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Original Article

Laparoscopic radical surgery in early-stage cervical cancer: short-term and long-term outcomes and survival analysis

Hongying He[1,4], Zhijun Yang[1], Jieqing Zhang[1], Desheng Yao[1], Jiangtao Fan[2], Renfeng Zhao[3], Dingyuan Zeng[4], Xiaoxia Hu[3], Zhong Lin[5], He Wang[1], Zhongmian Pan[1], Yanming Jiang[6], Li Li[1]

[1]Department of Gynecologic Oncology, The Affiliated Tumor Hospital of Guangxi Medical University, Nanning, China; [2]Department of Gynecology, The First Affiliated Hospital of Guangxi Medical University, Nanning, China; [3]Department of Gynecology, The People's Hospital of Guangxi Zhuang Autonomous Region, Nanning, China; [4]Department of Gynecological Oncology, The Fourth Affiliated Hospital of Guangxi Medical University, Liuzhou, China; [5]Department of Gynecology, Ruikang Hospital Affiliated to Guangxi University of Chinese Medicine, Nanning, China; [6]Department of Gynecology, The Liuzhou People's Hospital, Liuzhou, China

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Abstract: The purpose of this study was to compare the long-term survival outcomes between laparoscopic radical hysterectomy (LRH) and open radical hysterectomy (ORH) in early-stage cervical cancer. A multi-center retrospective study was conducted in 1,863 patients who underwent either LRH (n=1,071) or ORH (n=792) between January 2007 and May 2014, for FIGO stage IA2-IIA2 cervical cancer. We observed significant differences in operating time, estimated blood loss, complications of vascular injury, return of bowel movement, removal of Foley catheter, post-operative hospital stay, post-operative complications and wound dehiscence between the LRH group and the ORH group ($P<0.05$). We did not find any significant difference in the number of lymph nodes removed, overall intra-operative complications, the length of parametrial resection and vaginal cuff, the degree of incontinence, recurrence rate, 5-year overall survival (OS) rate and 5-year disease-free survival (DFS) rate between the two groups ($P>0.05$). In addition, we found a significant difference in the 12-month post-operative period for incontinence and sexual dysfunction between the nerve-sparing LRH subgroup and the ORH group, as measured by a stratified analysis of the ICIQ-FLUTS and FSFI (six different domains) questionnaire scores, $P<0.05$). In univariate analyses, tumor dimension, clinical stage, deep stromal invasion, LVSI, and LN metastasis significantly affected the 5-year OS and 5-year DFS ($P<0.05$). In multivariate analyses, pathological type, clinical stage, LVSI, and LN metastasis were independent of prognostic factors ($P<0.05$). LRH for early-stage cervical cancer reduced the estimated blood loss and accelerated the post-operative recovery compared to a laparotomy. The nerve-sparing LRH, in particular improved the quality of life after surgery. Finally, LRH has a similar survival prognosis as ORH.

Keywords: Cervical cancer, laparoscopic radical hysterectomy, open radical hysterectomy, quality of life, survival analysis

Introduction

Cervical cancer is the third most common cancer in women worldwide and the second most common in developing regions [1]. Worldwide, about 530,000 new cases were reported in 2008, but this is estimated to exceed 665,000 cases by 2020 [2]. A standard primary treatment for early-stage cervical cancer is open radical hysterectomy (ORH) combined with pelvic lymphadenectomy. An alternate procedure called laparoscopic radical hysterectomy (LRH), was reported by Canis and Nezhat *et al* [3, 4] and, since then, several retrospective studies have documented the advantages of LRH in early-stage cervical cancer treatment [5-7]. However, only a few studies [8] have reported the impact of surgical excision on the long-term quality of life and the associated complications of pelvic floor and sexual function. Therefore, the aim of this multi-center retrospective study was to compare surgical excisions between the LRH and ORH procedures, with respect to complications, pelvic floor function, sexual function,

Table 1. Patients distribution during the two periods, in the six hospitals

	LRH (1071)		ORH (n=792)	
	(2007.1-2010.1)	(2011.1-2014.2)	(2007.1-2010.12)	(2011.1-2014.2)
Tumor-GXMU	182 (33.3%)	365 (66.7%)	293 (77.5%)	85 (22.5%)
NO.1-GXMU	23 (34.3%)	44 (65.7%)	40 (58.8%)	28 (41.2%)
People's-GXZAR	34 (46.6%)	39 (53.4%)	56 (69.1%)	25 (30.9%)
NO.4-GXMU	98 (32.1%)	207 (67.95)	153 (80.5%)	37 (19.5%)
RuiKang-GXCMU	20 (43.5%)	26 (56.5%)	25 (78.1%)	7 (21.9%)
People's-Liuzhou	15 (45.5%)	18 (54.5%)	21 (48.8%)	22 (51.2%)
Total	372 (34.7%)	699 (65.3%)	588 (74.2%)	204 (25.8%)

Abbreviations: Tumor-GXMU, Affiliated Tumor Hospital of Guangxi Medical University, NO.1-GXMU, The First Affiliated Hospital of Guangxi Medical University, People-GXZAR, The People's Hospital of Guangxi Zhuang Autonomous Region, NO.4-GXMU, the Fourth Affiliated Hospital of Guangxi Medical University, RuiKang-GXCMU, RuiKang Affiliated Hospital to Guangxi University of Chinese Medicine, People-Liuzhou, The Liuzhou People's hospital.

long-term survival outcomes, and to analyze the risk factors for the prognosis of LRH.

Materials and methods

Study population

We identified 1,863 patients, from six third-grade class-A hospitals in Guangxi province, who underwent radical hysterectomy from January 1, 2007 to May 28, 2014 for International Federation of Gynecology and Obstetrics (FIGO) stage Ia2 to IIa2 cervical cancer, All patients in this study underwent a pathological diagnosis, completed a medical record with the relevant information, and were not previously treated. The participating six hospitals included Affiliated Tumor Hospital of Guangxi Medical University, the First Affiliated Hospital of Guangxi Medical University, The People's Hospital of Guangxi Zhuang Autonomous Region, the Fourth Affiliated Hospital of Guangxi Medical University, RuiKang Affiliated Hospital of Guangxi University of Chinese Medicine and The Liuzhou People's Hospital. The 1,863 patients were divided into 2 groups based on the type of surgical procedure that they had undergone; LRH group (n=1,071) and ORH group (n=792). The patient distribution in the six hospitals, over two different time periods (from January 2007 to December 2010 and from January 2011 to May 2014), is shown in **Table 1**. Before surgery, all patients were diagnosed pathologically from tissue biopsies and were examined by two or more experienced gynecologic oncologists to confirm the clinical stage (FIGO 2009) of cervical cancer. In addition, a written consent was obtained from all patients. The choice of the operative procedure (LRH or ORH) was based on the patient's preferences after a thorough discussion of the risks and benefits of both procedures. The clinical and pathological characteristics of the patients in the two groups are presented in **Table 2**.

Procedures

All patients underwent either a radical or a modified radical hysterectomy combined with a pelvic and/or para-aortic lymph node dissection. Stage IA2 patients underwent a modified radical hysterectomy; LRH (6.5%, 70/1,071), ORH (8.3%, 66/792). The remaining patients (> stage IA2) underwent a radical hysterectomy; LRH (93.5%, 1,001/1,071), ORH (91.7%, 726/792). In addition, of the 1,071 LRH patients, 236 (22%) underwent a nerve-sparing (NS) radical hysterectomy; most of these cases were patients from the second time period (2011.01.01~2014.02.28). In younger patients with squamous cell carcinoma (age <45 years) who needed to preserve their ovarian function, we partly left a hemi-ovary or bilateral ovaries. We examined the frozen section to confirm that no metastasis had occured. However, if the patients had FIGO stages IB2 or IIA2, they underwent one or two cycles of neoadjuvant chemotherapy [PF or TP (TC) regimen. The TP (TC) regimen included: 3 weekly paclitaxel 175 mg/m^2 on day 1 plus 3-hour intravenous infusion followed by platinum 70 mg/m^2 or carboplatin (AUC=5) on day 1 plus 1-hour intravenous infusion. The PF regimen included: 3 weekly platinum 70 mg/m^2 on day 1 plus 96-hour continuous intravenous infusion of 5-fluorouracil

Table 2. Clinical and pathological characteristics of patients

Variable	LRH (n=1071)	ORH (n=792)	*p*-value
Age (years) (Mean logic)	46.2 years	45.9 years	0.586
BMI (Kg/m^2) (Mean ms) (M)	22.3 an ms	22.4 an ms	0.834
FIGO (2009) stage [n (%)]			
IA2	70 (6.5%)	66 (8.3%)	0.885
IB1	632 (59.0%)	456 (57.6%)	
IB2	132 (12.4%)	95 (11.9%)	
IIA1	162 (15.1%)	116 (14.6%)	
IIA2	75 (7.0%)	59 (7.5%)	
Histological grade [n (%)]			
High-grade	63 (5.9%)	37 (4.6%)	0.569
Medium-grade	112 (10.5%)	94 (12.0%)	
Low-grade	896 (83.6%)	661 (83.4%)	
Histology [n (%)]			
Squamous	814 (76.0%)	615 (77.6%)	0.748
Adenocarcinoma	119 (11.1%)	91 (11.6%)	
Adenosquamous	75 (7.0%)	51 (6.4%)	
Others	63 (5.9%)	35 (4.4%)	
Tumor size [n (%)]			
≤4 cm	860 (80.3%)	636 (80.3%)	1.000
>4 cm	211 (19.7%)	156 (19.7%)	
Deep stromal invasion [n (%)]			
Yes	291 (27.2%)	310 (39.1%)	<0.001
No	780 (72.8%)	482 (50.9%)	
Lymph node metastasis [n (%)]			
Positive	217 (20.3%)	147 (18.5%)	0.546
Negative	854 (79.7%)	645 (81.5%)	
LVSI [n (%)]			
Positive	63 (5.9%)	73 (9.2%)	0.078
Negative	1008(94.1%)	719 (90.8%)	
NACT [n (%)]			
Yes	185 (17.3%)	143 (18.1%)	0.79
No	886 (82.7%)	649 (81.9%)	

Abbreviations: BMI, body mass index; FIGO, International Federation of Gynecology and Obstetrics; LVSI, Lymphatic vascular stroma invasion; NACT, Neoadjuvant chemotherapy, SD, standard deviation.

1000 mg/m^2]. After surgery, patients with high risk intermediate factors were recommended for adjuvant treatment (radiotherapy or chemo-radiotherapy).

Both ORH and LRH procedures were performed under general anesthesia. For laparoscopic surgery, patients underwent insertion of a Foley urinary catheter and cup-type uterine manipulator after anesthesia. Carbon dioxide pneumoperitoneum was achieved using a Veres needle and a pressure not higher than 15 mmHg. 5 trocars were placed: a 10 mm trocar between the umbilicus and the xiphoid for laparoscopy, a 5 mm trocar in the left lower abdomen, an additional 10 mm trocar in the left lower abdomen 2 cm above the umbilicus line for excision of the para-aortic lymph nodes and two 5 mm trocars in the McBuney point and anti-McBuney point. Pelvic and para-aortic lymph nodes were coagulated and cut with Ultrasonic scalpel and bipolar cautery. LigaSure or Ultrasonic scalpel was used for the isolation and ligation of ovary vessels. In cases where the patients needed to preserve ovaries, ovaries were fixed to the paracolic sulci 5 cm above the anterior superior iliac spine. Both round ligaments were coagulated and cut. Both broad ligaments were transected 3-4 cm (width). The ureter was cleaned of all surrounding tissues and dissected from the uterine artery. Both the sacrouterine ligaments, cardinal ligaments and the paravaginal tissues were transected (3 cm width). The vagina was transected (3-4 cm width). The specimens, including the uterus, cervix and lymph nodes were removed vaginally. Finally, the vaginal stump was closed by laparoscopy, the abdominal cavity drainage-tube was placed, and the laparoscopic access point was closed.

The main point of laparoscopic nerve-sparing (NS) radical hysterectomy [9] was to avoid dissection of the tissue below the ureter to preserve innervation of the bladder. The vesicouterine ligament was transected, and the bladder was further mobilized inferiorly, with care taken to preserve the nervous branches running from the inferior hypogastric plexus to the bladder. Then, the medial fibrous part of the uterosacral ligaments were separated from the nerves running in its lateral part.

The surgical procedures for ORH were nearly identical to those for LRH, except that, in ORH, a midline abdominal incision was made from

Table 3. Surgical outcomes in the two groups of patients

	LRH (n=1071)	ORH (n=792)	*P*-value
Operating time (min)	257.0 ± 68.8	238.2 ± 56.1	<0.05
Estimated blood loss (mL)	358.0 ± 314.2	703.8 ± 430.7	<0.05
Return of bowel movement (days)	2.5 ± 0.9	2.9 ± 0.8	<0.05
Removal of Foley catheter (days)	14.8 ± 6.9	18.1 ± 9.0	<0.05
Post-operative hospital stay (days)	19.4 ± 15.8	29.6 ± 21.1	<0.05

the pubic symphysis area to 3 cm above the umbilicus.

After surgery, patients with high risk factors [10], such as lymph node (LN) metastasis, parametrial invasion, vaginal resection margin involvement, tumor size >4 cm, depth of invasion >1/2, poorly differentiated and lymphovascular space invasion (LVSI), were recommended for adjuvant therapy; radiotherapy included external irradiation and brachytherapy. External irradiation was given at a dose of 46-50 Gy (1.8 Gy/fraction) once daily, 5 fractions per week; vaginal brachytherapy was given at a dose of 10 Gy. Concurrent chemoradiotherapy was given with weekly cisplatin 40 mg/m^2 intravenously for 4-6 cycles.

Outcomes

Operative variables as determined from the operative report, included operating time (OT: defined as the time from skin incision to skin closure), estimated blood loss (EBL), lymph nodes removed, return of bowel movement, removal of Foley catheter, post-operative hospital stay, the length of parametrial resection and vaginal cuff, intra and post-operative complications.

Other variables included questionnaires covering pelvic floor function (International Consultation on Incontinence Questionnairel-Female Urinary Tract Symptoms, ICIQ-LUTS) and sexual function (Female Sexual Function Index, FSFI). Patients were evaluated pre-operation (baseline) and 12 months post-operation. This research was a multi-center retrospective study covering many years. The patients from the first period (2007.01.01~2010.12.31) were surveyed on pelvic floor and sexual function post-operation but not at baseline (or pre-operation). However, patients from the second period (2011.01.01~2014.02.28) were evaluated for pelvic floor function and sexual function before surgery and at a 12-month period after surgery.

The International Consultation on Incontinence Questionnaire Female Lower Urinary Tract Symptoms (ICIQ-FLUTS) is a 12-item questionnaire that was derived from the Bristol Female Lower Urinary Tract questionnaire and measures female lower urinary tract symptoms and the frequency of experiencing an inconvenient symptom (urinary-related quality of life); score 0 being no symptoms and score 48 being severe overall filling/voiding/incontinence symptoms. The degree of inconvenience of each symptom is measured on a Likert scale of 0 (least inconvenient) to 10 (extremely inconvenient). According to the degree of stress urinary incontinence (SUI) in the ICIQ-FLUTS questionnaire score standard, symptoms occurring less than 10 days in a period of 4 weeks score as mild SUI (1 point), occurring 10-20 days score as moderate SUI (2 points), occurring more than 20 days score as severe SUI (3 points), occurring every day score as serious SUI [11]. This questionnaire has been translated in Chinese dialects [12, 13]. Sexual functions of the study participants were assessed with the Female Sexual Function Index (FSFI); assessments were made twice: baseline and 12 months after surgery. This questionnaire was also translated in Chinese dialects [14, 15]. The survey is a brief, anonymous multi-dimensional, questionnaire that is used to assess sexual function by asking 19 questions [16]. The questions are grouped and scored for the domains of sexual desire (two questions), arousal (four questions), lubrication (four questions), orgasm (three questions), satisfaction (three questions), and pain during sexual intercourse (three questions). Domain factors are 0.6 for desire, 0.3 for arousal and lubrication, and 0.4 for orgasm, satisfaction, and pain. The total score was obtained by adding for each of the domains the sum of the scores and multiplying these sums by the domain factor. Therefore, the total FSFI score ranges from 2-36. A total score of 26.55 or less suggests female sexual dysfunction (FSD) [17].

Patient follow-up was conducted through letters, telephone interviews and e-mail. If letters or e-mails were not answered after four attempts or phones were shut down, contact was made to either the patient's unit or the police station. In cases where no information was returned, the patient was reported as "lost

Table 4. Intra- and post-operative complications

	LRH (n=1071)	ORH (n=792)	*P*-value
Intra-operative complications	87 (8.1%)	85 (10.7%)	0.068
Organ injury (Urinary tract and gastrointestinal tract)	43 (4.0%)	24 (3.0%)	0.297
Vessel injury	28 (2.6%)	61 (7.7%)	<0.001
Post-operative complications	362 (33.8%)	318 (40.2%)	0.007
Urinary retention	257 (24.0%)	222 (28.0%)	0.06
Wound dehiscence	7 (0.7%)	32 (4.0%)	<0.001
Febrile morbidity	78 (7.3%)	56 (7.1%)	0.925

Table 5. The extent of surgical excision

	LRH (n=1071)	ORH (n=792)	*P*-value
Length of the left parametrial resection (cm)	2.5 ± 0.8	2.7 ± 0.7	0.719
Length of the right parametrial resection (cm)	2.6 ± 0.3	2.7 ± 0.2	0.652
Length of vaginal tissue resection (cm)	2.4 ± 0.7	2.2 ± 0.7	0.437
Number of lymph node removed (n)	21.1 ± 8.4	20.4 ± 8.4	0.233

Table 6. ICIQ-FLUTS questionnaires scores at 12 months after surgery

	NS-LRH (n=236)	ORH (n=198)	*P*-value
Urinary incontinence [n (%)]	67 (28.4%)	71 (35.9%)	0.004
Mild	43 (18.2%)	47 (23.7%)	0.980
Moderate	15 (6.4%)	16 (8.1%)	
Severe	5 (2.1%)	5 (2.5%)	
Serious	4 (1.7%)	3 (1.5%)	

for follow-up". The follow-up deadline was May 31, 2015.

Statistical analysis

Statistical analysis was performed using the Stata software package (SPSS 20.0). Categorical variables were reported as the number of cases (n) and proportion (%), while continuous variables were reported as median and range values, *t*-tests and chi-square tests were used for statistical analysis. The log-rank test was used to compare the Kaplan-Meier curves for survival outcomes. The Cox proportional hazards model was used to obtain the hazard ratio for treatment comparison and its 95% confidence interval (CI). A *P*-value of <0.05 was considered statistically significant.

Results

Surgical outcome data

The data for surgical outcomes is presented in **Table 3**. The operating time in the LRH group was significantly longer than that in the ORH group (257.0 versus 238.2 min, *P*<0.05), but the estimated blood loss (358.0 versus 703.8 ml, *P*<0.05), return of bowel movement (2.5 versus 2.9 days, *P*<0.05), removal of Foley catheter (14.8 versus 18.1 days, *P*<0.05) and post-operative hospital stay (19.4 versus 29.6 days, *P*<0.05) for the LRH group were significantly shorter than that for the ORH group.

Intra- and post-operative complications

Although the two groups had similar rates of intra-operative complications (8.1% versus 10.7%, *P*=0.068), the rate of vessel injury was significantly higher in the ORH group than in the LRH group (2.6% versus 7.7%, *P*<0.001). The rate of post-operative complications was also significantly higher in the ORH group than in the LRH group (33.8% versus 40.1%, *P*=0.007). The rate of urinary retention (24.0% versus 28.0%, *P*=0.060) and wound dehiscence (0.7% versus 4.1%, *P*<0.001) were higher in the ORH group than in the LRH group, although the difference in Febrile morbidity (7.3% versus 7.1%, *P*=0.925) was not statistically significant (**Table 4**).

The extent of surgical excision

No statistical difference was found between the number of lymph nodes removed in the LRH group compared to the ORH group (21.1 versus 20.4, *P*=0.233). The length of the left parametrial resection (3 versus 2.7 cm, *P*<0.05), the length of the right parametrial resection (3 versus 2.7 cm, *P*<0.05) and the length of vaginal tissue resection (3 versus 2.8 cm, *P*<0.05) were also not significantly different between the two groups (**Table 5**).

Table 7. FSFI scores at 12 months after surgery between NS-LRH group and ORH groups

	LRH (n=978)	ORH (n=708)	*P*-value
Sexual interest	4.3 ± 1.1	3.9 ± 1.1	0
Sexual arousal	3.5 ± 1.3	3.2 ± 1.2	0.001
Lubrication	4.8 ± 0.9	4.6 ± 0.7	0.01
Orgasm	4.3 ± 1.0	4.0 ± 0.9	0
Sexual satisfaction	4.2 ± 1.2	3.6 ± 1.0	0
Sexual pain	4.5 ± 1.1	4.3 ± 1.0	0.016

Pelvic floor dysfunction

The ICIQ-FLUTS questionnaire survey was used to assess urinary incontinence 12 months after surgery. In the second period of the survey, (2011.01.01~2014.02.28), the questionnaire included both pre-operative baseline and 12-month post-operative information. In the LRH group, the total number of urinary incontinence cases 12 months after surgery was 191 (33.3%, 191/573). Of these, mild urinary incontinence occurred in 128 cases (22.3%, 128/573), moderate urinary incontinence occurred in 44 cases (7.7%, 44/573), severe urinary incontinence occurred in 12 cases (2.1%, 12/573), and serious urinary incontinence occurred in 7 cases (1.2%, 7/573). The total number of urinary incontinence cases 12 months after surgery in the ORH group was 71 cases (35.9%, 71/198). Of these, mild urinary incontinence occurred in 47 cases (23.7%, 47/198), moderate urinary incontinence occurred in 16 cases (8.1%, 16/198), severe urinary incontinence occurred in 5 cases (2.5%, 5/198), and serious urinary incontinence occurred in 3 cases (1.5%, 3/198). There was no significant difference in the incidence of total urinary incontinence and in the degrees of urinary incontinence after surgery (P>0.05) between the two groups.

Stratified analysis of 236 patients from the NS-LRH group and 198 patients from the ORH group from the same time period indicated that the frequency of urinary incontinence was fewer in the NS-LRH group than that in the ORH group (28.4% versus 34.7%, P=0.004). However, no statistical difference was found for the degree of incontinence between the NS-LRH group and the ORH group (P=0.980) (**Table 6**).

Sexual dysfunction

Except for dead, "lost for follow up" and asexual patients, the FSFI was used to assess sexual problems after surgery. In the second period of the study (2011.01.01 to 2014.02.28) FSFI was obtained from patients before the operation (baseline) and at 12 months after the operation. FSFI evaluated questions in six different domains, that included sexual desire, sexual arousal, lubrication, orgasm, sexual satisfaction, and sexual pain.

No statistical difference was observed between the two groups (P>0.05). In the LRH group, sexual dysfunction (FSFI<26.55) was reported in 161 cases before surgery (28.1%, 161/573), and in 313 cases 12 months after surgery (54.7%, 313/573); In the ORH group, sexual dysfunction was reported in 52 cases before surgery (26.3%, 52/198), and in 113 cases 12 months post surgery (57.1%, 113/198); No statistical difference was observed between the two groups (P=0.574, P=0.361).

Stratified analysis of 236 patients from the NS-LRH group and 198 patients from the ORH group over the same time period showed that the scores from the six domains were better in the NS-LRH group than in the ORH group (P<0.05) (**Table 7**). The total FSFI scores <26.55 before surgery did not differ between the NS-LRH and ORH groups (27.5% versus 25.7%, P=0.493), but were significantly different after surgery (47.1% versus 56.1%, P= 0.001).

Recurrence and survival outcomes

The average follow-up time was 52 months (ranging from 13-95 months) and 69 months (ranging from 14-101 months) for the LRH group and ORH group, respectively. We observed a 3.5% (35/1007) recurrence rate in the LRH group, where the number of patients where local pelvic recurrence occurred was 14 and the number of patients where metastasis occurred was 21. The recurrence rate was 4.7% (35/740) in the ORH group, where the local pelvic recurrence was 16 and metastasis number was 19 patients, but the difference between the two groups was not statistically significant. (P=0.269).

LRH was associated with similar survival outcomes as ORH. The 5-year OS was 94.0% and 90.2% for the LRH group and the ORH group, respectively, (P=0.260). The 5-year DFS rate was 93.9% and 89.1% for the LRH group and the ORH group, respectively (P=0.292) (**Figures 1** and **2**).

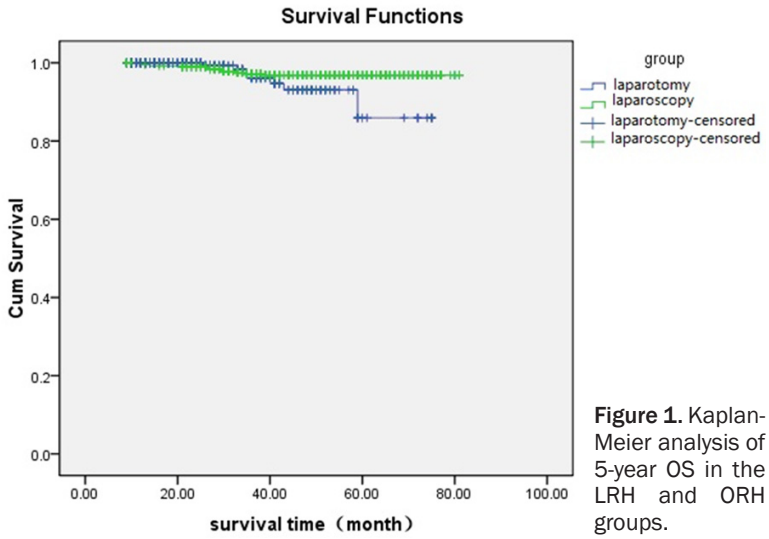

Figure 1. Kaplan-Meier analysis of 5-year OS in the LRH and ORH groups.

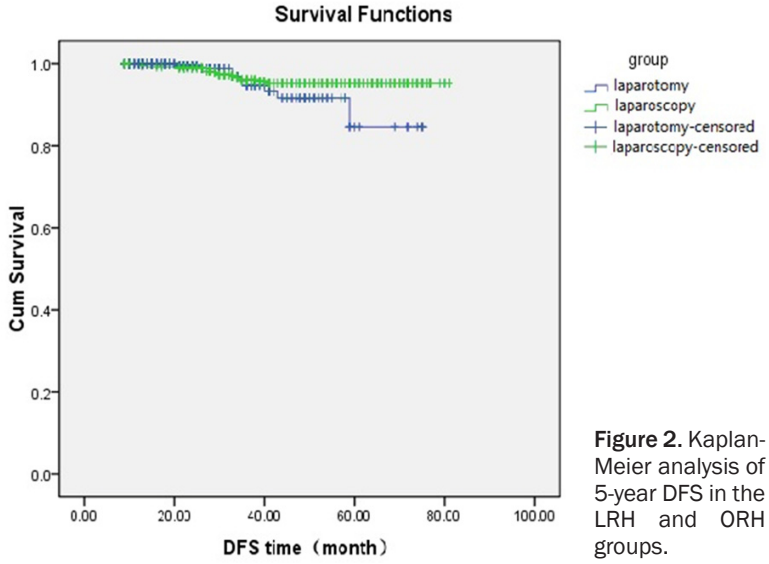

Figure 2. Kaplan-Meier analysis of 5-year DFS in the LRH and ORH groups.

The average follow-up time was 24 months (ranging from 14-53 months) for the NS-LRH group and 37 months (ranging from 15-53 months) for the ORH group in the second period (2011.01.01~2014.02.28). We observed a recurrence rate of 8.05% (19/236) in the NS-LRH group. The recurrence rate was 4.04% (8/198) in the ORH group; the difference was not statistically significant between the two groups (P=0.11). The overall survival rate of the NS-LRH group and the ORH group were 92% and 90%, respectively. No statistical difference between the two groups (P=0.053) was observed (**Figure 3**).

Univariate analyses revealed that tumor size >4 cm (P<0.001), FIGO stage Ib2 and IIa2 (P<0.001), cervical stromal invasion >1/2 (P<0.001), presence of lymphovascular space invasion (P=0.011) and lymph node metastasis (P< 0.001) were significantly associated with a decreased 5-year OS. Furthermore, tumor size >4 cm, FIGO stage Ib2 and IIa2, cervical stromal invasion >1/2 and lymph node metastasis were significantly associated with a decreased 5-year DFS (P<0.001) (**Table 8**).

In multivariate analyses, non-squamous (P=0.045), FIGO stage Ib2 and IIa2 (P=0.000) and presence of lymphovascular space invasion (P= 0.000) were significantly associated with a decreased 5-year OS. Furthermore, FIGO stage Ib2 and IIa2 (P=0.000), positive lymphovascular space invasion (P=0.008) and lymph node metastasis (P= 0.013) were significantly associated with a decreased 5-year DFS (**Table 9**).

Discussion

For nearly 20 years, a number of studies have investigated the surgical outcomes of LRH and assessed the safety and feasibility of this procedure [18-20]. Consistent with previous reports, we found that patients who underwent LRH had significantly reduced blood loss, faster recovery of bowel function, faster removal of Foley catheter and shorter post-operative hospital stay than those who underwent ORH. In fact, in our study, post-operative hospital stay was 19.4 and 29.6 days in the LRH and ORH groups, respectively, which is in accordance with other Chinese hospitals, but remarkably longer than hospital stays in Western hospitals. This is most likely due to Insurance policies in China, where most patients prefer to stay in the hospital as long as possible or until the catheter is removed. However, LRH has an increased operating time compared with ORH. Cao SJ et al [21] reported that the for the initial 16 cases per-

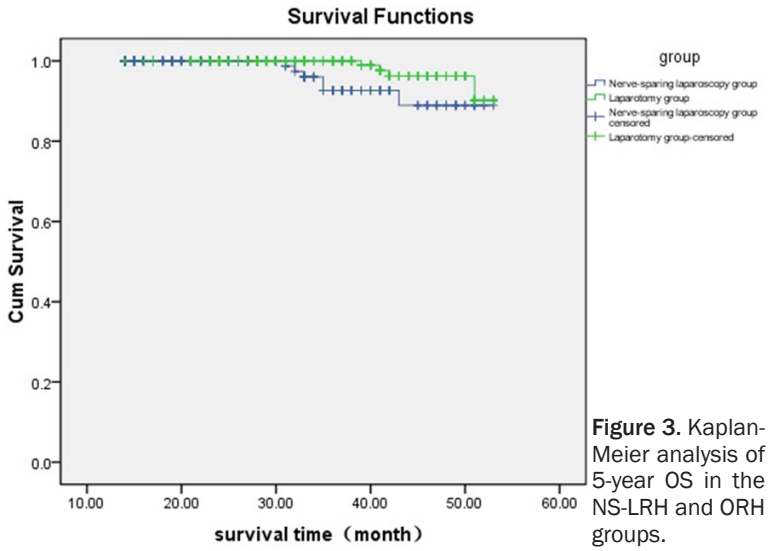

Figure 3. Kaplan-Meier analysis of 5-year OS in the NS-LRH and ORH groups.

Table 8. Univariate analysis of factors predicting survival

Variable	N	5-year OS (%)	*P*	5-year DFS (%)	*P*
Age (years)					
≤35	298	92.2	0.069	91.2	0.376
>35	1565	94		93.7	
Tumor size (cm)					
≤4	1528	92.9	<0.001	92.5	<0.001
>4	335	85.3		78.7	
Histology					
Squamous	1425	91.6	0.879	91.4	0.835
Non-Squamous	438	90.6		90	
Histological grade					
High/Medium	302	94	0.439	93.8	0.623
Low	1561	92.7		92.6	
Clinic stage					
Ia2+Ib1+IIa1	1053	94	<0.001	93.5	<0.001
Ib2+IIa2	810	85.1		78.4	
Stromal invasion					
≤1/2	1408	92	<0.001	91.2	<0.001
>1/2	455	87.6		86	
LVSI					
No	1744	92.4		90.8	0.092
Yes	119	88	0.011	86.7	
LN metastasis					
No	1461	92	<0.001	91.7	<0.001
Yes	402	86.7		85	
Preoperative NACT					
No	1535	92.5	0.8	91.3	0.855
Yes	328	93.3		92.3	
Surgery group					
LRH	1071	93	0.26	91.4	0.292
ORH	792	92.2		89.9	

Abbreviations: DFS, disease-free survival; LVSI, Lymphatic vascular stroma invasion; LN, Lymph node; NACT, Neoadjuvant chemotherapy; LRH, laparoscopic radical hysterectomy; ORH, Open radical hysterectomy.

formed in the LRH group, the operating time was longer than the ORH group, although there was no significant difference between the two groups (250.3 ± 38.18 min vs. 243.9 ± 45.5 min, $P>0.05$). For the final 17 cases, the operating time for LRH was shorter compared to ORH and there was a significant difference in operating time between the two groups (205.9 ± 36.98 vs. 243.9 ± 45.5 min, $P<0.05$). These data suggest that as surgeons get more experienced with the technique, the operating time gets shorter. Laparoscopic imaging systems expose the surgical field more clearly and provide a more extended view than traditional open surgery; this contributes to less tissue damage, less vascular injury and inflammation, decrease in abdominal disruption, and better preservation of internal homeostasis, and therefore the recovery of bowel function is faster, the indwelling catheter time is shorter, resulting in a shorter post-operative hospital stay. Furthermore, since the surgery is mainly completed by coagulation, bleeding caused during operations is reduced.

Our study shows that the total number of cases of intra-operative complications in LRH were similar to ORH, while the incidence of intra-operative vascular injury, urinary retention and wound dehiscence were reduced. This is consistent with data reported by Nam et al [22]. However, Li G et al [23] reported no statistically significant difference between intra-operative complications and post-operative complications. Thus, the inci-

Table 9. Multivariate analysis of factors predicting survival

Variable	N	5-year OS		5-year DFS	
		OR (95% CI)	*P*	OR (95% CI)	*P*-value
Age (years)					
≤35	298	-	-	-	-
>35	1565				
Tumor size (cm)					
≤4	1528	-	-	-	-
>4	335				
Histology					
Squamous	1425	4.06	0.045	-	-
Non-Squamous	438	(1.03-15.98)			
Histological grade					
High/Medium	302	-	-	-	-
Low	1561				
Clinic stage					
Ia2+Ib1+IIa1	1053	177.92	0	152.73	0
Ib2+IIa2	810	(52.76-599.91)		(56.78-410.85)	
Stromal invasion					
≤1/2	1408	-	-	-	-
>1/2	455				
LVSI					
No	1744	0.109	0	0.21	0.008
Yes	119	(0.03-0.38)		(0.07-0.67)	
LN metastasis					
No	1461	-	-	0.36	0.013
Yes	402			(0.16-0.81)	
NACT					
No	1535	-	-	-	-
Yes	328				
Surgery group					
LRH	1071	-	-	-	-
ORH	792				

Abbreviations: DFS, disease-free survival; LVSI, Lymphatic vascular stroma invasion; LN, Lymph node; NACT, Neoadjuvant chemotherapy; LRH, laparoscopic radical hysterectomy; ORH, Open radical hysterectomy.

dence of LRH complications is associated with laparoscopic instruments, the patient's disease status, familiarity with the anatomy of the pelvic cavity, experience of the surgeon, and so on.

Our study shows that the number of lymph nodes that were removed, the length of the parametrial resection and the length of vaginal tissue resection showed no statistical difference between the LRH and ORH groups. The completeness of resection of the tumor is free from any influence. Simsek et al [24] reported similar results. However, Naik et al [25] found that the length of vaginal tissue resection was superior in the ORH group. In the second time period, the incidence rate of urinary incontinence and the different degrees of urinary incontinence 12 months after surgery, as measured by the ICIQ-FLUTS questionnaire rating, showed no significant difference between the two groups ($P>0.05$). Stratified analysis in the NS-LRH group and ORH group in the same period showed that the frequency of urinary incontinence was fewer in the NS-LRH group than that in the ORH group ($P=0.004$). However, no statistical difference was found between the degree of incontinence in the two groups (P=0.98). Laterza et al [26] reported that LRH, compared to ORH, reduced the post-operative occurrence of urge incontinence, increased bladder sensation and constipation by obstructed defecation. In addition, they reported no significant difference in sexual dysfunction based on the FSFI questionnaire rating for the period of 12 months before and after the operation, in patients in the second time period (P>0.05). After stratified analysis in the NS-LRH group and the ORH group in the same period, we found significant differences in sexual dysfunction in the period 12 months after the operation; this is evident from the different scores for the two groups in the six-domain questionnaire ($P<0.05$). In contrast, Laterza et al [27] reported that these problems were not statistically significant between the two groups. The results of our study showed that the NS-LRH group had improved pelvic floor function and sexual function compared to the ORH group. Currently, many studies have confirmed that preserving the pelvic autonomic nerve is what makes the difference

in post-operative improvement in pelvic floor and sexual function [28, 29].

However, an important limitation of retrospective studies is the inherent bias; many studies use a variety of methods to assess the quality of life (including pelvic floor function and sexual function) and lack a uniform standard for evaluation and statistical analysis. Therefore, to obtain high quality evidence we strongly recommend that future studies should have a defined long-term life quality index, a unified standard and effective assessment tools. Moreover, our study showed no significant difference in the 5-year OS rate and DFS rate, compared to the recurrence rate between the two groups (P>0.05). This is consistent with other studies in the literature [30, 31]. Meanwhile, no significant difference in the overall survival rate between the NS-LRH and the ORH groups in the same time period was observed (*P*>0.05). It was not clear if the nerve-sparing method influenced the prognosis [32].

In this study, 1,863 cases of cervical cancer patients were analyzed for prognostic factors. Univariate analyses showed that lymph node metastasis, depth of cervical stromal invasion, and LVSI were associated with the prognosis of cervical cancer. Age, histological type, tumor size, clinical stage and histological grade had no significant effect on the prognosis. Multivariate analyses showed that lymph node status and depth of invasion were independent predicting factors. The results suggest that the patients with cervical stromal invasion depth >1/2 and lymph node metastasis had poor prognosis, not including LVSI. These results may be due to the comprehensive effects of the multivariate analyses on the prognosis, but the effect of LVSI should also be noted. Our results are consistent with other studies [33, 34].

In conclusion, the current retrospective study showed that compared with ORH, LRH results in reduced blood loss, post-operative complications, indwelling catheter time and post-operative hospital stay; the prognosis is similar to the laparotomy. However, the nerve-sparing procedure has the advantage of improving long-term pelvic floor function and sexual function after surgery. Therefore, training of laparoscopic surgeons should be strengthened and promoted in hospitals where conditions permit. This study is a multi-center, retrospective study, with many differences in laparoscopic equipments and surgical techniques; therefore the quality of evidence is low. In the future, a good, multi-center, prospective randomized controlled study needs to be designed, to further test the long-term quality of life and survival of patients with early-stage cervical cancer.

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Disclosure of conflict of interest

None.

Address correspondence to: Li Li, Department of Gynecologic Oncology, The Affiliated Tumor Hospital of Guangxi Medical University, Nanning 530021, China. E-mail: lili@gxmu.edu.cn

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