The influence of learning curve of robot-assisted laparoscopy on oncological outcomes in early stage cervical cancer: an observational cohort study

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Abstract

Objective: To investigate the learning curve of robot-assisted laparoscopy in early stage cervical cancer and quantify impact on oncological outcomes. **Design:** Observational cohort study. **Setting:** Tertiary referral centre with one surgical team. **Population:** All early stage cervical cancer patients treated consecutively with robot-assisted laparoscopy between 2007 and 2017. **Methods:** With multivariate risk-adjusted cumulative sum analysis (RA-CUSUM), we assessed the learning curve of robot-assisted laparoscopy of a single surgical team based on cervical cancer recurrence. Subsequently, a survival analysis was conducted comparing oncological outcomes of patients treated during different phases of the learning curve. **Main Outcome Measures:** Surgical proficiency based on recurrence, survival rates in the different learning phases. **Results:** 165 cervical cancers patients were operated by robot-assisted laparoscopy, with a median follow-up of 57 months (range 3-132 months). The RA-CUSUM analysis demonstrated two phases of the learning curve: a learning phase of 61 procedures (group 1) and an experienced phase representing the 104 procedures thereafter (group 2). The 5-year disease free survival was 80.2% in group 1 and 91.1% in group 2 (P = 0.040). Both the 5-year disease-specific survival and overall survival significantly increased after the learning phase. **Conclusion:** The learning phase of robot-assisted laparoscopy in early stage cervical cancer in this institutional cohort is at least 61 procedures, with higher survival rates in the patients treated thereafter. The learning curve of robot-assisted laparoscopy affects oncological outcomes and warrants more attention in the design of future studies. **Funding:** None. **Keywords:** Cervical cancer, robot-assisted laparoscopy, learning curve, RA-CUSUM, recurrence, survival.

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Introduction

The perioperative advantages of robot-assisted laparoscopy have resulted in its widespread adoption in the treatment of early stage cervical cancer. Numerous observational studies and meta-analyses report superior results in blood loss, hospital stay and complication rates compared with the laparotomic approach.[1-4] In addition, equal survival rates of robot-assisted laparoscopy and laparotomy were suggested.[5-8] However, a recent trial by Ramirez et al., which randomised between minimally invasive surgery (MIS) and laparotomy, showed a significantly increased recurrence rate and reduced overall survival in patients receiving MIS for FIGO stage IA1-IB1 cervical cancer.[9] The MIS arm of this trial consisted predominately of conventional laparoscopy with only 15.6% of the patients operated by robot-assisted surgery. Multiple subsequent observational studies have substantiated these results regarding MIS[10-13], while others reported non-inferiority of recurrence and survival rates after (specifically) robot-assisted surgery.[14-16]

A large population-based cohort study in Sweden, where cervical cancer surgery is highly centralised, recently concluded it to be safe to continue with robot-assisted surgery when performed by experienced, high-volume surgeons.[14] In the previous studies, the learning curve effect on oncological outcomes in cervical cancer – specifically in robot-assisted laparoscopy – is not yet reported. This could be a potential confounder and could offer a possible explanation for the conflicting reports. In addition, until today the literature available on learning curves has mainly focused on the duration of surgery only.[17-20] To analyse proficiency in robot-assisted laparoscopy the oncological outcome should be considered the foremost relevant parameter. In other oncological diseases, for instance prostate cancer, it has been shown that oncological outcomes are associated with the learning curve of robot-assisted surgery but the amount of procedures needed to reach an accepted plateau of the learning curve varies widely and requires further research.[21,22]

The objective of this study is to investigate the learning curve of a single surgical team and its effect on the risk of cervical cancer recurrence and to quantify impact on survival. By using a multivariate risk-adjusted cumulative sum analysis we aim to establish the number of surgeries needed to ascertain – oncological – proficiency in robot-assisted laparoscopy in the treatment of early stage cervical cancer.

Methods

Design

We performed an observational cohort study reporting on all patients treated consecutively with robot-assisted laparoscopy for early stage cervical cancer (FIGO stage IA1, IA2, IB1 and IIA1 according to 2009 FIGO staging and guidelines[23]) between 1 December 2007 and 1 April 2017. Inclusion criteria were a histopathologically proven carcinoma of the cervix and the intention to perform robot-assisted radical surgery as primary treatment. Patients were excluded in case of an ongoing pregnancy or when treated with neoadjuvant chemotherapy. All procedures were part of standard clinical care, for which informed consent was obtained.

The primary outcome of interest was surgical proficiency, based on cervical recurrence rate. Secondary outcomes were disease-free survival (DFS), disease-specific survival (DSS) and overall survival (OS) in the different learning phases. Survival was defined as the time interval between date of diagnosis or first visit and date of disease recurrence diagnosis (DFS) or death due to the sequelae of cervical cancer (DSS) or death from any cause (OS).

Surgical technique

All surgical procedures were performed at a tertiary referral centre by a surgical team consisting of two gynaecological oncologists (RV, RZ) with similar experience in robot-assisted operation techniques. In all patients with early stage cervical cancer and an indication for radical surgery, the da Vinci (S until 2010 and Si until 2017) Surgical System (Intuitive Surgical, Sunnyvale, USA) was used. Robot-assisted laparoscopy was the standard of care, with laparotomy only performed in 10 cases during the inclusion period for those who had an absolute contra-indication (e.g. advanced pregnancy, large uterus*)*.Primary surgical treatment for early stage cervical cancer consisted typically of robot-assisted pelvic sentinel lymph node (SLN) evaluation and systematic lymph node dissection (PLND) combined with radical hysterectomy or radical vaginal trachelectomy when fertility preservation was desired and the maximum tumour diameter was [?]2 cm. When sentinel nodes were found to be positive on frozen section, the intended radical uterine surgery was discontinued and chemoradiation initiated. In case of unexpected finding of cervical cancer after simple hysterectomy (for benign indication), primary treatment was expanded with robot-assisted PLND and parametrectomy. Details on the surgical techniques performed at our institution have been previously described.[5,24]

Data collection

Parameters were extracted from the institutional medical records. The clinical, surgical, histopathological and follow-up data collected from medical records included: age at diagnosis, body mass index (BMI, in kg/m^2), history of abdominal surgery, ASA classification (American Society of Anaesthesiologists), FIGO stage (2009), type of procedure, tumour histology and size, lymph vascular space invasion (LVSI), nodal count and status, parametrial involvement, vaginal involvement, positive resection margins, adjuvant or adjusted treatment (the latter due to intraoperative finding of positive lymph nodes), disease recurrence, time and sites of recurrence and survival information. Disease recurrence was defined as the local and/or distant (outside the inner pelvis) presence of malignant tissue originating from the primary tumour, determined clinically, radiographically and/or histopathologically. Death records were verified using the municipal Personal Records Database.

Oncological follow-up was performed for a total of five years according to national guidelines consisting of ambulant visits to a gynaecological oncologist at intermissions of three months (first year), four months (second year) and six months up to five years of follow-up.

Statistical analysis

To evaluate the learning curve of robot-assisted laparoscopy, a risk-adjusted cumulative sum (RA-CUSUM) statistical analysis was performed. The cumulative sum (CUSUM) procedure has been validated to monitor surgical outcomes and is able to detect small changes over time in the surgical performance.[25,26] The RA-CUSUM is an extension of this statistical method by adjusting for each patient's individual risk of surgical failure through the use of a likelihood-based scoring method[25]. We defined surgical failure as cervical cancer recurrence. As the estimated risk of recurrence varies among patients, a multivariate risk adjustment is essential. The probability of recurrence for each patient was modelled by a logistic regression analysis. The variables included in the risk model were based on prior results.[27] We limited this model to 3 degrees of freedom to prevent overfitting. Sensitivity analyses with different models were tested in the RA-CUSUM to ensure that the presented data is robust.

The RA-CUSUM chart plots the function:

$$(1) \quad \mathrm{X}_t = \max\ (0, X_{t-1} +\ W_t)\,, \quad t = 1, 2, 3, \ldots$$

Where $X_0 = 0$ and W_t is the weight assigned to the $t$he procedure. In this study, each value of t corresponds to a new patient receiving a robot-assisted procedure. The weights W_t are given by:

$$(2) \quad \mathrm{W}_t = \begin{cases} \log\left[\frac{1-p_t+R_0p_t}{1-p_t+R_Ap_t}\right] & \text{if patient t develops no recurrence} \\ \log\left[\frac{(1-p_t+R_0p_t)R_A}{(1-p_t+R_Ap_t)R_0}\right] & \text{if patient t develops recurrence} \end{cases}$$

Where p_t is the probability of recurrence for each patient calculated from the probability of recurrence model; $R_0 = 1$represents the odds ratio under the null hypothesis; $R_A$represents the odds ratio under the alternate hypothesis. Following Steiner et al. we used two RA-CUSUM procedures.[25] The first, here referred to as RA-CUSUM+, is designed to detect a doubling of the odds of recurrence ($R_A = 2$). The second one, here referred to as RA-CUSUM-, is designed to detect a halving of the odds of recurrence ($R_A = 0.5$) (based on a similar analysis in robot-assisted hemicolectomy by Parisi et al.[28]).

Both RA-CUSUM procedures can be presented in one plot, with RA-CUSUM+ plotting the function X_t as described above (1), and RA-CUSUM- plotting the function:

$$(3) \quad Z_t = \min\ (0, Z_{t-1} -\ W_t)\,, \quad t = 1, 2, 3, \ldots$$

Where $Z_0 = 0$ and W_t is provided by the formerly described function (2).

To summarise, the RA-CUSUM plots the difference between the cumulative expected occurrence of an event (here: recurrence) and the actual observation. In the upper RA-CUSUM+ chart, the curve moves up for every case with recurrence and down for every case without recurrence. The magnitude by which the line ascends or descends is determined by the difference between the observed and expected probability of recurrence. For instance, if a patient modelled as having a high probability of recurrence subsequently develops a recurrence, the curve ascends less (i.e. small penalty) than it would if a recurrence is diagnosed in a low risk modelled patient (i.e. larger penalty). In the lower RA-CUSUM- chart, surgical success is indicated by a negative drift of the curve.

Based on the RA-CUSUM plot, the "learning phase" of robot-assisted laparoscopy at our institution was determined. The procedures performed during this first phase were compared with the rest of the procedures performed thereafter. The Statistical Package for the Social Sciences version 25.0.2 (SPSS; International Business Machines, Armonk, NY USA) was used for modelling analysis and the RA-CUSUM analyses were performed using Microsoft Excel 2010 for Windows. As we performed an intention-to-treat analysis, cases where radical hysterectomy was aborted because of positive lymph nodes were included in the analysis.

Comparisons of continuous variables were conducted using the Mann-Whitney U test. Categorical data were reported as proportions and compared between groups using χ^2-test or Fisher exact test as appropriate. Survival curves for both groups were estimated using Kaplan Meier method and differences between the two groups were compared using log-rank test. Statistical tests were two-sided with significance set at $P< 0.05$, with confidence intervals (CI) at the 95% level.

Results

Population The study population consisted of 165 patients with a median age of 40 years (range 23-81 years) and median BMI was 24 kg/m^2(range 18-41 kg/m^2). The majority (90.3%) were staged as FIGO IB1. One robot-assisted procedure was converted to conventional laparoscopy because of technical difficulties. There were no conversions to laparotomy. A total of 145 (87.9%) procedures were preceded by SLN evaluation and in 84.1% of these cases the sentinel nodes were detected bilaterally. Due to lymphatic tumour involvement radical hysterectomy was omitted in 13 patients (7.9%) and subsequently primary treatment was adjusted to chemoradiation. Another 22 patients (13.3%) received adjuvant radiotherapy or chemoradiation because of post-operative histopathological findings of positive lymph nodes (n = 5), parametrial invasion (n = 4), positive (n = 1) or narrow (<5 mm, n = 6) resection margins, extensive LVSI (n = 1) or a combination of any of these criteria (n = 5). One of the patients with micrometastasis in one lymph node did not receive adjuvant chemoradiation due to contra-indications for radiotherapy. The median follow-up duration was 57 months (range 3-132 months).

Risk model and sensitivity analysis

In order to determine the learning curve with RA-CUSUM multiple risk models, obtained with logistic regression, were tested. The first risk of recurrence model containing three independent variables – age, parametrial involvement and lymph node status – was overall significant (P = 0.009). However, only age and lymph node status were unique significant variables (OR 1.05 (CI 1.01-1.09) and OR 4.23 (CI 1.32-13.57), respectively). Due to the majority of patients being staged IB1, FIGO stage was not included. When replacing parametrial involvement and lymph node status with adjuvant or adjusted treatment, which summarises multiple prognostic factors, this variable yielded a more significant risk model (P = 0.001) and a strong association to recurrent disease (OR = 3.85 (CI 1.46 – 10.16)). The final model used for the RA-CUSUM chart (below) included age and adjuvant or adjusted treatment. Outcomes of the RA-CUSUM did not change substantially for the various models.

Learning curve

The RA-CUSUM chart is displayed in *Figure 1* . The RA-CUSUM+ chart shows a peak at 61 procedures, where after a consistent decrease is observed and the RA-CUSUM+ chart moves towards zero indicating satisfactory results with respect to the predicted recurrence rates. Hence, the first 61 procedures comprise the learning phase for the surgical team. In the 20 procedures thereafter, representing the first part of the experienced phase, surgical performance is still improving as the chart moves further negatively, indicating a decrease of surgical failure as presented by the RA-CUSUM- chart. From procedure 81 onwards the RA-CUSUM- chart stabilises, indicating the plateau of the learning curve has been reached.

As a sensitivity analysis, RA-CUSUM plots were constructed for the different risk models as described earlier, all showing an identical learning phase of 61 procedures.

Based on the RA-CUSUM plot the patients were divided into two groups: group 1 (the learning phase; procedure 1-61) and group 2 (the experienced phase; procedure 62-165).

Patient characteristics and survival by learning phases

Table 1 shows the baseline characteristics of the patients treated during the two phases. Apart from follow-up duration no significant differences were found. The median follow-up duration was 62 months (range 14-132 months) in group 1 (case 1-61) and 43 months (range 3-91 months) in group 2 (case 62-165) ($P < 0.001$). In both groups the majority of patients completed a three-year follow up (90.2% in group 1 vs. 80.8% in group 2, $P = 0.168$).

In total, 20 patients (12.1%) were diagnosed with recurrent disease within five years; 12 patients (19.7%) in group 1 and eight patients (7.7%) in group 2 ($P = 0.028$). In both group 1 and group 2 seven patients presented with locoregional recurrence (11.5% and 6.7%, respectively), four patients in group 1 (6.6%) and no patient in group 2 presented with distant recurrence and one patient in both group 1 and group 2 presented with a combination of locoregional and distant recurrence (1.6% and 1.0%, respectively). The 5-year DFS was 80.2% in group 1 and 91.1% in group 2 ($P = 0.040$) (Figure 2A). The 3-year DFS did not differ significantly between the groups (83.6% vs 92.8%,$P = 0.064$). Of the ten patients with recurrent disease who were alive at the time of analysis, five were treated curatively (three in group 1 and two in group 2) and five patients are currently on palliative treatment.

A total of 12 patients died within five years follow up, ten of whom died of cervical cancer; nine patients (14.8%) in group 1 and one patient (1.0%) in group 2. Both the DSS and OS at five years of follow up differed significantly between the two groups, in favour of group 2: 84.7% vs 97.7% ($P = 0.002$) (Figure 2B) and 84.7% vs 94.8% ($P = 0.018$) (Figure 2C), respectively.

Discussion

Main findings

This is the first study, using RA-CUSUM analysis, to evaluate the length of the learning period of robot-assisted laparoscopy on oncological outcomes. Our results suggest an institutional learning phase of at least 61 procedures, showing a decreasing recurrence rate with increasing experience. The 5-year DFS and DSS significantly improved in patients treated after this initial learning phase. The 5-year DFS and OS in our cohort are comparable with other recent studies on robot-assisted surgery in the treatment of cervical cancer[6,8,14] and moreover, similar to the national recurrence and survival rates for early stage cervical cancer in The Netherlands.[29] When regarding the 4.5-year DFS, the outcome parameter provided in the Laparoscopic Approach in Cervical Cancer (LACC) trial, we found that 93% of the patients treated during the experienced phase (group 2) were free of recurrence at 4.5 years of follow-up. This is substantially higher than the 4.5-year DFS of 86% reported in the MIS arm of the LACC trial.[9]Unfortunately, the exact MIS volume and (RA-CUSUM based) individual learning curves are unknown for the inclusion centres of the LACC trial. Furthermore, their surgical proficiency assurance was limited to providing data from (a minimum of) any 10 laparoscopic surgeries and two procedural videos, which in light of our main findings could be considered insufficient.

Strengths and Limitations

Since we started with robot-assisted surgery at our institution at the end of 2007 it was the standard of care for early stage cervical cancer, thus minimizing the risk of selection bias in our analysis. Another strength is that, in contrast to other studies on this subject, we performed a formal CUSUM analysis, which is considered the reference standard for studying surgical learning curves and recently emerged in other surgical fields.[30,31] Also, given the objective outcome parameters (i.e. mortality), misclassification of the outcome status (i.e. information bias) is unlikely to have occurred.

There were several limitations to this study. First, the shorter follow-up time of the second group, inherent to the more recent surgery date in this group, could have led to overestimation of the learning curve effect. This effect is likely to be limited as the majority of the recurrences occurred in the first three years of follow-up, which 80.8% of the patients in group 2 completed (not significantly different from the first group). Also, survival analysis with Kaplan Meier plots corrects for differences in individual follow-up through censoring thus still providing reliable data. Secondly, other robot-assisted procedures were also performed in the period from December 2007 to April 2017 for high grade and serous endometrial cancer, which reinforces our finding that one needs at least 61 procedures before reaching surgical proficiency. The variety of robot-assisted procedures is an inescapable reality in the daily practice of a high-volume oncological centre and represents a practice comparable to other tertiary referral centres. This also applies to the diversity in the surgical treatments given to these relatively young patients with cervical cancer. Preservation of fertility is often desired and, if possible, radical surgery is performed without removal of the uterus. We chose to include all primary radical robot-assisted laparoscopies in early stage cervical cancer since the robot-assisted actions require equal surgical proficiency. Inevitably, individual learning curves may differ, but we did not do a per surgeon analysis. In any case, for daily practice institutional performance is more important than individual performance. In the end, teams will consist of both experienced and less experienced surgeons which should guarantee maintenance of team proficiency at an optimal level. Lastly, our analysis may have been affected by residual confounding, resulting from several factors contributing to the risk of recurrence, such as age, FIGO stage, parametrial involvement and lymph node status, all related to DFS.[27] By using RA-CUSUM analysis we adjusted for these risk differences between patients but the limited number of events in some variables restricted the comprehensiveness of our model.

Interpretation

Until now, studies highlighting the impact of learning curve on oncological outcomes in gynaecology mainly focused on conventional laparoscopy. A recent retrospective cohort study by Liu et al. showed that the adoption of conventional laparoscopy for the treatment of cervical cancer initially resulted in a significant reduction of DFS survival rates.[32] In the years thereafter the survival rates in that study gradually improved up to the level before the adoption of conventional laparoscopy which strongly suggests an effect of a learning curve.[32]

Compared with conventional laparoscopy, the learning process of robot-assisted surgery was originally perceived as shorter. After the adoption of the robot-assisted approach, it was stated that the 3D view of robotic laparoscopy allows for a significantly better performance and faster improvement in learning curve than conventional laparoscopy with 2D view.[33] Which specific part of robot-assisted radical hysterectomy (RRH) or robot-assisted PLND contributes to the learning curve the most, remains to be established. From their data on the different parts of robot-assisted surgery in endometrial cancer, Seamon et al. concluded that hysterectomies – and in particular the closure of the vaginal cuff – had the longest learning curve.[34]

Another recent study suggested an impact of the learning curve on oncological outcomes after robot-assisted surgery in cervical cancer patients.[35] Chong et al. reported inferior OS after RRH during the learning period compared with conventional laparoscopic radical hysterectomy (LRH) performed by experienced surgeons, though not significant (P- value of 0.07).[35] Given the small study size ($n = 65$) and the absence of a CUSUM analysis, the exact length of the learning curve could not be defined in that study.

With the use of RA-CUSUM analysis we approached the absolute number of procedures needed for a single surgical team to obtain robotic proficiency. More importantly, we were able to demonstrate the impact of the learning curve on the oncological outcomes of early stage cervical cancer patients. Our results underscore the necessity of a validated learning curriculum to make the learning process of an innovative surgical technique as effective and short as possible.[20,33] Nowadays, simulation training should be mandatory and followed by robot-assisted procedures using dual consoles. This allows for direct supervision of new trainees by a certified proctor. Further research in larger populations and other centres is needed to be able to determine to what extent the length of the initial learning phase will be universally applicable.

Furthermore, we propose that the learning curve effect on oncological outcomes should be included in the design of future studies – including posthoc analyses of existing trials – comparing the safety of innovative and common surgical treatments.

Conclusion

This single institution study, with one surgical team over a period of ten years, suggests the initial learning phase of robot-assisted laparoscopy in early stage cervical cancer to be at least 61 procedures, with a significant increase in disease-free survival and disease-specific survival after this initial learning phase. Overall, robot-assisted laparoscopy in patients with early stage cervical cancer shows high survival rates, comparable with observational results both historically after open surgery as well as currently in national surveys of robot-assisted surgery, when performed by an experienced surgical team. The impact of the learning curve of robot-assisted surgery on oncological outcomes warrants more attention and should be included in future studies on the safety of robot-assisted surgery.

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Disclosure of interests

R.P.Z. is a proctor for robot-assisted surgery in gynaecological oncology on behalf of Intuitive Surgical. All other authors declare they have no conflicts of interest related to the presented research.

Contribution to authorship

I.G.T.B., J.P.H., C.G.G. and R.P.Z. designed the study. R.H.M.V. and R.P.Z. performed all robotic surgeries. Data collection was carried out by J.P.H. and I.G.T.B. The statistical analysis was done by I.G.T.B. and the subsequent results interpreted by I.G.T.B., J.P.H., C.G.G. and R.P.Z. The manuscript was drafted by I.G.T.B., J.P.H. and C.G.G. , which was critically revised and approved by H.W.R.S., I.M.J.S., R.H.M.V. and R.P.Z.

Details of ethics approval

This study was based on the departmental complication and treatment outcome register for robot-assisted surgery, which is maintained as a part of standard clinical care and primarily aims to improve that care. The institutional review board was consulted and, in accordance to Dutch law, waived approval requirements for the use of the fully anonymised data.

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Table 1. Baseline characteristics of the two groups divided by the learning curve analysis.

	Group 1 (n=61)	Group 2 (n=104)	P
Age (years), median (range)	39 (24 – 81)	40 (23 – 81)	0.94
BMI (kg/m^2), median (range)	23.1 (19.3 – 31.6)	24.2 (18.0 – 41.0)	0.27
History of abdominal surgery	19 (31,1)	33 (31,7)	1.00
ASA score[a]	60	104	0.22
1	44 (73.3)	86 (82.7)	
[?]2	16 (26.7)	18 (17.3)	
FIGO stage			1.00[b]
IA1 and IA2	4 (6.6)	7 (6.7)	
IB1 and IIA	57(93.4)	97 (93.3)	
Histology			0.58
Squamous cell	41 (67.2)	71 (68.3)	
Adenocarcinoma	17 (27.9)	24 (23.1)	
Other (adenosquamous, clearcell, villoglandular)	3 (4.9)	9 (8.7)	
Grade [c]	60	102	0.26
I	10 (16.7)	27 (26.5)	
II	36 (60.0)	49 (48.0)	
III	14 (23.3)	26 (25.5)	
Type of procedure			0.38
PLND and RH	43 (70.5)	59 (56.7)	
PLND and RVT	8 (13.1)	20 (19.2)	
PLND only	4 (6.6)	9 (8.7)	
Other[d]	6 (9.8)	16 (15.4)	
SN procedure performed	53 (86.9)	92 (88.5)	0.96
LN harvested (excluding SN only), median (range)	27 (12-56)	24 (10-61)	0.31
LN harvested (excluding SN only)			
<17 lymph nodes harvested[e]	2 (3.3)	11 (11.0)	0.13[b]
[?]17 lymph nodes harvested	58 (96.7)	89 (89.0)	
Positive LN status	7 (11.5)	14 (13.5)	0.90
Positive LVSI	28 (45.9)	47 (46.1)	1.00
Positive parametrial involvement	4 (6.6)	4 (3.8)	0.47[b]
Adjuvant or adjusted treatment	15 (24.6)	20 (19.2)	0.54
Radiotherapy	10 (16.4)	8 (7.7)	0.22
Chemoradiation	5 (8.2)	12 (11.5)	

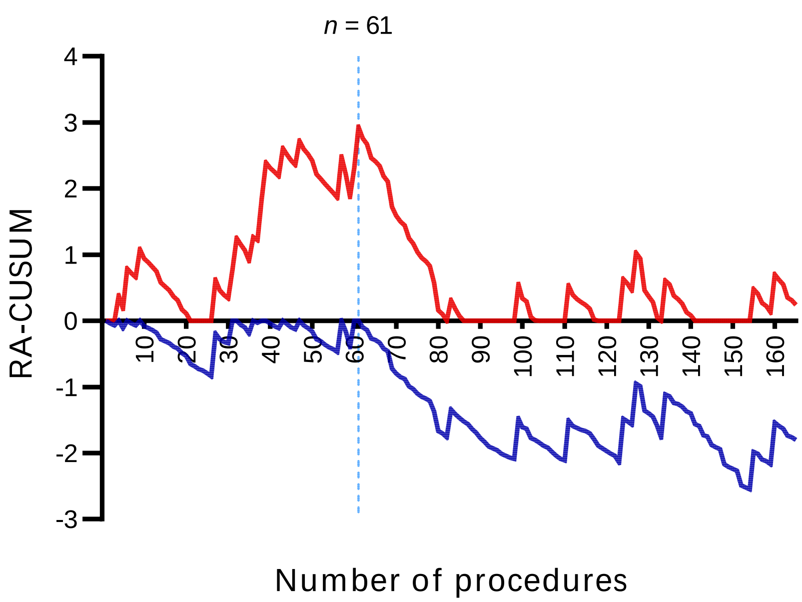
	Group 1 (n=61)	Group 2 (n=104)	P
Follow up duration (months), median (range)	62 (14-132)	43 (3-91)	<0.001[f]

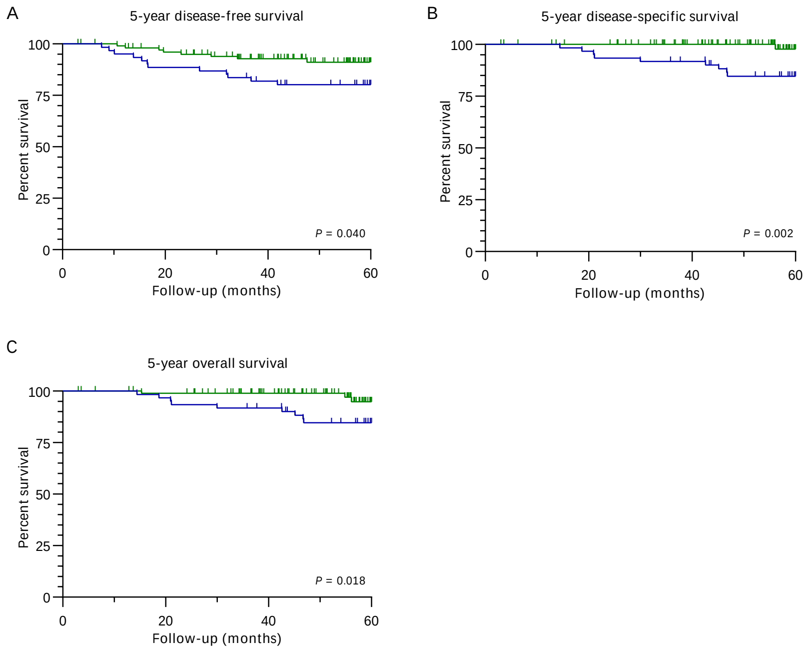
Data are presented as No. (%). Percentages may not total 100 because of rounding. BMI, body mass index. ASA, American Society of Anesthesiologists. FIGO, International Federation of Gynecology and Obstetrics; PLND, pelvic lymph node dissection; RH, radical hysterectomy; RVT, radical vaginal trachelectomy; SN, sentinel node; LN, lymph node; LVSI, lymph-vascular space invasion. Pearson's Chi squared test and Mann-Whitney U test were used for categorical data and median values, respectively, unless otherwise specified.[a]1 system missing; [b]Fisher's exact test (>20% expected count <5);[c] Three system missings (one villoglandular);[d] robot parametrectomy with PLND (n=10), robot RH only +/- SN (n=3), robot PLND with simple hysterectomy (n=1), laparoscopic PLND +SN expanded with robot RH (n=1), robot LN sampling because of suspected nodes (n=1), RVT + robot SN (n=2), robot PLND + SN with conisation (n=1), robot PLND + SN with radical cervical resection after supravaginal hysterectomy (n=1), robot RH with laparoscopic PLND + SN in two tempi (n=1), robot PLND + SN, RVT in another centre (n=1);[e] Cut-off based on earlier publication[36]; [f] Statistically significant.

FIGURE LEGENDS

Figure 1. The learning curve of robot-assisted laparoscopy for recurrent cervical cancer. The X-axis indicates the number of procedures performed. The Y-axis indicates the cumulative sum of success and failure of the surgical team in terms of recurrence, adjusted for the probabilities from the risk model. The RA-CUSUM+ (red) is designed to detect decrease in surgical performance while RA-CUSUM- (blue) is designed to detect increase in the surgical performance. Both curves move upward for surgical failure and downward for surgical success.

Figure 2. Kaplan-Meier survival curves for patients treated during the learning phase (blue) or the experiences phase (green). (A) Five-year disease-free survival. (B) Five-year disease-specific survival. (C) Five-year overall survival.




A
5-year disease-free survival
Percent survival
100
75
50
25
0
P = 0.040
0
20
40
60
Follow-up (months)
B
5-year disease-specific survival
Percent survival
100
75
50
25
0
P = 0.002
0
20
40
60
Follow-up (months)
C
5-year overall survival
Percent survival
100
75
50
25
0
P = 0.018
0
20
40
60
Follow-up (months)