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ENDOMETRIAL CANCER (G SEL, SECTION EDITOR)

Robotic Surgery in Endometrial Cancer

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Abstract

Purpose of Review The number of minimal invasive gynecological oncological operations performed especially for endometrial cancer is increasing rapidly parallel with the increase in robotic systems in hospitals. This paper focuses on evaluating the studies comparing robotic surgery with laparoscopic and open surgery in patients with endometrial cancer in light of current literature.

Recent Findings When the current literature is examined, it is seen that the results of robotic surgery have similar results to laparoscopy such as length of hospital stay, postoperative pain, recovery in a short time, and less blood vessels, and they are disadvantageous in terms of cost compared with laparoscopy. When compared with laparotomy, it is emphasized that there is no difference in terms of intraoperative oncologic surgery results and it is a method that can be chosen as a minimally invasive surgery option especially in obese patients because of its ergonomics.

Summary Although there is no randomized controlled study comparing the results of laparoscopic and open surgery with robotic surgery, retrospective data suggests that perioperative morbidity in robotic surgery is less and improves in terms of intraoperative surgical outcomes. As with benign gynecological procedures, randomized controlled trials are needed to identify patients who may benefit from robotic surgery and to better define clinical outcomes. It should be noted that randomized controlled trials comparing surgical and robotic-assisted surgery with laparoscopy are lacking and most of them are derived from retrospective data.

Keywords Robotic surgery · Endometrial cancer · Minimal invasive surgery

Introduction

Endometrial carcinoma is the most common gynecologic malignancy in the USA and is the fourth most common cancer in women [1]. Most of the patients are diagnosed at an early stage (stage I) and 5-year survival rates are over 95% at early stages. Surgical treatment of endometrial cancer involves hysterectomy, resection of adnexal structures, and appropriate surgical staging in patients with a risk for extra uterine disease [2]. Endometrial cancer patients are classified to risk groups to guide adjuvant therapy use. In low risk group (stage I endometrioid, grades 1–2, < 50% myometrial invasion, lymphovascular space invasion (LVSI) negative), lymphadenectomy is not recommended and in intermediate risk group (stage I endometrioid, grades 1–2, > 50% myometrial invasion, LVSI negative), lymphadenectomy can be considered for staging purposes [3]. Modern methods used in the treatment of endometrial cancer include laparotomy, laparoscopy, and a more novel approach, robotic-assisted surgery [4]. In the early 1990s, laparoscopy was shown to be an applicable surgical approach in the staging of endometrial cancer [5]. Advantages introduced by minimally invasive surgery include decreased blood loss, fewer blood transfusions, less postoperative pain, shorter duration of hospitalization, faster healing time, and better cosmetic results [6]. A randomized controlled trial GOG-LAP 2 was published in 2009 and the importance of minimally invasive surgery in endometrial cancer has been shown by the fact that patients with endometrial cancer operated by laparoscopy have better short-term surgical results than laparotomy [7]. In continuation of the study which was published in 2012, progression-free survival and overall survival rates were found to be similar when compared with laparotomy.

Despite all these advantages, minimally invasive surgery is not used as commonly as desired in gynecological oncology. Technical limitations of laparoscopy are main reasons for the limited use of laparoscopic gynecological operations.

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Disadvantages of laparoscopy include the need for use of camera during operation by an assistant in helping to the surgeon, especially for 2D images, hand tremor, and limitations in ergonomics [8]. In addition, processes such as suturing and knot tying became more difficult due to movement limitations of the laparoscopic instruments. Since the instruments are not completely ergonomic, the surgeon becomes significantly exhausted especially during complex operations such as endometrial staging procedures including pelvic and para-aortic lymphadenectomy. New technologies are being developed to overcome the limitation of laparoscopic surgery. High-density halogen and xenon light sources, advanced hand instruments, and electrosurgery devices have been developed and finally robotics has been implemented. Today, robotic surgery represents the final step in minimally invasive surgery. Advantages of robotic surgery over laparoscopy include obtaining 3D images, enabling direct visualization by eye–hand axes, increased number of basic hand movements of laparoscopic devices (from 4 to 7), ease of left-hand usage, easier suturing, easier knot tying, elimination of hand tremor, being less exhausting for the surgeon, shorter learning time, less need for transition to laparotomy, and enabling performing more complex procedures [9].

According to a recent report by the manufacturer of robotic surgical system, the number of robotic surgical systems in the USA increased from 800 to 2001 and from 200 to 443 in Europe between 2007 and 2013. By 2013, the number of robotic surgeries performed worldwide has exceeded 1.5 million [10]. According to a survey conducted in 2010, it was reported that 95% of the gynecological oncology fellow had a robotic surgery platform and 95% received training [11]. In the same study, they emphasized that 74% of the fellow received training for robotic lymph node dissection. Robotic surgery is used in 5114 centers and its annual growth is expected to be more than 13–17% [12]. The number of gynecological oncological operations performed is increasing rapidly parallel with the increase in robotic systems in hospitals.

Obesity, which is one of the important risk factors of endometrial cancer, is rapidly becoming epidemic all over the world. According to a recent study, 68% of women with early stage endometrial cancer were obese [13]. Unfortunately, obesity sometimes restricts laparoscopy in terms of ventilation problems and providing CO_2 pneumoperitoneum. Standard laparotomy is a suboptimal procedure due to complications related to wound infection and prolonged recovery time. The use of robots in gynecological oncology has led to significant improvements. Preliminary experience shows that robotic-assisted laparoscopy is a good minimally invasive method for obese patients. Gehring et al. performed a study of endometrial cancer staging including 36 obese (BMI 30–30.9) and 13 morbidly obese (BMI > 40) patients with an operation time of 189 min (111–263), mean blood loss of 50 mL (25–300), and mean number of lymph nodes 31.4 (6–73) [14].

There are many studies in the literature providing that endometrial staging results in robotic-assisted surgery are comparable with laparoscopy and laparotomy. Some of the preliminary data on endometrial staging with robotic surgery are presented in this section. Boggess et al. compared the results of staging of endometrial cancer with laparotomy ($n = 138$), laparoscopy ($n = 81$), and robotic-assisted surgery ($n = 103$). In the robotic group, shorter operation time, less estimated blood loss, and transfusion rate were obtained compared with laparoscopy [4]. In the robotic group, the number of lymph nodes (mean 32.9) was highest and the estimated blood loss (74.5 mL) was the lowest. The mean hospital stay was 4.4 days in patients who underwent laparotomy, 1.2 days in the laparoscopy group and 1 day in the robotic group. Operation times were 146.5, 213.4, and 191.2 min in laparotomy, laparoscopy, and robotic group, respectively. The rate of postoperative complications was less in the robotic group compared with laparoscopy (5.9–29.7%; $p < 0.0001$). In the robotic and laparoscopy group, the rates of transition to laparotomy were similar. As a result, they emphasized that robotic surgery can be applied and preferred to laparoscopy in staging of endometrial cancer. Hoekstra et al. evaluated the results of endometrial staging in laparoscopy, laparotomy, and robotic-assisted surgery in 69 patients [15]. The operation time in the robotic and laparotomy groups was less than laparoscopy ($p = 0.023$). No significant difference was found between the three groups in terms of lymph nodes ($p < 0.0001$). The lowest blood loss was calculated in the robotic group ($p < 0.0001$). Mean hospital stay was found to be 1 day in the groups with minimally invasive surgery. As a result, they emphasized that robotic surgery provided many important improvements in terms of perioperative outcomes when compared with laparoscopy and laparotomy and increased the tendency towards robotic surgery in staging of endometrial cancer. In their studies involving 158 patients made by Veljovich and colleagues, the results of patients undergoing robotic assisting and laparotomy with endometrial staging were compared [16]. In the robotic surgery group ($n = 25$), there were 8 major and 13 minor complications. The operation time (283 min) was longer in the robotic surgery group ($p < 0.001$). However, estimated blood loss and length of hospital stay were less than open surgery ($p < 0.001$). In conclusion, although the operation time was longer, robotic surgery could be preferred in terms of the number of lymph nodes obtained, length of hospital stay, and estimated blood loss.

DeNardis et al. compared the results of 106 patients who underwent laparotomy and 56 patients with endometrial cancer undergoing robotic-assisted surgery [17]. Conversion to laparotomy was done in 5.4% of robotic cases due to intraoperative causes. The major perioperative complication was 3.6% in the robotic patient group, while the incidence of complications was 20.8% in open surgery ($p = 0.007$). In conclusion, since robotic surgery provides a reduction in perioperative morbidity, they emphasized that it can be preferred in patients with high body mass index and morbidity risk. Gehrig et al. compared laparoscopy ($n = 32$) and robotic-assisted ($n = 49$) surgery for staging obese and morbidly obese endometrial cancer patients and emphasized that they obtained better staging results with robot in obese patients [14]. It is very difficult to see the details of pelvic anatomy as in open conventional surgery, especially in obese patients and it depends on the good exposition of the surgical field. However, with the help of the 3D image provided by the robotic system, the surgeon is able to evaluate the entire pelvis anatomy in detail and dissect easily in obese patients.

In a large prospective non-randomized study conducted by Paley et al. in 2011, 377 robotic endometrial cancer staging were compared with 131 laparotomy staging [18]. In the laparotomy group, wound infection, urological injury, and bleeding, which were serious complications, were 3 times higher. The length of hospital stay was 1.4 days in the robotic surgery group and 5.3 days in the laparotomy group ($p = 0.0001$).

The majority of the studies including the comparison of minimal invasive surgical techniques and laparotomy are non-randomized controlled trials. After the preliminary studies comparing the robotic surgery with laparotomy and laparoscopy, systematic reviews and meta-analysis have been published.

One of the meta-analysis related to comparison of safety and affectivity of robotic hysterectomy versus conventional laparoscopy and laparotomy for endometrial cancer included 37 studies ($n = 3511$) [19]. Overall complication rates are lower in robotic group than laparotomy (RR 0.37 95% CI 0.29–0.49). Intraoperative and postoperative complications for robotic group versus open hysterectomy were significantly lower in robotic group (RR = 0.43, 95% CI 0.25–0.76, RR 0.48; 95% CI 0.35–0.66 respectively). Vaginal cuff dehiscence rates in the robotic group were higher than the laparotomy group (RR 3.11; 95% CI 1.42–6.80). When comparing the robotic group with the laparoscopy group, intraoperative complication rates were lower in robotic group, but there was no significant difference between groups including postoperative complications. There are two studies in the meta-analysis that included the overall and disease-free survival rates and revealed no clinically meaningful significant difference both between robotic versus laparoscopy and robotic versus laparotomy [20–21].

Chen et al. reported a meta-analysis including robotic-assisted versus conventional laparoscopic surgery for endometrial cancer staging [22]. There were a total of 2015 patients identified: 912 in the robotic group and 1193 in the laparoscopic group. Conversion to laparotomy due to exposure difficulty, dense adhesions, and vascular injury was found less in the robotic group (RR 0.4; CI 95%, 0.25–0.64). Fewer complications in the robotic group than laparoscopy group (RR 0.72; CI 95%, 0.55–0.95; $p = 0.02$). Also, less blood loss in robotic group was found than in laparoscopy group. There were no significant difference between two groups regarding the length of the operation and total lymph nodes harvested (WMD, 13.28 min; 95% CI from −6.66 to 33.22; $p = 0.19$ and WDM, 0.86; 95% CI from −2.24 to 3.96; $p = 0.59$, respectively). The incidences of readmission and transfusion were significantly lower, whereas vaginal cuff dehiscence was significantly higher in robotic hysterectomy and open hysterectomy.

In a systematic review by Gaia et al., 8 different studies involving 1591 patients were examined and 589 robotic surgery patients were found to have less blood loss compared with the 396 laparoscopy group and less than 606 laparotomy groups ($p < 0.005$) [23]. Although the transition to laparotomy was higher in the laparoscopy group compared with the robotic group, it was not statistically significant (4.6% versus 9.9%). The number of removed lymph nodes, perioperative complication rates, gastrointestinal injury, urological injury, and vaginal cuff dehiscence rates were found to be the same in all three methods. Operation time was similar in the robotic group by laparoscopy (219 min versus 209 min $p = \text{NS}$), but longer than the laparotomy group (207 min versus 130 min $p < 0.005$).

In a review published in 2017, there were 14 studies comparing robotic surgery and laparoscopic surgery, 11 studies comparing open surgery with robotic surgery, and one randomized clinical trial [24]. Robotic surgery compared with laparoscopic surgery; as a result of 14 observational studies comparing the duration of the hospital stay, it was found to be less in the robotic surgery groups, whereas there was inconsistency in the studies involving shorter operation time findings in laparoscopic surgery. In the largest series, which included 1433 patients with Barrie et al., the operative time was shorter in terms of not only hysterectomy but also pelvic/para-aortic lymphadenectomy [25]. These results support the results of the studies of Maenpaa et al., the only randomized trial involving 99 patients so far [26]. However, there was no difference in terms of length of hospital stay, number of lymph nodes removed, and estimated blood loss. While conversion to laparotomy was 5 in the laparoscopic group, no conversion was seen in the robotic surgery group. According to these results, Maenpaa et al. emphasized that robotic surgery is an effective and reliable surgical alternative in endometrial cancer staging. In the majority of studies, estimated blood loss was less in the robotic surgery group. When the number of lymph nodes removed was compared, robotic surgery was superior in 4 studies and laparoscopic surgery was superior in 3 studies, but no difference was found in 4 studies. In 11 studies which compared robotic surgery with laparotomy, robotic surgery was found to be superior in terms of estimated blood loss and length of hospital stay [24]. In the study performed by El Sahwi et al., the operation time in the robotic surgery group was found to be shorter than in open surgery, while Hinshaw et al. found similar in their studies, and in all other studies, longer operative times in the robotic surgery groups [27–28]. When the numbers of removed lymph nodes were examined, robotic surgery was superior in 5 studies and open surgery in 2 studies, but no difference was found in 5 studies. From an economic point of view, although it seems to be costly due to the cost of the first institutionalized and dispensable parts of robotic surgery, costs have been found to be less costly in some studies when compared with open surgery considering other parameters such as length of hospital stay after surgery.

A total of 1218 patients were evaluated in a systematic review of 8 studies including comparison of robotic surgery and laparoscopic surgery [29]. The length of hospital stay was less in the robotic group. Although there is a downward trend in operation times compared with laparoscopy, there is no continuity between studies. In most studies, estimated blood loss was less in robotic surgery. There was no difference between the two groups in terms of lymph node number. In addition, some studies showed a faster recovery time in the robotic surgery group. In 8 studies comparing robotic surgery with abdominal surgery (robotic 642 patients versus 835 abdominal), shorter hospital stay and less estimated blood loss were found in the robotic surgery group. Although the duration of the operation in the robotic surgery group was much longer than laparotomy, there was no significant difference in the number of lymph nodes removed. In two studies, the direct and indirect costs were compared in terms of cost of robotic surgery and open surgery, and robotic surgery was more advantageous than open surgery due to short hospital stay (8212 $ versus 12,943 $, $p = 0.001$).

In a systematic review and meta-analysis of 8075 patients (3830 robotic and 4245 laparoscopic) comparing the results of robotic and laparoscopic surgery in endometrial cancer published in 2017, 36 studies were included, including 33 retrospective studies, two case-control studies, and one randomized controlled trial. In terms of operative time, no difference was found between the two groups in the meta-analysis, while the hospital stay was shorter in the robotic group (0.46 days, 95% CI 0.26 versus 0.66). Less blood loss (57.74 mL, 95% CI 38.29 to 77.20), less transition to laparotomy (RR = 0.41, 95% CI 0.29 to 0.59), and fewer complications were detected in the robotic approach (RR = 0.82, 95% CI 0.72 to 0.93). Robotic surgery was found to be more costly than laparoscopy ($ 1746.20, 95% CI $ 63.37 to $ 3429.03) [30•].

The systematic review and meta-analysis related to robotic versus laparoscopic surgery for endometrial cancer was published by Xie et al. [31]. There were a total of 19 studies including 3056 patients. Lower estimated blood loss was found in the robotic group (WMD 77.65; 95% CI 105.58 to −49.72). Also, hospital stay and conversion to laparotomy rates were in favor of the robotic group. The incidence of intraoperative visceral injury, operation time, transfusion rate, and total number of lymph node harvested were similar between groups and there were no statistical significant differences.

A recent meta-analysis comparing conversion and complication rates of laparoscopic and robotic hysterectomy in endometrial cancer patients with obesity was published [32••]. The study included 10.800 endometrial cancer patients with obesity. Conversion from laparoscopy and robotic surgery proportions were found 6.5% (95% CI 4.3–9.9) and 5.5% (3.3–9.1) respectively among patients' body mass index > 30, and 7.0% (3.2–14.5) and 3.8% (1.4–9.9) among patients with BMI > 40. Intolerance of Trendelenburg position in patients with morbid obesity may reduce conversion rates if the endometrial staging is performed via robotic surgery rather than laparoscopic surgery.

Robotic Single-Port Surgery in Endometrial Cancer

In a study by Corrado et al., single-port surgery has been shown to be safe for both hysterectomy and pelvic lymph node dissection [33]. The researchers prospectively collected data from patients with FIGO stage 1 or occult stage II endometrial cancer. The study included 125 patients. The average docking time was 11 min, console time was 80 min, and total operation time was 122 min. Estimated blood loss was 50 mL. One patient was switched to vaginal surgery due to lung ventilation problems. Pelvic lymph node dissection was performed in 16.8% of the patients and the mean number of lymph nodes removed was 13. While the mean length of hospital stay was 2 days, no intraoperative complications were reported. Although the authors emphasize that single-port robotic surgery is technically feasible and safe in patients with stage I–II endometrial cancer, there are not enough randomized prospective studies in the current literature.

In their systematic review which included robotic laparoendoscopic single-site surgeries performed in 2018, Matanes et al. emphasized that the new route would be the same in advanced minimally invasive surgery, and that better cosmetic results were obtained and patient morbidity could be reduced compared with multi-port surgery [34]. Four hundred fifty-two publications on this subject have been reviewed and finally 36 articles have been included. They concluded that R-LESS surgery can be performed, safe, and equal to LESS surgery. In addition, they emphasized that shorter recovery time, less postoperative pain, and better cosmetic results were obtained with robotic multi-pot surgeries. However, large randomized prospective studies should be performed in terms of definitive results.

Conclusion

Although there is no randomized controlled study comparing the results of laparoscopic and open surgery with robotic surgery, retrospective data suggests that perioperative morbidity in robotic surgery is less and improves in terms of intraoperative surgical outcomes. As with benign gynecological procedures, randomized controlled trials are needed to identify patients who may benefit from robotic surgery and to better define clinical outcomes. It should be noted that randomized controlled trials comparing surgical and robotic-assisted surgery to laparoscopy are lacking and most of them are derived from retrospective data.

Compliance with Ethical Standards

Conflict of Interest Ahmet Göçmen and Fatih Şanlıkan declare they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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