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Robot-assisted versus open radical hysterectomy: A multi-institutional experience for early-stage cervical cancer[☆]

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Abstract

Objective: To compare perioperative and clinico-pathological outcomes of patients with early-stage cervical cancer who underwent robot-assisted radical hysterectomy (RRH) and open radical hysterectomy (ORH).

Methods: This retrospective multi-center study abstracted demographic, clinico-pathological and perioperative outcomes data from medical records of 491 cervical cancer patients treated with RRH (n = 259) ORH (n = 232) between 2005 and 2011 at two American and one Norwegian University Cancer Centres.

Results: Mean estimated blood loss (EBL) and transfusion rates were less for RRH than for ORH (97 vs. 49 mL, $p < 0.001$, and 3% vs. 7%, $p = 0.018$, respectively). Mean length of hospital stay (LOS) was significantly shorter in RRH versus ORH (1.8 vs. 5.1 days, $p < 0.001$). Mean operative time was longer for RRH than ORH (220 vs. 156 min, $p < 0.001$). Although overall complications were similar ($p = 0.49$), intra-operative complications were less common in the RRH group than ORH (4% vs. 10%, $p = 0.004$). In multivariate regression analyses longer operative time, less EBL and intra-operative complications, shorter LOS, and more pre-operative cone were significantly associated with RRH versus ORH. Recurrence and death rates were not statistically different for the two groups at a mean follow-up time of 39 months ($p = 1.00$ and $p = 0.48$, respectively).

Conclusions: RRH had improved clinical outcomes compared to ORH in the treatment of early-stage cervical cancer in terms of EBL, intra-operative complications, transfusion rates, LOS, and pre-operative cone. Disease recurrence and survival were comparable for the two procedures.

Keywords: Early-stage; Cervical cancer; Robotic radical hysterectomy; Open radical hysterectomy; Intra-operative complications; Morbidity; Recurrence; Survival

Introduction

Cervical cancer is the fourth most common cancer in women with an estimated 528,000 new cases worldwide in 2012. The estimated number of deaths in 2012 from cervical cancer was 266,000 worldwide, accounting for 7.5% of all female cancer deaths.[1]

☆ Previous presentation: Parts of this study were presented at a Scientific Plenary Session of the 46th Annual Meeting on Women's Cancer, Society of Gynecologic Oncology (SGO), in Chicago, IL, March 2015.

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The first open radical hysterectomy (ORH) was performed by Ernst Wertheim[2] in 1898, and the technique was modified by Joe Vincent Meigs[3] in 1944 who added pelvic lymphadenectomy to the original Wertheim procedure and published his series of 100 patients.[4] ORH has been the standard surgical treatment for early-stage cervical cancer since then. In the past three decades, gynecologic oncological surgeons have introduced minimally invasive surgical techniques in order to potentially improve both surgical and oncological outcomes while reducing the intra and post-operative complications and morbidity.

The first total laparoscopic radical hysterectomy (TLRH) with pelvic lymphadenectomy was reported by Michael Canis[5] in 1989. Since then, TLRH has gained acceptance as a feasible alternative to ORH due to reported benefits in terms of less blood loss, shorter hospital stay, and less post-operative analgesic needs.[5–9] Despite these advantages, TLRH has not been widely adopted in surgical practice. Lack of adoption has been attributed to the limitations of traditional laparoscopic tools, leading to a prolonged learning curve and ergonomic challenges for surgeons.[10–14]

Robot-assisted laparoscopic (computer-enhanced laparoscopic) techniques utilizing the da Vinci® Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA) emerged in the mid 2000s with the potential to overcome many of the recognized limitations of "straight-stick" laparoscopic tools available for complex gynecologic procedures. The advantages offered by robotic technology include a three-dimensional magnified camera system, tremor filtration, and seven degrees of instrument mobility inside the body ("wristed movement"), and improved ergonomics. There is convincing observational evidence that the intuitive nature of the robotic surgical system also has an additional advantage in terms of a shorter surgeon learning curve compared to traditional laparoscopy.[15,16]

In the last decade, the indications for clinical application of robotic surgery in gynecological oncology have been rapidly expanded. Shortly after the U.S. Food & Drug Administration (FDA) clearance for gynecologic surgery in 2005,[17] the first robot-assisted laparoscopic radical hysterectomy (RRH) for cervical cancer was reported by Bilal M. Sert[18] followed by several larger case series with historical controls demonstrating feasibility and potential benefits of RRH for treating patients with early-stage cervical cancer.[19–24] However, very few well-designed, matched case–control studies with adequate sample sizes have compared the results of ORH versus RRH.[22,25–28] Therefore, in this multi-center retrospective study with sufficient sample size, we did a comparative analysis of our data on early-stage cervical cancer patients who underwent either RRH or ORH with respect to intra-operative, clinico-pathological, and post-operative outcomes. We also reviewed previous comparative studies of such patients on these clinical outcomes.

Materials and methods

Patient samples

After excluding 26 patients who had received neoadjuvant chemotherapy, we identified 491 patients with early-stage cervical cancer who underwent Type II or Type III radical hysterectomy from 2005 to 2011 (Table 1). Cases were recruited from one European center (Oslo, Norway) and two American centers (Chapel Hill, NC and Orlando, FL). The sample distribution was 156 (32%) from Chapel Hill, 170 (35%) from Orlando, and 165 (33%) from Oslo. All patients (RRH = 259 and ORH = 232) were consecutively collected at each institution, beginning from close in time to the initiation of their respective robotic surgery programs.

Data collection

The local institutional review boards (IRBs) of the three centers approved the study for retrospective data collection. The operative, clinico-pathological and survival data were abstracted from the patients' medical records and included: age, body mass index (BMI), skin-to-skin operative time, estimated blood loss (EBL), hospital length of stay (LOS), tumor histology, FIGO stage, tumor size, positive surgical margins, lymphovascular space invasion (LVSI), lymph node yields, positive nodes present, transfusion volume, time to recurrence and/or death, pre-operative cone rate, cervical infiltration, disease recurrence and survival information. Clinic charts were reviewed for intra-operative and post-operative complications. Intra-operative complications happened during the surgery, while post-operative complication happened from end of surgery to 30 days post-operatively. The latter complication was coded according the Accordion Severity Classification 1: mild complications; 2: moderate complications; 3: Severe complications; and 4: post-operative death.[29]

The BMI was calculated as kilograms/meter^2 (kg/m^2). The EBL during operation was dichotomized as $<$150 mL or $\geq$150 mL, but not in the regression analyses. Correspondingly, length of stay (LOS) was dichotomized as $\leq$3 days or $>$3 days, but used as a continuous variable in the regression analyses. LVSI was defined as the presence of malignant cells in cervical stromal epithelial-lined spaces. Cervical tumor size was defined as the greatest measured diameter of the cervical lesion measured by the pathologist on the both cone and gross specimens. Comorbidity concerned the presence of other relevant somatic diseases such as hypertension and previous myocardial infarction, etc. Depth of stromal invasion was measured in millimeters (mm) from the basement membrane and categorized into thirds of the entire cervical stromal width.

Disease recurrence was determined clinically, radiographically, and/or histologically. The time-to-recurrence was calculated from the date of surgery until the patient

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Table 1
Characteristics of the clinico-pathological factors of robot versus open surgery groups.

Variables	Robot surgery (n = 259)	Open surgery (n = 232)	*p*-Value	Total sample (n = 491)
	Mean (SD)	*Mean (SD)*		*Mean (SD)*
Age at surgery, years	44.5 (11.7)	46.7 (12.2)	**0.04**	45.4 (12.0)
Follow-up time, months	34.6 (21.7)	45.2 (28.5)	**<0.001**[a]	39.6 (25.6)
Body mass index, kg/m^2	27.6 (6.5)	27.4 (6.6)	0.89	27.5 (6.6)
Operative time, minutes	220 (53)	156 (57)	**<0.001**	190 (64)
	N (%)	*N (%)*		*N (%)*
Treatment center				
Chapel Hill, NC	121 (47)	35 (15)	**<0.001**	156 (32)
Orlando, FL	79 (30)	91 (39)		170 (35)
Oslo, Norway	59 (23)	106 (46)		165 (33)
Estimated blood loss				
<150 mL	206 (80)	10 (4)	**<0.001**	216 (44)
≥150 mL	53 (20)	222 (96)		275 (56)
Hospitalization time				
≤3 days	156 (60)	35 (15)	**<0.001**	191 (39)
>3 days	103 (40)	197 (85)		300 (61)
Tumor size				
≤1.20 cm	129 (50)	101 (43)	0.16	230 (47)
>1.20 cm	130 (50)	131 (57)		261 (53)
Positive LVSI	88 (37)	92 (41)	0.35	180 (39)
Positive surgical margins	9 (4)	15 (7)	0.13	24 (5)
No of lymph nodes removed				
<20	96 (37)	94 (41)	0.35	190 (39)
≥20	163 (63)	134 (59)		297 (61)
Histology				
Squamous	146 (57)	135 (59)	0.76	281 (58)
Adenocarcinoma	94 (36)	83 (35)		177 (35)
Adenosquamous	8 (3)	6 (3)		14 (3)
Others	11 (4)	6 (3)		17 (4)
FIGO stages				
IA1 + IA2	36 (14)	22 (10)	0.13	58 (12)
IB1	206 (80)	183 (80)		389 (80)
≥IB2	17 (6)	24 (10)		41 (8)
Recurrence rate	23 (9)	21 (9)	1.00[b]	44 (9)
Death rate	7 (3)	9 (4)	0.48[b]	16 (3)
Intra-operative complications	9 (4)	23 (10)	**0.004**	32 (7)
Post-operative complications				
Grade I	17 (7)	18 (8)	0.73	35 (7)
Grade II	50 (19)	38 (16)	0.41	88 (18)
Grade III	8 (3)	5 (2)	0.58	13 (3)
Lymphocyst	4 (2)	8 (3)	0.24	12 (2)
Lymphedema	5 (2)	4 (2)	1.00	9 (2)
Transfusions rate	7 (3)	17 (7)	**0.018**	24 (5)
Pre-operative cone rate	175 (68)	101 (44)	**<0.001**	276 (56)
Post-operative radio-chemotherapy	70 (27)	76 (33)	0.17	146 (30)
Comorbidity	24 (9)	44 (19)	**0.002**	68 (14)
Positive nodes	25 (10)	29 (12)	0.49	54 (11)
Cervical infiltration	*N = 147*	*N = 195*		*N = 342*
None	40 (27)	7 (3)	**<0.001**	47 (14)
Outer 1/3	42 (29)	58 (30)		100 (29)
Inner 1/3	36 (24)	72 (37)		108 (32)
Middle 1/3	29 (20)	58 (30)		87 (25)

Bold represents p value ≤ 0.05.
Abbreviations: LVSI = lymphovascular space invasion; FIGO − International Federation of Gynecology & Obstetrics.
[a] Non-parametric Kruskal Wallis.
[b] Adjusted for follow-up time.

was noted to have disease recurrence. The disease-specific survival was defined as those patients who died from complications of cervical cancer and/or of the cancer progression. The overall survival was calculated from the date of surgery to the date of death (or the last follow-up date if the patient is alive), using a National Registry system associated with the Social Security System to confirm death records.

Surgical management

Stage IA1 with positive LVSI and stage IA2 patients were operated using Piver Type II techniques. Stage IB1 + IB2 patients were operated with Piver Type III radical hysterectomy. The surgical procedure for the Piver Type II and Type III ORH cases and RRH cases at all three participating institutions has been described previously.[20,24,30] All surgeons who participated in the study were competent in both surgical procedures although the RRH data sets included the learning curve time periods for the robotic-assisted procedure.

Supplementary treatment

Post-operative adjuvant therapies included external-beam radiotherapy delivered by a four field technique of 4100−5040 cGy ± weekly cisplatin ± brachytherapy; whole pelvic radiation therapy (WPRT) alone, or brachytherapy alone. Post-operative radiotherapy was administered for close (<3 mm) and positive surgical margins, lymph node metastasis or in case of parametrial invasion.[31] Patients with stage IB disease with negative lymph nodes, but with two or more of the following features: deep stromal invasion, capillary space involvement, and tumor diameter >4 cm also received post-operative radiotherapy according to updated GOG-92 study.[32] Salvage therapies included: intensity-modulated radiation therapy to a specific site of recurrence; WPRT ± chemotherapy, combination chemotherapy, and debulking/exenteration surgical procedures.

Statistical analyses

Between-group differences on continuous variables were analyzed with independent samples *t*-tests, and on categorical variables with chi-square tests. In case of skewed distributions, non-parametric tests were used. In order to evaluate strength of associations, bivariate and multivariable logistic regression analyses were used, and the strength of associations were expressed as odds ratios (OR) with 95% confidence intervals (95% CI). Kaplan−Meier plots were made for recurrence and death rates between the groups, and the log-rank test was applied for the eventual significant differences. The level of significance was set at $p < 0.05$, and all tests were two-tailed. The statistical software used was IBM SPSS for Windows version 20.0 (IBM Corp., Armonk, NY, USA).

Results

General characteristics of the sample

The general characteristics of the surgical groups are shown in Table 1. The mean age of patients at surgery was 45.4 ± 12.0 years, and the BMI was 27.5 ± 6.6 kg/m^2, which did not differ significantly between the surgical groups. The mean follow-up time after surgery was 39.6 ± 25.6 months for both groups combined.

Between-group comparisons

ORH cases had longer follow-up time than RRH ($p < 0.001$) secondary to the introduction of robotic surgery in 2006 with increasing numbers of cases in 2007 and 2008 as robotic surgery replaced laparotomy. The mean operation time was significantly longer ($p < 0.001$) and EBL <150 mL was more frequent ($p < 0.001$) in the RRH group. The rate of LOS ≤3 days was higher ($p < 0.001$) and the rate of intra-operative complication was lower ($p = 0.004$) in the RRH group. No significant between-group differences were observed for positive LVSI, positive surgical margins, number of lymph nodes retrieved, or concerning histology of the cervical cancers, FIGO stages, or the grading of post-operative complications between the two groups (Table 1).

The transfusion rate was lower ($p = 0.018$) in the RRH group, as was the transfusion rate, while no significant between-group differences were observed for post-operative chemotherapy. The pre-operative cone rate was lower in the ORH group ($p < 0.001$), but that group had higher rate of comorbidity ($p = 0.002$). Data on cervical stromal infiltration was only reported in 342 patients (66%), and such infiltration was significantly more common in the ORH group (Table 1).

Findings of the regression analyses

The significant between-group differences observed in Table 1 were confirmed in the bivariate logistic regression analyses with surgical groups as dependent variable (Table 2). In the multivariable analysis, longer operative time, less EBL and intra-operative complications, shorter LOS, and more pre-operative conization procedures remained significantly associated with the RRH group compared to the ORH group.

Findings of recurrence-free and overall survival analyses

Despite a relatively long-term follow-up analysis, the recurrence-free survival and overall survival did not differ significantly between the groups, and the Kaplan−Meier plots did not show significance between-group differences on the log-rank tests (Figs. 1 and 2). The mean recurrence and overall survival rates did not differ significantly between the groups (Table 1).

Review of previous studies

Table 3 gives an overview of key findings of eight studies comparing RRH and ORH including the present

Table 2
Bivariate and multivariable logistic regression analyses of independent variables with robot-assisted versus open surgery (reference) groups of patients with cervical cancer.

Variables	Bivariate analysis			Multivariable analysis		
	OR	95% CI	*p*-Value	OR	95% CI	*p*-Value
Age at surgery	0.99	0.97–0.99	**0.04**	1.01	0.97–1.04	0.77
Operation time	1.02	1.02–1.03	**<0.001**	1.03	1.02–1.04	**<0.001**
Estimated blood loss	0.98	0.98–0.99	**<0.001**	0.98	0.97–0.99	**<0.001**
Follow-up time	0.98	0.98–0.99	**<0.001**	0.99	0.98–1.01	0.40
Length of hospital stay	0.78	0.72–0.84	**<0.001**	0.88	0.78–0.99	**0.04**
Intra-operative complications	0.32	0.15–0.72	**0.006**	0.17	0.03–0.91	**0.04**
Transfusion given	0.35	0.14–0.86	**0.023**	0.75	0.11–5.27	0.77
Comorbidity present	0.44	0.26–0.74	**0.002**	1.05	0.34–3.26	0.94
Pre-operative cone	2.70	1.87–3.90	**<0.001**	3.15	1.43–6.91	**0.002**

Bold represents p value ≤ 0.05.
Abbreviations: OR = odds ratio; CI = confidence interval.

study.[20,22,25,27,28,33] All studies except our study have group sample sizes <64 cases, while ours were 259 for RRH and 232 for ORH. In all studies except the ones by Geisler et al.[25] and Cantrell et al.,[33] the operative time was longer for robotic than open surgery. In all studies the EBL and the transfusion rates were significantly lower and the LOS shorter in the RRH versus ORH group. In all studies other than Nam et al.[27] and our study the proportions of post-operative complications were higher in the ORH group.

Discussion

In our study the RRH group had significantly longer operative time, but lower rates of EBL <159 mL, intra-operative complications, transfusion rate, LOS ≤3 days, comorbidity, and more pre-operative conization compared to the ORH group. The review of previous studies of RRH versus ORH including this study showed that the operation time was longer, the transfusion rates significantly lower, and the LOS shorter in the RRH group

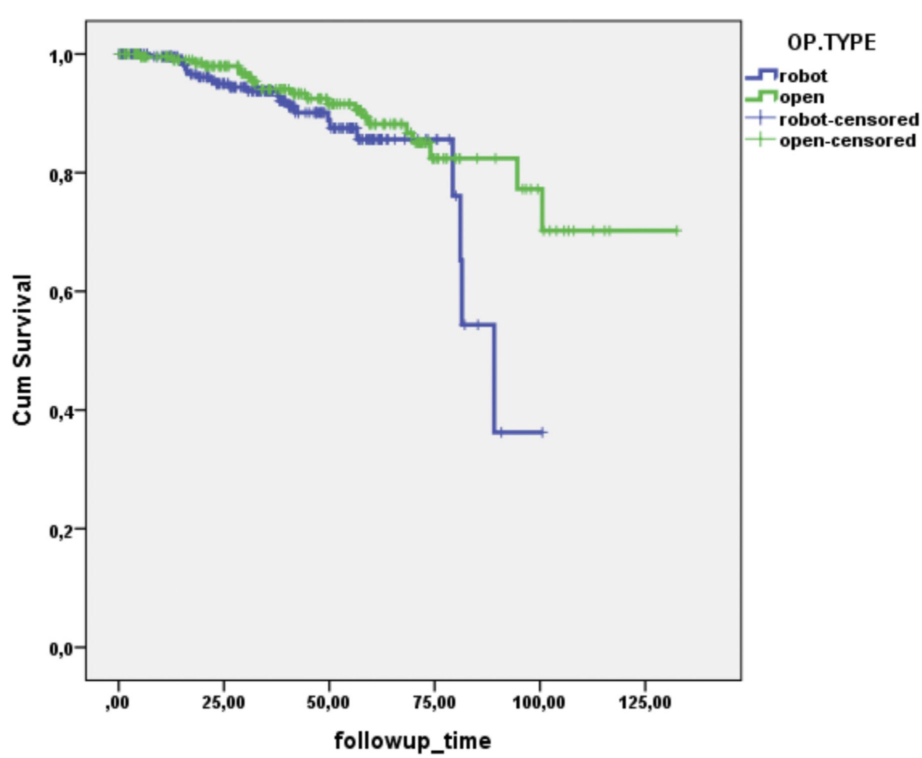

Figure 1. Kaplan–Meier plot of recurrence in the RRH and OPH groups (log-rank test $p = 0.12$).

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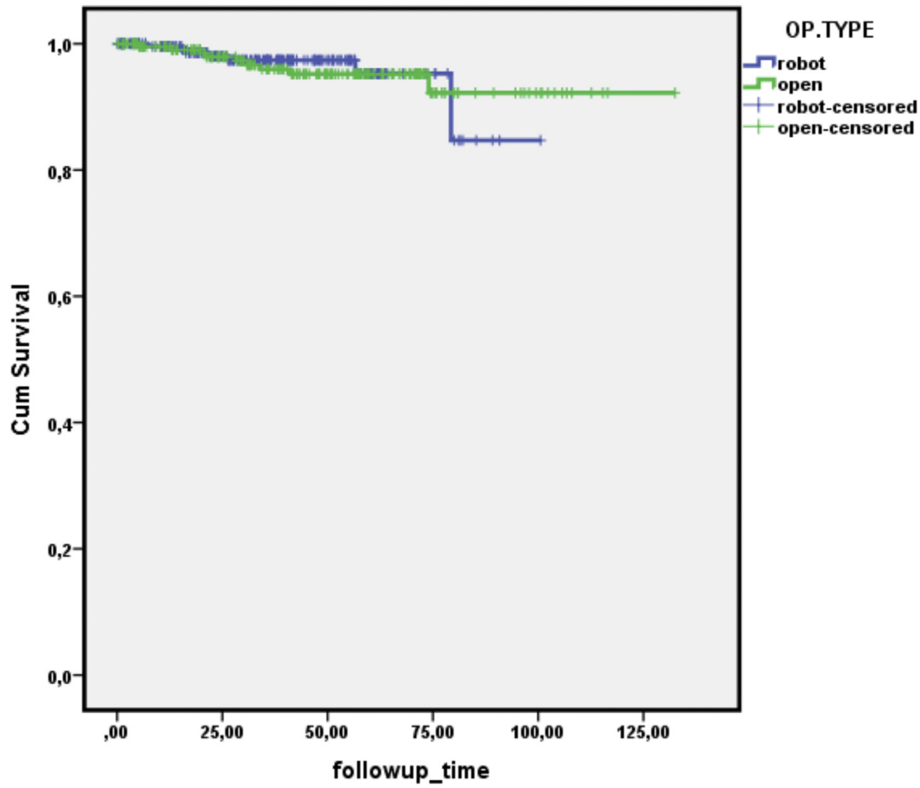

Figure 2. Kaplan–Meier plot of deaths in the RRH and OPH groups (log-rank test $p = 0.85$).

Table 3
Summary of the key characteristics of previously reported studies comparing the RRH (Robot) and ORH (Open) procedures for patients with cervical cancer.

Variables	Ko et al. [2008] n = 48		Boggess et al. [2008] n = 100		Maggioni et al. [2009] n = 80		Geisler et al. [2010] n = 60		Schreuder et al. [2010] n = 27		Nam et al. [2010] n = 64		Cantrell et al. [2010] N = 127		Sert et al. [2015] n = 491	
Surgery	Robot	Open	Robot	Open	Robot	Open	Robot	Open	Robot	Open	Robot	Open	Robot	Open	Robot	Open
Patients (n)	16	32	51	49	40	40	30	30	13	14	32	32	63	64	259	232
BMI	28	27	29	26	24	24	34	32	ND[1]	ND[1]	22	22	28	25	28	27
Mean																
Median																
Operative time[2]	270	203	211	248	272	199	154	166	434	225	220	210	213	240	219	156
Mean																
Median																
EBL[3]	82	666	97	417	78	221	165	323	300	2000	221	532	50	400	97	431
Mean																
Median																
Transfusion rates (%)	6	31	0	4	8	23	0	7	ND	ND	3	64	ND	ND	3	7
LOS[4]	1.7	4.9	1.0	3.2	3.7	5.0	1.4	2.8	4	9	11.6	16.9	1	4	2.9	5.2
Mean																
Median																
Lymph nodes[5]	16	17	34	23	20	26	24	26	29	26	20	24	29	24	25	23
Mean																
Median																
Complications[6]																
Intra-operative	0	3	ND	ND	5	13	ND	ND	8	0	3	0	2	2	4	10
Post-operative	13	22	8	16	33	55	ND	ND	0	21	84	59	3	5	29	26

Abbreviations: [1] ND = no data; RRH = robot-assisted radical hysterectomy; ORH = open radical hysterectomy; BMI = body mass index; [2] Operat time = skin-to-skin operation time in minutes; [3] EBL = estimated blood loss in milliliters; [4] LOS = hospital length-of-stay in days; [5] Lymph nodes removed; [6] Operative complications (%).

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compared to ORH one. Most studies observed that the proportions of post-operative complications were more frequent with ORH,[20,22,26,34] while so was not the case for graded post-operative complications in our study.

Comparison with previous studies

Given the large sample sizes of the two groups in our study insight into the somewhat conflicting findings in studies with smaller patient cohorts may be evident. The potential benefits of RRH include decreased EBL, fewer transfusions, shorter LOS, low conversion to laparoscopy/laparotomy and possibly fewer intra-operative complications.[35,36] However, this result comes with the expense of longer operative times, at least during learning phases of the robotic procedures compared to ORH.[15,37] In addition, since fellows in training participated in most procedures, multiple learning curves are likely represented, although this may hold true for ORH cases as well.

Since the performance of the first laparoscopic hysterectomy by Harry Reich[38] and first laparoscopic radical hysterectomy by Michael Canis[5] more than 25 years ago gynecologic surgeons have argued about the comparability of the minimally invasive and traditional laparotomy procedure. This argument was renewed with the performance of the first robotic-assisted radical hysterectomy about a decade ago.[18]

Several other studies have demonstrated a significant increase in operative time associated with the robotic approach.[22,26,28] On the other hand, Boggess et al., Geisler et al., and Cantrell et al. have found longer operative time with open surgery compared to the robotic approaches in their respective training centers.[20,25,33] This result may partly be explained by educational purposes and the learning curves of assistants and residents, and by additional procedures such as peritoneal washing, sentinel lymph nodes procedures and supra-pubic catheter placement. It is more important to note the actual mean time difference between the two surgical procedures is approximately about 20—40 min. This time-difference for RRH may be acceptable when compared to the benefits of reduced blood loss, shorter LOS, fewer intra-operative complications and likely quicker return to normal activities associated with the robotic procedures which is more precise and has minimal tissue damage. We can also see the cosmetic outcomes comparing abdominal incision after ORH and five small trocar incisions after RRH (Figs. 3 and 4). We might expect that robotic operative times may decrease on subsequent analyses of more mature operative experiences, remote to learning curve phases.

In this study we noted a significantly lower rate of EBL ≥150 mL in the RRH group, similar to all other previous studies.[20,22,25—28,33] Among the 458 patients whose records included information on blood loss 81% was less than <150 mL among RRH, whereas 96% of open procedures led to blood loss of >150 mL ($p < 0.001$). In addition 7% of ORH patients required blood transfusion in association with open radical hysterectomy compared to 3% of patients who had RRH ($p = 0.018$). These results are also comparable with several other previous single-institution observational studies and reports.[20,22,25—27]

We also demonstrated lower LOS for RRH group compared to ORH ($p < 0.001$) in this study. Not all single institutional series reported a reduction in LOS, likely influenced by social norms in their respective countries regarding hospitalization requirements. In 61% of the cases in the current study 20 or more lymph nodes were removed, with no difference between the two procedure groups. These results are comparable with several other studies comparing early experiences with RRH and ORH,[25—28,33] indicating that lymph node dissections are comparable. Therefore we would not necessarily expect differences in survival secondary to inadequate lymph node assessment.

Most of the studies comparing RRH and ORH have not analyzed use of post-operative adjuvant therapies.[39] All

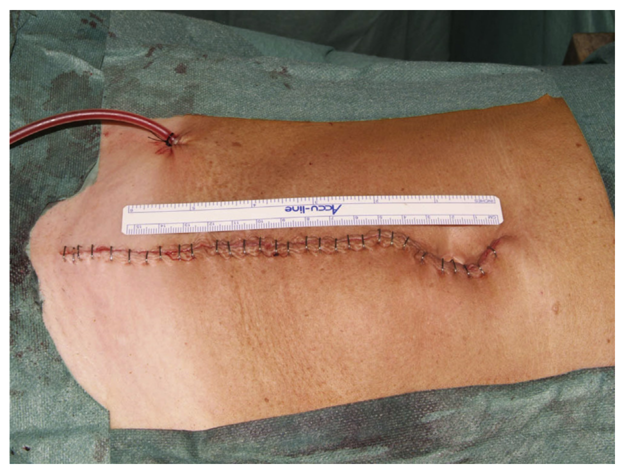

Figure 3. Abdominal incision after ORH.

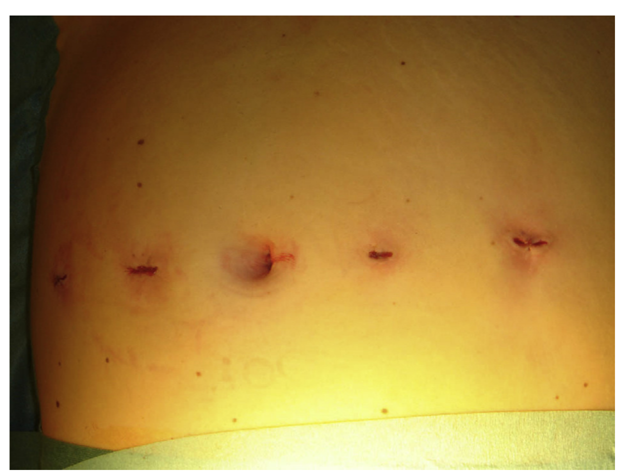

Figure 4. Five small trocar incisions after RRH.

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three institutions have primarily used Sedlis' criteria for use of post-operative adjuvant therapy in node negative patients following radical hysterectomy.[31] In this study; post-operative radiotherapy with concomitant chemotherapy was given to 27% of the RRH versus 33% of ORH cases ($p = 0.17$). This finding is within the reported post-operative adjuvant therapy usually of 25%–80% of cases.[40–42] These results from single institutions are relatively small retrospective studies without uniform criteria for adjuvant therapy decides prospectively, and none of them are randomized controlled trials. Significant differences in patient selection and/or institutional treatment philosophy could explain the wide variation in reported use of adjuvant therapies.

Summary of main findings

By merging data from three university centers our sample sizes achieved adequate statistical power to compare surgical and survival outcomes between robot-assisted and open radical hysterectomy cases in early-stage cervical cancer. We observed that ten variables were significantly associated with operation type (surgical approach). In multivariable logistic regression analyses, five independent variables remained significantly associated with RRH for early-stage cervical cancer versus ORH, namely longer operation time, less EBL >150 mL and LOS >3 days LOS, fewer intra-operative complications, and higher pre-operative conization rate.

Clinical implications

RRH has several significant advantages compared to ORH as a surgical technique.[43] Estimated blood loss, transfusions, and hospital LOS were all improved with the RRH approach, despite the learning curve experiences reported. Operative times were longer with RRH, but will likely improve with experience. There were no differences observed in disease recurrence or survival, although follow-up time in the RRH patients shorter than ORH patients. In our retrospective study we were unable to analyze cost mainly due to the differences in health insurance systems and cost infrastructures in the countries of origin of this study. The literature on cost data is also conflicting. Halliday reported significantly higher costs for ORH compared to RRH, however amortization costs for the robotic surgical unit were not included.[44] Hospital costs of robot-assisted laparoscopic surgery are higher than alternatives but clinical effectiveness data are limited.[45] Robotic surgery has the potential to become cost-effective in centers with high case-loads that reduce the per-case amortization costs while industry competition over time will likely reduce the cost of the robotic instrumentation and maintenance, making robotic technology more affordable and cost-effective.[46] Clearly the transition from ORH to RRH (not previously witnessed with standard laparoscopy) has reduced hospital LOS which is a major component of cost in the US. And may potentially speed return to normal activities which has other economic benefits. Future studies will need to assess all these factors when cost-effectiveness is analyzed.

Strength and limitations

The primary strength of our study is our sample size and inclusion of three geographically distinct centers with multiple surgeons. Another strength is our review of previous studies showing common agreements and disagreements across many studies. A potential limitation is the merging of data from three university centers without adequate quality assurance of common definitions of variables. For example, we lacked staging of intra complications. We utilized the Accordion grading system of surgical complications reported by Strasberg et al.[29] (Table 1). Another limitation concerns the variation in treatment coverage. In Norway hospital treatment in general is for free, while in the United States such treatment is covered by a variety of insurances. Such administrative differences could influence patient recruitment and selection of surgical modality. A further limitation is missing data concerning with some variables. A large number of surgeons were involved in the procedures from each institution with no information on individual learning curves regarding robot surgery which limits interpretation of the data with respect to "learning curves", or determination of what proportion of cases were beyond individual surgeon's learning curves. Lastly, the follow-up time for RRH cases was relatively short compared to ORH, however beyond 24 months when the majority of recurrences in cervical cancer are expected to occur.

Conclusions

Recurrence of disease and deaths for patients with early-stage cervical cancer treated with robotic radical hysterectomy were comparable to that of open radical hysterectomy. RRH cases were observed to have significantly less EBL, transfusion needs, LOS, and fewer intra-operative complications in spite of longer operative times and had similar rates of graded post-operative complications.

Robot-assisted laparoscopic procedures account for a rapidly growing proportion of all hysterectomies performed in the United States and Europe. In the absence of randomized trials to compare clinical outcomes with open radical hysterectomy retrospective comparisons such as in the present study can be hypothesis generating and at least guide clinical management with some degree of uncertainty. Results from this study should be further evaluated in a larger multi-center setting with mature surgical experiences. We eagerly await the results of a phase III randomized clinical trial of laparoscopic or robotic radical hysterectomy versus abdominal radical hysterectomy in patients with early-stage cervical cancer that was initiated in January 2008 and has an estimated study completion date July 2022.[47]

Conflict of interest statement

All co-authors declare that there are no conflicts of interest associated with this manuscript, except Dr. Robert W. Holloway has received compensation for advanced training programs from Intuitive Surgical, Inc. (Sunnyvale, CA).

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