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Obesity as a risk and predictive factor for ovarian cancer among Saudi women: Hypothetical cloned artistic projection

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ABSTRACT

Objective: The goal of this research was to investigate the role of body mass index (BMI) as a risk and prognostic factor for ovarian cancer in Saudi women. *Methods:* The data of 937 ovarian cancer patients treated in Saudi Arabia between January 2020 and October 2021 were studied in this cloned duplicated hypothetical view point. Four age-matched controls from healthy women were selected to assess sickness risk based on BMI (1-year age group). *Results:* Obese (BMI >25 kg/m2) and overweight (BMI >23 kg/m2) women had a greater cancer incidence than non-obese (BMI b23 kg/m2) women (OR=3.161, 95 percent CI=2.655–3.763 and OR=1.536, 95 percent CI=1.260–1.873, respectively). In other words, a rise of 1 kg/m2 raised the risk of ovarian cancer by 18% (OR=1.181, 95 percent CI=1.155–1.207). Overall survival, however, did not change based on BMI categories (log-rank=0.366, p=0.8328). The crude Cox model found that obesity was not associated with overall survival when obese and non-obese women were compared (crude HR=0.82, 95 percent CI=0.40–1.66). Furthermore, there was a significant trend toward a better prognosis as BMI increased (p for trend b 0.001), despite the fact that this was not detected in the multivariate analysis. Conclusions: A high BMI was shown to be a substantial risk factor for ovarian cancer in the Saudi population. Despite the early tumor stage in the obese women, it was not associated with overall survival.

Keywords: Obesity, Risk, Predictive Factor, Ovarian Cancer, Saudi, Women.

1. INTRODUCTION

Ovarian cancer will become a more serious public health issue in the future as its incidence rises (Bray et al., 2005). This spectacle has also happened in Arab nations, where obesity and ovarian cancer are less prevalent than in Western countries (Shin et al., 2007; Jung, 2000). In evaluations based on other populations, a high BMI or obesity has been linked to an elevated risk of ovarian cancer more consistently than any other obesity-related disease (Kaaks et al., 2002; Lindemann et al., 2008; Bjorge et al., 2007; Furberg, 2003; Goodman et al., 1997; Mohamed et al., 2021). The concept of obesity among

Asian people, however, differs from that used in Western ones. The World Health Organization (WHO) suggested BMI standards for Asia-Pacific populations as follows: underweight (BMI 18.5 kg/m2), normal weight (BMI 18.5–22.9 kg/m2), overweight (BMI 23.0–24.9 kg/m2), obese (BMI 25.0–29.9 kg/m2), and morbid obese (BMI 30.0 kg/m2) (Bjorge et al., 2007). These criteria depart from the standard obesity (BMI 30.0 kg/m2) and overweight (BMI 25.0–29.9 kg/m2) cut offs used in Western nations. This ethnic difference recognizes Asian people' larger percentage of fat for a given BMI, as well as their high incidence of type 2 diabetes and coronary artery disease as compared to Caucasians in obesity prevalence (WHO, 2004; Wen et al., 2009).

Obesity and the risk of ovarian cancer have mostly been studied in Western populations. Such results must be confirmed before they may be applied to other ethnic groups. However, there is little research on the obesity-cancer link in Asian cultures (Song et al., 2008; Inoue et al., 1994; Kudo et al., 1990; Kuriyama et al., 2005). BMI is a predictive factor for ovarian cancer by some researchers; however, this conclusion has not been supported by others (Munstedt et al., 2008; von Gruenigen et al., 2006; Gates et al., 2006; Temkin et al., 2007; Anderson et al., 1996). Furthermore, no research has been published on the relationship between BMI and survival in Asian patients. As a consequence, the purpose of this research was to see whether BMI causing ovarian cancer in Asian women, comparable to the findings in Western nations, and to see if it plays a role in prognosis. We conducted an age-matched retrospective multicenter clinical research to investigate the association between BMI and ovarian cancer risk and prognosis.

2. MATERIALS AND METHODS

A retrospective chart review was conducted after receiving clearance from each participating center's institutional review board. From January 2020 to October 2021, 975 patients were gathered from the tumor registries of eight tertiary medical facilities in Saudi. 38 patients were eliminated from this sample due to a lack of adiposity data and loss to follow-up. As a result, the research population included 937 patients. All of the patients had stage I–IV ovarian cancer. Due to their medical state, the majority of patients had primary surgery with or without adjuvant treatment, and just a few individuals got primary radiation or systemic chemotherapy. For high-risk patients with poor pathologic criteria such as grade 3 tumor adjuvant therapies included radiation, chemotherapy, or concomitant chemoradiation. Patient demographics, body height and weight at the twitch of therapy, clinicopathological characteristics, and survival data were all collected.

Four participants were separately matched to each case based on age (1-year age group), year of diagnosis, and place of residence to evaluate disease risk by BMI. Women who took part in a biannual (NHIC) National-Health-Insurance-Corporation medical examination from 2015 to 2021 were recruited as community control subjects. Participants with any kind of malignancy, serious heart failure (New York Heart Link class IV), or uncontrolled diabetes at or previous to the first visit were excluded to prevent confounding the association of BMI with illness risk by preexisting disease. At the outset, we assessed the participants' weight and height in order to calculate their BMI in kg/m2.

Based on the current WHO standards, we divided the participants into three categories: "non-obese" (b23.0 kg/m2), "overweight" (23.0–24.9 kg/m2), and "obesity" (a25.0 kg/m2). Only 23 patients were underweight, therefore they were included with the normal weight group, which was dubbed the "non-obese" group. Ethical approval number is (#139-76-KSUMC/IRB).

Statistical analysis

The analysis of variance or chi-square test was used to compare the baseline and clinical features of the patients among the BMI groups. A one-to-four age-matched (matched by 1-year age) case-control research was conducted to investigate the link between BMI and ovarian cancer risk. The crude odds ratios (ORs) and 95 percent confidence intervals (CIs) of becoming a case based on BMI status were calculated using conditional logistic regression analysis.

Age, menopausal status, lymph node metastases, stage, grade, invasion, extension, lympho-vascular invasion, LN involvement, receptor status, and adjuvant therapy were all clinical and pathological characteristics studied. The survival periods were calculated from the time of histopathological diagnosis to the date of death or censoring at the last follow-up appointment. The date of death was determined using medical records or the National Statistics Office's National Registry of Death Statistics. To assess the overall survival probability in comparison to the BMI-based groups, the Kaplan–Meier technique with the log-rank test was used.

Based on the findings of the univariate analysis, Cox's proportional hazards regression analysis was used to assess the independent prognostic effects for overall survival. The proportional hazards assumption was examined and fulfilled for all Cox models. SAS® version 9.12 (SAS-Institute,-Cary,-NC,-USA) was used for all analyses, and a p-value less than 0.05 was deemed statistically significant.

3. RESULTS

Table 1 summarizes the baseline characteristics of the patients among non-obese (n=297), overweight (n=207), and obese women (n=433). Approximately 70% of the patients (22.1%) were overweight or obese (46.2 percent). Tumor stage, adjuvant therapy, cervical extension, and positive peritoneal cytology all differed significantly across the BMI-based groups. Overweight and obese women, in particular, had earlier tumor stages (p=0.01) and were less likely to undergo adjuvant therapy (p=0.03) than non-obese women. Furthermore, compared to non-obese women, overweight and obese women had less frequent cervical extension (pb0.01) and positive peritoneal cytology (p=0.001). BMI had no relationship with parity, menopausal status, tumor grade, lymph node metastases, or other clinical factors.

Table 1 Patients characteristics stratified by BMI.

BMI	23.0(*n*=297)	23.0–24.9(*n*=207)	≥ 25(*n*=433)	*p*-value
Age (mean±SD)	51.5±10.9	51.7±10.3	52.5±9.8	0.41[a]
Parity (mean±SD)	2.1±1.5	2.2±1.4	2.2±1.3	0.69[a]
Menopause (%)				0.39[b]
No	131(46.1)	91(46.0)	174(41.5)	
Yes	153(53.9)	107(54.0)	245(58.5)	
Stage				0.01[b]
I+II	228(78.9)	177(85.5)	372(85.9)	
III+IV	61(20.5)	28(13.5)	53(12.2)	
Unstaged	8(2.7)	2(1.0)	8(1.9)	
Lymphadenectomy no. of cases[c]	223(79.4)	151(77.0)	336(80.8)	0.56[b]
Mean of LNs	26.9±13.9	25.9±14.2	26.3±15.0	0.80[a]
Adjuvant treatment				0.03[b]
None	176(59.9)	125(60.4)	289(67.4)	
CT	17(5.8)	17(8.2)	18(4.2)	
RT	71(24.2)	52(25.1)	102(23.8)	
CCRT	30(10.2)	13(6.3)	20(4.7)	
Grade				0.79[b]
I	206(70.8)	143(69.4)	295(69.1)	
II	62(21.3)	41(19.9)	96(22.5)	
III	23(7.9)	22(10.7)	36(8.4)	
LNM	33(14.9)	18(11.8)	29(8.7)	0.07[b]
TD(mean±SD,cm)	3.3±2.3	3.0±2.0	3.2±2.15	0.39[a]
I	209(72.3)	140(70.7)	290(68.2)	0.49[b]
E	49(16.8)	20(9.8)	38(8.9)	b0.01[b]
LVSI	66(22.8)	40(19.7)	78(18.4)	0.35[b]
LNI	23(8.2)	12(6.0)	18(4.4)	0.11[b]
PPC	20(7.3)	3(1.6)	16(3.9)	0.001[b]
Receptor status				0.91[b]
ER+/PR+	75(55.6)	39(52.0)	99(52.9)	
ER+/PR−	10(7.4)	8(10.7)	12(6.4)	
ER−/PR+	19(14.1)	11(14.7)	33(17.7)	
ER−/PR−	31(23.0)	17(22.7)	43(23.0)	

BMI stands for body mass index; CT stands for chemotherapy; RT stands for radiation therapy; CCRT stands for concurrent chemoradiation; LNM stands for lymph node metastasis; TD stands for tumor diameter; I stands for invasion; E stands for extension; LVSI stands for lympho-vascular space invasion; AI stands for lymph node involvement; PPC stands for positive peritoneal cytology; ER stands for estrogen receptor; PR stands for progesterone receptor; Column percentages are represented by figures in parentheses; ANOVA test p-values are computed; The chi-square test is used to get b p-values; c After missing data are removed, percentages are calculated.

The mean BMI of patients and controls was 25.174.31 kg/m2 and 23.203.05 kg/m2, respectively (pb0.0001). Figure 1 depicts the association between overweightness and the risk of ovarian cancer. The obese women had a median value of 27.41 kg/m2 (range 25.0–49.7 kg/m2). Obese women (BMI 25 kg/m2) had a more than three-fold higher risk of developing ovarian cancer than non-obese women (BMI b23 kg/m2) (OR=3.161, 95 percent CI=2.655–3.763). Overweight women (23 kg/m2BMIb25 kg/m2) had a higher risk than non-obese women (BMI b23 kg/m2) (OR=1.536, 95 percent CI=1.260–1.873). That is, an increase of 1 kg/m2 increased the incidence of ovarian cancer by 18% (OR=1.181, 95 percent CI=1.155–1.207).

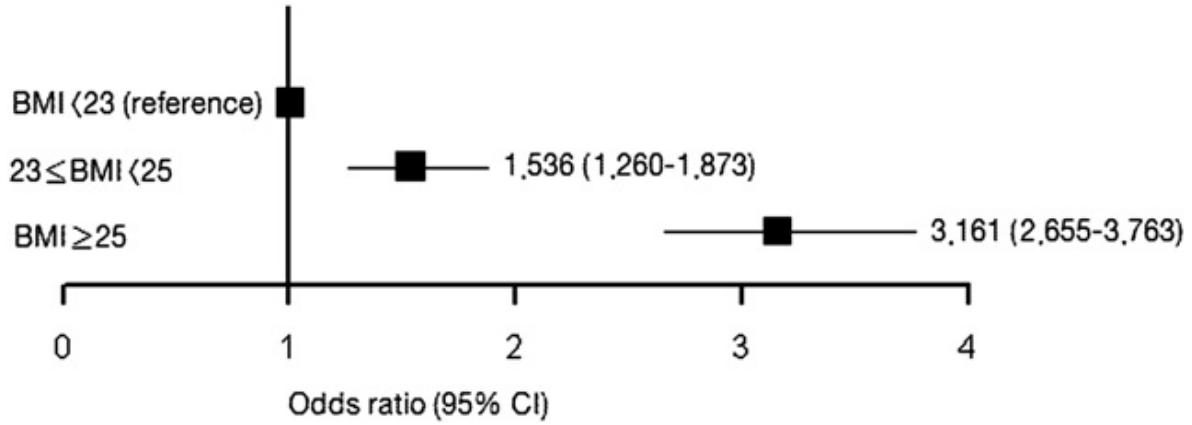

Figure 1 Cancer odds ratios (ORs) based on BMI; conditional logistic regression analysis was conducted, and 95 percent confidence intervals are shown in parentheses.

Furthermore, we investigated if BMI may be a prognostic factor in women with ovarian cancer. Despite the earlier tumor stage detected in the obese women, the Kaplan–Meier analysis demonstrated no significant difference in overall survival across three BMI-based groups: non-obese, overweight, and obese women (log-rank=0.366, df=2, p=0.8328) (Fig. 2). The crude Cox model in Fig. 3 demonstrates that obesity had no effect on patients' overall survival when compared to non-obese women (crude HR=0.82, 95 percent CI=0.40– 1.66). However, there was a statistically significant trend indicating a better prognosis with increasing increments of BMI (p for trend b0.001). A multivariate Cox regression analysis was performed to assess the true effects of incremental increases in BMI on overall survival, including variables such as, tumor grade-tumor stage, -menopause status, -adjuvant treatment, -patient age and LVSI, which were significant prognostic factors based on the results of the univariate Cox regression analysis (data not shown).

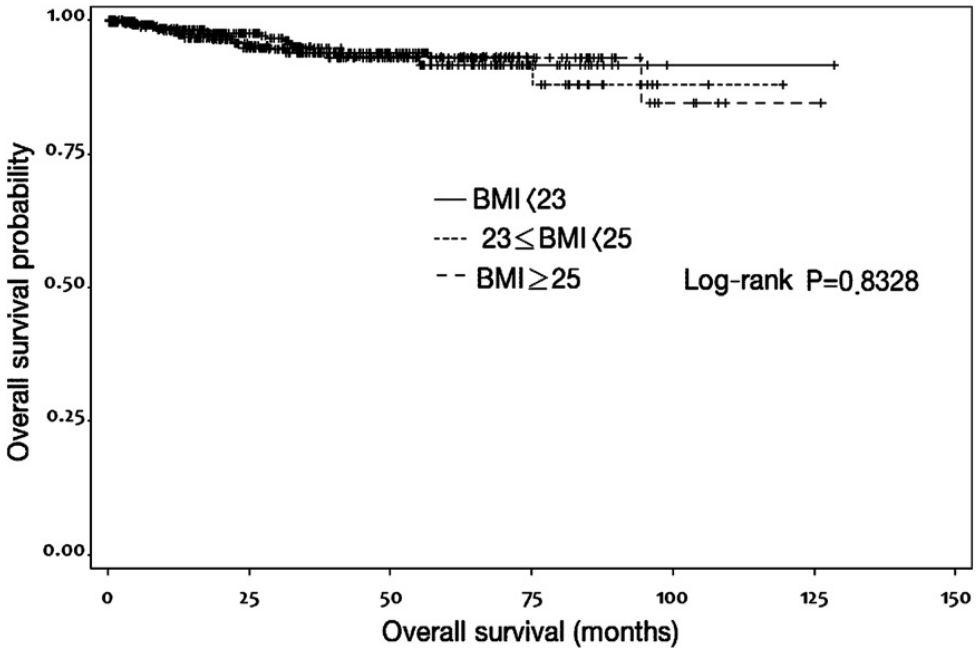

Figure 2 shows a Kaplan–Meier study of overall survival in non-obese, overweight, and obese women.

The multivariate Cox regression analysis did not reveal that BMI was linked with overall survival, and the significance of p for trend is lost after adjusting for the six confounding variables. A stepwise regression of all variables revealed that only stage (HR=3.37, 95 percent CI=1.55–7.35) and LVSI (HR=2.75, 95 percent CI=1.27–5.95) were significant predictors of survival; age, menopause status, tumor grade, and adjuvant treatment provided no significant improvement in prognostic ability. To maximize the probable trend related with increasing BMI increments, an additional Cox regression was conducted (Fig. 4) comparing underweight (b18.5 kg/m2, n=23) and obese women (b25.0 kg/m2, n=433) women. Underweight women had a poorer prognosis than obese women (crude HR=4.21, 95% CI=0.97–18.30, p=0.06). However, in a full model that included BMI and the six covariates, the predictive ability of underweight women was not detected (adjusted HR=3.42, 95 percent CI=0.75–15.57, p=0.11).

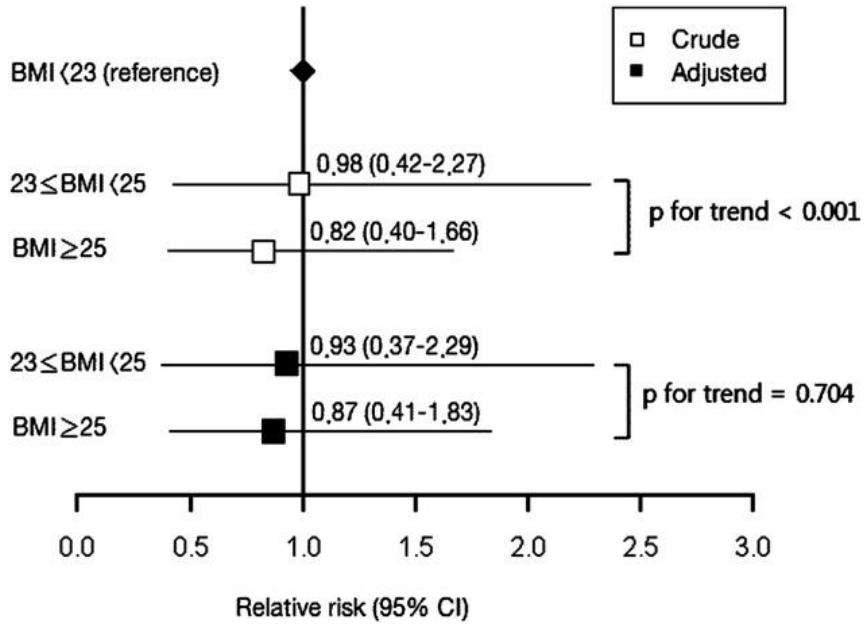

Figure 3 shows the cancer risk ratios (HRs) for non-obese, overweight, and obese women; crude values were calculated using Univariate Cox proportional hazards regression analysis. After correcting for patient age, menopause, tumor stage, grade, adjuvant therapy, and lympho-vascular space invasion, adjusted estimates were produced using multivariate Cox regression analysis.

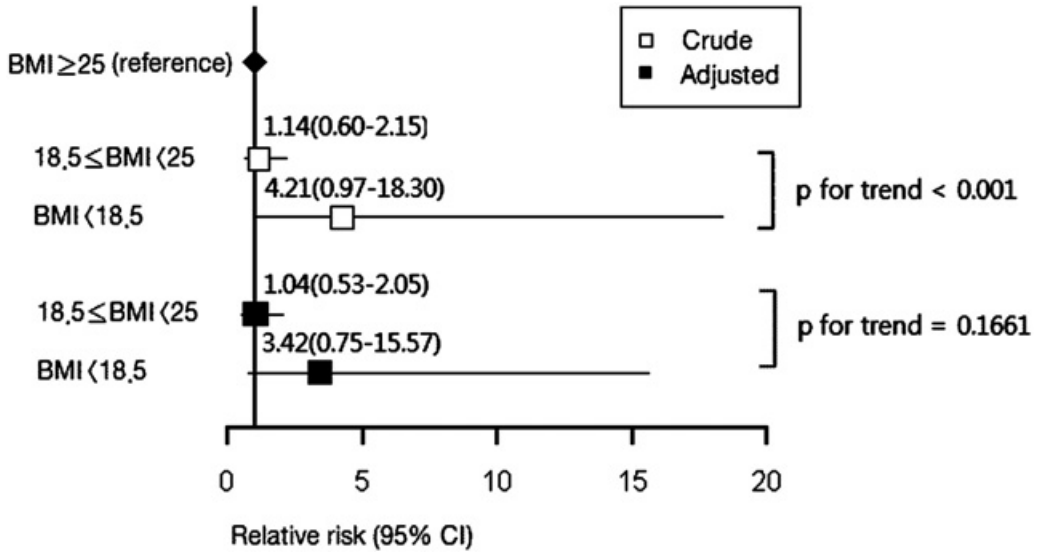

Figure 4 shows the cancer risk ratios (HRs) for underweight, normal-overweight, and obese women;

4. DISCUSSION

In Western research, a BMI of 30 kg/m2 corresponds to the obese category (Ogden et al., 2006). Only 109 (18.4 percent) and seven (0.8 percent) of patients in the current research had BMIs of 30 kg/m2 and 40 kg/m2, respectively, although more than half of Western patients had a BMI of 30 kg/m2 (Gates et al., 2006; Temkin et al., 2007; Anderson et al., 1996). This research group had a lower BMI when compared to Western nations. Given that Asians, such as Koreans, have different BMI patterns than the North American population (Ogden et al., 2006) and that extreme obesity with a BMI of 40 kg/m2 is uncommon in Korea, in the development of ovarian cancer in Asian populations. To evaluate the particular dangers of an Asian population, the Asian-Pacific obesity guidelines were utilized to analyze ovarian cancer risk and prognosis. In the Asian population investigated, we discovered that having a high BMI or being obese was a substantial risk factor for ovarian cancer. Obese women (BMI 25 kg/m2) showed a more than threefold greater incidence of ovarian cancer in this research group compared to non-obese women (BMI b23.0 kg/m2). BMI, on the other hand, had no effect on the overall survival of ovarian cancer patients.

Obesity or a high BMI was revealed to be a risk factor for ovarian cancer in an Asian population, which is consistent with previous research on Western populations (Kaaks et al., 2002; Lindemann et al., 2008; Bjorge et al., 2007; Furberg, 2003; Goodman et al., 1997). We verified the link of BMI with ovarian cancer risk using obesity recommendations for Asian-Pacific populations, and discovered that not only obese but also overweight women were at risk for disease development (IARC, 2000). To yet, it is unclear if obesity affects the prognosis of ovarian cancer. With the ultimate objective of individualizing cancer therapy, we tried to identify groups with a poorer prognosis depending on BMI. Obese women have a better prognosis for ovarian cancer because they had a greater prevalence of better-differentiated, more common ovarian histology, less invasive adenocarcinomas, a lower frequency of lymph node metastases, and fewer cases with positive cytology (Everett et al., 2003; Pavelka et al., 2004). Furthermore, obese individuals had much greater baseline nutritional resources to assist them cope with the adverse effects of metastatic illness and tumor cachexia (Van Cutsem & Arends, 2005).

Obese women, on the other hand, may be at a greater risk of overall mortality, mostly from cardiovascular reasons (Adams et al., 2006). One recent investigation found that obese individuals had a considerable prognostic benefit. Munstedt et al., (2008) reported that obesity impacted overall survival positively in a retrospective analysis of 1180 ovarian malignancies. Other researchers, however, have not corroborated this (von Gruenigen et al., 2006; Gates et al., 2006; Temkin et al., 2007; Anderson et al., 1996). Our research found no link between BMI and the prognosis of ovarian cancer in an Asian population, contradicting earlier studies that found a link between BMI and the prognosis of ovarian cancer. After multivariate corrections, the minor tendency toward a better prognosis among obese patients was no longer apparent, and this finding was supported by the Cox regression comparing underweight, normal-overweight, and obese women (Fig. 4). As a consequence, our data indicated that the identified confounders contributed to the poor prognosis of underweight women.

Furthermore, while using BMI as a prognosticator, we observed the features of our research population in comparison to previous studies (Munstedt et al., 2008; von Gruenigen et al., 2006; Gates et al., 2006; Temkin et al., 2007; Anderson et al., 1996). We included only ovarian histology in our study to enhance any conclusions by excluding other histology. Obese patients (46.2%) did not have a more differentiated histology or were younger; nonetheless, they had more early stage disease than the non-obese group. The selection bias of the control participants, as well as the dearth of epidemiologic data on the study population, must be addressed when interpreting our findings. In this research, the controls were NHIC program members, whereas the cases were hospitalized. Our community controls might be representative of the whole Korean population. Furthermore, the case and control groups were collected in the same location and roughly at the same time, with a significant number of age-matched controls.

Strength of this research was that almost 80% of the patients had a complete lymphadenectomy, and the mean number of retrieved nodes for each BMI-based group was comparable. This article was cloned from a recent research which was conducted on Korean women diagnosed with endometrioid uterine cancer (Jeong et al., 2010). We did something similar to artistic projection as creating a hypothetical research on Saudi women in preparation for finding a relationship between excess weight and ovarian cancer and opening the door to implementing this research hypothesis on the ground by other researchers who have a plenty of resources, time, money and effort. This kind of pseudo research is a new modality allowing the young burnt-out clinicians not to be deprived from promotion.

5. CONCLUSION

In conclusion, our data demonstrated that having a high BMI or being obese was a major risk factor for ovarian cancer in a Saudi population, although it was not connected with overall survival. Despite the fact that the patient was obese, a comprehensive lymphadenectomy appeared to have been accomplished. This shows that obese women have a lower proclivity for under staging.

Because the surgery was conducted by gynecological oncologists, the staging was correct and thorough monitoring was given. The results for the survival study came from patient information based on sufficient treatment and follow-up.

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Author Contributions

Details of contribution of each author regard manuscript writing and preparation first, second and third.

Ethical approval

The study was approved by the Medical Ethics Committee of King Saïd University (Ethical clearance number (#139-76-KSUMC/IRB)).

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Conflict of interests

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

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