Thai Journal of Obstetrics and Gynaecology
September 2025, Vol. 33, No. 5, pp. 419-431

GYNAECOLOGY

The Association between Preoperative Body Mass Index and Survival Outcome in Endometrial Cancer

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ABSTRACT

Objectives: This research examined the predictive value of preoperative body mass index (BMI) for progression-free survival (PFS) and overall survival (OS) of endometrial cancer (EC) patients, as well as the correlation between BMI and surgical outcomes.

Materials and Methods: EC patients who had surgery between January 2016 and October 2022 were retrospectively analyzed. Survival rates, surgical specifics, and clinicopathological features were evaluated. Survival studies employed Cox proportional hazards models and Kaplan-Meier curves.

Results: Of 252 EC patients studied, 31% were obese (BMI ≥ 30 kg/m^2). In obese individuals, endometrioid G1 histology and early-stage disease were favorable clinicopathological characteristics. Most obese people were not given adjuvant therapy. Obese individuals had a lessened paraaortic lymphadenectomy frequency. Adjuvant radiation treatment and an Eastern Cooperative Oncology Group performance level of 1 were the only significant predictors of PFS in the multivariate analysis. Age, advanced stage, histology, and surgical quality predicted OS. Patients with BMI < 30 and ≥ 30 kg/m^2 showed comparable PFS, per Kaplan–Meier curves. Obese individuals had a slightly higher 5-year OS rate.

Conclusion: EC patients' preoperative BMI affects surgical care and results. Technical difficulties during surgery reduce the frequency of full staging in obese individuals. BMI did not affect PFS, however, it may preserve OS in EC patients.

Keywords: endometrial cancer, obesity, surgical outcomes, survival.

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Received: 2 December 2024, **Revised:** 20 May 2025, **Accepted:** 28 May 2025

ความสัมพันธ์ระหว่างดัชนีมวลกายก่อนการผ่าตัดและผลลัพธ์การรอดชีวิตในผู้ป่วยมะเร็งเยื่อบุโพรงมดลูก

พลอยทราย ตั้งอมตะกุล, กมัยธร เทียนทอง

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาความสัมพันธ์ระหว่างดัชนีมวลกายก่อนการผ่าตัดต่อการรอดชีวิตปลอดโรค และการรอดชีวิตรวมในผู้ป่วยมะเร็งเยื่อบุโพรงมดลูก รวมถึงศึกษาความสัมพันธ์ระหว่างดัชนีมวลกายก่อนการผ่าตัดและผลลัพธ์การผ่าตัด*

วัสดุและวิธีการ: *การวิเคราะห์ข้อมูลแบบย้อนหลังในผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกที่ได้รับการผ่าตัดระหว่างเดือนมกราคม พ.ศ. 2559 ถึงเดือนตุลาคม พ.ศ. 2565 โดยประเมินอัตราการรอดชีวิต รายละเอียดการผ่าตัด ลักษณะทางคลินิกและพยาธิวิทยา ใช้แบบจำลองความเสี่ยงสัมพัทธ์แบบ Cox และกราฟ Kaplan-Meier เพื่อทำนายการรอดชีวิต*

ผลการศึกษา: *ในกลุ่มผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกจำนวน 252 ราย พบว่าร้อยละ 31 มีภาวะอ้วน (ค่าดัชนีมวลกายก่อนการผ่าตัด ≥ 30 กิโลกรัมต่อตารางเมตร) ในกลุ่มผู้ป่วยที่อ้วนพบว่ามีลักษณะทางคลินิกและพยาธิวิทยาที่ไม่รุนแรง เช่น พยาธิวิทยาของเนื้อเยื่อประเภท endometrioid เกรด 1 และระยะโรคในระยะแรก ผู้ป่วยส่วนใหญ่ในกลุ่มนี้ไม่ได้รับการรักษาเสริม และพบว่ามีอัตราการผ่าตัดเอาน้ำเหลืองหลอดเลือดเออร์ตาต่ำ การวิเคราะห์หลายตัวแปรพบว่า การรักษาเสริมด้วยรังสีรักษาและระดับสมรรถภาพทางร่างกายของ Eastern Cooperative Oncology Group (ECOG) ที่ระดับ 1 เป็นตัวพยากรณ์ที่สำคัญสำหรับการรอดชีวิตปลอดโรค นอกจากนี้ อายุ ระยะของโรคที่รุนแรง พยาธิวิทยาของเนื้อเยื่อและคุณภาพการผ่าตัดเป็นตัวการพยากรณ์ที่สำคัญสำหรับการรอดชีวิต การวิเคราะห์ Kaplan-Meier พบว่า ไม่มีความแตกต่างที่มีนัยสำคัญในการรอดชีวิตปลอดโรค ระหว่างผู้ป่วยที่มีค่าดัชนีมวลกายก่อนการผ่าตัด < 30 กิโลกรัมต่อตารางเมตร และผู้ป่วยที่มีค่าดัชนีมวลกายก่อนการผ่าตัด ≥ 30 กิโลกรัมต่อตารางเมตร อย่างไรก็ตาม ผู้ที่มีภาวะอ้วนมีอัตราการรอดชีวิตรวมที่ 5 ปีสูงขึ้นเล็กน้อย*

สรุป: *ค่าดัชนีมวลกายก่อนการผ่าตัดในผู้ป่วยมะเร็งเยื่อบุโพรงมดลูกส่งผลต่อการดูแลและผลลัพธ์การผ่าตัด ผู้ที่มีภาวะอ้วนมีความยากลำบากทางเทคนิคในระหว่างการผ่าตัด ทำให้การผ่าตัดเพื่อกำหนดระยะของโรคไม่สมบูรณ์ ค่าดัชนีมวลกายก่อนการผ่าตัดไม่มีผลกระทบต่อการรอดชีวิตปลอดโรค แต่มีแนวโน้มเพิ่มการรอดชีวิตรวมในผู้ป่วยมะเร็งเยื่อบุโพรงมดลูก*

คำสำคัญ: *มะเร็งเยื่อบุโพรงมดลูก, ภาวะอ้วน, ผลลัพธ์การผ่าตัด, การรอดชีวิต*

Introduction

Over the past ten years, endometrial cancer (EC), the sixth most common cancer globally, has increased in frequency. Although incidence rates in Asian nations are generally lower than those in Western nations[1], new data from Cancer in Thailand Vol. 10 represent a 6.7 age-standardized incidence rate per 100,000 women (2016–2018). Consequently, EC has surpassed cervical cancer to become the second most common gynecologic cancer[2].

Multiple risk factors for EC have been identified, including obesity, advanced age, unopposed estrogen exposure, and nulliparity. Among all cancers, EC has the strongest association with obesity[3]. Epidemiologic and histologic evidence suggests that EC can be stratified into types I and II[4]. Type I EC is primarily estrogen-dependent and associated with excess endogenous estrogen secondary to obesity. It typically exhibits low-grade histology and carries a more favorable prognosis than type II EC[5].

Individuals with an obesity-related body mass index (BMI) (> 25 kg/m^2) are twice as likely to develop EC as those with a normal BMI. A BMI of 30 kg/m^2 or higher is considered obese. Additionally, for women with severe obesity (BMI of ≥ 35 kg/m^2), the risk is even higher, at 4.7 times higher. Furthermore, linked to a number of comorbid conditions are cardiovascular disease, diabetes mellitus, obstructive sleep apnea, and hypertension. Patients with EC may have worse prognoses as a result of these conditions, which also raise the risk of perioperative complications[6].

Currently, combined with or without a lymphadenectomy, total hysterectomy and bilateral salpingo-oophorectomy, are the standard treatments for EC. This surgical procedure can be performed through traditional laparotomy or minimally invasive approaches without compromising survival outcomes. When high-grade histology or an advanced disease stage is detected, pelvic and paraaortic lymphadenectomy is necessary to guide appropriate adjuvant therapies such as radiotherapy, chemotherapy, or both. However, performing surgery on obese patients presents challenges, including difficulties operating in a deep operative field, a heightened risk of surgical complications, a prolonged hospital stay, and increased healthcare costs. Because of these challenges, surgeons may even opt to avoid complete surgical staging, including lymphadenectomy[7]. Obesity can also pose obstacles to the delivery of adjuvant treatments. Consequently, patients with obesity may receive inadequate treatment, potentially impacting their survival outcomes[8].

This study's main goal was to determine the predictive value of preoperative BMI in order to forecast patients with EC's overall survival (OS) and progression-free survival (PFS). The second objective was to investigate the association between preoperative BMI and surgical outcomes in this particular patient population.

Materials and Methods

From January 2016 to October 2022, one super-tertiary hospital served as the site of this retrospective cohort study. We got institutional review board ethical approval from Rajavithi Hospital, Thailand (IRB number 056/2022). EC-diagnosed patients who had undergone bilateral salpingo-oophorectomy and total hysterectomy, with or without lymphadenectomy, were included in the registry. Surgeons specializing in gynecologic oncology at our hospital carried out the surgeries using laparoscopic or traditional laparotomy techniques. Individuals who had incomplete medical records and synchronous cancer were not allowed to participate in the research. The patient selection process is illustrated in Fig. 1. The staging system for surgery was determined by applying the 2009 revision of the International Federation of Gynecology and Obstetrics (FIGO). According to FIGO staging and the likelihood of recurrence, postoperative adjuvant therapies, such as chemotherapy, radiotherapy, or a combination of the two, were given.

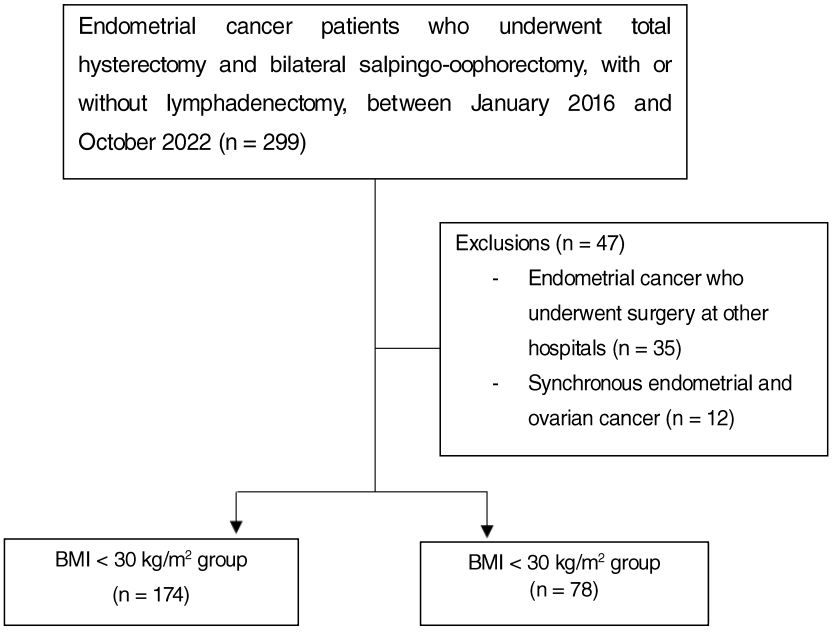

Fig. 1. Flowchart of patient selection.

Clinicopathological data were obtained from the medical records and included baseline characteristics (age at cancer diagnosis, performance status according to the Eastern Cooperative Oncology Group [ECOG], preoperative BMI, comorbidities, and currently taking medications), preoperative serum albumin level, histologic subtype, grading, and nodal status. Surgical details were also collected, including the operation date, operative findings, surgical procedure, operative duration, estimated blood loss, and residual tumor status. Other recorded variables included FIGO staging, intraoperative and postoperative complications occurring within 30 days after the operation, type and date of postoperative adjuvant treatment, and length of hospital stay. Patients were divided into two groups according to their preoperative BMI: non-obese patients (BMI of < 30 kg/m^2) and the obese group (BMI of ≥ 30 kg/m^2). The World Health Organization's international classification served as the basis for this classification of adult obesity.

The patients' care team from the gynecological oncology department routinely checked them in as outpatients after their treatment. Imaging studies were conducted on patients suspected to have recurrent disease. For such patients, treatment decisions were made based on the site and extent of the disease. Follow-up data, including the date of recurrence, site of recurrent disease, and last follow-up period, were obtained from the medical records. Disease recurrence was confirmed either histologically or clinically based on imaging findings. Both the imaging study date and the histopathological confirmation date were used to determine the date of recurrence. Through civil registration databases, the death date and cause were discovered.

In this study, PFS and OS were the main survival outcomes that were examined. The PFS was calculated by measuring the interval between the date of the operation and the date of any cause's recurrence or demise, whichever occurred first. From

the date of the operation until the patient's death from any cause or, if they were still alive at the conclusion of the study, the last follow-up date, OS was defined.

Using reference numbers from a study by Gaballa et al, the formula for testing two independent proportions served as the basis for calculating the sample size[9]. Patients with EC with a BMI of < 30 and ≥ 30 kg/m^2 had 5-year PFS rates of 78% and 58%, respectively, in the reference study. With a ratio of 2:1, the power was set to 80%, the type I error at 0.05, and the sample size was calculated to be 124 patients in the non-obese group and 62 patients in the obese group. The study aimed to include at least 137 patients with EC in the non-obese group and 69 in the obese group, taking into account a dropout rate of 10% statistical evaluation.

Statistical analysis

The chi-square test was used to analyze the categorical variables comparing patients with EC with a BMI of < 30 versus ≥ 30 kg/m^2. Frequencies and percentages of the outcomes were displayed. For normally distributed data, which were reported as mean ± standard deviation, the continuous data were evaluated using the student's t-test; for non-normally distributed data, which were reported as median and range, the Mann-Whiney U test was utilized. The Kaplan–Meier method was used to estimate the survival curves for OS and PFS. To evaluate the relationship between variables and survival outcomes, univariate and multivariate Cox regression analyses were run, taking into account covariates with a p value of < 0.1 from the univariate analysis. For the entire cohort, risk ratios (HRs) and 95% confidence intervals (CI) were provided. The statistical analyses conducted with Stata version 17 (StataCorp, College Station, TX, USA) revealed a statistically significant difference when p values of < 0.05 or when the null hypothesis was excluded by 95% CI.

Results

The study included 252 patients with EC who underwent surgery at a single super-tertiary hospital between January 2016 and October 2022. 78 (31%) and 174 (69%) of these patients had BMIs of ≥ 30 kg/m^2 and < 30 kg/m^2, respectively. The average BMI values for the obesity and non-obesity groups were 34.83 kg/m^2 and 24.11 kg/m^2, respectively. According to BMI, Table 1 displays the clinicopathological features of the patients. Individuals who had a BMI of 30 kg/m^2 or higher were considerably younger (mean age, 54.83 ± 11.52 vs 58.79 ± 9.93 years; p=0.006) and exhibited a greater occurrence of hypertension (64.1% vs 47.1%, p=0.013) and additional comorbidities like cardiovascular or thyroid conditions (15.4% vs 6.3%, p=0.021). Additionally, a greater percentage of patients with a BMI of 30 kg/m^2 were assigned to FIGO stage I (75.6% vs 60.3% compared to 60.9%, p = 0.023) and had endometrioid G1 histology (60.3% vs 38.5%, p = 0.001). Furthermore, the proportion of patients who did not receive adjuvant treatment was significantly higher in the obese group (47.4% vs 27%, p < 0.002).

The operative data and surgical complications are shown in Table 2 based on BMI. The laparotomy technique was used for surgery in 82% of the cases. Less frequently than patients with a BMI of < 30 kg/m^2, patients with a BMI of ≥ 30 kg/m^2 underwent paraaortic lymph node sampling, bilateral pelvic lymph node dissection, bilateral salpingo-oophorectomy, and total hysterectomy (35.9% vs 67.2%, p < 0.001). Furthermore, no discernible variations were found in terms of the amount of residual illness, the estimated blood loss, the length of the operation, the hospital stay, or the intraoperative complications. Postoperative complications, including fever, bowel ileus, and surgical site infection, were rare and failed to identify any statistically significant distinctions between the two groups.

Table 1. Clinicopathological characteristics according to BMI.

	BMI < 30 kg/m² (n = 174)	BMI ≥ 30 kg/m² (n = 78)	p value
Age (years)	58.79 ± 9.93	54.83 ± 11.52	0.006*
Co-morbidity			
No	99 (56.9%)	52 (66.7%)	0.143
DM	47 (27%)	25 (32.1%)	0.413
HT	82 (47.1%)	50 (64.1%)	0.013*
DLP	41 (23.6%)	26 (33.3%)	0.105
Other	11 (6.3%)	12 (15.4%)	0.021*
Current medication			
ASA	22 (12.6%)	10 (12.8%)	0.969
MFM	43 (24.7%)	23 (29.5%)	0.426
Statin	47 (27%)	30 (38.5%)	0.068
Other	77 (44.3%)	46 (59%)	0.031*
Preoperative Albumin (g/dL)	4.32 ± 0.45	4.33 ± 0.38	0.811
Previous abdominal surgery	26 (14.9%)	10 (12.8%)	0.656
ECOG			
0	127 (73%)	61 (78.2%)	0.379
1	47 (27%)	17 (21.8%)	0.379
Preoperative adjuvant treatment			
No	173 (99.4%)	78 (100%)	0.502
Radiation	1 (0.6%)	0 (0%)	0.502
FIGO Stage			
I	106 (60.9%)	59 (75.6%)	0.023*
II	18 (10.3%)	5 (6.4%)	0.316
III	38 (21.8%)	12 (15.4%)	0.235
IV	12 (6.9%)	2 (2.6%)	0.165
Histology			
Endometrioid G1	67 (38.5%)	47 (60.3%)	0.001*
Endometrioid G2	35 (20.1%)	21 (26.9%)	0.229
Endometrioid G3	41 (23.6%)	4 (5.1%)	<0.001*
Carcinosarcoma	12 (6.9%)	1 (1.3%)	0.063
Serous carcinoma	5 (2.9%)	2 (2.6%)	0.890
Clear cell carcinoma	14 (8%)	3 (3.8%)	0.219
Adjuvant treatment			
No	47 (27%)	37 (47.4%)	0.002*
Radiation	46 (26.4%)	24 (30.8%)	0.478
Chemotherapy	61 (35.1%)	11 (14.1%)	0.001*
Chemotherapy and Radiation	20 (11.5%)	6 (7.7%)	0.359

DM: Diabetes Mellitus, HT: Hypertension, DLP: Dyslipidemia, ASA: Aspirin, MFM: Metformin

Table 2. Operative data and surgical complications according to BMI.

	BMI < 30 kg/m² (n = 174)	BMI ≥ 30 kg/m² (n = 78)	p value
Type of operation			
TAH with BSO	8 (4.6%)	14 (17.9%)	0.001*
TAH with BSO with BPND	39 (22.4%)	26 (33.3%)	0.067
TAH with BSO with BPND with PANS	98 (56.3%)	22 (28.2%)	< 0.001*
TLH with BSO	1 (0.6%)	3 (3.8%)	0.055
TLH with BSO with BPND	9 (5.2%)	7 (9%)	0.253
TLH with BSO with BPND with PANS	19 (10.9%)	6 (7.7%)	0.428
Residual disease			
No	160 (92%)	76 (97.4%)	0.099
< 1 cm	4 (2.3%)	1 (1.3%)	0.593
≥ 1 cm	10 (5.7%)	1 (1.3%)	0.109
Estimated blood loss (ml)	546.26 ± 268.54	313.33 ± 217.42	0.367
Operative time (minutes)	172.19 ± 46.77	169.04 ± 49.23	0.627
Hospital stays (days)	4.9 ± 2.75	4.46 ± 1.53	0.192
Intraoperative complications			
Blood transfusion	19 (10.9%)	3 (3.8%)	0.066
Bowel injury	2 (1.1%)	1 (1.3%)	0.929
Other	4 (2.3%)	0 (0%)	0.177
Postoperative complications			
Surgical site infection	4 (2.3%)	1 (1.3%)	0.593
Postoperative fever	2 (1.1%)	1 (1.3%)	0.929
Other	0 (0%)	1 (1.3%)	0.135

TAH: Total abdominal hysterectomy, TLH: Total laparoscopic hysterectomy, BSO: Bilateral salpingo-oophorectomy, BPND: Bilateral pelvic lymph node dissection, PANS: Paraaortic lymph node sampling

In Table 3, the PFS univariate and multivariate analysis results are displayed. The univariate analysis revealed that non-endometrioid histology, high-grade histology, adjuvant radiation therapy, adjuvant combined chemotherapy and radiation, low preoperative albumin level (< 3.5 g/dL), ECOG performance status of 1, FIGO stage III/IV, and non-optimal surgery were independent poor prognostic factors for PFS. When aspirin was taken, the chance of recurrence was also significantly decreased. The only significant prognostic factors for PFS that remained in the multivariate analysis, however, were an ECOG performance status of 1 (adjusted HR [95% CI] 2.71 [1.31–5.6]; p = 0.007) and adjuvant radiation therapy (adjusted HR [95% CI] 4.03 [1.22–13.29]; p = 0.022).

Table 4 displays the OS univariate and multivariate analysis results. An age > 60 years, a low preoperative albumin level (< 3.5 g/dL), ECOG performance status of 1, FIGO stage III/IV, non-endometrioid histology, high-grade histology, adjuvant chemotherapy, adjuvant combined chemotherapy and radiation, lymphadenectomy, were found to be separate poor prognostic factors for OS, as was suboptimal surgery. Hypertension and aspirin use were linked to a significantly lower risk of death among patients with a BMI of ≥ 30 kg/m². In the multivariate analysis, an age of > 60 years, non-endometrioid histology, FIGO stage III/IV, and suboptimal surgery continued to be highly unfavorable prognostic factors for OS. Furthermore, in the multivariate analysis, hypertension significantly reduced the risk of death.

Table 3. Univariate and multivariate analysis of prognostic factors for PFS.

Characteristics	Univariate		Multivariate	
	HR (95% CI)	p value	Adjusted HR (95% CI)	p value
BMI (kg/m^2)				
< 30	1			
≥ 30	0.8 (0.39, 1.66)	0.552		
Age (years)				
< 60	1			
≥ 60	1.48 (0.77, 2.82)	0.238		
Underlying disease				
No	1.31 (0.69, 2.5)	0.411		
DM	0.91 (0.44, 1.89)	0.806		
HT	0.6 (0.31, 1.16)	0.131		
DLP	0.89 (0.42, 1.88)	0.754		
Current medication				
ASA	0.17 (0.02, 1.27)	0.084*	0.16 (0.02, 1.17)	0.071
MFM	1.04 (0.5, 2.15)	0.919		
Statin	0.84 (0.41, 1.73)	0.635		
Preoperative albumin (g/dL)				
≥ 3.5	1		1	
< 3.5	3.78 (1.34, 10.69)	0.012*	2.86 (0.81, 10.19)	0.104
ECOG				
0	1		1	
1	3.52 (1.85, 6.71)	<0.001*	2.71 (1.31, 5.6)	0.007*
FIGO Stage				
I/II	1		1	
III/IV	2.81 (1.47, 5.37)	0.002*	1.3 (0.56, 3.03)	0.539
Histology				
Endometrioid	1		1	
Non-endometrioid	2.81 (1.39, 5.69)	0.004*	1.85 (0.75, 4.55)	0.181
Adjuvant treatment				
No	1		1	
Radiation	3.51 (1.12, 11.04)	0.031*	4.03 (1.22, 13.29)	0.022*
Chemotherapy	1.66 (0.3, 9.04)	0.56		
Chemotherapy and radiation	6.91 (2.36, 20.24)	<0.001*	0.81 (0.14, 4.73)	0.818
Type of operation				
Laparotomy	1			
Laparoscopy	1.13 (0.5, 2.58)	0.768		
Lymphadenectomy				
No	1			
BPND	0.98 (0.31, 3.03)	0.966		
BPND and PANS	0.96 (0.33, 2.79)	0.939		
Optimal surgery				
Yes	1		1	
No	2.65 (1.03, 6.81)	0.043*	1.03 (0.32, 0.33)	0.96

DM: Diabetes Mellitus, HT: Hypertension, DLP: Dyslipidemia, ASA: Aspirin, MFM: Metformin, BPND: Bilateral pelvic lymph node dissection, PANS: Paraaortic lymph node sampling

Table 4. Univariate and multivariate analysis of prognostic factors for OS.

Characteristics	Univariate		Multivariate	
	HR (95% CI)	p value	Adjusted HR (95% CI)	p value
BMI (kg/m^2)				
< 30	1		1	
≥ 30	0.46 (0.22, 0.94)	0.035*	0.84 (0.37, 1.9)	0.676
Age (years)				
< 60	1		1	
≥ 60	2.37 (1.33, 4.23)	0.003*	2.79 (1.43, 5.43)	0.003*
Underlying disease				
No	1.32 (0.75, 2.29)	0.334		
DM	1.06 (0.58, 1.94)	0.854		
HT	0.57 (0.32, 1.01)	0.053*	0.41 (0.2, 0.83)	0.014*
DLP	0.76 (0.39, 1.48)	0.417		
Current medication				
ASA	0.26 (0.06, 1.05)	0.058*	0.27 (0.06, 1.2)	0.085
MFM	0.96 (0.51, 1.81)	0.91		
Statin	0.88 (0.47, 1.63)	0.677		
Pre-operative albumin (g/dL)				
≥ 3.5	1		1	
< 3.5	6.11 (2.6, 14.36)	<0.001*	2.28 (0.75, 6.91)	0.145
ECOG				
0	1		1	
1	2.64 (1.51, 4.61)	0.001*	1.98 (0.97, 4.07)	0.062
FIGO Stage				
I/II	1		1	
III/IV	3.05 (1.75, 5.32)	<0.001*	2.74 (1.06, 7.12)	0.038*
Histology				
Endometrioid	1		1	
Non-endometrioid	4.12 (2.29, 7.41)	<0.001*	2.67 (1.18, 6.03)	0.018*
Adjuvant treatment				
No	1		1	
Radiation	1.91 (0.83, 4.41)	0.13		
Chemotherapy	2.45 (0.87, 6.87)	0.09*	0.6 (0.18, 1.97)	0.397
Chemotherapy and radiation	3.08 (1.41, 6.73)	0.005*	0.64 (0.2, 2.05)	0.449
Type of operation				
Laparotomy	1			
Laparoscopy	0.8 (0.4, 1.6)	0.527		
Lymphadenectomy				
No	1		1	
BPND	3.78 (1.17, 12.23)	0.027*	1.32 (0.39, 4.52)	0.656
BPND and PANS	8.29 (3.85, 17.85)	<0.001*	1.09 (0.34, 3.48)	0.88
Optimal surgery				
Yes	1		1	
No	6.24 (3.18, 12.21)	<0.001*	2.72 (1.12, 6.61)	0.027*

DM: Diabetes Mellitus, HT: Hypertension, DLP: Dyslipidemia, ASA: Aspirin, MFM: Metformin, BPND: Bilateral pelvic lymph node dissection, PANS: Paraaortic lymph node sampling

The Kaplan-Meier survival analyses for overall PFS is presented in Fig. 2a. The overall 5-year PFS rates were 85.6% (95% CI 79.4%–90.0%) in the non-obese group and 87.2% (95% CI 77.5%–92.9%) in the obese group, with a median follow-up period of 68 months. Although the obese group exhibited a slightly higher PFS rate than the non-obese group, the difference was not statistically significant (p = 0.552). When stratified by disease stage, as illustrated in Fig. 3, early-stage patients had 5-year PFS rates of 89.5% (95% CI 82.6%–93.8%) in the non-obese group and 92.9% (95% CI 82.2%–96.7%) in the obese group (p = 0.367). Although the trend suggests a slightly better PFS in obese patients, no statistically significant difference was observed. Furthermore, advanced-stage patients exhibited lower 5-year PFS rates, with the non-obese group at 75.5% (95% CI 61.0%–85.3%) and the obese group at 64.3% (95% CI 34.3%–83.3%), though this difference was not statistically significant (p = 0.457).

The Kaplan-Meier survival analyses for overall OS is shown in Fig. 2b. The overall 5-year OS rate was significantly higher in the obese group (88.5%, 95% CI 79.0%–93.8%) compared to the non-obese group (79.2%, 95% CI 72.4%–84.5%), with a statistically significant correlation observed (p = 0.03) via Cox proportional hazards regression analysis. When stratified by stage as shown in Fig. 4, early-stage patients had 5-year OS rates of 84.7% (95% CI, 77.0%–89.9%) in the non-obese group and 93.8% (95% CI, 84.2%–97.6%) in the obese group (p = 0.026). However, in advanced-stage disease, OS rates were comparable between the two groups (65.4%, 95% CI 50.4%–76.9% for non-obese vs 64.3%, 95% CI 34.3%–83.3% for obese), with no statistically significant difference (p = 0.876).

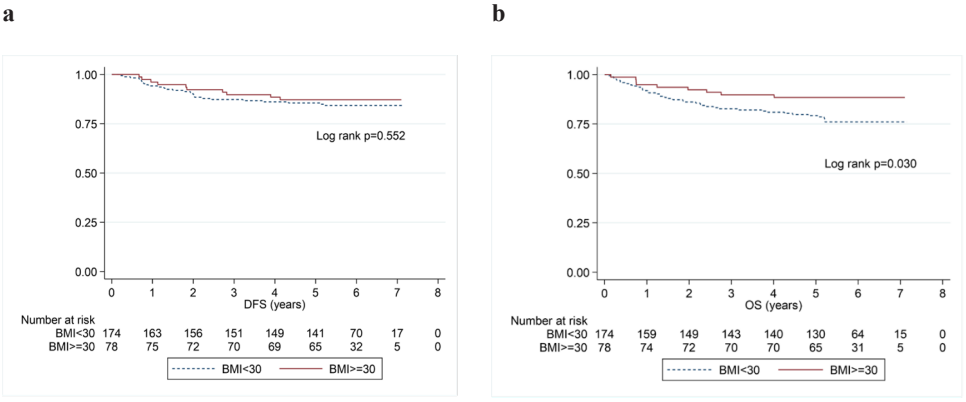

Fig. 2. Kaplan Meier Curves of overall PFS (a) and OS (b).

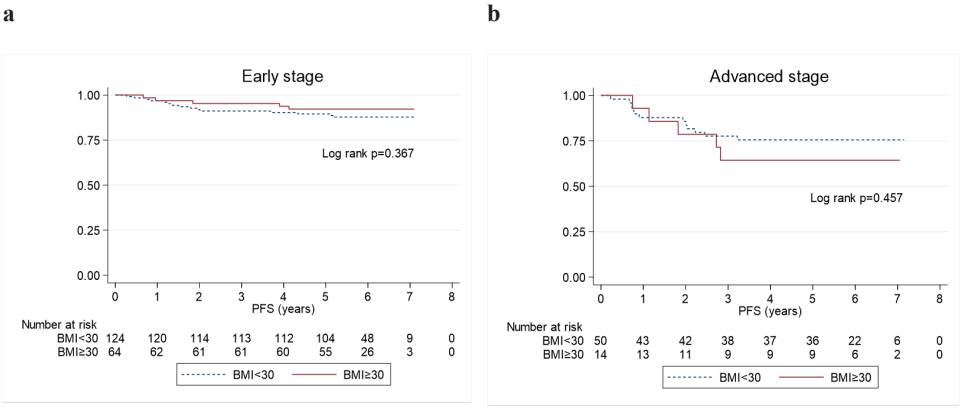

Fig. 3. Kaplan Meier Curves of PFS stratified by early (a) and advanced disease stages (b).

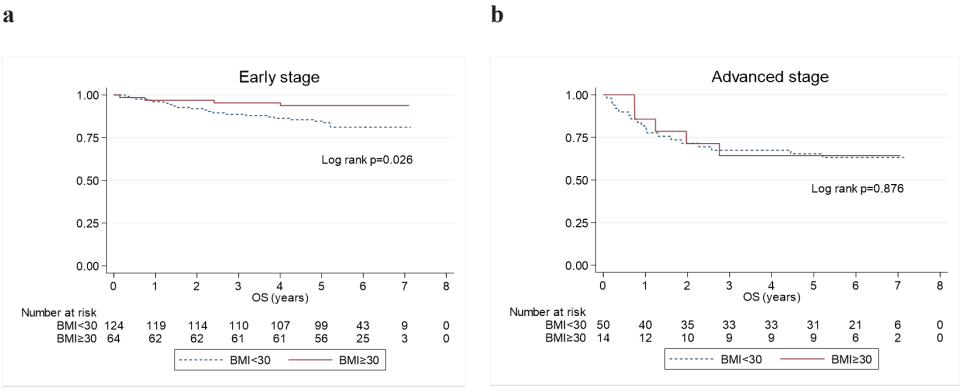

Fig. 4. Kaplan Meier Curves of OS stratified by early (a) and advanced disease stages (b).

Discussion

As an established risk factor for several metabolic diseases and cancers, including EC, obesity is a well-known public health concern. There are two subsets of EC: type I and type II. Eighty percent of EC cases are type I tumors, which are often dependent on estrogen, have low-grade endometrioid histology, and often develop against a backdrop of hyperplasia. On the other hand, type II tumors are commonly associated with high-grade features, arise within atrophic endometrium, and are less likely to be estrogen dependent. Obesity has been linked to a 2.7-time increase in type I tumor development and a 1.8-time increase in type II tumor development in women. Furthermore, individuals with metabolic syndrome a condition characterized by the co-occurrence of abdominal obesity, diabetes mellitus, hypertension, and dyslipidemia—have a two fold increased risk of developing EC[10].

Numerous mechanisms mediate the hormonal impact of obesity on EC. Adipocytes in the peripheral fat of obese people use aromatase to convert androgens to estrone and estradiol. Additionally, sex hormone-binding globulin levels are linked to decreased in obesity, which raises levels of bioactive estrogen. Estrogen metabolites function as mutagens, forming adducts with DNA and causing a build-up of double-stranded DNA breaks, which exacerbates genetic instability. Additionally contributing to cellular stress and genetic instability, adipokine-mediated inflammation and the production of mitochondrial reactive oxygen species in obesity further encourage mutagenesis[11].

For patients with gynecologic cancer, treatment modalities that are adversely affected by obesity include radiation, chemotherapy, and surgery. Due to variables including body weight and comorbidities that may reduce surgical tolerance or feasibility, obese patients may have difficulty obtaining standard care. The fact that obesity is commonly linked to other comorbid conditions like diabetes mellitus, cardiovascular disease, and obstructive sleep apnea complicates the safe administration of surgical procedures even more[12]. Regardless of whether the surgery was done via laparotomy or laparoscopy, the rate of pelvic lymph node dissection in the current study was similar across the BMI groups. However, patients who had a BMI of ≥ 30 kg/m^2 and underwent surgical staging by laparotomy had a significantly lower rate of paraaortic lymph node sampling. This finding implies that, in comparison to patients with a BMI of < 30 kg/m^2, patients who are obese may have inadequate lymph node assessment due to the technical difficulties in exposing and accessing the deep surgical fields. This kind of data is crucial for directing adjuvant treatments. In patients with a BMI of ≥ 30 kg/m^2, we also observed a trend toward shorter operative times, shorter hospital stays, and lower estimated blood loss volumes. This trend may be related to the lower rate of complete surgical staging

in this population. Between the two BMI groups, there were no appreciable variations in intraoperative or postoperative complications, though. In contrast, a comprehensive analysis found that women with a BMI below 30 kg/m^2 had considerably reduced estimated blood loss, shorter operational times, shorter hospital stays, and decreased incidence of perioperative problems compared to women with a BMI of 30 kg/m^2 or above[13]. In the present study, the higher rate of no adjuvant treatment in the obesity group can be attributed to the higher percentages of younger patients, FIGO stage I disease, and low-grade histology. This finding contrasted with another study in which the need for adjuvant treatment was similar between obese and non-obese patients[14].

Obesity's effect on PFS and OS in EC patients is still debatable[15, 16]. A prospective cohort study with > 900,000 participants revealed that a BMI of > 40 kg/m^2 was linked to a 60% increased risk of dying from any cancer. For patients with a BMI of 30-34 and > 40 kg/m^2, the relative risk of dying from EC ranged from 2.53 to 6.25, respectively[17]. In our study, we found a higher overall OS rate in patients with a BMI of ≥ 30 kg/m^2, despite the low rate of complete surgical staging in this population. The lower FIGO stage and the greater frequency of low-grade histology may explain this finding. This result remained significant even after stratifying patients in the early-stage group. However, in advanced-stage disease, the survival advantage was no longer apparent. This suggests that the potential protective effect of obesity may be limited to early-stage disease, whereas in advanced-stage cases, other factors such as tumor burden, treatment resistance, and comorbidities may play a more significant role in survival outcomes. We also discovered a higher incidence of type I EC in obese patients, which was consistent with other studies[9, 18]. Furthermore, the univariate analysis significantly linked aspirin use to a lower risk of death and recurrence; however, the multivariate analysis did not support this association. Arem along with others15 examined 12 researches on the prognosis for EC and obesity. In 7 of these 12 studies, the BMI and specific mortality did not consistently correlate, according to the authors; however, some studies suggested that obesity patients had lower grades and stages as well as higher all-cause mortality[15]. Güzel and associates compared to patients with a BMI of < 40 kg/m^2, there was a non-statistically significant trend toward lower PFS and OS in patients with morbid obesity[19]. In an ancillary data analysis from the Gynecologic Oncology Group LAP2 study, obesity was associated with death from all causes but not from cancer[7]. An independent study conducted by Gaballa and colleagues revealed no connection between survival and obesity. The correlation between obesity and enhanced OS raises intriguing questions about the underlying mechanisms[9]. More research is needed to understand the complex interactions between obesity, tumor biology, and treatment response in patients with EC.

The retrospective cohort study design, along with its performance at a single academic cancer center recognized for its aggressive surgical management, is a noteworthy strength. Nevertheless, it's critical to acknowledge the study's three main limitations. To begin with, the retrospective design of the study has built-in limitations, including biases and a reliance on easily accessible medical records. Second, the study cohort comprised only a small number of laparoscopic surgeries. It's possible that the small sample size had an impact on the actual surgical results, particularly in terms of the estimated blood loss and operating time. Third, the survival analysis did not account for cause-specific mortality, which may affect the interpretation of overall survival outcomes. It is therefore important to use caution when extrapolating the results of this study to broaden demographics or different surgical contexts.

Conclusion

Our findings suggested that patients with EC who had a BMI of ≥ 30 kg/m^2 exhibited no significant difference in PFS but had significantly longer OS than those with a BMI of < 30 kg/m^2. Adjuvant radiation therapy and an ECOG performance status of 1 were found to be independent predictors of PFS. Older age

(> 60 years), advanced FIGO stage (III/IV), non-endometrioid histology, and non-optimal surgery were significantly poor prognostic factors for OS.

Potential conflicts of interest

The authors declare no conflicts of interest.

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