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# Concurrent Learning Curves of 3-Dimensional and Robotic-Assisted Laparoscopic Radical Hysterectomy for Early-Stage Cervical Cancer Using 2-Dimensional Laparoscopic Radical Hysterectomy as a Benchmark: A Single Surgeon's Experience

Authors' Contribution:  
Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

BCEF 1 **Ding Ding\***  
BCF 1 **Hongyuan Jiang\***  
B 1 **Jichan Nie**  
ABCEG 1,2 **Xishi Liu**  
ACEFG 1,2 **Sun-Wei Guo**

1 Department of Gynecology, Shanghai Obstetrics and Gynecology Hospital, Fudan University, Shanghai, P.R. China  
2 Shanghai Key Laboratory of Female Reproductive Endocrine-Related Diseases, Fudan University, Shanghai, P.R. China

**Corresponding Authors:**  
**Source of support:**

\* Ding Ding and Hongyuan Jiang contributed equally to this work  
Xishi Liu, e-mail: lxsdoc@hotmail.com, Sun-Wei Guo, e-mail: hoxa10@outlook.com

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**Background:** For early-stage cervical cancers, radical hysterectomy (RH) with pelvic lymphadenectomy has been the standard care. This study compared the learning curves and intra-, peri-, and post-operative outcomes for 3-dimensional laparoscopic RH (3D-LRH) and robotic-assisted (RA)-LRH by a surgeon highly skilled in 2-dimensional (2D)-LRH for treatment of early-stage cervical cancer.





**Material/Methods:** Two hundred and thirty-nine patients with early-stage cervical cancer (FIGO stage: Ia2–IIa2) admitted to Shanghai Obstetrics and Gynecology Hospital, Fudan University were recruited into this prospective study: 54, 85, and 100 patients underwent 2D-, 3D-, and RA-LRH, respectively and were followed up. Patients' demographic, clinical, and operative information was retrieved and compared. CUSUM (cumulative summation) analysis using a benchmark derived from previously performed 2D-LRHs.

**Results:** Both 3D- and RA-LRH had a steep learning curve. 3D-LRH was superior to 2D- and RA-LRH in terms of significantly shorter operating time. For all approaches, the operating time was associated with the uterus size of the patient and was not affected by other parameters. All approaches of LRH yielded comparable radicality and operative results other than operative time.

**Conclusions:** Both 3D- and RA-LRH approaches had similar radicality, and intra-operative and post-operative complication rates, however, 3D-LRH had the shortest operating time and lowest amount of blood loss. After reaching proficiency, RA-LRH had comparable operating time with that of 2D-LRH, and might be even shorter in cases where surgeon has acquired more experience. In countries where labor costs are low; 3D-LRH might be preferable to 2D- and RA-LRH for early-stage cervical cancer.

**MeSH Keywords:** **Hysterectomy • Laparoscopes • Robotics • Uterine Cervical Neoplasms**

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## Background

Cervical cancer is ranked as the 7<sup>th</sup> in incidence and the 10<sup>th</sup> in mortality for cancers worldwide [1]. It is the second most common female-specific cancer after breast cancer, accounting for approximately 8% of both total cancer cases and total cancer deaths in women [2], and the 9<sup>th</sup> leading cause for cancer-related years of life lost [1]. While the incidence of new cases and the mortality rate for cervical cancer have both been gradually decreasing in the United States and many parts of the world [1], the number of newly diagnosed cases appears to be increasing in the coastal regions of China [3,4].

For early-stage cervical cancers, radical hysterectomy (RH) with pelvic lymphadenectomy has been the standard care, and in conjunction with tailored adjuvant therapy is now widely accepted [5,6]. Since the first reports in the early 1990s [7,8], laparoscopic RH (LRH) has been shown to be superior in terms of decreased blood loss, shorter hospital stay, and shorter recovery time compared with traditional, abdominal RH [9–12]. While the uptake of LRH in the West appears to be slow [13,14], LRH has become the standard of care in major teaching hospitals in China since the turn of the century [15,16].

With the approval of the Da Vinci<sup>®</sup> surgical system by the US Food and Drug Administration for use in gynecological procedures a decade ago, robotic-assisted (RA)-LRH has emerged as an alternative minimally invasive surgical approach. Shorter learning curve, 3-dimensional (3D) view, camera stability, tremor reduction, improved dexterity, and the ease of movement overcome several shortcomings of conventional, or 2D-laparoscopy [17] and have made the RA-LRH attractive despite much higher cost [18–20]. Systematic reviews indicate that there is little difference in surgical outcomes between RA-LRH and 2D-LRH but the former has a higher cost [21–23].

Shortly after the report of first cases of LRH in the early 1990s, 3D laparoscopy was introduced and its first use in gynecology was reported in 1993 [24]. While it addressed the issue of lack of depth perception and spatial orientation, it was not widely adopted due to degraded viewing condition from poor image resolution and the requirement to wear uncomfortable goggles that easily cause surgeon fatigue [25,26]. However, 3D laparoscopy has been improved dramatically over the last 5 years with the advent of the 4<sup>th</sup>-generation 3D system with a high resolution and more ergonomic glasses. Published studies on the non-gynecological use of 3D laparoscopy suggest that it is superior to 2D laparoscopy [27–30] and, in the hands of expert surgeons, even better than RA laparoscopy [31].

We started LRH in 2009 for patients with early-stage cervical cancer and so far nearly 2900 LRHs have been performed in our hospital as of the writing of this paper, with the author

(XSL) alone having performed operations for over 830 cases before embarking on RA-LRH in early 2015. About 3 months after the acquirement of a Da Vinci<sup>®</sup> surgical system IS3000, we also acquired 3D laparoscopy (Olympus, Japan), and we have been performing both RA-LRH and 3D-LRH since mid-2015.

RH and lymph node dissection for early-stage cervical cancer are complex gynecological procedures, and, as such, there must be learning curves to acquire competency. Since we learned to perform the 2 surgical approaches nearly concurrently, we had an opportunity to assess and compare the learning curves for the 2 approaches. In addition, since we had performed extensive 2D-LRH before embarking on 3D-LRH and RA-LRH, and because 2D-LRH was also performed during the first 7 months of 2015, we had an opportunity to compare these 3 procedures. To the best of our knowledge, there have been no published report on 3D-LRH, and it is unclear which of these 3 approaches is best suitable for LRH, and also unclear what the strengths and weakness of these 3 approaches are when performing LRH for early-stage cervical cancer.

In this study, we assessed and compared the learning curves of 3D and RA procedures and also compared intra-, peri-, and post-operative outcomes of these 2 approaches to LRH for early-stage cervical cancer. All surgeries were performed by a single surgeon and within the same time period, using a benchmark derived from previous extensive 2D-LRH cases series by the same surgeon.

## Material and Methods

### Surgical instruments

We have used conventional 2D laparoscopy (EvisExera II CV-180 & CLV-180, Olympus, Tokyo, Japan) for radical hysterectomy since 2009. Our 3D laparoscopy (LTF-190-10-3D, Olympus) became operational in February 2015. The Da Vinci<sup>®</sup> S<sup>1</sup><sup>HD</sup> surgical system IS3000 (Intuitive Surgical, Inc., Sunnyvale, CA, USA) was installed in an operating room dedicated to robotic surgery at our hospital in February 2015, and this equipment was shared by 5 surgical teams in the Gynecology Department of our hospital, with each team having exclusive access to the operating room on one particular week day. The surgeon (XSL) and her team were certified by the Chinese University of Hong Kong Jockey Club Minimally Invasive Surgical Skills Centre for robotic surgery.

### Patient recruitment and data collection

Women newly diagnosed with invasive cervical cancer of International Federation of Gynecology and Obstetrics (FIGO) stages IA2–IIA2 were eligible for this study. While this study started in early February 2015, recruitment for RA-LRH did not begin until early March, and for 3D-LRH, it did not begin until

early June. When it was decided to perform 3D-LRH in June, the assignment of patients to either 2D-, 3D-, and RA-LRH was made quasi-randomly but the choice to do RA-LRH was made based largely on the availability of the robotic system, which was assigned to our team on a particular day of the week. After late June, more patients were able to receive 3D-LRH. After over a dozen 3D-LRH cases, when the surgical team was convinced that they felt more comfortable with 3D-LRH, it was decided to switch completely to 3D-LRH. Once this decision was made, the choice as to which approach to use was made to ensure each arm of the study had at least 50 patients with no consideration for age, FIGO stage, or other considerations.

A total of 239 patients were recruited for this study: 54, 85, and 100 patients received 2D-, 3D-, or RA-LRH, respectively. All patients consented to the selection of operation. All cases were operated by the same surgeon (XSL) in February 2015 through June 2016. All surgical data were prospectively recorded. For all cases, data were collected on demographics, body mass index (BMI), uterus size (measured by ultrasonography), intra-, peri-, and post-operative variables such as operative time, estimated blood loss, measures of LRH radicality, lymph node counts, and complications. While the surgical team (XSL and JN) had access to information that could identify individual participants during data collection, all participants' identities were anonymized with numerical IDs when transcribed to an Excel spreadsheet and analyzed by the study analyst (SWG) who had no knowledge of the participants' personal information.

The extent of the resection in the radical technique followed the Mayo classification of radical hysterectomies reported in 1975 [32]. All pathologic specimens were reviewed by 2 experienced gynecologic pathologists. Prior to sectioning the specimen, gross measurements of cardinal ligament and vaginal cuff length were recorded. Operating time (OT) for all 3 groups was defined to be the "skin-to-skin" time, that is the time interval from skin incision to the completion of skin closure. The amount of blood loss during an operation was estimated by the difference in the total amount of suctioned and irrigation fluids. Disease recurrence was determined clinically, radiographically, and/or histologically.

This study was approved by the Ethics Review Committee of Shanghai Obstetrics and Gynecology Hospital, Fudan University. And it was also registered on the China Clinical Trial Registration Center (Registration No. ChiCTR-ONC-17013611).

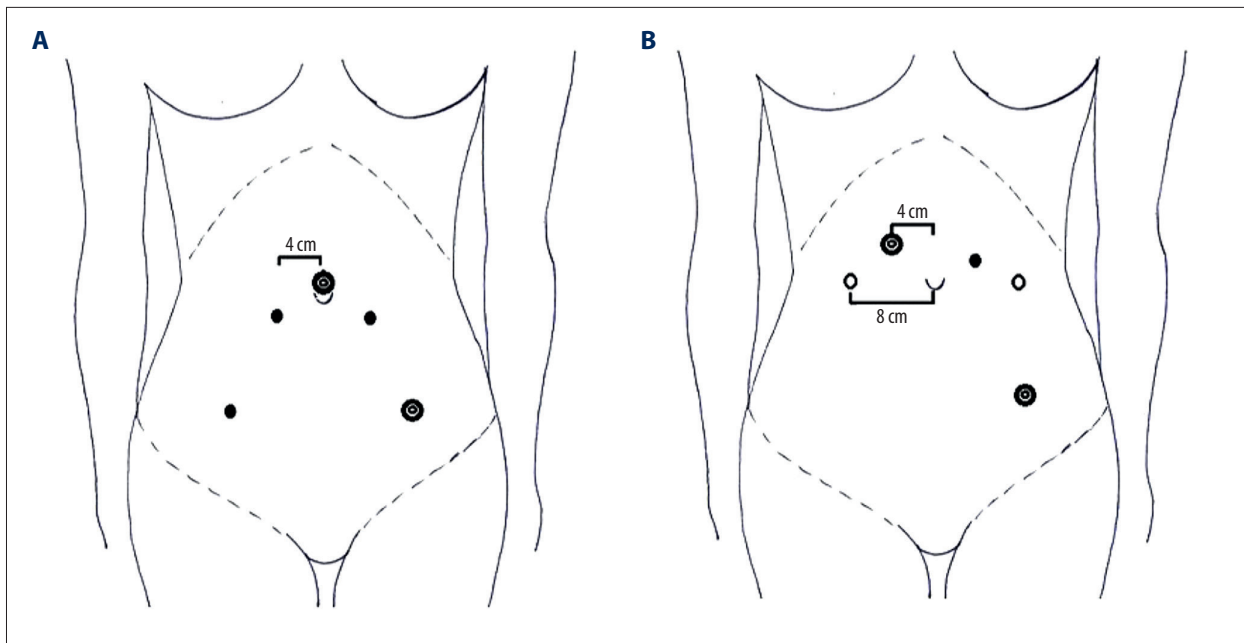
### Surgical procedures

Under general anesthesia, the patient was put in a lithotomy-Trendelenburg position. For 2D- and 3D-LRH, a 12-mm trocar was inserted as the camera port through a vertical incision right in the umbilicus. One pair of 5-mm trocars were placed

symmetrically approximately 4 cm away from the umbilicus, slightly below the horizontal line passing through the umbilicus. Another pair of trocars, one 5 mm and the other 12 mm, were inserted bilaterally at the outer one-third of the iliac spine umbilicus line symmetrically (Figure 1A). For robotic procedures, 5 trocars with 3 robotic arms were used for port placement: a 12-mm trocar was placed 4-cm right and 4-cm higher away from the umbilicus for the camera. Two working robotic arms were attached to an 8-mm reusable trocar placed 8 cm to the umbilicus bilaterally. An additional pair of ancillary trocars, one 5-mm and the other 12-mm in diameter, were inserted at the left upper quadrant and the left outer one-third of the iliac spine umbilicus line, respectively (Figure 1B). An intrauterine manipulator was used to manipulate the uterus so the vesical-vagina fold and rectal-vagina fold could be exposed easily.

For 2D- and 3D-LRH, the major energy device used was a HARMONIC ACE® (Ethicon Endo-Surgery, Cincinnati, OH, USA). For RA-LRH, a pair of mono-polar scissors and a fenestrated bipolar grasper were used. For 2D-LRH, the 2D-HD Olympus camera with a 10-mm 30-degree laparoscope was used. For 3D-LRH, the 3D high definition (HD) Olympus camera with a 10-mm 0-degree lens dual-channel stereo-laparoscope was employed.

For all approaches, LRH (Piver III/Type C) and pelvic lymphadenectomy were performed as described previously [8,33], but with some variations. After pelvic lymphadenectomy, the ureter was dissected off the lateral peritoneum down to the ureter tunnel. For patients who opted for ovarian removal, the infundibulo-pelvic ligament was excised, while for patients who intended to preserve their ovaries, the ovarian ligament was cut. The uterus was manipulated to the anterior to expose the rectal-vagina-peritoneum fold, followed by incision of the fold. The rectum was separated from the vagina and pushed to the posterior, exposing the pararectal space. The bladder peritoneum fold was then incised, and the bladder was moved forward from the anterior vaginal wall. The uterine artery was isolated and cut at its origin. On dissection of vessels over the ureter, the tunnel was developed by placing ventral traction on the uterine vessels and freeing the ureter from the adventitial attachments of the vessels medial and ventral. The anterior vesico-uterine ligament was divided and incised. The posterior vesico-uterine ligament was also incised. The same procedure was performed on both sides. Both cardinal and sacral ligaments were exposed and dissected as in a type III radical hysterectomy, exposing the paravesical and pararectal space. The parametrial tissues were incised, followed by the circumferential incision of the upper vaginal part with a 3-cm margin underneath the vagina fornix. Tissue samples were taken from the vagina and measured. The vagina cuff was then closed with a running locking suture. The peritoneum from the surface underneath the bladder was sewn to the surface of the rectum



**Figure 1.** Schematic diagram showing the port placement for robotic-assisted and 2-dimensional/3-dimensional laparoscopic radical hysterectomy. (A) Robotic radical hysterectomy. (B) Laparoscopic radical hysterectomy. For both A and B, ● denotes the placement of a 5-mm trocar, ○, a 8-mm trocar, and ⊙, a 12-mm trocar.

with 0 MONOCRYL sutures. In case of ovarian preservation, the ovaries were transposed to the abdominal sidewall up out of the pelvis at this time using 0-Vicryl suture on a CT-1 needle.

For both 2D and 3D laparoscopic surgeries, the surgeon and her assistants (if willing) sat on a wooden high stool (approximately 92 cm from the sitting plane to the ground level) during the entire course of the surgery. Foley catheters were extracted after 3 weeks for all patients. The residual urine volume was assessed after self-voiding; if the volume was greater than 100 mL, the catheter was reinserted for an additional week.

### Statistical analysis

The comparison of distributions of continuous variables between or among 2 or more groups was made using the Wilcoxon rank-sum test and Kruskal-Wallis test, respectively. Spearman's correlation coefficient was used when evaluating correlations between 2 variables. Fisher's exact test was used when comparing the count data between 2 groups. Multiple linear regression analysis was carried out to evaluate whether the OT or amount of blood loss was associated with factors such as the approach of LRH (RA or 3D versus 2D), age, stage, tumor size, lymphovascular space involvement, stromal infiltration, parametrial involvement, vaginal involvement, presence of positive obturator nodes, metastasis to the pelvic cavity, sequence of surgery, and other variables such as the radicality of the LRH (length of vaginal tissues and cardinal ligament tissues removed, number of lymph nodes retrieved).

A logistic regression model was used to see whether the occurrence of complication was associated with the approach of LRH (RA or 3D versus 2D), age, stage, tumor size, lymphovascular space involvement, stromal infiltration, parametrial involvement, vaginal involvement, presence of positive obturator nodes, metastasis to the pelvic cavity, sequence of surgery, and other variables such as the radicality of the LRH (length of vaginal tissues and cardinal ligament tissues removed, number of lymph nodes retrieved). To view the general trend of OT chronologically as the surgeries were performed, we used the smooth spline routine, lowess, in R.

CUSUM analysis was used to further analyze the learning curve. Following Yim et al. [34], and in the spirit of the cumulative summation test [35], the CUSUM score for the  $i$ th surgery was calculated using the following formula:

$$S_i = S_{i-1} + (t_{i-m}) \text{ for } i=1,2,\dots, n.$$

with the initial value  $S_0=0$  and where  $t_i$  is the OT (or the amount of blood loss) for the  $i$ th surgery,  $m$  is the benchmark/target/reference,  $t_{i-m}$  essentially measures the deviation of the outcome measure (i.e., the OT) from the benchmark  $m$  for the  $i$ th surgery. Here  $m$  was taken to be the average operating time for 2D-LRH, which was more or less stabilized due to the large number of such procedure performed. Thus, it can be used as a benchmark or reference. If  $t_i$  is longer than the benchmark time  $m$ , then  $t_{i-m} > 0$ , otherwise  $t_{i-m} \leq 0$ .  $S_i$  is basically the cumulative sum of accumulated deviations calculated up to the  $i$ th surgery.

**Table 1.** Characteristics of recruited patients undergone 2D-, 3D- and RA-LRH.

Variable	2D-LRH (n=54)	3D-LRH (n=85)	RA-LRH (n=100)	P-value
Age (in years)				
Mean ±SD	46.2±9.1	46.2±9.9	47.1±9.5	0.83
Median (range)	47.0 (29–64)	47.0 (29–67)	46.5 (28–66)	
Body mass index (BMI)				
Mean ±SD	22.0±2.4	21.9±2.5	22.5±2.6	0.18
Median (range)	21.6(17.2–28.0)	21.4(17.3–31.7)	22.3(17.2–32.9)	
Uterus size (dm <sup>3</sup> )				
Mean ±SD	65.8±43.3	62.3±51.8	52.3±30.5	0.23
Median (range)	61.3(8.6–217.7)	41.3(7.8–346.5)	41.3(5.4–176.9)	
FIGO Stage				
Ia2	7 (13.0%)	4 (4.7%)	14 (14.0%)	0.004
Ib1	29 (53.7%)	47 (55.3%)	60 (60.0%)	
Ib2	2 (3.7%)	13 (15.3%)	5 (5.0%)	
IIa1	12 (22.2%)	21 (24.7%)	21 (21.0%)	
IIa2	4 (7.4%)	0 (0.0%)	0 (0.0%)	
Histology				
Squamous carcinoma	42 (77.8%)	60 (82.2%)	69 (72.6%)	0.14
Adenocarcinoma	12 (22.2%)	10 (13.7%)	25 (26.3%)	
Neuroendocrine	0 (0.0%)	3 (4.1%)	1 (1.1%)	
Average diameter of the tumor (cm)				
Mean ±SD	2.42±1.26	2.92±1.22	2.47±1.02	0.013
Median (range)	2.0 (0.2–6.0)	3.0 (0.5–8.0)	2.0 (0.5–5.0)	
Lymphovascular space involvement				
No	35 (64.8%)	58 (68.2%)	73 (73.0%)	0.55
Yes	19 (35.2%)	27 (31.8%)	27 (27.0%)	
Deep stromal infiltration				
No	32 (59.3%)	33 (45.2%)	53 (55.8%)	0.24
Yes	22 (40.7%)	40 (54.8%)	42 (44.2%)	
Depth of stromal infiltration				
Microscopic	6 (11.1%)	3 (3.5%)	14 (14.0%)	0.17
Shallow	26 (48.1%)	35 (41.1%)	42 (42.0%)	
Deep	15 (27.8%)	37 (43.5%)	34 (34.0%)	
Whole	7 (13.0%)	10 (11.8%)	10 (10.0%)	
Bilateral parametrial involvement				
No	52 (96.3%)	80 (94.1%)	96 (96.0%)	0.79
Yes	2 (3.7%)	5 (5.9%)	4 (4.0%)	
Vaginal involvement				
No	37 (68.5%)	56 (65.9%)	79 (79.0%)	0.11
Yes	17 (31.5%)	29 (34.1%)	21 (21.0%)	
Metastasis in pelvic lymph node				
No	50 (92.6%)	68 (80.0%)	94 (94.0%)	0.009
Yes	4 (7.4%)	17 (20.0%)	6 (6.0%)	
Metastasis in parametrial lymph node				
No	52 (96.3%)	78 (91.8%)	96 (96.0%)	0.44
Yes	2 (3.7%)	7 (8.2%)	4 (4.0%)	



**Table 1 continued.** Characteristics of recruited patients undergone 2D-, 3D- and RA-LRH.

Variable	2D-LRH (n=54)	3D-LRH (n=85)	RA-LRH (n=100)	P-value
Positive obturator nodes				
No	51 (94.4%)	76 (89.4%)	95 (95.0%)	0.32
Yes	3 (5.6%)	9 (10.6%)	5 (5.0%)	
Presence of positive iliac lymph node				
No	51 (94.4%)	78 (91.8%)	95 (95.0%)	0.66
Yes	3 (5.6%)	7 (8.2%)	5 (5.0%)	
Presence of positive common iliac lymph node				
No	48 (88.9%)	76 (89.4%)	95 (95.0%)	0.24
Yes	6 (11.1%)	9 (10.6%)	5 (5.0%)	

RA-LRH – robotic-assisted laparoscopic radical hysterectomy; 3D-LRH – 3-dimensional laparoscopic radical hysterectomy;  
SD – standard deviation; FIGO – International Federation of Gynecology and Obstetrics.

When the CUSUM score was plotted against the surgical sequence, a positive slope of the plot indicates a longer OT with greater deviation from the benchmark, particularly when such scores are in the positive domain. In contrast, a negative slope of the plot would suggest an overall better performance than the benchmark, and indicate a proficiency phase with progressive improvement in surgical skills or shorter OT. Normally, a surgeon would have a CUSUM plot that appears initially to have a positive slope, representing his/her learning process and the performance that is below the par of the benchmark since the term  $t_i - m$  would be a positive value and thus  $S_i \geq S_{i-1}$ . If the surgeon acquires enough experience so that his/her surgical performance is on par with or even better that of the benchmark, then the term  $t_i - m \leq 0$  and thus  $S_i \leq S_{i-1}$ , resulting in a negative slope of the CUSUM curve. Hence the CUSUM plot should resemble an inverted U or V, with the apex or the peak representing the turning point or period from an apprentice to a proficient practitioner.

P-values of less than 0.05 were considered statistically significant. Following convention, P-values of less than 0.10 were considered statistically significant for interaction terms in the linear regression. All computations were made with R 3.3.1 [36] ([www.r-project.org](http://www.r-project.org)).

## Results

The demographic and clinical characteristics for the 3 groups of patients are listed in Table 1. We can see that the 3 groups were very comparable except the 3D-LRH group had slightly more patients with squamous carcinoma and the 2D-LRH group had significantly more patients with lymphovascular space involvement and the presence of positive common iliac lymph nodes. Viewing age, BMI and uterus size chronologically revealed that there were no discernable differences among the

3 groups, while the 3D-LRH group had more patients in FIGO stage Ib2 and larger average tumor diameter (Supplementary Figure 1 in Supplemental Information, Table 1).

In all 3 LRH approaches, there was no conversion. Hence, the conversion rate was significantly lower than the previously reported rate of 1.5% ( $P=0.026$ ) [37]. The intra-, peri-, and post-operative results are summarized in Table 2. It can be seen from Table 2 that while most of the peri- and post-operative results were comparable among the 3 groups, there was a significant difference in OT: the RA-LRH group had the longest OT ( $171.6 \pm 38.8$  minutes), the 2D-LRH group had significantly shorter OT ( $151.6 \pm 30.7$  minutes), while the 3D-LRH group had the shortest OT ( $111.8 \pm 21.7$  minutes) (Table 2). The LRH with the shortest OT was achieved by a 3D-LRH, with 56 minutes or less OT compared to 60 minutes; while the longest LRH was achieved by a RA-LRH (the 26<sup>th</sup> RA-LRH procedure performed), which took 285 minutes or 4 hours and 45 minutes.

### Operative time (OT): descriptive analysis for learning curve effect

To see whether there was a learning curve effect, we plotted the OT, widely considered as surrogate measure for surgical proficiency, in a chronological fashion for the 3 approaches, as shown in Figure 2. While the OT appeared to stay constant for the 2D-LRH as expected, it was progressively decreased for both 3D-LRH and RA-LRH, however, for 3D-LRH the learning curve appeared to tamper off from January 2016, or starting with the 52<sup>nd</sup> case (Figure 2A). In fact, OT correlated negatively with the number of LRHs or the sequence of the operation for both 3D-LRH and RA-LRH ( $r=-0.27$ ,  $P=0.012$ , and  $r=-0.50$ ,  $P=1.2 \times 10^{-7}$ , respectively), but, expectedly, not for 2D-LRH ( $r=0.03$ ,  $P=0.85$ ), indicating that there was indeed a strong learning curve effect for both 3D- and RA- but not for 2D-LRH.

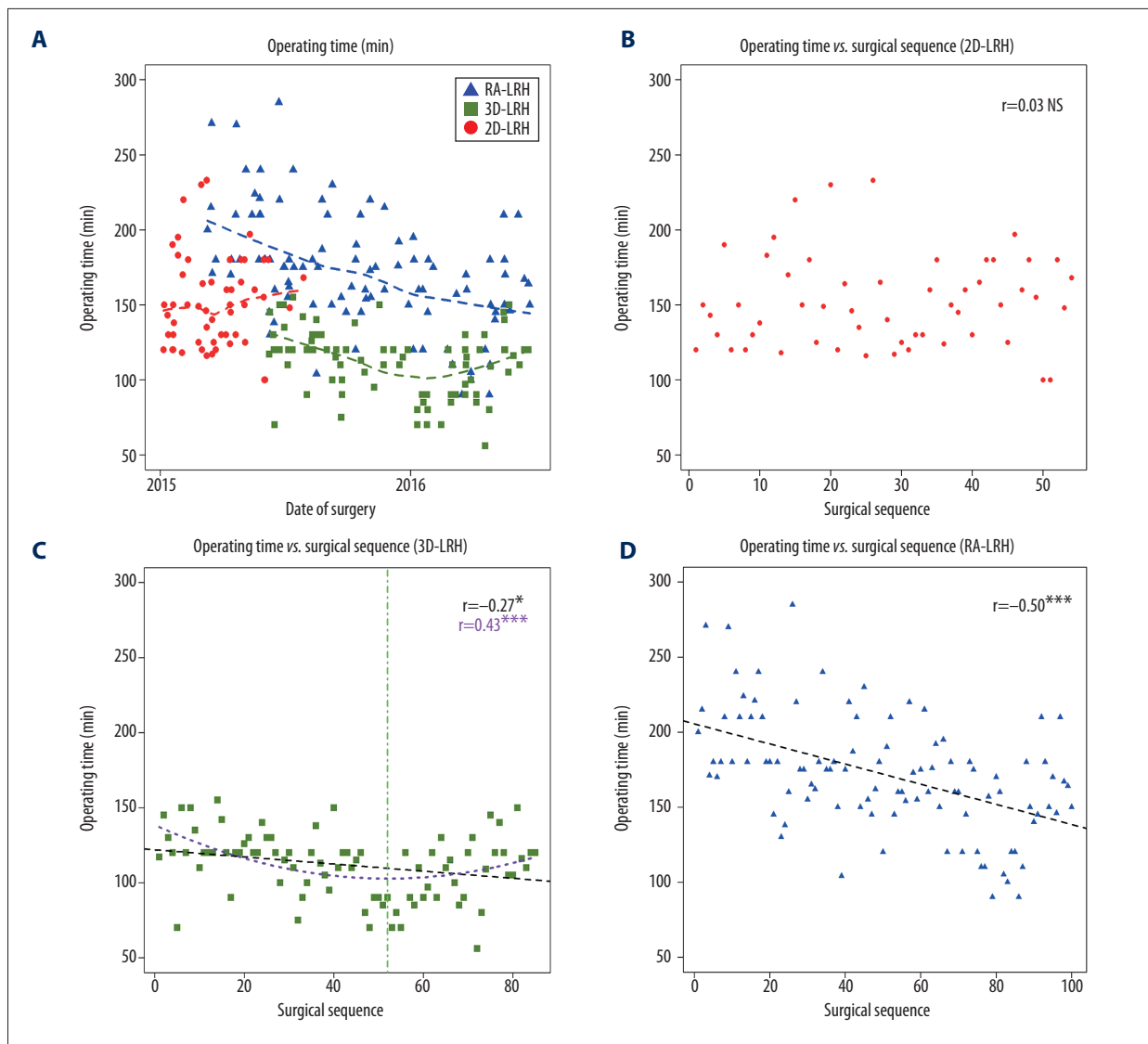
**Table 2.** Intraoperative, perioperative and postoperative data.

Variable	2D-LRH (n=54)	3D-LRH (n=85)	RA-LRH (n=100)	P-value
Operating time (min)				
Mean ±SD	151.6±30.7	111.8±21.7 <sup>a</sup>	171.6±38.8 <sup>b</sup>	<2.2×10 <sup>-16</sup>
Median (range)	149.5 (100–233)	117.0 (56–155)	172.0 (90–285)	
Amount of blood loss (mL)				
Mean ±SD	233.5±151.3	211.6±174.2	317.5±231.5 <sup>c</sup>	0.0004
Median (range)	200 (30–700)	200 (20–1500)	200 (100–1300)	
Blood transfusion				
No	52 (96.3%)	82 (96.5%)	89 (89.0%)	0.095
Yes	2 (3.7%)	3 (3.5%)	11 (11.0%)	
Ovarian preservation				
No	34 (63.0%)	52 (61.2%)	61 (61.0%)	0.97
Yes	20 (37.0%)	33 (38.8%)	39 (39.0%)	
Length of resected vaginal wall (cm)				
At 12 o'clock	2.97±0.58	2.97±0.52	2.78±0.62	0.09
At 3 o'clock	3.00±0.50	3.03±0.57	2.91±0.65	0.96
At 6 o'clock	3.06±0.57	3.22±0.68	3.05±0.67	0.44
At 9 o'clock	3.00±0.65	2.96±0.52	2.84±0.64	0.45
Length of resected cardinal ligament tissue (cm)				
Left	3.11±0.27	3.08±0.31	2.99±0.51	0.65
Right	3.02±0.31	3.04±0.37	2.97±0.43	0.91
Number of lymph nodes retrieved	21.7±3.8	23.0±3.8	22.4±3.9	0.06
Complication				
Urethral fistula	0 (0.0%)	0 (0.0%)	1 (1.0%)	0.64
Hydronephrosis	1 (1.9%)	5 (5.9%)	3 (3.0%)	
Post-operation hemorrhage	0 (0.0%)	1 (1.2%)	0 (0.0%)	0.38
Total	1 (1.9%)	6 (7.1%)	4 (4.0%)	
Length of hospital stay (day)				
Mean ±SD	10.4±3.7	10.7±3.1	10.9±3.4	0.25
Median (range)	10 (6–25)	10 (6–23)	10 (6–23)	
Refractory urinary retention 3 weeks after operation				
No	47 (87.0%)	81 (95.3%)	97 (97.0%)	0.055
Yes	7 (13.0%)	4 (4.7%)	3 (3.0%)	
Post-operative chemotherapy				
No	26 (48.1%)	35 (41.2%)	60 (60.0%)	0.035
Yes	28 (51.9%)	50 (58.8%)	40 (40.0%)	
Post-operative radiotherapy				
No	34 (63.0%)	61 (71.8%)	75 (75.0%)	0.29
Yes	20 (37.0%)	24 (28.2%)	25 (25.0%)	

<sup>a</sup> Indicates  $P < 0.001$  as compared with the 2D-LRH group; <sup>b</sup> Indicates  $P < 0.01$  as compared with the 2D-LRH group; <sup>c</sup> Indicates  $P < 0.05$  as compared with the 2D-LRH group. 2D-LRH – 2-dimensional laparoscopic radical hysterectomy; 3D-LRH – 3-dimensional laparoscopic radical hysterectomy; RA-LRH – robotic-assisted laparoscopic radical hysterectomy; SD – standard deviation; FIGO – International Federation of Gynecology and Obstetrics.

We also plotted OT versus surgical sequence for all 3 LRH approaches (Figure 2B–2D). As expected, there was no effect for 2D-LRH (Figure 2B), the effect was barely significant for 3D-LRH ( $R^2=0.07$ ,  $P=0.012$ ; Figure 2C), and most prominent effect was for RA-LRH ( $R^2=0.25$ ,  $P=1.2 \times 10^{-7}$ ; Figure 2D), especially for RA-LRH as seen by higher (negative) correlation coefficient

(–0.50 versus –0.27) and steeper regression line (Figure 2C, 2D). Interestingly, as the OT curve for 3D-LRH appeared to reach its nadir at the 52<sup>nd</sup> surgery (Figure 2C), a quadratic regression centered at 52 apparently fit the data better than linear regression ( $R^2=0.18$  versus  $R^2=0.07$ ,  $P=4.3 \times 10^{-5}$  versus 0.012, respectively).



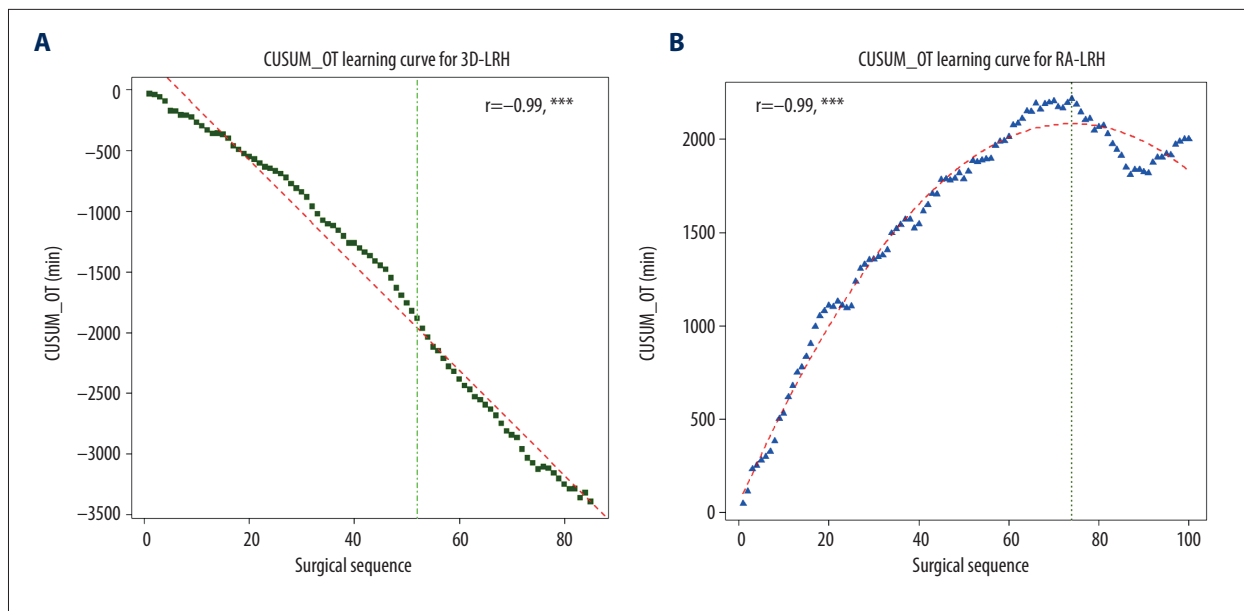
**Figure 2.** Chronological record of operating time of all operations by 3 different approaches of radical hysterectomy (A), by 2D-LRH only (B), by 3D-LRH only (C), and by RA-LRH only (D). Each blue, triangle dot represents 1 case of robotically assisted LRH. Each square dot in olive drab represents one 3D-LRH. Each round dot in red represents one 2D-LRH. The dashed lines are the smoothed spline of the data. 2D-LRH – 2-dimensional laparoscopic radical hysterectomy; 3D-LRH – 3-dimensional laparoscopic radical hysterectomy; RA-LRH – robotic-assisted laparoscopic radical hysterectomy.

Multiple linear regression (MLR) analysis on the OT (log-transformed to improve normality) incorporating age, BMI, uterus size, tumor stage, tumor size, lymphovascular space involvement, stromal infiltration, parametrial involvement, vaginal involvement, presence of positive obturator nodes, metastasis to the pelvic cavity, sequence of surgery, ovarian preservation or not, and other variables such as the radicality of the LRH, indicated that the uterus size was positively associated with the OT ( $P=0.026$ ); RA-LRH was positively associated ( $P=3.2 \times 10^{-7}$ ), but 3D-LRH was negatively associated ( $P=9.6 \times 10^{-13}$ ) with OT, yet for RA-LRH, the sequence of surgery decreased the OT ( $P=0.024$ , respectively;  $R^2=0.52$ ).

**CUSUM analysis of OT**

To further investigate the learning curve, we calculated the  $CUSUM_{OT}$  using the average OT for 2D-LRH as the benchmark. Figure 3 shows the  $CUSUM_{OT}$  for both 3D- and RA-LRH. It can be seen from Figure 3A that for 3D-LRH, the CUSUM plot was nearly a straight line with a negative slope (Figure 3A). A linear regression line provided a nearly perfect fit ( $R^2=0.99$ ,  $P<2.2 \times 10^{-16}$ ). A closer look at the plot indicated that the data could be fitted better by 2-piece linear regression lines, one stopped at the 52<sup>nd</sup> LRH and the other started at the 53<sup>rd</sup> LRH (Figure 3A). Of note, the CUSUM curve was all in the negative





**Figure 3.** (A) The CUSUM plot of operating time for 3D-LRH versus surgical sequence using the average 2D-LRH operating time as a benchmark. (B) The CUSUM plot of operating time for RA-LRH versus surgical sequence using the average 2D-LRH operating time as a benchmark. The dashed lines are regression lines: a linear regression in (A) and a quadratic regression in (B). The vertical dashed line in (A) and the dotted line in (B) indicate the apparent turning point in 3D-LRH and RA-LRH learning process, respectively. The number listed is the Pearson's correlation coefficient. \*\*\*  $P < 0.001$ . CUSUM – cumulative summation; 3D-LRH – 3-dimensional laparoscopic radical hysterectomy; RA-LRH – robotic-assisted laparoscopic radical hysterectomy.

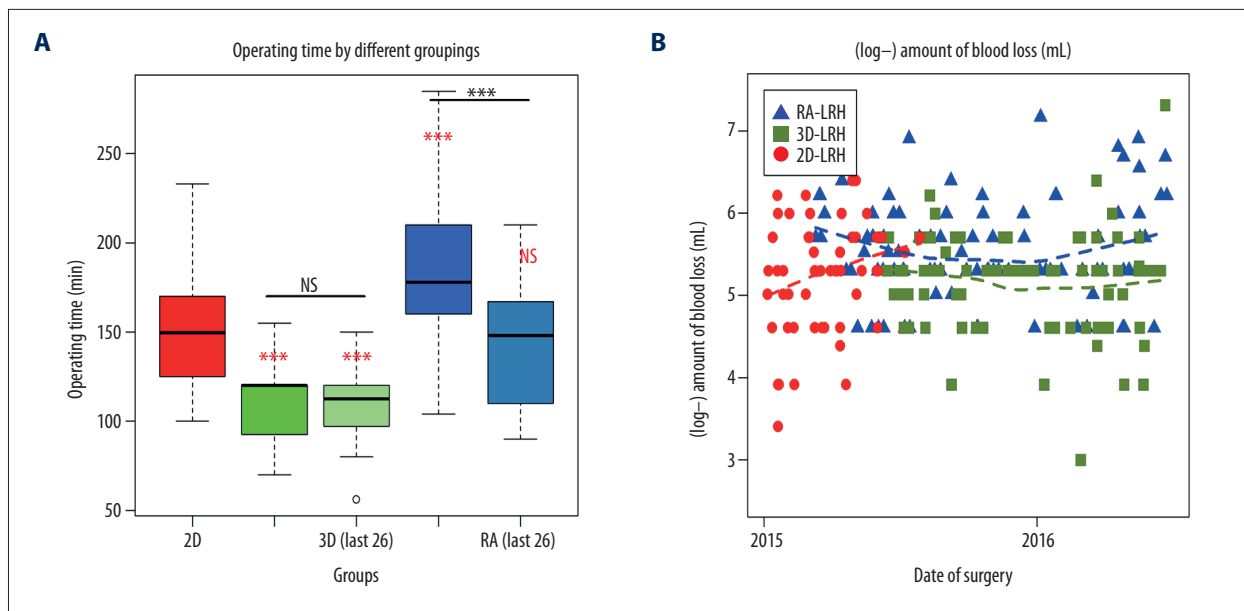
domain, indicating that the OT for 3D-LRH was consistently shorter than that of 2D-LRH. In contrast, the CUSUM plot for RA-LRH looked like a truncated and inverted “V” with the apex located at the 74<sup>th</sup> RA-LRH, suggesting that for the first 74 or so surgeries, the OT was consistently longer than the benchmark and deviated greatly from it. However, at around the 74<sup>th</sup> RA-LRH, the CUSUM appeared to have reached its peak and began to go down (Figure 3B). This plot was best modeled as a quadratic linear regression with the apex at the 74<sup>th</sup> surgery, and the fit was nearly perfect ( $R^2=0.99$ ,  $P < 2.2 \times 10^{-16}$ ). As the CUSUM scores were all in the positive domain, this indicated that the OT for RA-LRH deviated greatly from the benchmark and was longer than that of 2D-LRH for the first 74 or so RA-LRHs. Starting from the 75<sup>th</sup> case, however, the CUSUM began to go down, suggesting that the OT ceased to deviate from the benchmark and the OT was shorter or comparable to that of 2D-LRH. We note that the CUSUM plots would have been quite different (Supplementary Figure 2A, 2B), if the average OT for 3D- and RA-LRH were used as the respective benchmarks.

In view of this, we compared the OT for the last 26 surgeries in the RA-LRH group (since 100 minus 74=26) to the last 26 surgeries in the 3D-LRH group to their respective first set of surgeries (first 74 RAs and first 59 3Ds) and found that there were significant differences in OT between the last 26 cases and the earlier surgeries in both groups (both  $P$ -values  $< 0.001$ ; Figure 4A).

In particular, while the OT was significantly longer than that of 2D-LRH for the first 74 RA-LRH cases ( $181.6 \pm 35.6$  minutes versus  $151.6 \pm 30.7$  minutes;  $P = 3.5 \times 10^{-6}$ ), the difference disappeared for the last 26 cases of RA-LRH ( $136.9 \pm 33.5$  minutes versus  $151.6 \pm 30.7$  minutes;  $P = 0.09$ ; Figure 4A). Remarkably, the OT for the first 59 3D-LRH cases was still significantly shorter than that of the 2D-LRH group ( $115.4 \pm 22.7$  minutes versus  $151.6 \pm 30.7$  minutes;  $P = 1.4 \times 10^{-9}$ ). For the 3D-LRH group and RA-LRH group, the mean OT of the last 26 cases was reduced by 15.9% and 24.3% respectively, compared with the earlier cases. Of note, the average OT of the last 26 3D-LRH cases was significantly shorter than that of 2D-LRH by an average of 34.4% ( $97.1 \pm 20.8$  minutes versus  $151.6 \pm 30.7$  minutes;  $P = 2.6 \times 10^{-9}$ ). Since the decreasing trend of the RA-LRH OT showed no sign of abating (Figure 2A, 2D), whereas that of 2D-LRH had stabilized, it seemed that the OT for RA-LRH could eventually be shorter than that of 2D-LRH, especially given that the  $CUSUM_{OT}$  for RA-LRH appeared to have reached its peak at the 74<sup>th</sup> surgery (Figure 3B).

### The amount of blood loss

For the estimated amount of blood loss, the learning curve effect appeared to be much less pronounced than that of OT or even somewhat subdued (Figure 4B). There was a significant difference in the amount of blood loss during surgery among the 3 groups ( $P = 0.0004$ ), and the pair-wise comparison



**Figure 4.** (A) Boxplot of the operating time by different groupings. The 3D-LRH and RA-LRH cases were both divided into subgroups: the last 26 cases and the previous cases, since the CUSUM analysis indicated that the 74<sup>th</sup> case in the RA-LRH was a turning point, signaling proficiency. The symbols for statistical significance indicate the comparison between the 2D-LRH and the indicated group (in red). \*\*\*  $P < 0.001$ . NS – not significant ( $P > 0.05$ ). (B) Chronological record of the amount of blood loss (log-transformed) of all operations by 3 different approaches of LRH. Each blue triangle dot represents 1 case of RA-LRH. Each square dot in olive drab represents one 3D-LRH. Each round dot in red represents one 2D-LRH. The dashed lines are the smoothed spline of the data. 3D-LRH – 3-dimensional laparoscopic radical hysterectomy; RA – robotic-assisted; CUSUM – cumulative summation.

indicated significant difference between RA-LRH and 2D-LRH ( $317.5 \pm 231.5$  mL versus  $223.5 \pm 151.3$  mL,  $P = 0.019$ ) and between RA-LRH and 3D-LRH ( $317.5 \pm 231.5$  mL versus  $211.6 \pm 174.2$  mL;  $P = 0.0004$ ) but not between 2D- and 3D-LRH ( $P = 0.38$ ; Table 2). However, the magnitude of the difference seemed to be rather small (Figure 4B). No significant correlation with the surgical sequence was found (both  $P$ -values  $> 0.44$  for 3D- and RA-LRH). Judging from Figure 4B, it seemed that for both 3D- and RA-LRH, the learning curve tapered off much sooner than that for OT (Figure 2A). In fact, the difference in the amount of blood loss was no longer significant when the 2D-LRH group data was compared to the data from the last 26 cases each of the other two procedures (all  $P$ -values  $> 0.09$ ).

MLR analysis on the amount of blood loss (log-transformed to improve normality) incorporating the same set of covariables used for OT indicated that both 3D- and RA-LRH interacted with the surgical sequence, and the interaction terms were negatively associated ( $P = 0.047$  and  $P = 0.093$ , respectively), while RA-LRH was positively associated with the amount of blood loss ( $P = 0.007$ ). However, the amount of variation explained by these co-variables was nearly negligibly small ( $R^2 = 0.09$ ), indicating that there were other factors, yet to be identified, that are associated the amount of blood loss. In other words, there was no significant difference in the amount of blood loss between 2D- and 3D-LRH when other factors were controlled for,

and for both 3D- and RA-LRH there was a very weak learning curve effect. Age, disease severity (FIGO stage, tumor size, etc), ovarian preservation or not, BMI, and the radicality of the surgery had no impact on the amount of blood loss. There was no difference in the transfusion rates among the 3 approaches (Supplementary Figure 3A, Table 2).

### LRH radicality

The 3 LRH approaches had comparable surgical radicality. For example, the average length of excised vaginal tissue in the 2D-, 3D-, and RA-LRH groups were 3.01 cm ( $\pm 0.40$ ), 3.04 cm ( $\pm 0.38$ ), and 2.90 cm ( $\pm 0.48$ ), respectively ( $P = 0.12$ ; Table 2, Supplementary Figure 3B). Other measures of radicality in the 3 groups, such as the average length of removed cardinal ligament tissue, and the number of lymph nodes retrieved during LRH were very comparable (Table 2, Supplementary Figure 3C, 3D). MLR analyses did not identify any particular factors that were associated with these measures of radicality.

### Intra- and post-operative complications

The complication rate for 2D-, 3D-, and RA-LRH was 1.9%, 7.1%, and 4.0%, respectively, with the overall complication rate of 4.6%. While a chronological rendition of their occurrences seemed to suggest that for 3D-LRH, the complications appeared to occur in

a random fashion (Supplementary Figure 3E), there was no significant difference in the overall complication rate among the 3 groups ( $P=0.38$ ; Table 2). The combined complication rate of all 3 procedures was 11 out of 239 cases (4.6%), which was in line with the reported 6% for 2D-LRH, or 5.8% in a previous report [21].

Among these 11 complications, ureteral fistula was found in 1 patient (9.1%), who was treated by implantation of ureter into her bladder after an unsuccessful implantation of ureteral stents. Hydronephrosis was found in 9 patients (81.8%), who were successfully treated by implantation of ureteral stents that were removed 2–3 months later without any incidence. Post-operative hemorrhage was found in 1 patient (9.1%) in the 3D-LRH group, due to diffusive bleeding at the cardinal ligament, which was remedied by a second laparoscopic surgery. In all approaches of LRH in this study, there was no incident of wound infection or intestinal obstruction (Table 2).

### Recurrence

Recurrence was found in 2 patients (0.8%). One patient who had small cell neuroendocrine carcinoma of the cervix had remote metastasis to the pelvic cavity, vulva, and lung at 5 months after surgery. The other patient, who had squamous carcinoma of the cervix with no apparent high-risk factors, had recurrence in the pelvic cavity at 5 months after surgery.

### Discussion

In this study, we found that in treating patients with early-stage cervical cancer, both 3D- and RA-LRH had a strong learning curve effect, manifested most prominently by progressively decreasing OT as the surgeon acquired more surgical experience. In this study, 3D-LRH appeared to be superior to 2D-LRH and RA-LRH in terms of significantly shorter OT whether the learning curve effect was accounted for or not. The 3D-LRH also results in significantly less blood loss than RA-LRH, but blood loss was comparable to that of 2D-LRH. While initially the RA-LRH OT was longer than that of 2D-LRH, after about 70 cases the OT was comparable to that of 2D-LRH and is likely to become shorter if more experience is gained.

Our study had several strengths. First, all operations were performed by a single surgeon, thus eliminating any possible difference in experience, skill level, dexterity, or training and making the comparison more reliable. Second, the 2 new surgical approaches, 3D-LRH and RA-LRH, were introduced at the hospital almost at the same time and were performed almost concurrently during the study period. Since the surgeon was a novice to both 3D and robotic systems, there was no inherent bias in favor or against either 3D or the robotic procedures. As such, the comparison that we made should be considered

objective and fair, without any bias due to differences in experience, skill level, or training. In particular, since the assignment was quasi-random, the comparison should be free of any conceivable bias in favor or against any particular approach. Third, with few exceptions for multi-center studies, our study has, especially for RA-LRH, a larger sample size than most studies that have reported on the use of a robotic system for early-stage cervical cancer within a single institution, and certainly by a single surgeon (see, for example, summary tables in 3 previously published reports [21,34,38]). A larger sample size permits more observations, which can help to avoid premature conclusions that surgical proficiency can be achieved in 9 or 20 cases. Fourth, this study not only measured traditional outcome parameters such as OT and amount of blood loss, but also measured parameters of LRH radicality and factors that might impact learning curves, such as uterus size and BMI. Lastly, for both newly introduced LRH approaches, we used the same benchmark that was derived from our extensive 2D-LRH case series, which should be more objective. Indeed, since the learning curves for new surgical approaches were more or less linear, the use of the overall mean would often invariably yield a second-order parabola [34,39], as seen in Supplementary Figure 2 for our data. In fact, the use of a well-defined benchmark is more in line with the spirit of CUSUM analysis [35] and of the learning curve CUSUM where a target is set [40]. One can argue that the overall mean might not be appropriate for a target or benchmark, since as more experience is gained and surgical skills improved, the overall mean OT would surely be reduced progressively.

This study also had several limitations. First, this study reported results from a single well-experienced surgeon, who had extensive 2D-LRH experience. As such, our findings might not be applicable to surgeons with less experience. Given that most hysterectomies are performed by laparotomy, even in developed countries such as the United States [41], it might be difficult to fully appreciate the benefits of 3D-LRH if 2D-LRH experience is inadequate or simply lacking. Second, this study was not a randomized clinical trial, and as such, the comparison between different RH approaches might be subject to certain biases. However, as we see in Table 1 and Supplementary Figures 1 and 3, the 3 groups are fairly comparable. Future randomized studies are certainly warranted to compare 3D- and RA-LRH, especially for long-term outcomes.

For all approaches of LRH, the OT was not related to BMI of the patients being operated on, and OT was not affected by patient age, disease severity such as FIGO stage or tumor size, radicality of the LRH, or whether ovarian preservation procedure was performed or not. However, the OT was positively associated with the uterus size. All 3 approaches of LRH yielded comparable radicality and intra- and post-operative results other than OT and the amount of blood loss. This finding was

consistent with published studies reporting comparable surgical outcomes between 2D- and RA-LRH [21,42–46].

Consistent with the findings reported for non-gynecological laparoscopic surgeries [27–30], we found 3D- was superior to 2D-LRH. This was due to the fact that, compared with 2D laparoscopy, 3D laparoscopy offers a stereoscopic vision of the surgical field, giving a realistic sense of spatial perception that enhances the exposure of finer anatomic structures and the precision movements of the surgeon, such as suturing, knotting, and dissection [29]. With the help of a 3D-HD Olympus monitor, all of the members of the surgical team can see in 3D by wearing polarized goggles. The resultant 3D vision not only provides surgeons a high-definition image that exposes fine anatomical structures but also facilitates the placement of laparoscopic instrument at the desired place, because the depth perception of 3D makes the interstitial space magnified during operation. Thus, enhanced precision in locating the target field of operation, as well as placement of surgical instruments, makes tasks such as ureteral dissection, the development of the vesico-uterine space and rectal-uterine space, and the exposure of cardinal ligament easier and simpler than its 2D counterpart. However, the surgeon in charge cannot maneuver the 3D-vision camera at will as can be done using the robotic system, because the 3D-vision camera has to be held by an assistant. Hence this procedure needs an experienced assistant to work closely with the surgeon.

For surgeons already familiar with 2D-LRH, the learning curve for 3D-LRH is very steep, as shown in this study. Just as reported previously [30], in this study, the surgeon and her assistant quickly adapted to the 3D system and within 10 minutes of the first-ever 3D-LRH became quite comfortable with the system. With added stereoscopic vision of the surgical field and high-fidelity images, the 3D system is easier than its 2D counterpart to handle tasks such as the dissection of the ureter and uterine vessels and the release of the ureter from the adventitial attachments of the vessels medial and ventral. This may explain why 3D-LRH took less OT than the familiar 2D-LRH in our series. Compared with the robotic system, 3D laparoscopy has the same stereoscopic vision of the surgical field, yet it also has better tactile feedback than the former when performing tasks such as suturing and tissue separation, hence the 3D-LRH learning curve is very steep for surgeons experienced with the 2D-LRH. RA-LRH resulted in slightly more blood loss. This might be attributable to the use of the monopolar scissors in the robotic system as opposed to the HARMONIC ACE in the 2D- and 3D-LRH. HARMONIC ACE can perform a better job in coagulation than the monopolar scissors.

Our study also echoes a previous report that, for surgeons with advanced surgical skills, their OT with a 3D laparoscopy is shorter than with a robotic laparoscopy and thus might not benefit in terms of OT as much from the latter, even though

3D is reported to benefit the novices OT through steep learning curve [31]. Robotic laparoscopy is radically different from the traditional 2D system. As such, there is a learning curve even for experts on 2D laparoscopy. In contrast, 3D laparoscopy is nearly identical to the 2D counterpart, which explains a steep learning curve for 3D-LRH. Our study also agrees with a recent report that the use of RA radical nephrectomy was not associated with increased risk of any major complications but was associated with prolonged OT and higher hospital costs compared with laparoscopic surgery [23].

The Da Vinci® system allows surgeons to be free from the conventional bedside operation approach and provides them overall control of the instruments and camera. In contrast, surgeons stand erect during the entire course of an operation when performing 2D or 3D laparoscopy, and this position is by no means ergonomically optimal, especially when high-volume operations are routine. In our case, however, we used a high stool so that the surgeon (and her assistant, if they chose to) sat while operating. This position, while not entirely ergonomic, was quite comfortable and helped alleviate discomfort.

With more flexible graspers that can move in 360 degrees, Da Vinci® makes tasks such as ligation of arteries and suturing easier than conventional 2D laparoscopy. As in 3D-LRH, robotic 3D-HD vision also gives the operator better depth perception and wider vision, which enhances her surgical performance. However, it lacks tactile feedback. Hence it poses more challenge than the 2D or 3D system when performing tasks typical to gynecological surgery, i.e., when handling tissues, such as cardinal ligaments, that are often stretched with tension. In addition, the assistant's field of vision is different from the surgeon's: while the former sees the surgical field in 2D, the latter, in 3D. This discrepancy can sometimes cause discord between the 2, slowing down the operation. This may explain the longer OT for RA-LRH compared to 3D-LRH. However, due to the strong learning curve effect, the OT difference compared to 2D-LRH in our study diminished after about 74 cases and the decrease in OT appeared to be unabated, suggesting that the OT for RA-LRH might eventually become shorter than that of 2D-LRH as experience is gained through more surgeries. Of course, RA-LRH costs much more than either 2D- LRH or 3D-LRH. We summarized the advantages and disadvantages of the 3 approaches of LRH in Table 3.

Despite the learning curve effect in 3D- and RA-LRH, there was no significant differences in the duration of hospital stay among the 3 LRH approaches. The seemingly longer hospital stay reported in this study for all 3 approaches of LRH, in comparison with those published [21], we attributable to several reasons. 1) The higher percentage (52.7%) of post-operative adjuvant therapy; and 2) current health insurance policies (provided by the same government-sponsored plan) that provide substantially more coverage for in-patient medication than out-patient

**Table 3.** A ledger book for the comparison of 3 approaches of LRH.

Item	2D-LRH	3D-LRH	RA-LRH	Remark
Set-up time	5 min	5 min	~15 min	
3D view	No	Yes	Yes	
Congruence in surgical vision between the surgeon and his/her assistant	Yes	Yes	No	In 3D, the assistant can also see 3D by wearing a pair of polarized glasses.
Primary source of energy used in coagulation	Ultrasound	Ultrasound	Electric (monopolar scissors-)	
Effectiveness in coagulation	Effective	Effective	Inferior to 2D and 3D systems	
Flexible graspers, scissors and needle holders that can move in 360°	No	No	Yes	
Ease in suturing tissues stretched with tension	Yes	Yes	No	
Learning curve	Flat	Steep (for expert surgeons)	Steep	
Operating time	Fast	Fast	Slower	
Touch sensation	Yes	Yes	No	
Tremor control	No	No	Yes	
Dexterity	Requires training	Requires training	Improved	
Ergonomics	Not very comfortable, but a high stool can be made to alleviate the discomfort	Not very comfortable, but a high stool can be made to alleviate the discomfort	Very comfortable	
Minimal invasiveness	Excellent	Excellent	Excellent	
Cost	Low	Higher than 2D but much lower than RA-LRH	High	
Complication rate	Low	Low	Low	
Amount of blood loss	Low	Lowest	Slightly higher than 3D	
Time to recovery	Fast	Fast	Fast	
Long-term survival	Satisfactory [50]	Unknown, but presumably similar to the 2D	Similar to the 2D [50]	

RA-LRH – robotic-assisted laparoscopic radical hysterectomy; 3D – 3-dimensional; 2D – 2-dimensional.

medication, which practically provides a powerful inducement for longer hospital stay. Yan et al. reported an average of 12 days of hospital stay for LRH in Wenzhou, China [47].

Our study corroborated the assertion by Yim et al. [34] that CUSUM analysis should be used for assessing surgical proficiency. Indeed, our study clearly showed that quite different conclusions could be reached just by using the plot of OT versus

surgical sequence without using a CUSUM analysis. CUSUM analysis is now a well-accepted method for assessing proficiency for learning a complex procedure or skill [35,48–50]. For OT, which is a complex parameter reflecting proficiency as well as dexterity, we felt that a well-justified benchmark should be used for the CUSUM analysis instead of the overall mean of the OT during the learning process. Apparently, different benchmarks might yield different conclusions.



## Conclusions

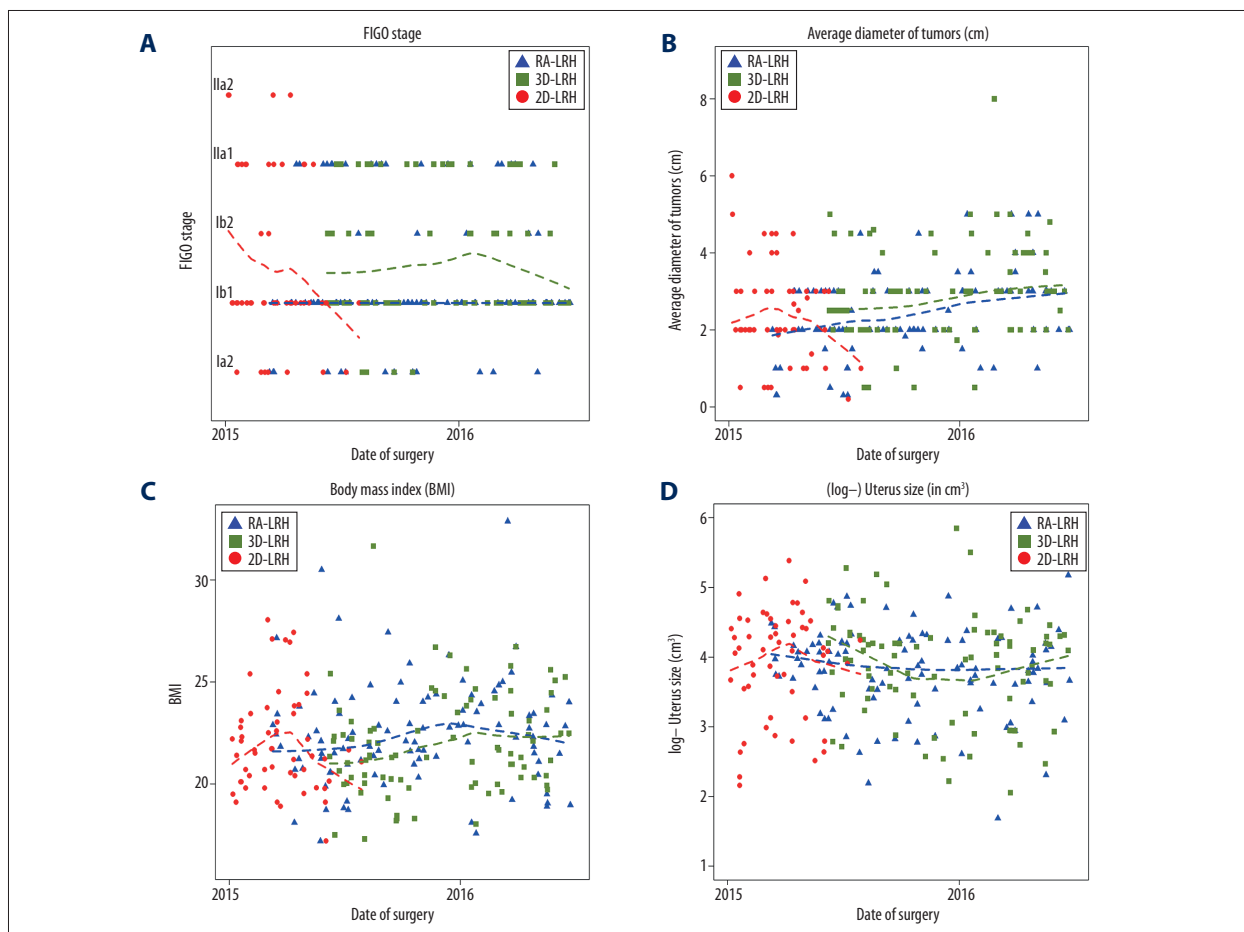
Mastering 3D- or RA-LRH had a steep learning curve for an experienced surgeon with an excellent command of 2D laparoscopy. In our experience, 3D-LRH was superior to 2D-LRH and RA-LRH in terms of significantly shorter OT and slightly less blood loss than RA-LRH. For all approaches, the OT correlated positively with patient's uterus size, and was not affected by patient's age, disease severity such as FIGO stage or tumor size, radicality of the LRH, or whether ovarian preservation procedure was performed or not. All 3 approaches of LRH had comparable radicality, and intra- and post-operative complication rates other than OT and the amount of blood loss. While

RA-LRH is currently much more expensive than either 2D-LRH or 3D-LRH, it might still be attractive if the cost of 1 extra MD-level assistant and his or her training are taken into the economic equation. In addition, technological advancement in the future might further improve the current robotic systems, hopefully making them better and less costly. But until that day comes, 3D-LRH is, in our view, a winner for early-stage cervical cancer in the hands of experienced surgeons, especially in countries where labor costs are low.

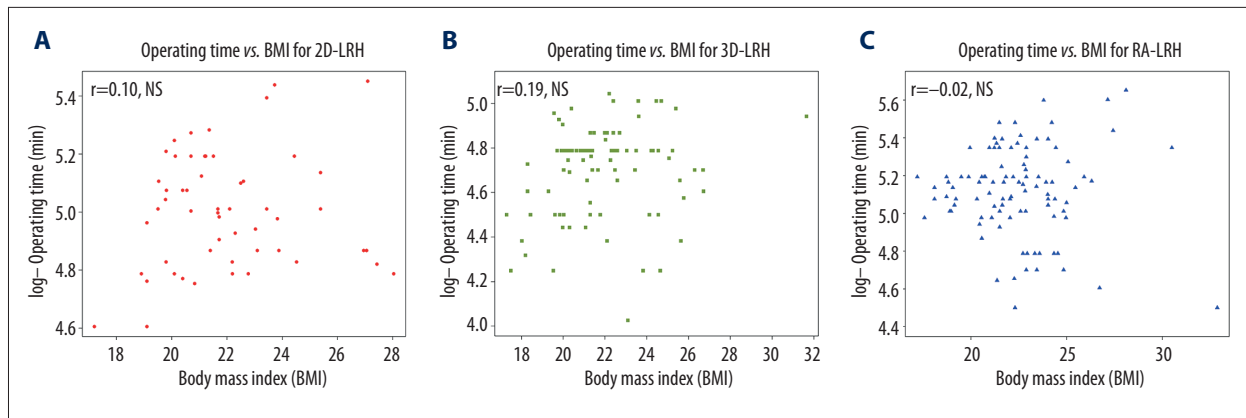
## Conflicts of interest

None.

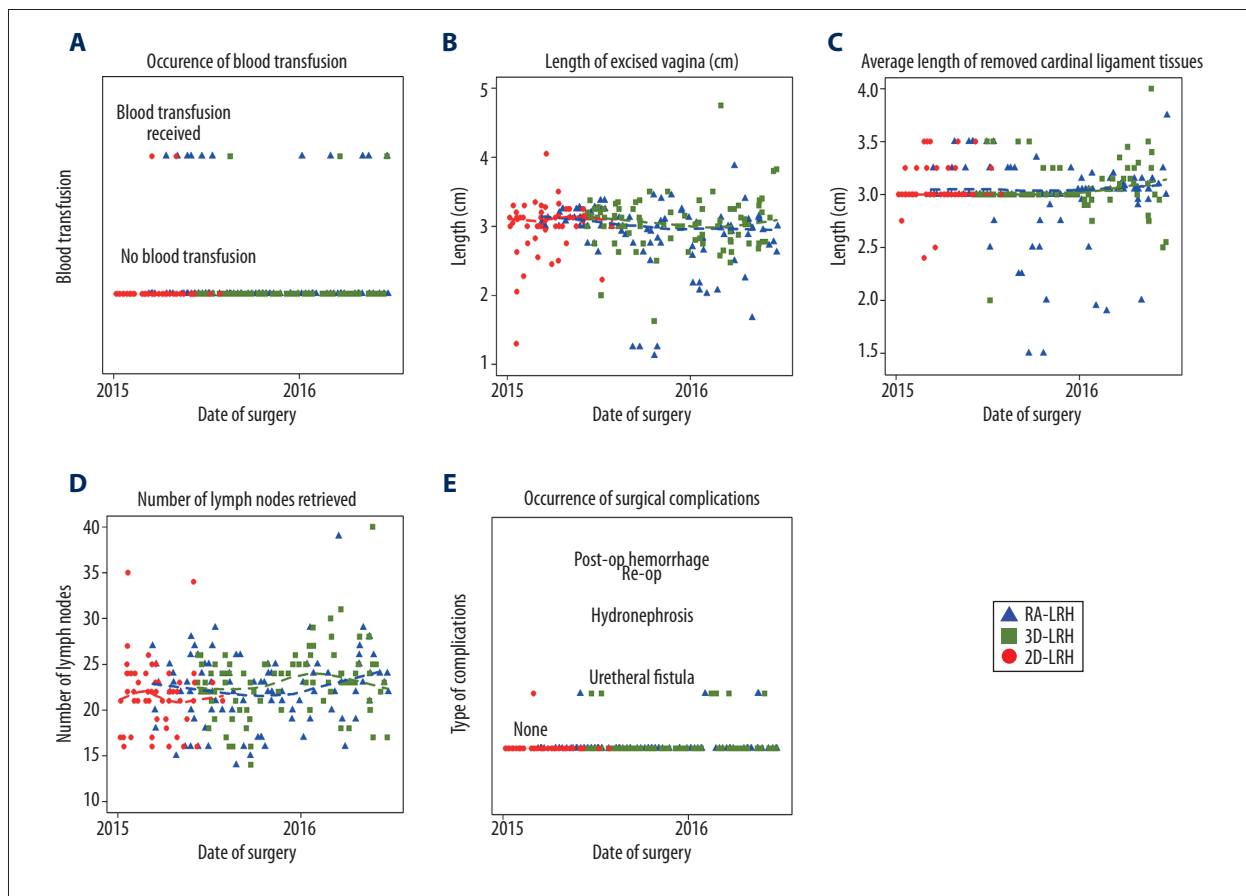
## Supplementary Figures



**Supplementary Figure 1.** Chronological data. (A) Chronological record of FIGO stages of all operations by mode of radical hysterectomy. (B) Chronological record of the average diameters of tumors (in cm) of all operations by mode of radical hysterectomy. (C) Chronological record of body mass index (BMI) of patients of all operations by mode of radical hysterectomy. (D) Chronological record of (log-transformed) uterus size of patients of all operations by mode of radical hysterectomy. Each blue triangle dot represents one case of RA-LRH. Each square dot in olive drab represents one 3D-LRH. Each round dot in red represents one 2D-LRH. The dashed lines are the smoothed spline of the data. FIGO – International Federation of Gynecology and Obstetrics; RA-LRH – robotic-assisted laparoscopic radical hysterectomy; 3D-LRH – 3-dimensional laparoscopic radical hysterectomy.



**Supplementary Figure 2.** (A–C) The CUSUM plots. (A) The CUSUM plot of operating time for 3D-LRH versus surgical sequence using the average 3D-LRH operating time as a benchmark. (B) The CUSUM plot of operating time for RA-LRH versus surgical sequence using the average RA-LRH operating time as a benchmark. CUSUM – cumulative summation; 3D-LRH – 3-dimensional laparoscopic radical hysterectomy; RA-LRH – robotic-assisted laparoscopic radical hysterectomy.



**Supplementary Figure 3.** Chronological data. Chronological record of blood transfusion (A), the length of excised vaginal tissues (in cm) (B), the length of removed cardinal ligament tissues (in cm) (C), the number of lymph nodes retrieved (D), and the occurrence of various surgical complications (E) in all operations by mode of LRH. Each blue, triangle dot represents one case of RA-LRH. Each square dot in olive drab represents one 3D-LRH. Each round dot in red represents one 2D-LRH. The dashed lines are the smoothed spline of the data. RA-LRH – robotic-assisted laparoscopic radical hysterectomy; 3D-LRH – 3-dimensional laparoscopic radical hysterectomy.

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