

The impact of robotic surgery on gynecologic oncology

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The objective of this article was to review the published scientific literature pertaining to robotic surgery and its applications in gynecologic malignancies and to summarize the impact of robotic surgery on the field of gynecologic oncology. Summarizing data from different gynecologic disease-sites, robotic-assisted surgery is safe, feasible, and demonstrates equivalent histopathologic and oncologic outcomes. In general, benefits to robotic surgery include decreased blood loss, fewer perioperative complications and decreased length of hospital stay. Disadvantages include accessibility to robot surgical systems, decreased haptic sensation and fixed cost as well as cost of disposable equipment. As robotic surgery becomes readily available it will be imperative to develop standardized training modalities. Further research is needed to validate the role of robotic surgery in the treatment of gynecologic malignancies.

Keywords: Gynecologic malignancies, Robotic surgery

INTRODUCTION

Since the approval of the da Vinci robotic surgical system (Intuitive Surgical Inc., Sunnyvale, CA, USA) by the Food and Drug Administration for use in gynecologic procedures in April of 2005, over 100 publications have explored the role of robotic surgery in gynecologic malignancies. Worldwide, robotic technology is being rapidly adopted with the number of robotic-assisted procedures being performed nearly tripling from 80,000 in 2007 to 205,000 in 2009. In a similar time frame, the number of da Vinci robotic systems installed in US hospitals grew by approximately 75% from 800 to around 1,400 [1]. The benefits of robotic surgery as a minimally invasive surgical technique parallel those of traditional laparoscopy, with the added advantages of overcoming several barriers to the use

of laparoscopy, such as limitations of the human hand (seven degrees of movement and elimination of hand tremors), elimination of the fulcrum effect of laparoscopy (the robotic arms imitate the movements of the surgeon's hand), improved visualization (three-dimensional stereoscopic imaging), and increased independence of the operating surgeon, thus enabling the robotic-assisted management of gynecologic malignancies to become more widely utilized. In a recent survey of the members of the Society of Gynecologic Oncologist (SGO) examining the trends in laparoscopic and robotic surgery, 27% of respondents indicated that they performed robotic-assisted surgery, and 66% indicated that they planned to increase their use of robotic-assisted surgery in the future citing limited access to robotic systems as a common reason for not already adopting robotic technology [2]. In addition to limited access primarily secondary to cost, robotic surgery has several other potential drawbacks including lack of haptic feedback, bulky machine habitus, and need for additional staff and training. Robotic technology in gynecology remains in its infancy with most articles supporting its use being limited to case series, retrospective cohorts and case control studies. The purpose of this review is to summarize the available literature

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on robotic surgery and its impact on the field of gynecologic oncology.

CERVICAL CANCER

Since the first published report of robotic radical hysterectomy in 2006 [3], several publications have evaluated the safety, feasibility and efficacy of a robotic-assisted laparoscopic radical hysterectomy and bilateral pelvic lymphadenectomy for the treatment of early stage (IA2 and IB1) cervical cancer. In a pilot case-control study designed to evaluate the safety and efficacy of robotic radical hysterectomy and bilateral pelvic lymphadenectomy among patients with early stage cervical cancer, there was no significant difference in operative time, number of lymph nodes excised, and length of the excised parametrial tissue compared to patients who underwent laparoscopic radical hysterectomy [4]. There was, however, significantly less blood loss (71 mL vs. 160 mL) and shorter length of hospital stay (4 days vs. 8 days) in the robotic-assisted group ($p < 0.05$). In a retrospective clinical review of ten early stage cervical cancers, Kim et al. [5], report successful completion of each attempted operation with no conversion to laparotomy with a median operative time of 207 minutes (range, 120 to 240 minutes), a median docking time of 26 minutes (range, 10 to 45 minutes), mean estimated blood loss of 355 mL, and an average of 27.6 pelvic lymph nodes removed (range, 12 to 52). More importantly there were no ureteral injuries or fistulae. Collectively, these initial studies demonstrated the safety and feasibility of performing radical hysterectomies with a robotic-assisted approach.

Several comparative analyses of different modalities of radical hysterectomy also exist in the literature. Nezhat et al. [6], compared intraoperative, pathologic and postoperative outcomes of 13 patients who underwent robotic radical hysterectomy to 21 patients who underwent laparoscopic radical hysterectomy, and found no significant difference in operative time, mean estimated blood loss and pelvic nodal counts. At the conclusion of follow-up, neither group had experienced a recurrence, leading the authors to conclude that robotic radical hysterectomy appears to be equivalent to laparoscopic radical hysterectomy. In a case-control study, Boggess et al. [7], compared 51 patients who underwent robotic radical hysterectomy with 49 patients who underwent open radical hysterectomy and found significant differences in estimated blood loss, operative time and nodal counts all in favor of the robotic radical hysterectomy cohort, leading the authors to conclude that robotic radical hysterectomy is feasible and may be favorable over open radical hysterectomy in patients with early

stage cervical cancer.

In a recently published retrospective comparative series of robotic radical hysterectomy with laparoscopic radical hysterectomy or open abdominal radical hysterectomy, Magrina et al. [8], provide the only comparison of the three available surgical modalities. The mean operative times for patients in the robotic, laparoscopic, and open cohorts were 190, 220, and 167 minutes, respectively; the mean estimated blood loss was 133, 208, and 443 mL, respectively; and the mean length of stay was 1.7, 2.4, and 3.6 days, respectively. There were no reported differences in intraoperative or postoperative complications and no conversions in the minimally invasive groups.

Despite the presumed equivalency of a minimally invasive surgical approach to radical hysterectomy, to date there is no completed prospective comparison that is adequately powered to classify a robotic or laparoscopic radical hysterectomy as an equivalent surgical approach to open radical hysterectomy. A multicenter phase III randomized clinical trial comparing robotic or laparoscopic radical hysterectomy with abdominal radical hysterectomy in patients with early stage cervical cancer is currently underway [9]. The aim of this study is to show the equivalence of the minimally invasive surgical approach versus the abdominal approach with a two phase protocol. The primary endpoint of the first phase is rate of enrollment and the primary endpoint of the second phase is to determine equivalence with respect to disease-free survival with 80% power. Secondary endpoints include treatment-related morbidity, cost and cost effectiveness, patterns of recurrence, quality of life, pelvic floor function, feasibility of intraoperative sentinel lymph node sampling, and overall survival.

Given the stated advantages of minimally invasive surgery, employment of the da Vinci robotic surgical system has given surgeons the opportunity to perform complex gynecologic oncology procedures through a minimally invasive approach. One such example of this is radical trachelectomy. Radical trachelectomy is an appropriate alternative to radical hysterectomy in appropriately selected patients with early stage cervical cancer. Although reports of laparoscopic radical trachelectomy exist [10,11], the laparoscopic approach has not been widely accepted secondary to the complexity of the procedure and the required advanced skill of the surgeon. With the advantages in surgical instrumentation the robotic surgical system affords, robotic radical trachelectomy appears to be a feasible alternative to the open or vaginal approach. In the largest reported series of patients who underwent robotic radical trachelectomy to date, the authors compared the robotics approach to historical controls and found that the robotics approach was associated with less blood loss, a lower transfusion rate, fewer intraoperative and postoperative

complications and a shorter length of hospitalization without compromising histopathologic outcomes such as parametrial length or node counts [12].

Failure to detect occult nodal metastases in patients with locally advanced cervical cancer (IB2-IVA) can lead to suboptimal treatment. In a prospective correlation of surgical findings with positron emission tomography/computed tomography (PET/CT), patients underwent preoperative PET/CT followed by laparoscopic extraperitoneal para-aortic lymphadenectomy [13]. Among the 26 patients with negative pelvic and para-aortic lymph nodes on PET/CT, 3 (12%) had histopathologically positive para-aortic nodes. Of the 27 patients with positive pelvic but negative para-aortic lymph nodes on PET/CT, 6 (22%) had histopathologically positive para-aortic lymph nodes. Eleven (18.3%) patients had a treatment modification based on surgical findings, highlighting the importance of surgical staging in patients with locally advanced cervical cancer. The extraperitoneal approach to para-aortic lymphadenectomy overcomes limitations of the transperitoneal approach including, obesity, short intestinal mesentery, distended bowel, intestinal adhesions. Robotic technology provides additional advantages over traditional laparoscopic instrumentation, particularly when working in a limited surgical field during extraperitoneal para-aortic lymphadenectomy. Margina et al. [14] described the development of robotic extraperitoneal lymphadenectomy using two female torso cadavers and the feasibility of selective aortic lymphadenectomy in a patient with advanced cervical cancer. Similarly, Vergote et al. [15] report on the first series of robotic retroperitoneal para-aortic lymphadenectomy in patients with advanced cervical cancer, and concluded that the robotic procedure was technically easier than the laparoscopic approach.

ENDOMETRIAL CANCER

Because of the associated risk factors for endometrial cancer, including obesity and multiple medical comorbidities, patients with endometrial cancer often represent relatively unfit surgical candidates at greater risk for surgical morbidity. Minimally invasive surgery has been championed as a means of reducing surgical morbidity. In a survey to members of the SGO examining trends in laparoscopy and robotic surgery, there was a 12% increase in the number of SGO members who preferred to use laparoscopy in oncologic cases in which both laparoscopy and laparotomy offered equal results, with surgical staging of endometrial cancer being the most common indication for laparoscopy [2].

In the same survey, 27% of respondents indicated that they

used the robot surgical system for gynecologic procedures. Reasons for the expanded use of minimally invasive surgery include studies documenting the feasibility, effectiveness and equivalency of a laparoscopic surgical approach in patients with early stage endometrial cancer. Zullo et al. [16,17] performed a randomized trial comparing laparoscopy and laparotomy in patients with early stage uterine cancer, and found that laparoscopy was as feasible and safe as the open approach with no difference in recurrence rates or death and a significant improvement in quality of life for the first 3 years after surgery. In a prospective comparison of laparoscopy to laparotomy for endometrial cancer staging, the Lap-2 trial, conducted by the Gynecologic Oncology Group (GOG), demonstrated the feasibility of laparoscopy with equivalent positive cytology rates, proportion of advanced stage diagnoses, and node positivity compared to laparotomy [18]. In addition, laparoscopy had an improved safety profile with fewer grade ≥ 2 postoperative events and shorter hospital stay. Laparoscopy was associated with less postoperative pain, earlier resumption of normal activity, earlier return to work, and significant improvement in quality of life. Tozzi et al. [19] were the first to report on differences in survival outcomes among patients undergoing laparoscopic versus open approach to endometrial cancer. Overall survival rates showed no significant difference between the two groups: 86% in the laparotomy group compared to 90% in the laparoscopy group, respectively.

Although prospective comparisons of robotic endometrial cancer surgery to other modalities of surgical staging are lacking, data demonstrating the benefits of laparoscopy can be extrapolated and combined with existing reports regarding robotics and endometrial cancer surgery. Paley et al. [20] report on the surgical outcomes of the first 377 consecutive cases of women who underwent endometrial cancer staging with robotic surgery compared to 131 women who underwent abdominal hysterectomy with surgical staging in the year prior to initiation a robotic surgery program at their institution. There were no significant differences between the groups with respect to age, BMI, medical comorbidities, or number of previous abdominal surgeries. Operative times were longer in the robotic surgery group, but nodal counts, length of stay and estimated blood loss all favored the robotics cohort. In addition, women undergoing open surgery experienced significantly higher major complications compared to women undergoing robotics surgery (26% vs. 6.4%, $p < 0.001$). The most significant reduction was in the incidence of wound separation or dehiscence, infectious complications, and ureteral injury or acute renal failure in the robotic surgery group. The authors estimate that the incorporation of robotic

surgery into their minimally invasive surgery program was most significant for endometrial cancer patients with a 12.5-fold increase in endometrial cancer patients receiving staging surgery via a robotic minimally invasive surgical approach. This shift towards robotic surgery for endometrial cancer is similar to the experience of other minimally invasive surgical programs across the country [21]. A potential reason for rapid incorporation of a robotics approach to endometrial cancer staging procedures is the steeper learning curve in comparison to laparoscopic hysterectomy with lymphadenectomy. Lim et al. [22] compared the learning curve and outcomes of the first 122 patients who underwent a robotic hysterectomy with lymphadenectomy to the first 122 patients who underwent a similar laparoscopic approach. They found robotic hysterectomy with lymphadenectomy had a faster learning curve in comparison to laparoscopic hysterectomy with lymphadenectomy with comparable adequacy of surgical staging between the two surgical methods. In addition, robotic hysterectomy with lymphadenectomy was associated with shorter hospitalization, less blood loss, fewer intraoperative and major complications, and a lower rate of conversion to an open procedure.

OVARIAN CANCER

Given the effectiveness and feasibility of minimally invasive surgery in the management and staging of other early gynecologic malignancies, there is now expanding interest of the role of minimally invasive surgical approaches in the management of ovarian cancer. There is controversy surrounding implementation of minimally invasive surgical approaches with regards to ovarian cancer management secondary to the concern that meticulous exploration of the peritoneal cavity is neither safe nor feasible using laparoscopy because of limited range of motion, visibility and haptic sensation. Consequently, there is limited data regarding the efficacy of minimally invasive surgery and specifically robotic surgery in the management of ovarian cancer.

Borderline ovarian tumors account for approximately 10-15% of cases of early stage epithelial ovarian cancer, and as a result surgical staging of borderline ovarian tumors is recommended secondary to the risk of under diagnosis of invasive epithelial ovarian cancer on frozen section. In the largest review to date, Fauvet et al. [23] compared women with ovarian borderline tumors who underwent surgical staging with laparoscopy to laparotomy retrospectively, and found that women in the laparoscopy group had a significantly lower rate of complete surgical staging likely secondary to a high rate of conservative

surgery in the laparoscopy group. However, there was no significant difference in recurrences rate between patients in the laparoscopy group in comparison to the laparotomy group (12.1% vs. 9.1%). There was a relatively high rate of conversion to open in the laparoscopy group (28.2%) secondary to expected ovarian cancer, large volume tumor and adhesions, stressing the importance of adequate patient selection when attempting a minimally invasive surgical approach.

Approximately 15% of women with epithelial ovarian cancer will have early stage disease at diagnosis and require comprehensive surgical staging to provide adequate prognostic information and treatment planning. Patients with presumed early stage ovarian cancer identify a cohort of epithelial ovarian cancer patients that could potentially benefit from the reduced morbidity of a minimally invasive surgical approach. Tozzi et al. [24] identified 24 patients with FIGO stage IA or IB ovarian or fallopian tube carcinoma who underwent comprehensive laparoscopic staging. There were no intraoperative complications. The mean operative time was 176 minutes. The mean number of pelvic lymph nodes removed was 19.8 and the mean number of para-aortic lymph nodes removed was 19.6. The mean progression-free survival rate was 91.6% and the overall survival rate was 100%. In a second study performed by the GOG, the feasibility of completion laparoscopic staging for women with incompletely staged ovarian, fallopian tube, or primary peritoneal carcinoma was examined. Women who underwent laparoscopy had significantly less estimated blood loss and shorter hospital stay than women who underwent laparotomy with equivalent operative times and numbers of lymph nodes obtained [25]. Of note in this study, there was a relatively high conversion rate (23%), a high complication rate (19%), and lack of follow-up data on disease progression and overall survival. Nezhat et al. [26] performed a retrospective review of 36 patients who underwent laparoscopic staging for presumed early stage ovarian and fallopian tube carcinoma. There were 4 retrospective postoperative complications, and 78% had their disease upstaged. The mean follow-up was 55.9 months and there were 3 recurrences in patients who underwent conservative surgery with an overall survival rate of 100%. Secondary to the proposed technological advantages of robotic surgery, Magrina et al. [27] performed a retrospective case-control analysis of 25 patients with epithelial ovarian cancer undergoing robotic surgical treatment in comparison with patients treated by laparoscopy and laparotomy. Patients in this study were not limited to apparent early stage disease. There was a significant increase in the mean operative time among patients in the robotics cohort. In contrast, patients in the robotic surgery group had less blood loss and the shortest mean length of hospital stay com-

pared to laparoscopy or laparotomy. Patients were subdivided according to the extent of surgery by the type and number of procedures required to achieve adequate cytoreduction, and they concluded that laparoscopy or robotics are preferable to laparotomy for patients with ovarian cancer requiring primary tumor excision along with one additional major procedure. Laparotomy is preferred for those patients requiring two or more additional major procedures. As one would expect, removal of all disease, and not the surgical approach, is the most important factor in influencing survival. Despite limited retrospective data, it does appear that minimally invasive surgical staging of presumed early stage ovarian cancer is safe and effective when performed by a trained gynecologic oncologist; however, the disadvantages of robotic surgery will likely limit application of the robotic surgery approach to carefully selected patients with epithelial ovarian cancer.

COST OF ROBOTIC SURGERY

In reviewing the available literature it becomes apparent that robotic technology is safe and allows completion of more complex surgical procedures via a minimally invasive surgical approach, but at relatively high costs. In a recent cost comparison of robotic surgery, laparoscopy, and laparotomy, cost estimates were fit into three separate models: a societal perspective, and a hospital perspective with and without robotic costs included [28]. The societal model included in patient hospital cost, robotic expenses, lost wages of patient and caregiver cost. The hospital models included inpatient hospital costs with and without the cost of the robot. As one would expect, from an economic perspective, laparoscopy was the least costly approach among all three models utilized in this study. In addition, from the societal perspective, the shorter hospital stay and recovery time associated with minimally invasive surgery is reflected in the lower overall cost of both laparoscopy and robotics from a societal perspective when compared to the open approach. In both of the hospital models, with and without robotic cost, the traditional laparoscopic techniques remained the least expensive technique. The most significant contributor causing robotic surgery to remain more expensive than traditional laparoscopy was the cost of disposable equipment. Disposable equipment for traditional laparoscopy versus robotic surgery was \$1,138 and \$2,210, respectively, not including the upfront fixed cost of the robot ranging from \$1 million to \$2.5 million per unit, or the cost of the maintenance contract [1]. Unfortunately, despite the existence of unique diagnosis and procedure codes for robotic-assisted procedures, there is no higher reimbursement rate for robotic assisted

procedures from US Medicare or private insurers.

IMPACT ON TRAINEE EDUCATION

In a recent survey of gynecologic oncology training programs, 78% of fellows in training reported a need for more minimally invasive surgical training [29]. As new surgical techniques and instrumentation are brought to the forefront, efficient training of residents and fellows is imperative. With the constraints of the 80 hour work week restrictions, trainees have less exposure to a variety of surgical cases, stressing the importance of a defined surgical curriculum. Development of training protocols serves as a dual purpose in that it also provides trainees with objective documentation of competency as they seek jobs at the completion of training and credentialing in robotic surgery. Lastly, medical simulation training is the focus of recent governmental expenditures in that the Agency for Healthcare Research and Quality has awarded \$5 million in grants for simulation research projects [30].

In a recent systematic review of randomized controlled trials evaluating the effectiveness of virtual reality training for laparoscopic surgery, Gurusamy et al. [31], concluded that virtual reality training resulted in a greater reduction in operating time, error and unnecessary movements in comparison to standard laparoscopic training in which the trainee observes an experienced surgeon. In a separate study, trainees in an obstetrics and gynecology residency program were randomized to receive proficiency-based virtual reality simulator training in laparoscopic salpingectomy or standard clinical education [32]. Those in the simulator trained group performed superiorly to those in the standard education group. Defined robotic surgical training protocols are now starting to emerge. Geller et al. [30] describe a protocol that includes online instruction and 2 hands-on modules that evaluate platform set-up and surgical skills with plans to reassess the effectiveness of their model as their trainees progress through residency and fellowship with an ultimate goal of establishing a proficiency level.

CONCLUSIONS

Our review of the literature establishes a role for robotic surgery in early stage cervical and endometrial cancer, advanced cervical cancer, fertility sparing procedures for the treatment of cervical cancer, and early stage ovarian cancer. Surgeons should expect further research to validate the application of

robotic surgery in the treatment of these particular malignancies and clinical scenarios.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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