Update on minimally invasive surgery in the management of gynecologic malignancies: focus on robotic laparoscopic systems

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Laparoscopic management of gynecologic malignancies has experienced an unparalled expansion in the last 10–15 years, driven by tremendous advances in technology, medicine and surgical techniques. The best example of this comes from the adoption of robotic technology for minimally invasive procedures. These procedures and other minimally invasive laparoscopic procedures are now being explored, defined and are gaining wide acceptance for treatment of endometrial, cervical, and ovarian cancer treatment. When compared with standard open techniques in large studies, minimally invasive procedures seem to offer similar or improved survival with the added benefits of faster recovery, decreased blood loss, decreased pain, and improved quality of life. Ongoing clinical trials will undoubtedly encourage future and current laparoscopic surgeons to deploy this exciting technology to fulfill the surgical extirpation of malignant disease while providing patients with the most minimally invasive approach.

Since the late 1980s, significant advances have been made in the development and implementation of minimally invasive surgical procedures for gynecologic malignancies, particularly cancers of the uterus and cervix. The published literature on advanced minimally invasive procedures in gynecologic oncology has grown steadily during the past quarter century and currently numbers over 100 reports.[1] Technology has improved significantly since the late 1980s with the development of more powerful computers and more sophisticated optical systems and surgical instrumentation. These technical developments have enabled surgeons to perform minimally invasive procedures once thought to be infeasible. Laparoscopy is now available for most patients with endometrial and cervical cancer and is gaining popularity among advanced laparoscopists for use in staging early ovarian cancer or selecting patients for neoadjuvant chemotherapy. This review chronicles the increasing use of laparoscopic procedures for the management of gynecologic malignancies. The emerging role of robotic laparoscopic procedures will be explored, with particular focus on the da Vinci® Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA).

Evolution of the robotic surgical platform

The military was the first group to show an interest in using robotic systems for performing surgeries. The focus of initial development was the capability of robotic surgical procedures to be performed on soldiers near or at the frontline of battle by surgeons based in a noncombat area. This technological concept developed by the military provided a framework for engineers and technicians in the private sector to adapt and enhance robotic surgery for use in the health care industry.
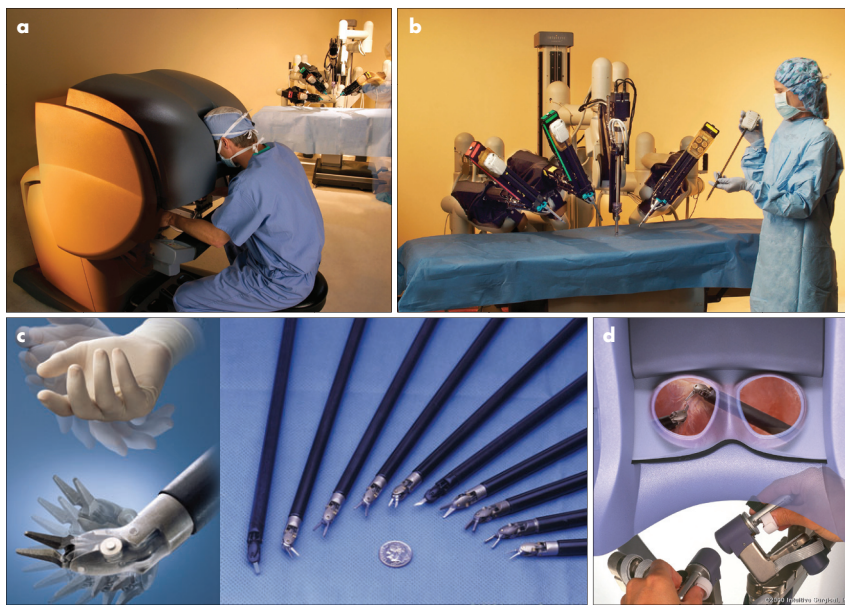
Early robotic systems for laparoscopic procedures

Initial attempts to use robotics for laparoscopic procedures involved the Automated Endoscopic System for Optimal Positioning (AESOP®) device (Computer Motion, Inc., Goleta, CA). This voice-activated system allows the surgeon to control robotic motions via specific verbal commands.

FIGURE 1 Primary components of the da Vinci® Surgical System. (**a**) The da Vinci Surgical System is manipulated via master controls located on this console. While seated on an ergonomically designed, backless chair, the surgeon views a three-dimensional (3D) image of the surgical field. The surgeon's first and second digits of the left and right hands fit into the master controls, which transmit the surgeon's hand, wrist, and finger movements into precise, real-time movements of the EndoWrist® Instruments inside the patient. (**b**) The patient-side cart consists of 3 or 4 robotic arms, 2 or 3 of which house instruments and 1, the endoscope. The arms pivot at 1- to 2-cm port sites, thereby executing the surgeon's transmitted movements. The patient-side surgical assistant team member installs and changes EndoWrist Instruments and supervises the patient side aspects during surgery. (**c**) The surgeon can select from among a wide variety of EndoWrist Instruments during a procedure. The instruments allow for seven degrees of freedom, which mimic the movements of the surgeon's hands, wrists, and fingers. Each instrument is designed for a specific task, such as suturing, grasping, or incising tissue. Several instruments can also provide monopolar or bipolar cauterization. Quick-release levers allow for rapid exchange of instruments by the surgical assistant. (**d**) The InSite Vision System provides the surgeon with 3D endoscopic visualization. The processing technology enhances the surgeon's view through image synchronizers, high-intensity illuminators, and camera control units. Controls on the console enable the surgeon to revert to two-dimensional images.

AESOP was used mainly for the manipulation of the endoscopic camera. Initial evaluation of AESOP in 50 patients indicated that surgeons could perform routine gynecologic endoscopic surgical procedures more rapidly using the device.[2]

Technological advances led to the development, also by Computer Motion Inc., of the ZEUS™ Robotic System. This device made use of 3 robotically controlled arms that were directly connected, via cables, to a surgical table and a work station with a surgeon/robotic console. The first robotic-assisted cardiovascular bypass surgery performed in the United States used ZEUS.[3]

da Vinci Surgical System

The next development in robotic surgery was telesurgery, ie, surgery that can be performed by surgeons separated physically from the patient. This approach was pioneered by Intuitive Surgical Inc., with the development of the da Vinci Surgical System. The da Vinci system consists of four primary components: the surgeon's console, the patient-side cart, proprietary EndoWrist® Instruments, and the three-dimensional (3D) InSite® Vision System (Figure 1). The surgeon's console is connected electronically to the surgical arena via the Internet; as a result, the surgeon can be hundreds of miles away from the patient. The system translates the movements of the surgeon's hands into robotic manipulation intraoperatively, which allows the surgeon to manipulate the laparoscopic surgical instruments remotely.

The da Vinci Surgical System is approved in the United States and Europe and is being used in over 300 hospitals. According to Intuitive surgical devices company, the *da Vinci*™ Surgical System is cleared in the United States and Europe and is being used at roughly 600 sites worldwide. The *da Vinci* System, which sells for about $1.5 million, has been used in more than 100,000 procedures since it was introduced in 1999. The US Food and Drug Administration has cleared the da Vinci® Surgical System for adult and pediatric use in urologic surgical procedures, general laparoscopic surgical procedures, gynecologic laparoscopic surgical procedures, general non-cardiovascular thoracoscopic surgical procedures and thoracoscopically assisted cardiotomy procedures. To date, the system has been used in such procedures as radical prostatectomy, nephrectomy, ureteral reimplantation, cholecystectomy, Nissen fundoplication, splenectomy, simple and radical hysterectomy, pelvic and aortic nodal dissection, myomectomy, and mitral valve repair.

Use in gynecologic oncology. The da Vinci Surgical System was approved for gynecologic use only recently, in April 2005. Thus, widespread application of the system within the specialty of gynecology or the subspecialty of gynecologic oncology has not yet occurred. To date, the published literature on robotic applications in gynecology and gynecologic oncology is limited despite the fact that 400,000 hysterectomies are performed in the United States annually.[4–10] Most of the published reports have been institutional pilot series examining the feasibility of the da Vinci Surgical System for use in patients with benign gynecologic disease.[4–10]

Procedures that have been performed to date in patients with gynecologic malignancies include simple hysterectomy, modified radical hysterectomy, radical hysterectomy, pelvic and aortic lymph node dissections, and adnexal surgery. The most promising applications of the system in gynecologic oncology appear to be in the management of early-stage endometrial and cervical cancers. In addition, the system has been used to perform surgical staging procedures in patients with endometrial and cervical cancers, and data from small series have been presented at national and regional meetings. All of the reports thus far have demonstrated the system's safety and feasibility.[4–12] Large prospective trials of the da Vinci system in gynecologic oncology have yet to be conducted, however.

Minimally invasive surgery in endometrial cancer

Standard laparoscopic procedures

Recent publications have highlighted the adoption of minimally invasive laparoscopic techniques in the management of endometrial cancer. The laparoscopy (LAP) II trial performed by the Gynecologic Oncology Group (GOG) and 100 participating gynecologic oncologists at 30 institutions was the largest prospective randomized trial of laparoscopy versus laparotomy for the comprehensive staging of patients with endometrial cancer. In this trial 1,696 patients were randomized (2:1) to laparoscopy and 920, to laparotomy. The study results showed that both groups were adequately staged; conversion to a traditional approach occurred in 26% of the patients who underwent a laparoscopic procedure.[13] Patients in the laparoscopy group had a lower incidence of perioperative complications compared with those in the laparotomy group (14% vs 21%), as well as a 50% reduction in postoperative stay (2 vs 4 days).[13] Interestingly 70% of pa-

tients with a body mass index (BMI) of 32 were adequately staged laparoscopically. Analysis of quality of life (QOL) in a subgroup of 782 patients (524 randomized to laparoscopy and 258, to laparotomy) from the LAP II trial showed QOL improvements in the laparoscopy group during the first 6 weeks after surgery. These patients had improved physical functioning, resumption to normal activity, personal appearance, and immediate postoperative pain scores.[13]

Another recently completed study comparing abdominal hysterectomy with laparoscopic hysterectomy for the treatment of endometrial cancer was presented at the 35th Annual Meeting of the Western Association of Gynecologic Oncologists in 2006.[14] In this study, Leiserowitz et al compared data on the two procedures from the California Cancer Registry (CCR) linked to the California Office of Statewide Health Planning and Development (OSHPD) hospital discharge database, 1997–2001. ICD-9-CM codes for diagnostic categories and procedures were identified from the combined database, and information on patient demographics, medical comorbidities, type of surgery, hospital outcomes, and cancer characteristics was compiled.

A total of 13,172 patients underwent a standard total abdominal hysterectomy (TAH) and 1,044, a laparoscopic-assisted vaginal hysterectomy (LAVH). Interestingly, lymph nodes were assessed in fewer than 40% of the patients in both groups. Both overall survival (Figure 2) and cause-specific survival were significantly worse (both $P < 0.0001$) in TAH-treated patients than in LAVH-treated patients, even after adjustment for age, grade, stage, presence of comorbidities, positive nodes, and use of radiation therapy; however, only in patients with grade 1 endometrial cancers, overall survival did not differ ($P = 0.058$) between TAH- and LAVH-treated patients (Figure 3).[14] Metastatic lymph

nodes were uncommon in both groups (4.21% [LAVH] vs 7.05% [TAH]). Although the LAVH and TAH groups incurred similar hospital charges, the LAVH group had a shorter length of stay.[14] Mortality was equivalent in the two groups; however, the LAVH group had decreased short-term morbidity.[14]

Many other smaller studies of laparoscopic surgery published over the last 10 years have consistently demonstrated slightly increased operative times with lower blood loss, shorter hospital stays, fewer postop-
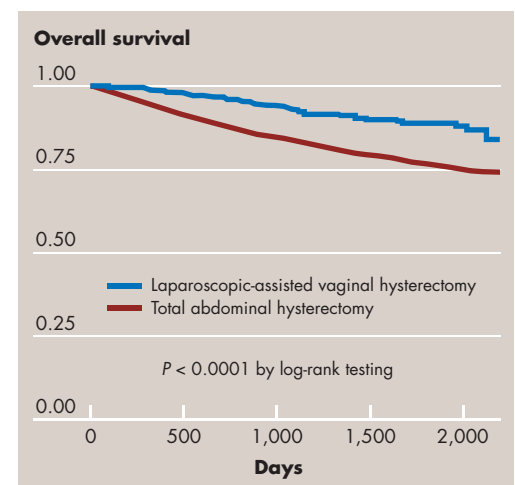
FIGURE 2 Overall survival of patients with endometrial cancer: laparoscopic-assisted vaginal hysterectomy versus total abdominal hysterectomy.
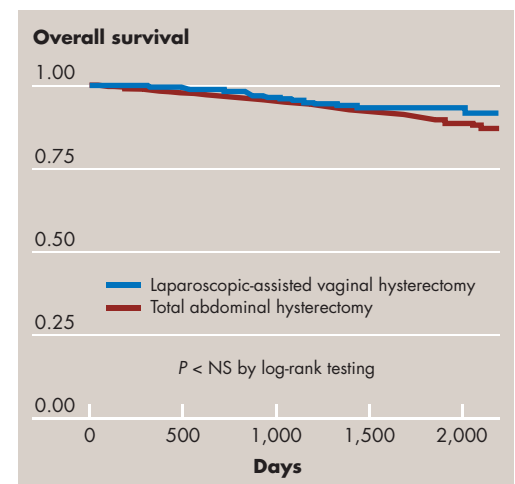
FIGURE 3 Overall survival of patients with grade I endometrial cancer: laparoscopic-assisted vaginal hysterectomy versus total abdominal hysterectomy.

TABLE 1

Pilot series evaluating the utility of da Vinci® Surgical System–assisted robotic procedures in gynecologic oncology

Procedure	Indication	OR time (min)	EBL (mL)	BMI	LOS (days)	Operative complications/ postoperative complications
USO/BSO ± DH	Benign gynecologic disease (n = 10)	121	113	27	0.6	None
DH-BSO-pelvic ± aortic node dissection	Endometrial cancer (n = 9)	177	100	30	1.0	None
DRH	Carcinoma in situ (n = 1); early-stage cervical cancer (n = 2)	225	108	25	2.5	One conversion to laparotomy

OR = operating room; EBL = estimated blood loss; BMI = body mass index; LOS = length of stay; USO/BSO = unilateral or bilateral salpingo-oophorectomy; DH = da Vinci–assisted laparoscopic hysterectomy; DRH = da Vinci–assisted radical hysterectomy

erative complications, and similar or improved nodal counts and survival rates in patients with early-stage endometrial cancer.[15–20] It is not as clear what the outcome of a laparoscopic vs a standard open procedure would be in patients suspected of having distant metastases prior to surgery.

da Vinci–assisted laparoscopic procedures

Only two reports detailing the use of the da Vinci system in the management of patients with endometrial cancer have been published to date. Marchal et al described the use of telerobotic-assisted laparoscopic hysterectomy to manage 12 patients with stage I endometrial cancer. No operative complications occurred, and the authors concluded that robotics can be safely used to perform gynecologic oncology procedures.[11] Reynolds et al detailed their preliminary experience using robot-assisted laparoscopic staging procedures in the management of seven patients with endometrial cancer. No conversions to laparotomy were required. Mean blood loss was 50 mL, and median hospital stay was 2 days.[12]

Preliminary results of our pilot series on the utilization of the da Vinci Surgical System are summarized in Table 1. A total of 22 patients were surgically managed with a robotic approach: 10 patients with benign gy-

necologic disease, 9 patients with endometrial cancer, 1 patient with carcinoma in situ, and 2 patients with early-stage cervical cancer. Procedures performed included simple hysterectomy, modified radical hysterectomy, pelvic and aortic nodal dissection, and adnexal surgery. For all patients, mean blood loss was 110 mL and mean hospital stay was 1 day. Only one patient required conversion to laparotomy.

Although the published literature on applications of the da Vinci Surgical System in gynecology and gynecologic oncology is small, numerous investigators have presented their experience using the system in such procedures as simple hysterectomy, radical hysterectomy, and pelvic and aortic nodal dissections in the management of endometrial cancer as well as cervical cancer (see below).

Minimally invasive surgery in cervical cancer

Minimally invasive surgery has been used in the treatment of patients with early-stage (stage I) cervical cancer and, more controversially, for surgical staging, typically in patients with stages II–IV disease. The advent of improved laparoscopic devices from trocars to instruments has allowed for rapid progress for both treatment and staging.

Treatment

Standard laparoscopic procedures. Patients with stage Ia1 disease and no

lymphovascular space invasion can be managed with a LAVH. Patients with International Federation of Gynecology and Obstetrics (FIGO) stages Ia2–Ib1 squamous lesions may be managed with a laparoscopic-assisted radical hysterectomy. Most authors agree that FIGO stage Ib2 squamous lesions and adenocarcinomas are more satisfactorily managed with an open radical hysterectomy procedure or with chemotherapy and whole pelvic radiation therapy and brachytherapy. Various authors have used either a type II or III hysterectomy performed laparoscopically, including pelvic lymphadenectomy, to manage stages Ia2–Ib1 cervical cancer.[21–24] Table 2 summarizes available data on the use of total laparoscopic radical hysterectomy (type II or III) with laparoscopic pelvic lymphadenectomy in patients with stage I cervical cancer.

Steed et al compared their data on 71 patients with FIGO stage I cervical cancer who underwent total laparoscopic hysterectomy to a time-matched control group of 205 patients who underwent a radical abdominal hysterectomy. Comparison of the laparoscopy vs open hysterectomy groups showed an increase in operating room time (3.5 vs 2.5 hours), a reduction in estimated blood loss (300 vs 500 mL), a decrease in length of stay (1 day vs 5 days), an increase in intraoperative complications (13% vs

TABLE 2

Laparoscopic radical hysterectomy in FIGO stage I cervical cancer

Study (year)	Number of patients	PLN, mean number	(+) PLN	OR time, mean (min)	EBL (mL)	LOS (days)	Complications	Follow-up, median (mo)	DFS, n (%)
Spirtos et al[21] (2002)	78	24	12%	205	225	3	15%	67*	70 (90%)
Abu-Rustum et al[22] (2003)	19	26	5%	371	301	5	53%	4–28†	19 (100%)
Steed et al[23] (2004)	71	NA	7%	210	300	1	13%	17	67 (94%)
Gil-Moreno et al[24] (2005)	27	19	11%	285	400	5	26%	32	27 (100%)

FIGO = International Federation of Gynecology and Obstetrics; PLN = pelvic lymph nodes; (+) PLN = patients with positive lymph node metastases; OR = operating room; EBL = estimated blood loss; LOS = length of stay; DFS = disease-free survival at time of follow-up

* Intraoperative and postoperative complications   † Range

4%), and no difference in postoperative complications or 2-year disease-free survival.[23]

Results of these studies support the feasibility of the laparoscopic approach for radical hysterectomy. The increase in operative time and intraoperative complications associated with the laparoscopic approach suggest areas in need of improvement, whereas the decreases in length of stay and estimated blood loss and the faster postoperative recovery seem to offer advantages over the standard open approach.

da Vinci–assisted procedures. To date, the results of approximately 50 da Vinci–assisted radical hysterectomies for cervical cancer have been reported at regional or national meetings. These data are encouraging in that the successful use of the da Vinci system in advanced and difficult gynecologic oncology procedures is being reproduced by a small number of investigators. The da Vinci system is currently being used to perform total laparoscopic radical hysterectomy in patients with cervical cancer at several institutions of laparoscopic excellence, and data on outcomes, including survival, are expected within the next year. Completion of further studies will be needed to determine the utility of the da Vinci system for total laparoscopic radical hysterectomy in these patients.

Staging

Patients with bulky FIGO stage Ib2 cervical cancers and FIGO stages II–IV are often treated with external-beam radiation in combination with chemotherapy. The risk of pelvic and para-aortic metastatic disease increases substantially as stage increases. In 1996 Finan et al defined the risk of positive pelvic metastatic disease to be 43% in patients with FIGO stage Ib2 disease and the risk of positive para-aortic disease to be 5%.[25] Stehman et al have shown that the presence of para-aortic metastatic disease is the greatest predictor of survival by stage in patients with cervical cancer, and is associated with a substantial reduction in survival (Table 3).[26]

These studies demonstrate the importance of evaluating the nodal basins prior to standard pelvic radiotherapy. Identifying positive metastatic nodes allows the radiation oncologist to tailor the radiated fields to treat 1 level above the metastatic site. Lymphadenectomy remains the gold standard for assessing the nodal basins. Several groups have successfully performed lymphadenectomy via a laparoscopic extraperitoneal approach; laparascopic staging has had few complications,and has uncovered a high incidence of occult nodal metastasis not revealed by computed tomography, magnetic resonance imaging, or positron emission tomog-

raphy.[1,27,32–35] To date, there have been no reports on the use of the da Vinci Surgical System for the nodal staging of locally advanced cervical cancers.

Minimally invasive surgery in ovarian cancer

The cornerstone of ovarian cancer treatment is optimal surgical debulking, with the aim of leaving the smallest possible amount of residual tumor. Once aggressive surgical debulking has been done, the addition of chemotherapy has the greatest chance of achieving a successful outcome. The standard of care for patients found to have ovarian cancer includes surgical staging in addition to optimal tumor debulking. More than 70% of ovarian cancer patients present at an advanced stage, which likely precludes the use of a laparoscopic approach for optimal debulking. Consequently, the laparoscope is often relegated to a diagnostic purpose in patients with widely

TABLE 3

Percentage of patients with metastatic disease in the pelvic lymph nodes [(+) PLN] and para-aortic lymph nodes [(+) PALN]

FIGO stage	(+) PLN	(+) PALN
I	15.4%	5%
II	28.6%	21%
III	47.0%	31%

FIGO = International Federation of Gynecology and Obstetrics
Adapted from Stehman et al[27]

metastatic ovarian cancer. However, in patients with early-stage disease, it is possible to use a laparoscopic approach not only for staging but also for optimal tumor debulking.[28–31]

Second-look surgery for patients with ovarian cancer has largely been abandoned in the United States; however, laparoscopic second-look procedures may serve a purpose in research protocols. Incompletely staged patients at times may benefit from a minimally invasive approach if the disease is thought to be confined to the ovary. Surgeons who lack the expertise in managing a suspicious adnexal mass are potentially placing patients at unnecessary risk of an unsatisfactory outcome or a second surgery.

Conclusions

Laparoscopy has been increasingly accepted by gynecologists and is also gaining momentum for utilization by gynecologic oncologists, as evidenced by its increasing spectrum of use in the treatment of malignancies of the cervix, uterus, and ovaries. Application of the laparoscopic approach has been shown to be feasible in all of these disease sites. When compared with standard open techniques in large studies, minimally invasive procedures seem to offer similar or improved survival with the added benefits of faster recovery and improved QOL.[13-14]

Widespread acceptance of laparoscopy has been inhibited by its slow learning curve, unfamiliarity of surgeons with the devices, and increased operative time. When used by surgeons who are proficient in the technology, however, laparoscopic procedures are associated with quicker patient recovery, shortened time of return to work, and decreased hospital stay compared with open procedures. Furthermore, surgeons who perform laparoscopic surgery can, over time, achieve operative times that are equal to or lower than times achieved by surgeons performing open procedures

on similar patients.[13-14]

Robotic-assisted surgery represents the latest advance in minimally invasive surgery, and the da Vinci is the most recent innovation in robotic-assisted surgical systems. Hopefully, this newest technology, which seeks to overcome the limitations of standard laparoscopy, will lead to more widespread acceptance of minimally invasive procedures.

Many experts of laparoscopic surgery who have also used the da Vinci Surgical System believe that robotic-assisted procedures have a steep learning curve and the system helps to facilitate the use of laparoscopy to approach challenging cases. It logically follows that laparoscopic procedures now accepted as viable options for the treatment of endometrial, cervical, and ovarian cancer could be performed using the da Vinci system after appropriate training of expert laparoscopists.

Currently, there exist no standardized criteria to identify patients with a gynecologic malignancy who are candidates for a minimally invasive surgical approach. Various practitioners have used such criteria as BMI < 35; age 18–75 years; no more than 1 or 2 prior laparotomies without evidence of extensive pelvic adhesions; medically fit for surgery; and clinical stage I endometrial, cervical, or ovarian carcinoma to identify patients eligible for minimally invasive surgery. Only a small proportion of practicing gynecologic oncologists have received formal fellowship training on how to perform advanced minimally invasive procedures. The selection of patients and level of difficulty of the minimally invasive procedures offered will vary between practitioners and will typically reflect the surgeon's skill and competency. Until minimally invasive procedures have gained widespread acceptance among gynecologic oncologists, patients should seek out local, regional, or nationally recognized experts in these procedures.

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Conflicts of interest: Dr. Tillmanns is a speaker for GlaxoSmithKline, Ortho-Biotech, Genzyme, Valley Lab, anticipate consultant and proctor for Intuitive Surgical. Dr. Lowe is a consultant for Intuitive Surgical and Valley Labs.