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Original Research

Short-term outcomes for patients with endometrial cancer who received robot-assisted modified radical hysterectomy: A retrospective observational study

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Objective: Minimally invasive surgery is a standard treatment for endometrial cancer patients with uterine-confined disease. Robot-assisted surgery has been covered under public insurance since 2018 in Japan. The aim of the current study was to compare the short-term outcomes between robot-assisted modified radical hysterectomy (RAMRH) and total laparoscopic modified radical hysterectomy (TLMRH). *Methods*: A total of 190 patients with endometrial cancer who had undergone RAMRH or TLMRH were retrospectively reviewed. Short-term outcomes, including surgical time, estimated blood loss, complications, and hospital stay, were compared between the groups. *Results*: Among 190 patients, including 67 with RAMRH and 123 with TLMRH, the median (interquartile range [IQR]) surgical time was 247 (IQR: 221-313) min in RAMRH and 271 (IQR: 236-280) min in TLMRH. The estimated blood loss was less than 10 mL in most cases. There was 1 major vessel injury and 1 vescio-vaginal fistula in the RAMRH group. In contrast, there were 2 bladder injuries, 1 bowel injury, 2 obturator nerve injuries, 1 major vessel injury, and 2 pelvic abscesses in the TLMRH group. The median hospital stay was 10 (IQR: 10-10) days in RAMRH and 9 (IQR: 9-10) days in TLMRH. *Conclusion*: Robot-assisted procedures were not associated with poorer short-term outcomes than laparoscopy in patients with endometrial cancer.

Keywords

Endometrial cancer; Robot assisted hysterectomy; Laparoscopic hysterectomy; Minimally invasive surgery

1. Introduction

Minimally invasive surgery, including robot-assisted or laparoscopic hysterectomy, for patients with endometrial cancer has been performed worldwide [1]. According to the National Comprehensive Cancer Network (NCCN) guidelines, total hysterectomy, bilateral salpingo-oophorectomy, and lymph node assessments for endometrial cancer patients can be performed via any surgical route, including laparoscopic, robotic, vaginal, and abdominal, although the standard approach in cases of apparent uterine-confined disease is to perform the procedure via a minimally invasive approach. However, the NCCN guidelines also note that laparotomy may still be required for patients with metastatic presentations [2]. Robot-assisted hysterectomy has been performed since 2002 in the United States [3]. The percentage of endometrial cancer patients undergoing this procedure in the United States increased from 9.5% in 2008 to 56.8% in 2015 [4].

Abdominal hysterectomy has been performed for patients with endometrial cancer in Japan; however, laparoscopic hysterectomy has been covered under public insurance since 2014 for stage IA endometrial cancer. Robot-assisted hysterectomy was also covered under public insurance in 2018. Similar to other countries, minimally invasive approaches have been standard treatments for early endometrial cancer patients in Japan. Furthermore, the rate of robot-assisted hysterectomy is increasing rapidly. The aim of the current study was to compare the short-term outcomes between robot-assisted modified radical hysterectomy (RAMRH) and total laparoscopic modified hysterectomy (TLMRH).

2. Materials and methods

2.1 Participants

Of the patients with endometrial cancer who had undergone RAMRH or TLMRH and bilateral salpingo-oophorectomy with or without lymph node dissection at the Osaka Medical College in Japan between September 2017 and August 2020, 190 were eligible for the study and were retrospectively reviewed.

Patients who met the following criteria were eligible for inclusion in the study: (1) planned robot-assisted or laparoscopic hysterectomy with salpingo-oophorectomy for low-risk endometrial cancer (FIGO stage IA with grade 1 or 2 endometrioid carcinoma); (2) correct information available from medical records; and (3) no chemotherapy or radiotherapy performed before surgery. Most patients had undergone sentinel node biopsy. Pelvic lymph node dissection was per-

Table 1. Characteristics of the patients who underwent robot-assisted modified radical hysterectomy and total laparoscopic modified radical hysterectomy for endometrial cancer.

	RAMRH	TLMRH	*P* value
Number of patients	67	123	
Age (years)*	56.5 ± 10.1	57.9 ± 11.1	0.40
BMI*	24.4 ± 6.2	24.7 ± 5.4	0.80
FIGO stage (%)			
IA	62 (92.5)	97 (78.9)	0.01
IB	3 (4.5)	13 (10.6)	0.15
III	2 (3.0)	10 (8.1)	0.16
IV	0	3 (2.4)	0.20
Histological type (%)			
Endometrioid G1 or G2	63 (94.0)	117 (95.1)	0.75
Endometrioid G3	2 (3.0)	3 (2.4)	0.83
Serous	2 (3.0)	2 (1.6)	0.53
Carcinosarcoma	0	1 (0.8)	0.46
Approach to lymph nodes (%)			
No dissection	0	8 (6.5)	0.03
SNNS	57 (85.1)	84 (68.3)	0.01
PLD	6 (9.0)	22 (17.9)	0.10
PLD + laparoscopic PAND	4 (6.0)	2 (1.6)	0.10
Conversion to laparotomy (%)	0	7 (5.7)	0.70
Complications (%)	2 (3.0)	8 (6.5)	0.03
Bladder injury	0	2	0.29
Bowel injury	0	1	0.46
Obturator nerve injury	0	2	0.29
Major vessel injury	1	1	0.66
Vesico vaginal fistula	1	0	0.17
Pelvic abscess	0	2	0.29
Median surgical time (IQR), min	247 (221-313)	271 (236-280)	0.90
Mean surgical time* (min)	281 ± 83	283 ± 72	0.90
Estimated blood loss (%)			
< 10 mL	56 (83.6)	87 (70.7)	0.045
≥ 10 mL	11 (16.7)	36 (29.3)	0.045
Blood transfusion	1	0	0.17
Median hospital stay (IQR), day	9 (8-9)	10 (10-10)	0.04

* According to an analysis of variance (mean ± standard deviation); RAMRH, robot-assisted modified radical hysterectomy; TLMRH, total laparoscopic modified radical hysterectomy; BMI, body mass index; FIGO, International Federation of Gynecology and Obstetrics; SNNS, sentinel node navigation surgery; PLD, pelvic lymph node dissection; PAND, para-aortic node dissection; IQR, interquartile range.

formed for patients with large tumours or those who did not wish to undergo sentinel node biopsy. Lymph node assessment was not performed for older patients or for those with complications. Omentectomy was performed for patients who tested positive for intraperitoneal cytology. Laparoscopic or abdominal para-aortic lymph node dissection was performed for patients who were diagnosed with stage IB disease or high-grade tumours at the time of surgery. Abdominal conversion was performed for patients with advanced disease. Although patients could choose between robot or laparoscopy, we could plan the robot-assisted hysterectomy for only once a week at our hospital.

In the current study, TLMRH was performed in more than 300 cases at the beginning of the study, while RAMRH was performed for the first time. Robot-assisted para-aortic lymph node dissection is not covered by public insurance; thus, patients who were considered to be at a lower risk received RAMRH, while those at a higher risk received TLMRH.

2.2 Surgical procedures

We have previously reported the procedures of the surgery [5–7] and sentinel node biopsy [8, 9]. The intra-abdominal procedures of robot-assisted and laparoscopic surgery are the same. Robot-assisted surgery was performed using the da Vinci Si system in 15 cases and the Xi system in 52 cases. Fig. 1 shows the arrangement of ports for both robot-assisted and laparoscopic surgery. The patients were positioned at an inclination angle of 25° for robot surgery and 10° for laparoscopy with the lithotomy. Both, TLMRH and RAMRH, were performed by two surgeons who are experts in gynaecologic oncology. Each surgeon had an experience of performing TLMRH for more than 100 patients at the beginning of the study, while surgeons performed RAMRH for the first time in the current study. In the first 20 cases, RAMRH was performed by two surgeons, and in the remaining 47 cases, it was performed by one surgeon.

2.3 Statistical analyses

All statistical analyses were performed using the JMP software program (version. 15.1.0). Continuous variables are expressed as median (interquartile range [IQR]) or mean ± standard deviation. The Mann-Whitney U-test was used to compare continuous variables, and Fisher's exact test was used to compare frequencies (non-continuous variables). *P*-values < 0.05 were considered to indicate statistical significance.

3. Results

Among the 190 patients with clinically low-risk endometrial cancer who had undergone minimally invasive surgery, 67 had undergone RAMRH and 123 had undergone TLMRH. The mean age was not markedly different between the groups (56.5 ± 10.1 vs. 57.9 ± 11.1 years, $P = 0.4$). The body mass index was not markedly different between the groups (24.4 ± 6.2 vs. 24.7 ± 5.4, $P = 0.8$). In the RAMRH group, 62 (92.5%) patients had stage IA disease, 3 (4.5%) had stage IB disease, and 2 (3.0%) had stage III disease. In the TLMRH group, 97 (78.9%) had stage IA disease, 13 (10.6%) had stage IB disease, 10 (8.1%) had stage III disease, and 3 (2.4%) had stage IV disease. Histologically, in the RAMRH group, 63 (94.0%) patients had grade 1 or 2 endometrioid carcinoma, 2 (3%) had grade 3 endometrioid carcinoma, and 2 (3.0%) had serous carcinoma. In contrast, in the TLMRH group, 117 (95.1%) patients had grade 1 or 2 endometrioid carcinoma, 2 (2.4%) had grade 3 carcinoma, 2 (1.6%) had serous carcinoma, and 1 (0.8%) had carcinosarcoma. In the RAMRH group, 57

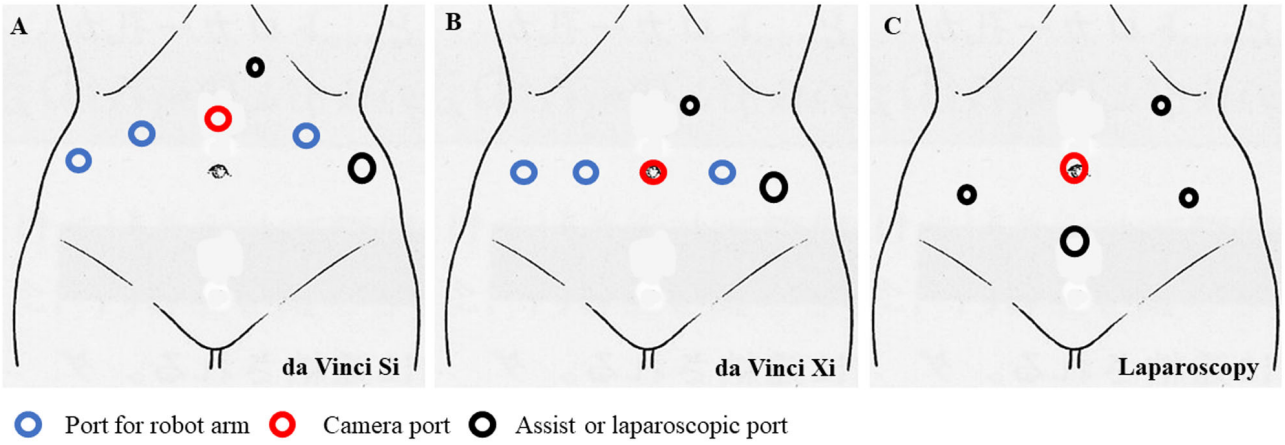

Fig. 1. Port arrangement. (A) Robot-assisted surgery (da Vinci Si) (B) Robot-assisted surgery (da Vinci Xi) (C) Laparoscopic surgery.

(85.1%) patients underwent sentinel node navigation surgery (SNNS), 6 (9.0%) underwent pelvic lymph node dissection (PLD), and 4 (6.0%) underwent PLD and laparoscopic para-aortic lymph node dissection (PAND). In the TLMRH group, the lymph node status was not assessed in 8 (6.5%) patients, 84 (68.3%) underwent SNNS, 22 (17.9%) underwent PLD, and 2 (1.6%) underwent laparoscopic PLD and PAND. Seven (5.7%) patients converted to laparotomy because of advanced disease. There were 2 (3.0%) complications ($\geq$ grade III on the Clavien-Dindo classification) in the RAMRH and 8 (6.5%) in the TLMRH group. In the RAMRH group, 1 major vessel injury occurred during surgery and 1 vesico vaginal fistula was found after surgery. In the TLMRH group, there were 2 bladder injuries, 1 bowel injury, 2 obturator nerve injuries, and 1 major vessel injury during surgery. A pelvic abscess was found in 2 patients after surgery. The median surgical time was 247 (IQR: 221-313) min for RAMRH and 271 (IQR: 236-280) min for TLMRH. The mean surgical time was 281 $\pm$ 83 min for RAMRH and 283 $\pm$ 72 min for TLMRH. There were no significant differences between the groups (P = 0.9). The estimated blood loss was less than 10 mL in most cases; 83.6% of the patients in the RAMRH group and 70.7% of the patients in the TLMRH group had less than 10 mL blood loss at surgery. There was 1 blood transfusion in the RAMRH group. In contrast, no patient received blood transfusion in the TLMRH group. The median hospital stay after surgery was 9 (IQR: 8-9) days in the RAMRH group and 10 (IQR: 10-10) days in the TLMRH group (Table. 1).

Fig. 2 shows the surgical time, console time, and estimated blood loss in each case of RAMRH. The surgical time and console time decreased with the progress in the number of cases. The estimated blood loss was less than 10 mL in most cases. One patient had 2100 mL blood loss during surgery due to a large amount of bleeding occurring in the right vesicouterine ligament. Eight units of RBCs were transfused in this case. Fig. 3 shows the learning curve of the RAMRH. The mean and median docking times were 27.4 $\pm$ 7.8 and 26 (IQR: 20-32) min, respectively, with y = -0.28 + 37. The mean and median operation times were 280 $\pm$ 83 and 247 (IQR: 220-270) min, respectively, with y = -1.8x + 340. The mean and median console times were 199 $\pm$ 53 and 188 (IQR: 157-229) min, respectively, with y = -1.7x + 257.

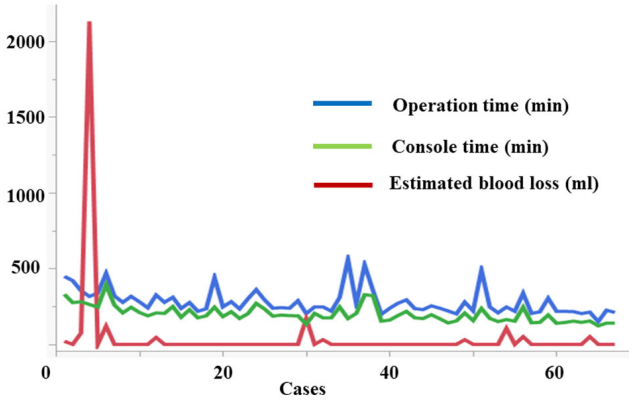

Fig. 2. All parameters in robot-assisted modified radical hysterectomy for patients with low-risk endometrial cancer. Operation time and console time decreased with each case. Estimated blood loss was less than 10 mL in most cases.

4. Discussion

Total hysterectomy and bilateral salpingo-oophorectomy with lymph node assessment have been performed as primary treatments for uterine-confined endometrial cancer. Although this procedure may be performed through any surgical route, including abdominal, vaginal, laparoscopic, and robotic, minimally invasive approaches are considered as standard approaches for apparent uterine-confined disease [10]. Several meta-analyses, randomised trials, systematic reviews, and population-based studies have shown that minimally invasive approaches are preferred because of lower rates of surgical site infection, transfusion, venous thromboembolism, decreased hospital stay, and lower cost of care, without compromising on the oncologic outcomes.

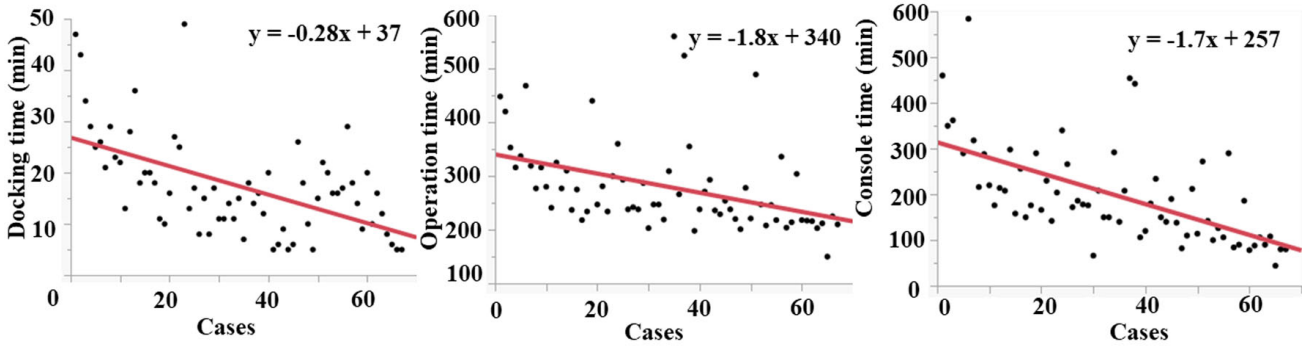

Fig. 3. Learning curve in robot-assisted modified radical hysterectomy for low-risk endometrial cancer. Trends in docking time, operation time and console time with robot-assisted modified radical hysterectomy. The mean and median docking times were 27.4 ± 7.8 and 26 (IQR: 20-32) min, respectively. The mean and median operation times were 280 ± 83 and 247 (IQR: 220-270) min, respectively. The mean and median console times were 199 ± 53 and 188 (IQR: 157-229) min, respectively. y = -0.28x + 37 in docking time, y = -1.8x + 340 in operation time, and y = -1.7x + 257 in console time, where x = 67 cases.

For these reasons, robot-assisted laparoscopic hysterectomy is preferred over abdominal hysterectomy and considered to be a standard surgery for uterine-confined endometrial cancer [11–14].

There have been several meta-analyses of surgery for endometrial cancer comparing robot-assisted and laparoscopic hysterectomy. Robot-assisted hysterectomy had fewer complications and lower estimated blood loss than laparoscopic hysterectomy. The number of removed pelvic lymph nodes did not differ between robot-assisted and laparoscopic surgery [15–20]. The long-term oncologic outcomes were not different between robot-assisted and laparoscopic surgery [21, 22]. Siestro *et al.* reported the long-term prognosis of patients with endometrial cancer who underwent robotic, laparoscopic, and abdominal hysterectomy. Among the 363 patients with endometrial cancer, 175 underwent robot-assisted hysterectomy, 101 underwent laparoscopic hysterectomy, and 87 underwent abdominal hysterectomy with a median follow-up period of 51.4 months (minimum of 2 years). The surgical route did not affect the 5-year survival rate. The recurrence rate was 10.9% for robotic hysterectomy and 12.9% for laparoscopic hysterectomy. The rate of low-risk patients was about 50% in both the robot and laparoscopy groups. Cardenas *et al.* reported the long-term prognosis among 415 patients with endometrial cancer who had undergone minimally invasive surgery. In this study, 183 patients had undergone robot-assisted hysterectomy and 232 had undergone laparoscopic hysterectomy with a median follow-up period of 38 months. Overall survival (3-year survival rate, 93.3% vs. 93.6%, P = 0.9) and disease-free survival (3-years disease-free survival rate, 83.3% vs. 88.4%, P = 0.9) were not different between the groups. The recurrence rate was 14.8% in the robotic and 12.1% in the laparoscopic procedure. In the study described above, the rate of low-risk disease was 70%. In our study, it was 89.5% for RAMRH and 77.2% for TLMRH. No patient had recurrence in the RAMRH group with a median follow-up period of 8 (IQR: 5-19) months. Three patients (2.4%) had recurrence in the TLMRH group with a median follow-up period of 12 (IQR: 4-19) months. In Japan, minimally invasive hysterectomy for endometrial cancer is covered under public insurance, however, the indication is stage IA disease; most patients with stage IB or more advanced disease undergo open surgery. Further research with a larger number of participants is needed to assess long-term oncologic outcomes in Japan.

Traditionally, we performed extra-fascial total abdominal hysterectomy for endometrial cancer in our institution. Since laparoscopic and robot-assisted surgery are new methods, modified radical hysterectomy was selected as a reliable method for performing extra-fascial hysterectomy [7, 10]. However, several studies have shown that a more aggressive surgical approach does not improve prognosis in open surgery [23–25].

Generally, the cost of robotic surgery is more expensive than that of laparoscopy. However, the difference in cost between the robot and laparoscopy decreases with bulk orders of instruments. In our institution, robotic surgery is commonly used for patients with stomach cancer, lung cancer, colon cancer, prostate cancer, kidney cancer, bladder cancer, and uterine cancer. Furthermore, education and the development of new techniques is highly prioritized since our institution is a medical college.

In the current study, the mean length of hospital stay was 9-10 days, which was much longer than that in most studies from Western Europe and the United States. Since the cost of medical care in Japan is extremely low compared to other countries, patients are more inclined towards receiving medical care. Furthermore, due to the complicated social health insurance system in Japan, each hospital calculates the approximate length of hospital stay for hospital management. At our hospital, for patients with endometrial cancer, the length of hospital stays for RAMRH and TLMRH is 9 and 10 days, respectively.

The present study has a few limitations that cannot be overlooked. First, the sample size was relatively small. Second, the evaluation of lymph node status was not the same between the groups. Third, there was a bias in the choice of robot or laparoscopy. Given that this was a retrospective observational comparative study, our results must be confirmed in further investigations, such as a prospective cohort study.

5. Conclusions

The short-term outcomes were not significantly different between RAMRH and TLMRH for low-risk endometrial cancer.

Abbreviations

IQR, interquartile range; NCCN, National Comprehensive Cancer Network; PAND, para-aortic lymph node dissection; PLD, pelvic lymph node dissection; RAMRH, robot-assisted modified radical hysterectomy; TLMRH, total laparoscopic modified radical hysterectomy.

Author contributions

TT, SU, KT, and KK designed the research study. SM, ST, HK, TK, SF, and YT performed data collection and curation. TT, KT, KK, and MO wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Osaka Medical College Research Review Board (2015-11), and all patients provided written informed consent.

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Conflict of interest

The authors declare no competing interests. The authors alone are responsible for the content and writing of the paper.

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