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Original Article

Impact of Obesity on Surgical Treatment for Endometrial Cancer: A Multicenter Study Comparing Laparoscopy vs Open Surgery, with Propensity-Matched Analysis

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ABSTRACT **Objective:** To evaluate the impact of obesity on the outcomes of surgical treatment for endometrial cancer in general and also comparing laparoscopic and open abdominal approach.

Design: Retrospective case-control study (Canadian Task Force classification II-1).

Setting: Obstetrics and Gynecology Department, University of Insubria, Varese, Catholic University of the Sacred Heart, Rome, International School of Surgical Anatomy, Sacred Heart Hospital, Negrar, and Sant'Orsola-Malpighi Hospital, Bologna, Italy.

Patients: Data of consecutive patients who underwent surgery for endometrial cancer in 4 centers were reviewed. Univariate and multivariable analyses were performed. Adjustment for potential selection bias in surgical approach was made using propensity score (PS) matching.

Interventions: Laparoscopic or open surgical treatment for endometrial cancer.

Measurements and Main Results: A total of 1266 patients were included, including 764 in the laparoscopy group and 502 in the open surgery group. A total of 391 patients (30.9%) were obese, including 238 (18.8%) with class I obesity, 89 (7%) with class II obesity, and 64 (5.1%) with class III obesity. The total number of complications, risk of wound complications, and venous thromboembolic events were higher in obese women compared with nonobese women. Blood transfusions, incidence/severity of postoperative complications, and postoperative hospital stay were significantly higher in the open surgery group compared with the laparoscopy group, irrespective of obesity. These differences remained significant in both multivariable analysis and PS-matched analysis. The percentage of patients who received lymphadenectomy declined significantly in patients with BMI ≥ 40 in both the laparoscopy and open surgery groups. Conversions from the initially intended minimally invasive approach to open surgery were 1.1% to 2.2% for women with BMI <40, but increased in those with BMI ≥ 40 (8.6%; $p = .05$). PS analysis showed a lower complication rate, shorter hospital stay, and greater likelihood of receiving lymphadenectomy in obese women in the laparoscopic group.

Conclusion: Laparoscopy for endometrial cancer retains its advantages over open surgery, even in obese patients. However, operating on obese patients can be challenging regardless of the surgical approach taken, especially in

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The increasing rates of obesity in developed countries represent a concern not only for obesity's etiologic role in several diseases (including endometrial malignancy) [1–8], but also because obesity negatively affects anesthesiologic parameters and surgical performance, potentially increasing the risk of perioperative complications [9,10]. Surgery in morbidly obese patients can be challenging, and the ability to perform endometrial cancer staging may be impaired even in highly skilled operators [11].

The recent publication of 3 large randomized controlled trials (RCTs) [12–14] has validated laparoscopic surgery as an alternative to traditional open surgery for treating women with endometrial cancer [15]. Minimally invasive surgery is associated with fewer postoperative complications compared with an open approach [15], without affecting oncologic outcomes [16]. However, extreme obesity traditionally has been considered a relative contraindication to laparoscopic surgery. In these patients, a thicker panniculus reduces the range of movement of the laparoscopic instruments, and steep Trendelenburg position must be avoided and the redundancy of the bowel loops hinders proper exposure of the pelvic structures [8,9]. Some previous small studies have focused on the effects of adiposity on surgical outcomes of laparoscopic surgery and abdominal surgery [17–20], but common experience suggests that open surgery is usually preferred for an extremely obese patient with endometrial cancer [21,22]. A recent subanalysis of a RCT suggested that minimally invasive surgery is not cost-effective in obese women [13]; however, the literature remains devoid of solid, adequately powered studies on this issue.

Based on the foregoing considerations, the aim of the present study was to evaluate the impact of obesity and of its severity on perioperative outcomes of surgical treatment for endometrial cancer, comparing laparoscopic and open approaches.

Materials and Methods

The study involved patients from 4 institutions. We enrolled all consecutive women who underwent surgical treatment for histologically proven endometrial cancer either by laparoscopy or by open surgery between January 2000 and March 2013. In all involved institutions, research activities involving the study of existing data are exempt from the requirement for Institutional Review Board approval.

Surgical staging included peritoneal washing and total hysterectomy with bilateral salpingo-oophorectomy with or without pelvic/para-aortic lymphadenectomy. Details of the technique used for both laparoscopic and open approach have been provided elsewhere [23,24]. All procedures were performed by surgeons with extensive training and experience in gynecologic oncology and in advanced minimally invasive surgery.

Patients with stage IV disease according to the International Federation of Gynecology and Obstetrics (FIGO) classification [25], those with <6 months follow-up, those with incomplete clinical/histological data, and those who did not undergo hysterectomy were excluded from the final analysis.

Patients were divided according to the intended initial surgical approach. Data were stratified according to adiposity class: BMI <25 (normal weight), BMI ≥25 and <30 (overweight), BMI ≥30 and <35 (obesity class I), BMI ≥35 and <40 (obesity class II), and BMI ≥40 (obesity class III).

Preoperative evaluation of expected anesthesiologic risk was based on the American Society of Anesthesiology (ASA) score and patient performance status [26]. The decision as to whether or not to perform pelvic/para-aortic lymphadenectomy was based on preoperative and intraoperative uterine risk factors and the expected anesthesia risk.

The laparoscopy and open approach were compared with respect to baseline characteristics, perioperative data, and surgical and long-term outcomes. The management and outcome of each postoperative complication were recorded to grade severity based on the Clavien-Dindo scoring system [27]. FIGO surgical stage [25], tumor grade, and histopathological type were recorded for each patient. Following surgery, patients were examined every 3 months for 2 years, then every 6 months for the next 3 years, and yearly thereafter.

Statistical Analysis

Statistical analysis was performed with Prism 5 for Windows (GraphPad Software, San Diego, CA) and Stata version 11.2 (StataCorp, College Station, TX). Statistical significance was considered achieved for $p < .05$ (2-tailed). Normality testing (D'Agostino-Pearson test) was performed to determine whether continuous variables were sampled from a Gaussian distribution. Then comparisons between 2 group of continuous variables were done using the independent-samples t test or Mann-Whitney U test, as appropriate. Comparisons of more than 2 groups were done using 1-way analysis of variance (ANOVA). Post hoc analysis was performed with Bonferroni posttest. Categorical covariates were compared using the χ^2 test.

Univariate analysis followed by multiple logistic regression were performed to identify factors associated with perioperative outcomes. Factors with at least a tendency toward association on univariate analysis ($p < .10$) were then entered into a multiple logistic regression model with performance of lymphadenectomy (yes/no), blood transfusion (yes/no), intraoperative complications (yes/no), postoperative complications (yes/no), and postoperative complications grade ≥2 according to the Clavien-Dindo classification [27] as dependent variables, to identify characteristics independently associated with laparoscopic or open surgery. Multiple linear regression was performed to assess the presence of independent associations between surgical approach and the number of lymph nodes removed and length of hospital stay.

Because of nonrandom treatment allocation, a propensity score (PS) model was used to reduce bias resulting from differences in observed covariates between the laparoscopic and open surgery groups. Analyses using PS methods attempt to emulate randomized comparisons, because they allow comparisons between patient groups that are on average similar on all considered confounders. The PS for an individual is defined as the probability of having been treated with an intervention based on variables measured at or before the time of treatment. To generate PSs, a nonparsimonious logistic regression model incorporating variables felt to be predictors of treatment assignment was developed with laparoscopic approach as the dependent variable. The choice of covariates potentially related to the treatment arm included in the PS model was based on univariate analysis and clinical knowledge. Patient age, tumor stage, grading, histotype, ASA score, time of treatment, and institution were included in the PS model. Women in the open group were matched 1:1 to women in the laparoscopic group, creating pairs of laparoscopic and open surgery cases so as to minimize the total within-pair differences in the PS. The success of matching was assessed for each variable using standardized differences. A successful balance was inferred if the residual imbalance for all confounders was <5%.

Results

The study group comprised a total of 1266 patients with endometrial cancer, including 764 initially approached with laparoscopy and 502 in initially approached through open surgery. A total of 391 (30.9%) patients were obese. In the laparoscopic group, 260 patients (34%) were of normal weight, 274 (35.9%) were overweight, 137 (17.9%) were obese class I, 58 (7.6%) were obese class II, and 35 (4.6%) were obese class III. In the open surgery group, the corresponding figures were 179 (35.7%), 162 (32.3%), 101 (20.1%), 31 (6.2%), and 29 (5.8%) ($p = .13$). No between-group differences were observed in the proportions of women included in any of the body weight classes. Table 1 reports the patients' baseline demographic and pathological characteristics. A significantly higher proportion of women in the open surgery group had a worse ASA score ($p < .001$) and a more serious stage of disease ($p < .001$).

Estimated blood loss, need for blood transfusions, postoperative complications and severity of postoperative adverse events, and hospital stay were significantly ($p < .05$) higher in the open surgery group, whereas, the percentage of patients who underwent lymphadenectomy, the number of lymph nodes removed and the rate of intraoperative complications did not differ between groups in both univariate analysis (Supplementary Table 1) and multivariate analysis, adjusting for stage and grade of disease, chronological age, and ASA score (Table 2). A total of 502 patients per group were included in the PS analysis. Propensity matching of cases between the 2 groups confirmed these findings, and

Table 1

Demographic and pathological data

Characteristic	Laparoscopy	Open surgery	p value
Age, yr, mean ± SD	62.2 ± 11.5	63.2 ± 11.3	.99
Elderly (≥75 yr), n (%)	115 (15)	90 (17.9)	.17
BMI, median (range)	27 (15.8–60.4)	27 (15.9–62.3)	.78
Obese, n (%)	230 (30.1)	161 (32.1)	.49
No vaginal birth, n/N (%)	179/753 (23.8)	135/489 (27.6)	.13
Previous open abdominal surgery, n/N, (%)	330/705 (46.8)	227/466 (48.7)	.52
ASA score ≥2, n (%)	154 (20.2)	229 (45.6)	<.001
Stage ≥ 2, n/N (%)	100/747 (13.4)	161 (32.9)	<.001
Type II histology, n (%)	115 (15.1)	92 (18.3)	.11

ASA = American Society of Anesthesiologists; BMI = body mass index.

Table 2

Surgical outcomes on univariate and multivariate analysis (adjusting for stage and grade of disease, chronological age, and American Society of Anesthesiologists score), and on propensity-matched analysis

Outcome	Approach	Univariate analysis	Multivariate analysis	Propensity-matched analysis
Lymphadenectomy	*Laparoscopy*	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Open	0.93 (0.73 to 1.17)	0.91 (0.70 to 1.18)	**0.72 (0.55 to 0.94)**
Number of lymph nodes removed	*Laparoscopy*	Ref	Ref	Ref
	Open	0.36 (−1.28 to 2.01)	0.42 (−1.28 to 2.12)	0.66 (−1.15 to 2.53)
Blood transfusions	*Laparoscopy*	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Open	**4.13 (2.51 to 6.79)**	**3.31 (1.91 to 5.73)**	**5.51 (2.85 to 10.66)**
Intraoperative complications	*Laparoscopy*	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Open	1.54 (0.71 to 3.26)	1.28 (0.54 to 3.01)	**3.65 (1.41 to 29.63)**
Postoperative complications	*Laparoscopy*	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Open	**2.16 (1.59 to 2.94)**	**1.88 (1.34 to 2.63)**	**1.69 (1.21 to 2.37)**
Complications Clavien-Dindo ≥2	*Laparoscopy*	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Open	**2.11 (1.44 to 3.11)**	**1.78 (1.17 to 2.70)**	**2.31 (1.46 to 3.63)**
Postoperative hospital stay, d	*Laparoscopy*	Ref	Ref	Ref
	Open	**3.73 (3.23 to 4.22)**	**3.48 (2.96 to 4.01)**	**4.32 (3.67 to 4.96)**

Significant data are in bold type.

showed a higher rate of intraoperative complications in the open surgery group compared with the laparoscopic surgery group (Table 2).

Stratifying patients according to degree of obesity, we observed that the percentage of subjects who received blood transfusions, the incidence and severity of postoperative complications, and the postoperative hospital stay were significantly higher in the open surgery group, in both non-obese (BMI <30) and obese (BMI ≥30) women (Table 3). Among morbidly obese women (BMI ≥40), only hospital stay remained significantly shorter in the laparoscopic group compared with the open surgery group, although the proportions of lymphadenectomies and blood transfusions were lower, and the number of lymph nodes removed higher, in the laparoscopic group.

In terms of obesity class, the proportion of patients who underwent lymphadenectomy did not change significantly with increasing obesity up to class II. A significantly ($p < .05$) lower proportion of patients with BMI ≥40 underwent lymphadenectomy. The extent of this reduction was

Table 3

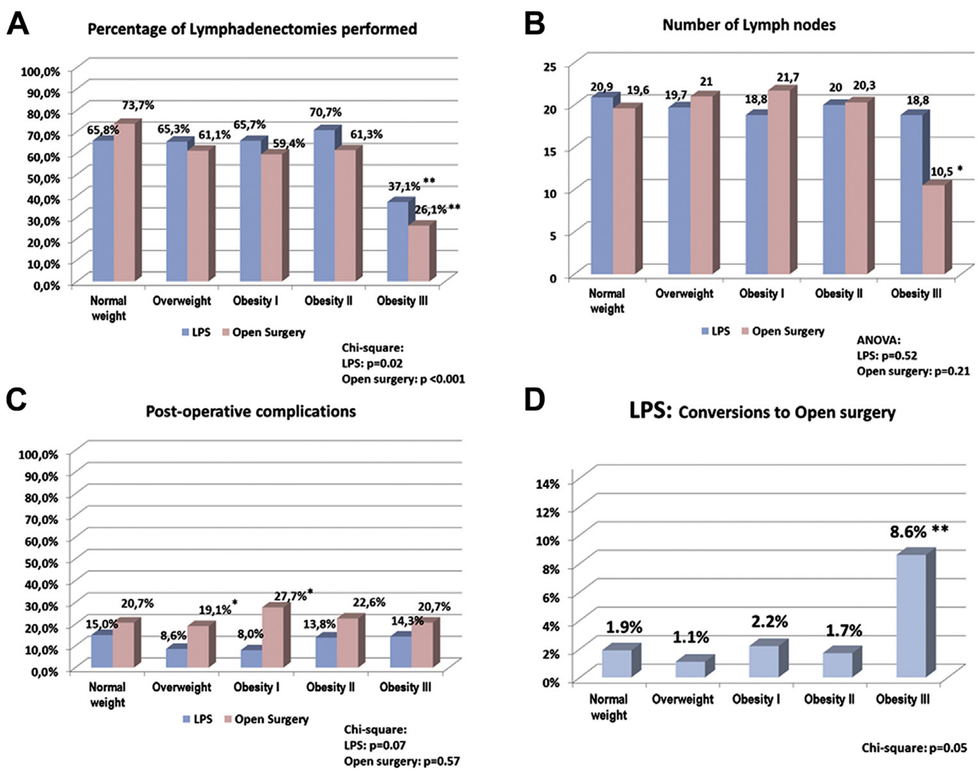
Comparison of laparoscopic and open approaches with stratification on degree of obesity

		BMI<30		**BMI ≥30**		BMI ≥40	
Outcome	**Approach**	n (%)	OR (95% CI)	n (%)	OR (95% CI)	n (%)	OR (95% CI)
Lymphadenectomy, n (%)	*Laparoscopy*	350 (65.5)	1.00 (reference)	144 (62.6)	1.00 (reference)	13 (37.1)	1.00 (reference)
	Open	231 (67.7)	1.11 (0.83 to 1.47)	85 (52.8)	0.67 (0.44 to 1.01)	6 (20.7)	0.44 (0.14 to 1.37)
Number of lymph nodes removed, mean ± SD	*Laparoscopy*	20.3 ± 10.5	Ref	19.1 ± 10.4	Ref	18.8 ± 12.8	Ref
	Open	20.2 ± 13.1	−0.1 (−2 to 1.9)	20.6 ± 13.7	1.5 (−1.7 to 4.6)	10.5 ± 7.6	−8.3 (−20.4 to 3.73)
Blood transfusions, n (%)	*Laparoscopy*	20 (3.8)	1.00 (reference)	3 (1.3)	1.00 (reference)	1 (2.9)	1.00 (reference)
	Open	31 (9.1)	**2.57 (1.44 to 4.59)**	26 (16.2)	**14.57 (4.34 to 49.06)**	3 (10.3)	3.9 (0.38 to 39.9)
Intraoperative complications, n (%)	*Laparoscopy*	11 (2.1)	1.00 (reference)	3 (1.3)	1.00 (reference)	0	1.00 (reference)
	Open	12 (3.5)	1.73 (0.76 to 3.96)	2 (1.2)	0.95 (0.16 to 5.76)	0	–
Postoperative complications, n (%)	*Laparoscopy*	63 (11.8)	1.00 (reference)	24 (10.4)	1.00 (reference)	5 (14.3)	1.00 (reference)
	Open	68 (19.9)	**1.86 (1.28 to 2.71)**	41 (25.5)	**2.93 (1.69 to 5.09)**	6 (20.7)	1.56 (0.42 to 5.77)
Complications Clavien Dindo score ≥2, n (%)	*Laparoscopy*	36 (6.7)	1.00 (reference)	15 (6.5)	1.00 (reference)	3 (8.6)	1.00 (reference)
	Open	37 (10.9)	**1.68 (1.04 to 2.72)**	29 (18)	**3.15 (1.63 to 6.09)**	2 (6.9)	0.79 (0.12 to 5.08)
Postoperative hospital stay, d, mean ± SD	*Laparoscopy*	3.6 ± 2.8	Ref	3.3 ± 2.5	Ref	3.6 ± 2.3	(reference)
	Open	7.5 ± 6.2	**3.9 (3.2 to 4.5)**	6.8 ± 4.4	**3.5 (2.8 to 4.2)**	6.9 ± 4.3	**3.3 (1.4 to 5.1)**

BMI = body mass index; CI = confidence interval; OR = odds ratio; SD = standard deviation. Significant data are in bold type.

Fig. 1

(A) Percentage of lymphadenectomies in the laparoscopic *vs*. open surgery groups, with stratification on the five different classes of body weight. **(B)** Number of lymph nodes removed in the laparoscopic vs open surgery groups, with stratification on the 5 different classes of body weight. **(C)** Postoperative complication rate in the laparoscopic *vs*. open surgery groups, with stratification on the 5 different classes of body weight. **(D)** Percentage of conversion to open surgery in the laparoscopic group across the 5 classes of body weight. *Statistically significant between the 2 surgical approaches (favors laparoscopy). **Statistically significant within the same surgical group compared with the reference (i.e. normal weight class; BMI <25).



similar in the laparoscopic and open surgery groups. This decrease was confirmed after multivariable adjustment for confounding factors (Fig. 1A). The number of lymph nodes removed was similar across the 5 BMI classes in the women who underwent laparoscopy, whereas in the open surgery group it was significantly lower in women with class III obesity compared with normal-weight women (Fig. 1B). Fig. 1C shows the rate of postoperative complications across the 5 BMI classes, and Fig. 1D shows conversions from an initially intended minimally invasive approach to open surgery. As shown in Fig. 1D, conversions were uncommon (1.1%–2.2%) in women with BMI <40, but much more common in morbidly obese patients (8.6%; p = .05).

When stratifying patients based on the severity of obesity, regardless of surgical approach, we found that the proportion of women who underwent lymphadenectomy was stable up to class II obesity (>60% in all classes), and then decreased dramatically to a low of 30% in women with BMI ≥40. In addition, when lymphadenectomy was done, the median number of lymph nodes removed was between 18 and 22 in women with BMI up to 40, and was significantly lower (16) in those with class III obesity.

The proportion of patients undergoing para-aortic lymphadenectomy was 9.7% (74 of 764) in the laparoscopic group and 10.8% (54 of 502) in the open surgery group (p = .52). Among obese patients, para-aortic lymphadenectomy was performed in 7.4% (17 of 230) obese patients in the laparoscopic group and in 8% (13 of 161) of those in the open group (p = 1.00). No significant difference in the likelihood of undergoing para-aortic lymphadenectomy was found between obese and nonobese women within the same surgical approach group (laparoscopic or open).

PS-matched analysis after stratification on different classes of obesity (Table 4) shows that patients in the open surgery group were less likely to undergo lymphadenectomy and had longer hospital stays irrespective of BMI. In the laparoscopic group, women with BMI ≥30 had also an advantage in terms of lower risk of both intraoperative and postoperative complications (Table 4).

A detailed analysis of the complications according to the type of adverse event, the surgical approach chosen, and the presence or absence of obesity found significantly higher rate of surgical site complications, risk of

Table 4

Comparison of laparoscopic and open approaches with propensity-matched stratification on degree of obesity

Outcome	Approach	BMI <30, OR (95% CI)	BMI ≥30, OR (95% CI)	BMI ≥40, OR (95% CI)
Lymphadenectomy	Laparoscopy	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Open	**0.61 (0.43 to 0.87)**	**0.43 (0.27 to 0.69)**	**0.24 (0.08 to 0.77)**
Number of lymph nodes removed	Laparoscopy	Reference	Reference	Reference
	Open	0.9 (−1.2 to 3)	−1 (−5 to 3)	**−17.3 (−35 to −0.3)**
Blood transfusions	Laparoscopy	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Open	**2.65 (1.33 to 5.27)**	**3.12 (1.40 to 6.93)**	0.44 (0.10 to 1.47)
Intraoperative complications	Laparoscopy	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Open	0.64 (0.29 to 1.38)	**5.23 (2.31 to 31.76)**	–
Postoperative complications	Laparoscopy	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Open	**1.62 (1.07 to 2.46)**	**6.33 (2.37 to 16.91)**	2.58 (0.18 to 12.91)
Complications Clavien-Dindo score ≥2	Laparoscopy	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Open	1.48 (0.87 to 2.50)	**3.15 (1.63 to 6.09)**	2.64 (0.49 to 14.16)
Postoperative hospital stay, d	Laparoscopy	Reference	Reference	Reference
	Open	**4.4 (3.5 to 5.3)**	**3.9 (2.9 to 4.6)**	**2.3 (0.6 to 4.5)**

BMI = body mass index; CI = confidence interval; OR = odds ratio. Significant data are in bold type.

thromboembolism, and total number of adverse events among obese patients compared with nonobese patients (Table 5). The risk of wound complications was higher in the open surgery group, irrespective of BMI. Bowel lesions were more frequent in the open surgery group in patients with BMI <30; conversely, venous thromboembolism was more common among obese patients in the open surgery group compared with those in the laparoscopic group.

Discussion

Obesity, especially extreme obesity, has long been considered a factor that potentially limits the ability to perform laparoscopic interventions [9,10,28,29]. Apart from the use of a vaginal approach (which preclude the possibility of assessing or at least exploring the nodal status), in common clinical practice, open surgery is traditionally advocated when a morbidly obese patient requires surgery for endometrial cancer. Our study, based on a large multicenter experience, calls this view into question and suggests that laparoscopy for endometrial cancer has advantages over open surgery even in obese patients.

Of interest is how our findings strongly suggest the difficulties inherent in performing operations in morbidly obese women affected by endometrial cancer, irrespective of the

Table 5

Complications (intraoperative and postoperative), according to the presence/absence of obesity and surgical approach

	BMI <30 (n = 875)				BMI ≥30 (n = 391)				
Complication	Total, n (%)	Laparoscopy (n = 534), n (%)	Open (n = 341), n (%)	p value	Total, n (%)	Laparoscopy (n = 230), n (%)	Open (n = 161), n (%)	p value	p value, obese vs nonobese
Urinary lesions	22 (2.5)	14 (2.6)	8 (2.3)	1.00	4 (1)	3 (1.3)	1 (0.6)	.65	.09
Bowel lesions	15 (1.7)	4 (0.7)	11 (3.2)	**.01**	6 (1.5)	3 (1.3)	3 (1.9)	.69	1.00
Vascular complications	9 (1)	8 (1.5)	1 (0.3)	.16	3 (0.8)	1 (0.4)	2 (1.2)	.57	.76
Wound complications (including vaginal dehiscence)	26 (3)	8 (1.5)	18 (5.3)	**.002**	22 (5.6)	8 (3.5)	14 (8.7)	**.04**	**.02**
Postoperative fever	21 (2.4)	12 (2.2)	9 (2.6)	.82	13 (3.3)	9 (3.9)	4 (2.5)	.57	.35
Venous thromboembolism	6 (0.7)	2 (0.4)	4 (1.2)	.21	10 (2.6)	1 (0.4)	9 (5.6)	**.002**	**.01**
Other complications	51 (5.8)	26 (4.9)	25 (7.3)	.14	29 (7.4)	13 (5.6)	16 (9.9)	.11	.31
Total complications	150 (17.1)	74 (13.9)	76 (22.3)	**.002**	87 (22.3)	38 (16.5)	49 (30.4)	**.001**	**.03**

BMI = body mass index. Patients may have had multiple complications. Significant values are in bold type.

surgical approach chosen, whether open or minimally invasive. Table 5 shows a greater total number of adverse events, greater risk of thromboembolism, and higher rate of wound complications in obese women compared with nonobese women. Excessive adiposity poses several problems to the surgical team far beyond difficulties maintaining Trendelenburg positioning and positive intra-abdominal pressure. Analyzing the difficulties of operating on obese patients must take other factors into account as well, such as surgeon fatigue and inability to correctly expose and develop the anatomic spaces. Moreover, the postoperative course may be more complicated and prolonged, resulting in a greater risk of postoperative complications. These factors have little or no relationship with the use or not of a minimally invasive approach, but rather apply to surgery in general.

As a confirmation to the foregoing considerations, our data indicate a dramatic reduction in the percentage of women with BMI ≥40 who underwent lymphadenectomy in both the laparoscopic and open surgery groups. However, when matching patients for well-known confounders (i.e., patient age, tumor stage, grading, histotype, ASA score, time of treatment, and institution) using PS analysis, a significant tendency toward a lower rate of lymphadenectomy was observed in the open surgery group. The utility of nodal dissection in treating endometrial cancer remains a matter of passionate debate [30], and any inference on this issue is far beyond the scope of the present study.

A recent subanalysis of the LAP 2 trial by the Gynecologic Oncology Group (GOG) showed a lower tendency to develop aggressive tumors in very obese women [7]; consequently, these women receive less benefit from nodal dissection [30]. Moreover, morbidly obese women have a higher incidence of medical comorbidities, which may influence the surgeon in choosing a more prudent intervention to avoid anesthesia problems [7]. In the present study, the decision of whether or not to perform nodal dissection was based on uterine risk factors and anesthesia considerations. As demonstrated by a recent Italian multicenter survey, treatment protocols for endometrial cancer vary widely among institutions [31]. This is due mainly to controversial scientific questions and to the availability of facilities in each center; however, in the present study, the reduced percentage of lymphadenectomies suggests that factors unrelated to oncologic indications or anesthesia difficulties may have played some role in reducing the extent of surgical efforts in women with class III obesity. The common belief that laparoscopic surgery reduces surgeons' ability to accomplish nodal dissection is called into question by the results of our PS-matched analysis. Furthermore, our data show that the likelihood of undergoing complete nodal staging with para-aortic lymphadenectomy is not influenced by the surgical approach, even in obese patients.

Another important finding of the present study is the steep decline in nodal yield in women with BMI ≥40 when data from the 2 surgical approaches were pooled. In the laparoscopic group, however, the number of lymph nodes removed was not affected by BMI. Again, this finding challenges the common belief that laparoscopic surgery is inferior to an open approach in terms of the ability to visualize the surgical field and develop anatomic spaces in cases of excessive adiposity.

Overall, the incidence and severity of postoperative complications were lower for both nonobese and obese women in the laparoscopic group compared with the open surgery group. This finding could not be confirmed in women with BMI ≥40, however, probably owing to the low incidence of adverse events in that subgroup.

Analyzing the conversions from an initial laparoscopic approach to unintended laparotomy, the percentage of laparoscopic failures in our series approached 2% throughout the BMI classes up BMI 40, and then increased rapidly to 8.6% in patients with BMI ≥40. In general, these figures compare well with the available randomized series of laparoscopic treatment of endometrial cancer. The LACE RCT, conducted in 19 tertiary gynecologic cancer centers in Australia, New Zealand, and Hong Kong, reported a 3.7% overall conversion rate from laparoscopy to open surgery, similar to our findings (no stratification on the 5 different BMI classes was available) [14], whereas the GOG LAP2 trial published in 2009 registered a conversion rate of >25% in their study population [12].

Recently, Bijen et al [17], in a subanalysis of a randomized trial performed in The Netherlands, concluded that laparoscopy is not cost-effective in obese women, and suggested that open surgery should be preferred, particularly in women with BMI ≥35. The limited sample size, the impressive conversion rate (35% at BMI ≥35), and the choice to not perform lymphadenectomy (as per protocol indication) preclude generalization of these results.

Although previous preliminary smaller studies have suggested that laparoscopy may be of value for obese women with endometrial cancer [18–20], solid data on a large cohort of patients were lacking. For this reason, we designed and conducted the present study.

In a comparison of laparoscopic procedures for endometrial cancer and traditional open surgery in nonrandomized studies, selection bias frequently occurs favoring the endoscopic technique, because surgeons choose the most ideal patients when embarking on technically demanding minimally invasive procedures. Retrospective studies are prone to the common intrinsic limitations of any chart review, particularly selection bias. To minimize shortcomings in the estimation of treatment effect, we used the PS method to compare patient groups that were on average similar in terms of all observed confounders. It must be acknowledged that the PS methodology offers a powerful strategy for controlling for selection bias, but although randomization will balance, in expectation, both measured and unmeasured confounders between groups, the PS-matched analysis is based only on measured baseline variables. Therefore, within a stratum of subjects matched on the PS, there is the potential risk of treatment groups still being imbalanced in unmeasured characteristics. However, given that no previous randomized trial has compared laparoscopic and open surgery in obese women affected by endometrial cancer, appropriate multi-institutional observational studies represent for the moment the highest level of clinical research available pragmatically in this scenario.

Conclusion

In conclusion, although previous RCTs had clearly shown that the laparoscopic approach to treating endometrial cancer is not only feasible, effective, and oncologically safe, but also associated with lower postoperative morbidity and a better adverse event profile compared with an open abdominal approach [9–12], still no adequately powered study had explored whether these advantages can be extended (and in what measure) to obese and morbidly obese women. Our data show that laparoscopy is superior (or at least equivalent) to open surgery in patients with endometrial cancer, even in cases of morbid adiposity. In particular, minimally invasive surgery allows for faster recovery and a greater likelihood of retroperitoneal staging.

Our findings are important not only for academic discussion, but also for patient treatment; women affected by endometrial cancer may need adjuvant therapy. Considering that obese patients are at increased risk for a prolonged and more complicated postoperative course, a surgical approach that reduces overall surgical morbidity may have beneficial consequences on long-term outcomes. This speculation remains to be confirmed by specifically designed trials, however.

Although limited by the absence of randomization, our data appear to be of value, owing to the large number of patients included. The retrospective nature of our analysis of prospectively collected data provides a picture of the real clinical scenario that may be encountered in high-volume referral oncologic centers, beyond the strict and selective recruitment rules that must be observed during enrollment in randomized trials. Moreover, our use of PS-matched analysis approximates our results to those of a randomized trial, further reinforcing our conclusions.

Supplementary Data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jmig.2015.08.007.

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