Impact of morbid obesity in surgical management of endometrial cancer: surgical morbidity, clinical and pathological aspects

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Summary

Objective: To evaluate the effect of body mass index (BMI) on clinical, surgical, pathologic features, and surgical morbidity in the management of patients with endometrial cancer.

Materials & Methods: All endometrial cancer patients who were surgically treated in our institution between January 1, 2003 and January 1, 2006 were eligible for the study. Forty-two out of 60 patients were included in the analysis from our cancer database. The patients were divided into three groups: BMI < 30, BMI 30-40, BMI > 40. Statistical analysis was performed by SPSS for Windows (version 11; SPSS, Inc., Chicago, IL).

Results: Lymphadenectomy as part of surgical staging was performed in 90.5% of all patients. Although patients with a BMI > 40 were less likely to have positive lymph vascular space invasion (LVSI) ($p = 0.042$), chance of deep myometrial invasion and positive lymph nodes (18%) were the same as for patients with a BMI < 30. Patients with a BMI > 40 had statistically longer operating times when compared to patients with a BMI < 40 ($p = 0.039$). Wound separation rate was statistically higher in the morbidly obese patients ($p = 0.01$). Average number of lymph nodes removed, hospital days, intraoperative and overall postoperative complication rates did not differ among the three groups ($p > 0.05$).

Conclusions: This study confirms that comprehensive surgical staging can be performed adequately and safely in obese and morbidly obese endometrial cancer patients with no difference in length of hospital stay, intraoperative or postoperative complications. As a result adjuvant treatment of morbidly obese patients can be planned accordingly preventing under or over treatment.

Key words: Morbid obesity; Endometrial carcinoma; Surgical management; Lmphadenectomy.

Introduction

Endometrial cancer is the most common gynecologic malignancy, ranking fourth among malignancies in women overall [1]. Most of the risk factors for this type of cancer are related to estrogen excess; endogenous or exogenous. Obesity is a constantly increasing health problem as more people are overweight and obese, and leisure time physical activity is increasing only slightly. The risk of developing endometrial carcinoma parallels the increase in degree of obesity, such that women who are 5-10 kg overweight have a two-fold increased risk while women who are overweight > 25 kg have a ten-fold increased risk [2]. Morbid obesity is not only a known risk factor but also a feature, which can play a role in the selection of a conservative therapeutic regimen for endometrial carcinoma. This is based on the general assumption that obesity negatively impacts surgical management due to increased intraoperative and postoperative complications, inadequate lymph node yield, and increased incidence of comorbid conditions like hypertension, diabetes mellitus and cardiopulmonary diseases that complicate the postoperative course [3]. Data on the effects of obesity on surgical staging in endometrial carcinoma is rare in the literature. Despite lack of evidence supporting these assumptions some authors have suggested vaginal hysterectomy without a formal surgical staging in this group of obese patients [4-6].

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We aimed to look at the effect of obesity on the selection of type of surgery and to assess the adequacy and safety of comprehensive surgical staging in morbidly obese compared to non obese endometrial cancer patients. We also investigated the effect of obesity on surgical morbidity, clinical and pathologic factors in this group of patients by stratification according to body mass index (BMI).

Materials & Methods

All patients with endometrial carcinoma, who were surgically treated in Baskent University School of Medicine by one of two gynecologic oncologists between January 1, 2003 and January 1, 2006, were identified for the study. Forty-two out of 60 patients were included in the study and these patients underwent analysis from our cancer database. Eighteen patients were excluded because of incomplete information in their medical records; all these patients were operated on at a time when patient data were not recorded prospectively. We stratified patients according to their BMI, calculated on admission. Patients were considered as having normal or ideal weight with a BMI < 30, and obese when they had a BMI between 30 and 40, whereas they were labeled morbidly obese with a BMI > 40 [7]. BMI was calculated by dividing weight in kilograms by the height in meters squared. Clinical data collected included age at diagnosis, height, weight, BMI, and comorbid conditions. Comorbid conditions searched for included hypertension, diabetes, pulmonary disease, cardiac disease, thyroid disease and peptic ulcer. Pulmonary disease was defined as patients having asthma, chronic obstructive pulmonary disease (COPD), chronic bronchitis, bronchiectasis, restrictive lung disease, or emphysema. Pathologic data collected included histology,

grade, myometrial invasion, lymph vascular space invasion (LVSI), peritoneal cytology, lymph node status and stage.

Surgical data collected included operative time, estimated blood loss, type of surgery, average number of lymph nodes retrieved, intraoperative complications, postoperative complications and number of hospital days. Intraoperative complications specifically searched for included ureteral injury, bladder injury, bowel injury, and vessel injury. Recorded complications other than these were also included. Postoperative complications that were looked at included wound dehiscence, serous discharge, fever over 38°C on two separate occasions, sepsis, atelectasia, ileus, deep venous thrombosis, pulmonary emboli, urinary tract infection and postoperative death.

Statistical analysis

Data were analyzed using SPSS for Windows (version 11; SPSS, Inc., Chicago, IL). Anova and chi-square tests were used to compare groups. Post hoc analysis was performed by the Bonferroni test. The difference between women with a BMI ≥ 40 and women with a BMI < 40 was analyzed by the independent Student's t-test. Homogeneity of variances was calculated by Levene's test and Lilliefors significance correction test. The Mann-Whitney U test was used where appropriate.

Results

Mean age of the entire study population was 60 (range: 45-72 years). There was no statistical difference in age between ideal weight and obese and morbidly obese groups of patients (p = 0.468).

Among all patients 47% had hypertension, and 81% of patients with a BMI > 40 had hypertension, which was statistically significantly higher than patients with a BMI < 30 who had hypertension in 55% (p = 0.01). Also, COPD was found in 18% of morbidly obese patients whereas no patients in the ideal body weight group had COPD (p = 0.05). Incidence of diabetes, hypothyroidism, peptic ulcer disease, or cardiac disease did not differ among groups (p > 0.05) (Table 1).

Lymphadenectomy as part of surgical staging was performed in 90.5% of all patients, and there was no difference between three groups. Among patients with a BMI > 40, 90% had complete surgical staging including lymphadenectomy, and statistically there was no difference compared to patients with a BMI < 30, who had 88% complete surgical staging (p = 0.983). The most commonly performed procedure was total abdominal hysterectomy (TAH) with bilateral salpingo-oophorectomy (BSO), omentectomy, peritoneal cytology, and lymph node dissection (LND), which was performed on 25 (59.5%) patients. TAH+BSO, peritoneal cytology, and LND were performed on eight (19%) patients. Among the patients undergoing complete surgical staging, 19% had only pelvic lymphadenectomy performed, and all others had both pelvic and paraaortic lymph node dissection. The average number of lymph nodes removed was 26 (range: 9-53), and there was no difference among the three groups. Lymph nodes were positive for metastasis in 23% of the patients who underwent LND. Positive lymph nodes were detected in 20% of patients with a BMI > 40 which was not statistically different than other patients with a BMI < 30 and a BMI 30-40 (p = 0.950). In terms of estimated blood loss there was statistically no difference between three groups (p = 0.484). However, patients with a BMI > 40 had longer operating times (234 min vs 201 min.) when compared to patients with a BMI < 40, and this difference was statistically significant (p = 0.039) (Table 2).

Table 1. — *Comorbidity stratified by BMI.*

	BMI < 30 (n = 9)	BMI 30-40 (n = 22)	BMI > 40 (n = 11)	Total (n = 42)	
Mean age (years)	61	58	61	60	p = 0.468
Comorbid conditions					
Hypertension	5 (55.6%)	6 (27.3%)	9 (81.8%)	20 (47.6%)	p = 0.01
Diabetes Mellitus	4 (44.4%)	4 (18.2)	2 (18.2%)	10 (23.8%)	p = 0.261
COPD*	0 (0%)	0 (0%)	2 (18.2%)	2 (4.8%)	p = 0.05
Hypothyroidism	1 (11.1%)	1 (4.5%)	0 (0%)	2 (4.8%)	p = 0.509
Peptic ulcer	0 (0%)	1 (4.5%)	1 (9.1%)	2 (4.8%)	p = 0.635
Cardiac disease	0 (0%)	0 (0%)	1 (9.1%)	1 (2.4%)	p = 0.236

* Chronic obstructive pulmonary disease.

The most common histological type was endometrioid adenocarcinoma. Patients with a BMI > 40 had a higher rate of having endometrioid histology (90% vs 66%) and a lower rate of papillary serous or clear cell histology (0% vs 22%) than patients with a BMI < 30, although these figures did not reach statistical significance (p = 0.834). There was no difference between the three groups in terms of myometrial invasion, peritoneal cytology, and stage (p > 0.05). Although morbidly obese patients had no grade 3 tumors, there was no difference in tumor grades as compared to patients with ideal body weight (p = 0.054). Lymphovascular space involvement (LVSI) was negative in 100% of patients with a BMI > 40, whereas 55% of patients with a BMI < 30 had positive LVSI, which was a statistically significant difference (p = 0.04) (Table 3).

When we analyzed intraoperative complications we found bleeding of more than 1000 cc in only 4.7% of our study population and there was no difference among the three groups. We did not have any ureteral injuries. Also there were no bowel injuries, bladder injuries and we did not encounter any vessel injuries. Of our patients 11% needed blood transfusions averaging two units. Two (22%) patients with a BMI < 30, one (4.5%) patient with a BMI between 30 and 40, and two (18%) patients with a BMI > 40 received blood transfusions. There was no difference between morbidly obese and ideal weight patients in terms of blood transfusion rates. Intraoperative complications did not differ among the three groups (p = 0.292).

When we analyzed postoperative complications, there was no difference in the three groups in terms of wound infection, urinary tract infections, occurrence of lymphocele, deep vein thrombosis, sepsis, pneumonia, cardiological events and ileus. The only statistically significant difference was wound dehiscence, which occurred in three (27%) patients with a BMI > 40, whereas no patient in other groups had such a complication (p = 0.01). When calculated for all patients wound dehiscence was observed in 7%. However, overall postoperative complication rates did not differ among the three groups (p = 0.368). There were no postoperative deaths.

Discussion

Obesity is a known risk factor for type I endometrial carcinoma due to excess aromatization of androstenedione in the adipose tissues to estrone, leading to a

Table 2. — *Surgical features stratified by BMI.*

	BMI < 30 (n = 9)	BMI 30-40 (n = 22)	BMI > 40 (n = 11)	Total	p value
Type of Surgery					0.122
TAH/BSO/LND/OMT/APP/CYT	3 (33.3%)	1 (4.5%)	0 (0%)	4 (9.5%)	
TAH/BSO/LND/OMT/CYT	3 (33.3%)	15 (68.2%)	7 (63.6%)	25 (59.5%)	
TAH/BSO/LND/CYT	1 (11.1%)	4 (18.2%)	3 (27.3%)	8 (19%)	
TAH/BSO/PERIT CYT	1 (11.1%)	2 (9.1%)	1 (9.1%)	4 (9.5%)	
MOD RAD HYST/BSO/LND/OMT/CYT	1 (11.1%)	0 (0%)	0 (0%)	1 (2.4%)	
LYMPHADENECTOMY	8 (88.9%)	20 (90.9%)	10 (90.9%)	38 (90.5%)	0.983
LN status (positive)	2 (25%)	5 (25%)	2 (20%)	9 (23.7%)	0.95
Mean number of LNs retrieved (min-max)	24.1 (14-34)	27 (10-53)	25.7 (12-47)	26 (10-53)	0.812
EBL (cc) (mean)	325	430	447	412	0.484
Operative time (min) (mean)*	186	207	234	209	0.039
Hospital days (mean)	6.3	5.5	7.1	6.1	0.083

* BMI > 40 vs BMI < 40; TAH/BSO/LND: total abdominal hysterectomy and lymph node dissection; EBL: estimated blood loss; OMT/APP/PERIT CYT: omentectomy/appendectomy/peritoneal cytology; MOD RAD HYST: modified radical hysterectomy.

Table 3. — *Histopathologic features stratified by BMI.*

	BMI < 30 (n = 9)	BMI 30-40 (n = 22)	BMI > 40 (n = 11)	Total (n = 42)	
Histology					p = 0.834
Endometrioid	6 (66.7%)	17 (77.3%)	10 (90.9%)	33 (78.6%)	
Adenosquamous	1 (11.1%)	2 (9.1%)	1 (9.1%)	4 (9.5%)	
Serous	1 (11.1%)	2 (9.1%)	0 (0%)	3 (7.1%)	
Clear cell	1 (11.1%)	1 (4.5%)	0 (0%)	2 (4.8%)	
Stage					p = 0.249
I	4 (44.4%)	15 (68.2%)	6 (54.5%)	25 (59.5%)	
II	2 (22.2%)	2 (9.1%)	3 (27.3%)	7 (16.7%)	
III	1 (11.1%)	5 (22.7%)	1 (9.1%)	7 (16.7%)	
IV	2 (22.2%)	0 (0%)	1 (9.1%)	3 (7.1%)	
LVSI					p = 0.042
negative	5 (55.6%)	18 (81.8%)	11 (100%)	34 (81%)	
positive	4 (44.4%)	4 (18.2%)	0 (0%)	8 (19%)	
Myometrial Invasion					p = 0.670
none	1 (11.1%)	3 (13.6%)	1 (9.1%)	5 (11.9%)	
< 50%	4 (44.4%)	14 (63.6%)	5 (45.5%)	23 (54.8%)	
> 50%	4 (44.4%)	5(22.7%)	5(45.5%)	14 (33.3%)	
Grade					p = 0.054
1	3 (33.3%)	12 (54.5%)	2 (18.2%)	17 (40.5%)	
2	5 (55.6%)	6 (27.3%)	9 (81.8%)	20 (47.6%)	
3	1 (11.1%)	4 (18.2%)	0 (0%)	5 (11.9%)	
Cytology					p = 0.314
negative	7 (77.8%)	21 (95.5%)	10 (90.9%)	38 (90.5%)	
positive	2 (22.2%)	1 (4.5%)	1 (9.1%)	4 (9.5%)	

chronic low dose estrogen exposure [8]. Obesity is also related to increased risk for diseases such as hypertension, chronic obstructive pulmonary disease and diabetes as well as several malignancies [9].

In many gynecologic oncology centers, the decision to perform lymphadenectomy in endometrial carcinoma is made according to the preoperative or intraoperative risk factors for lymph node metastasis such as grade, myometrial invasion and histology. However, grade is worse in 20-30% of endometrial biopsy specimens after hysterectomy specimens are evaluated [10, 11] and determining the true extent of myometrial invasion, even with frozen section analysis, has been shown to be limited [12]. Omitting lymphadenectomy in these seemingly low-risk patients may lead to inappropriate postoperative management, since staging will impact postoperative treatment in nearly 30% of these patients [13]. Furthermore, several prior studies have suggested a therapeutic benefit to the performance of selective lymphadenectomy for endometrial cancer [14-17].

A number of alternative management strategies such as panniculectomy, simple vaginal hysterectomy or even high-dose rate brachytherapy have been suggested for morbidly obese patients, partly due to technical difficulties and partly with the assumption that complete surgical staging might not be safe and adequate for these patients [4-6, 18, 19]. However, we have confirmed the studies Everett *et. al.* [20] and Pavelka *et. al.* [21] by showing that comprehensive surgical staging in morbidly obese endometrial cancer patients is both safe and adequate with no increase in intraoperative or postoperative complications. This information is important due to the fact that the aforementioned alternative management strategies might have high complication rates apart from

not being standard treatment. In accordance with that, Nyugen TV *et. al.* [19] reported a 21% acute and late toxicity in morbidly obese patients undergoing high-dose rate brachytherapy.

Another reason for a less than standard surgery in the literature for morbidly obese patients is that these patients have a tendency towards slightly more favorable histopathologic disease characteristics [3]. However, we have shown like Everett *et. al.* [20] that they have the same risk of having extrauterine disease occurrence as slim patients with endometrial cancer. In our study, 18% of all our morbidly obese patients had extrauterine disease found in their lymph nodes, which would have been missed if they had not had lymph node dissection. Moreover, our data showed that morbidly obese patients could have the same percentage of deep myometrial invasion as ideal weight patients.

Our study is important because 26% of our patients were morbidly obese. There are still scarce data on morbidly obese endometrial cancer patients, and in those studies, a lower percentage of patients with a BMI > 40 compared to ideal body weight patients had undergone lymphadenectomy. In our study the percentage of patients with a BMI > 40 and a BMI < 30, who had lymphadenectomy were not different statistically, being 90% and 88%, respectively. The rate of morbidly obese patients undergoing lymphadenectomy, which is 90%, is higher compared to 64.5% in the study of Everett *et al.* [20], and 36% in Anderson *et al.'s* study [3]. In our study, 20% of morbidly obese patients who had lymphadenectomy had positive lymph nodes, which is higher than other authors' data, however this might be because we did systematic lymph node dissection rather than sampling in most of our patients, reflected in the higher number of nodes that were retrieved.

Although pelvic surgery in the morbidly obese patient is technically difficult, it is still possible to perform staging surgery in an appropriate manner utilizing some surgical adaptations. Accordingly, some authors have suggested panniculectomy, supraumbilical midline incisions, the use of suitable retractors and longer instruments [18]. In our morbidly obese patients, we sutured the edge of the peritoneum to the skin to improve exposure, as suggested by Morrow and Curtin [22]. This takes up the slack in the pelvic peritoneum anterior to the round ligament.

In conclusion, we have shown, in accordance with other authors, that morbidly obese women with endometrial carcinoma have the same risk of extrauterine disease and a significant chance of having lymph node metastasis. Although technically challenging, comprehensive surgical staging in this group of patients is safe and adequate in terms of lymph node yield; it is also important for planning adjuvant treatment without undertreating or overtreating these patients, hence preventing unnecessary complications.

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