of statistical heterogeneity.<sup>17</sup> We utilized a fixed-effects model in the absence of significant heterogeneity and a random-effects model in the presence of significant heterogeneity. We prespecified subgroup analyses according to the study design including matched populations and concurrent controls. Also we performed a sensitivity analysis with only studies with  $\geq 90\%$  stage I in both groups.

## Results

We identified 1798 potentially relevant studies from electronic databases and selected 126 for full text review. Of these, 108 studies were excluded and four reports were found during our manual searches (Fig. 1).<sup>12–14,18–36</sup>

### Study characteristics

Table 1 shows the characteristics of the 22 studies included. Five<sup>12,14,33,34,36</sup> of these studies included comparisons across all three groups, 15<sup>12,14,19,20,23–25,27–30,32–34,36</sup> examined RH versus OH, and 11<sup>12–14,21,22,26,31,33–36</sup> examined RH versus LH. Of the 15 studies comparing RH with OH, all except one<sup>34</sup> were single-center studies. Eleven of these were nonconcurrent cohort

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