Impact of Surgeons' Experience on Oncologic Outcomes in Women Undergoing Laparoscopic Radical Hysterectomy for Cervical Cancer: A Comparison of the First 50 and last 50 Cases

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Abstract

Objectives: To compare the oncological outcomes of the first 50 laparoscopic radical hysterectomy (LRH) surgeries with the last 50 LRH, performed by high volume surgeons, for cervical cancer patients.

Design: A nationwide multicentre retrospective cohort study

Setting: Clinical diagnosis and treatment of cervical cancer patients in mainland China (Four C) database.

Population: women with early cervical cancer undergone LRH.

Methods: We retrospectively analyzed the oncological outcomes of 1004 cervical cancer patients who underwent LRH performed by 19 surgeons. They were divided into two groups according to the sequence of operations, the first 50 and the last 50 patients with LRH. Kaplan-Meier survival analysis and log-rank test, Cox proportional risk regression model and propensity score matching were used.

Main Outcome Measures: 5-year overall survival (OS) and disease-free survival (DFS) rates.

Results: There were no significant differences in the 5-year OS and DFS between first 50 patients with LRH group (n=413) and last 50 patients with LRH group (n=591) (OS: p=0.388; DFS: p=0.226). The last 50 cases of LRH was not an independent risk factor for OS and DFS in early cervical cancer patients (p=0.830, p=0.300). After propensity score matching, similar outcomes were observed (n=364:364，OS:P = 0.764; DFS:P = 0.705).

Conclusions: The oncological outcomes of the first 50 LRH surgeries were similar to those of the last 50 surgeries in patients with early-stage cervical cancer. Increase in the surgeons' experience did not improve significantly with oncological outcomes of patients with early stage cervical cancer after LRH.

1. Introduction

Radical hysterectomy in combination with pelvic lymphadenectomy is the standard treatment for non-fertility sparing stage IA1 cervical cancer with positive lymphovascular space invasion (LVSI) to stage IIA2 cervical cancer. NCCN guideline[1] used to indicate that laparotomy or minimally invasive surgery (MIS) are acceptable for patients with early stage cervical cancer. Due to these suggestions, MIS was widely used. However, in November 2018, Ramirez et al. [2] published a multicentre, phase III randomized controlled trial in the New England Journal of Medicine, which reported that laparoscopic radical hysterectomy(LRH) was associated with worse OS and DFS rates after 4.5 years in patients with early stage cervical cancer than was abdominal radical hysterectomy (ARH). In the same period, retrospective cohort data from Melamed et al.[3] were also published, and LRH was reported to result in a shorter OS than ARH. These two studies overturned the traditional understanding of laparoscopic surgery in gynecologic oncology. *Cervical Cancer Guidelines (Version 3.2019)* released by NCCN Clinical Practice

Guidelines in Oncology in 2019 [4] no longer recommends laparoscopic surgery as the preferred surgical approach for the treatment of early stage cervical cancer .

Although these two studies suggested that the long-term prognosis was poor for patients that underwent LRH with early stage cervical cancer, the study did not provide reasons for the poor efficacy of laparoscopy. Among many possible causes, surgical experience was often thought to influence oncological outcomes. Therefore, we suggest a hypothesis: was the surgeons' experience one of the reasons for the poor outcomes of LRH surgery? However, the previous studies on the learning curve of LRH for early stage cervical cancer focused on operative techniques such as operation time, bleeding volume, incidence of intraoperative and postoperative complications and perioperative outcomes, rarely focused on long-term oncological outcomes and ignored the influence of surgeons' experience on the long-term oncological outcomes of patients with early stage cervical cancer. In addition, in most of the studies, single-center, single-surgeon and small samples were included.

To test this hypothesis, we explored whether the experience of surgeons affects the efficacy of LRH based on the clinical diagnosis and treatment of cervical cancer in China database. This study is a multicenter retrospective study. We compare the oncological outcomes of the first 50 LRH surgeries and the last 50 LRH surgeries of surgeons for patients with early stage cervical cancer.

2. Materials And Methods

2.1 Data Source

The data used in this study is from the Clinical Diagnosis and Treatment for Cervical Cancer in China (Four C) Database, which covers 46 313 patients with cervical cancer in 37 hospitals in mainland China from January 2004 to December 2016. The establishment of this database was approved by the Ethics Committee of the Southern Hospital of Southern Medical University. The ethical approval number is NEEC-2017-135, and the clinical research registration number is CHiCTR1800017778 (International Clinical Trials Registry Platform Search Port, http://apps.who.int/trialsearch/).

All follow-up procedures were carried out by trained gynecological oncology staff at each centre to keep the patients' personal data confidential and to provide disease management guidance at the same time. The follow-up information was gathered through the return visit system or telephone follow-up, including survival status, time of death, recurrence time, recurrence site, treatment after recurrence. The oncological outcomes were estimated according to the recorded information, and the last day of the return visit or telephone follow-up was defined as the last follow-up. We follow-up all patients, but the follow-up rate of oncological outcomes was 72.7% in this database. Detailed data collection requirements and database establishment processes were described in our previously published study. [5,6]

Laparoscopic cervical cancer surgery started to be conducted in all participating institutions after 2004,so the first LRH cases performed by surgeons after this year were included in this database. In this study,

more than 600 surgeons were enrolled. In the database, 19 surgeons who completed more than 100 cases of LRH were enrolled. The operation cases were sorted according to the operation date. The first 50 patients with LRH were considered a group and the last 50 patients with LRH were considered another group. The patients were grouped according to the date of the operation, regardless of whether they met the inclusion or exclusion criteria.

In this database, the FIGO stage was recorded and corrected by tumour size according to the FIGO 2009 staging system. Tumour size was evaluated using magnetic resonance imaging, computed tomography, ultrasound, physical examination or postoperative pathological records.

2.2 Inclusion and exclusion criteria

The patients' inclusion criteria were as follows: age 18 years or older; cervical cancer diagnosis of FIGO stage IA1 with positive LVSI to stage IIA2; squamous cell carcinoma, adenocarcinoma, or adenosquamous cell carcinoma; a history of laparoscopic surgery; type QM-B or QM-C [7] hysterectomy with pelvic lymphadenectomy with or without paraaortic lymphadenectomy; and a postoperative survival outcome. Surgeons who performed 100 or more LRH surgeries were also included, and we excluded patients if they had neoadjuvant chemotherapy or radiotherapy before surgery. Patients with pregnancy or other types of malignant tumours were excluded, too.

In subgroup analyses, the standard postoperative adjuvant therapy was defined as cervical cancer patients with one or more high-risk factors (lymph node metastasis, parametrial involvement, and surgical margin invasion) or patients with two or more intermediate-risk factors (deep cervical stromal invasion, tumor size > 4 cm, and LVSI were received radiotherapy or chemo-radiotherapy. [8]

2.3 Outcome measures

The overall 5-year survival rate (OS) and disease-free survival rate (DFS) were calculated. OS was defined as the time from diagnosis to death for any reason. DFS was defined as the time from diagnosis to death or recurrence for any reason. Data regarding patients with no evidence of recurrence or death were censored at the date of last follow-up.

2.4 Statistical methods

Metrological data were expressed as the mean (+ standard deviation) and categorized data by percentage (%). The Kaplan-Meier curve was used to describe the changes in survival outcomes, and the log-rank test was used to compare the differences in survival curves among groups. A Cox proportional risk regression model was used to adjust for case mix, determine independent risk factors, and calculate the relevant risk and 95% confidence interval. The statistical software used was SPSS 23.0 (SPSS Inc., Chicago, IL, USA). $P < 0.050$ was considered statistically significant. In the multivariate model, we also included the following known variables that may affect prognosis to reduce confounding effects: FIGO stage, age, histology, tumour size, depth of the stromal invasion, LVSI, lymph node metastasis, surgical margin invasion, parametrial tumour invasion, and postoperative adjuvant treatment.

To control confounding factors, each patient in the first 50 patients with LRH group was matched to one patient in last 50 patients with LRH group using the known risk factors for recurrence or death using propensity score matching (PSM).

3. Results

A total of 46 313 patients with cervical cancer were included from the large database on the clinical diagnosis and treatment of cervical cancer in China. 7670 patents received LRH, and there were 19 surgeons operating more than 100 LRH. The mean LRH of 19 surgeons is 201.2 ± 85.2 (range 102 to 375). According to the inclusion and exclusion criteria, 1004 patients with early stage cervical cancer were finally included. The data filtering process is shown in Fig. 1.

Median follow-up of censored cases was 35.3 months (interquartile range, 26.0–51). Clinico-pathologic characteristics of two groups before and post matching are shown in Table 1. The first 50 patients with LRH group was younger than another group. In both groups, patients with IB1 stage disease accounted for most(66.1% vs. 65.0%). The first 50 patients with LRH group were more likely to have lower stage disease, whereas the last 50 patients with LRH group were more likely to have higher stage disease. Tumours in the first 50 patients with LRH group were less likely to have lymphovascular space invasion and deep stromal invasion (all, $P < 0.05$).

Table 1
Clinical and pathological parameters of first 50 patients with LRH group and last 50 patients with LRH group

	before matched		***P***	**after matched**		***P***
Characteristic	**First 50 patients with LRH(n = 413)**	**Last 50 patients with LRH(n = 591)**		**First 50 patients with LRH(n = 364)**	**Last 50 patientes with LRH(n = 364)**	
Age(years)	**46.3 ± 8.913**	**49.1 ± 9.637**	**< 0.001**	47.1 ± 8.789	47.3 ± 9.137	0.701
FIGO stage			**< 0.001**			0.191
IA	13(3.1%)	13(2.2%)		11(3.0%)	10(2.7%)	
IB1	273(66.1%)	384(65.0%)		257(70.6%)	268(73.6%)	
IB2	35(8.5%)	48(8.1%)		32(8.8%)	30(8.2%)	
IIA1	56(13.6%)	111(18.8%)		50(13.7%)	50(13.7%)	
IIA2	7(1.7%)	28(4.7%)		7(1.9%)	0(0.0%)	
IB/IIA	29(7.0%)	7(1.2%)		7(1.9%)	6(1.6%)	
Histologic type			0.307			0.732
Squamous cell carcinoma	368(89.1%)	509(86.1%)		320(87.9%)	313(86.0%)	
Adenocarcinoma	37(9.0%)	71(12.0%)		36(9.9%)	41(11.3%)	
Adenosquamous carcinoma	8(1.9%)	11(1.9%)		8(2.2%)	10(2.7%)	
Tumour size			**< 0.001**			0.495
≤ 4 cm	342(82.8%)	508(86.0%)		318(87.4%)	328(90.1%)	
4 cm	42(10.2%)	76(12.9%)		39(10.7%)	30(8.2%)	
Unknows	29(7.0%)	7(1.2%)		7(1.9%)	6(1.6%)	
LVSI			**< 0.001**			0.672
Negative	363(87.9%)	426(72.1%)		314(86.3%)	310(85.2%)	
Positive	50(12.1%)	165(27.9%)		50(13.7%)	54(14.8%)	
Stromal invasion depth			**0.021**			0.868

	before matched		*P*	after matched		*P*
Characteristic	**First 50 patients with LRH(n = 413)**	**Last 50 patients with LRH(n = 591)**		**First 50 patients with LRH(n = 364)**	**Last 50 patientes with LRH(n = 364)**	
≤ 1/2	202(48.9%)	237(40.1%)		175(48.1%)	181(49.7%)	
1/2	176(42.6%)	298(50.4%)		158(43.4%)	155(42.6%)	
Unknows	35(8.5%)	56(9.5%)		31(8.5%)	28(7.7%)	
Parametrium			0.573			0.362
Negative	406(98.3%)	578(97.8%)		357(98.1%)	360(98.9%)	
Positive	7(1.7%)	13(2.2%)		7(1.9%)	4(1.1%)	
Surgical margin			0.135			0.704
Negative	404(97.8%)	585(99.0%)		361(99.2%)	360(98.9%)	
Positive	9(2.2%)	6(1.0%)		3(0.8%)	4(1.1%)	
pelvic lymph nodes			0.836			0.128
Negative	346(83.8%)	498(84.3%)		308(84.6%)	322(88.5%)	
Positive	67(16.2%)	93(15.7%)		56(15.4%)	42(11.5%)	
postoperative treatment			0.185			0.103
Standard treatment	187(45.3%)	305(51.6%)		170(46.7%)	187(51.4%)	
Insufficient treatment	52(12.6%)	75(12.7%)		42(11.5%)	27(7.4%)	
Over treatment	163(39.5%)	200(33.8%)		150(41.2%)	144(39.6%)	
Uncertain	11(2.7%)	11(1.9%)		2(0.5%)	6(1.6%)	

There was no difference in 5-year OS and DFS between the first 50 patients with LRH group (n = 413) and the last 50 patients with LRH group (n = 591) (OS: 94.6% vs 96.6%, P = 0.388; DFS: 87.6% vs 90.5%, P = 0.226) (see in Fig. 2). Cox multivariate analysis (see in Table 3) showed that surgical experience was not an independent risk factor for poor OS in patients with early stage cervical cancer (p = 0.830) or an independent risk factor for poor DFS (p = 0.300).

Table 3

Association of Surgical Experience of LRH and Survival outcome of first 50 patients with LRH group and last 50 patients with LRH group (n = 1004)

Parameters	Multivariate analysis for 5-year OS			Multivariate analysis for 5-year DFS		
	HR	95.0% CI	P	HR	95%CI	p
Age(years)	-	-	0.703	-	-	0.736
Surgeons' experience	-	-	0.830	-	-	0.300
FIGO stage	-	-	0.447	-	-	0.765
Histologic type	-	-	0.241		-	0.049
Squamous cell carcinoma				1(Ref)	-	-
Adenocarcinoma	-	-	-	1.471	0.775–2.793	0.238
Adenosquamous carcinoma	-	-	-	3.209	1.164–8.845	0.024
Tumour size	-	-	0.419	-	-	0.944
LVSI	-	-	0.042	-	-	0.718
Negative	1(Ref)	-	-	-	-	-
Positive	2.252	1.030–4.927	0.042	-	-	-
Stromal invasion depth	-	-	0.019	-	-	0.011
≤ 1/2	1(Ref)	-	-	1(Ref)	-	-
> 1/2	3.954	1.465–10.669	0.007	2.208	1.296–3.761	0.004
unknows	4.253	1.136–15.924	0.032	2.227	1.011–4.909	0.047
Parametrium	-	-	0.159	-	-	0.792
Surgical margin	-	-	0.413	-	-	0.655
pelvic lymph nodes	-	-	0.159	2.685	1.661–4.340	0.000
postoperative treatment	-	-	0.903	-	-	0.689
Multicollinearity test and cox proportional hazard regression models were used for analysis.						
Proportional hazard assumption was tested and showed no interaction with time.						
Bold indicates significant P-value.						

After propensity score matching, a total of 728 patients (364 in first 50 patients with LRH group and 364 in last 50 patients with LRH group) met the criteria for inclusion. The baseline data of patients after

matching were consistent (Table 1). OS was 93.8% in group first 50 patients with LRH group and 96.9% in group last 50 patients with LRH group (see in Fig. 2). There was no significant difference in OS between the two groups (p = 0.764). Cox multivariate analysis (see in Table 4) showed that LRH surgical experience was not associated with OS in patients with early stage cervical cancer (p = 0.410). DFS was 87.2% in first 50 patients with LRH group and 91.8% in last 50 patients with LRH group. There was no significant difference in DFS between the two groups (p = 0.705). Cox multivariate analysis showed that the experience of LRH surgery was not correlated with DFS in patients with early stage cervical cancer (p = 0.522).

Table 4
After matched, association of Surgical Experience of LRH and Survival outcome of first 50 patients with LRH group and last 50 patients with LRH group (n = 728)

Parameters	Multivariate analysis for 5-year OS			Multivariate analysis for 5-year DFS		
	HR	95.0% CI	P	HR	95%CI	p
Age(years)	-	-	0.264	-	-	0.728
Surgeons' experience	-	-	0.767	-	-	0.522
FIGO stage	-	-	0.546	-	-	0.614
Histologic type	-	-	0.434	-	-	0.034
Squamous cell carcinoma	-	-	-	1(Ref)	-	-
Adenocarcinoma	-	-	-	1.584	0.772–3.247	0.209
Adenosquamous carcinoma	-	-	-	3.543	1.266–9.919	0.016
Tumour size	-	-	0.018	-	-	0.461
≤ 4 cm	1(Ref)			-	-	-
4 cm	1.160	0.332–4.047	0.816	-	-	-
Unknows	6.141	1.744–21.621	0.005	-	-	-
LVSI	-	-	0.073	-	-	0.610
Stromal invasion depth	-	-	0.015	-	-	0.008
≤ 1/2	1(Ref)	-	-	1(Ref)	-	-
> 1/2	4.334	1.422–13.213	0.010	2.421	1.310–4.474	0.005
unknows	6.325	1.576–25.380	0.009	3.133	1.268–7.740	0.013
Parametrium	-	-	0.508	-	-	0.465
Surgical margin	-	-	0.563	-	-	0.363
pelvic lymph nodes	-	-	0.334	3.030	1.717–5.347	0.000
postoperative treatment	-	-	0.731	-	-	0.715
Multicollinearity test and cox proportional hazard regression models were used for analysis.						
Proportional hazard assumption was tested and showed no interaction with time.						
Bold indicates significant P-value.						

The same results were obtained from the subgroup analysis of standard postoperative adjuvant therapy(Fig. 3,Table 5–6). The baselines of FIGO staging, histological type, tumour size, LVSI, cervical stromal invation depth and surgical margin were not consistent between the two groups (Table 2). The OS was 95.6% in first 50 patients with LRH group (n = 187) and 95.8% in last 50 patients with LRH group (n = 305) before standard treatment (see in Fig. 3). There was no significant difference in OS between the two groups (p = 0.189). Cox multivariate analysis (see in Table 5) showed that LRH surgical experience was not associated with OS in patients with early stage cervical cancer (p = 0.189). DFS was 90.2% in first 50 patients with LRH group and 92.2% in last 50 patients with LRH group (see in Fig. 3). There was no significant difference in DFS between the two groups (p = 0.280). Cox multivariate analysis showed that LRH operation experience was not related to DFS in patients with early stage cervical cancer (p = 0.516). The similar result were obtained after matching (see in Table 2 and Table 6).

Table 2
Clinical and pathological parameters of standart post-operative therapy subgroup of first and last 50 patients with LRH

	before matched		***P***	**after matched**		***P***
Characteristic	**First 50 patients with LRH(n = 187)**	**Last 50 patients with LRH(n = 305)**		**First 50 patients with LRH(n = 166)**	**Last 50 patients with LRH(n = 166)**	
Age(years)	**46.9 ± 8.499**	**48.0 ± 9.901**	**0.221**	**46.9 ± 8.327**	**47.1 ± 9.753**	**0.799**
FIGO stage			**0.002**			0.999
IA	11(5.9%)	8(2.6%)		6(3.6%)	7(4.2%)	
IB1	127(67.9%)	205(67.2%)		122(73.5%)	120(72.3%)	
IB2	20(10.7%)	29(9.5%)		18(10.8%)	18(10.8%)	
IIA1	18(9.6%)	40(13.1%)		16(9.6%)	16(9.6%)	
IIA2	4(2.1%)	22(7.2%)		3(1.8%)	4(2.4%)	
IB/IIA	7(3.7%)	1(0.3%)		1(0.6%)	1(0.6%)	
Histologic type			0.040			0.845
Squamous cell carcinoma	175(93.6%)	263(86.2%)		156(94.0%)	155(93.4%)	
Adenocarcinoma	10(5.3%)	36(11.8%)		9(5.4%)	9(5.4%)	
Adenosquamous carcinoma	2(1.1%)	6(2.0%)		1(0.6%)	2(1.2%)	
Tumour size			0.009			0.987
≤ 4 cm	156(83.4%)	253(83.0%)		144(86.7%)	143(86.1%)	
4 cm	24(12.8%)	51(16.7%)		21(12.7%)	22(13.3%)	
Unknows	7(3.7%)	1(0.3%)		1(0.6%)	1(0.6%)	
LVSI			< 0.001			0.875
Negative	161(86.1%)	210(68.9%)		142(85.5%)	143(86.1%)	
Positive	26(13.9%)	95(31.1%)		24(14.5%)	23(13.9%)	
Stromal invasion depth			**0.002**			**0.992**

Legends

	before matched		*P*	after matched		*P*
Characteristic	**First 50 patients with LRH(n = 187)**	**Last 50 patients with LRH(n = 305)**		**First 50 patients with LRH(n = 166)**	**Last 50 patients with LRH(n = 166)**	
≤ 1/2	110(58.8%)	144(47.2%)		99(59.6%)	100(60.2%)	
1/2	56(29.9%)	139(45.6%)		50(30.1%)	49(29.5%)	
Unknows	21(11.2%)	22(7.2%)		17(10.2%)	17(10.2%)	
Parametrium			0.736			0.474
Negative	183(97.9%)	297(97.4%)		163(98.2%)	161(97.0%)	
Positive	4(2.1%)	8(2.6%)		3(1.8%)	5(3.0%)	
Surgical margin			0.030			1.000
Negative	181(96.8%)	303(99.3%)		164(98.8%)	164(98.8%)	
Positive	6(3.2%)	2(0.7%)		2(1.2%)	2(1.2%)	
pelvic lymph nodes			0.834			0.104
Negative	150(80.2%)	247(81.0%)		133(80.1%)	144(86.7%)	
Positive	37(19.8%)	58(19.0%)		33(19.9%)	22(13.3%)	
Legends						

Table 5

Association of Surgical Experience of LRH and Survival outcome of standart post-operative therapy subgroup of first and last 50 patients with LRH (n = 492)

Parameters	Multivariate analysis for 5-year OS			Multivariate analysis for 5-year DFS		
	HR	95.0% CI	P	HR	95%CI	p
Age(years)	-	-	0.945	-	-	0.142
Surgeons' experience	-	-	0.162	-	-	0.294
FIGO stage	-	-	0.263	-	-	0.259
Histologic type	-	-	0.096	-	-	0.008
Squamous cell carcinoma	-	-	-	1(Ref)	-	-
Adenocarcinoma	-	-	-	2.575	0.956–6.934	0.061
Adenosquamous carcinoma	-	-	-	8.067	1.818–35.788	0.006
Tumour size	-	-	0.142	-	-	0.176
LVSI	-	-	0.801	-	-	0.278
Stromal invasion depth	-	-	0.304	-	-	0.079
Parametrium	-	-	0.500	-	-	0.311
Surgical margin	-	-	0.601	-	-	0.458
pelvic lymph nodes	-	-	0.015	-	-	0.011
Negative	1(Ref)	-	-	1(Ref)	-	-
Positive	4.651	1.344–16.089	0.015	2.765	1.262–6.061	0.011
Multicollinearity test and cox proportional hazard regression models were used for analysis.						
Proportional hazard assumption was tested and showed no interaction with time.						
Bold indicates significant P-value.						

Table 6
After matched, association of Surgical Experience of LRH and Survival outcome of standart post-operative therapy subgroup of first and last 50 patients with LRH **(n = 332)**

Parameters	Multivariate analysis for 5-year OS			Multivariate analysis for 5-year DFS		
	HR	95.0% CI	P	HR	95%CI	p
Age(years)	-	-	0.191	-	-	0.876
Surgeons' experience	-	-	0.725	-	-	0.604
FIGO stage	-	-	0.902	-	-	0.580
Histologic type	-	-	0.055	-	-	0.400
Tumour size	-	-	0.917	-	-	0.739
LVSI	-	-	0.157	-	-	0.057
Stromal invasion depth	-	-	0.743	-	-	0.137
Parametrium	-	-	0.616	-	-	0.516
Surgical margin	-	-	0.746	-	-	0.634
pelvic lymph nodes	-	-	0.022	-	-	0.084
Negative	1(Ref)	-	-	-	-	-
Positive	8.153	1.562–48.805	0.022	-	-	-
postoperative treatment	-	-	0.191	-	-	0.876
Multicollinearity test and cox proportional hazard regression models were used for analysis.						
Proportional hazard assumption was tested and showed no interaction with time.						
Bold indicates significant P-value.						

4. Discussion

Our study found that long-term oncological outcomes in patients with early stage cervical cancer did not improve significantly with increased surgical experience for high LRH volume surgeons.

The inclusion and exclusion criteria are relatively loose in the general analysis, and the results could reflect the influence of surgeons' LRH experience on survival outcomes of early stage cervical cancer patients. In matched cohort studies, the patients' baseline data were more uniform than those in the RWD, and mixed bias could be effectively controlled. However, the external validity of the results was poor, which meant that the ability to generalize the results to other groups of patients with cervical cancer was limited.[21,22] In this study, general analysis and matched cohort studies were consistent and mutually

validated, which improved the reliability of the results.[23] This further confirmed that the surgical experience of LRH surgeons was not related to the oncological outcomes of the patients.

At present, there are no original articles to study the reasons for the worse laparoscopic oncologic outcome of women with cervical cancer from the perspective of the experience of surgeons, but after the publication of LACC study, some articles [9–12] discussed whether the experience of surgeons could be one of the reasons for the worse laparoscopic oncologic outcome of women with cervical cancer. However, previous studies analyzed fewer institutions, surgeons and fewer patients than this study. For example, Chong et al. [13] compared the earliest 50 patients with LRH of a surgeon in a single center with the next 50 patients with LRH in patients with locally advanced cervical cancer. With an increase in surgical experience, the operation time, hospitalization days, time to recover normal residual urine and blood transfusion decreased, the number of lymph nodes obtained increased, and the intraoperative and postoperative complications decreased significantly. For each group, the five-year OS rates were 96% and 92%, and the five-year DFS rates were 92% and 90%. The differences were not statistically significant, and the study did not provide a reason for the lack of significant differences in long-term oncological outcomes. However, our finding differ from another study of surgeon experience on prostate cancer. Vickers et al.[14] conducted a retrospective cohort study of 4702 patients with prostate cancer treated by laparoscopy. A total of 29 surgeons from 7 hospitals participated in the study. It was found that the 5-year recurrence rate was 16.3%, 11.0% and 7.1% ($p = 0.038$) for patients treated by surgeons with 10, 250 and 750 laparoscopic surgeries, respectively, and that the increase in surgical experience was associated with the oncological outcomes of patients with prostate cancer.

Matsuo et al. [15] conducted a nationwide multicenter retrospective study on the RH surgical volume of early stage cervical cancer. A total of 5964 patients with stage IB1-IIB cervical cancer were enrolled from 2004 to 2008. It was found that RH surgical volume may be a prognostic factor for early stage cervical cancer. High surgical volume hospitals may be associated with a reduced risk for local recurrence and an improved survival rate. In this study, there were fewer than 32 RH operations in low volume hospitals, 32 to 104 RH operations in medium volume hospitals and more than 105 RH operations in high volume hospitals over a five-year period. However, the number of surgeries in hospitals could not fully equal to the experience of the surgeons. High-volume hospitals also have doctors with less experience in surgery, and low-volume hospitals also have surgeons with a high surgical volume. The lack of information on surgical approaches in this study means that researchers cannot adjust for the confounding factors of surgical approaches to oncological outcomes. Recent studies such as the study by Ramirez et al.[2] suggest that LRH is associated with poor oncological outcomes in patients with early stage cervical cancer. This study addresses the lack of research on surgeons' experience and surgical approaches highlighted in Matsuo et al.. [15]

Our study found that the oncological outcomes of patients with early stage cervical cancer was not affected by the LRH experience of surgeons. According to literatures on the learning curve of laparoscopic surgery for cervical cancer, surgeons need 20–50 surgeries to master laparoscopic surgery.

[13,16–20] Therefore, number 50 was selected as the cutting point of surgical experience in this study to compare the oncologic outcomes of the first 50 surgeries and the last 50 surgeries of surgeons with more than 100 surgeries. Our database collected consecutive surgical cases (both open and laparoscopic) of more than 600 surgeons. We screened 7,670 patients who underwent laparoscopic QM-B and C2 hysterectomy. Among them, there are 19 surgeons having more than 100 LRH surgeries, so 1,900 patients with their first 50 and last 50 surgeries were included in this study. On the basis of these 1,900 patients, we strictly included and excluded the following criteria. Finally, 1004 patients were selected for oncologic outcome analysis, including 413 patients in the first 50 LRH group and 591 patients in the last 50 LRH group.

Patients enrolled in this study received postoperative adjuvant therapy according to NCCN and FIGO guidelines. FIGO guideline in 2018 [8] mentioned that postoperative adjuvant therapy was added to patients, with any two of three factors intermediate- risk prognostic factors or with any one of high-risk prognostic factors. The high-risk prognostic factors included positive surgical margins or lymph node metastases or parametrial spread, and the intermediate- risk prognostic factors included tumor size more than 4 cm, lymphovascular invasion, deep stromal invasion. This study is a retrospective study. The earliest cases started from 2004, and Sedlis standard was officially recommended by NCCN guideline in 2015 [24]. Therefore, the standards adopted in this study are not completely consistent with Sedlis standard.

The similar survival outcome were observed in both general and subgroup analysis, before or after matching. It might be explained by the following reason. The first cervical cancer surgery case of this study has been recorded since January 2004 when LRH had been introduced in mainland China not so long. Only few experienced surgeons with a high volume of ARH started LRH. Most of the nineteen surgeons in our study were those surgeons who were pioneers on LRH, their enriched surgical experience of ARH helped them to conquer the difficulty on transferring ARH to LRH, so they mastered LRH technique more easily. It might explain why the 5-year OS and DFS results in the first 50 patients with LRH group were not poorer than the last 50 patients with LRH group in this study.

We acknowledge several limitations in this study. First, this study only analyzed the effect of LRH surgical experience on the efficacy of LRH, without considering the effect of ARH experience on the efficacy of LRH. Second, this study is a retrospective study, although multivariate analysis and propensity score matching could effectively control for known confounding factors, the impact of confounding factors on result could not be eliminated completely. Third, this study only analyzed the overall survival rate and disease-free survival rate but did not analyze the recurrence patterns, which requires further study. Fourth, there may be differences in the writing standards of cases and reports in different hospitals, leading to a lack of some clinical data. Fifth, in China, gynecologists perform laparoscopic radical hysterectomy with Wertheim-Meigs operation. Patients with stage IB1 to IIA2 cervical cancer underwent QM-C radical hysterectomy and pelvic lymph node dissection. Patients with stage IA1 with positive LVSI to IA2 cervical cancer underwent QM-B radical hysterectomy. However, this study is a retrospective study. It is a pity that

this database lacks specific surgical procedures. Whether we used a uterine manipulation, or made a vaginal stuff is not available.

5. Conclusion

The oncological outcomes of the first 50 surgeries performed by high-volume LRH surgeons were similar to those of the last 50 surgeries in patients with early stage cervical cancer. The long-term oncological outcomes of LRH in patients with stage IA1 with positive LVSI to stage IIA2 cervical cancer did not improve with an increase in surgeons' experience.

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the Ethics Committee of the Nanfang Hospital of Southern Medical University (approval number NFEC-2017-135 and clinical trial number CHiCTR1800017778; International Clinical Trials Registry Platform Search Port, http://apps.who.int/trialsearch/); registration date: August 14, 2018. Written consent to participate in the study was provided by all patients.

Consent for publication

Not Applicable.

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests to disclose.

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Authors' contributions

1. Pengfei Li did the literature search, data collection, data analysis and interpretation, drafted and revised the manuscript
2. Shan Kang conceived and designed the study, interpreted the data, developed and revised the manuscript.
3. Jianxin Guo conceived and designed the study, interpreted the data, developed and revised the manuscript.
4. Shiqi Liang did the literature search, data analysis and interpretation and figures, drafted and revised the manuscript.
5. Ying Yang conceived, designed the study, interpreted the data. conceived, designed the study, interpreted the data.
6. Shaoguang Wang conceived, designed the study, interpreted the data.
7. Xiaonong Bin did the data analysis and interpretation.
8. Jinghe Lang conceived, designed and supervised the study.
9. Ping Liu conceived, designed and supervised the study.
10. Chunlin Chen conceived, designed and supervised the study.

All authors read and approved the final manuscript.

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Figures

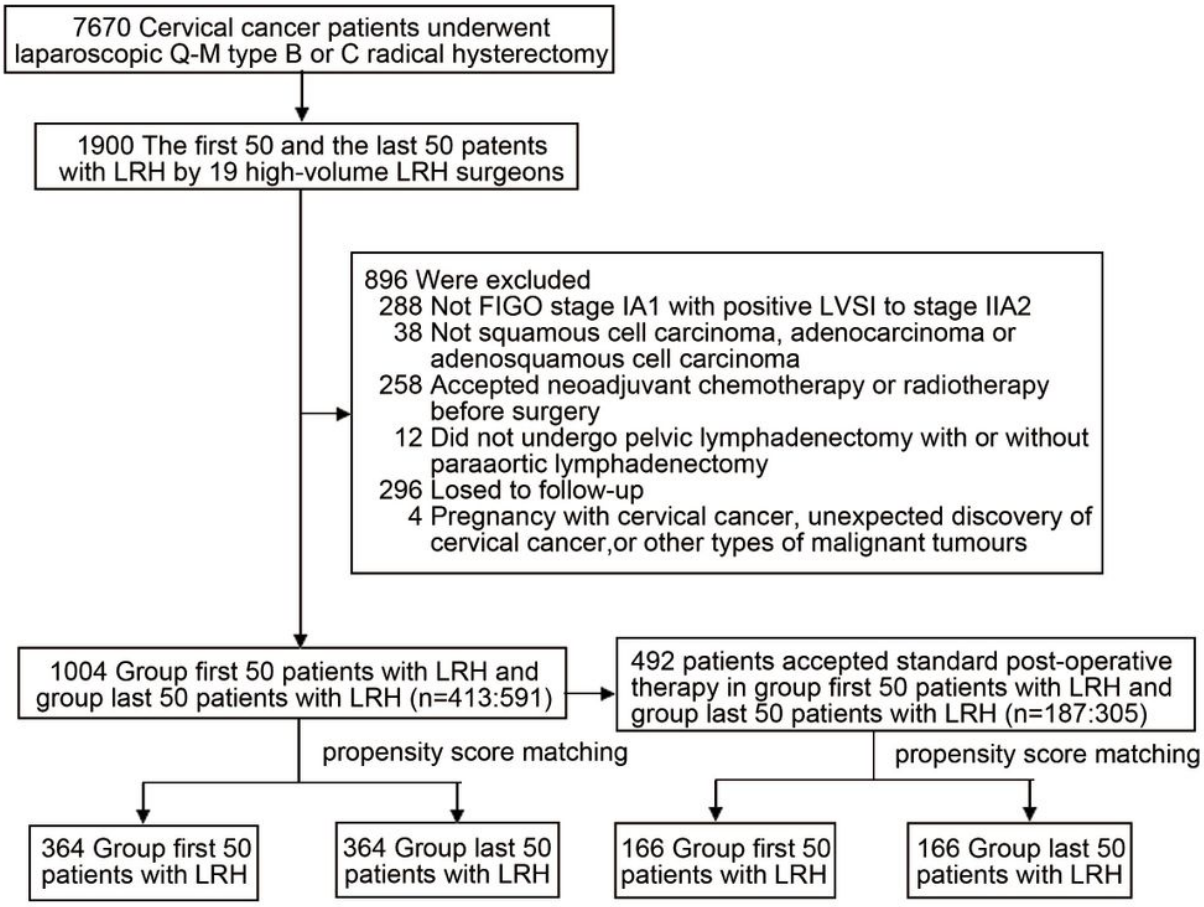

Figure 1

Study population.

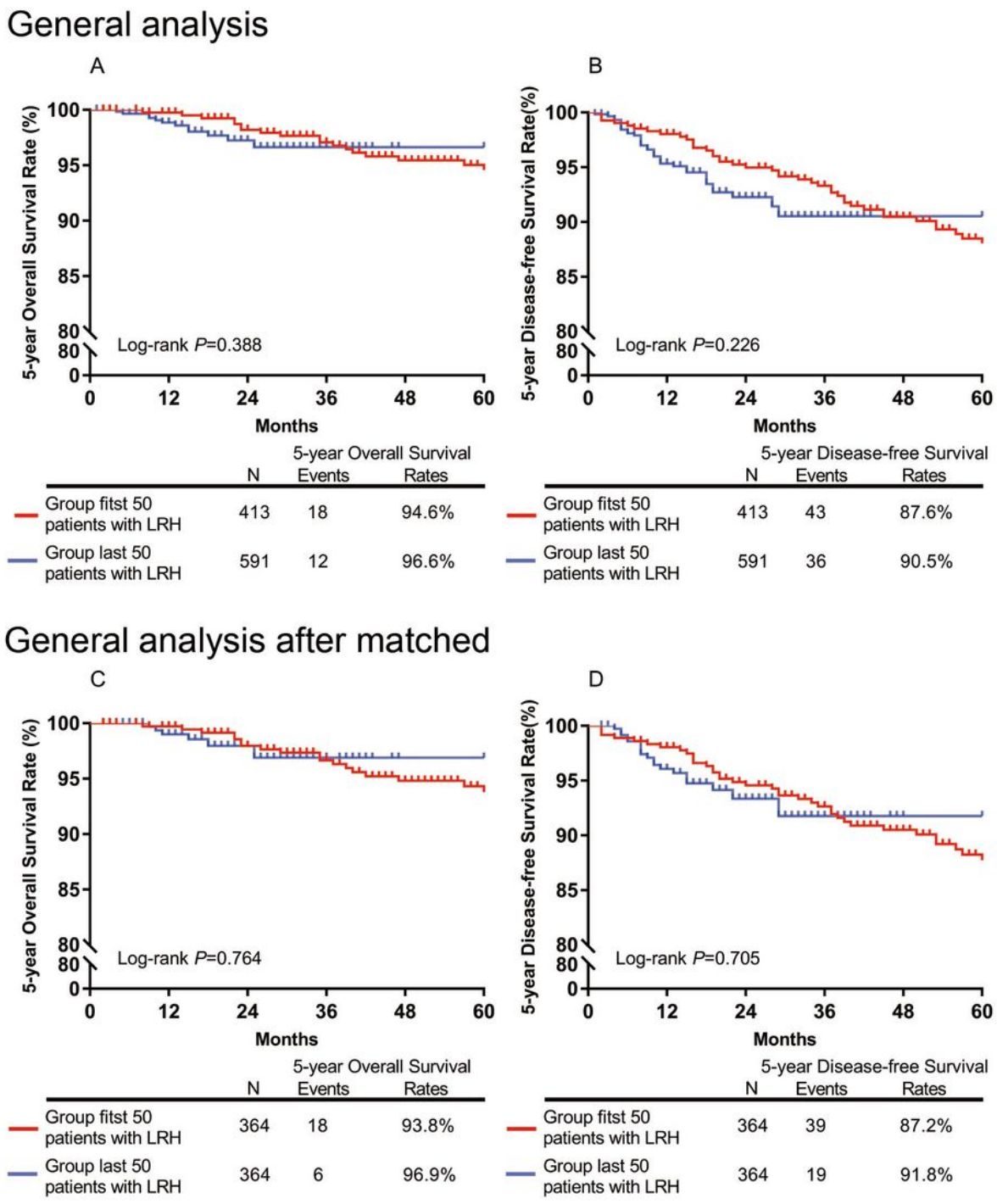

Figure 2

Survival analysis of the first 50 patients with LRH group and the last 50 patients with LRH group (A,B) and after propensity score matching(C,D). The 5-year OS(A) and 5-year DFS(B) were not associated with surgeons' experience while comparing the first 50 cases to last 50 cases(OS:94.6% vs 96.6%, p=0.388; DFS:87.6% vs 90.5%, p=0.226). After PSM, similar result were observed in the 5-year OS(C) and 5-year DFS(D) (93.8% vs 96.9%, P = 0.764; 87.2% vs 91.8%, P = 0.705).

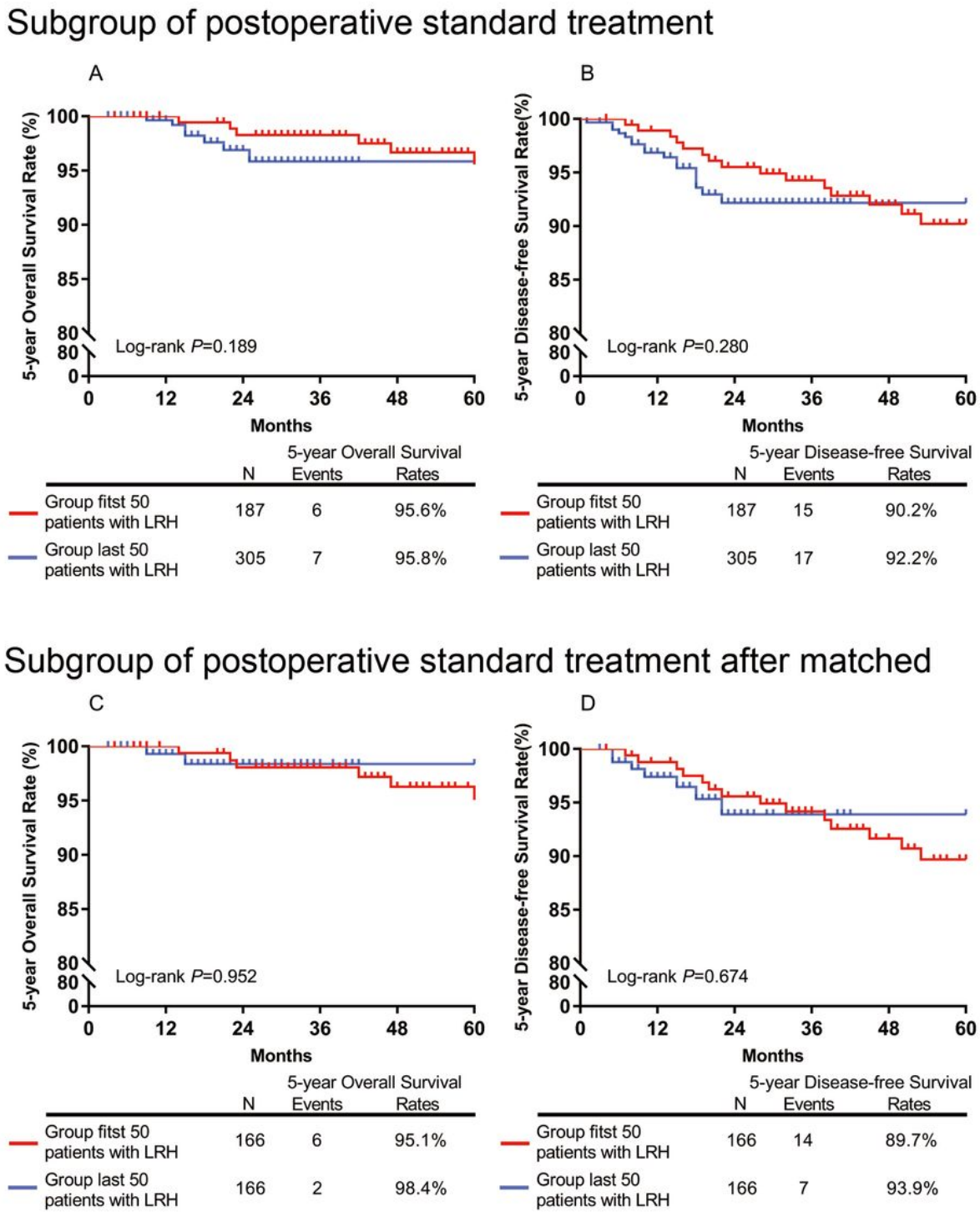

Figure 3

Survival analysis of the first 50 patients with LRH group and the last 50 patients with LRH group in the subgroup of standard postoperative therapy(A,B) and after propensity score matching(C,D). For patients received standard postoperative therapy after LRH, the 5-year OS(A) and 5-year DFS(B) were not associated with surgeons' experience while comparing the first 50 cases to last 50 cases (OS: 95.6% vs

95.8%, P = 0.189; DFS: 90.2% vs 92.2%, P = 0.280). After PSM, similar result were observed in the 5-year OS(C) and 5-year DFS(D) (OS: 95.1% vs 98.4%, P = 0.952; DFS: 89.7% vs 93.9%, P = 0.674).