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Original Research

Laparoscopic nerve-sparing radical hysterectomy for bulky cervical cancer (≥6 cm) after neoadjuvant chemotherapy: A multicenter prospective cohort study

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HIGHLIGHTS

- To evaluate the clinical outcomes of laparoscopic nerve-sparing radical hysterectomy (LNRH) for bulky stage cervical cancer (lesion ≥ 6 cm) after neoadjuvant chemotherapy (NAC).
- The LNRH after NAC with TC for bulky stage cervical cancer confirmed to the urinary and intestinal function recovered better.
- The latest study of the patients with bulky stage cervical cancer subjected to this therapeutic strategy.

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ABSTRACT

Objective: The study aimed to evaluate the clinical outcomes of laparoscopic nerve-sparing radical hysterectomy (LNRH) for bulky-stage cervical cancer (lesion ≥ 6 cm) after neoadjuvant chemotherapy (NAC).

Methods: This study prospective recruited patients with pathology-confirmed cervical cancer presenting as a bulky mass (lesion ≥ 6 cm). Subjects included patients who underwent laparoscopic radical surgery. They were assigned to one of two groups by surgical method: patients who underwent LNRH after NAC and patients who underwent classical laparoscopic radical hysterectomy (LRH) after NAC. We compared the patients' general clinical characteristics, surgical profiles, pathological findings and adjuvant therapies between the two groups. Recovery of bladder and intestinal function was evaluated by questionnaire. Patients were followed for up to 1 year to determine the maintenance of effect.

Results: Compared with patients treated with LRH, patients who underwent LNRH presented no significant differences in age, surgery characteristics, pathological findings, adjuvant therapies or main adverse effects. The mean duration of residual urine <50 mL in the LNRH group was 11 days, much shorter than that in the LRH group (18 days; $P < 0.001$). The period of passage of gas by anus was shorter (38.9 ± 4.1 h) in LNRH patients than that in LRH patients (56.5 ± 4.0 h; $P < 0.001$). The urinary and intestinal symptoms were evaluated 1 year after surgery. The recovery of urinary and intestinal function of patients was better in the LNRH group than in the LRH group.

Conclusion: LNRH is a safe and feasible surgical management for bulky-stage cervical cancer patients (lesion ≥ 6 cm), and after NAC, the urinary and intestinal function of patients in LNRH group showed better recovery compared with functions in the LRH group. The technique is relatively new, and its oncologic efficiency has not yet been fully established. Prospective randomised controlled studies with an increased number of patients and long-term postoperative follow-up should be carried out to investigate the effect of this therapeutic strategy for bulky-stage cervical cancer.

1. Introduction

Cervical cancer is still the second most common malignancy and second most common cause of cancer-related death in women

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worldwide [1]. Conventional surgical management of cervical cancer is radical hysterectomy (RH), which is associated with postoperative morbidities such as bladder dysfunction, sexual dysfunction and colorectal motility disorders [2–4]. Damage to the pelvic nerve plexus (inferior hypogastric plexus) and its vesical branches is the main cause of dysfunction. The pelvic automatic nerves are the pathway for the neurogenic control of rectal and bladder functions. They supply blood vessels of the female internal genitals and are involved in the neural control of the lubrication-swelling response [5]. Improving surgical treatment, as well as postoperative quality of life, is an increasingly important challenge for women diagnosed with cervical cancer.

Compared with conventional RH, laparoscopic radical hysterectomy (LRH) is now performed routinely around the world, because it is minimally invasive [6]. However, LRH still leads to substantial rates of postoperative morbidity. As surgical technology has developed, the magnified horizon of laparoscopes has allowed clearer visualisation of structures such as nerve branches. Laparoscopic nerve-sparing radical hysterectomy (LNRH) has been developed for early-stage cervical carcinoma, with a technical procedure already established [7–9]. In this procedure, advantages such as preserving sexual, bladder and bowel function associated with the pelvic nerve plexus and its vesical branches, are preserved [7,9].

However, patients with bulky-stage cervical cancer are difficult to manage because of the high recurrence rate and worse prognosis. Neoadjuvant chemotherapy (NAC) before RH has been widely used in bulky cervical cancer, with the purpose of reducing tumour size, lowering the difficulty of operation and reducing the risk factors of recurrence. LNRH has become increasingly common in early-stage cervical cancer and locally advanced cervical cancer after NAC [10]. Nevertheless, no systematic research that particularly concentrates on LNRH for cervical cancer patients with a bulky mass (lesion $\geq$ 6 cm) exists. Therefore, the present study sought to testify the surgical outcomes of LNRH for bulky mass cervical cancer (lesion $\geq$ 6 cm) after NAC.

2. Materials and methods

2.1. Study subjects

This study was conducted prospectively in three medical centres, in patients with bulky cervical cancer (2009 FIGO staging IB2 orIIA2) with a lesion $\geq$ 6 cm, from December 2012 to March 2015. The inclusion criteria were as follows: patients without any evidence of parametrical invasion or lymph node metastasis on preoperative pelvic examination, magnetic resonance imaging and positron emission tomography/computed tomography examinations. Exclusion criteria included neuroendocrine histology, history of psychiatric disease, pathologically proven distant metastasis, urinary dysfunction preoperative and another coexisting malignancy. Patients with an adequate follow-up duration of more than one year after the surgery were included in the analysis. The study design was approved by the appropriate ethics review board of Clinical Medical College of Lanzhou University. All participants signed the written informed consent.

2.2. NAC treatment regimens

All patients received NAC with 2 or 3 courses of paclitaxel plus carboplatin (TC) treatment before surgery [11]. Courses of NAC were administered 21 days apart, with an intravenous paclitaxel dosage of 175 mg/m^2 and intravenous carboplatin with area under the curve (AUC) 6 mg/mL per min, both administered on Day 1. A maximum of 3 courses of NAC were administered to each patient. Within 4 weeks after the last course of NAC, patients were re-evaluated with physical and imaging examination. The response of tumour was assessed according to the revised Response Evaluation Criteria In Solid Tumours (RECIST) guideline in 2009 [12].

2.3. Operative technique

All operations were performed by surgeons skilled in LRH and LNRH for one year before this study. Before starting surgery, the Trendelenburg position was not exaggerated. An intrauterine manipulator was inserted vaginally. Pneumoperitoneum was created by a Veress needle introduced in the umbilicus. CO_2 was used for inflation, and pressure was kept at about 10–12 mm Hg. The LRH technique followed previous study [13]. The surgical steps and the technique used for LNRH resemble those described by Ju-Won Roh and Dong Ock Lee [14].

2.4. Data collection and follow-up

For each patient, recorded parameters including clinical characteristics (age, body mass index [BMI], operative time [OT], hospital stay, estimated blood loss [EBL], recover time of bowel motility, days for residual urine <50 mL, adjuvant therapy), histopathologic characteristics (histology, FIGO stage, tumour size, paracervical length, vaginal length, number of pelvic lymph nodes removed), immediate morbidities, and duration of follow-up. 'Immediate complications' were defined as bladder, ureter or rectal injury in surgery.

2.5. Statistical analysis

Continuous variables were assessed for normal distribution and expressed as mean with standard deviation (SD) and median with range or percentage (%), as appropriate. Student's *t*-test was used for analysis of the normally distributed, descriptive continuous variables. Categorical variables were expressed as absolute numbers or percentages. Chi-square test or Fisher's exact test was used to compare qualitative variables. All of the statistical analyses were performed using the SPSS 17.0 software (SPSS Inc., Chicago, Illinois, USA). A $p < 0.05$ was considered statistically significant.

3. Results

3.1. Characteristics of enrolled patients

From December 2012 to March 2015, 84 consecutive patients with cervical cancer FIGO stage IB2 or IIA2 were enrolled in three medical centres. After excluding patients with neuroendocrine histology ($n = 1$) and pathologically confirmed distant metastasis ($n = 3$), 80 patients qualified for the study and were assigned to either the RH group or the LNRH group. After assignment, one patient declined NAC with TC in the LRH group, and one patient was without sensitivity for NAC with TC in LNRH group; therefore, the two patients were excluded from the study. Further, one patient in each group was lost to follow-up within one year after the surgery. In the final analysis, 76 patients (38 in the LNRH group and 38 in the LRH group) were included. The flow diagram of the patients enrolled in this study is shown in Fig. 1.

The detailed clinical characteristics of the enrolled patients in both groups are presented in Table 1. Data analysed on the characteristics of patients undergoing the two types of procedures included age, BMI, FIGO stage, tumour size and histologic type. Of these parameters, there was no significant difference between the LNRH group and the LRH group.