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Robotic Surgery for Cervical Cancer

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The development of robotic technology has facilitated the application of minimally invasive techniques for the treatment and evaluation of patients with early, advanced, and recurrent cervical cancer. The application of robotic technology for selected patients with cervical cancer and the data available in the literature are addressed in the present review paper. The robotic radical hysterectomy technique developed at the Mayo Clinic Arizona is presented with data comparing 27 patients who underwent the robotic procedure with 2 matched groups of patients treated by laparoscopic (N = 31), and laparotomic radical hysterectomy (N = 35). A few other studies confirmed the feasibility and safety of robotic radical hysterectomy and comparisons to either to the laparoscopic or open approach were discussed. Based on data from the literature, minimally invasive techniques including laparoscopy and robotics are preferable to laparotomy for patients requiring radical hysterectomy, with some advantages noted for robotics over laparoscopy. A prospective randomised trial is currently being perfomred under the auspices of the American Association of Gyneoclogic Laparoscopists comparing minimally invasive radical hysterectomy (laparoscopy or robotics) with laparotomy. For early cervical cancer radical parametrectomy and fertility preserving trachelectomy have been performed using robotic technology and been shown to be feasible, safe, and easier to perform when compared to the laparoscopic approach. Similar benefits have been noted in the treatment of advanced and recurrent cervical cancer where complex procedures such as extraperitoneal paraortic lymphadenectomy and pelvic exenteration have been required. Conclusion: Robotic technology better facilitates the surgical approach as compared to laparoscopy for technically challenging operations performed to treat primary, early or advanced, and recurrent cervical cancer. Although patient advantages are similar or slightly improved with robotics, there are multiple advantages for surgeons.

Key Words: Cervical cancer, treatment, minimally invasive surgery, robotic surgery

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INTRODUCTION

The development of robotic technology has facilitated the application of minimally invasive techniques for the treatment and evaluation of patients with early, advanced, and recurrent cervical cancer. The use of a robotic system in preset laboratory drills has been associated with faster performance times, increased accuracy, enhanced dexterity, faster suturing, and reduced number of errors when compared to conventional laparoscopic instrumentation.[1] Complex operations, such as radical hysterectomy, can be addressed in a more efficient fashion and the skills to perform this procedure are acquired not only in a shorter time but by a larger number of laparotomy surgeons who encountered difficulties with conventional laparoscopy. The application of robotic technology for selected patients with cervical cancer will be addressed here.

EARLY CERVICAL CANCER

Robotic radical hysterectomy

For early cervical cancer robotic and laparoscopic radical hysterectomy have been shown to have advantages for patients over the laparotomy approach in terms of blood loss, blood transfusions, complications, and length of hospital stay, with the exception of prolonged operating times.[2-5] Similar recurrence and cure rates have been reported when comparing the results of both techniques.[2-5] However, a prospective randomized trial comparing minimally invasive radical hysterectomy (laparoscopy or robotics) with laparotomy has never been performed but is being performed

at present under the auspices of the American Association of Gyneoclogic Laparoscopists.[6]

Our surgical approach for the performance of robotic radical hysterectomy has been described elsewhere.[7] A summary of the important steps is addressed here.

Technique

Operative set-up and instrumentation

Patients are placed in the semi-lithotomy position. Four trocars are used: a 12-mm transumbilical optical trocar, two 8-mm robotic trocars, and a 10-mm assistant trocar. The Trendelenburg position is necessary until all bowels are out of the pelvis to a maximum of 30 degrees. No uterine manipulator is used but a vaginal probe (Apple Medical, Marlborough, MA, USA) and a colpo-occluder balloon (Rumi Colpo-occluder, Cooper Medical, Trumbull, CT, USA).

The robotic column is placed between the patient's feet. An EndoWrist PK grasper (Intuitive Inc., Sunnyvale, CA, USA) and an EndoWrist monopolar spatula (Intuitive Inc.) are used with the left and right robotic arms, respectively. An Endo Wrist Prograsper (Intuitive Inc.) is used in the fourth robotic arm whenever used. An EndoWrist needle holder (Intuitive Inc.) is used for vaginal cuff closure switching the monopolar spatula.

Surgical technique

The extent of paracervical resection of the radical technique according to the Mayo classification of radical hysterectomy has been described elsewhere,[8] and is applied to our robotic technique. After dissection of the paravesical and pararectal spaces, the external iliac nodes, the obturator nodes, the nodes of the hypogastric artery, and common iliac nodal groups are removed bilaterally using the PK grasper and monopolar spatula.

The lateral parametrium is transected at the origin of the branches from the internal iliac artery and vein with successive applications of the EnSeal vessel-sealing bipolar device (SurgRx, Inc., Redwood city, CA, USA; Ethicon Endo-Surgery, Inc.), to the level of the deep uterine vein dorsally. This preserves the parasympathetic pelvic splachnic nerves. The uterosacral ligaments are transected with the EnSeal at the level of the anterior rectal wall toward the upper-posterior vaginal wall, which preserves the caudal portion of the sympathetic nerves in that area. An additional portion of the sympathetics can be preserved if separated from the lateral portion of the uterosacral ligaments.

Once the bladder is dissected from the cervix and upper vagina, the ventral and dorsal portions of the vesicouterine ligament are transected with the EnSeal. With the ureter elevated, the paravaginal tissues are divided with the EnSeal below the level of transection of the lateral parametrium and uterosacral ligament. The vagina is transected circumferentially with the monopolar spatula and the uterus is removed vaginally.

The vaginal cuff is closed with 2 continuous sutures of 2-0 Vicryl precut at 15 cm and with a fastened Lapra-Ty (Ethicon Endo Surgery, Cincinnati, OH, USA) at their end.

RESULTS

During the period of April 20, 2003 to September 16, 2006, a total of 523 patients underwent robotic surgery for gynecologic conditions at the Mayo Clinic Arizona. Among them, 27 patients underwent robotic radical hysterectomy for the primary treatment of gynecologic cancer. Our first radical hysterectomy was performed on April 9, 2003. These patients were compared to 2 matched groups of patients (laparoscopy, N = 31, and laparotomy, N = 35) by age, BMI, site and type of malignancy, FIGO staging, uterine size, and type of radical hysterectomy.

The mean operating time was significantly longer for the laparoscopic (220.4 minutes) group compared to both robotic (189.9 minutes) and laparotomy (166.8 minutes) groups ($p < 0.001$). The mean blood loss (443 mL; 133 mL; 208 respectively), mean rate of blood loss (2.6 mL; 0.7 mL; 0.9 mL respectively), and mean length of hospital stay (3.6 days; 1.7 days; 2.4 days, respectively) were significantly higher for the laparotomy group compared to both robotic and laparoscopic groups ($p < 0.05$). There were no difference in the number of lymph nodes, and intra or post-operative

complications among the 3 groups.

At a mean length of follow up of 27.1 months (range, 10 - 50 months), none of the patients with cervical cancer have experienced recurrence.

Based on these and other data, laparoscopy and robotics are preferable to laparotomy for the treatment of early stage cervical cancer. Robotic surgery offers a shorter operating time and numerous other advantages for the surgeon.[9-14]

LITERATURE REVIEW

Robotic radical hysterectomy

The first published report regarding robotic radical hysterectomy was in 2006.[9] In 2007, a pilot case-control study designed to evaluate the feasibility and efficacy of robotic-assisted laparoscopic radical hysterectomy and bilateral pelvic lymph node dissection for early cervical cancer was reported in 7 consecutive patients, compared to 8 patients treated with conventional total laparoscopic radical hysterectomy.[10] There were no statistically significant differences observed in the 2 groups in regards to operation time (241 vs 300 minutes), number of lymph nodes, and length of resected parametrial tissue, whereas significantly less bleeding (71 vs 160 mL) and shorter hospital stay (4 vs 8 days) were described in the robotic-assisted group ($p < 0.05$).

A retrospective clinical review of 10, stage IA2-IB1 cervical cancer patients who underwent robotic-assisted radical hysterectomy was published by Kim YT et al. in February 2008. No conversion to laparotomy was observed, mean operative time was 207 minutes, and mean estimated blood loss was 355 mL, the average number of resected pelvic lymph nodes was 27.6, no ureteral injuries or fistula complications were described.[11] The authors concluded that robotic radical hysterectomy for selected early cervical cancer cases is feasible and associated with low morbidity.

Fanning J et al. performed robotic radical hysterectomies in 20 consecutive stage IA-IIA cervical cancer patients.[12] Mean operative time was 6.5 hours, mean estimated blood loss was 300 mL, the average number of pelvic lymph nodes was 18, and all the patients went home on post-operative day 1. Even though the operative time seems to be long compared to other series, the authors concluded that the improved vision and intra-abdominal articulation of the robot provide an advantage in performing the most difficult steps of radical hysterectomy, such as unroofing and dissection of the distal ureter.

Nezhat FR et al. compared the intra-operative, pathologic, and post-operative outcomes of robotic radical hysterectomy to total laparoscopic radical hysterectomy in 13 and 21 patients with early stage cervical cancer, respectively. No statistical differences were observed regarding operative time (323 vs 318 minutes), estimated blood loss (157 vs 200 mL) and mean pelvic nodes count (25 vs 31).[13] There were no recurrences in either group with a mean follow-up time of 12 months in the robotic group and 29 months in the laparoscopic group. Their conclusion was that robotic radical hysterectomy appears to be equivalent to total laparoscopic radical hysterectomy with respect to operative time, blood loss, hospital stay, and oncologic outcome.

Boggess JF et al. recently published a case-control study of robotic-assisted type III radical hysterectomy (RHA) with pelvic lymph node dissection performed in 51 patients compared with 49 patients who underwent open radical hysterectomy (ORH).[14] There were significant differences between the groups with regard to operative blood loss ($p < 0.0001$), operative time ($p = 0.0002$), and lymph node retrieval ($p = 0.0003$), all of which were in favor of the RAH cohort. Hospital stay for RAH group was 1 day, compared with a 3.2-day average hospitalization for the cohort with ORH. The authors' conclusion was that robotic type III radical hysterectomy with pelvic node dissection is feasible and may be preferable over open radical hysterectomy in patients with early-stage cervical cancer.

The results described above confirmed similar patient benefits as it has been shown with the use of laparoscopy as compared to laparotomy for cervical, endometrial, and colorectal cancer patients.[15-22] However, while previous reports demonstrated longer operating times for robotics, the mean operating times for robotics and laparotomy were similar in our hands, and significantly

shorter as compared to laparoscopy.[15] In addition, as compared to laparoscopy, robotic patients undergoing the radical technique had significantly less blood loss and those who underwent the modified radical technique had a significantly shorter hospitalization. In summary, minimally invasive techniques, laparoscopy, and robotics are preferable to laparotomy for patients requiring radical hysterectomy, with some advantages noted for robotics over laparoscopy.

A phase III randomized clinical trial comparing laparoscopic or robotic radical hysterectomy (TLRH/TRRH) with abdominal radical hysterectomy (TARH) in patients with early stage cervical cancer is being performed under the auspices of the AAGL.[6] The aim of the study is to show the equivalence of the laparoscopic or robotic approach versus the abdominal approach following a 2-phase protocol. In the first phase, 100 patients will be randomized (1 : 1) to receive either TLRH/TRRH or TARH, with the rate of enrollment being the primary end point. In the second phase, recruitment will be extended by another 640 patients in a 1 : 1 TLRH/TRRH : TARH allocation, to determine equivalence with respect to disease-free survival. Equivalence will be assumed if the difference in disease-free survival does not exceed 7% at 4 years. Secondary outcomes will be treatment-related morbidity, costs and cost effectiveness, patterns of recurrence, quality of life, pelvic floor function, feasibility of intraoperative sentinel node sampling, and overall survival. This trial will be sufficiently powered to show the equivalence of primary and secondary outcomes for this patient population, which will allow patients and health administrators to make an informed choice of surgical alternatives in collaboration with gynecologic oncology surgeons.

Robotic radical parametrectomy

Treatment options for patients with undiagnosed cervical cancer discovered incidentally on a simple hysterectomy specimen include adjuvant radiation therapy or radical parametrectomy, which includes removal of the upper vagina, lateral parametria, and regional lymph nodes. Traditionally radical parametrectomy has been performed by laparotomy, with few cases described by laparoscopic-assisted vaginal or total laparoscopic approach.[23-25]

Ramirez PT et al. reported the first 5 patients treated by robotic radical parametrectomy and pelvic lymphadenectomy.[26] The median operative time was 365 minutes, estimated blood loss was 100 mL, the median number of pelvic lymph nodes was 14, and there were no conversion to laparotomy. There was 1 intra-operative cystomy and 1 patient experienced 2 post-operative complications, a vesicovaginal fistula, and a lymphocyst. The authors' concluded that robotic radical parametrectomy and bilateral pelvic lymphadenectomy is feasible and safe and can be performed with an acceptable complication rate.

Robotic radical trachelectomy

Vaginal radical trachelectomy in conjunction with laparoscopic pelvic lymphadenectomy to preserve fertility in women with early cervical cancer is now well established and considered to be as safe as traditional radical hysterectomy when strict selection criteria are met.[27-30] A few cases of various extent of laparoscopy in conjunction with a final vaginal approach and 1 case of total laparoscopic radical trachelectomy have been described.[31-34] The first report of a robotic radical trachelectomy for fertility sparing in stage IB1 adenocarcinoma of the cervix was published by Person J et al., who reported 2 cases of robotic radical trachelectomy and pelvic lymphadenectomy performed in 2 nullipaurous women with early stage cervical cancer.[35] The duration of the surgeries were 387 and 358 minutes, respectively. The long operative time was justified by the authors as a product of the novelty of the procedure and waiting time for frozen section. No perioperative complications were observed. Their conclusion was that robotic radical trachelectomy is a safe and feasible alternative to a combined laparoscopic and vaginal approach.

Geisler JP et al. in October 2008, published another case report of a robotic radical trachelectomy in a stage IB1 adenosarcoma of the cervix, operating time was 172 minutes and the estimated blood loss was 100 mL.[36]

Advanced cervical cancer

Nodal dissection, transperitoneal and extraperitoneal

Laparoscopic pelvic and paraaotic lymph node staging is widely used in patients with advanced cervical cancer prior to initiation of primary chemo-radiation therapy due to lack of sensitivity of imaging techniques. This approach has been shown to be feasible and safe.[37-39] An extended pelvic and para-aortic lymphadenectomy can reliably and safely be performed robotically in the management of gynecological malignancies. The robotic system aids in performing a meticulous dissection and in adhering to sound oncologic principles. For the robotic approach data are available for both pelvic and para-aortic lymphadenectomy performed during staging procedure for endometrial, cervical, or early ovarian cancers.[1,9-15,40]

Extraperitoneal para-aortic laparoscopic lymphadenectomy is preferable to reduce the risk of adhesions prior to chemioradiation treatments and for obese patients where the transperitoneal approach can be more difficult or impossible. Data are available for the laparoscopic approach, both in terms of safety and feasibility.[41-44] Recently, Vergote I et al. reported on 5 patients with stage IIb-IIIb cervical carcinoma undergoing robotic retroperitoneal para-aortic lymphadenectomy. The authors concluded the robotic procedure was technically easier than the laparoscopic approach.[45]

At the Mayo Clinic Arizona, a robotic extraperitoneal infrarenal aortic lymphadenectomy technique was developed in fresh-frozen cadavers and successfully applied to patients, and will be the basis for an upcoming paper.[46]

Recurrent cervical cancer

Robotic pelvic exenteration

Treatment of patients with recurrent cervical carcinoma after initial primary surgery or chemoradiation is based on a single or combination of treatment modalities such as radiotherapy, chemotherapy, and various surgical procedures.[47,48] Minimally invasive surgery may improve the outcome of patients with bulky residual tumors after chemoradiation for locally advanced cervical cancer and for lateral pelvic wall recurrence. In case of central pelvic recurrence after surgery and adjuvant radiation treatment, pelvic exenteration is the only therapeutic approach with curative goals. Women facing an exenterative procedure should undergo a comprehensive evaluation to make sure there is no evidence of unresectable or metastatic disease that would make them unsuitable candidates for exenteration. The laparoscopic approach for a pre-treatment evaluation in patients with recurrent cervical cancer has already shown to be paramount to select adequate candidates for exenterative procedure similarly a pre-exenteration robotic evaluation can be easily performed.[49,50]

Pruthi RS et al. recently described the technique of robotic-assisted laparoscopic anterior pelvic exenteration performed in 12 women for clinically localized bladder cancer.[51] Nine patients underwent ileal conduit diversion and 3 patients underwent an orthotopic neobladder. In all cases, the urinary diversion was performed extracorporeally. Mean operating room time was 4.6 hours and the mean surgical blood loss was 221 mL. Mean time to flatus was 1.9 days and 2.4 days to bowel movement, and time to discharge 4.8 days. There were 2 postoperative complications (17%) in 2 patients. The authors' initial experience with robotic-assisted laparoscopic anterior pelvic exenteration appears to be favorable with acceptable operative, pathologic, and short-term clinical outcomes. However, the oncological outcomes of these new, minimally invasive surgical approaches need to be carefully verified through more experience to adequately evaluate and validate these procedures as appropriate surgical and oncologic options.

CONCLUSION

For technically challenging operations performed to treat primary, early or advanced, and recurrent cervical cancer, robotic technology facilitates the surgical approach better in comparison to laparoscopy due to its steady 3-dimensional visualization, instrumentation with articulating tips, and an adaptive downscaling of the surgeons movements without tremor. Although patient advantages are similar or slightly improved with robotics, there are multiple advantages for the surgeons. The present randomized clinical trial

will most likely confirm the advantages of the minimally invasive approach over laparotomy.[6]

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