RESEARCH ARTICLE

Effect of Laparoscopic Nerve-sparing Radical Hysterectomy on Bladder Function, Intestinal Function Recovery and Quality of Sexual Life in Patients with Cervical Carcinoma

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Abstract

Objective: To investigate bladder and intestinal function recovery and quality of sexual life after laparoscopic nerve-sparing radical hysterectomy (LNRH) for treatment of early invasive cervical carcinoma. Methods: Subjects included patients who underwent radical hysterectomy by laparotomy who were randomly assigned to 2 groups: 30 patients who underwent LNRH and 35 classical laparoscopic radical hysterectomy (LRH). We assessed the patients general clinical information, surgical characteristics, pathological findings, and adjuvant therapies. A urodynamic study was used to assess bladder function. Intestinal function recovery and quality of sexual life were evaluated by questionnaire. Results: No significant differences were found in age, surgery characteristics, pathological findings, adjuvant therapies, and main adverse effects between the 2 groups. The mean duration of the postoperative catheterization (DPC) in group LNRH was shorter than that in group LRH ($P < 0.001$). The maximum flow rate, maximum cystometric capacity , maximum detrusor pressure and urinary complications in group LNRH were better than those in group LRH. The quality of sexual life evaluated according to the female sexual function index (FSFI) was better in group LNRH than in those who underwent LRH. The intestinal function of patients in group LNRH also recovered better compared with patients in group LRH.

Keywords: Cervical cancer - laparoscopic nerve-sparing radical hysterectomy - bladder function - quality of sexual life

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Introduction

Cervical cancer is still the second most common malignancy and second most common cause of cancer-related death in women worldwide. Conventional radical hysterectomy causes damage to the pelvic autonomic nerves, which is believed to lead to impaired bladder function, defecation problems, and sexual dysfunction (Jensen et al., 2004; Bergmark et al., 2006; Pieterse et al., 2006). The pelvic automatic nerves are the pathway for the neurogenic control of rectal and bladder function and they supply blood vessels of the female internal genitals and are involved in the neural control of the lubrication-swelling response (Trimbos et al., 2001). It is reported that approximately 15% of all cervical cancers occur in women under the age of 40 (Covens et al., 2001). So except for prolong the survival period, more work need to do for improving the quality of life. With the development of the technology, the magnified view of laparoscopes has allowed a clearer visualization of structures such as nervous branches, thus favoring the adoption of nerve-sparing techniques, during radical procedures (Liang et al., 2010; Park et al., 2011).

First developed in Japan, a nerve-sparing modification of the Wertheim operation has been routinely applied to radical hysterectomy for cervical cancer in the Leiden University Medical Center (LUMC) since approximately 2001.

Beneficial effects of the nerve-sparing operation technique, compared with non-nerve-sparing procedures, have been reported on sexual functioning, bladder function, and bowel function (Sakuragi et al., 2005; Todo et al., 2006; Pieterse et al., 2007).

Traditional treatment for cervical cancer consists of radical surgery or radiotherapy; however, neither method spares fertility, and either can lead to psychosexual dysfunction and decreased quality of life. Neoadjuvant chemotherapy (NACT) prior to surgery is an alternative option that does not affect genital functions. Successful pregnancy following NACT demonstrates that NACT and adjuvant chemotherapy do not always affect fertility or eliminate the chance for pregnancy. The ability of NACT to reduce tumour volume and virtually sterilize micrometastases may be due to an uncompromised tumour blood supply and a population of chemosensitive tumour cells. Thus, NACT allows for a less-extensive dissection

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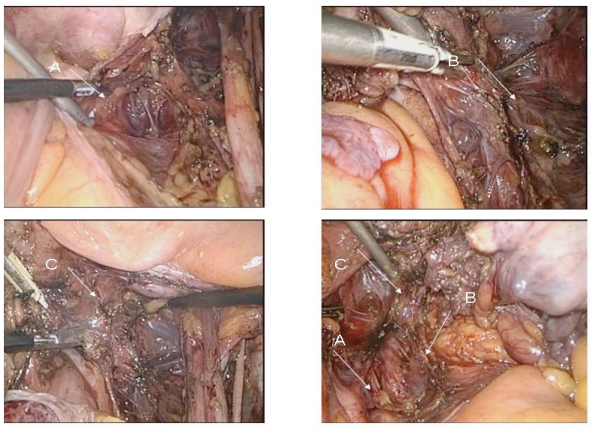

Figure 1. The Key Steps of the LNRH. A shows the separation of the hypogastric nerve (lateral uterosacral ligament), B shows the pelvic splanchnic nerve, C shows the retained the bladder branch nerve.The pelvic splanchnic and hypogastric nerves and bladder branch nerve were preserved during transection of the cardinal ligament in LNRH patients (Figure 1).

of the cervix instead of radical hysterectomy while preserving the effectiveness of the treatment (Hwang et al., 2001; Selvaggi et al., 2006).

This study was a study to evaluate the effect of laparoscopic radical nerve-sparing hysterectomy plus systematic bilateral pelvic lymphadenectomy (LNRH) versus traditional laparoscopic radical hysterectomy (LRH) on the quality of bladder, intestinal and sex function on early cervical carcinoma patients with or without neoadjuvant chemotherapy.

Materials and Methods

This study was conducted prospectively in patients with early uterine cervical carcinoma (2009 FIGO staging Ia2 to IIa2) who treated with or without NACT followed by either nerve-sparing LRH or non nerve-sparing LRH at Qingdao Municipal Hospital. Patients receiving either types of hysterectomy gave informed consent. This study was approved by the Ethics Committee of Qingdao Municipal Hospital. Cisplatin-based adjuvant chemotherapy was administered in 1–2 courses before surgery depending on tolerance and response. Exclusion criteria included a history of voiding dysfunction, previous pelvic radiotherapy, previous pelvic reconstruction, and brain/spinal cord diseases. In addition, patients with pathologically confirmed metastasis to the lymph nodes were excluded.

All operations were performed by board-certified gynecological oncology surgeons who were skilled at laparoscopic operations at the Qingdao Municipal Hospital. The classification of hysterectomy was based on the new definition by Querleu and Morrow (Querleu et al., 2008) The pelvic splanchnic and hypogastric nerves were preserved during transection of the cardinal ligament in LNRH patients. The details of the surgery were reported in this article (Long et al., 2013).

The lengths of operations, blood loss, the duration of postoperative stay, operation-related complications were compared in patients from the two groups. The bladder

Table 1. Comparison of Characteristics between Patients Undergoing LRH with or without Nerve-sparing Techniques

Characteristics	LNRH (n = 30)	LRH (n =35)
Age (y)	43 (range, 32-54)	46 (range, 38-61)
Histology		
Squamous cell carcinoma	25	29
Adenocarcinoma	5	6
Operative time (min)	240 (range, 210-270)	200 (range, 190-220)
Blood loss (mL)	162 (range, 50-550)	205 (range, 50-750)
Tumor size (cm)	1.5	2.3
Parametrial involvement	0	0
Positive pelvic lymph node	1	3
Positive paraaortic lymph node	0	0
Positive section margin	0	0
Operation-related complications		
Bladder injuring	0	0
Fistula/ureter injuring	0	0
GI injury	0	0
NACT		
No	25	30
Yes	5	5

function recovery evaluation consists of 2 parts. The patients' catheterizations had been kept since operation until the residual urine volume was less than 100 mL and the draining time was recorded. As many patients who received RH complained about abnormal bladder function within 1 year, the UDS was carried out in 6 to 12 months after surgery, analyzing indexes such as maximum flow rate (MFR), maximum cystometric capacity (MCBC), maximum detrusor pressure (MDP). All women who underwent LRH or LNRH were asked to complete a questionnaire regarding symptoms of frequency/urgency, nocturia, dysuria, urinary retention, incontinence, bowel rectal function, fecal incontinence, air incontinence, able to distinguish air from feces 1 year after the surgery. The quality of sexual life (QOL) was evaluated by female sexual function index (FSFI) 1 year after the operation.
Statistical analysis: The results are expressed as means standard deviation (SD) or percentage (%), as appropriate. We checked for normality of distribution of all variables with continuous data. The Mann-Whitney test was used to assess the difference in medians between LNRH and LRH because of non-normality of distribution SPSS17.0 statistical package. Categorical data used the Fisher's exact test. The SPSS17.0 statistical package was used for all analyses. All tests were two-tail and $P< 0.05$ was considered statistically significant.

Results

The pelvic splanchnic and hypogastric nerves and bladder branch nerve were preserved during transection of the cardinal ligament in LNRH patients (Figure 1).

Between March 2010 and March 2014, 30 patients with early stage cervical cancer were recruited prospectively at a tertiary referral medical center to receive LNRH or LRH. Of these patients, 5 patients were stage FIGO Ia2,

Table 2. Bladder Function Assessment

	LNRH	LRH	*P*
NDPC, d		14	15
Mean±SD	11.03±2.21	18.13±6.00	0.000
UDS		7	9
MCBC, mean ±SD, mL	323.16±22.62	422.27±31.31	0.000
MFR, mean ±SD, mL/s	19.89±3.03	12.14±1.83	0.000
MDP, mean ±SD, cmH_2O	39.11±5.01	26.72±5.22	0.000

MFR, indicates maximum flow rate; MCBC, indicates maximum cystometric capacity; MDP, indicates maximum detrusor pressure

Table 3. Comparison of Postoperative Urinary Symptoms between Patients Undergoing LNRH and LRH

Characteristics	LNRH (n=30)*	LRH (n =35)*	*p*
Frequency/urgency symptoms	3	15	<0.01
Nocturia	2	13	<0.01
Dysuria	1	9	<0.05
Urinary retention	0	7	<0.05
Incontinence	5	17	<0.01

20 patients were Ib1, 10 patients were Ib2, 20 patients were stageIIa1 and 5 patients were stageIIa 2. Of these patients, 30 underwent LNRH and 35 underwent LRH. 5 LNRH and 5 LRH patients were treated with Cisplatin-based NACT. The patients were aged from 32 to 61 years (mean age 44.5 years). Data analyzed on the characteristics between patients undergoing the two types of procedures included age, tumor size, operation time, blood loss, and complications (Table 1). Of these parameters, there was no significant difference between the two groups.

Bladder Function Recovery

The mean duration of the postoperative catheterization (DPC) in group LNRH was 11.03 days, much shorter than that in group LRH (18.13 days; $P < 0.001$). All these patients had received UDS before surgery. The preoperative data of UDS are all within the reference range; no significant difference was found between the 2 groups ($P > 0.05$). The maximum flow rate, maximum cystometric capacity , maximum detrusor pressure in group LNRH were better than those in group LRH ($P < 0.000$) (Table 2)

The urinary symptoms were evaluated 1 year after surgery. There was a significant reduction in the incidence of postoperative self-catheterization and a reduction in the period of bladder function recovery in those whose pelvic nerves were preserved versus those whose were not. 1 year postoperatively, urinary complications such as nocturia, urgency and frequency, postoperative urine retention, and dysuria were significantly different (Table 3).

The quality of sexual life was evaluated according to female sexual function index (FSFI) 1 year after surgery. The sexual life score in group LNRH was better than that in group RH (Table 4). The FSFI score ≤23 was considered as dissatisfied sexual function. The total score in group LNRH was 23.34+3.69, including 3 cases of score ≥30, 13 cases of score 23-30 and 13 cases of score ≤23. The total score in group LRH was 17.57+2.28, including 0 cases of score ≥30, 3 cases of score 23-30 and 27 cases of score ≤23. The LNRH group was better in sexual desire, sexual arousal, vagina lubrication, orgasm and sexual satisfaction than that in group LRH ($P<0.05$). There was no significant difference in algopareunia between two groups.

Table 4. The Quality of Sexual Life Evaluated According to Female Sexual Function Index(FSFI)

	LNRH Score	LRH Score	*P*
Total	23.34+3.69	17.57+2.28	0.000
Sexual desire	3.60+0.80	2.60+0.53	0.002
Sexual arousal	3.52+0.85	2.60+0.74	0.016
Vagina lubrication	3.95+0.70	2.75+0.78	0.001
Orgasm	3.49+0.88	2.73+0.83	0.046
Sexual satisfaction	4.36+0.81	2.63+0.84	0.000
Algopareunia	4.33+0.71	4.17+0.67	0.583

Table 5. The Intestinal Function Assessment

	LNRH	LRH	*P*
N	30	35	
Passage of gas by anus (hours after surgery)	39.97±3.84	57.50±4.01	0.000
Bowel rectal function			
Normal	28 (93%)	32 (91%)	
Constipation	2 (7%)	3 (9%)	
Fecal incontinence			
Never	0	0	NA
Seldom	0	4	
Air incontinence			
Never	0	0	NA
Seldom	0	2	
Able to distinguish			
No air from feces	0	0	NA
Not always	0	3	

The period of passage of gas by anus was shorter (39.97±3.84 hours) in LNRH patients than that in LRH patients (57.50±4.01 hours). The intestinal function of patients in group LNRH recovered better compared with patients in group LRH. In analyzing the responses to the questionnaires, no statistical differences were detected between the two groups for bowel-rectal quality of life.

Discussion

Serious bladder dysfunction has been reported in up to 10% to 32% of RH surgery patients. Intestinal dysfunction also occurs frequently after RH, but is generally less problematic, especially in long-term cases. Excessive mobilization of the rectum and/or caudal and lateral dissections of the uterosacral ligaments may result in partial denervation of autonomic fibers. However, the effects of surgery on intestinal function are incompletely understood (Fotiou et al., 1997). Sexual dysfunction also occurs after RH, especially in patients undergoing adjuvant radiotherapy (RT), but this issue is generally less investigated (Bergmark et al., 1999; Jensen et al., 2004). In women with CC, treatment causes changes in vaginal anatomy and function. These negative sequelae could derive from damage to the sympathetic and parasympathetic nervous systems. Nerve-sparing RH (NSRH) may provide a possibility to improve QoL and reduce bladder, sexual, and intestinal dysfunctions, without compromising radicality (Samlal et al., 1996;

Hockel et al., 1998; Bergmark et al., 1999; Possover et al., 2000; Trimbos et al., 2001; Jensen et al., 2004; Raspagliesi et al., 2004).

In the present study, the major peri-operative complications of the NSRH group and the control group, such as intestinal obstruction, urinary system injury, DVT, and lymphocyst, did not differ significantly, which suggests that NSRH has not raised the risk of organ injury in the operating field. In addition, there were no obvious differences between the 2 subgroups in aspects such as duration of surgery, intraoperative blood loss, incision healing, postoperative fever, and antibiotics use. Present data have indicated that NSRH does not extend the risk of surgery approaches and perioperative surveillance. Depending on our data and other scholars' achievements, (Sakuragi et al., 2005; Papp et al., 2006; Park et al., 2010).

The QOL in the NSRH group evaluated 1 year after operation was obviously better than that in the control group. Meanwhile, a deeper analysis showed that QOL in the NSRH group improved compared with that in the control group, especially in social and family life, emotional well-being, working status, and the symptom correlated with the operating field. However, NSRH effectively preserves sympathetic and parasympathetic branches of the autonomous innervation on pelvic organs. That indeed maintains the function of organs within the operating field and actually release the symptoms correlated with operation that degrade QOL, including dysuria, constipation, and sexual dissatisfaction. Thus, the patients who received NSRH are less disturbed by the adverse effect of surgery, which improves their emotional stability and working initiative. In that circumstance, they integrate into family and community activities better and obtain a higher quality of life.

In conclusion, our observation suggests that LNRH is a safe and reliable procedure for early invasive cervical carcinoma, sacrificing no surgical radicality and causing no increase in complications. It also shows that LNRH effectively improves the bladder function, intestinal function recovery and the quality of sexual life in patients with FIGO stages IB1 and IIA. However, the result of our study can still be limited by the number of patients enrolled in the study and the time of follow-up. Further prospective randomized controlled studies with an increased number of patients should be carried out investigating the effect of LNRH on bladder function recovery and QOL improvement as well as long-term postoperative follow-up.

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