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ORIGINAL CONTRIBUTIONS

Obesity in Patients with Endometrial Cancer: May It Affect the Surgical Outcomes of Laparoscopic Approach?

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Abstract

Objective To evaluate the impact of obesity on surgical outcomes for women with endometrial cancer (EC) managed by laparoscopic surgery. Minimal invasive surgery has been incorporated in the surgical management of EC, improving perioperative outcomes. However, this approach may become more challenging in case of obesity. So it is important to accurately evaluate and establish the most appropriate surgical approach for these patients.

Materials and Methods From January 2008 through April 2016, we conducted a prospective observational study, including all consecutive patients with a histological diagnosis of EC undergoing surgical staging by laparoscopy at our institution. Patients were classified in two groups (obese vs non-obese) according to their body mass index. Information about short- and long-term outcomes were recorded and analyzed during an outpatient follow-up.

Results Between January 2008 and April 2016, 83 women underwent laparoscopic surgery for EC at our institution. Forty-six (56.6%) of them were classified as obese. Surgical outcomes were similar in both groups. No significant difference was reported in surgical time, number of lymph nodes removed, blood loss, length of hospital stay, and incidence of intra- or postoperative complications. Also, long-term outcomes did not show any statistical significant difference: recurrence rate was 6.4% (3/47) among obese patients and 13.9% (5/36) among non-obese ($p = 0.251$). No difference was reported even in time to recurrence (log-rank $p = 0.280$) and in survival time (log-tank $p = 0.132$) between the two groups.

Conclusions Our results show that obesity did not impair the outcomes of laparoscopic surgery for EC. This surgical approach may be offered to obese patients with the same level of safety, radicality, and efficiency as for the normal-weight population.

Keywords Endometrial cancer · Laparoscopy · Obesity · Surgical approach

Introduction

Endometrial cancer (EC) is an important health problem especially in developed countries where obesity, one of its main risk factor, is spreading [1, 2]. It is the sixth most common cancer in women worldwide, and the most common gynecologic malignancy in the developed world [3]. It has been well demonstrated that unopposed excess of endogenous estrogen related to obesity is a significant risk factor for type I endometrial cancer [4]. Obesity, defined as body mass index (BMI) ≥ 30 kg/m^2, is associated with a 2.6-fold increase in EC risk, compared with normal-weight women (BMI < 25 kg/m^2). While in case of severe obesity (BMI ≥ 35 kg/m^2), the risk is 4.7-fold increased [3]. In clinical practice, more than two-thirds of women with EC are obese [4, 5], and experts predict that by 2030, about half of the general population will have a BMI ≥ 30 kg/m^2 [6]. Due to this data, we will face an increasing number of women with EC and obesity. At present, in case of suspected early stage disease, surgery at diagnosis is the cornerstone of management. The traditional surgical approach consisted of laparotomy to perform total hysterectomy and bilateral salpingo-oophorectomy, with or without lymphadenectomy [7]. Obesity is associated with higher risk of

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surgical complications, thus demanding further interventions, longer hospital stay, and increased healthcare costs [8]. In the last two decades, minimal invasive surgery has been incorporated in the surgical management of EC, improving perioperative outcomes without compromising survival [9–11]. However, a minimal invasive approach may become more challenging, with increased operative time and high rate of conversion into laparotomy [12]. So it is important for these patients to accurately evaluate and establish the most appropriate surgical approach.

The aim of our study is to assess the impact of obesity on surgical outcomes for women with EC managed by laparoscopic surgery.

Material and Methods

We conducted a prospective observational study including all consecutive patients with a histological diagnosis of EC undergoing surgical staging by laparoscopy (LPS) at our institution, from January 2008 through April 2016.

For each patient, evaluation of tumor extension was conducted firstly by clinical and ultrasound examination. Image study was added to all patients, magnetic resonance imaging (MRI) and/or positron emission tomography/computed tomography (PET/CT) to evaluate the existence of distant metastases.

Patients with stage IV disease, according to the International Federation of Gynecology and Obstetrics (FIGO) classification, not eligible for initial surgical management, were excluded from the study.

Patients were classified in two groups according to their body mass index, obese when BMI ≥ 30 kg/m^2 and normal weight when BMI < 30 kg/m^2, according to the International Classification of adult obesity (WHO).

The surgical procedure was performed at our institution by the same team of surgeons from the Oncology Unit of Obstetrics and Gynecology Service. Surgical staging included exploration of the abdominal cavity, peritoneal washing cytology, total hysterectomy, bilateral adnexectomy, and pelvic with or without para-aortic lymphadenectomy.

Staging of patients was performed according to the 1988 International Federation of Gynecology and Obstetrics (FIGO) classification until the end of 2009, and then, it was substituted by the new 2009 FIGO staging guidelines, after its publication [13].

Adjuvant treatment was conducted by the Services of Medical Oncology and Radiotherapy of our center depending on the final stage.

Outpatient follow-up after surgery was performed every 3 months during the first 2 years, every 6 months until the fifth year, and annually until the tenth year.

The following variables were recorded and analyzed for each patient: age, body mass index (BMI), operative time, intra- and postoperative complications, number of lymph nodes obtained, histological type of cancer, difference in hemoglobin and hematocrit before and after surgery, length of hospital stay, need for adjuvant treatment, tumor recurrence, and death.

The initial data analysis was evaluated with a descriptive statistical approach. For inferential analysis, the Kolmogorov-Smirnov test was firstly used to assess normal distribution of the samples. Then, Student's t test was used for normally distributed variables, while Mann-Whitney test was applied to variables with non-normal distribution. For qualitative variables, the χ^2 test was used. Statistical significance was set at $p < 0.05$.

Survival analysis was performed with Kaplan-Meier estimate, and log-rank test was then applied. SPSS (Statistical Package for Social Science) N21 was used for the analysis.

Results

During the study period, 83 women underwent laparoscopic (LPS) surgery for EC at our institution. Of these patients, 46 (56.6%) were classified as obese (BMI ≥ 30 kg/m^2) while 36 (43.4%) had normal weight (BMI < 30 kg/m^2). The mean body mass index in the first group was 34.5 kg/m^2 (± 4.9) while it was 26.3 kg/m^2 (± 2.6) in the second one. Patients' baseline demographic and pathological characteristics were not significantly different, as shown in Table 1.

Table 1 Demographic and pathological characteristics

	47 obese patients no. (%) or means (SD)	36 non-obese patients no. (%) or means (SD)	p value
Age	63.9 ± 11.1	59.89 ± 11.9	0.117
BMI	34.5 ± 4.9	26.3 ± 2.6	< 0.001
Staging			
Low stage (< III)	36 (76.6%)	30 (83.3%)	0.701
High stage (≥III)	9 (19.1%)	6 (16.7%)	
Histological type			
Endometrioid	44 (93.6%)	34 (94.4%)	0.297
Non-endometrioid	3 (6.4%)	2 (5.6%)	

Table 2 Surgical outcomes according to BMI

Outcome	47 obese patients no. (%) or means (SD)	36 non-obese patients no. (%) or means (SD)	*p* value
Surgical time (minutes)	179.6 ± 21.4	185.3 ± 26.1	0.267
Hb reduction (mg/dl)	2.0 ± 1.1	2.1 ± 1.1	0.606
Ht reduction (%)	5.3 ± 2.9	6.0 ± 3.1	0.249
Intraoperative complications	3 (8.5%)	2 (5.6%)	0.875
Postoperative complications	5 (21.3%)	1 (8.3%)	0.171
Lymph nodes removed tot.	13.1 ± 7.1	13.1 ± 7.0	0.733
-Pelvic	13.1 ± 7.1	12.5 ± 6.4	0.674
-Aortic	0.02 ± 0.15	0.64 ± 2.50	0.181
Hospital stay (days)	4.4 ± 2.3	3.9 ± 1.4	0.600

Table 2 presents the surgical outcomes of patients who underwent LPS surgery. Surgical outcomes were similar in both groups (Table 2). No significant difference was reported in surgical time, blood loss (estimated by the difference in hemoglobin and hematocrit level before and after surgery), or intraoperative complications, with an overall incidence of 6.0% (5/83). Among obese patients, the incidence was 6.4%, reporting one bladder perforation and two ureteral lesions, while in the other group, the incidence was 5.6%, with one case of bladder perforation, and one case reporting anesthetic complication.

The rate of any postoperative complication among the entire cohort was 7.2% (10.6% in the obesity group, 2.8% in the normal-weight group), which consisted of two surgical wound infections, one pelvic abscess, one seroma in the operative port (umbilical trocar), and one case of temporary dysarthria. The number of lymph nodes removed was similar in both groups, with a mean number of 13.1 (± 7.1) among obese patients, and 13.1 (± 7.0) among non-obese women. Also, the length of hospital stay was similar ($p = 0.600$) between obese and normal-weight groups, with a mean length of 4.4 (± 2.3) days and 3.9 (± 1.4) days, respectively.

Twenty-five obese (53.2%) and 23 (3.9%) normal-weight patients needed adjuvant therapy after laparoscopic procedure, not highlighting any significant difference between the two groups ($p = 0.448$).

Long-term outcomes were collected and analyzed during the outpatient follow-up and are summarized in Table 3: We report an overall recurrence rate of 9.6% (8/83), 6.4% (3/47) among obese patients and 13.9% (5/36) among non-obese, with a no statistically significant difference ($p = 0.251$). Only two cases of death due to progression of the neoplastic disease occurred in the study period, both in the non-obese group ($p = 0.102$). No difference was reported even in time to recurrence and in survival time between the two groups.

Survival analyses was finally performed using Kaplan-Meier estimate (Figs. 1 and 2). No difference in survival time was demonstrated comparing obese and non-obese patients (log-rank $p = 0.132$), even if comparing separately those with high stage (log-rank $p = 0.186$) and those with low stage (log-rank $p = 0.329$). The same result was obtained in evaluating time to recurrence with Kaplan-Meier estimate (log-rank $p = 0.280$).

Discussion

In our series, 56.6% of patients with endometrial cancer had a BMI ≥ 30 kg/m^2, consistent with previous study that demonstrated that almost two-thirds of endometrial cancer patients are obese [4, 5, 14]. Indeed, the relation between excess adiposity and cancer development, in particular endometrial

Table 3 Long-term outcomes according to BMI

Outcome	47 obese patients no. (%) or means (SD)	36 non-obese patients no. (%) or means (SD)	*p* value
Need for adjuvant therapy	25 (53.2%)	23 (63.9%)	0.448
-Brachytherapy	17 (36.2%)	14 (38.9%)	
-External radiotherapy	5 (10.6%)	6 (16.7%)	
-Chemoradiotherapy	3 (6.4%)	3 (8.3%)	
Recurrence	3 (6.4%)	5 (13.9%)	0.251
Mortality	0	2 (5.6%)	0.102
Time to recurrence (months)	59.1 ± 30.1	64.2 ± 33.2	0.378
Survival time (months)	61.0 ± 27.8	69.5 ± 29.7	0.154

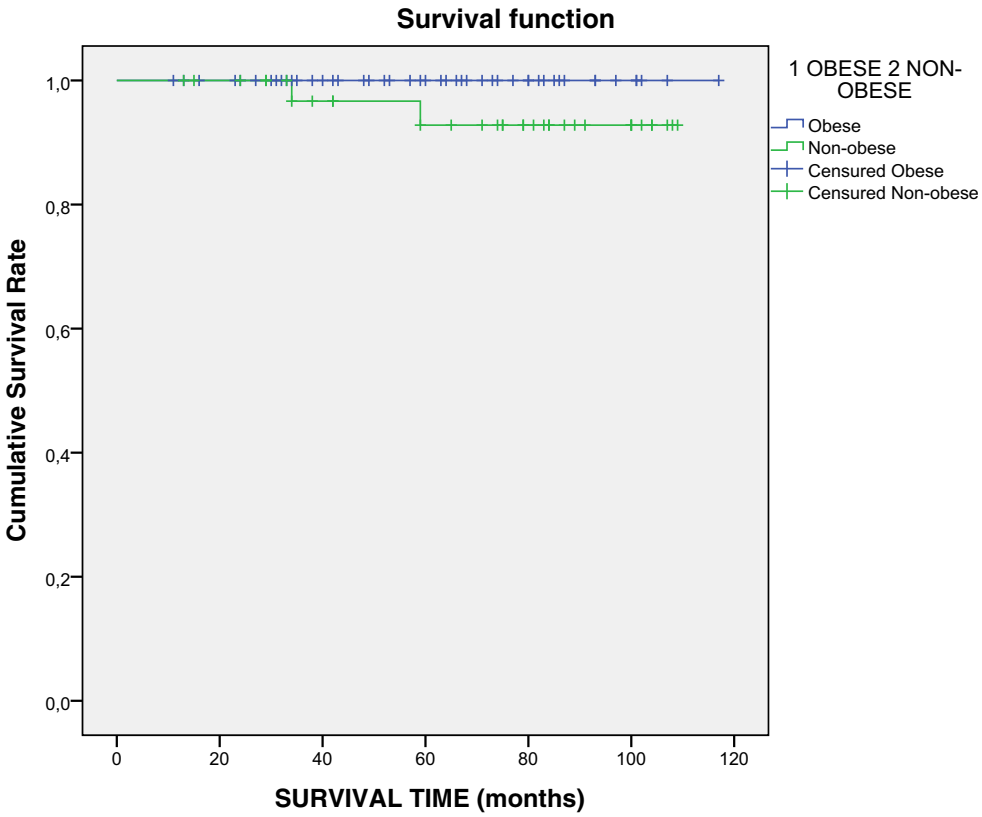

Fig. 1 Survival time in obese vs non-obese patients (Kaplan-Meier estimate). No difference in survival time was demonstrated comparing obese and non-obese patients (log-rank $p = 0.132$)

cancer, is well described in literature [15, 16]. Some adipose tissue–derived factors, like leptin, caveolin 1, serum amyloid A, and alterations in fibroblast growth factors levels, which participate in metabolic control and inflammation process,

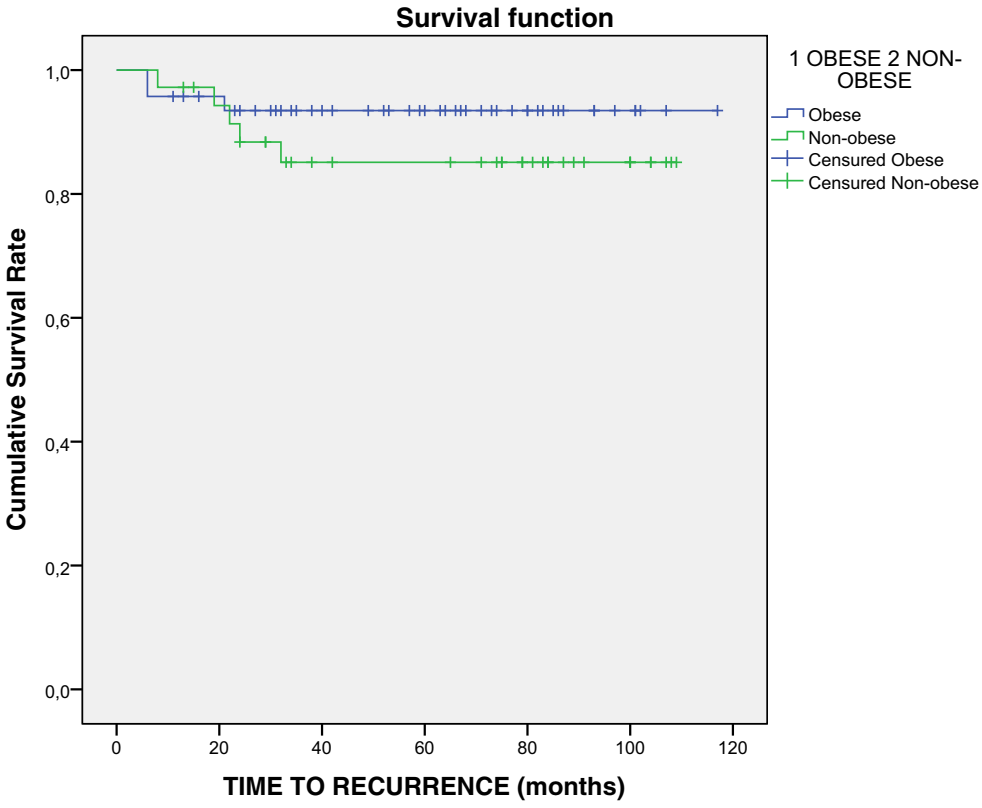

Fig. 2 Time to recurrence in obese vs non-obese patients (Kaplan-Meier estimate). No difference in time to recurrence was demonstrated comparing obese and non-obese patients (log-rank $p = 0.280$)

may be related to carcinogenesis promotion [17–20]. There was no difference between BMI groups as baseline demographic and pathological characteristics. Obesity, usually associated with high healthcare cost in a variety of surgical fields, due to postoperative complications and longer hospital stay [21], did not show to affect surgical outcomes in our study. Our results confirmed the safety and effectiveness of laparoscopic approach for these patients, as described in previous studies [5, 22, 23]. Data about other comorbidities, such as hypertension, diabetes, dyslipidemia, and related treatment among the patients were not available. This aspect represents a limitation of our study and could be addressed in future works. One of the most common concerns about the use of minimally invasive approach is the increased operative time associated with obesity. In our series, all patients underwent laparoscopic procedure (with hysterectomy, oophorectomy, and lymphadenectomy) with no significant difference in surgical time between obese and non-obese patients. This result is interesting if compared with those from other studies, which reported longer operative times for obese patients when a minimally invasive approach was used [5, 11, 12, 24]. However, in some of these studies, the difference was of marginal clinical importance, thus not justifying avoiding the use of laparoscopic approach in these patients.

No difference was noted in intraoperative and postoperative complications between BMI groups, and short-term perioperative outcomes were similar. Blood loss, which was similar in the two groups, was estimated from the difference between preoperative and postoperative hemoglobin and hematocrit levels, as the total volume of blood loss was altered by the peritoneal washing. Also, the length of hospital stay was similar between obese and non-obese patients. These results are supported also by other studies, which assessed the efficacy of laparoscopic approach in obese women with endometrial cancer [5, 25]. For these patients, minimal invasive surgery may improve not only perioperative outcomes and quality of life, but may also have a significant impact on healthcare costs, especially in morbidly obese patients, by reducing the incidence of perioperative complications, length of hospital stay, and need for readmission [22].

Also, the number of lymph nodes removed was similar among the two groups, while in some studies the obesity conditioned the possibility to perform a lymphadenectomy, thus compromising the staging process [25].

Need for adjuvant treatment was similar between the two groups, and also, recurrence and mortality rate did not show any significant difference. The survival analysis performed with Kaplan-Meier indicated no differences in time to recurrence and survival time between obese and non-obese patients, thus suggesting that the same radicality may be reached with minimal invasive surgery also in case of obesity, when performed by skilled surgeons.

Our results show that obesity did not impair the outcomes of laparoscopic surgery for endometrial cancer. This surgical approach may be offered to obese patients with the same level of safety, radicality, and efficiency as for the normal-weight population. Laparoscopy is not only feasible but also beneficial for obese women affected by endometrial cancer, by decreasing the incidence of perioperative complication, without compromising long-term outcomes. However, it is important for these patients to be referred to surgeons with experience in laparoscopic surgery in women with high BMI, in order to optimize the benefit of this minimal invasive approach.

Compliance with Ethical Standards

Conflict of Interest The authors declare that there are no conflicts of interest.

Statement of Institutional Review Board Approval The Ethics Committee of our Institutions does not require an approval for this kind of research, as this is an observational study.

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