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Robotic surgery for gynecologic cancers: indications, techniques and controversies

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Abstract

Minimally invasive surgery for gynecologic cancers is associated with fewer postoperative complications including less blood loss and quicker recovery time compared to traditional laparotomy. The robotic platform has allowed patients access to minimally invasive surgery due to its increased utilization by gynecologic oncologists. Many surgeons have embraced the robotic platform due to its technological advances over traditional laparoscopy including high-definition 3D optics, wristed instrumentation, camera stability and improved ergonomics. While robotic surgery continues as a mainstay in the management of gynecologic cancers, it remains controversial in regards to its cost effectiveness and more recently, its long-term impact on clinical and oncologic outcomes. A strong component of the justification of this surgical platform is based on extrapolated data from traditional laparoscopy despite limited prospective randomized trials for robotic-assisted surgery. In this review, we highlight the use of robotic surgery in the management of gynecologic cancers in special populations: fertility sparing patients, the morbidly obese, the elderly, and patients with a favorable response to neoadjuvant chemotherapy.

Keywords

gynecologic cancer; minimally invasive surgery; robotic surgery; sentinel lymph node

Historical Notes

It is best estimated that Leonardo da Vinci (1452–1519) first sketched his prototype for a robotic mechanical knight over five centuries ago. While many centuries later, the namesake surgical platform has transformed the field of minimally invasive surgery. Da Vinci's robotic knight consisted of a complex core of mechanical devices that is thought to be human powered. The two operating systems of the robot included those with 3° of freedom (legs, ankles, knees and hips) and those with 4° of freedom (shoulder, elbows, wrists and hands).¹ Da Vinci's mechanical designs were far ahead of the development of any formal design prints. Similarly, da Vinci's contribution to anatomy and anatomic illustration were far ahead of the contemporary scientific work that would occur almost two centuries later.² (Fig. 1)

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Conflict of Interest

The authors have no conflicts of interest to declare.

The namesake robotic platform thus captures the essence of Da Vinci's work including the novel pursuit of mechanical and robotic design in addition to his pursuit of anatomic knowledge. (Fig. 2)

While the concept of robotic design may have been first introduced by Leonardo da Vinci, the field of 'telesurgery' or the ability to operate at a remote site with the use of robotic technology is an emerging area of interest.³ The ability to offer complex minimally invasive surgery at a site remote from the patient offers the potential to bring a more advanced level of care in remote areas, potentially saving lives around the world. Not only can this type of technology help in humanitarian situations with limited access, the military has also pursued this type of technology to assist in emergency areas.⁴ This type of 'telecommunication' and 'telesurgery' can be applied in a wide variety of clinical scenarios allowing patients access to a skilled surgeon remotely. Ongoing research is being conducted to better understand the amount of distance possible for remote telesurgery to be feasible.^{5,6}

The da Vinci Surgical System (Intuitive Surgical Inc.) was first introduced in 2000 as the first robotic surgical system approved by the US Food and Drug Administration (FDA). The surgical platform was eventually approved for use in gynecologic malignancies in 2005. It is estimated that more than 6 million surgeries have been performed globally using the surgical platform (www.davincisurgery.com). Since its initial approval, the utilization of the Da Vinci robotic platform has rapidly increased in the field of gynecologic oncology. While much of the debate surrounding the adoption of robotic surgery has focused on the cost effectiveness and the immediate postsurgical outcomes, the benefits of improved ergonomics and advanced instrumentation are important considerations in surgeon preference (Table 1). There are few large randomized control trials that investigate the potential discrepancy between laparoscopic and robotic surgery and also robotic versus open surgery. More recently, long-term safety concerns regarding oncologic outcomes associated with minimally invasive surgery (laparoscopy and robotic-assistance) in the management of early cervical cancer has led the US FDA to issue a 'safety communication'. In February 28, 2019, the US FDA cited 'limited, preliminary evidence' that the use of robotically assisted surgical devices for the treatment or prevention of cancers (e.g., breast and cervical) may be associated with diminished long term-survival. The FDA acknowledged that while robotically assisted devices allow for quicker recovery and improved surgical technique, limited studies have been performed to evaluate the specific oncologic clinical outcomes such as local cancer recurrence, disease free interval, or overall survival.⁷

Current Indications

Cervical cancer

Despite increased access to cervical cancer screening and implementation of human papillomavirus (HPV) vaccination programs, in 2018 there were approximately 569 847 cases of cervical cancer diagnosed worldwide.⁸ In the United States, in 2020 there are an estimated 13,800 new cases and 4,290 disease related deaths.⁹ For decades, abdominal radical hysterectomy had been the standard of care for the surgical management of early FIGO stage cervical cancer with 5-year overall survival rates greater than 80%.¹⁰ According to the National Comprehensive Cancer Network (NCCN) guidelines, radical hysterectomy

remains the standard surgical treatment for early FIGO stage cervical cancer.¹¹ Unlike an extrafacial hysterectomy, a radical hysterectomy is a complex surgery to perform and teach. It requires development of the pararectal, paravesical, vesicouterine, and rectovaginal spaces, ligation of the uterine arteries at their origin along the internal iliac arteries, bilateral ureterolysis from the pelvic brim to bladder insertion, resection of the cardinal ligaments at the pelvic sidewall, resection of the uterosacral ligaments at the pelvic floor (sacrum), and removal of one quarter to one third of the proximal vagina. (3). Bilateral pelvic lymphadenectomy is also routinely performed as part of a radical hysterectomy.

Historically, either an open or minimally invasive (laparoscopic or robotic) surgical approach was acceptable for radical hysterectomy (4). The first robotic-assisted radical hysterectomy was reported in 2005 and prompted the beginning of a national trend toward increasing usage of the robotic platform. Between 2008 and 2015, 3563 radical hysterectomies were performed based on the National Inpatient Sample (NIS) data, of which 27.5% were performed using a minimally invasive approach (robotic and laparoscopic).¹³ Prior studies have demonstrated that compared to an open approach, minimally invasive (laparoscopic or robotic) techniques are associated with decreased blood loss, fewer complications, and a shorter hospital stay.^{13–16} Additional retrospective studies demonstrated no differences between robotic-assisted radical hysterectomy and open surgery in regards to recurrence rates or death (Table 2).^{12,16}

Following the publication of the Laparoscopic Approach to Cervical Cancer (LACC trial; [Clinicaltrials.gov NCT00614211](https://clinicaltrials.gov/ct2/show/study/NCT00614211)) in October 2018, the safety of a minimally invasive approach to radical hysterectomy for early cervical cancer was significantly challenged. Ramirez *et al.* published a prospective, randomized trial involving stages IA1 (lymphovascular invasion), IA2, or IB1; with patients who underwent a minimally invasive approach having a lower rate of disease-free survival at 4.5 years, 86.0% (MIS) compared to 96.5% for open surgery (difference of –10.6 percentage points; 95% CI –16.44.7; p=0.87 for non-inferiority).¹⁷ Of the minimally invasive surgical patients, approximately 84.4% underwent laparoscopy and 15.6% robot-assisted surgery. The study was prematurely closed due to an imbalance in deaths between the groups, with differences in overall survival rates at 3 years 93.8% (MIS) and 99.0% (open). As a companion piece published alongside the LACC trial, Melamed *et al.* analyzed the National Cancer Database and Surveillance, Epidemiology and End Results (SEER) database, demonstrating a decline in relative survival, with patients who underwent minimally invasive surgery having a worse 4-year mortality rate of 9.1% compared to 5.3% among those who underwent open surgery. In subgroup analysis, however, the hazard ratio for death for patients with tumors <2 cm were statistically similar.¹⁸ There remains significant concerns regarding the inherent flaws of a database study with the biases associated with retrospective analyses. Similarly, Doo *et al.* retrospectively evaluated patients with stage IB1 cervical cancer and found no difference in perioperative complications; however, on multivariate analysis found that robotic radical hysterectomy or tumor size ≥ 2 cm (irrespective of surgical approach), were independently associated with recurrence and death.¹⁹

The LACC study highlights several challenges when designing surgical randomized trials including limited selection criteria of participating surgeons regarding volume and baseline

outcomes, as well as the standardization of surgical technique, including learning curves. Radical hysterectomy at baseline is a complex surgery to learn and to teach, however, trying to perform this surgery using a minimally invasive approach such as laparoscopy can also lead to significant variation in technique and skill. The LACC trial was performed across 33 centers in 13 countries over a 9-year period. In order for a surgeon to be considered for the trial, they were required to have a minimum of 10 documented cases as the primary surgeon, a proven track record with clinical research and hospital privileges and to have submitted 1 unedited surgical video. While there has been significant research showing improved outcomes with decreased recurrence risk and improved survival in high-volume centers, surgical volume was not a component in surgeon selection.²⁰ Additionally, the majority of centers participating in the study were outside of the United States (27/33 centers), where there is limited oversight and regulation of surgical training compared to the rigor of US-based Gynecologic Oncology training programs.

An additional challenge included the standardization of surgical technique to improve study uniformity. In the LACC trial, unlike other surgical trials, there was no standardization or documentation required by the participating center to assess the performance of appropriate surgical technique during the study period. For patients randomized to the minimally invasive arm, it was up to the surgeon to decide between a laparoscopic vs robotic approach, with 16% of patients undergoing robotic-assisted radical hysterectomy (RRH). Concern for a lack of uniformity in surgical technique is also supported by the inconsistent finding of similar postoperative complication rates between the MIS and open radical hysterectomy groups (25 vs 26%). The similar rates between the two groups is contradictory to many studies that have demonstrated less blood loss, decreased operative time, fewer blood transfusions and shorter length of stay with MIS (Table 2). Additionally, key elements in robotic-assisted surgery that may make this approach more similar to open surgery compared to laparoscopy, including improved visualization and depth perception with 3D technology, efficiency in suturing, and more precise dissections were not accounted for during the study period in either surgeon reported outcomes or pathologic specimen analysis. While the landmark LACC trial is the highest level of evidence published to date, currently MIS may still be an acceptable option in select cases. Only 16% of patients underwent RRH and therefore the extrapolation of data is difficult to interpret. Additional information is needed to better understand why a minimally invasive approach may be resulting in worse survival for early stage cervical cancer patients undergoing radical hysterectomy.

Intrauterine manipulator

Following the landmark LACC trial, significant attention has been directed to the specific surgical techniques used in minimally invasive surgery that could be contributing to the overall survival differences which includes the use of the intrauterine manipulator. Unlike open surgery, upward traction on the uterus with the use of an intrauterine manipulator is a critical step in allowing adequate exposure to safely perform the procedure. Although it has been hypothesized that the introduction of a uterine manipulator may disrupt tumor and cause dissemination of cancer cells, this has been refuted by several studies that have failed

to show a difference in the risk of recurrence or overall survival in the management of endometrial cancer.^{21–24}

The use of the manipulator for cervical cancer remains slightly more controversial. Rakowski *et al.* retrospectively evaluated clinical-data and tumor pathology from open and robotic-assisted radical hysterectomy cases and found no difference in depth of invasion, lymphovascular space invasion, or parametrial involvement.²⁵ There are only case reports of artefactual displacement of CIN III to fallopian tubes during laparoscopic hysterectomy with use of the intrauterine manipulator; however, this raises a theoretical mechanism of cervical cancer cell dissemination into the peritoneal cavity.²⁶

Special populations

Tumors 2 cm—A major limitation of the LACC trial was the inability to generalize the results of the trial to ‘low risk’ cervical cancer cases including tumors of less than 2 cm due to the trial being under-powered.¹⁷ Additionally, in the companion retrospective SEER database study, there was no survival difference observed between the two surgical methods for patients with a tumor of less than 2 cm.¹⁸ The significance of the 2 cm size cut-off has also been incorporated in the most updated FIGO cervical cancer staging, suggesting that this tumor size is of oncologic significance.²⁷ Therefore, given the limited data in patients with small lesions or < 2 cm, among appropriately selected cases, robotically assisted surgery may still be an appropriate option after thorough counseling.^{28,29}

Fertility sparing—While the standard treatment for early-stage cervical cancer remains radical hysterectomy with pelvic lymphadenectomy, in patients who desire future fertility, the option of radical trachelectomy with pelvic lymphadenectomy may be considered. Several prognostic factors have been identified including histology, LVSI, and deep stromal invasion when comparing radical trachelectomy to radical hysterectomy for management.³⁰ Tumor size remains controversial with several studies demonstrating conflicting results regarding outcomes for tumors greater or less than 2 cm.^{31,32} There remains limited data regarding the role and outcomes of robotically assisted trachelectomy for cervical cancer. Currently, a multinational study (IRTA study) assessing differences between an open vs minimally invasive (robotic or laparoscopic) approach to radical trachelectomy is underway and will help inform clinical practice.

Endometrial cancer

In 2019, there will be an estimated 65,620 new cases of endometrial cancer diagnosed and 12,590 deaths attributed to the disease in the United States.⁹ The current treatment for early-stage endometrial cancer includes an extrafascial hysterectomy, bilateral salpingo-oophorectomy with or without a pelvic lymphadenectomy or aortic lymph node sampling. Unlike cervical cancer, there are several landmark randomized controlled trials that have evaluated the safety and feasibility of minimally invasive surgery in the management of endometrial cancer. The Gynecologic Oncology Group LAP2 Study (GOG-LAP2; [Clinicaltrials.gov NCT00002706](https://clinicaltrials.gov/NCT00002706)) was the first trial that demonstrated improved short-term surgical outcomes including shorter hospital stay and fewer complications with laparoscopy compared to open surgery.³³ Notably, the conversion rate from laparoscopy to open surgery

was 26%. The study evaluated more than 2500 patients, and reported no difference in overall survival or recurrence between the two arms.³⁴ Additional studies include the Laparoscopic Approach to Cancer of the Endometrium (LACE; [Clinicaltrials.gov NCT00096408](https://clinicaltrials.gov/ct2/show/study/NCT00096408)) trial, a multinational, randomized trial evaluating laparoscopic vs open hysterectomy, which again showed no difference in disease-free survival or overall survival at 4.5 years.³⁵

To date, there are no large randomized trials comparing laparoscopy, laparotomy and robotic-assisted surgery in the management of endometrial cancers. A systematic review published in 2010 compared all three surgical modalities (laparoscopy, laparotomy and robotic assistance) and analyzed eight studies which included 1591 patients. Robotic surgery was associated with less blood loss compared to both laparoscopy and laparotomy, operative times were longer with robotic and laparoscopy (however both were similar) than laparotomy, and length of stay was shorter for minimally invasive approaches. The conversion rates for laparotomy were 4.0% for robotic-assisted and 9.9% for laparoscopy; however, this difference was not statistically significant.³⁶ Ran *et al.* also conducted a meta-analysis in 2014, which included 22 studies that compared the three surgical approaches and similarly concluded that robotic surgery is safe and may be beneficial over traditional laparoscopy. They found similar operative times between laparoscopy and robotic approaches however demonstrated less blood loss and lower conversion rates in robotic cases.³⁷ In 2019, a Danish study prospectively reviewing outcomes of early-stage endometrial cancer cases found that abdominal hysterectomy was associated with increased odds of severe complications compared to a minimally invasive approach (OR, 2.58; 95% CI 1.80–3.70) and was associated with higher mortality compared to laparoscopic and robotic approaches (laparoscopic HR 1.42; 95% CI 1.02–1.97 and HR 1.70; 95% CI 1.31–2.19, respectively).³⁸

At this time, the evidence continues to support the use of minimally invasive surgery over laparotomy in the management of early stage endometrial cancer. Several studies have also suggested a benefit in robotic assistance over laparoscopy, which has been associated with decreased blood loss and lower conversion rates to open surgery. Additional randomized studies are needed to assess the long-term oncologic outcomes.

Surgical techniques

At our institution, patients are counseled prior to surgery regarding postoperative care including the option for same-day discharge, which is routinely offered with the exception of patients with significant medical co-morbidities. Prior to surgery, we use a 'T-Score' system to stratify patients based on several factors: BMI (body mass index), uterine size, history of abdominal surgeries, vaginal parity and cardiopulmonary reserve (Table 3). This scoring system allows for appropriate pre-operative counseling on the success of a robotic-assisted approach. Mechanical bowel prep or antibiotics are not routinely administered prior to surgery; however, if a para-aortic lymphadenectomy is highly anticipated, Miralax with two bisacodyl tablets are prescribed to improve visibility. We routinely use a TrenGuard 450 Trendelenburg restraint, which aims to eliminate patients sliding in Trendelenburg position by placing stabilizing pillows to effectively act as a 'speed bump'. This technology can secure patients up to 450 pounds in up to 40° of Trendelenburg. In positioning obese patients,

we recommend a stepwise approach by testing ventilator pressures by incrementally placing the patient in steep Trendelenburg. For high-risk patients, we also recommend placement of two peripheral intravenous cannulae prior to tucking arms to improve access in the event of major bleeding in addition to having a laparotomy tray available in the room. In our experience, uterine manipulation is helpful to improve visibility and safety. We routinely use the V-Care disposable uterine manipulator (ConMed).

For abdominal entry, we anesthetize port sites with 0.5% bupivacaine, and prefer direct entry method with an 8 mm optical trocar under direct visualization prior to CO₂ insufflation. The four DaVinci robotic ports are 8 mm in size but we recommend making a 9 mm incision at each entry site in order to facilitate smooth placement (without excessive pressure due to skin dystocia) of each cannula using the clear plastic tapered obturator for Xi arms 1, 2, and 4. The placement of the camera port depends on the patient's body habitus, uterine size, and the need for para-aortic lymphadenectomy; this port is generally placed 23–27 cm superior to the pubic symphysis. A zerodegree camera lens is placed in the third arm of the Xi, monopolar scissors are placed in the fourth arm, a bipolar fenestrated grasper is placed in the second arm, and a double fenestrated pro-grasp is placed in the first arm. The robot is side-docked on the left side of the patient. (Fig. 3) After delivery of the uterus through the vagina, a sterile lap is placed within a glove to occlude the vagina during cuff closure. The monopolar and bipolar instruments are exchanged for a DaVinci Mega Suturecut Needle Driver and DaVinci Mega Needle Driver, respectively. 0 vicryl ct-1 sutures x 2 are then introduced via the assistant port and vaginal cuff closure is accomplished with surgeon's knots at each angle and then a running locking stitch towards the center of the cuff where the sutures are tied together and the needles removed and retrieved through the assistant port. Following the running of one side of the cuff, the double fenestrated pro-grasp can be used to maintain upward traction on the cuff and tension on the repair while the surgeon begins the closure on the opposite side.

The placement of the five ports follows a gentle 'rainbow' pattern on the abdomen with the assistant port in the right lower quadrant, directly opposite the DaVinci Xi arm 1 in the left lower quadrant. When pelvic lymphadenectomy is anticipated, we use a 12 mm AirSeal System Insufflation (ConMed) and have the console surgeon use the robot to assist the surgical assistant in closing the 12 mm port with 0 vicryl suture delivered with the Carter Thomason Fascial Closure Device to prevent hernia formation. When lymphadenectomy is not planned, we use a 5 mm assistant port and pass 0 vicryl ct-2 sutures x 2 through the Xi arm 1 port for vaginal cuff closure. Once both sutures have been delivered, the surgeon can place one needle into the undersurface of the anterior abdominal wall for security and the surgical assistant replaces the double fenestrated pro-grasp in the Xi arm 1 to facilitate vaginal cuff closure. The needles are then returned through the Xi arm 1. Finally, for women with large uteri (12–14 cm or greater) that cannot be delivered transvaginally, a small mini-laparotomy incision in the direction of Pfannensteil can be performed with the robot remaining docked; the uterus is delivered through the incision which is then quickly repaired and the console surgeon then proceeds to close the vaginal cuff robotically.

Sentinel lymphadenectomy and firefly fluorescence

The sentinel lymph node (SLN) algorithm was first incorporated into the NCCN guidelines for patients with endometrial cancer in 2014.³⁹ Since 2011, there has been a rapid increase in the use of SLN to detect nodal metastasis, with the most notable increase observed in women undergoing robotic-assisted hysterectomy.⁴⁰ The FIRES trial ([Clinicaltrials.gov NCT01673022](https://clinicaltrials.gov/ct2/show/study/NCT01673022)) is a multicenter, prospective, cohort study with 385 patients enrolled of which 340 underwent sentinel lymph node mapping using indocyanine green (ICG) and fluorescence imaging with complete pelvic lymphadenectomy. Of these patients, 41 (12%) patients had positive nodes, of whom 36 had at least one mapped sentinel lymph node. Nodal metastases were identified in 97% (35/36) of the sentinel lymph nodes resulting in a sensitivity of 97.2% and a negative predictive value of 99.6%.⁴¹ Several studies have also compared the SLN detection rate with ICG compared to blue dye and found a superior detection rate with ICG (detection rate ICG 90.9% vs blue dye 64.4%, $p < 0.0001$).^{42,43}

At our institution, for low-risk patients defined as endometrioid adenocarcinoma with <50% myometrial invasion, we have historically used intraoperative frozen section with Mayo criteria to triage patients for lymphadenectomy. Patients without myometrial invasion, grade 1 or 2, or with a tumor size ≤ 2 cm are omitted from undergoing routine lymphadenectomy. Compared to the Mayo Clinic historical algorithm, the Memorial Sloan Kettering (MSK) surgical algorithm incorporated SLN mapping in all endometrial cancer staging in addition to the removal of any suspicious nodes. If there was no mapping on a hemi-pelvis, a side-specific lymphadenectomy was performed with para-aortic lymphadenectomy at the surgeon's discretion. In combination with the MSK algorithm, patients who undergo unsuccessful mapping of a hemi-pelvis, application of these criteria have been used selectively to omit them from undergoing lymphadenectomy by Mayo criteria. When reviewed retrospectively, Leiteo *et al.* found an increased proportion of patients undergoing pelvic lymph node excision with the SLN algorithm versus the selective Mayo LND algorithm, however fewer lymph nodes were removed with the SLN protocol. Overall, both approaches were without any compromise on short-term oncologic outcomes with similar 3-year overall survival.⁴⁴

We use a sentinel lymph node mapping protocol similar to the procedure presented in the FIRES trial. After induction of anesthesia, a standardized dose of 0.5 mg/mL of ICG tracer is injected into the cervix. This concentration is achieved by creating a dilution of 1 mL of the ICG solution (2.5 mg/mL) into 4 mL of sterile water. Using a 22-G spinal needle, 1 cc of the ICG solution is then injected into the cervix at 3 and 9 o'clock of the ectocervix approximately 1 cm deep, and an additional 1cc is injected superficially at both sites. Following entry into the peritoneal cavity using the da Vinci Xi surgical robot, the ICG tracer can be used to visualize the lymphatic channels. Firefly fluorescence imaging for da Vinci Surgical System contains an 806 nm laser light source that allows ICG to fluoresce when illuminated. The fluorescent light is then captured with a special camera device that allows the ICG to be displayed in the visible light spectrum.⁴⁵ Mapping is considered successful after observing a channel from the cervix leading to at least one lymph node in the hemi-pelvis. Following sentinel lymph node removal, specimens are routinely processed using the ultra-staging protocol. Sentinel lymph nodes are cut at 3 mm intervals; both

hematoxylin and eosin (H&E) and pancytokeratin immunohistochemistry staining are performed. Metastatic disease is defined as either macro- with greater than 2 mm of disease, micro- with 0.2–2 mm of disease volume, or isolated tumor cells with foci less than 2 mm in greatest dimension.

Para-aortic lymphadenectomy

While lymph node status is required for the complete FIGO surgical staging of endometrial cancer, the routine systematic use of para-aortic lymphadenectomy remains controversial.³⁹ Similar to what has been previously described, we use a center docked trans-peritoneal approach for para-aortic lymphadenectomy.^{46–48} The omentum and small bowel are carefully moved into the left upper quadrant using a Ray-Tec sponge to allow for adequate visualization. The procedure then starts with an incision of the peritoneum along the right common iliac artery medial to the ureter. This allows mobilization of the cecum cephalad. The bedside assistant then laterally retracts the ureter and ovarian vessels. Once the peritoneum is opened, the psoas muscle and genitofemoral nerve are identified. The dissection is extended to the bifurcation of the aorta allowing for removal of the common iliac lymph nodes with development of pedicles using monopolar cautery. The bedside assistant gently grasps the small bowel peritoneum then to adequately expose the duodenum and aorta to allow the dissection to continue along the entire surface of the inferior vena cava to the level of the reflection of the duodenum. The first arm is then used to retract the duodenum above the renal vein allowing for exposure. The lymph nodes are then dissected from the left renal vein to the inferior mesenteric artery (IMA) with blunt dissection and monopolar cautery, with care to avoid perforating lumbar vessels. Dissecting below the IMA down to the external iliac then completes the lymphadenectomy. We recommend that all major lymphatic trunks be bipolar cauterized or clipped to minimize the development of lymphoceles. The left ureter can be identified by making a small window in the mesentery of the sigmoid colon.

Special populations

Obese patients—Surgery remains the primary treatment for endometrial cancer, and the approach used has a significant impact on the morbidity and cost associated with the management of obese patients. Obesity is a well-established risk factor for the development of endometrial cancer.⁴⁹ In obese patients, similar benefits have been demonstrated with minimally invasive surgery.⁵⁰ When evaluating the role of robotic surgery, several retrospective studies have shown findings consistent with prior studies evaluating laparoscopy.^{51–53} In 2008, Gehrig *et al.* retrospectively reviewed outcomes for obese and morbidly obese patients undergoing laparoscopy versus robotic-assisted surgery and found that robotic surgery was associated with shorter operative time ($P = 0.0004$), less blood loss ($P < 0.0001$), increased lymph node retrieval ($P = 0.004$) and shorter hospital stay ($P = 0.01199$).⁵² When evaluating robotic surgery in super-morbidly obese patients (BMI > 50 kg/m²), a retrospective analysis of 168 patients found similar outcomes between supermorbidly obese patients compared to those with a lower BMI (length of stay, blood loss, complications, number of lymph nodes), suggesting that robotic surgery is a feasible option for these patients.⁵⁴ While robotic surgery in the obese patient with endometrial cancer is safe and feasible, there is still limited prospective data evaluating the long-term

oncologic outcomes as well as cost effectiveness. For example while, Chan *et al.* demonstrated similar outcomes between laparoscopy and robotic-assisted surgical management in regards to intraoperative and postoperative complications, this study went further in highlighting the increased charges incurred with robotic surgery versus laparoscopy.⁵⁵ For morbidly obese women, we use a step-wise approach of graduated placement into steep Trendelenburg position (5 degrees at a time) allowing the patient to equilibrate as the anesthesiologist monitors tidal volumes and peak pressures. With this technique we have successfully provided minimally invasive robotic surgery to women with BMI 60–82.

Elderly—As life expectancy continues to increase in industrialized nations, we anticipate increasing rates of gynecologic malignancies diagnosed during later decades in life. This will likely present more challenging medical and surgical clinical scenarios. Surgery is often avoided altogether in some high-risk scenarios leading to significant undertreatment. Although most studies in these populations are retrospective, similar outcomes have been observed with decreased morbidity associated with laparoscopic surgery.^{56,57} In a retrospective analysis of patients from the Gynecologic Oncology Group LAP2 trial randomizing patients to laparotomy vs laparoscopy, patients greater than 60 years old experienced significantly less morbidity in the laparoscopic group. Patients across all ages experienced shorter hospital stay in the laparoscopy group, however, when stratifying by age, patients ≥ 60 years old with laparotomy had higher rates of antibiotic administration ($P < 0.001$), ileus ($P < 0.001$), pneumonias ($P = 0.48$), deep vein thrombosis ($P = 0.035$) and arrhythmias ($P = 0.01$) compared to laparoscopy.⁵⁸ Leiteo *et al.* retrospectively evaluated 982 patients who underwent robotic surgery for gynecologic cancer which were stratified by three age groups: 65–74, 75–84, and ≥ 85 years old. In multivariate analysis, ≥ 85 years was independently associated with 90-day mortality (4%), however, overall mortality rate remained low (0.5%) in the study.⁵⁹ While much of the data applied to the aging population is extrapolated from laparoscopic surgery, a similar benefit may be conferred by robotic surgery; however, randomized data are limited.

Ovarian cancer

Despite being an effective form of treatment for endometrial cancer, there are few studies evaluating the role of robotic-assisted surgery in the initial staging or management of recurrent ovarian cancer. Currently, 15–25% of patients with ovarian cancer will be diagnosed at an early stage in the United States, thus complete surgical staging is a critical component of prognosis and treatment planning. According to NCCN guidelines, complete surgical staging should include hysterectomy, bilateral salpingo-oophorectomy, omentectomy, pelvic and para-aortic lymphadenectomy and peritoneal biopsies.⁶⁰ Given the multiquadrant disease distribution, it has been argued that it is insufficient to assess disease in anatomically challenging locations (lesser sac, Morison's pouch, mesentery) with MIS, arguing in favor of open surgery for intra-abdominal evaluation. Given the risk of tumor spillage and multiquadrant disease, robotic-assisted surgery or MIS is not recommended for the management of early or advanced stage ovarian cancer.⁶¹

Special population

Neoadjuvant chemotherapy—There remains a lack of consensus on the superiority of neoadjuvant chemotherapy followed by interval cytoreductive surgery in the primary management of ovarian cancer.^{62–65} The results of the Japan Clinical Oncology Group JCOG 0602 and the SCORPION trial ([Clinicaltrials.gov NCT01461850](https://clinicaltrials.gov/ct2/show/study/NCT01461850)) are pending in addition to several ongoing studies (the Trial on Radical Upfront Surgery in Advanced Ovarian Cancer [TRUST] trial; [Clinicaltrials.gov NCT02828618](https://clinicaltrials.gov/ct2/show/study/NCT02828618) and Study of Upfront Surgery Versus Neoadjuvant Chemotherapy in Patients with Advanced Ovarian Cancer (SUNNY) trial; [Clinicaltrials.gov NCT02859038](https://clinicaltrials.gov/ct2/show/study/NCT02859038)).^{62,63} Current NCCN guidelines recommend that neoadjuvant chemotherapy be considered for patients with bulky stage III or IV disease following an assessment by a gynecologic oncologist.⁶⁰ Patients often respond to neoadjuvant chemotherapy and can have a complete response with absent gross residual disease prior to surgery. In this clinical context, the decision to perform robotic surgery requires extensive patient counseling and at minimum the following criteria: a normal CA-125, post-chemotherapy imaging scan without any evidence of disease (including an absence of ascites), a normal pelvic exam under anesthesia, and laparoscopic evaluation confirming an absence of visible disease or ascites.

Discussion

Robotic-assisted surgery has transformed the field of gynecologic oncology over the last 15 years. This minimally invasive surgical platform has allowed an increasing number of patients access to the immediate benefits of MIS, including less blood loss, shorter hospital stays, decreased wound complications, and quicker recovery time. Telesurgery and the ability for surgeons to operate remotely with robotic technology is emerging as an area of research. Recently, a robotic-assisted percutaneous coronary intervention was successfully performed at a site 10 miles away in Ahmedabad, India.⁶ While the field continues to move forward with more applications, it remains critical in the field of oncology that we continue to assess the oncologic safety. While many studies during the initial uptake of minimally invasive techniques consistently demonstrated the improved short-term outcomes for patients with less morbidity, additional studies including the LACC trial have challenged the MIS approach citing worse oncologic outcomes. While the FDA has issued a safety warning in regards to the robotic platform, a very small percentage of women underwent robotic surgery in the LACC trial. These limitations should be strongly considered when designing future randomized surgical trials. Additional randomized clinical trials are needed to better guide gynecologic oncologists in deciding the most appropriate surgical approach to optimize patient outcomes and appropriately triage patients.

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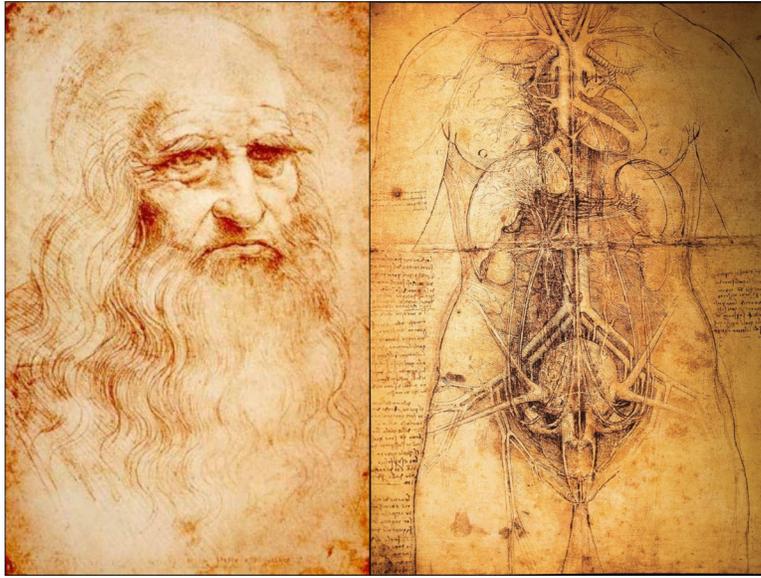


Figure 1. Self-portrait of Leonardo da Vinci (1452–1519) and his detailed sketch of female anatomy.



Figure 2. Construction of Leonardo da Vinci's mechanical drummer and mechanical knight, on display in Berlin. Designed around 1495 for a pageant in Milan, the Robotic Knight consisted of a life-size suite of armor filled with gears and wheels connected to an elaborate pulley and cable system allowing for independent motion (sitting down, standing up, moving its head, lifting its visor, and even playing the drums; rumors also suggested the Knight had the secret ability to write messages and draw pictures). This prototype was built by roboticist Mark Rosheim in 2002.

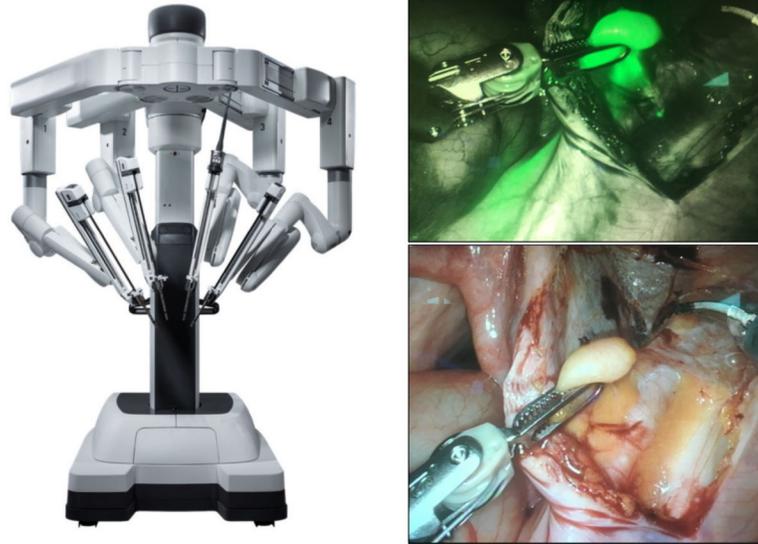


Figure 3. The DaVinci Xi Surgical Robot and DaVinci Robot Firefly™ technology demonstrating sentinel lymphatic mapping for endometrial cancer through which near-infrared light excites indocyanine green tracer to emit a fluorescent signal. Images from Dr. Tewari's surgical practice.

Table 1

Advantages of Minimally Invasive Surgery (MIS, laparoscopic and robotic) compared to Laparotomy;
Advantages of Laparoscopy compared to Robotics.

MIS	Laparotomy
<ul style="list-style-type: none"> • Hospitalization not required (decreased hospital costs, reduced likelihood of contracting hospital-acquired infection) • Improved cosmesis and reduced risk of cellulitis, superficial wound separation, need for Wound VAC, hernia formation requiring mesh, diasthesis, evisceration with acidosis, intra-abdominal adhesions with associated discomfort, hazardous subsequent surgery, and small bowel obstruction • Less time to reach postoperative milestones (voiding, ambulation, regular diet, bowel function, pain control, driving, exercise, return to work) • Visualization magnified (less blood loss, fewer blood transfusions, fewer complications) 	<ul style="list-style-type: none"> • Tactile feedback • Ability to remove large organs intact • Shorter operating times (reduced OR costs, less exposure to inhalational anesthetics, more efficient use of surgeon's time) • Expeditious control of catastrophic hemorrhage • More complex operations possible
Laparoscopic	Robotic
<ul style="list-style-type: none"> • Haptic feedback • Cost-effective • Fewer and smaller incisions • Avoidance of prolonged Trendelenberg • Flexibility in instrument configuration 	<ul style="list-style-type: none"> • Ergonomically superior • Intuitive nature • Camera stabilization • Wristed instrumentation with improved dexterity (precision with dissection, ease of suturing, facilitates development of surgical planes in areas riddled with disease) • Motion dampening sensors (tremor filtration) • Depth perception due to 3D camera (less blood loss, reduced transfusions, reduced complications) • May facilitate MIS for morbidly obese • Lower conversion rate to open surgery

Table 2

Selected publications of robotic surgery in cervical cancer

Source/year	Study design	Groups	Disease	Number of patients				Significance
				Total	RRH	LRH	ARH	
Boggess 2008	Case control	RRH vs ARH	Early stage cervix	100	51	—	49	First case series of RRR, RRR associated with shorter operative time, LOS, less blood loss; similar complication rate
Magrina 2008	Prospective	RRH vs LRH vs ARH	Stage IA2-IB2 cervix and corpus	57	18	18	21	First study comparing RRR and LRH to ARH, shorter operating times for RRR with similar outcomes to LRH
Nezhat 2008	Retrospective	RRH vs LRH	Stage IA1-IIA cervix	43	13	30	—	RRH similar to LRH in operative time, blood loss, hospital stay and oncologic outcome
Maggioni 2009	Prospective	RRH vs ARH	Stage IA2-IIA cervix	80	40	—	40	RRH associated with decreased EBL and LOS; increased operative time; no difference in complications
Cantrell 2010	Retrospective	RRH vs ARH	Stage IA1-IB cervix	127	63	—	64	No statistical difference in PFS or OS compared to historical cohort of ARH
Soliman 2011	Retrospective	RRH vs LRH vs ARH	Stage IA1-IBA cervix and corpus	95	34	31	30	MIS associated with less EBL, LOS; trend toward higher conversion rate in LRH compared to RRR, shorter operative time with ARH
Tinelli 2011	Prospective	RRH vs LRH	Stage IA1-IB cervix	99	23	76	—	No difference in blood loss, LOS, recurrence rates, longer operative time for LRH
Wright 2012	Population-based retrospective	RRH vs LRH vs ARH	Cervix (stage unknown)	1894	67	217	1610	ARH associated with increased perioperative complications, MIS associated with lower transfusion rates and LOS
Kim 2014	Retrospective case-control	RRH vs LRH	Stage I-IIA cervix	92	23	69	—	RRH associated with less EBL, longer operative time; no difference in complications or 3-year recurrence free survival
Shazly 2014	Meta-analysis	RRH vs LRH vs ARH	Stage IA1-IIA cervix	4013	1013	710	2290	RRH superior to ARH with lower EBL, LOS, wound and febrile morbidities; RRR comparable to LRH in short-term outcomes
Kong 2016	Retrospective case-control	RRH vs LRH vs ARH	Stage IB-IIA cervix	128	20	108	—	Disease recurrence higher in RRR/LRH with intracorporeal colpotomy vs LRH vaginal colpotomy (16 vs 5.1%, $P = 0.057$)
Sert 2016	Retrospective	RRH vs ARH	Early stage cervix	491	259	—	232	RRH less EBL, LOS, longer operative time; recurrence and death rates similar at 3 years
Mendivil 2016	Retrospective case-control	RRH vs LRH vs ARH	Early stage cervix	146	58	49	39	ARH associated with increased LOS; EBL; LRH shorter operative times; no difference in OS or PFS
Zanagolo 2016	Retrospective case-control	RRH vs ARH	Early stage cervix	307	203	—	104	RRH associated with less EBL, LOS; no difference in OS or PFS at 3 years
Diver 2017	Retrospective cohort	RRH vs LRH vs ARH	Stage IA-IBB cervix	383	71	30	282	Similar OS and recurrence between MIS and ARH, ARH associated with increased EBL and LOS
Pellegrino 2017	Long-term follow-up of prospective study	RRH vs LRH	Stage IA1-IIA2 cervix	52	34	18	—	RRH associated with decreased EBL, similar operative time; OS at 59 months (RRH 100% vs LRH 83%)
Shah 2017	Retrospective case-control	RRH vs ARH	Stage IA1-IB2 cervix	311	109	—	202	RRH associated with less EBL, LOS, complications; no difference in PFS or OS

Source/year	Study design	Groups	Disease	Number of patients				Significance
				Total	RRH	LRH	ARH	
Chong 2018	Retrospective	RRH vs LRH	Early stage cervix	125	65	60	—	RRH associated with longer operative time; OS lower in RRH compared to LRH ($P=0.0762$), no difference in recurrence pattern ($P=0.7$) however peritoneal recurrence only in RRH group
Gallotta 2018	Retrospective	RRH vs LRH vs ARH	Stage IA2-IB2 cervix	210	70	140	—	RRH associated with longer operative time; no difference in 3-year DFS or OS
Jim 2018	Meta-analysis	RRH vs LRH vs ARH	Stage I-II cervix	2100	n/a	n/a	n/a	17 studies included; RRH and LRH lower EBL and LOS compared to ARH
Ramirez 2018	Prospective phase III RCT	RRH/LRH vs ARH	Stage IA1-IB1 cervix	631	269	49	312	Disease free survival lower in LRH/RRH (86%) compared to ARH (96.5%) and overall survival (93% vs 99%)
Melamed 2018	Population-based cohort study	RRH/LRH vs ARH	Stage IA2-IB1	2461	978	247	1236	Increased 4 year mortality in LRH/RRH group (9.1%) compared to ARH (5.3%)
Siesto 2019	Retrospective case series	RRH vs ARH	Stage IA-IIA1 cervix	91	91	—	—	RRH 40 month follow-up, DFS 90.4% (95% CI 85.3-95.6) and OS 94.5% (95% CI 91.8-97.2)
Matanes 2019	Retrospective	RRH vs ARH	Early stage cervix	98	74	—	24	Recurrence rate lower in RRH (17% vs 7%); no difference in OS or PFS at 46 months
Zhang 2019	Meta-analysis	RRH vs LRH vs ARH	Cervix	2197	932	373	892	12 studies included, RRH less EBL, shorter LOS compared to ORH; no difference between RRH and LRH in tumor recurrence
Doo 2019	Retrospective	RRH vs ARH	Stage IB1 cervix	105	49	—	49	No difference in recurrence risk, PFS or OS; however in tumors > 2 cm higher risk of recurrence in RRH, higher risk of recurrence (30 vs 8%, $P=0.006$) and shorter PFS (HR 0.31)
Alfonzo 2019	Population-based cohort	RRH vs ARH	Stage IA1-IB cervix	864	628	—	236	No difference in 5-year OS or DFS between open and robotic groups
Cusimano 2019	Population-based retrospective	RRH vs LRH vs ARH	Cervix	958	49	424	483	MIS associated with increased rates of death and recurrence compared to OH in patients with IB disease but not IA disease

Abbreviations: ARH, abdominal radical hysterectomy; LRH, laparoscopic radical hysterectomy; RRH, robotic-assisted radical hysterectomy.

Table 3

T-score, preoperative assessment for minimally invasive approach to hysterectomy

Points	BMI	Uterine size (cm)	Abdominal surgeries	Vaginal parity	Cardiopulmonary reserve
0	30	10	None	Prior vaginal birth(s)	No significant medical co-morbidities
1	31–44	11–13	LTC/S only and/or LSC	No prior vaginal births	Mild-to-moderate medical co-morbidities (eg, mild hypertension)
2	45	>13	Midline vertical or other exploratory	C/S only	Significant co-morbidities (eg, history of cardiac arrest, severe hypertension, aortic stenosis, pulmonary fibrosis, etc)

BMI, body mass index; C/S, cesarean section; LSC, laparoscopy; LTC/S, low transverse cesarean section. The T score (Tewari score) is calculated by adding the points for the five components listed in the table.