Impact of obesity on surgical and pathological outcomes in women with endometrial cancer undergoing robotic-assisted surgical staging

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ABSTRACT

One of every three women in the United States is obese. Obesity is a well-known risk factor for the development of EC, and is associated with up to 46% of all cases. Endometrial cancer (EC) is the most common gynecologic cancer. The aim of this study was to evaluate the effect of obesity on patients undergoing robotic-assisted (RA) laparoscopic surgical staging for endometrial cancer. This is a multi-institutional retrospective cohort study of patients undergoing RA surgical management of EC. All patients underwent comprehensive surgical staging including hysterectomy, bilaterally salpingoophorectomy, pelvic lymphadenectomy and when feasible paraaortic lymphadenectomy. Surgical and pathologic outcomes of obese (BMI ≥30) versus non-obese women (BMI <30) were compared. From 2013-2017, 103 patients were identified. 67 were obese and the remaining 36 were non-obese. There was no significant statistical difference in total operative time, FIGO grade or depth of myometrial invasion between the obese and non-obese cohort. We observed an increase in EBL in the obese vs non-obese cohorts (p=0.007). Additionally, we observed an increase incidence of adverse events in the obese patient cohort, complicating 10.45% (7/67) of cases, compared to the non-obese cohort 5.56% (2/36). Of these complications, only the obese patient cohort suffered from intraoperative complications (3/67), including thermal injury, arrhythmia and airway management problem. There were no intraoperative adverse events in the non-obese cohort. Obese patients were more likely to have a final pathologic diagnosis of endometriod adenocarcinoma (89%) versus those in the non-obese cohort (75%). In conclusion, obese patients undergoing RA surgical management of EC is associated with a significant increase in EBL in obese compared with non-obese patients. Obesity appears to confer increased risk of intraoperative and postoperative complications. Obese women are more likely to be diagnosed with endometriod adenocarcinoma on final pathology.

Keywords: Endometrial cancer, obesity, robotic-assisted surgical staging, endometriod adenocarcinoma, comprehensive surgical staging

INTRODUCTION

Obesity is an epidemic. One of every three women in the United States is obese[1]. Endometrial cancer is the most common gynecologic cancer, the American Cancer Society estimates that there will be 61,380 new cases will be diagnosed in 2017[2]. Obesity is a well-known risk factor for the development of endometrial cancer, and is associated with up to 46% of all cases[3,4]. The majority of these cases are Type I, endometriod adenocarcinoma, which is typically diagnosed at early stage and has an overall positive prognosis[5,6]. The corner stone of treatment of endometrial cancer is surgery. Overtime, the traditional practice of staging laparotomy has been replaced by minimally invasive approaches, including comprehensive robotic-assisted laparoscopic surgical staging. Generally, it is believed that obesity confers additional surgical risk, compared to non-obese patients undergoing the same surgical procedure. Including increased operative times, poor exposure, inadequate lymph node dissection, increase average blood loss and an increase in both intra-operative and post-operative complications[6,7]. The Gynecologic Oncology Group Study Lap 2 demonstrated the safety and feasibility of laparoscopic staging compared to open laparotomy for the management of endometrial cancer in a non-obese patient population[8]. Laparoscopy was associated with shorter length of stay and fewer post-operative complications, with the disadvantage of longer total operative time[8]. Since the LAP2, multiple studies have sought to determine the role of minimally invasive surgery in the obese patient with
endometrial carcinoma. Several series have demonstrated low conversion to laparotomy and equally successful lymphadenectomy in patients undergoing robotic staging, as well as shorter hospital stay, lower transfusion rate and less wound complications.[3,9]. At our institution, almost all patients who undergo surgical management of endometrial cancer, do so via robotic assisted laparoscopic comprehensive surgical staging. We seek to evaluate the outcomes of obese versus non-obese patients undergoing robotic assisted surgical management of endometrial cancer.

METHODS
A retrospective cohort study of women who underwent robotic assisted surgical management of endometrial cancer at the State University of Buffalo, University Hospital and Good Samaritan Hospital Medical Center. This study was approved by the Institutional Review Board of both institutions. Eligibility criteria included a pre-operative pathologic diagnosis of complex atypical hyperplasia or endometrial cancer based on preoperative endometrial biopsy or dilatation and curettage. Robotic assisted laparoscopic surgical staging was performed, including hysterectomy, bilateral salpingo-oophorectomy and pelvic and para-aortic lymph node dissection when indicated and feasible. A retrospective chart review was performed on these patients.

Data collected included patient demographics, operative statistics, perioperative complications and pathologic details. Demographics included patient age, body mass index (BMI) calculated as weight in kilograms divided by the square of height in meters (kg/m2), and co-morbidities. Operative statistics included procedure performed, length of surgery and estimated blood loss. Pathologic details included uterine weight, final pathologic diagnosis, depth of invasion, lymph node metastasis and lymphovascular space invasion. Pathologic subtypes were divided as either endometriod adenocarcinoma or non-endometriod. The non-endometriod group included the following histologies; serous, clear cell, squamous and undifferentiated carcinoma. Every robotic procedure was performed on the da Vinci Surgical System (Intuitive Surgical, Sunnydale, CA). We then compared outcomes between obese and non-obese patients, specific areas of interest included total operative times, estimated blood loss, grade, depth of myometrial invasion and pathologic subtype. Data was analyzed using Chi-square, Fischer’s exact test, ANOVA and student’s t-test where appropriate. Statistical significance was set at p < 0.05.

RESULTS
A total of 103 patients underwent robotic-assisted surgical staging for endometrial cancer. There were 67 obese (BMI ≥30) and 36 non-obese (BMI <30) patients included. The mean BMI of the obese patient cohort was 42.05 kg/m2, and the mean BMI of the non-obese cohort was 24.86 kg/m2. There were no significant differences in age or comorbidities between the two cohorts (Table 1). There were no conversions to laparotomy in either group. Our study showed the mean operative time was greater in the obese patient cohort compared to the non-obese group, but the difference was not statistically significant, 217.13 versus 197.67 minutes, respectively (p 0.159). There was a significantly greater EBL in obese compared to non-obese women, 61.3 mL and 39.4 mL respectively (p 0.007) (Table 2). There was an increase incidence of adverse events in the obese patient cohort, complicating 10.45% (7/67) of cases, compared to the non-obese cohort, with a complication rate of only 5.56% (2/36). Of these complications, only the obese patient cohort suffered from intraoperative complications (3/67), including thermal injury, arrhythmia and airway management problem. There were no intraoperative adverse events in the non-obese cohort. Five patients in the obese cohort suffered from postoperative complications including intra-abdominal hematoma formation requiring blood transfusion, thermal urologic injury, ileus, readmission secondary to dehydration and one patient required return to the operating room for small bowel obstruction and strangulated umbilical hernia. The two postoperative adverse events observed in the non-obese cohort included a case of cellulitis at incision site and ileus.

Final pathologic outcomes were analyzed. We compared the histologic subtype, FIGO grade and depth of myometrial invasion between obese and non-obese patient cohorts. The final pathology of the obese patient cohort was predominantly endometriod adenocarcinoma, 89% of the patients. Non-endometriod types accounted for only 7.4% of
cases in obese women, and complex atypical hyperplasia was the final pathologic diagnosis in 2.9%. Endometriod adenocarcinoma was also the most common pathologic diagnosis in the non-obese cohort, accounting for 75% of cases, but this group had a notably higher incident of non-endometriod types, 22%. In patients with endometriod adenocarcinoma, FIGO grade did not differ significantly between obese and non-obese groups (p 0.1553). Depth of myometrial invasion also did not differ significantly between cohorts (p 0.665).

**DISCUSSION**

The primary management of endometrial cancer is surgery. The Gynecologic Oncology Group LAP2 trial is the largest prospective trial comparing open versus laparoscopic surgical management of endometrial cancer. The primary outcome of this trial was equivalent intraoperative outcomes and recurrence rate, as well as reduced post-operative complications observed in the laparoscopic group[8]. However, the average BMI of patients undergoing laparoscopy and laparotomy was low, only 28 kg/m² and 29 kg/m², respectively. Additionally, the conversion rate to laparotomy increased dramatically with increasing BMI. The average conversion rate of the entire cohort was 25%, but increased to 57.1% with BMI greater than 40. It is generally accepted that obesity confers patients’ greater surgical risks and leads to more challenges for the surgeon, including poor exposure, greater blood loss, and an increase in both intraoperative and postoperative complications[6,7].

In 2005, the FDA approved the use of robotics in pelvic surgery[10]. Robotic surgery has several advantages when compared to traditional laparoscopy, including increased instrument range of motion, tremor filtration, high definition 3-D viewing, absence of fulcrum effect and ease of learning[11,12]. A large single-center prospective study of patients undergoing robotic-assisted surgery for gynecologic malignancy demonstrated a decrease in mortality in comparison to laparotomy, this study included both obese and non-obese women[13].

There are few studies evaluating the effect of BMI on outcomes in patients undergoing robotic assisted surgical management of endometrial carcinoma. In a series by Gallo et al., there was no difference in EBL, operative time, length of stay or complications when comparing obese versus non-obese women[14]. Conversely, a larger study by Menderes et al. found significantly higher EBL and length of stay related to increasing BMI in patients undergoing robotic assisted surgical staging[15]. Our results were in agreement with Gallo et al. in regard to total operative time, we found no significant difference between obese and non-obese patients. Regarding EBL, our outcomes coincided with the findings of Menderes et al. We found statistically significant increase in EBL in obese compared to non-obese patients undergoing robotic-assisted surgical staging. We observed an average blood loss of 61.3 mL in obese patients and 39.4 mL non-obese patients (p 0.007). However, this overall low blood loss in both groups did not lead to more blood transfusions, and is likely little clinical significance.

Obesity is a well-documented risk factor for endometrial carcinoma, it has been associated with up to 46% of all endometrial cancers, most commonly endometriod adenocarcinoma[4,16]. The principal mechanism behind this finding is the aromatization of androstenedione to estrone in adipose cells. In accordance with this, our results demonstrate a greater percentage of endometriod adenocarcinoma, when compared to other histologic subtypes, in obese women. The weaknesses of our study include the retrospective design and the lack of long-term follow up data. Further areas of study include prospective trials and evaluation of long term outcomes of obese women undergoing robotic-assisted surgical management of endometrial carcinoma.

**CONCLUSION**

Obesity does not appear to increase the operative time in women undergoing robotic-assisted surgical management of endometrial cancer. Although the EBL was significantly greater in obese women, this

**Table 1: Pre-operative patient characteristics**

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Obese (N = 67)</th>
<th>Non-Obese (N = 36)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>42.06</td>
<td>24.9</td>
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</tr>
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<td>Range</td>
<td>30.1-67.7</td>
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**Table 2: Surgical outcomes**

<table>
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<tr>
<th>Procedure Time (minutes)</th>
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<th>Non-Obese (N=36)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
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<td>197.67</td>
<td></td>
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<tr>
<td>Range</td>
<td>89-435</td>
<td>95-337</td>
<td>0.159</td>
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<table>
<thead>
<tr>
<th>EBL (mL)</th>
<th>Obese (N=67)</th>
<th>Non-Obese (N=36)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>61.34</td>
<td>39.44</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>25-250</td>
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<td>0.007</td>
</tr>
</tbody>
</table>
difference is not likely to be clinically significant, and did not lead to a higher incidence of blood transfusion. Obesity appears to be a risk factor for complications in both the intraoperative and postoperative period. Endometrioid adenocarcinoma accounts for a greater percentage of disease in obese women with endometrial cancer, compared to non-obese women.

Compliance with ethical standards

1. There were no sources of funding involved with this study.

2. This retrospective study was approved by the internal review board of both institutions: Good Samaritan Hospital Medical Center and University of Buffalo, State University of New York, University Hospital.

3. Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

4. All contributing authors have no conflicts of interests and received no sources of funding.

REFERENCES


