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# Current Evidence Regarding the Role of Robot-Assisted Surgery in Gynecological Oncology

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## Abstract

Minimal invasive surgery has completely transformed the surgical practice over the last few decades with numerous benefits for patients and healthcare organizations. These advantages are especially profound in robot-assisted surgery which involves a more ergonomic approach for the surgeon and also eliminates the tremor and improves dexterity. In this review we explore the latest developments regarding the use of robot-assisted surgery in the field of gynecological oncology. In more detail, robot-assisted surgery is already established as the method of choice in treating uterine cancer and newer data show that it plays an important role in the group of patients undergoing interval debulking surgery for ovarian cancer, as a growing number of surgeons perform this operation with the use of the robot. The role of robotic surgery in the group of patients with advanced ovarian cancer undergoing primary maximal effort cytoreductive surgery is still controversial, mainly due to the risk of surgical upstaging and limited views of the peritoneal surfaces. Finally, minimal invasive surgery is currently not routinely utilized in the treatment of cervical cancer; however, this might change in the near future when newer data are published.

## Introduction and Background

Minimal Invasive Surgery (MIS) has been a major breakthrough in the last few decades with its benefits completely changing the surgical practice and training field [1]. The advantages are especially profound in Robot-Assisted Surgery (RAS) and include a more ergonomic and less tiring experience for the surgeon, the elimination of tremor, better dexterity, and a shorter learning curve compared to Conventional Laparoscopic Surgery (CLS) [2]. RAS also offers a better quality of care for the patient as it is related to a lower incidence of surgical complications, less blood loss, faster recovery, and smaller incisions compared to CLS [2].

RAS has gained much popularity in Gynecological Oncology with more and more surgeons abandoning the open or even the laparoscopic approach in its favor [3]. It is imperative, however, that the safety, oncological efficacy, cost-effectiveness, short and long-term results on patient morbidity and mortality of this new method, are assessed and compared to those of open surgery and laparoscopy to define the gold standard approach for the treatment of each cancer group.

The purpose of this literature review is to present the newest evidence regarding the role of RAS in the treatment of endometrial, cervical, and ovarian cancer patients compared to laparoscopy and laparotomy.

## Methods

A search for relevant studies was performed in major databases (PubMed, MEDLINE, Ovid). A combination of terms including "robot, robotic surgery, gynecological oncology, gynecological cancer, minimal invasive surgery" was used. Papers published from 1/1/2020 onwards were included in the review. Case reports, cost effectiveness analyses and studies not in English language were excluded from the review. The reference lists of included studies were also searched to identify more studies that might have been missed during the initial database search. A total of 81 relevant studies have been identified and included in our review.

## Review

### Endometrial cancer

The superiority of MIS in the management of endometrial cancer has been well-established

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since the LAP2 [4,5] and LACE trial [6]. This is also supported by more recent evidence [7]. Comparing RAS with LT, a 2023 meta-analysis has demonstrated that RAS is associated with better Overall Survival (OS), Remission-Free Survival (RFS), and disease-specific survival and concludes that it offers superior long-term oncological outcomes [8]. Better OS and fewer postoperative complications were also reported in a study published in 2021 as well as no difference in recurrence rates for stage I endometrial cancer [9]. The same study also highlights that through RAS it is possible to discharge the patient on the same day of surgery. Another meta-analysis published in 2021 reported lower blood loss, blood transfusion volume, hospital stay length, re-admission, and re-operation rate, fewer complications, and increased operative time for patients who underwent RAS compared to those who underwent LT [10], which is also in accordance with the findings of a 2021 review [7]. Favorable results towards RAS have also been showcased by a 2023 German nationwide registry analysis; LT was found to be related to a higher risk of in-hospital mortality and long postoperative mechanical ventilation as well as longer in-hospital stay compared to MIS [11]. The same study reported a higher probability of home discharge to women who underwent Robot-Assisted Surgery (RAS) compared to those who underwent conventional laparoscopy, but no difference in risk of prolonged ventilation and hospital stay. The safety and efficacy of the robotic 3-arm approach have also been evaluated and compared to that of LT by a 2020 study [12], which found no statistically significant differences in OS and Disease-Free Survival (DFS) between the two methods.

Two meta-analyses also display favorable results for RAS compared to CLS for the treatment of endometrial cancer [8,10]. More specifically, RAS was found to offer equivalent OS, RFS, and DSS to CLS [8] but with reduced estimated blood loss, intraoperative complications, hospital stay length, and conversion rate, but increased readmission [10]. Uwins et al. [7] also report no difference in lymph node yield between the two techniques but a shorter learning curve for RAS. Another 2020 meta-analysis compared robotic *vs.* laparo-endoscopic single-site hysterectomy and found that the robotic approach was associated with less blood loss and shorter hospital stay, while the operation time, complication rate, and multiport conversion rate were not significantly different between the two methods [13]. It is important, however, to point out that there is also some evidence that CLS may have better long-term results than RAS for endometrial cancer, as a 2022 retrospective study demonstrated poorer OS, RFS, and DSS for RAS compared to CLS and a shorter median time to first recurrence [14].

The advantages of RAS are even more prominent in the obese population, which is associated with an increased number of perioperative complications such as increased intraoperative blood loss, surgical site infections, wound separation, thromboembolism, and anesthetic complications [3,7]. As was previously described, RAS is linked to a reduced intraoperative complication rate compared to LT and CLS. The reduced length of stay in hospital and increased mobility compared to LT are linked to reduced thromboembolism, while the smaller incisions are related to less frequent surgical site infections [3]. It has been found that the morbidly obese who receive RAS treatment, experience similar rates of complications to non-obese women as well as similar length of stay, blood loss, and lymph node yield [7,15]. Additionally, based on the results of two 2020 studies, RAS compared to LT for the treatment of endometrial cancer in women with BMI ≥ 30, is associated with better OS and relative survival as well as with better quality of life measures and faster return to normal activities [16,17]. Finally, comparing RAS and CLS for endometrial cancer in the morbidly obese, a 2020 study found lower blood loss for RAS but with no difference in postoperative hemoglobin, longer operation times, and no difference in adverse events [18]. Conversion to LT is also lower in RAS compared to CLS, which is important for minimizing complication rates [3]. Another population that has benefited more from the development of RAS is the elderly population because of their frailty and comorbidities [7]. It is known that elderly women treated with LT for endometrial cancer showcase higher complication percentages, higher mortality, and longer hospital stay [19]. The same study demonstrated that the RAS approach significantly decreases the risk for overall and perioperative complications as well as the length of hospital stay compared to LT [19]. It is also important that according to the same study, the risk reduction went up with age. On the contrary, no difference was found regarding intra-operative and overall minor complications.

## Cervical cancer

MIS was utilized for years in the treatment of cervical cancer, however the findings of the LACC trial [20] in 2018, which reported statistically significant poorer OS and disease-free survival in the population undergoing radical hysterectomy *via* the minimally invasive approach compared to open surgery, led to a shift in practice in many countries with major cancer society's now recommending an open approach to perform a radical hysterectomy in their guidelines [21,22]. Hence, the current utilization of MIS techniques and consequently robotic approaches, are limited.

Despite its practice-changing results, LACC trial received criticism regarding its design, methodology and differences in the surgical skills of the surgeons performing the operations, all of which are well-known limitations of surgical [23]. In addition, a recent meta-analysis has reported on the use and safety of MIS in cervical cancer [24] with similar results to LACC trial.

In a retrospective study comparing open and robotic radical hysterectomy for cervical cancer, the authors concluded that the robotic approach was associated with poorer OS and PFS compared to laparotomy, despite the fact that radicality was comparable between the 2 groups [25]. Hence, it is possible that the difference observed in the oncologic outcomes is related to surgical technique leading to tumor spread, the use of uterine manipulators or colpotomy related peritoneal spillage.

It seems that the landscape of cervical cancer surgical treatment is once again changing, as the recently reported SHAPE trial concluded that simple hysterectomy for low-risk, early-stage cervical cancer has a non-inferior pelvic recurrence rate at 3 years compared to radical hysterectomy [26]. It has also highlighted the significantly fewer complications and better quality of life of the patients in the simple hysterectomy group. Moreover, there are currently 2 prospective trials comparing robotic surgery to open surgery for the treatment of early-stage cervical cancer [27,28]. These trials incorporate techniques to reduce tumor spread such as vaginal colpotomy and avoiding the use of uterine manipulators. Their results are still awaited but they are likely to change the surgical practice if positive for robotic approach.

In conclusion, the use of MIS and robotic techniques for the treatment of cervical cancer in the era of LACC trial is limited. However, newer trials comparing the robotic approach *vs.* conventional laparotomy are currently in the recruitment phase and potential results in favor of robotic surgery, could lead to another

shift in surgical practice. The robotic approach could also be utilized in performing simple hysterectomy in patients who fit the SHAPE trial criteria, as it is associated with the well-known and previously discussed benefits of reduced hospital stay, pain and complications.

### Ovarian cancer

The use of MIS in the treatment of ovarian cancer is still controversial, with one of the main concerns being the need for a thorough exploration of all the peritoneal cavity quadrants to identify and remove all the visible disease, which can be challenging in MIS and especially in CLS. Another issue is the possibility of disease spreading during the minimally invasive manipulations [3,29]. Gallotta et al. [29] however, highlight the advantages of MIS in the perioperative outcomes as well as the evolution of RAS technology which allows good intraperitoneal exploration and execution of complicated procedures such as aortic lymphadenectomy or omentectomy.

Regarding early-stage ovarian cancer, there is evidence that RAS is an acceptable approach for appropriately selected patients, taking into account characteristics like obesity and comorbidities, as long as it is done by an experienced surgeon, as this approach offers disease control, survival, and recurrence rate equivalent to LT [29,30]. In accordance with this, a 2022 retrospective case-cohort study showcased similar mean operative times and pelvic/para-aortic lymph node yield when comparing robotic (after laparoscopic Salpingo-Oophorectomy of a suspicious adnexal mass) to open surgical staging [31]. Another large-scale retrospective cohort study, using the National Cancer Database, compared the RAS with the CLS approach for stage I epithelial ovarian cancer and showed no significant difference in the 1-year, 3-year, and 5-year survival rates of the two groups, but a lower conversion to LT rate for the RAS group [32].

Many authors remain skeptical about the role of RAS for primary debulking surgery in advanced ovarian cancer due to the high risk of intraperitoneal rupture of the mass and limited views of all the peritoneal surfaces, which is of paramount importance in maximal effort cytoreductive surgery [3]. However, its role in patients who are candidates for Neoadjuvant Chemotherapy (NACT) followed by Interval Debulking Surgery (IDS) is much clearer [3,29]. Authors of two reviews suggest that there is no difference in residual disease rates after surgery between MIS and LT, between MIS and LT, while also highlighting the better perioperative results, shorter hospital stay time, and higher 5-year OS rates in the MIS group [3,29]. A 2020 systematic review also reports much better OS and Progression-Free Survival (PFS) when comparing patients who underwent RAS with those who also underwent LT at some point in their treatment [33] whereas a single-center retrospective cohort study reported similar OS and PFS among patients who underwent robotic-IDS or open-IDS [34].

In summary, the role of RAS in ovarian cancer remains unclear, hence most authors however suggest that large prospective, randomized studies are required to precisely define the role of robotic-IDS in advanced ovarian cancer, such as the ongoing LANCE trial, the results of which could possibly change the current practice in the treatment of this type of cancer [29,31,33].

## Conclusion

In conclusion, in this comprehensive review we have presented the latest data regarding the use of RAS in gynecological oncology. Despite its benefits for patients, hospitals and surgeons, the use of RAS in gynecological oncology is still controversial. In more detail, RAS is widely adopted in the treatment of endometrial cancer, whereas it has limited use in the treatment of cervical and ovarian cancer. Results of ongoing trials exploring the safety of RAS in cervical and ovarian cancer are still awaited. Large prospective studies and clinical trials are definitely needed in order for RAS to be widely adopted in gynecological oncology.

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