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BODY MASS INDEX AND GRADING HISTOPATOLOGI ENDOMETRIOID ENDOMETRIAL CARCINOMA

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ABSTRACT
Endometrioid endometrial carcinoma is a malignant primary epithelial tumor in the endometrium, in the form of a glandular neoplasm with an acinar, papillary, or solid pattern, which can invade the myometrium. Histological grading is determined based on structural differentiation and cell atypia. Body mass index is calculated by dividing body weight by height in the square. The exact cause of endometrioid endometrial carcinoma is unknown. Still, most cases are associated with chronic estrogen stimulation of the endometrium, which triggers endometrial hyperplasia as a precursor to endometrioid endometrial carcinoma. Objective to assess the relationship between body mass index and histopathological grading of endometrioid endometrial carcinoma. Formalin-fixed paraffin tissue blocks from 31 patients with endometrioid endometrial carcinoma were used to examine the relationship between body mass index and histopathological grading. Baseline characteristics of the samples were obtained through medical records or pathology archives. The relationship between body mass index categories and histopathological grading was analyzed using the Kruskal-Wallis test. There was no significant relationship between body mass index and endometrioid endometrial carcinoma histopathological grading ($p>0.05$). The high body mass index category was not always associated with high histopathological grading of endometrioid endometrial carcinoma.

Keywords: body mass index; endometrioid endometrial carcinoma; grading histopathology

INTRODUCTION

Endometrial carcinoma is the most common cancer of the female reproductive system in developed countries and was reported to affect 320,000 women and cause 76,000 deaths globally in 2012. It is the third leading cause of cancer-related deaths in women. The incidence of this cancer has been rising, with newer statistics indicating that in 2020, over 417,000 cases were reported worldwide (Makker et al., 2022). In developed countries, 75% of cases of endometrial carcinoma occur in patients aged around 60 years during the postmenopausal period, so the most common symptom is postmenopausal bleeding (Barczyński et al., 2023). Evidence on the association between high Body Mass Index (BMI), and the risk of endometrial cancer, including subtypes in Asian populations is still limited (Harvey et al., 2023). Di Indonesia, penelitian terakhir mendapatkan prevalensi karsinoma endometrium mencapai 7,2 kasus per tahun. Usia penderita karsinoma endometrium cenderung lebih muda, yaitu sebanyak 63,9% pada usia ≥50 tahun dan sebanyak 12,5% pada usia ≤ 40 tahun (Sofyan et al., 2020). The most common types based on histology are endometrioid endometrial carcinoma (EEC) about 75-80%, serous papillary carcinoma 5-10% and clear cell carcinoma 3-5%. Serous papillary carcinoma and clear cell carcinoma are aggressive types (Bogani et al., 2021).

Excess estrogen hormone is suspected as the cause of endometrial carcinoma. The ovaries produce and release estrogen, but fat tissue also has the power to convert some hormones into estrogen. The more fat tissue, the more hormones are converted into estrogen, thus increasing estrogen levels in women and increasing the risk of endometrial carcinoma (Monnin et al., 2023). Some experts believe that there is a relationship between weight gain and the incidence of endometrial carcinoma (Smrz et al., 2021). According to previous research, it was revealed that there is a relationship between obesity and the risk

of endometrial carcinoma and women with normal body weight with endometrial carcinoma may have a better survival rate than those with obesity (Anggraeni et al., 2021).

BMI is a simple, inexpensive, and non-invasive method for measuring body fat, calculated by dividing body weight (kg) by the square of height (m^2). Although only height and weight are used, BMI has been shown to correlate with body fat and future health risks. High BMI can predict morbidity and mortality, making it an effective tool for screening obesity and its health risks (Sruthi et al., 2023). Previous studies have suggested that weight gain and obesity can increase the risk of endometrial carcinoma. The greatest risk is in women who have a ≥35% increase from normal BMI or women who average ≥1% increase from normal BMI over the period from age 21 years. In Japanese and Americans, a 5% increase from normal BMI increases the risk of endometrial carcinoma (Dikaiou et al., 2024). According to the World Health Organization, cancer differentiation for EEC is based on histological structure and cell atypia. This grading is grouped based on the degree of differentiation of EEC as seen from the solid, non-squamous, or non-morula growth pattern. The nuclear grade is determined by variations in the size and shape of the nucleus, chromatin distribution, and nucleoli size (Soslow et al., 2019). Therefore, this study aimed to assess the relationship between body mass index and histopathological grading of endometrioid endometrial carcinoma.

METHOD

The study was an associative descriptive study with a cross-sectional approach. This study was conducted at the Gynecology Oncology Polyclinic/Inpatient Unit, Anatomic Pathology Unit of Medan General Hospital, Anatomic Pathology Laboratory and Integrated Laboratory of the Faculty of Medicine, University of North Sumatra for 4 months. 31 people were involved in this study. The research sample was searched through data storage software and the label number of the slide or paraffin block histopathologically diagnosed as EEC that met the inclusion and exclusion criteria was obtained. The medical record that was histopathologically diagnosed as EEC was then recorded as the patient's BMI status. Inclusion criteria: adequate and representative histopathologically diagnosed slides and paraffin blocks with clinical data in the form of BMI. Exclusion criteria: 1) slides or paraffin blocks recorded according to the data storage device, lost or damaged so that they cannot be re-evaluated and/or re-cut; 2) slides that after review are not EEC; and 3) slides or paraffin blocks that do not include BMI in the medical record. EEC is graded by looking at the architecture, if ≤ 5% dense growth is considered grade 1 6-50% dense growth is considered grade 2, and 63 > 50% is considered grade 3 / high-grade. Body mass index is calculated by comparing body weight with height, calculated by dividing body weight in kilograms by height in meters squared. Data were analyzed using the Kruskal-Wallis test. The research has received permission from the Health Research Ethics Committee of the Faculty of Medicine, University of North Sumatra No. 522/TGL/KEPK FK USU-RSUP HAM/2019.

RESULT

Table 1 shows that the average age is 53.4 years with a standard deviation of 14.1. The youngest age group suffering from EEC is the 21-26 year age group with a sample size of 1 case (3.2%), in detail the age of the sufferer is 21 years with a norm weight BMI category and diagnosed as EEC grade III. While the oldest age is the 81-86 year age group with a sample size of 1 case (3.2%), in detail the age of the sufferer is 84 years with a norm weight BMI category and diagnosed as EEC grade III. The age distribution of EEC sufferers is mostly in the 51-56 year age group with a sample size of 9 cases (29.0%).

Table 1.
Characteristics of EEC sufferers based on age (n=31)

Age	f	%
Age, mean±SD, year	53,4 ± 14,1	
21 – 26	1	3,2
27 - 32	2	6,5
33 – 38	1	3,2
39 – 44	2	6,5
45 – 50	6	19,3
51 – 56	9	29,0
57 – 62	2	6,5
63 – 68	2	6,5
69 – 74	4	12,9
75 – 80	1	3,2
81 - 86	1	3,2

Table 2.
Histopathology grading of EEC patients (n=31)

Grading	f	%
Grade I	14	45,2
Grade II	8	25,8
Grade III	9	29,0

Table 2 shows that EEC patients with histopathological grading Grade I were 14 people (45.2%), Grade II were 8 people (25.8%), and Grade III were 9 people (29.0%).

Table 3.
BMI categories in EEC patients (n=31)

BMI	f	%
Underweight	2	6,5
Normoweight	15	48,4
Overweight	8	25,8
Obesity	6	19,3

Table 3 shows that the underweight category is 2 people (6.5%), the norm weight is 15 people (48.4%), overweight is 8 people (25.8%), and obesity is 6 people (19.3%).

Table 4.
BMI Distribution Based on EEC Sufferer Grading

Body Mass Index	Grading						p-value
	Grade I		Grade II		Grade III		
	f	%	f	%	f	%	
Underweight	1	50,0	1	50,0	0	0	0,563
Nomoweight	5	33,3	4	26,7	6	40,0	
Overweight	4	50,0	2	25,0	2	25,0	
Obesity	4	66,6	1	16,7	1	16,7	

*Uji Kruskal-Wallis p>0,005

Table 4 indicates that underweight patients were evenly distributed between grade I and grade II (50.0% each), with no cases in grade III. Norm weight patients showed 33.3% in grade I, 26.7% in grade II, and 40.0% in grade III. Overweight patients had 50.0% in grade I, 25.0% in grade II, and 25.0% in grade III. Obese patients were predominantly in grade I (66.6%), with 16.7% in both grade II and grade III.

DISCUSSION

EEC is a primary epithelial malignant tumor in the endometrium, a glandular neoplasm that shows an acinar, papillary, or partially solid configuration and has the potential to affect the myometrium (Saglam, 2024). Most cases of EEC are often associated with endometrium exposed to estrogen stimulation. In this study, it was found that from 31 samples of EEC sufferers, most of them occurred in the age range of 51-56 years (29.0%). This condition is by previous research where the age of EEC sufferers was ≥50 years (Macaron et al., 2023). Meanwhile, another study found that the average age of EEC sufferers was 67.1 years with a standard deviation of ±11.9 years (Patton et al., 2024). This study also found that the highest number of EEC sufferers was grade I, namely 14 people (45.2%). This is by previous research which stated that the highest number of EEC sufferers was grade I, namely 380 people (64.3%) (Firmansyah et al., 2022). Meanwhile, another study found that the highest number of EEC sufferers were in histopathology grade III (Trifanescu et al., 2018).

Characteristics of EEC patients based on BMI category in EEC patients from this study, the norm weight category was found to be the highest with 15 people (48.4%). While in previous studies the highest figure was in the obesity category (66.3%) (Hashmi et al., 2020). Some experts believe that there is a relationship between weight gain and the occurrence of EEC where excess estrogen hormone is suspected as the cause. This excess estrogen produced will be stored cumulatively, considered to increase the risk of endometrial carcinoma (Bukato et al., 2024). Several factors are known to influence the development of EEC including (1) obesity, (2) diabetes, (3) hypertension, (4) infertility, and (5) exposure to unopposed estrogen (estrogen used in estrogen replacement therapy without the administration of progestin to prevent side effects). Prolonged estrogen replacement therapy and estrogen-secreting ovarian tumors increase the risk of endometrioid endometrial carcinoma (Chou et al., 2024).

The relationship between BMI and histopathology grading of EEC patients in this study found that the obesity category with histopathology grading grade I had the highest incidence (66.6%). This is due to the results of previous studies that found the obesity category with histopathology grading grade I as the highest incidence (60.9%) (Mardiah et al., 2021). However, the results of the analysis of the relationship between BMI and histopathology grading of EEC patients in this study obtained a p-value = 0.563 ($p>0.05$) which showed no significant relationship. This may be the BMI data or weight and height of patients who came to the Medan General Hospital, assessed at the same time. The possibility of patients suffering from EEC occurred long before the patient came to the Medan General Hospital.

But from this study, something is interesting even though statistically the relationship between BMI and EEC histopathology grading is not significant. The consistency of overweight and obesity characteristics appears to be consistent in grade I with the highest incidence and decreases along with the increase in EEC histopathology grading. There is a tendency for overweight and obesity to be most often found in grade I. While in grade II and grade III, the incidence rate decreases. This may be due to the patient's declining health due to the disease, or it may be due to the patient's psychological state towards the disease. Side effects of therapy also cannot be ruled out as a cause of the decrease in the patient's BMI category along with the course of the disease.

CONCLUSION

There was no significant relationship between the BMI category and EEC histopathology grading. The average age of EEC patients was 53.4 ± 14.1. with most patients in the 51-56 years age group (29%). The frequency distribution of EEC patients with histopathology grading grade I was the most common, namely 14 people (45.2%). The most dominant BMI category found in EEC patients was norm weight with the number of patients being 15 people (48.4%). It is advisable to obtain the patient's BMI or height and weight status at the initial stage when the patient is diagnosed with EEC.

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