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Original Article

# Systematic review of laparoscopic comprehensive staging surgery in early stage ovarian cancer: A meta-analysis

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ABSTRACT

*Objective:* To assess the clinical outcomes of laparoscopic comprehensive staging surgery in early stage ovarian cancer.

*Materials and methods:* Electronic literature searches were conducted in Embase, MEDLINE, Cochrane Library, China Biology Medicine, and Chinese National Knowledge Infrastructure, and literature on laparoscopy versus laparotomy for comprehensive staging surgery was retrieved. The literature was selected according to certain inclusion criteria. Data were extracted from these studies and the quality of the included studies was assessed. The meta-analysis was conducted using the Review Manager 5.2 software.

*Results:* A total of 11 nonrandomized controlled trials involving 591 cases were included. The pooled data indicated less intraoperative blood loss, lower postoperative complication rates, shorter postoperative hospital stays, and lower postoperative recurrence rates in the laparoscopy group. There were no significant differences in operative time, harvested lymph node number, intraoperative complications, or mortality.

*Conclusion:* For comprehensive staging surgery, laparoscopy was equivalent to or even better than conventional laparotomy for early ovarian cancer. More robust evidence should be explored for precise verification.

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## Introduction

Ovarian cancer represents 2.4–5.6% of all female malignancies and has the highest mortality rate for women who develop gynecologic malignancies [1,2]. Women with advanced ovarian cancer have a 5-year survival rate of <50%, but those with Stage I ovarian cancer have a 5-year survival rate of 85–90% [3]. However, in clinical practice, Stage I ovarian cancer is usually found incidentally during routine ultrasonography, laparoscopy, or laparotomy for an ovarian cyst or presumed benign tumors [4,5]. Furthermore, for patients with Stage I ovarian cancer, >30% are upstaged after comprehensive surgical staging because of microscopic metastatic disease [2,6].

According to the International Federation of Gynecology and Obstetrics (FIGO), standard management for apparent early stage disease is complete surgical staging, including total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and paraaortic lymph node dissection, infracolic omentectomy, multiple peritoneal washing, and multiple peritoneal biopsies during a generous laparotomy [2]. The FIGO guidelines indicated that there are three independent factors affecting the survival of all patients with ovarian cancers: stage of cancer at diagnosis, histological grade, and volume of residual disease after surgery [7]. Thus, it is of significant importance to stage early stage ovarian cancer (EOC) to predict patients' prognosis adequately. Furthermore, staging information is a crucial factor for deciding the appropriate adjuvant therapy for most gynecologic oncologists [4]; in addition, fertility sparing treatment may be appropriately offered to young women as requested if Stage I disease is confirmed [6].

The conventional approach for ovarian cancer is surgical exploration through a midline vertical abdominal incision [4]. However, recent developments in laparoscopy for staging provide an attractive option for optimal surgical and oncologic outcomes, although the cost of laparoscopy is higher than that of laparotomy [4]. The feasibility, safety, and advantages of laparoscopic staging surgery for ovarian cancer are well established [2,4]. The advantages of laparoscopy over laparotomy are better intraoperative

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visualization, improved cosmesis, less blood loss, decreased postoperative complications such as wound infections and small bowel ileus, a shorter hospital stay, and a faster recovery [8–10].

However, laparoscopic staging surgery for EOC is not without controversy, and only a few studies are available to help elucidate whether laparoscopy is a proper management tool for EOC because of difficulty in recruiting a sufficient number of patients [4]. Concerns over minimally invasive surgery for EOC are the carbon dioxide effect, dissemination occurring from the exfoliation of tumor cells, and a high risk of intraoperative tumor rupture due to limitations in laparoscopic staging surgery [4,11]. Because of recent advances in laparoscopic techniques and instruments, early concerns have been largely unfounded [10,12]. As evidence is gradually accumulated, laparoscopic staging of EOC has at least equivalent, although not significantly superior, surgical–pathological outcomes and middle-range oncologic results as a conventional treatment approach [10]. No vital evidence exists to determine the efficacy and safety of laparoscopic surgery versus laparotomy for staging EOC, and only a descriptive systematic review [9] and a quantitative meta-analysis [12] involving no Chinese populations were available. Therefore, we aimed to conduct a meta-analysis of laparoscopic comprehensive staging surgery for patients with EOC.

## Materials and methods

### *Literature search*

A thorough literature search was performed by two independent researchers using the key words “ovarian cancer”, “early stage”, “laparoscopy”, “staging surgery”, and “staging laparoscopy” in MEDLINE (from December 1969), Embase (from September 1974), the Cochrane Library (from February 1990), China Biology Medicine (from 1987), and Chinese National Knowledge Infrastructure (from 1999) for all articles published (to March 2014). Abstracts of trials that were identified through electronic searches were further reviewed, and those with original data that specifically provided useful operative outcomes were retrieved for detailed evaluation.

### *Study selection*

The inclusion criteria for studies that were subject to our meta-analysis were as follows: (1) *study design:* randomized controlled trials (RCTs) or well-designed nonrandomized controlled trials with no confinement on allocation concealment, blinding, or districts; (2) *patients:* individuals diagnosed with EOC; (3) *intervention*: the experimental group had laparoscopic staging surgery, and the control group had a laparotomy; and (4) *outcomes*: operative time, intraoperative blood loss, time to first postoperative flatus, number of resected pelvic lymph nodes, intraoperative or postoperative complication rate, recurrence rate, etc.

The exclusion criteria were as follows: (1) comments, reviews, and editorials; (2) incomplete original data or studies with only abstracts available; (3) case reports, case series, and noncontrolled researches; (4) studies in which laparoscopic surgery was performed for diagnostic biopsy instead of radical treatment; and (5) overlapping articles, and in cases of duplicate study populations, only the larger study was included in our analysis.

### *Data extraction*

Two independent researchers reviewed the literature by strictly following the inclusion/exclusion criteria. After analyzing each study, the following variables showing operative outcomes were examined: (1) operation time [mean ± standard deviation (SD), minutes]; (2) intraoperative blood loss (mean ± SD, mL); (3) pelvic lymphadenectomy number; (4) para-aortic lymphadenectomy number; (5) time to first postoperative flatus; (6) intraoperative complications; (7) postoperative complications; (8) hospital stays; (9) recurrence rate during follow-up after staging surgery; (10) postoperative mortality rate; and (11) rate of intraoperative tumor rupture. While examining these variables, data presented as a median value and a range were converted to a mean value and SD using the formula proposed by Hozo et al [13].

### *Methodological quality assessment*

Two authors independently assessed the risk of bias according to the *Cochrane Handbook for Systematic Reviews of Interventions* [14]. We evaluated the risk of bias in the included studies using the Review Manager software (RevMan version 5.2; The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark), which included the following key domains: (1) sequence generation; (2) allocation sequence concealment; (3) blinding; (4) incomplete outcome data; (5) selective outcome reporting; and (6) other potential sources of bias.

### *Data analysis*

The analysis was performed using RevMan version 5.2 (The Nordic Cochrane Center). The $\chi^2$ test was used to assess heterogeneity. A $p$ value <0.10 was considered statistically significant. The $I^2$ statistic was used to estimate the degree of heterogeneity. Dichotomous data are presented as relative risks with 95% confidence intervals (CIs). We analyzed the data based on an intention-to-treat principle. If no heterogeneity was detected, a fixed effects model was used to analyze the data. A random effects model was used if there was any unexplained heterogeneity. The authors of the included studies were contacted to supply any missing data. If a sufficient number of eligible trials (>10 studies) existed, a funnel plot analysis was conducted to assess reporting biases [15]. We conducted a subgroup analysis to test for differences between results published in English and Chinese.

## Results

A total of 565 potentially relevant studies regarding laparoscopic comprehensive staging surgery and EOC were identified, among which 432 studies were in English, and the remaining 133 studies were in Chinese. Five hundred and thirty-two studies were initially excluded for various reasons: 481 irrelevant studies were excluded after reviewing the titles and abstracts; a few other studies were excluded because they were case reports ($n = 5$), reviews ($n = 6$), and duplicates ($n = 40$). After reviewing and analyzing the clinical outcomes of the initially selected studies, only 11 trials with 591 EOC patients were identified that satisfied the inclusion/exclusion criteria, of which five studies were published in English and six studies were published in Chinese (Fig. 1). The methodological quality of the included trials is presented in Fig. 2.

The included 11 studies [2,4,16–24] involved 591 participants and were all nonrandomized controlled trials comparing laparoscopy with laparotomy for the staging of EOC patients. The baseline characteristics of all 591 EOC patients are summarized in Table 1. There were 235 patients in the laparoscopy group and 356 patients in the laparotomy group, and no statistically significant differences in age, body mass index, clinical staging, pathological pattern, or histological grading were observed between the two groups.

The operative time (minutes) between the two groups was investigated with statistical heterogeneity among the results of all studies ($I^2 = 77\%$; $p < 0.00001$), and therefore a random effect

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