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Safety and effectiveness of robotic hysterectomy versus conventional laparoscopic hysterectomy in patients with cervical cancer in China

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Abstract

Objective The aim of this study was to compare the safety and effectiveness of robotic hysterectomy (RH) with conventional laparoscopic hysterectomy (LH) for the treatment of cervical cancer using multivariate regressions.

Methods We designed a retrospective single-center study and consecutively collected patients with cervical cancer from February 2014 to October 2017. Data extraction was performed by two independent researchers. The surgical outcomes include operative time, estimated blood loss, number of lymph nodes, time to first flatus, time to a full diet, time to remove drainage tube, length of hospital stay, and postoperative complication.

Results A total of 152 patients with cervical cancer were collected in our study including 92 patients who underwent RH and 60 patients who underwent LH. Both groups have similar characteristics. The RH group showed shorter operative time (Coe − 42.89; 95% CI − 74.39 to 11.39; $P=0.008$) and more number of lymph nodes (Coe 6.06; 95% CI 2.46–9.66; $p=0.001$) than the LH group. As for the postoperative parameters, the RH group showed shorter time to remove drainage tube (Coe − 0.89; 95% CI –1.62 to –0.15; $p=0.019$) and length of hospital stay (Coe − 6.40; 95% CI − 10.19 to − 2.95; $p=0.001$). No significant difference was found between the groups in estimated blood loss (Coe 34.64; 95% CI − 33.08 to 102.37; $p=0.314$), time to first flatus (Coe 0.11; 95% CI − 0.38 to 0.61; $p=0.652$), time to a full diet (Coe − 0.24; 95% CI − 0.54 to 0.06, $p=0.118$), and postoperative complication (OR 0.84; 95% CI 0.35–1.98; $p=0.685$).

Conclusion The results from this study suggest that RH is safe and effective as LH but robotic surgery significantly contributed to the feasibility of alternative treatment options for cervical cancer patients.

Keywords Cervical cancer · Robotic hysterectomy · Conventional laparoscopic hysterectomy

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Introduction

Cervical cancer is the most common disease among gynecological malignant tumors and seriously endangers women health [1]. Hysterectomy is the main surgical treatment for cervical cancer [2].

Laparoscopic surgery provides advantages including less blood loss, faster recovery, shorter hospital stay, and smaller abdominal incision compared to laparotomy [3–6]. However, laparoscopic hysterectomy (LH) has some drawbacks. Robotic hysterectomy (RH) overcomes the disadvantages of laparoscopy because of the three-dimensional view, wide range motion with wristed instruments, and the stability of surgeon's operation [7, 8]. Therefore, robotic surgery is likely to become popular but only if its safety and effectiveness are verified.

Several studies are available on the evaluation of RH safety and effectiveness compared to LH. Kim et al. [9] reported longer operative time and shorter estimated blood loss for RH versus LH. Other studies indicated shorter operative time and estimated blood loss for RH versus LH [10, 11]. However, the safety and effectiveness of RH compared to LH are still controversial, and none of these studies took into consideration the potential confounders (e.g., average GDP per capita, comorbidities and other factors). To our knowledge, most of the comparative studies on hysterectomy have been conducted in the United States and in Europe, but limited studies are available on this comparison in the mainland of China.

Therefore, this study used multivariate regressions to evaluate the surgical safety and clinical effectiveness of RH versus LH for cervical cancer in China.

Methods

Study design and patients

A retrospective single-center study was designed and a total number of 152 patients with cervical cancer, aged 47.45 ± 9.72 years, were consecutively collected from February 2014 to October 2017 which included 92 patients subjected to RH and 60 subjected to LH. Patients' diagnosis of cervical cancer was confirmed by histopathology. Patients were included in this study if International Federation of Gynecology and Obstetrics (FIGO) clinical staging was from IA to IIB. All patients had prior consent to the operation and the patient's data use has been approved by the Ethics Committee of Gansu Provincial Hospital.

Surgical treatment

The robotic system used was a da Vinci robot (Intuitive Surgical Inc, Sunnyvale, CA, USA) and conventional laparoscopy was performed using a multiport instrument. All procedures were performed by surgeons experienced in advanced laparoscopic gynecological procedures. It means each surgeon has worked in the department of gynecology for more than 10 years and has performed 30 cervical cancer operations. Our gynecological team has five people who can perform cervical cancer surgery, including four qualified for robotic surgery. The surgical team consisted of a chief resident or fellow as surgical assistant at the bedside or at the caudal part of the patient for uterine manipulation. After general anesthesia, the patient was placed in dorsal lithotomy and steep Trendelenburg position. Specific surgical procedures were conducted following the NCCN Clinical Practice Guidelines in Oncology. In brief, the procedure consisted of eight component parts: (1) development of the paravesical and pararectal spaces, (2) right and left pelvic lymphadenectomy from common iliac nodes to bilateral inguinal nodes, (3) ureteral dissection, (4) ligation and dissection of the uterine artery, (5) development of the vesicouterine and rectovaginal spaces, (6) resection of the parametria, (7) resection of the upper vagina, and (8) vaginal cuff closure. Simple hysterectomy means that some patients received simple hysterectomy for the first time and the postoperative pathological diagnosis was upgraded and supplemented again.

Data collection

Data extraction was performed by two independent researchers from the medical records collected at the study center. Data were referred to patient characteristics (age, body mass index, average GDP per capita, FIGO stage, pathology and comorbidities) and perioperative parameters. Postoperative complications and total costs were also included. Disagreements between the two researchers were resolved by discussion and consensus. We divided age into four grades on the basis of interquartile range.

Outcomes

RH and LH safety and effectiveness were evaluated by measuring operative time, estimated blood loss, number of removed lymph nodes, time to first flatus, time to a full diet, time to remove drainage tube, total drainage volume, length of hospital stay and postoperative complications. The operative time was recorded from the anesthesia to the end of wound closure. Blood loss was measured by subtracting

the irrigation fluid volume used from the total amount of the fluid in the suction apparatus. The number of removed lymph nodes from cervical cancer patients was measured. The time to first flatus was defined as the time from the end of the surgery to the time of spontaneous elimination of intestinal gas. The drainage tube was removed after operation according to the drainage amount. The time to a full diet was defined as the time from the end of the surgery to the time of intake of solid food. The length of hospital stay was defined as the number of postoperative days until the patient was discharged. Postoperative complications were defined as those occurring during hospitalization, including paralytic ileus, phlebothrombosis and rectovaginal fistula.

Statistical analysis

Statistical analyses were performed using Stata software, version 12.0 (Stata Corp). Data are presented as mean ± SD or as percentage (%) of the total number (*n*). Continuous variables with normal distribution were compared using Student's *t* test. Wilcoxon's rank testing was used for non-normal distribution data. Categorical data were analyzed with crosstabs and the Pearson Chi-squared test or Fisher's exact test. Correction for confounding factors was performed by multivariate linear model or logistic regression. All comparisons were two sided and a 5% level of significance was used.

Results

Patient characteristics are shown in Table 1. No statistical differences were observed between the two groups regarding age, nationality, average GDP per capita, preoperative blood sugar, staging, and pathology. Surgical procedure between the two groups was significantly different ($p < 0.001$). In terms of comorbidities, diabetes, hypertension, gynecological inflammation and anemia were significantly different between the two groups. However, no differences were observed in cardiovascular, peripheral vascular and other gynecological comorbidities between the two groups (Table 1).

The operative time was 306.63 ± 91.98 min and 323.25 ± 88.05 min in the RH and LH groups, respectively, and the difference was not significant. The estimated blood loss was 232.72 ± 216.49 ml and 207.50 ± 107.68 ml in the RH and LH groups, respectively, with no significant difference. The number of removed lymph nodes was 29.45 ± 9.78 and 21.05 ± 11.22 ($p < 0.001$) in the RH and LH groups, respectively.

The time to first flatus was 3.32 ± 1.30 days and 3.17 ± 1.22 days in the RH and LH group, respectively, and the difference was not significant. The time to a full diet was 3.48 ± 1.44 days and 3.47 ± 1.35 days in the RH and LH groups, respectively, and the difference was not significant. The time to remove drainage tube was 5.38 ± 2.25 days and 6.38 ± 3.77 days in the RH and LH groups, respectively, and the difference was not significant. The length of hospital stay was 10.40 ± 5.39 days and 18.23 ± 16.26 days in RH and LH groups, respectively, and the difference was not significant. The incidence of postoperative complications was not significantly different. The patients who were transferred to the intensive care unit after surgery were two in the robot group and none in the laparoscopy group (Table 2).

The multivariate regression analysis of operative time is shown in Table 3. The average operation time was reduced by 42.89 min in the robotic group compared to laparoscopic group after adjusting for potential confounders (coefficients − 42.89; 95% CI − 74.39 to 11.39; $p = 0.008$). The operative time was also associated with surgical procedures, number of removed lymph nodes, and estimated blood loss.

The hospitalization time of the RH group was 6.40 days shorter than that of the LH group after adjusting for potential confounders (coefficients − 6.40; 95% CI − 10.19 to − 2.95; $p = 0.001$). In addition, the other most important influencing factors were the operative time, total drainage volume, gynecological inflammatory comorbidities and age (Table 4). The model for time to remove drainage tube showed that time for RH was 0.89 days shorter than LH on average per patient after adjusting potential confounders (coefficients − 0.89; 95% CI − 1.62 to − 0.15; $p = 0.019$). Other parameters considered were total drainage volume, postoperative complications, surgical procedures and time to first flatus (Table 5).

The number of removed lymph nodes in the RH group was 6.06 more than the LH group influenced by surgical procedure and comorbidities in a multivariate regression analysis (Table 5). In terms of estimated blood loss, the two groups did not show any statistical difference (coefficients 34.64; 95% CI − 33.08 to 102.37) after adjusting for other potential confounders (Table 5). Similar results were obtained when time to first flatus and time to a full diet were compared in the two groups since the differences were not statistically significant (coefficients 0.11 and − 0.24; 95% CI − 0.38 to 0.61 and − 0.54 to 0.06) (Table 5). The multivariate linear model associated with total costs showed that the RH group was associated with increased costs compared with conventional LH group (coefficients 18,064.3 95% CI 14,830.84–21,297.75; $p < 0.001$) (Table 5). Furthermore, the odds of having postoperative complications in the RH group was 0.84 times more compared to LH group after adjusting for potential confounders, but no statistically significant difference was observed (OR 0.84; 95% CI 0.35–1.98) (Table 5).

Table 1 Demographic and clinical characteristics

Variables	RH *n* (92)	LH *n* (60)	*p*
Characteristics			
Age, *n* (%)			
≤ 42	23 (25.5)	17 (28.3)	0.153*
≥ 43 and ≤ 46	25 (28.6)	10 (16.7)	
≥ 47 and ≤ 51	18 (19.4)	20 (33.3)	
≥ 52	26 (26.5)	13 (21.7)	
Nationality, *n* (%)			
The Han nationality	90 (97.8)	55 (91.7)	0.169*
Other	2 (2.2)	5 (8.3)	
Average GDP per capita (CNY)	108.14 ± 1.46	108.12 ± 1.72	0.662†
Preoperative blood sugar (mmol/l)	5.64 ± 1.55	5.42 ± 1.29	0.259†
Staging, *n* (%)			
I a	7 (7.6)	9 (15.0)	0.171*
I b	48 (52.2)	34 (56.7)	
II a	24 (26.1)	14 (23.3)	
II b	13 (14.1)	3 (5.0)	
Pathology, *n* (%)			
Squamous	86 (93.5)	55 (91.7)	0.558*
Adenocarcinoma	6 (6.5)	5 (8.3)	
Surgical			
Procedures, *n* (%)			
Simple hysterectomy[a]	0 (0.0)	8 (13.3)	0.001*
Radical hysterectomy	92 (100.0)	52 (86.7)	
Comorbidities, *n* (%)			
Hypertension	14 (15.2)	2 (3.3)	0.020*
Diabetes	13 (14.1)	1 (1.7)	0.009*
Cardiovascular diseases	7 (7.6)	5 (8.3)	0.576*
Peripheral vascular diseases	7 (7.6)	3 (5.0)	0.465*
Gynecological inflammations	75 (81.5)	39 (65.0)	0.021*
Other gynecological diseases	35 (38.0)	21 (35.0)	0.704*
Degree of anemia			
No	53 (57.6)	43 (71.7)	0.026*
Mild	20 (21.7)	14 (23.3)	
Moderate	19 (20.7)	3 (5.0)	
Total costs (CNY)	52,393.36 ± 9959.29	41,413.49 ± 21,748.74	< 0.001†

Date are presented as mean ± SD or as percentage (%) of the total number (*n*)

*Chi-squared test

†Wilcoxon's rank testing

[a]Some patients received simple hysterectomy for the first time and the postoperative pathological diagnosis was upgraded and supplemented again

Discussion

Multivariate regression was used to evaluate the surgical safety and clinical effectiveness of RH versus LH for cervical cancer in China. The results showed that the RH group had shorter operative time, length of hospital stay, and time to remove the drainage tube and a greater number of lymph nodes removed than the LH group. However, estimated blood loss, time to first flatus, time to a full diet and postoperative complications were similar between RH and LH groups.

Regarding operative time, RH was shorter than LH, which was consistent with recent studies [10–12]. In contrast, several studies indicated that RH has a longer operating time [9, 13, 14], and other studies demonstrated that the operative time of both groups was similar [15, 16]. The difference might be due to the following reasons: (1) previous studies reported that robotic surgery has been suggested to facilitate

Table 2 Outcomes of RH versus LH

Outcomes	RH	LH	*p*
Operative time (min)	306.63 ± 91.98	323.25 ± 88.05	0.109†
Estimated blood loss (ml)	232.72 ± 216.49	207.50 ± 107.68	0.706†
Time to first flatus (days)	3.32 ± 1.30	3.17 ± 1.22	0.384†
Time to a full diet (days)	3.48 ± 1.44	3.47 ± 1.35	0.951†
Time to remove drainage tube (days)	5.38 ± 2.25	6.38 ± 3.77	0.009†
Total drainage volume (ml)	452.45 ± 323.85	706.55 ± 1025.00	0.991†
Length of hospital stay (days)	10.40 ± 5.39	18.23 ± 16.26	0.202†
Number of removed lymph nodes	29.45 ± 9.78	21.05 ± 11.22	< 0.001†
Postoperative complication, *n* (%)			
No	86 (93.5)	56 (93.3)	0.770*
Paralytic ileus	4 (4.3)	3 (5.0)	
Phlebothrombosis	1 (1.1)	1 (1.7)	
Rectovaginal fistula	1 (1.1)	0 (0.0)	
Intensive care unit, *n* (%)	2 (2.2)	0 (0.0)	0.673*

Date are presented as mean ± SD or as percentage (%) of the total number (*n*)

*Chi-square test

†Wilcoxon's rank testing

Table 3 The multivariate regression analysis of operative time

Factors	Coe[a]	95% CI[b]	*p*
Group (robot)	− 42.89	− 74.39 to − 11.39	0.008
Age, *n* (%)			
≤ 42	Referent		
≥ 43 and ≤ 46	28.14	− 11.14 to 67.43	0.159
≥ 47 and ≤ 51	− 5.19	− 43.74 to 33.36	0.790
≥ 52	− 12.18	− 50.92 to 26.56	0.535
Nationality (other)	− 19.88	− 85.59 to 45.84	0.551
Average GDP per capita (CNY)	4.93	− 4.06 to 13.91	0.280
Surgical procedures			
Simple hysterectomy	Referent		
Radical hysterectomy	53.82	− 12.52 to 120.15	0.111
Estimated blood loss (ml)	0.16	0.08 to 0.24	< 0.001
Number of removed lymph nodes	1.28	− 0.17 to 2.72	0.083

[a]Coefficient

[b]95% confidence interval

lymph node removal in the treatment of various malignant tumors [17–19], while lymph node removal was not considered in the studies we mentioned above; (2) quite different definition of "operative time" was found among studies [20].

We found that the mean number of removed lymph nodes in the RH group was more than the LH group. Several studies demonstrated that no significant difference in the number of lymph nodes was found between two groups [13, 21, 22]. Yim et al. [22] explained that the lymph node counting method is not standardized. Furthermore, Chen et al. [13] reported that an increased precision with the laparoscope or robotic arm can increase lymph node removal, which is beneficial for the patient.

Our study also showed that the length of hospital stay was shorter in the RH group compared with the LH group. This was in accordance with three other studies [13, 16, 23]. However, Kim et al. [21] and Yim et al. [22] reported no significant difference in terms of length of hospital stay between the RH and LH groups. The main reason for a shorter postoperative hospital stay for patients after RH might be because patients had a faster recovery after surgery [24]. The different lengths of hospital stay results might be due to the different definitions of "length of hospital stay" [25]. In our study, the length of hospital stay stands for the duration from the first day after surgery to the hospital discharge. However, Kim et al. and Yim et al. did not have a clear definition of length of hospital stay. In this study, the length of hospital stay of both groups was longer than other recent studies [23, 26]. Maybe this is because cancer patients in Asia tend to stay longer in the hospital due to national health insurance subsidies as suggested by Chen et al. [13]. In addition, patients in our hospital had a recovery period after surgery and some patients performed postoperative chemotherapy.

Regarding time to remove the drainage tube, the result was shorter in the RH group than in the LH group. To the best of our knowledge, this study is the first study comparing RH and LH regarding the time to remove the drainage tube in hospitalization. Furthermore, the outcome might reflect patients' postoperative recovery.

Regarding the estimated blood loss, it was similar between the two groups in this study. In contrast, several

Table 4 The multivariate regression analysis of LOS

Factors	Coe[a]	95% CI[b]	*p*
Group (robot)	− 6.40	− 10.19 to − 2.95	0.001
Age, *n* (%)			
≤ 42	Referent		
≥ 43 and ≤ 46	− 5.55	− 10.21 to − 0.91	0.020
≥ 47 and ≤ 51	− 7.99	− 12.45 to − 3.52	0.001
≥ 52	− 9.79	− 14.24 to − 5.34	< 0.001
Nationality (others)	− 5.07	− 12.51to 2.38	0.180
Average GDP per capita (CNY)	0.03	− 1.01 to 1.07	0.960
Surgical procedures			
Simple hysterectomy	Referent		
Radical hysterectomy	4.16	− 3.36 to 11.68	0.276
Operative time (min)	0.04	0.02 to 0.05	< 0.001
Time to first flatus (days)	0.06	− 1.21 to 1.32	0.930
Total drainage volume (ml)	0.03	0.01 to 0.05	0.012
Postoperative complication (yes)	1.73	− 4.82 to 8.28	0.602
Intensive care unit (yes)	5.28	− 9.73 to 20.29	0.487
Comorbidities (yes)			
Gynecological inflammations	− 6.33	− 10.10 to − 2.55	0.001
Other gynecological diseases	2.71	− 0.71 to 6.14	0.120
Diabetes	0.92	− 4.59 to 6.44	0.742
Hypertension	1.17	− 4.56 to 6.90	0.686
Cardiovascular diseases	2.09	− 4.57 to 8.77	0.534
Peripheral vascular diseases	2.67	− 4.11 to 9.44	0.438
Degree of anemia			
No anemia	Referent		
Mild anemia	− 4.50	− 8.44 to − 0.56	0.026
Moderate anemia	− 2.98	− 7.69 to 1.74	0.214

[a]Coefficient

[b]95% confidence interval

previous studies reported that robotic surgery reduced blood loss compared with laparoscopic surgery [10, 14, 23]. Zanaqnolo et al. [27] recently published a review of robot-assisted surgery in gynecologic cancers and indicated shorter blood loss after robotic surgery. However, the reason for similar estimated blood loss between RH and LH groups might be due to a more direct vascular injury in LH leading to excessive blood loss [28].

We also found that the time to first flatus and time to a full diet were both similar between the two groups. Chen et al. [13] reported that the time to a full diet was not significant between the groups. Nie et al. [10] reported that time to first flatus after RH was superior to LH. These results could indicate that the robotic approach improves the short-term surgical outcomes of cervical neoplasm patients, thus, they might have a faster recovery after surgery [24].

In our study, we found that the risk of having postoperative complications was equal between both groups after adjusting for potential confounders. The same result was reported in two other studies [13, 21]. However, Corrado et al. [11] and Nie et al. [10] demonstrated that the RH group was associated with a lower rate of postoperative complications compared with the LH group. The difference among studies may be because of the different follow-up time and surgeon experience.

Our study showed that the robotic surgery required higher total costs in hospital than the laparoscopic surgery. This is consistent with previous studies [16, 22, 29, 30].

One of the strengths of this study is the multivariate regression analysis and the adjustment of the outcomes for potential confounders. Another strength is the more comprehensive outcomes in our study. However, the limitation of this study is that the outcome analysis was not adjusted with the potential impact of body mass index because of the lack of this parameter measurement in more than 30% of the LH group patients.

Conclusion

Based on the above outcome analysis, our study demonstrated that RH is safe and effective as LH but robotic surgery significantly contributed to the feasibility of alternative treatment options for cervical cancer patients. Further large-scale randomized multicenter studies are now required to guide future application of robotic system.

Table 5 The multivariate or logistic regression analysis of other outcomes

Models[d]	Coe[a]	95% CI[b]	*p*
Time to remove drainage tube			
Group (robot)	− 0.89	− 1.62 to − 0.15	0.019
Number of removed lymph nodes			
Group (robot)	6.06	2.46 to 9.66	0.001
Estimated blood loss (ml)			
Group (robot)	34.64	− 33.08 to 102.37	0.314
Time to first flatus (days)[e]			
Group (robot)	0.11	− 0.38 to 0.61	0.652
Time to a full diet (days)[f]			
Group (robot)	− 0.24	− 0.54 to 0.06	0.118
Total costs (CNY)[g]			
Group (robot)	18,064.3	14,830.84 to 21,297.75	< 0.001
Models[d]	OR[c]	95% CI	*p*
Postoperative complications[h]			
Group (robot)	0.84	0.35–1.98	0.685

[a]Coefficient

[b]95% confidence interval

[c]Odds ratio

[d]All multivariate linear or logistic regression models were adjusted for age, nationality, average GDP per capita, surgical procedure, and comorbidities

[e]Additionally adjusted for preoperative blood sugar, operative time, number of removed lymph nodes, and postoperative complication

[f]Additionally adjusted for number of removed lymph nodes and time to first flatus

[g]Additionally adjusted for operative time, length of hospital stay, number of removed lymph nodes, and postoperative complication

[h]Additionally adjusted for operative time, estimated blood loss, time to first flatus, time to a full diet, and time to remove drainage tube

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Author contributions LH: design of the study, data collection, data analysis, responsible for surgery, and manuscript writing. PY: design of the study and data analysis. LY: design of the study. RL: design of the study. RS: data collection. JL: responsible surgery. LW: data collection. XC: responsible surgery. KY: design of the study. TG: design of the study. HW: design of the study and responsible for surgery.

Compliance with ethical standards

Conflict of interest We declare that we have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of Gansu Provincial Hospital, China (Reference number: 2017-067).

Informed consent Informed consent was obtained from all individual participants.

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