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CLINICAL ARTICLE

Retrospective comparison of laparoscopic versus open radical hysterectomy after neoadjuvant chemotherapy for locally advanced cervical cancer

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ABSTRACT

Objective: To compare outcomes after laparoscopic radical hysterectomy (LRH) and abdominal radical hysterectomy (ARH) for locally advanced cervical cancer (LACC)after neoadjuvant chemotherapy (NACT). *Methods:* In a retrospective study, data were analyzed from patients with FIGO stage IB2–IIB cervical cancer who underwent LRH or ARH after NACT at Union Hospital, Wuhan, China, between January 2007 and August 2013.Perioperative outcomes and survival were compared. *Results:* Overall, 99 patients who underwent LRH and 30 who underwent ARH were included. Compared with ARH patients, LRH patients presented with lower-stage tumors ($P = 0.013$). Median operative time, number of harvested lymph nodes, and rate of positive surgical margins did not differ significantly between the groups, but LRH resulted in less blood loss (median 300 mL [range 20–1100] vs 375 mL [100–1200]; $P = 0.027$). There were two intraoperative complications and 23 postoperative complications in the LRH group, and 12 postoperative complications in the ARH group. No conversions occurred in the LRH group; all complications were managed without severe sequelae. As of March 2014, recurrence had been noted for 6(6.1%) LRH patients and 2 (6.7%) ARH patients. *Conclusion:* LRH was similar to ARH in terms of safety, feasibility, and morbidity, with less blood loss among women with LACC undergoing NACT. Long-term outcomes need to be documented.

1. Introduction

Uterine cervical cancer is the second most common gynecologic malignancy [1]. It is estimated that approximately 35% of cases are diagnosed at a regional stage of disease [2]. Locally advanced cervical cancer (LACC) refers to tumors of stage IB2, IIA, and IIB, as classified by the International Federation of Gynecology and Obstetrics (FIGO). The 5-year overall survival is 60% for patients with LACC, but 90% for those with early cervical cancer [3], suggesting that the treatment for women with LACC remains challenging.

Currently, the following modalities are considered to be acceptable interventions for LACC: concurrent chemoradiation [4], neoadjuvant chemotherapy (NACT) followed by radical hysterectomy and pelvic lymphadenectomy [5,6], and concurrent chemoradiation followed by adjuvant chemotherapy or radical surgery [7,8]. However, the advantages and disadvantages of these strategies remain under discussion.

The standard management for early cervical cancer is radical hysterectomy and pelvic lymphadenectomy—a procedure of high technical difficulty, complexity, and risk. Laparoscopic radical hysterectomy (LRH) with pelvic and aortic lymphadenectomy was first reported in 1993 by Nezhatet al. [9]. Since then, this procedure has been applied clinically in the treatment of early-stage cervical cancers, and its technical feasibility and safety have been reported in a series of studies [10–12]. However, there are few reports on LRH after NACT for the treatment of patients with LACC [6,13]. The aim of the present study was therefore to determine whether LRH is comparable to abdominal radical hysterectomy (ARH) in terms of surgical and oncologic outcomes among patients with LACC who underwent NACT.

2. Materials and methods

In a retrospective study, data were reviewed from patients with LACC (FIGO stage IB2–IIB) who underwent LRH or ARH after NACT at the Department of Gynecology and Obstetrics, Union Hospital, Huazhong University of Science and Technology, Wuhan, China, between January 1, 2007, and August 31, 2013. The study was approved by the ethics committee of Wuhan Union Hospital and patient consent was waived because the data were obtained retrospectively and analyzed anonymously.

At the study hospital, patients (aged <70 years) who had good performance status (Eastern Co-operative Oncology Group score 0–1) [14] with cervical cancer at stage IB2, IIA (≥4 cm), or IIB according to the

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1995 FIGO staging system [15] were candidates for NACT. A regimen of paclitaxel plus carboplatin, i.e. 135–175 mg/m^2 of liposome paclitaxel (Luye Pharma Group Ltd., Nanjing, China) combined with 400 mg of carboplatin (Qilu Pharma Ltd., China) every 4 weeks for three cycles, was used [16]. In a few cases, particularly in cases of early application of NACT in our department, irinotecan combined with carboplatin were administered. The response to NACT was evaluated by a pelvic examination and pelvic magnetic resonance imaging, performed before and 10 days after NACT in accordance with the Response Evaluation Criteria in Solid Tumors guideline [17]. After this evaluation, patients with a clinical response (complete or partial remission) or IB2 patients with stable disease underwent radical hysterectomy and pelvic lymphadenectomy within 3 weeks of the last chemotherapy cycle. Patients without a clinical response underwent radiation.

Querleu and Morrow type C2 radical hysterectomy was performed via laparoscopy or laparotomy, as described previously [18]. Systematic bilateral pelvic lymphadenectomy included dissection of the common iliac, external iliac, internal iliac, obturator, and deep inguinal lymph nodes.

All patients had a Foley catheter inserted for 10 days immediately after surgery. Bladder function was assessed after removal of the urinary catheter by performing post-void residual catheterization from day 10 after surgery. Patients with a post-void residual urine volume of greater than 100 mL (urinal retention) received a further Foley catheter and the residual urine volume was revaluated weekly until resumption of normal bladder function.

Patients with lymph node metastasis, parametrial involvement, positive surgical margins, or poorer responses to NACT (i.e., IB2 patients with stable disease) underwent adjuvant treatment. Follow-up was performed at stage-specific gradations in accordance with FIGO guidelines. The patients underwent follow-up examinations every 3 months for the first 2 years, every 6 months in the third year, and yearly thereafter.

For the present study, medical records were reviewed to collect data regarding the disease and therapy. The following parameters were recorded: age, body mass index, FIGO stage, response to NACT, pathologic findings, and perioperative outcomes.

Operative time was measured from the first skin incision to closure of the skin. Blood loss was measured as the sum of the suctioned fluids and the weight of the sponges minus the use of irrigation fluids at completion of the surgery. Postoperative complications were defined as those occurring within 30 days of surgery. Time to death was defined as the interval between surgery and death. Overall survival (OS) was defined as the time from surgery to death from any cause or to the date of last contact. Progression-free survival (PFS) was defined as the time from surgery to the first appearance of progressive disease or to the date of last contact.

Statistical analysis was performed with SPSS version 13.0 (SPSS Inc, Chicago, IL, USA). Comparisons between patients undergoing LRH and ARH were performed by using nonparametric statistics. Numeric parameters were expressed as the median and range, and the Mann–Whitney *U* test was used to examine the differences. Fisher exact test and the χ^2test were used to compare rates between the groups as appropriate. A two-tailed *P* value of less than 0.05 was considered statistically significant.

3. Results

During the study period, 148 patients with LACC received NACT. Among them, 129 with a clinical response after NACT underwent type C2 radical hysterectomy at the study institute. In total, 99 patients were operated via laparoscopy (LRH group) and 30 patients underwent open surgery (ARH group). There were no significant differences in age, body mass index, or pathologic findings between these two groups (Table 1). However, the LRH group presented with earlier tumor stages than the ARH group($P = 0.013$).

Table 1
Characteristics of the study patients by treatment.[a]

Characteristic	NACT + LRH (n = 99)	NACT + ARH (n = 30)	*P* value
Age, y	45 (31–63)	43.5 (30–61)	0.398
Obese	2 (2.0)	1 (3.3)	>0.99
FIGO stage			0.013
IB2	44 (44.4)	8 (26.7)	
IIA	49 (49.5)	15 (50.0)	
IIB	6 (6.1)	7 (23.3)	
Histotype			0.657
Squamous	84 (84.8)	27 (90.0)	
Adenocarcinoma	9 (9.1)	2 (6.7)	
Adenosquamous	2 (2.0)	1 (3.3)	
Unknown	4 (4.0)	0	
Histologic grading			0.398
Well differentiated	26 (26.3)	11 (36.7)	
Moderately differentiated	44 (44.4)	10 (33.3)	
Poorly differentiated	25 (25.3)	9 (30.0)	
Unknown	4 (4.0)	0	
Lymph node metastasis	25 (25.8)	8 (26.7)	>0.99
Parametrial involvement	3 (3.0)	3 (10.0)	0.143
NACT regimens			0.003
PC	98 (99.0)	25 (83.3)	
Platinum-based	1 (1.0)	5 (16.7)	
Response to NACT			0.703
Complete response	16 (16.5)	4 (13.3)	
Partial response	53 (54.6)	19 (63.3)	
Stable disease	28 (28.9)	7 (23.3)	
Disease progression	0	0	

Abbreviations: NACT, neoadjuvant chemotherapy; LRH, laparoscopic radical hysterectomy; ARH, abdominal radical hysterectomy; FIGO, International Federation of Gynecology and Obstetrics; PC, paclitaxel plus carboplatin.
[a] Values are given as median (range) or number (percentage), unless indicated otherwise.

Most of the patients (99.0% in the LRH group; 83.3% in the ARH group) received PC chemotherapy prior to surgery. A non-taxane-containing platinum-based regimen was used less frequently for LRH patients than for ARH patients (1.0% vs 16.7%, respectively; $P = 0.003$). The response to NACT was similar in the two groups ($P = 0.703$). The response rates (complete response plus partial response) were 71.1% and 76.6% in the LRH and the ARH groups, respectively (Table 1). Ten women in the LRH group and two in the ARH group had pathologically confirmed complete remission.

The surgical data are presented in Table 2. There was no significant difference in median operative times, estimated blood loss, number of

Table 2
Surgical outcomes of the study patients by treatment.[a]

Outcome	NACT + LRH (n = 99)	NACT + ARH (n = 30)	*P* value
Operative time, min	240 (170–3030)	255 (180–420)	0.441
Blood loss, mL	300 (20–1100)	375 (100–1200)	0.027
Lymph node count	25 (8–47)	20 (14–40)	0.085
Positive surgical margins	4 (4.1)	1 (3.3)	>0.99
Adjuvant therapy	30 (30.3)	11 (36.7)	0.511
Radiotherapy	20 (20.2)	9 (30.0)	0.318
Chemoradiation	10 (10.1)	2 (6.7)	0.731
Intraoperative complications	2 (2.0)	0	>0.99
Ureter injury	1 (1.0)	0	>0.99
Obturator nerve injury	1 (1.0)	0	>0.99
Postoperative complications	23 (23.3)	12 (40.0)	0.100
Bladder dysfunction	19 (19.2)	12 (40.0)	0.021
Long-term bladder dysfunction (>30 d)	7 (7.1)	3 (10.0)	0.697
Urinary tract fistula formation	1 (1.0)	0	>0.99
Deep vein thrombosis	1 (1.0)	0	>0.99
Lymphocele	2 (2.0)	0	>0.99

Abbreviations: NACT, neoadjuvant chemotherapy; LRH, laparoscopic radical hysterectomy; ARH, abdominal radical hysterectomy.
[a] Values are given as median (range) or number (percentage), unless indicated otherwise.