Challenges in Laparoscopic Surgery for Early-Stage Cervical Cancer Postprint

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Abstract

In recent years, laparoscopic minimally invasive surgery has been widely employed in the treatment of early-stage cervical cancer. Previous retrospective studies have demonstrated that minimally invasive surgery offers advantages of reduced intraoperative blood loss, shorter hospitalization duration, and accelerated postoperative recovery, while showing no significant difference in overall survival compared with conventional open surgery. However, a prospective multicenter randomized controlled clinical trial and a retrospective epidemiological study, both published in N Engl J Med on October 30, 2018, revealed that minimally invasive surgery increased mortality in early-stage cervical cancer. Although these findings do not completely negate the role of laparoscopy in treating early-stage cervical cancer, they should prompt surgeons to pay close attention and reflect: adherence to standardized oncological treatment principles is fundamental, and the selection of surgical approach should be based on patient characteristics, disease features, and the surgeon' s technical expertise.

Full Text

Challenges of Laparoscopic Surgery for Early-Stage Cervical Cancer

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Abstract

In recent years, minimally invasive laparoscopic surgery has been widely used for early-stage cervical cancer. Previous retrospective studies have shown that

minimally invasive surgery offers advantages including reduced intraoperative blood loss, shorter hospital stays, and lower postoperative complication rates compared to abdominal surgery, without compromising survival outcomes. However, a prospective multicenter randomized controlled trial and a retrospective epidemiological study published in the *New England Journal of Medicine* on October 30, 2018, demonstrated that minimally invasive surgery was associated with higher recurrence rates and lower disease-free survival in cervical cancer patients. While these results do not completely negate the role of laparoscopy in cervical cancer treatment, they warrant serious attention and reflection from surgeons. Standardized oncologic principles remain fundamental, and surgical approach selection should be based on patient characteristics, disease features, and surgeon expertise.

Keywords: laparoscopic surgery; early-stage cervical cancer; recurrence; disease-free survival

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Since the 1990s, rapid advances in science and technology have led to the development of new materials and techniques increasingly applied in medicine. Gynecologic oncologists have continuously pursued surgical approaches that minimize trauma while optimizing treatment outcomes. In this context, laparoscopic surgery has gradually found its application in gynecologic oncology. Through persistent efforts and practice, its use has expanded across an increasingly broad range of indications.

In 1992, Dargent et al. reported the first case of laparoscopic pelvic lymphadenectomy combined with laparoscopic-assisted radical vaginal hysterectomy (LARVH) for cervical cancer. That same year, American scholars Nezhat et al. described the first laparoscopic radical hysterectomy with pelvic lymphadenectomy. In 1993, Childers et al. reported laparoscopic staging for early endometrial cancer, and in 1994, Querleu et al. first published laparoscopic staging for early ovarian cancer. Since then, reports of laparoscopic applications in gynecologic malignancies have proliferated.

For patients with early-stage cervical cancer, laparoscopic radical hysterectomy (LRH) and retroperitoneal lymph node dissection have become widely adopted. The National Comprehensive Cancer Network (NCCN) guidelines have recommended minimally invasive surgery as an acceptable approach for early-stage cervical cancer, citing benefits such as reduced blood loss, shorter hospital stays, and lower complication rates, with comparable survival outcomes.

On October 30, 2018, the *New England Journal of Medicine* published two pivotal studies comparing minimally invasive versus open radical hysterectomy for early-stage cervical cancer. The prospective multicenter randomized controlled trial and retrospective epidemiological study both revealed that minimally invasive surgery was associated with increased mortality in early-stage cervical cancer. The trial showed that the minimally invasive group had a 10.6% lower disease-free survival rate (86% vs. 96.5%) and significantly lower overall sur-

vival compared to the open surgery group. The retrospective study found a 65% higher risk of death in the minimally invasive group (HR = 1.65). Notably, after the adoption of minimally invasive surgery in 2006, the annual overall survival rate decreased by 0.8%, despite having increased by 0.3% annually before 2000.

These findings, while disappointing, must be interpreted with caution. Every study has limitations. Although the randomized controlled trial enhanced patient coverage across centers, the average enrollment was only a few patients per center per year, with recurrent cases concentrated in just a few of the participating centers, suggesting that institutional or surgeon factors cannot be ignored. The studies also lacked specific data on recurrence patterns and causes of death, and did not analyze why minimally invasive surgery resulted in shorter survival. Furthermore, the results may not be generalizable to low-risk patients (tumor diameter <2 cm, no lymphovascular space invasion, negative lymph nodes), as the study populations were insufficient to compare survival outcomes in this subgroup.

The surgical community has raised concerns about potential technical limitations of laparoscopy. Reports of tumor metastasis at port sites and peritoneal surfaces have increased. Some researchers attribute this to pneumoperitoneum effects. Lin et al. conducted an animal study comparing tumor dissemination with and without pneumoperitoneum, finding that while both groups developed metastases, the pneumoperitoneum group showed diffuse peritoneal injury and changes. Electron microscopy revealed that CO2 pneumoperitoneum caused immediate mesothelial cell contraction, creating opportunities for tumor cell implantation. In vitro studies have shown that cervical cancer cells exposed to CO2 environments exhibit enhanced proliferative capacity after initial suppression, with weakened apoptosis.

Another critical concern involves the uterine manipulator. Kong et al. compared recurrence patterns after laparoscopic versus vaginal transection of the vaginal cuff, finding significantly higher metastasis rates when the cuff was transected laparoscopically (16.3% vs. 5.1%, p = 0.057), suggesting that vaginal removal may reduce the risk of intraperitoneal tumor spillage. The manipulator may cause tumor shedding during colpotomy, though proper selection and technique could mitigate this risk.

These results remind us to carefully reflect on and cautiously approach minimally invasive surgery for early cervical cancer. We must not completely negate the role of laparoscopy based solely on two studies, but rather analyze the underlying causes and improve our techniques. Patient selection is paramount. For large exophytic tumors (>3 cm), direct laparoscopic surgery should be avoided; instead, neoadjuvant chemotherapy followed by laparoscopy or primary open surgery should be considered.

Gynecologic oncologists must have a comprehensive understanding of intraoperative tumor-free principles: avoiding tumor rupture, protecting all incision sites,

minimizing pressure changes, and reducing frequent instrument exchanges. Attempting vaginal cuff transection without pneumoperitoneum during the final surgical stage may help reduce intraperitoneal dissemination risk.

To further establish the safety of minimally invasive surgery, China needs to launch prospective multicenter randomized controlled trials promptly. Laparoscopic surgery requires a substantial learning curve, and in many cases, inferior outcomes may reflect inadequate surgical skill rather than inherent flaws in the approach. We advocate for the concept of minimally invasive surgery but should not pursue laparoscopy for every case. Not all gynecologists need to adopt laparoscopic techniques.

For early-stage cervical cancer, surgical approach selection requires careful evaluation of patient characteristics, disease features, and surgeon expertise. We must balance efficacy and safety, continuously refine our techniques, and adhere to standardized oncologic principles. An experienced surgeon chooses the most appropriate approach based on the patient, disease, and available technology, rather than dogmatically pursuing laparoscopy in all cases.

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Note: Figure translations are in progress. See original paper for figures.