

Robotic-Assisted Fertility-Sparing Surgery for Early Ovarian Cancer

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ABSTRACT

Objective: To show the feasibility and safety of robotic-assisted laparoscopic fertility-sparing surgery for early-stage ovarian cancer in women of reproductive age.

Methods and Design: The first patient was a 29-year-old para 0 woman with well-differentiated endometrioid adenocarcinoma of the ovary and complex endometrial hyperplasia with marked atypia. The second patient was a 31-year-old para 0 woman with an immature grade 1 teratoma. Both patients underwent robotic-assisted laparoscopic surgical staging.

Results: In the first patient, there were no intra- or postoperative complications. Operative time was 5 hours 43 minutes and estimated blood loss was 100 mL. She was discharged home on postoperative day 1. She received 3 cycles of carboplatin and paclitaxel, as well as medroxyprogesterone acetate for the duration of chemotherapy. She conceived twice spontaneously since surgery and had two successful deliveries. She currently has no evidence of disease.

In the second patient, there were no intra- or postoperative complications. Operative time was 2 hours 52 minutes and estimated blood loss was 200 mL. She was discharged home on postoperative day 1. She declined adjuvant chemotherapy with bleomycin, etoposide, and cisplatin. She conceived spontaneously 4 months later and had a normal vaginal delivery. She currently has no evidence of disease.

Conclusions: Because fertility-sparing surgery is now accepted as a viable option in young women with early-stage ovarian cancer, less invasive techniques are being used. With the advent of robotic-assisted surgery and its advantages over conventional laparoscopy, we show that it is a safe and feasible approach in select patients. This is

the first reported series on robotic fertility-sparing surgery, but more research is needed.

Key Words: Ovarian cancer, Fertility-sparing surgery, Reproductive age women, Robotic surgery, Enhanced laparoscopic surgery.

INTRODUCTION

Although ovarian cancer is usually diagnosed in postmenopausal women, 12% of ovarian cancer cases occur in women of child-bearing age.¹

Epithelial ovarian carcinomas (EOCAs) comprise approximately 90% of all ovarian malignant tumors.² Several reports have estimated that 3% to 17% of all EOCAs occur in woman younger than 40 years of age.³ Ovarian germ cell tumors (GCTs) account for 20% to 25% of all ovarian neoplasms; however, only 3% are malignant. The peak incidence of GCTs is in young women or adolescent girls, accounting for 58% of all ovarian tumors in women younger than 20 years of age; one-third of these tumors are malignant.⁴

Traditionally, treatment consisted of complete surgical staging in the form of total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and pelvic and para-aortic lymphadenectomy. A more conservative approach is now being used with preservation of the uterus and contralateral ovary in patients with early-stage cancer who want to remain fertile.⁵

Although several authors have reported their experiences with laparoscopic fertility-sparing surgery, to our knowledge, there have been no reported cases of robotic-assisted fertility-sparing surgery. We present two cases of robotic-assisted fertility-sparing surgery in reproductive-aged women: one for EOCA and the other for GCT.

Both surgeries were performed at a university-affiliated teaching hospital by a board-certified gynecologist-oncologist proficient in robotic surgery and assisted by a surgical fellow specializing in minimally invasive gynecological surgery, as well as a resident.

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CASE 1

A 29-year-old woman (gravida 0 para 0)—5 feet 2 inches tall and weighing 120 lbs, with a body mass index of 21.95—without any significant past medical or surgical history presented for evaluation of infertility, at which time a left ovarian cyst was found. In November 2008, she underwent a laparoscopic left ovarian cystectomy, ablation of endometriosis, hysteroscopic polypectomy, and endometrial biopsy. Findings were significant for pelvic endometriosis and a left ovary adhered to the sidewall with a dermoid-appearing cyst, as well as an endometrial polyp. During separation of the cyst, inadvertent rupture occurred. The pathology of the cyst revealed a well-differentiated endometrioid adenocarcinoma with foci of squamous metaplasia, and the endometrial pathology showed proliferative endometrium and polypoid fragments of endometrium with complex endometrial hyperplasia with marked atypia. Subsequently, she was referred to our center for evaluation.

A positron emission tomography–computed tomography scan revealed a focus of activity corresponding to the uterus and increased activity in the ovaries bilaterally, however, with low standard uptake value (SUV) of 2 on the left and 2.1 on the right. *BRCA 1/2* were negative and a CA-125 marker was 10 U/mL.

After consultation with the patient and based on her desire for future fertility, in December 2008 she underwent fertility-sparing surgery in the form of an examination under anesthesia, exploratory laparoscopy, peritoneal washings, omentectomy, robotic-assisted laparoscopic left salpingo-oophorectomy, left extensive pelvic side wall dissection, ureterolysis, bilateral pelvic and para-aortic lymphadenectomy, multiple peritoneal biopsies, hysteroscopy, and dilation and curettage. Specifically because the ovary was severely attached to the side wall, to be certain that no metastatic disease remained, extensive resection of the left pelvic side wall, pararectal area, and left uterosacral ligament was performed.

Operative findings revealed an 8-cm uterus and no obvious signs of peritoneal carcinomatosis or ascites. The left ovary was attached to the left pelvic sidewall and contained necrotic tissue. The uterus and right fallopian tube and ovary were completely normal.

There were no intraoperative or postoperative complications, including port site metastasis. Total operative time was 5 hours 43 minutes, and estimated blood loss was 100 mL. She was discharged home on postoperative day 1. There were 17 peritoneal and diaphragmatic biopsy spec-

imens, 18 pelvic lymph nodes, and 13 para-aortic nodes and omentum, all of which were found to be benign. However, some biopsy specimens were positive for endometriosis. Endometrial curettings revealed complex hyperplasia with tubal metaplasia, no atypia, and follicular cysts and small foci of endometriosis of the left ovary. Peritoneal washing samples were negative for malignancy.

Based on recommendations from our hospital multidisciplinary tumor conference, she received 3 cycles of carboplatin and paclitaxel. In addition, because of the diagnosis of atypical hyperplasia, she also received medroxyprogesterone acetate for the duration of her chemotherapy.

She has conceived twice spontaneously since her surgery and had two successful pregnancies. At the time of this writing, she is currently without evidence of disease (46 months).

CASE 2

A 31-year-old woman (para 0)—5 feet 4 inches tall and weighing 162 lbs, with a body mass index of 27.8—with no significant past medical history presented to her gynecologist with left lower quadrant pain and a palpable mass on examination. Transvaginal ultrasonography revealed a complex cystic and solid lesion in the left adnexa measuring 7.4 × 7.3 × 9.7 cm. CA-125 marker reading was 6.7 U/mL, CA-19-9 was 8.2 U/mL, carcinoembryonic antigen (CEA) was 1.6 ng/mL, inhibin A was 24.7 pg/mL, and human chorionic gonadotropin was <0.5 mIU/mL. In February 2010, she underwent a laparoscopic cystectomy for presumed benign dermoid cyst; however, pathologic findings revealed an immature grade 1 teratoma. During the procedure, the cyst was inadvertently ruptured, and she was sent to our center for consultation.

A positron emission tomography–computed tomography scan was performed and demonstrated no evidence of intraperitoneal or retroperitoneal metastatic disease. Based on recommendations from our hospital multidisciplinary tumor conferences, she underwent robotic-assisted surgical staging in April 2010.

Operative findings revealed an 8-cm uterus with disseminated suspicious peritoneal lesions in different parts of the pelvic cavity ranging from 1 mm to 2 cm. The right fallopian tube and ovary were completely normal. The left ovary was severely attached to the pelvic sidewall with necrotic tissue. The mid and upper abdomen was normal except for a 2-mm lesion on the surface of the right diaphragm.

Peritoneal washings were obtained, and the robotic-assisted laparoscopic approach included resection of all peritoneal lesions and left salpingo-oophorectomy, with the infracolic omentectomy performed via conventional laparoscopy. A frozen section of one of the peritoneal lesions was positive for metastatic immature teratoma; based on that finding and also the low probability of the lymph nodes being affected, no lymphadenectomy was performed.

There were no intra- or postoperative complications, including port site metastasis. Total operative time was 2 hours 52 minutes, and estimated blood loss was 200 mL. She was discharged home on postoperative day 1. Pathology findings revealed teratomatous disease in the left ovary and 4 biopsy sites (rectum, cul-de-sac, pelvic side wall, and right broad ligament) with focally immature-appearing cartilage. The omentum was negative, endometrial curettings showed proliferative endometrium, and peritoneal washings were negative for malignancy.

Because her stage was IC, recommendation from a multidisciplinary tumor conference was that she be treated with three cycles of adjuvant chemotherapy in the form of bleomycin, etoposide, and cisplatin. However, the patient refused and opted for observation.

The patient conceived spontaneously and had a normal spontaneous vaginal delivery in March 2011. At 19 months' follow-up, she had no evidence of disease.

Operative Technique

Using general endotracheal anesthesia, the patients were placed in the dorsal lithotomy position using Allen stirrups with venodyne boots. In both cases, a standard Intuitive robotic platform (Intuitive Surgical, Sunnyvale, CA) was used. Port placement included a 12-mm primary, 4 cm above the umbilicus, 2 robotic 8-mm midlateral, and 10-mm and 5-mm ports in the right and left upper abdomen for introduction of ancillary instruments. After the robotic apparatus was docked, robotic bipolar and electrosurgical scissors are inserted and used for desiccation and cutting the tissues.⁶

After thorough laparoscopic evaluation of the abdominal and pelvic cavity and after obtaining peritoneal washings, the robot was docked and the robotic portion of the surgery proceeded. Adhesions were extensively lysed using a combination of sharp dissection and electrosurgery. The left ovary was mobilized from the pelvic sidewall, and a left pelvic wall dissection was performed. After identifying the ureter, the infundibulopelvic ligament was elec-

trodesiccated and the left tube and ovary were confined to a laparoscopy bag and removed from the abdominal cavity. An extensive resection of the left pelvic sidewall to the pararectal area and the left uterosacral ligament was performed, and all areas were inspected for possible metastatic disease.

In both cases, all peritoneal lesions were removed. Multiple biopsies from different parts of the anterior, posterior, left, right, pelvic, and abdominal wall were performed.

In the first case, lymphadenectomy was performed. For pelvic lymphadenectomy, after the pelvic side wall on each side was opened, the paravesical and pararectal spaces were developed and pelvic nodes were sampled from the external iliac vessels (from the mid common iliac artery to the deep circumflex vein), obturator fossa, and hypogastric vessels. The right tube and ovary were preserved. For the para-aortic lymphadenectomy, the posterior parietal peritoneum was incised over the right common iliac artery. The incision was extended all the way up to the gonadal vein on the right side and the renal vein on the left side. The ureters were identified, and the para-aortic nodes over the vena cava on the right side and on the left side from below and above the inferior mesenteric artery were sampled. The inferior mesenteric artery was electrodesiccated and cut to allow complete removal of all of the lymph nodes. The robotic apparatus was removed. Infracolic omentectomy was performed laparoscopically.^{7,8}

DISCUSSION

We present two successful cases of robotic-assisted laparoscopic fertility-sparing surgery for stage IC well-differentiated endometrioid adenocarcinoma and stage IC immature teratoma. Both patients were successfully treated, conceived spontaneously, and currently have no evidence of disease.

In both cases, surgical restaging was important, both to remove the affected ovary and to correctly stage the patients. This played a role in predicting future prognosis and in altering the decision for postoperative chemotherapy.

Zanetta et al.⁹ in 1997 published one of the earlier reports on fertility-sparing surgery for reproductive age women with epithelial ovarian cancer. They showed that this is an appropriate treatment option for early-stage patients with an acceptable oncological safety profile. Since then, several authors have published their results.

Case 1: Epithelial Ovarian Cancer

In 2002, Schilder et al.¹⁰ published a multi-institutional retrospective investigation on patients with stage IA and IC epithelial ovarian cancer who were treated with fertility-sparing surgery (in the form of unilateral adnexectomy). Patients with borderline malignancy were excluded. Fifty-two patients with stage I epithelial ovarian cancer treated from 1965 to 2000 at 8 participating institutions were identified. Forty-two patients had stage IA disease, and 10 had stage IC cancers. Cell type included 25 mucinous, 10 serous, 10 endometrioid, 5 clear cell, and 2 mixed histology; 38 were grade 1, 9 were grade 2, and 5 were grade 3. Twenty patients received adjuvant chemotherapy. Eight patients had second-look laparotomies and all were found to be negative. Duration of follow-up ranged from 6 to 426 months (median, 68 months). Tumor recurrence developed in 5 patients 8 to 78 months after the initial surgery. Nine patients underwent subsequent hysterectomy and contralateral oophorectomy for benign disease. The estimated survival was 98% at 5 years and 93% at 10 years. Twenty-four patients attempted to become pregnant, and 17 (71%) conceived. These 17 patients had 26 term deliveries (no congenital anomalies noted) and 5 spontaneous abortions. They concluded that fertility-sparing surgery should be considered as a treatment option in women with stage I epithelial ovarian cancer who desire future child-bearing.

Satoh et al.,¹¹ in 2010, attempted to systematically determine selection criteria for fertility-sparing surgery in stage I epithelial cancer. They examined 200 patients who underwent fertility-sparing surgery. A relapse of 8.5% was reported, with 27% of the relapsed patients presenting recurrence exclusively in the remaining ovary without any distant or peritoneal metastases. The authors concluded that with favorable histology (mucinous, serous, endometrioid, or mixed histology) and low grade (1 or 2), patients can safely undergo fertility-sparing surgery, even without postoperative chemotherapy. However, in cases of stage IA disease with clear cell histology or stage IC with unilateral ovarian involvement and unfavorable histology, the authors emphasized the need for adjuvant platinum-based chemotherapy.

On the basis of these and other studies, fertility-sparing surgery may be an option in patients with early-stage epithelial ovarian cancer; however, it should not be an option for patients with higher than stage I, synchronous endometrial cancer, grade 3 disease, hereditary syndromes, and poor histology (clear cell, anaplastic, and small cell).¹²

Case 2: Germ Cell Tumors

Germ cell tumors arise from primordial germ cells and comprise dysgerminomatous and nondysgerminomatous tumors, including yolk sac tumors (endodermal sinus tumors), immature teratomas, mixed germ cell tumors, pure embryonal carcinomas, and nongestational choriocarcinomas. They differ from epithelial ovarian cancers in that they predominantly involve one ovary and usually affect girls and women of reproductive age.

They are usually also chemosensitive and have specific tumor markers, which can aid in their diagnosis and management. Before more advanced chemotherapies were available, complete surgical removal and staging was the gold standard in treatment of GCTs. More recently, however, the management of these tumors in reproductive age women typically includes fertility-sparing surgery (preservation of the uterus and unaffected ovary) whenever appropriate, with a thorough staging procedure, followed by adjuvant chemotherapy consisting of bleomycin, etoposide, and cisplatin (except for stage IA or IB pure dysgerminoma and stage IA grade 1 immature teratoma).^{13,14} With the addition of postoperative chemotherapy, 90% to 95% of malignant GCTs are curable.¹⁵

In a review of the literature, Eskander et al.¹⁶ reported that of 515 patients with malignant GCTs treated conservatively, there were 185 pregnancies and 148 live births. Amenorrhea after completion of fertility-sparing surgery and chemotherapy was <3%. Only 9 patients had disease recurrence with a death rate of 3%.

In recent years, several authors have suggested that laparoscopic surgery is a feasible, safe, and adequate technique for surgical staging and debulking in ovarian cancer when compared with laparotomy. Furthermore, various advantages have been attributed to minimally invasive surgery, such as decreased hospital stay, quicker recovery times, and faster return to daily living without compromising oncological outcomes.^{7,17,18}

Reports in the literature on laparoscopic fertility-sparing surgery for ovarian cancer are scant. Muzii et al.¹⁹ performed a prospective study involving 27 patients who had already been operated on elsewhere for a presumably benign ovarian cyst. Pathology after the initial surgery revealed 12 low-malignant-potential neoplasms, 11 invasive epithelial ovarian carcinomas, 1 sex-cord stromal cell neoplasm, and 3 germ cell neoplasms. Patients underwent subsequent laparoscopic fertility-sparing surgery in the form of exploration of the peritoneal cavity, peritoneal washings, multiple peritoneal biopsies, unilateral adnex-

ectomy (except in borderline tumors), omentectomy, unilateral or bilateral pelvic and para-aortic lymph node sampling (except in borderline tumors, well-differentiated, mucinous, and granulosa cell tumors), endometrial biopsy, and appendectomy in mucinous tumors. Seven patients (26%) were upstaged and 6 received adjuvant platinum-based chemotherapy. There were two pregnancies, and the median follow-up was 20 months. All patients were alive at that time; however, one patient with International Federation of Gynecology and Obstetrics stage IC clear cell carcinoma had a recurrence 8 months after surgery. The authors concluded that laparoscopy is acceptable in surgical staging of patients with early-stage ovarian cancer undergoing conservative surgery with preservation of the uterus and contralateral ovary. Seracchioli et al.²⁰ performed a retrospective study on 19 patients with borderline ovarian tumors who underwent laparoscopy over a 3-year period, all of whom desired preservation of fertility. Mean follow-up was 42 ± 19 months. Of the 19 patients, 10 attempted pregnancy and 6 conceived spontaneously and carried to term without the disease interfering with gestation or follow-up period after surgery. They concluded that laparoscopic fertility-sparing surgery for borderline ovarian tumors is a safe option in women who desire future fertility without interfering with fertility and pregnancy outcomes. More recently, Hu et al.²¹ performed a retrospective study of young patients with epithelial ovarian cancer stage I, grade 1 in 8 institutions from January 1994 to December 2010. Ninety-four patients were treated with fertility-sparing surgery: 72 had laparotomies, 22 had laparoscopies, and 5 had laparoscopy that was converted to laparotomy intraoperatively. Median follow-up time was 58.7 months, and mean follow-up time was 58.7 months. Overall survival and disease-free survival rates declined in patients undergoing fertility-sparing surgery with increased histologic grade. In patients with early-stage disease, on the other hand, overall survival and disease-free survival were not affected by staging method. At the end of the follow-up, 7 of 12 patients had conceived. They concluded that fertility-sparing surgery could be considered for young patients with epithelial ovarian cancer stage I, grade 1 and that the surgical method may not significantly influence the prognosis.

Computer-enhanced telesurgery, known as robotic-assisted surgery, is the latest innovation in videoendoscopy, which profoundly revolutionized the concept of minimally invasive surgery in the past 3 decades. Operative laparoscopy has several advantages over laparotomy, including faster postoperative recuperation, shorter hospi-

talization course, cosmetic benefits, improved visualization, decreased blood loss, and fewer postoperative complications.^{22,23} Despite these advantages, there are several drawbacks to conventional videolaparoscopy, including 2-dimensional views, a slower learning curve, operator fatigue, counterintuitive hand movements, and tremor amplification.²⁴ With the advent of computer-enhanced surgery, some of these limitations can be overcome, allowing for improved visualization, coordination, and dexterity.²⁵ Furthermore, robotic surgery can be viewed as an extension of conventional laparoscopy, making the procedure more reproducible, especially in lengthy, complicated cases such as para-aortic and pelvic lymphadenectomy, as well as in obese patients. Furthermore, the surgeon is able to sit for the surgery, which is another advantage because this can decrease physician fatigue and long-term physical impairment.

CONCLUSION

Robotic-assisted surgery provides a 3-dimensional view, magnified stereovision, 7 degrees of freedom, tremor filtering, and improvement of the surgeons' ergonomic position during the surgery.²⁶ These are advantages that are desirable to robotic-assisted fertility-sparing surgery. To our knowledge, there have been no published reports on robotic-assisted laparoscopy for fertility-sparing surgery in ovarian cancer.

The two patients in this report were treated with conservative surgery via robotic-assisted laparoscopy, and both resulted in favorable outcomes. From this, it appears that robotic-assisted laparoscopic fertility-sparing surgery is both a feasible and acceptable option for low-grade and low-stage ovarian cancer in patients desiring future fertility.

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