Arch Gynecol Obstet (2012) 286:1269–1276
DOI 10.1007/s00404-012-2431-2

GYNECOLOGIC ONCOLOGY

Influence of body mass index on clinicopathologic features, surgical morbidity and outcome in patients with endometrial cancer

Ozgur Akbayır · Aytul Corbacıoglu Esmer · Ceyhun Numanoglu · B. Pinar Cılesız Goksedef · Aysu Akca · Lale Vuslat Bakır · Oguzhan Kuru

Received: 5 April 2012 / Accepted: 11 June 2012 / Published online: 24 June 2012

Abstract
Aim To examine the influence of obesity on the patient characteristics and clinicopathologic features of endometrial cancer, and to find how treatment and prognosis were affected by obesity in women with endometrial cancer.
Methods The data of 370 consecutive women operated for endometrial cancer were retrospectively reviewed. Patients were divided into three categories as <25, 25–29.9 and ≥30 according to BMI. All patients underwent primary surgical treatment including total abdominal hysterectomy, bilateral oophorectomy and peritoneal cytology. Pelvic lymphadenectomy was carried out for all patients except for those with no myometrial invasion regardless of the tumor grade or for whom it was technically impossible. Paraaortic lymphadenectomy was performed when pre- and intraoperative assessments suggested non-endometrioid or grade 3 endometrioid cancer, >50 % myometrial invasion and cervical involvement.
Results Patients with a BMI (body mass index) of <25 were significantly younger. Patients with a BMI of ≥30 were statistically less likely to have >50 % myometrial invasion and more likely to have stage I disease. There were no significant differences in the incidences of positive pelvic and paraaortic lymph nodes and tumor grades between the three groups. Also, there were no differences in surgery type, the mean of removed pelvic and paraaortic lymph node number, hospital stay, blood loss and complications between the groups. The patients with a BMI of ≥30 had significantly longer operating time. There were no statistically significant differences in recurrences, the median number of months at recurrence or the site of recurrence between the three groups, as well as the 5-year overall and disease-free survival of patients. Multivariate proportional hazard models identified stage III and IV disease as significant covariates for mortality rates, while stage III and IV disease, hypertension and pelvic irradiation were identified as significant covariates for recurrence rates.
Conclusion Positive peritoneal cytology, deep myometrial invasion and stage II–IV endometrial cancer were significantly more common in patients with a BMI of <25. There were no significant differences in tumor grade, surgical technique, surgical morbidity or adjuvant radiotherapy between the BMI groups. Recurrence and cancer-related mortality rates were not affected by the BMI.

Keywords Endometrial cancer · Body mass index · BMI · Obesity · Morbidity

O. Akbayır · A. Corbacıoglu Esmer · C. Numanoglu · A. Akca · L. V. Bakır · O. Kuru
Department of Obstetrics and Gynecology, Kanuni Sultan Suleyman Teaching and Research Hospital, Istanbul, Turkey

A. Corbacıoglu Esmer (✉)
Department of Obstetrics and Gynecology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Capa, Turkey
e-mail: aytulcorbacioglu@gmail.com

B. P. Cılesız Goksedef
Department of Gynecologic Oncology, Haseki Teaching and Research Hospital, Istanbul, Turkey

Introduction

Obesity is a major public health problem and a common cause of morbidity and mortality due to hypertension, type II diabetes mellitus, hyperlipidemia, pulmonary dysfunction and coronary artery disease [1]. Additionally, it contributes to the increased incidence and/or death from cancers of colon, breast, kidney, ovary, esophagus,

stomach, pancreas, gallbladder and liver [2]. Furthermore, the initiation and development of type I endometrial cancer is known to be influenced by obesity because of the changes in endogenous hormone metabolism [3]. Increased levels of peripheral estrogen create a mitogenic milieu initiating tumor formation [4]. Obesity elevates serum estrogen levels by decreasing serum levels of sex hormone-binding globulin (SHBG) or increasing the aromatization of androstenedione to estrogen in adipose tissue [3]. Leptin, a hormone secreted by white adipose tissue is also associated with cancerogenesis as it is a stimulator of angiogenesis and an activator of aromatase [5]. Not only obesity, but also the other components of metabolic syndrome (hypertension, dyslipidemia and glucose metabolic disturbance) are shown to be associated with endometrial cancer risk [3].

Even though obesity is a well-known risk factor for endometrial cancer [6, 7], the association between disease characteristics or outcome and obesity remains to be a controversial issue. While increased obesity was considered to be related with a lower grade by some authors [1, 8, 9], some of the studies did not find such an association [7, 10]. Similarly, the findings regarding the relation between early stage and obesity have been contradictory [6, 9]. Furthermore, some studies reported a decrease in mortality in obese patients due to the favorable tumor features [9, 11], whereas the others failed to find such a correlation [7] or found an increased risk of mortality [12].

The purpose of this paper was to examine the influence of obesity on the patient characteristics and clinicopathologic features of endometrial cancer. We also aimed to find how treatment and prognosis were affected by obesity in women with endometrial cancer.

Materials and methods

The data of 370 consecutive women operated for endometrial cancer at the Department of Gynecologic Oncology of Kanuni Sultan Suleyman Research and Teaching Hospital from January 2002 to December 2009 were retrospectively reviewed. All patients underwent primary surgical treatment including total abdominal hysterectomy, bilateral oophorectomy and peritoneal cytology. Pelvic lymphadenectomy (PLND) was carried out in all patients except for those with no myometrial invasion regardless of the tumor grade or for whom it was technically impossible. Paraaortic lymphadenectomy (PALND) was performed when pre- and intraoperative assessments suggested non-endometrioid or grade 3 endometrioid cancer, >50 % myometrial invasion and cervical involvement. PLND involved the removal of all lymphatic nodes including the common, external and internal iliac, and obturator lymph nodes. PALND was defined as the dissection of the nodes located from the bifurcation of the aorta to the level of the renal vein, including the region above the inferior mesenteric artery (IMA). Adjuvant therapy included intravaginal brachytherapy, pelvic and extended-field radiation, and chemotherapy.

Clinical data collected by reviewing the charts included age at diagnosis, height, weight, calculated body mass index (BMI), comorbid conditions (diabetes, hypertension, pulmonary disease, hypothyroidism), parity, smoking status, menopausal status, hormonal drug administration (HRT and ovulation induction) and disease characteristics (grade, stage, peritoneal cytology, the depth of myometrial invasion, cell type and lymph node status). The tumors were staged according to the 2009 FIGO staging system. Also, the data concerning intra- and postoperative findings including the extent of surgical procedure, the length of hospital stay, estimated blood loss, the duration of operation, the number of removed lymph nodes and surgical complications were gathered. Wound infection referred to diffuse hyperemia and edema of skin and subcutaneous tissue with purulent discharge, leukocytosis and fever with or without the separation of fascia and/or skin. Gastrointestinal system (GIS) injury involved the full-thickness injury of intestine and colon. Vascular injury involved the injury of venous or arterial vascular structure in the surgical site that necessitated repair or ligation. Lymphedema referred to late-onset uni/bilateral lower extremity edema regardless of the symptoms diagnosed after all other causes were ruled out. Radiation enteritis involved late-onset nausea, vomiting, diarrhea, intestinal obstruction and perforation after radiotherapy. Furthermore, we collected the data regarding the adjuvant therapy and outcome including the time from diagnosis to recurrence, the site of recurrence, the time from diagnosis to last follow-up or death, and the status at last follow-up. The data of women who did not attend our clinic for follow-up were obtained by telephone interview.

When the data were analyzed; patients were categorized into three groups as <25 (normal), 25–29.9 (overweighed) and >30 (obese) according to BMI. Frequency distributions were calculated for each of the variables. Pearson's χ^2 test was used to assess the association between categorical variables, and one-way analysis of variance was used to compare the distributions of continuous variables for the three groups. p values for difference in survival among groups were calculated by log-rank test. Factors that contributed to disease-related death and tumor recurrence (>60 age, BMI, hypertension, stage I disease, non-endometrioid histology, tumor grade, myometrial invasion, lymph node involvement or radiation) were included in Cox multivariate proportional hazards analyses. All statistical analyses were performed by the SPSS system (SPSS 15.0 for Windows 2000, Chicago, IL).

Results

A total of 370 patients with endometrial cancer were evaluated in this study; 24 patients were excluded due to incomplete data and 346 patients were analyzed. The mean age of the entire population was 56.1 ± 9.7 years. Patients with a BMI of <25 were significantly younger with a mean age of 52.1 ± 10.7 years ($p = 0.001$). The demographic characteristics of patients are shown in Table 1; 43.1 % of patients had hypertension and the incidence statistically increased with increasing BMI ($p = 0.001$); 21.4 % of patients had diabetes, and the incidence statistically increased with increasing BMI ($p = 0.004$). There were no differences between the groups in the incidences of other co-morbid conditions. Furthermore, the majority of patients were postmenopausal (72.5 %) and the incidence statistically increased with increasing BMI ($p = 0.001$).

Histopathological characteristics are shown in Table 2. The predominant histologic type was endometrioid adenocarcinoma. There were no statistically significant differences in tumor grades between the groups ($p = 0.68$). Patients with a BMI of ≥30 were statistically less likely to have >50 % myometrial invasion (MI) (24.4 % vs. 38.5 and 38.1 %, $p = 0.02$) and more likely to have stage I disease (88.1 vs. 71.2 % and 78.0 %, $p = 0.009$). The incidence of positive peritoneal cytology was statistically lower in patients with a BMI of ≥30 group compared to the other two groups (10.2 vs. 23.1 % and 17.8 %, $p = 0.03$). There were no significant differences in the incidences of positive pelvic and paraaortic lymph nodes between the three groups ($p = 0.39$ and 0.58, respectively).

Table 3 summarizes the treatment characteristics of the patients. There were no differences between the groups in surgery type, the mean of removed pelvic and paraaortic lymph node number, hospital stay, blood loss and complications. Patients with a BMI of ≥30 had significantly longer operating time than the other groups (135.5 ± 20.0 vs. 126.4 ± 8.8 and 124.7 ± 10.1, $p = 0.001$). Significantly less patients with a BMI ≥30 received chemotherapy (13.1 vs. 21.2 % and 25.4 %, $p = 0.02$).

The data on clinical outcome are shown in Table 4. The outcome data of 194 (56.1 %) patients were obtained. The mean follow-up time was 59.1 ± 30.1 months. Twenty-two patients (11.3 %) had recurrence or progressive disease. There was a trend toward fewer recurrences in patients with a BMI of ≥30, but it did not reach statistical significance (9.3 vs 12.5 % and 13.8 %) ($p = 0.65$). Also, there were no statistically significant differences in the median number of months at recurrence or the site of recurrence between the three groups. At the time of the last follow-up, 91.3 % of patients were alive, 7.7 % were dead of disease, and 1 % were dead of other causes without evidence of disease. There were no differences between the three groups in outcome ($p = 0.77$).

The 5-year estimated overall survival (OS) rates were 90.5, 91.3 and 92.9 % in patients with a BMI of <25, 25–29.9 and ≥30, respectively ($p = 0.90$) (Fig. 1). The 5-year disease-free survival (DFS) rates were 87, 84.9 and 89.0 % in patients with a BMI of <25, 25–29.9 and ≥30, respectively ($p = 0.62$) (Fig. 2). When we stratified patients according to stage, there were no statistically significant differences in 5-year OS and DFS rates between patients with a BMI of <25, 25–29.9 and ≥30. In patients with stage I disease, the 5-year OS rates were 100, 97.7 and 95.7 % ($p = 0.42$) and DFS rates were 100, 91.2 and 95.3 % ($p = 0.41$). There was no disease-related death in stage II patients and the 5-year DFS for stage II patients were 66.7, 66.7 and 66.7 % ($p = 0.96$). The 5-year OS and DFS rates for patients with stage III disease were 40, 53.3 and 60 % ($p = 0.96$) and 40, 51.2 and 60 % ($p = 0.76$),

Table 1 Demographic characteristics by BMI

	BMI <25	BMI 25–29.9	BMI ≥30	Total	*p*
Number of patients	52 (15.0 %)	118 (34.1 %)	176 (50.9 %)	346 (100 %)	–
Mean age	52.1 ± 10.7	58.05 ± 10.1	55.9 ± 8.8	56.1 ± 9.7	**0.001**
Comorbid conditions					
HT	11 (21.2 %)	49 (41.5 %)	89 (50.6 %)	149 (43.1 %)	**0.001**
Hypothyroidism	1 (1.9 %)	5 (4.2 %)	7 (4.0 %)	13 (3.8 %)	0.74
Pulmonary disease	2 (3.8 %)	0 (0 %)	6 (3.4 %)	8 (2.3 %)	0.11
DM	4 (7.7 %)	21 (17.8 %)	49 (27.8 %)	74 (21.4 %)	**0.004**
Breast cancer	0 (0.0 %)	1 (0.8 %)	4 (2.3 %)	5 (1.4 %)	0.23
Colon cancer	0 (0.0 %)	0 (0.0 %)	1 (0.6 %)	1 (0.3 %)	0.83
Parity	3.3 ± 2.2	3.34 ± 2.3	3.25 ± 1.8	3.3 ± 2.1	0.96
Smoking	11 (21.2 %)	11 (9.3 %)	21 (11.9 %)	43 (12.4 %)	0.09
Postmenopause	27 (51.9 %)	88 (74.6 %)	136 (77.3 %)	251 (72.5 %)	**0.001**
HRT use	0 (0 %)	1 (0.8 %)	2 (1.1 %)	3 (0.9 %)	0.73
Ovulation induction	2 (3.8 %)	4 (3.4 %)	5 (2.8 %)	11 (3.2 %)	0.92

BMI body mass index; *HT* hypertension; *DM* diabetes mellitus; *HRT* hormone replacement therapy

Table 2 Pathologic characteristics by BMI

	BMI <25	BMI 25–29.9	BMI ≥30	Total	*p*
Cell type					
Endometrioid	48 (92.3 %)	101 (85.6 %)	160 (90.9 %)	309 (89.3 %)	0.23
Non-endometrioid	4 (7.7 %)	17 (14.4 %)	16 (9.1 %)	37 (10.7 %)	
Grade					
1	18 (34.6 %)	35 (29.7 %)	61 (34.7 %)	114 (32.9 %)	0.68
2	24 (46.2 %)	55(46.6 %)	85 (48.3 %)	164 (47.4 %)	
3	10 (19.2 %)	28 (23.7 %)	30 (17.0 %)	68 (19.7 %)	
Depth of MI					
<50 %	32 (61.5 %)	73 (61.9 %)	133 (75.6 %)	238 (68.8 %)	**0.02**
>50 %	20 (38.5 %)	45 (38.1 %)	43 (24.4 %)	108 (31.2 %)	
Stage					
I	37 (71.2 %)	92 (78.0 %)	155 (88.1 %)	284 (82.1 %)	**0.009**
II	6 (11.5 %)	6 (5.1 %)	4 (2.3 %)	16 (4.6 %)	
III	9 (17.3 %)	15 (12.7 %)	15 (8.5 %)	39 (11.3 %)	
IV	0 (0.0 %)	5 (4.2 %)	2 (1.1 %)	7 (1.1 %)	
Peritoneal cytology					
Negative	40 (76.9 %)	97 (82.2 %)	158 (89.8 %)	295 (83.8 %)	**0.03**
Positive	12 (23.1 %)	21 (17.8 %)	18 (10.2 %)	51 (16.2 %)	
Lymph node status					
Sampled negative	45 (88.3 %)	99 (87.7 %)	153 (92.9 %)	297 (90.5 %)	0.19
Sampled positive	6 (11.7 %)	14 (12.3 %)	11 (7.1 %)	31 (9.4 %)	
Number of positive PLN	6 (11.5 %)	11 (9.5 %)	11 (6.3 %)	28 (8.1 %)	0.39
Number of positive PALN	3 (5.8 %)	5 (4.2 %)	5 (2.8 %)	13 (3.8 %)	0.58

BMI body mass index; *MI* myometrial invasion; *PLN* pelvic lymph node; *PALN* paraaortic lymph node

respectively. The number of patients with stage IV disease was not sufficient for the statistical analysis.

Table 5 shows the comparisons of 5-year survival rates of the BMI groups according to clinicopathological features. Among the patients with <25 of BMI, women over 60 years of age and who had diabetes, hypertension, non-endometrioid histology, deep myometrial invasion, stage II, III and IV disease, lymph node involvement and pelvic radiation had significantly lower disease-related and tumor-free survival rates. Among the patients with 25–29.9 of BMI, disease-related survival rates were significantly lower for women with non-endometrioid histology, deep MI, lymph node involvement, stage II, III and IV disease, and pelvic radiation, while tumor-free survival rates were lower for patients with greater FIGO stage. Among the patients with ≥30 of BMI, disease-related and tumor-free survival rates were significantly lower for women over 60 years of age and who had hypertension, non-endometrioid histology, deep myometrial invasion, stage II, III and IV disease, lymph node involvement and pelvic radiation. Multivariate proportional hazard models identified stage II, III and IV disease as significant covariates for mortality rates, while stage II, III and IV disease, hypertension and pelvic irradiation were identified as significant covariates for recurrence rates (Table 6).

Comments

BMI is a simple index that is commonly used to classify underweight, normal weight, overweight and obesity in adults. A BMI between 25.0 and 29.9 kg/m^2 is considered overweight, while obesity is defined as a BMI of ≥30 kg/m^2 [13]. Since overweight women have been reported to have a high risk of endometrial cancer like obese women [7], we classified the cohort into three groups according to BMI as <25, 25–29.9 and ≥30. We found that the rates of diabetes and hypertension statistically increased with increasing BMI, which is consistent with the findings of previous reports in the literature [1, 8, 14]. In addition, many authors reported that obese patients with endometrial carcinoma were significantly younger than nonobese women [4, 9, 15], which is in contradiction to our findings. The mean ages of patients at the time of surgery were 52.1 ± 10.7, 58.05 ± 10.1 and 55.9 ± 8.8 in normal weight, overweight and obese patients, respectively.

The relationship between obesity and histopathologic characteristics of endometrial cancer has been a controversial issue. We found that cancer confined to the uterus was more common in obese patients ($p = 0.009$), while the rates of positive peritoneal cytology and myometrial invasion >50 % were higher in patients with a BMI of <25 ($p = 0.03$ and $p = 0.02$, respectively). These findings are

Table 3 Treatment characteristics by BMI

	BMI <25	BMI 25–29.9	BMI ≥30	Total	*p*
Surgery type					
TAH + BSO[a]	1 (1.9 %)	5 (4.2 %)	12 (6.8 %)	18 (5.2 %)	0.16
PLND[b]	22 (42.3 %)	58 (49.2 %)	96 (54.5 %)	176 (50.9 %)	0.12
PLND + PALND[b]	29 (55.8 %)	55 (46.6 %)	68 (38.6 %)	152 (43.9 %)	0.07
Retrieved pelvic lymph node number (median range)	16 (5–28)	15 (5–46)	17 (3–35)	16 (3–46)	0.24
Retrieved paraaortic lymph node number (median range)	5 (1–16)	5 (1–12)	4 (1–12)	4 (1–16)	0.07
Operative time (min)	126.4 ± 8.8	124.7 ± 10.1	135.5 ± 20.0	130.3 ± 16.6	**0.001**
Estimated blood loss (ml)	300.6 ± 74.7	299.1 ± 92.2	301.7 ± 86.9	300.5 ± 86.8	0.96
Hospital stay (day)	7.1 ± 2.2	8.01 ± 2.4	8.6 ± 2.7	7.9 ± 2.5	0.34
Complications					
Early complications					
Wound infection	0 (0.0 %)	2 (1.7 %)	5 (2.8 %)	7 (2.0 %)	0.42
GIS injury	0 (0.0 %)	0 (0.0 %)	1 (0.6 %)	1 (0.3 %)	0.40
Vascular injury	1 (1.9 %)	5 (4.2 %)	2 (1.1 %)	8 (2.3 %)	0.21
Nerve injury	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	–
Late complications					
Wound separation (hernia)	2 (6.9 %)	8 (12.7 %)	17 (18.3 %)	27 (14.6 %)	0.27
Lymphocyst	3 (10.3 %)	2 (3.2 %)	9 (9.7 %)	14 (7.6 %)	0.26
Lymphedema	2 (6.9 %)	5 (7.9 %)	8 (8.6 %)	15 (8.1 %)	0.95
Radiation enteritis	1 (3.4 %)	2 (3.2 %)	2 (2.2 %)	5 (2.7 %)	0.89
Adjuvant RT					
Brachytherapy	36 (69.2 %)	93 (78.8 %)	125 (71.0 %)	254 (73.4 %)	0.25
Pelvic RT	20 (38.5 %)	50 (42.4 %)	55 (31.3 %)	125 (36.1 %)	0.14
Extended-field RT	4 (7.7 %)	6 (5.1 %)	6 (3.4 %)	16 (4.6 %)	0.41
Adjuvant RT + CT	11 (21.2 %)	30 (25.4 %)	23 (13.1 %)	64 (18.5 %)	**0.02**

BMI body mass index; *TAH* total abdominal hysterectomy; *BSO* bilateral salpingoophorectomy; *PLN* pelvic lymph node dissection; *PALND* paraaortic lymph node dissection; *RT* radiotherapy; *CT* chemotherapy

[a] Includes radical hysterectomy

[b] Additional to radical hysterectomy or TAH + BSO

Table 4 Outcome data by BMI

	BMI <25	BMI 25–29.9	BMI ≥30	Total	*p*
Number of followed patients	33 (63.5 %)	64 (54.2 %)	97 (55.1 %)	194 (56.1 %)	0.50
Follow-up duration (months)	54.1 ± 20.3	62.1 ± 32.7	58.8 ± 28.2	59.1 ± 30.1	0.47
Recurrence					
Number of patients	4 (12.5 %)	9 (13.8 %)	9 (9.3 %)	22 (11.3 %)	0.65
Median number of months	51.3 ± 31.9	60.1 ± 34.9	57.2 ± 29.2	57.1 ± 31.6	0.42
Recurrence site					
Vaginal vault	1 (3.1 %)	4 (6.2 %)	2(2.1 %)	7 (3.6 %)	0.91
Pelvic	1 (3.1 %)	2 (3.1 %)	2(2.1 %)	5 (2.6 %)	
Extrapelvic	2 (6.3 %)	3 (4.6 %)	5(5.1 %)	10 (5.1 %)	
Outcome					
Alive	30 (90.9 %)	58 (90.6 %)	89 (91.8 %)	177 (91.3 %)	0.77
All-cause death	3 (9.1 %)	6 (9.4 %)	8 (8.2 %)	17 (8.7 %)	
Cancer-related death	3 (9.1 %)	5 (7.8 %)	7 (7.2 %)	15 (7.7 %)	

BMI body mass index

consistent with the majority of studies in the literature [4, 7, 11]. However, Schmeler et al. [14] and Reeves et al. [6] could not find a significant association between the extent of tumor and BMI. Though obese patients with endometrial cancer were reported to be more likely to have endometrioid histology [1] and well-differentiated tumor [5] in many studies, we did not find such a relationship in our cohort as with the other series [4, 6, 14]. We also found that the number of positive PLN and PALN decreased with increasing BMI, but it did not reach statistical significance.

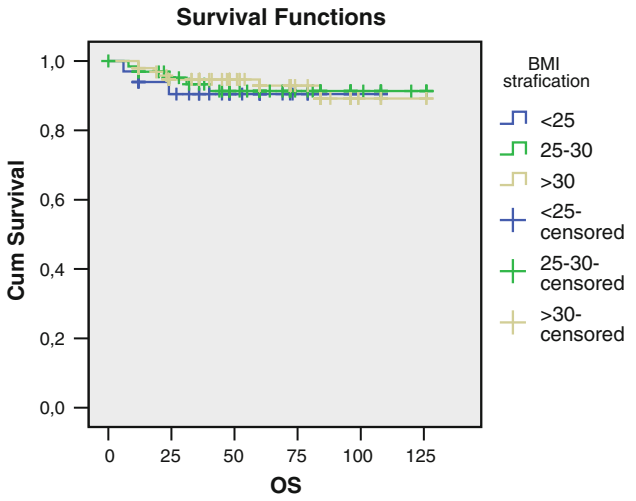

Fig. 1 *OS* (overall survival) Kaplan–Meier survival analysis for the groups

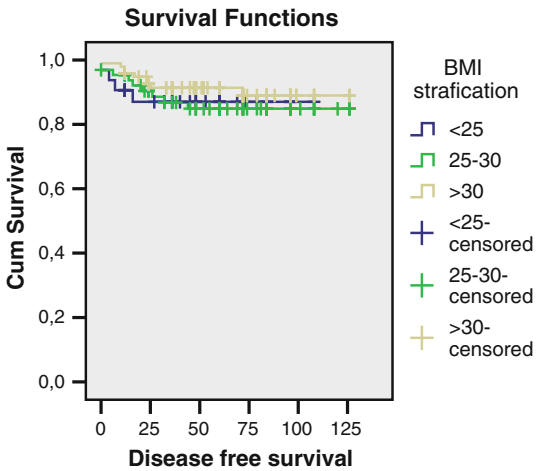

Fig. 2 DFS Kaplan–Meier survival analysis for the groups

This was in agreement with the findings reported in the study of Jeong et al. [7].

Obesity is considered to be a physical obstacle for complete surgical staging due to technical difficulties with exposure of tumor or lymphadenectomy and it is generally thought that obesity may cause increased intra- and post-operative complications as well as inadequate delivery of adjuvant radiation treatment [1]. Pavelka et al. [8] reported a significant difference in surgical staging and complete surgical staging rates between ideal body weight and morbidly obese groups. On the contrary, Martra et al. [10] in their study of 766 women performed lymphadenectomy in obese women as often as in nonobese patients, but the median nodal yield was significantly lower in the obese group. However, Everett et al. [1] stated that there was no difference in the average number of lymph nodes removed between the groups according to the BMI. Furthermore, in several studies, morbidly obese patients were reported to have significantly longer operative times and more blood loss compared with patients with normal weight, while wound infection and noninfectious wound breakdown significantly increased in patients with a BMI of >40 [1, 8]. Based on our findings, we believe that obesity is neither an obstacle for complete surgical staging nor a risky procedure with a high incidence of complications. We did not find any significant differences in the number of patients who underwent lymph node dissection as well as the number of retrieved lymph nodes between the groups. However, different from the previous studies, we analyzed women with a BMI of 30–40 and >40 in the same group and this might be the result of inconsistency with previous literature.

Jeong et al. [7] stated that obese and overweight women were significantly less likely to receive adjuvant therapy, as they tended to have an earlier stage of cancer. Similarly, Martra et al. [10] reported a significant 5 % decrease in odds of adjuvant pelvic radiation as BMI increased [7]. There was not a significant difference in adjuvant radiotherapy between the groups in our study, but the use of chemotherapy in addition to radiation was significantly more common in women with ideal weight compared with obese patients. This seems to be a result of favorable features of cancer in patients with a BMI of ≥30.

Due to the earlier stage and less invasive disease in obese patients, lower overall mortality rate has been shown to be associated with increasing BMI [11, 16]. In our cohort, although patients with a BMI of ≥30 had lower rates of overall mortality, it did not reach significance, which was consistent with the findings of Everett et al. [1]. We also stratified the cohort by stage to find the effect of obesity on outcome for each of the stages. There were no significant differences in overall or disease-free survival between the groups for each stage.

We also investigated the influence of risk factors on outcome in normal weight, overweight and obese patients. Stage II, III and IV disease had adverse effects on both 5-year overall and disease-free survival, while hypertension and pelvic irradiation adversely affected only disease-free survival. In contrast to the previous studies, diabetes did not have any effect on the overall and disease-free survival of total cohort. Steiner et al. [17] found a correlation between diabetes and survival in univariate analysis, but it lost its significance in multivariate analysis showing that diabetes was not a significant predictor of overall survival. Chia et al. [12] reported an increased risk of all-cause mortality (HRR = 1.7) but not endometrial cancer mortality in women with diabetes mellitus. However, Folsom et al. [18] reported that diabetes was associated with a poorer survival regardless of tumor stage and grade with the relative risks of 2.79 and 2.38 for overall and cancer-related death, respectively.

Table 5 Comparisons of 5-year survival rates of BMI groups according to clinicopathologic features

	Disease-related survival				Tumor free survival			
BMI	<25	25–29.9	≥30	Total	<25	25–29.9	≥30	Total
Age								
<60	95.8 %	94.9 %	97 %	96.2 %	92.2 %	87.8 %	95.4 %	92.4 %
>60	60 %	83.0 %	80.9 %	79.6 %	50 %	77.5 %	80.4 %	76.2 %
p	**0.005**	0.11	**0.004**	**0.0001**	**0.005**	0.25	**0.003**	**0.0001**
Diabetes mellitus								
Yes	0	100 %	91.3 %	91.4	0	90.9 %	87.0 %	85.8 %
No	93.3 %	89.8 %	93.6 %	92.1	89.8 %	83.9 %	93.6 %	89.2 %
p	**0.0001**	0.33	0.86	0.85	**0.0001**	0.80	0.42	0.58
Hypertension								
Yes	47.6 %	84.2 %	97.8 %	83.7 %	0 %	80.7 %	84.9 %	79.3 %
No	100 %	97.1 %	87.5 %	98.1 %	100 %	88.1 %	97.9 %	95.1 %
p	**0.0001**	0.09	**0.04**	**0.0001**	**0.0001**	0.40	**0.01**	**0.0001**
Histology								
Endometrioid	96.2 %	94.3 %	94.7 %	94.8 %	92.5 %	86.7 %	93 %	90.9 %
Non-endometrioid	33.3 %	68.6 %	68.6 %	63.1 %	33.3 %	68.6 %	68.6 %	63.1 %
p	**0.0001**	**0.025**	**0.007**	**0.0001**	**0.0001**	0.23	**0.03**	**0.0001**
Grade								
1	100 %	100 %	94.4 %	97.6 %	100 %	94.7 %	94 %	95.5 %
2 and 3	83.1 %	86.9 %	91.7 %	88.9 %	76.4 %	80 %	90 %	84.6 %
p	0.11	0.10	0.25	**0.01**	0.06	0.15	0.40	**0.02**
Depth of MI								
<1/2	100 %	95.2 %	96.3 %	96.6 %	100 %	88.1 %	95.9 %	93.8 %
>1/2	68.6 %	80.5 %	80.4 %	78.6 %	58.6 %	77.6 %	75.6 %	73.0 %
p	**0.006**	0.07	**0.001**	**0.0001**	**0.001**	0.21	**0.001**	**0.0001**
Stage								
I	100 %	97.7 %	95.7 %	98.0 %	100 %	91.3 %	95.3 %	96.6 %
II, III and IV	57.1 %	62.7 %	79.8 %	64.3 %	42.9 %	59.4 %	60 %	55.5 %
p	**0.0001**	**0.0001**	**0.003**	**0.0001**	**0.0001**	**0.001**	**0.0001**	**0.0001**
Pelvic irradiation								
Yes	97.1 %	81.2 %	78.5 %	78.9 %	63.6 %	79.1 %	72.7 %	73.7 %
No	100 %	97.1 %	98.5 %	98.3 %	100 %	88.9 %	98.6 %	95.6 %
p	**0.01**	**0.03**	**0.008**	**0.0001**	**0.004**	0.21	**0.0001**	**0.0001**
LNI								
Yes	33.3 %	65.5 %	60 %	55.4 %	33.3 %	64.3 %	60 %	52.4 %
No	96.7 %	96 %	94.8 %	95.5 %	93.1 %	88.2 %	93.1 %	91.5 %
p	**0.0001**	**0.002**	**0.001**	**0.0001**	**0.003**	0.06	**0.007**	**0.0001**
No. of pelvic LN								
≤8	100 %	100 %	100 %	100 %	100 %	85.7 %	100 %	94.1 %
>8	89.1 %	90 %	91.5 %	90.5 %	85.6 %	84.5 %	90.8 %	87.7 %
p	0.55	0.37	0.35	0.18	0.58	0.85	0.33	0.37

BMI body mass index; *MI* myometrial invasion; *LNI* lymph node invasion

In conclusion, we found that positive peritoneal cytology, deep myometrial invasion and stage II–IV endometrial cancer were significantly more common in patients with a BMI of <25, whereas grade, lymph node involvement and histologic type did not have an association with obesity. There were no significant differences in surgical technique, surgical morbidity or adjuvant radiotherapy rates between the BMI groups. Finally, recurrence and cancer-related mortality rates were not affected by the BMI. The main limitation of this study was that we could not trace all

Table 6 Hazard ratio for death and recurrence

	Death			Recurrence		
	HR	95 % CI	*p*	HR	95 % CI	*p*
Age >60-year	0.639	0.14–2.91	0.56	0.611	0.21–1.76	0.36
BMI						
<25	Ref.			Ref.		
25–30	0.822	0.15–4.29	0.81	1.916	0.48–7.50	0.35
>30	0.552	0.13–2.34	0.42	1.172	0.41–3.43	0.76
Hypertension	0.316	0.05–1.69	0.17	0.280	0.08–0.89	**0.03**
Stage II, III and IV	0.119	0.01–0.74	**0.02**	0.169	0.03–0.77	**0.02**
Non-endometrioid	0.337	0.10–2.18	0.47	1.059	0.32–3.48	0.92
Grade 2 and 3	0.231	0.02–2.19	0.20	0.416	0.11–1.54	0.19
>1/2 MI	0.278	0.06–1.18	0.08	0.442	0.15–1.23	0.12
LNI	1.856	0.28–12.03	0.51	3.451	0.67–17.63	0.13
Pelvic radiation	0.268	0.04–1.62	0.15	0.239	0.07–0.78	**0.01**

BMI body mass index; *MI* myometrial invasion; *LNI* lymph node invasion

patients, which resulted in the survival analysis of a smaller group of patients. We believe that larger studies regarding obesity and survival are needed to determine the impact of obesity on the prognosis of endometrial cancer.

Conflict of interest We declare that we have no conflict of interest.

References

1. Everett E, Tamimi H, Greer B, Swisher E, Paley P, Mandel L, Goff B (2003) The effect of body mass index on clinical/pathologic features, surgical morbidity, and outcome in patients with endometrial cancer. Gynecol Oncol 90:150–157
2. Fader AN, Arriba LN, Frasure HE, von Gruenigen VE (2009) Endometrial cancer and obesity: epidemiology, biomarkers, prevention and survivorship. Gynecol Oncol 114:121–127
3. Zhang Y, Liu Z, Yu X, Zhang X, Lü S, Chen X, Lü B (2010) The association between metabolic abnormality and endometrial cancer: a large case–control study in China. Gynecol Oncol 117:41–46
4. McCourt CK, Mutch DG, Gibb RK, Rader JS, Goodfellow PJ, Trinkaus K, Powell MA (2007) Body mass index: relationship to clinical, pathologic and features of microsatellite instability in endometrial cancer. Gynecol Oncol 104:535–539
5. Cymbaluk A, Chudecka-Glaz A, Rzepka-Górska I (2008) Leptin levels in serum depending on body mass index in patients with endometrial hyperplasia and cancer. Eur J Obstet Gynecol 136:74–77
6. Reeves KW, Carter GC, Rodabough RJ, Lane D, McNeeley SG, Stefanick ML, Paskett ED (2011) Obesity in relation to endometrial cancer risk and disease characteristics in the women's health initiative. Gynecol Oncol 121:376–382
7. Jeong NH, Lee JM, Lee JK, Kim JW, Cho CH, Kim SM, Seo SS, Park CY, Kim KT, Lee J (2010) Role of body mass index as a risk and prognostic factor of endometrioid uterine cancer in Korean women. Gynecol Oncol 118:24–28
8. Pavelka JC, Ben-Shachar I, Fowler JM, Rarnirez NC, Copeland LJ, Eaton LA, Manolitsas TP, Cohn DE (2004) Morbid obesity and endometrial cancer: surgical, clinical, and pathologic outcomes in surgically managed patients. Gynecol Oncol 95:588–592
9. Munstedt K, Wagner M, Kullmer U, Hackethal A, Frankee FE (2008) Influence of body mass index on prognosis in gynecological malignancies. Cancer Causes Control 19(9):909–916
10. Martra F, Kunos C, Gibbons H, Zola P, Galleto L, DeBernardo R, von Gruenigen V (2008) Adjuvant treatment and survival in obese women with endometrial cancer: an international collaborative study. Am J Obstet Gynecol 198:89.e1–89.e8
11. Anderson B, Connor JP, Andrews JI, Davic CS, Buller RE, Sorosky CI, Benda JA (1996) Obesity and prognosis in endometrial cancer. Am J Obstet Gynecol 174:1171–1178
12. Chia VM, Newcomb PA, Trentham-Dietz A, Hampton JM (2007) Obesity, diabetes, and other factors in relation to survival after endometrial cancer diagnosis. Int J Obstet Gynecol 17:441–446
13. Speroff L, Fritz FA (eds) (2005) Obesity. Clinical gynecologic endocrinology and infertility. Lippincott Williams & Wilkins, Philadelphia
14. Schmeler KM, Soliman PT, Sun CC, Slomovitz BM, Gershenson DM, Lu KH (2005) Endometrial cancer in young, normal-weight women. Gynecol Oncol 99:388–392
15. Lachance JA, Everett EN, Greer B, Mandel L, Swisher E, Tamimi H, Goff B (2006) The effect of age on clinical/pathologic features, surgical morbidity, and outcome in patients with endometrial cancer. Gynecol Oncol 101:470–475
16. Studzjinski Z, Zajevwski W (1982) Factors affecting the survival of 121 patients treated for endometrial carcinoma at a Polish hospital. Arch Gynecol Obstet Gynecol 143:569–573
17. Steiner E, Eicher O, Sagemuller J, Schmidt M, Pilch H, Tanner B et al (2003) Multivariate independent prognostic factors in endometrial carcinoma: a clinicopthologic study in 181 patients: 10 years experince at the Department of Obstetrics and Gynecology in Mainz University. Int J Gynecol Cancer 13:197–203
18. Folsom AR, Anderson KE, Sweeney C, Jacobs DR Jr (2004) Diabetes as a risk factor for death following endometrial cancer. Gynecol Oncol 94:740–745