Original Article

Robot-assisted Surgery with Para-aortic Lymphadenectomy for Endometrial Cancer: A Preliminary Report

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Abstract

Objectives: There are few reported cases of robot-assisted surgery for endometrial cancer with para-aortic lymphadenectomy (PAL) in Japan. Therefore, this study aimed to examine the clinical outcomes of robot-assisted surgery with PAL for endometrial cancer.

Materials and Methods: This retrospective cohort study was analyzed 13 endometrial cancer patients who underwent robotic surgery with PAL between January 2011 and October 2018 at our hospital. We examined their perioperative complications and oncological outcomes.

Results: The median follow-up period, median overall survival, and disease-free interval were 80 months, 79 months (61–120), and 79 months (5–120), respectively. There were two (15.3%) cases of perioperative complications of Clavien–Dindo Class II or higher and three (23.0%) cases of recurrence.

Conclusion: Our results showed that the surgical and oncological outcomes of robot-assisted surgery for endometrial cancer with PAL were comparable with those of other developed countries.

Keywords: Minimum invasive surgery, para-aortic lymphadenectomy, robotic surgery

Introduction

Recently, there has been an increase in the number of endometrial cancer patients undergoing minimally invasive surgeries and an expansion of the indications for these procedures worldwide.[1] Since April 2014, laparoscopic surgery for uterine cancer has been performed more often because it is covered by health insurance in Japan. Furthermore, our health insurance began covering robot-assisted surgery for endometrial cancer in April 2018. There are few reported cases of robot-assisted laparoscopy for endometrial cancer with para-aortic lymphadenectomy (PAL) in Japan. This study aimed to examine the clinical outcomes of robot-assisted surgery for endometrial cancer with PAL at our hospital.

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Materials and Methods

Patients

This study was a retrospective analysis in a single facility; it was approved by the Ethical Committee of Tokyo Medical University (No.TS2020-0269). All study participants provided informed consent. We performed robot-assisted surgery with PAL in 13 moderate or high-risk patients with endometrial cancer from January 2011 to October 2018. Patients in whom standard procedures could not be performed due to the presence of simultaneous multiple cancers or serious complications (such as heart failure and diabetes mellitus) at the time of the surgery were excluded. All patients underwent mechanical bowel preparation and

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lower extremity mechanical compression before surgery and received perioperative antibiotics and low-molecular-weight heparin after surgery. We analyzed these 13 patients. Data were collected from medical records, which included patient characteristics such as age, body mass index (BMI), medical complications, and history of previous abdominal surgery. Gynecological data were collected, including overall survival (OS), disease-free interval (DFI), recurrence rate, surgery duration, perioperative complications, bleeding amount, postoperative hospital stay, histological type grade, the International Federation of Gynecology and Obstetrics (FIGO) stage, number of dissected lymph nodes, lymph node metastasis, and adjuvant chemotherapy.

OS was calculated from the day of initial surgery to the end of June 2021, the final examination, or death. The DFI was from the day of initial surgery to the end of June 2021 or when recurrence was diagnosed. Perioperative complications were classified according to the Clavien–Dindo classification and events equivalent to Class II or higher were considered perioperative complications.

Surgical procedures and adjuvant chemotherapy

The surgeries were performed by a single surgeon using the da Vinci surgical system Si (Intuitive Surgical, Sunnyvale, CA, USA). The procedure of robot-assisted surgery included total hysterectomy, bilateral salpingo-oophorectomy, and bilateral para-aortic and pelvic lymph node dissection. All surgical procedures were performed under general anesthesia. The patient laid on the operating table with the gel pad in place and was placed in the Trendelenburg position using a levitator, after general anesthesia. Both arms were placed by the patient's side and shoulder blocks were used. The head position was 30° down when docking the robot.

We performed PAL by the da Vinci approaching from the foot side (reverse parallel docking). After PAL, the da Vinci was rolled out. We then turned around the da Vinci to approach from the head side (parallel docking) and performed a total hysterectomy and pelvic lymph node dissection [Figure 1].

When we performed PAL, da Vinci was placed in the reverse parallel docking position. When we performed the pelvic surgical procedure, da Vinci was placed in the parallel docking position.

First, pneumoperitoneum was achieved using a pneumoperitoneum needle at the navel. Next, a da Vinci camera port trocar was inserted 10 cm below the navel on the line running from the navel to the midpoint of the pubis using the Optiview method. Then three da Vinci trocars (8 mm in diameter) were inserted endoscopically. Next, a 12-mm assistant port was inserted between the 12-mm trocar under the navel and the 8-mm da Vinci trocar on the lower right abdomen.

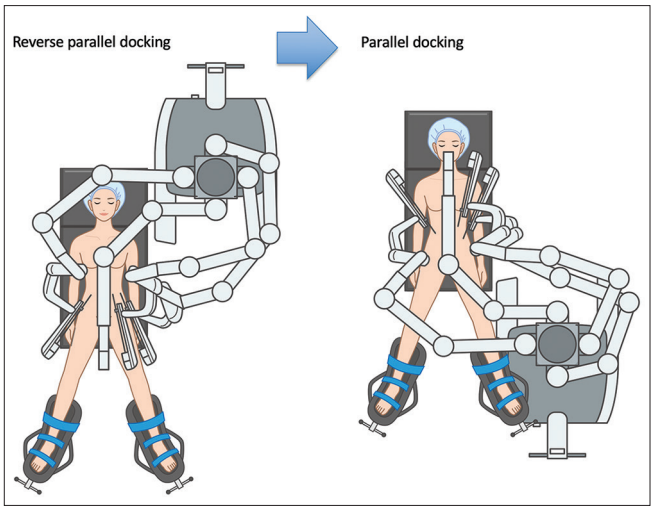

Figure 1: An image of the da Vinci surgical system docking

Furthermore, a 12-mm port was inserted from the umbilicus to 5 cm above it. After PAL, a da Vinci trocar was added to the patient's upper right navel and the da Vinci camera port and 12-mm port were exchanged [Figure 2].

A 0° camera was used throughout the procedure. A uterine manipulator was placed in the uterus after the bilateral fallopian tubes were sealed with a sealing device.

After surgery, we recommend postoperative adjuvant chemotherapy for patients at intermediate or high risk of recurrence by pathological examination. Chemotherapy consisted of docetaxel and carboplatin (DC) therapy (docetaxel: 70 mg/m^2 + carboplatin: AUC5–6) for three to six cycles.

Statistical analysis

We used SPSS version 26 (IBM Corp., Armonk, NY, USA) to perform the analysis. The number following the ± sign is a standard deviation. OS and disease-free survival were calculated by the Kaplan–Meier method.

Results

The median follow-up period, age, and BMI was 80 months, 57 (25–57) years, and 20.3 (17.4–32.3) kg/m^2, respectively. The median OS was 79 months (61–120). The estimated mean OS was 114.9 months (95% confidence interval [CI]: 93.1–136.7 months) [Figure 3], and the median DFI was 79 months (5–120). The estimated mean DFI was 102.8 months (95% CI: 76.0–129.6 months) [Figure 4], respectively.

Eight patients were FIGO Stage I (61.5%), two were Stage II (15.4%), one was Stage IIIA (7.7%), one was Stage IIIC1 (7.7%), and one was Stage IIIC2 (7.7%). The histological type was endometrioid carcinoma G1 in four patients (30.8%), endometrioid carcinoma G2 in two patients (15.4%), endometrioid carcinoma G3 in

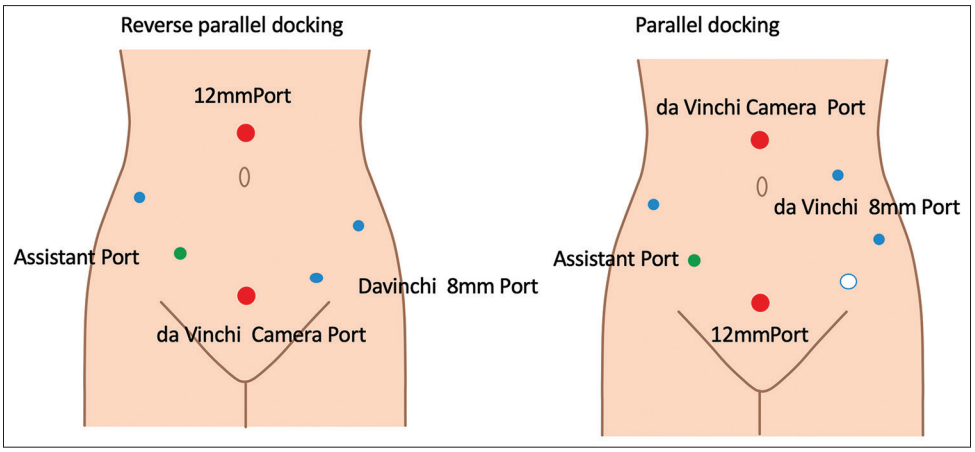

Figure 2: Port placement. Blue is the da Vinci 8-mm port. Red is the da Vinci camera port and 12-mm port. Green is the assistant port

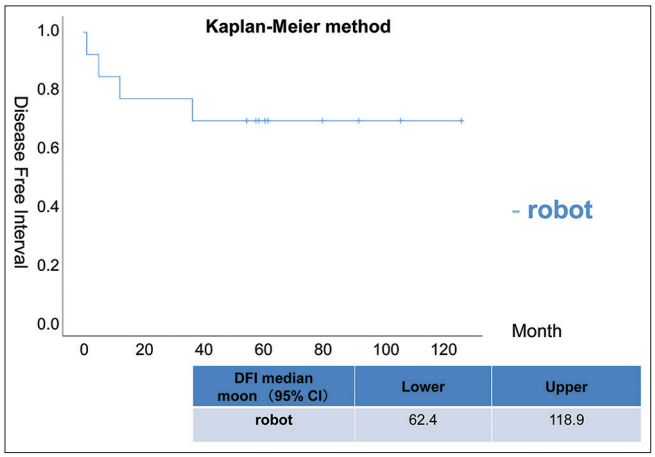

Figure 3: Kaplan–Meier curves of disease-free survival

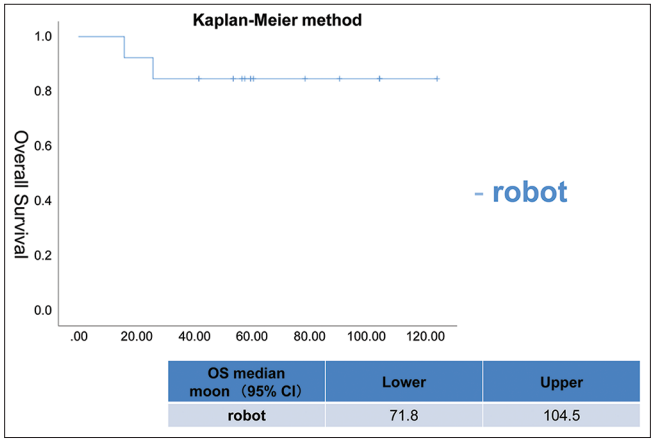

Figure 4: Kaplan–Meier curves of overall survival

five patients (38.4%), and clear-cell carcinoma in two patients (15.4%). The mean surgical time in the 13 patients was 396 (229–435) min, the total blood loss was 10 (10–3368) g, and the postoperative length of hospital was 3 (3–7) days. In addition, the number of pelvic and para-aortic lymph nodes dissected was 29 (21–69) and 16 (1–51), respectively. There were two (15.3%) cases of perioperative complications of Clavien–Dindo Class II or higher.

Seven patients (53.8%) received adjuvant chemotherapy, whereas two patients declined adjuvant chemotherapy. There were two cases of lymph node metastasis to the pelvic (left and right) and para-aortic lymph node areas. No recurrence has been observed in either case to date.

There were three cases (23.0%) of recurrence; recurrence case 1 was classified as pT1bN0M0 (FIGO IB), endometrioid carcinoma Grade 1. Ascites cytopathology was negative. Postoperatively, the patient was observed without adjuvant chemotherapy as the patient had requested. Recurrence was observed in the vaginal stump and pelvis 36 months after surgery. Recurrence case 2 was classified as pT2N0M0 (FIGO II), endometrioid carcinoma Grade 3. Ascites cytopathology was negative. Six cycles of DC therapy were administered as adjuvant chemotherapy. Recurrence was observed in the stump of the vagina, a right obturator lymph node, and the para-aortic lymph node area 5 months after surgery. Recurrence case 3 was classified as pT1aN0M0 (FIGO IA), endometrioid carcinoma Grade 2. Ascites cytopathology was positive. Three courses of DC therapy were administered as adjuvant chemotherapy. Recurrence was observed as peritoneal dissemination 12 months after surgery. There were no cases of port-site metastasis.

Discussion

Endometrial cancer is a common gynecological cancer in Japan.[2] When a patient is diagnosed with endometrial cancer, comprehensive surgical staging, which includes hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection or biopsy, and peritoneal cytology, is performed through laparotomy. It is known that endometrial cancer (even Stage I which is limited to the uterus) often presents with lymph node metastasis.[3]

Regional lymph nodes in endometrial cancer are widely distributed; they are not limited to the pelvic lymph nodes but extend to the para-aortic lymph nodes located inferior to the renal veins.[4,5] In surgeries for uterine malignancies, PAL is considered important for evaluating the stage and risk of recurrence and for treating enlarged retroperitoneal lymph nodes.[6] Para-aortic lymph node metastasis is an important prognostic factor in uterine cancer, and appropriate treatments should be added based on accurate staging of patients at moderate-to-high risk of recurrence.

The LAP2 trial showed no difference between laparoscopy and laparotomy in the comprehensive surgical staging of uterine cancer.[7] Recently, robot-assisted laparoscopic surgical staging for gynecological cancer has become an alternative treatment with no observed increase in complication rates, reduced blood loss, and equivalent number of dissected lymph nodes, compared with laparoscopic surgery.[8-10] The 2018 edition of the Japanese clinical guidelines for endometrial cancer states that laparoscopic surgery is recommended for endometrial cancers in patients at low risk of recurrence, as defined by the FIGO.[11] For endometrial cancer in patients at moderate-to-high risk of recurrence, it is controversial whether minimally invasive surgery (MIS) is superior to laparotomy.[3] There is still insufficient evidence and few investigations into the surgical techniques and outcomes have been carried out. It has also been reported that the recurrence rate is not significantly different between MIS and laparotomy, even in advanced endometrial cancer when the postoperative Stage is III or IV.[7,12] Some guidelines for endometrial cancer treatment do not recommend MIS for advanced cases (if it has advanced outside the uterine serous membrane).[13]

Robot-assisted surgery was first introduced in the field of gynecological malignancies by Reynolds *et al*.[14] Recently, many studies have reported that robot-assisted surgery was equal or superior to laparotomy and laparoscopic surgery in terms of perioperative surgical outcomes.[15-17] Unlike other developed countries, robotic surgery has not been widely performed in Japan. The Japan national health insurance had not covered robotic surgery previously. However, in April 2018, our national health system began covering robot-assisted laparoscopy for uterine malignancies, and the number of cases is increasing.[18] We performed surgery with PAL for uterine malignancies when no extrauterine infiltration was observed in preoperative examinations: (1) endometrioid carcinoma invading 1/2 or more of the muscle layer (Grades 1, 2), or (2) endometrioid carcinoma regardless of muscle layer invasion (Grade 3), and when the pathological features were determined to be of special type, such as serous. Our results are not different from those of previous reports in terms of postsurgical complications, recurrence-free survival, and OS.[19] Our surgical outcomes, including the number of lymph nodes dissected, amount of blood loss, length of hospital stay, and surgical time, were not different from those of previous studies. In addition, compared with previous reports, there was no obvious difference in the number of pelvic and para-aortic lymph nodes removed.[20,21] Robot-assisted surgery is believed to be superior to laparotomy in retroperitoneal lymphadenectomy. However, because our department elevates the pelvis to 30º, robot-assisted procedures are contraindicated in patients with serious systemic complications, cerebrovascular accident, respiratory dysfunction, or glaucoma; these cases should undergo laparotomy.[22-24]

In laparoscopic hysterectomy, inserting a uterine manipulator simplifies the surgery. However, more positives are detected in cytology when a manipulator is used.[25] Therefore, we inserted the manipulator after double sealing or clipping of both fallopian tubes with a sealing device; thus, the number of positives detected on ascites cytopathology did not increase.[26] Since robot-assisted surgery is less invasive than laparotomy, it reduces physical burden and is thought to shorten the postoperative length of stay. In terms of costs, these procedures not only reduce the financial burden on patients but are also believed to lower medical costs. In addition, the number of dissected pelvic and para-aortic lymph nodes did not differ among laparoscopic surgery, robot-assisted laparoscopy, and laparotomy.[27] It is believed that it is possible to maintain a level of curability in robot-assisted retroperitoneal lymphadenectomy similar to that in laparotomy.

Robot-assisted surgery was converted to laparotomy in one patient due to intraoperative bleeding from the inferior mesenteric artery. Another patient underwent emergency surgery for an incarcerated small bowel hernia following the insertion of a da Vinci port in the lateral abdomen 14 days after robot-assisted surgery. However, there were no cases of lymphatic leakage, ileus, or other complications that required treatment. In the early stage of endometrial cancer, port-site metastasis is reported to be as low as 0.3%.[28] We try to prevent port-site metastasis when lymph nodes are removed from the body by inserting a metallic tube into the port and then removing the lymph nodes from inside the tube or placing them in an isolation bag as soon as they are dissected. Four cases of recurrence were observed in this study. The recurrence rate was not less than that of laparotomy with PAL.[5] Moreover, the peculiar laparoscopic surgery recurrence type, such as port-site metastasis, was not found.[29] Every case of recurrence was found to be in the surgical field.

In Japan, AP therapy (doxorubicin: 60 mg/m^2 + cisplatin: 50 mg/m^2) or TC therapy (paclitaxel: 175 mg/m^2 + carboplatin:

AUC5–6) is recommended as an adjuvant for the high-risk group during recurrence.[10] However, AP therapy has been reported to have a high rate of occurrence of adverse events such as Grade 3/4 hematologic toxicity, gastrointestinal disorders, cardiotoxicity, and neurotoxicity.[30] The incidence of peripheral neuropathy is lower with DC therapy than TC therapy, and there is no significant difference in treatment response rate, disease-free survival, and OS.[31] Therefore, we recommend DC therapy for patients at high risk of recurrence.

This study has some limitations. First, it was conducted in a single facility, and the sample size was small. Second, when the pelvis needs to be elevated to 30°, robot-assisted procedures are contraindicated in patients with serious systemic complications, cerebrovascular accidents, respiratory dysfunction, or glaucoma. Third, radiation therapy was not used as adjuvant therapy in this study. Multiple randomized controlled trials have reported that it reduces pelvic recurrence but does not contribute to increase OS.[32,33] Therefore, adjuvant radiotherapy is generally not performed in Japan. This resulted in a selection bias. In the future, more cases need to be accumulated and more cases should be considered for oncological outcomes.

Conclusions

We present 13 cases of robot-assisted laparoscopy for endometrial cancer that included PAL for patients at moderate-to-high risk of recurrence. We will continue to accumulate cases and examine the optimal surgical methods and oncological outcomes.

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Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Conflicts of interest

Prof. Hirotaka Nishi, an editorial board member at *Gynecology and Minimally Invasive Therapy*, had no role in the peer review process of or decision to publish this article. The other authors declared no conflicts of interest in writing this paper.

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