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REVIEW ARTICLE

The roles and limitations of robotic surgery for obese endometrial cancer patients: a common challenge in gynecologic oncology

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Abstract In the United States, the epidemic of obesity is readily apparent in women diagnosed with endometrial cancer, the most common gynecologic malignancy. Overall, the benefits of minimally invasive surgery and its oncologic outcomes are similar among laparoscopy and robotic approaches. However, in stratifying obese patients by BMI, more data is needed on morbidly obese patients and their candidacy for robotic surgery along with the technical challenges of staging procedures. Cost analysis studies targeted specifically to the obese and morbidly obese patient is needed to further justify efforts at promoting robotic surgery in this patient population.

Keywords Gynecologic surgery · Robotic Surgery · Obesity · Endometrial cancer · Gynecologic oncology

Introduction

Obesity is preventable. In the United States, more than one-third or 78.6 million adults are obese [1]. The World Health Organization (WHO) classifies obesity as class I (BMI 30–34.9 kg/m^2), class II (BMI 35.00–39.9 kg/m^2) and class III (>40 kg/m^2) as a way of stratifying those patients at highest risk for developing comorbidities such as endometrial cancer [2]. Women with increased adipose tissue have an unopposed estrogen effect in the uterus predisposing them to endometrioid endometrial cancer (also known as type I uterine cancers). Typically, higher BMI patients have type I endometrial cancers, because this type of disease is related to increase estrogen exposure from adiposity. However, since obesity is preventable, even non-estrogen dependent endometrial cancer (type II, uterine papillary serous carcinomas and clear cell carcinomas) are being diagnosed in obese patients. While patients with a BMI between 30 and 39 kg/m^2 are common, the incidence of class II and III obesity is rising [3]. Since surgical staging is the standard of care for endometrial cancer, the challenge of managing obese women is even more pervasive in the gynecologic community.

The benefits of minimally invasive surgery have been established in the treatment of endometrial cancer. The gynecologic oncology group (GOG) LAP2 trial was a large phase 3 randomized study comparing laparoscopy to laparotomy in management of endometrial cancer (EC) [4]. The results demonstrated advantages in post-operative pain, length of stay, and reduction of complications with improved quality of life in the ensuing weeks after surgery with laparoscopy. There was no difference in recurrence rate, progression free survival (PFS) or overall survival (OS). This study established the role of minimally invasive surgery (MIS) in management of EC even with a 25.8 % conversion rate to laparotomy (LAP2). Increasing BMI was associated with failure to successfully complete laparoscopy (OR 1.11; 95 % CI 1.09–1.13 for every one-unit increase in BMI); nonetheless, this rate is exceedingly high in comparison to today's high volume gynecologic surgeons. Given the association of increased BMI with conversion in this study population, the median BMI in the laparoscopy group was

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only 28 kg/m^2 (interquartile range 24–34). Recognizing the clinical benefits of laparoscopy in endometrial cancer and its equivalence to open surgery, the adaptation of MIS in the management of EC is now an important goal.

Undoubtedly, obesity represents a challenge in incorporating traditional laparoscopy for primary surgical management. The thickness of the abdominal wall can cause difficulties in manipulating trocars and instruments along with the challenge it poses during anesthesia. Contemporary management of endometrial cancer in the United States, with its current obese population, has increasingly relied on robotic-assisted surgery to achieve the goal of minimally invasive surgery. Compared to conventional laparoscopy, robotics has the advantage of higher magnification, steady camera, and wristed instrumentation with a greater range of motion that may facilitate knot tying and suturing. It may provide an advantage in morbidly obese women in whom the resistance of the abdominal wall may prove to be a greater challenge during laparoscopy. The society of gynecologic oncology (SGO) has supported the use of the robotic platform for endometrial cancer patients and has noted the possible advantage to robotic surgery over traditional laparoscopy [5]. Nowhere are the benefits of MIS more pertinent than in the obese cancer patients with decreased abdominal wound infections, less blood loss, less pain and decreased length of hospital stay. Therefore, the aim of this review is to highlight the role and pitfalls of robotic surgery in the obese EC patients.

Methods

To perform a review of recent literature on obese patients with endometrial cancer, an electronic search of PubMed was performed from January 2008 until July 2014. A total of 24 articles were reviewed. Key words included, "gynecologic surgery," "robotic surgery," "obesity," "endometrial cancer," and "gynecologic oncology." All reference lists in the articles reviewed were also identified and utilized as pertinent studies. Papers were excluded if robotic surgery was not part of the research paper, or if benign disease was a primary outcome.

Results

Robotic surgical outcomes and complications in obese endometrial cancer patients

Table 1 illustrates the surgical outcomes for retrospective studies comparing robotics to laparoscopy or laparotomy

Table 1 Outcome comparisons of robotic surgery versus laparoscopy or laparotomy

	Patient (*n*)	Mean BMI	Obesity class (%)	Conversion (%)	Complications (%)
Seamon et al. [6]					
RH	109	40.0	I: 30 II: 21 III: 49	15.6	11.0
AH	191	40.0	I: 28 II: 23 III: 49	–	27.0
Seamon et al. [7]					
RH	105	34.2	I: 40 II: 32 III: 28	12.4	13.0
LH	76	28.7	I: 62 II: 35 III: 3	26.3	14.0
Subramaniam et al. [8]					
RH	73	39.8		11.0	4.1
LH	104	41.9		–	20.2
Gehrig et al. [13]					
RH	49	37.5	I: 33 II: 41 III: 26	2.3	6.5
LH	35	35.0	I: 50 II: 28 III: 22	–	17.3
Bernardini (2011)					
RH	45	40.3		8.9	4.4
AH	41	42.3		–	7.3
Tang et al. [10]					
RH	129	39.8		10.9	–
AH	110	40.3		–	–
DeNardis et al. [11]					
RH	56	28.5	III: 7	5.4	3.6
TH	106	34.0	III: 31	–	20.8
ElSahwi (2011)					
RH	155	34.5		–	10.0
AH	150	33.0		–	27.0
Menderes et al. [15]					
RH	364	34.8		0.8	–
Lau et al. [16]					
RH	108	–	I-II: 59 III: 46	–	–
Geppert et al. [18]					
RH	50	34.6	–	2	–
AH	64	32	–	–	–

for EC patients. The distributions of patients by surgical group and by WHO obesity class are outlined along with conversion and complication rates. Complications in these studies were not identically defined. However, for the majority of studies, "complications" referred to major adverse events such as bleeding, urinary and bowel injury.

The rate of conversion from a minimally invasive procedure to a laparotomy varied in these studies. One of the highest conversion rates seen was in a case control design by Seamon et al. [6] comparing robotics to laparotomy with the purpose of comparing adequacy of staging and surgical outcomes. Though their sample size was limited, the robotic arm had a conversion rate of 15.6 %. Mean BMI was matched in both arms, 39.6 for the robotic arm versus 39.9 in the open arm. There were more significant complications, such as blood loss, major vessel, nerve, gastrointestinal, and urinary injury in the laparotomy arm with a relative risk of 0.29 (0.13–0.65). Seamon et al. [7] also performed another comparison study between robotics and laparoscopy where the median BMI was significantly higher in the robotic arm. The conversion rate was lower in the robotic arm, 12 % versus 26 %, with poor exposure being the main reason for conversion in both arms. The majority of patients in this study however had a BMI less than 30. Similarly, Subramaniam et al. [8] compared 73 robotic cases to 104 open cases with a mean BMI of 39.8 in the robotic arm versus 41.9 in the open arm. There was a conversion rate of 11 % and significantly lower rate of complications in the robotic arm. In this study, uterine weight was also reported which was significantly higher in the laparotomy arm, begging the question of a possible selection bias even though routine imaging for uterine size was not performed. Certainly in retrospective comparison studies, it is important to note a potential for selection bias of more obese patients in either arm depending upon the investigator's hypothesis.

In studies looking at higher BMI, Bernardini et al. [9] looked at patients with BMI of 35 or greater; there were four conversions in 45 robotic patients with the majority being for large uterine size. Tang et al. [10] also compared robotics to laparotomy with a mean BMI in both groups that was above 39. Conversion was commonly related to poor exposure due to visceral adiposity or adhesions. In their comparison of robotic patients to open, DeNardis et al. [11] only reported a mean BMI of 28.5 in the robot group versus 34 in the open group with 31 % class III obesity in the open group versus only 7.1 % in the robot group. Robotic conversions were due to bleeding, large fibroids and pelvic adhesions. Major complications such as bleeding were more common in the open group.

Another retrospective study with 459 patients looked at the conversion from robotic surgery to laparotomy [12]. They had a median BMI of 30.8 (range 16.6–70.8) and of their 40 conversions (8.7 %) the BMI was higher in the conversion group with a median BMI or 36.6 (20.7–64.0). In their entire cohort, 254 (55.3 %) patients had endometrial cancer or hyperplasia. Adhesions and poor visualization were the most common reasons for conversion both before and after docking the robot. In all studies reviewed, mini-lap to remove the uterus did not count toward conversion.

Conversely, there were a few retrospective studies that had low conversion rates. Gehrig et al. [13] looked at 49 patients having robotic surgery versus 35 undergoing laparoscopy. In their cohort, they had 13 patients or 26 % with class III obesity versus 22 % in the laparoscopy group. They had no conversions in the robotics group and only two in the laparoscopy group. Both groups had no significant difference in complications. ElSahwi et al. [14] also compared robotic cases to open cases with the majority of patients having only class I obesity, mean BMI 34.5. There were no conversions. Menderes et al. [15] and Lau et al. [16] studied robotic cohorts alone with high percentages of class II and III patients to analyze the impact of BMI on endometrial cancer patients. Menderes et al. [15] reported few intra- and post-operative complications. The highest intra-operative complication was ureteral and bladder injury with seven patients combined and 24 patients with cardiac or pulmonary issues post-operatively. Three conversions were reported. Lau et al. [16] reported no conversions and the only difference in complications across BMI categories was for rehospitalization. Of those readmitted: one patient was found to have a double primary pancreatic cancer, one patient developed diverticulitis, and another developed pulmonary embolism.

There were additional studies which included EC patients who had robotic-assisted surgery; however, their operative outcomes were not recorded by their disease site. Gallo et al. [17] reviewed 442 cases of women who underwent robotic-assisted hysterectomy, with mean BMI in the non-obese, obese and morbid obese group as 25.1, 34.3 and 44.3, respectively. Overall conversion rate was 0.7 %, with one conversion in each group, and complication rate was similar in each of the three groups, with major complications accounting for 3.8, 4.5, and 4.0 %. Similarly, Geppert et al. [18] compared 50 robotic cases to 64 open cases with mean BMI of 34.6 in the robotic group and 32 in the open group. Complications were defined as prolonged hospital stays, readmissions or reoperations within first post-operative year, the need for intravenous antibiotics and blood transfusions. There was a conversion rate of 2 %. The robotic group had a shorter hospital stay. However, the laparotomy group experienced more complications including one reoperation for bowel obstruction, one bladder injury, five patients required intravenous antibiotics, and seven required blood transfusions. Comparatively, the robotic group had four significant complications, including a trocar hernia, vaginal bleeding, post-operative transfusion, ureter injury, and vaginal cuff dehiscence.

Vaginal cuff dehiscence was listed in three studies as a complication, but not stratified by BMI. There has been some attention drawn to the rate of vaginal cuff dehiscence in robotic surgery perhaps due to the increased use of thermal energy in MIS as opposed to open surgery when performing colpotomy. Other potential causes for vaginal cuff dehiscence include a shorter recovery period, and a return to normal day-to-day activity before the cuff has healed. More importantly, the magnified view afforded by robotic surgery, though allowing for higher resolution of the cuff, may lead surgeons to take less tissue while suturing than typically done in laparotomy. Tang et al. [10] reported increased vaginal cuff complications in the robotic arm, with six total patients developing cellulitis, seromas, hematomas, and dehiscence, respectively. In another review, Menderes et al. [15] reported cuff dehiscence as 0.8 %. ElSahwi et al. [14] reported a vaginal cuff dehiscence rate of 1.3 %; however, this complication was not significant between the robotic group and the open group.

A large retrospective by Backes et al. [19] looked specifically at complications including conversions in robotic surgery for endometrial cancer. They identified 503 patients with a mean BMI of 32 (range 17–70). They reported 32 conversions (6.4 %) and most commonly 40 % of cases were converted due to dense pelvic adhesions followed by poor visualization and inability to pack the bowel away (33 %). They reported two enterotomies, one ureteral injury and five vessel injuries. Post-operative complications were divided into those with completion of robotic staging and those that were converted. Post-operative ileus, and DVT were both significantly higher in the converted group, and those converted to laparotomy were more likely to have wound complications.

Pathologic outcomes and recurrence data

Table 2 highlights the staging, histopathology and node counts for specific studies of obese EC patients. While the majority of women had endometrioid endometrial cancer, a substantial number of studies reported women with type II cancers. The decision to perform lymphadenectomy as well as the extent of dissection in EC is controversial in gynecologic oncology. Overall, the data thus far demonstrate that mean pelvic node counts are similar if not increased in robotic cohorts as compared to open and laparoscopic cases. There may be a difference in para-aortic node counts especially in class II and III MIS patients. Lau et al. [16] demonstrated a significantly decreased number of para-aortic lymph nodes retrieved as BMI increased to class II and III. The number of para-aortic lymph nodes retrieved did not differ significantly from non-obese to morbidly obese groups; however, the number of patients able to undergo robotic para-aortic lymphadenectomy, as BMI increased, decreased significantly from 22 patients (44 %) to one patient (4.4 %), $p = 0.002$.

Data on lymphadenectomy is also related to conversion as in many cases the decision to convert was based upon lack of exposure. Part of the initial survey of a woman with endometrial cancer undergoing a MIS procedure is the assessment of exposure to perform lymphadenectomy especially if a para-aortic node dissection is anticipated. Therefore, if the conversion rate is related to BMI, then this is also a function of accomplishing an adequate staging procedure. Backes et al. in their study reported that the percentage of patients undergoing pelvic lymphadenectomy was lower as their median BMI increased. Therefore, the increasing BMI with possible lack of exposure may influence the surgeon's decision to perform node dissections with its subsequent increase in major bleeding, nerve injury, lymphocyst formation and ureteral injury.

Recently, there has been adaption of sentinel node algorithms in the surgical management of EC patients and incorporation into National Comprehensive Cancer Network guidelines [20]. However, Sinno et al. [21] in their comparison of isosulfan blue versus indocyanine green sentinel node mapping in robotic surgery for EC patients reported that BMI was adversely associated with mapping success both in univariate and multivariate analysis. With increased adiposity in the retroperitoneum, a sentinel node evaluation could be not only problematic but may also be less accurate.

With the increasing prevalence of obesity, the incidence of patients with higher BMI and type II uterine cancer is also significant. In Table 2, several studies included patients with type II histology most commonly uterine papillary serous carcinomas (UPSC). These studies, however, did not stratify BMI against the type II histology.

To establish the role of MIS for type II cancers, Fader et al. [22] looked at 191 patients who underwent either laparoscopic or robotic procedures for a high grade, UPSC, clear cell or mixed histology compared with 192 laparotomy patients. There were more mean lymph nodes removed in the MIS arm including para-aortic nodes. There was a 9.9 % conversion rate and in multivariate analysis, increasing BMI was associated with complications. After adjusting for age, stage and surgery type for every one-unit increase in BMI, the odds of a peri-operative event increased by 5 %. When controlling for stage, PFS and OS, the groups were not significant.

Several studies give relevant data on cancer recurrence for obese patients undergoing robotic surgery for EC. A large retrospective by Backes et al. [19] looked specifically at complications including conversions in robotic surgery for endometrial cancer. They identified 503 patients with a mean

Table 2 Evaluation of nodal counts in robotic versus laparoscopy and laparotomy

	Stage (%)	Histology	Grade (%)	Total mean node count	Pelvic mean node count	Aortic mean node count
Seamon et al. [6]						
RH	–	–	–	24.7 ($p = 0.45$)	18.5 ($p = 0.91$)	8.5 ($p = 0.11$)
AH	–	–	–	23.9	18.7	7.2
Seamon et al. [7]						
RH	I–II: 90 III–IV: 10	–	1: 66 2: 22 3: 12	–	21 ($p = 0.86$)	10 ($p = 0.09$)
LH	I–II: 91 III–IV: 9	–	1: 77 2: 12 3: 11	–	22	11
Subramaniam et al. [8]						
RH	–	–	1: 21.9 2: 53.4 3: 24.7	8.0 ($p = 0.51$)	–	–
LH	–	–	1: 21.2 2: 46.1 3: 32.7	7.2	–	–
Gehrig et al. [13]						
RH	I–II: 89.0 III–IV: 11	Endometrioid: 88 Serous: 6 Others: 6	1: 45 2: 33 3: 22	31.4 ($p = 0.004$)	21.7 ($p = 0.18$)	10.3 ($p = 0.01$)
LH	I–II: 81 III–IV: 19	Endometrioid: 84 Serous: 9 Others: 6	1: 28 2: 41 3: 31	24	18.4	7
Bernardini et al. [9]						
RH	I–II: 75.5 III–IV: 24.5	Endometrioid: 84.5 Others: 15.5	1: 60.0 2: 11.1 3: 11.1	–	18 ($p = 0.22$)	9 ($p = 0.37$)
AH	I–II: 78.0 III–IV: 22.0	Endometrioid: 80.5 Others: 19.5	1: 51.2 2: 12.2 3: 17.1	–	14	3
Tang et al. [10]						
RH	I–II: 93.1 III–IV: 6.3	–	1: 60.5 2: 25.6 3: 12.4	13.0 ($p = 0.06$)	10.7 ($p = 0.03$)	2.4 ($p = 0.70$)
AH	I–II: 90.9 III–IV: 8.2	–	1: 48.2 2: 37.3 3: 13.6	10.7	8.7	2
DeNardis et al. [11]						
RH	I–II: 89.0 III–IV: 11.0	Endometrioid: 89 Serous: 2 Others: 9	1: 70 2: 14 3: 16	18.6 ($p = 0.74$)	13.3 ($p = 0.49$)	6.5 ($p = 0.93$)
TH	I–II: 76.5 III–IV: 22.5	Endometrioid: 78.0 Serous: 11.0 Others: 11.0	1: 58.5 2: 19.0 3: 22.5	18	12.4	6.6
ElSahwi et al. [14]						
RH	I–II: 81.3 III–IV: 19.7	Endometrioid: 80.6 Others: 19.4	1–2: 76.8 3: 23.2	20.3 ($p = 0.95$)	–	–

Table 2 continued

	Stage (%)	Histology	Grade (%)	Total mean node count	Pelvic mean node count	Aortic mean node count
AH	I–II: 82.0	Endometrioid: 67.3	1–2: 57.3	20	–	–
	III–IV: 18 %	Others: 32.7	3: 42.7			
Menderes et al. [15]						
RH	I–II: 83.6	Endometrioid: 80.5	1: 40.7	19.9	15.9	3.6
	III–IV: 16.4	Serous: 12.9	2: 39.4			
		Others: 6.6	3: 19.9			
Lau et al. [16]						
RH	I–II: 83.0	Endometrioid: 77.8	1: 48.1	17.4	10.5 ($p = 0.9$)	5 ($p = 0.8$)
	III–IV: 17.0	Serous: 9.3	2: 22.2			
		Others: 12.0	3: 29.6			

BMI of 32 (range 17–70). Menderes et al. [15] noted recurrences were significantly higher in patients with a BMI of less than 30 even though operative outcomes including node counts were similar. Moreover, when they analyzed each histologic type including type II cancers, recurrence rates were consistently higher for patients with BMI less than 30. A possible explanation is the association with lower BMI patients and type II cancers; the authors report 11 % of patients with endometrioid endometrial cancer recurred as compared to 30 % of UPSC patients. Brudie et al. [23] found that the overall recurrence rate of 372 patients was 8.3 % regardless of histology, with recurrence free survival (RFS) and OS of 89.3 and 89.1 % of obese EC patients including both type I and II cancers. Mean BMI was 32.2 (range 19–70). Of the patients who had a recurrence, 42 % of patients had high-risk histologies such as papillary serous, clear cell and sarcomas, as compared to 38.7 % with endometrioid EC. More often, these patients recurred at the vaginal cuff, and rarely, at port sites (0.6 %).

Quality of life

Abitbol et al. [24] recruited 211 patients who underwent robotic surgery for any gynecologic cancer, to complete a functional assessment of cancer therapy-general (FACT-G) questionnaire at 1, 3 weeks, and 3, 6, and 12 months after surgery. Comparisons to those patients who were converted to open cases were not performed. Seventy percent of patients had endometrioid EC, and 37 % of patients had a BMI of greater than 30. Though initially patients reported a decrease in quality of life (QoL) within the first week, by week three and thereafter, functional well-being returned to baseline as did social well-being. The advantage of MIS as compared to laparotomy was also made evident by the improvement of emotional well-being at all post-operative visits after 1 week as compared to baseline.

Cost

There has been considerable controversy over the cost of performing robotic surgery as compared to laparoscopic or open procedures in gynecology. Specifically for endometrial cancer, Wright et al. [25] looked at 10,906 endometrial cancer patients and noted that the cost for utilizing the robot for EC was $9691 compared with $8237 for laparoscopy ($p = <0.01$). The cost difference decreased with increasing hospital volume. Stratification by BMI was not reported. Bell et al. [26] reviewed an overall procedure cost and clinical outcomes analysis of 110 patients with EC in robotic, laparoscopic and open cohorts. They reported in three groups higher turn-over times for the operating room between cases for robotics as compared to open. The costs of each group were as follows: open $12,943, laparoscopy $7569 and robotic $8212, but again this was not categorized by BMI.

It is imperative to address specifically high BMI EC patients in a separate cost model. By examining the current cost data on robotic surgery, the benefits of robotics on obese EC patients is not obvious and this is a major limitation in the MIS movement. Without further cost studies on obese EC patients, the use of robotics in this population from a global healthcare perspective is not substantiated even though there are vast clinical benefits. For example, an obese woman with EC who requires hysterectomy, a staging procedure would be at much greater risk with an open procedure experiencing a longer hospital stay, higher complications including wound infection, higher cost of inpatient and possible outpatients interventions to address complications. There also may be a delay in return to work, lost wages and longer time to economic output along with effects on family members which all may contribute to a much more significant overall cost.

Conclusion

The impact of obesity is astounding. From healthcare costs, societal costs and patient morbidity including death, the obesity epidemic is devastating to patients and is challenging for providers. From this review, overall complications are less if a patient can undergo a MIS procedure for EC, and robotics is often more feasible than laparoscopy when increased adiposity would otherwise limit appropriate dissection.

The limitations of robotics may be in the class II and III EC population, specifically those patients who need extended surgical staging with para-aortic lymphadenectomy. Prospective studies with sufficient numbers of morbidly obese patients undergoing surgery with high volume robotic surgeons are lacking. Additionally, with the advent of the new DaVinci Xi system, there may be distinct advantages in performing extended staging in obese patients that has yet to be demonstrated.

Future discussions are needed on specific surgical techniques and a dedicated learning curve for operating on morbidly obese patients. Included in this discussion is: exactly who is an appropriate obese EC candidate? Is uterine size a factor in successful completion of robotics in this population, and not just a patient's high BMI? In examining the data, it is clear that more effort is needed in defining the optimal robotic candidate, which would thus define the limitations of robotic surgery in this population. Additionally, more studies on obese candidates that may be successfully mapped using robotic sentinel node algorithms are needed.

The main pitfall in the credibility of robotics in the obese EC population is having adequate cost studies. From the data, to date, it is not immediately apparent that there is an overwhelming financial savings although the clinical benefits have been demonstrated. To move forward with robotics in this population, it is imperative that a clear financial advantage is demonstrated.

While the focus of this review is on robotic surgery in obese women, it is also important to address the value of preventative medicine. Education with regard to diet, nutrition, and exercise is paramount. The role of bariatric surgery in reducing the risk of endometrial cancer needs further development. It is possible in the future that combined EC staging and robotic bariatric procedures may be necessary in selecting morbidly obese patients with multiple co-morbidities to minimize a woman's overall perioperative risk. With the obesity epidemic on the rise, gynecologic oncologists must find innovative means to manage these challenging surgical patients in a safe, cost effective manner.

Conflict of interest The authors Drs. Shemshedini, Pradhan, Pua and Tedjarati have no conflicts of interest to report.

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