Research in Oncology
December 2016; Vol. 12, No. 2: 54-59
DOI: 10.21608/resoncol.2017.223.1007

Original Article

Effect of Body Mass Index on Survival in Patients with Epithelial Ovarian Cancer

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Introduction: Higher body mass index (BMI) is an independent and well-established prognostic factor in hormone-related cancers, such as breast and endometrial cancer. As a hormone-dependent cancer, ovarian cancer, however, has been linked inconsistently to obesity.
Aim: This work aimed to assess the association between BMI and ovarian cancer survival.
Methods: This retrospective study included 66 patients who were treated for epithelial ovarian cancer from January 2011 to April 2014. Clinical and epidemiological characteristics of patients were collected.
Time to progression and overall survival were calculated. BMI was calculated using the formula weight in kilograms divided by the square of the height in meters, and categorized according to World Health Organization classification.
Results: BMI indicated underweight in 3 patients (4.5%), healthy weight range in11 (16.7%), pre-obesity in 17 (25.8%), obesity class I in 13 (19.7%), obesity class II in 8 (12.1%) and obesity class III in 14 (21.2%). BMI did not associate significantly with disease stage (p=0.54), pathology (p=0.82), initial CA-125 level (p=0.61), platinum sensitivity (p=0.27), time to progression (p=0.58) or overall survival (p=0.87).
Conclusion: Our results suggest prevalence of obesity (relatively high) among Egyptian patients with epithelial ovarian cancer. Noteworthy, BMI had no significant association with disease stage, platinum sensitivity, time-to-progression or overall survival in the studied group.

Key words: Ovarian Carcinoma, Body mass index, Survival

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Submitted: 27-August-2016, **Revised: 6-**October-2016**, Accepted: 6-**November-2016

INTRODUCTION

Ovarian cancer is the sixth most commonly diagnosed gynecologic tumor and constitutes a leading cause of mortality within this group of tumors[1]. This is because of its typically insidious onset and late diagnosis. Subsequently, only about 40% of women with ovarian cancer can be still alive more than 5 years post-diagnosis[2].

This poor survival is largely attributable to the fact that most cases of ovarian cancer in developing countries are diagnosed with advanced stage[3].

In Egypt, ovarian cancer represents 4.7% of all female cancers. It is ranked as the third and comprises 40.7% of all gynecologic cancers[4].

Risk factors such as obesity, commonly measured by body mass index (BMI), have been found to associate with poorer survival in a number of cancers including breast, prostate, and colorectal cancer[5].

Relation between obesity and epithelial ovarian cancer is still unclear. It is hypothesized that elevated androgen level mediated by obesity in the presence of certain androgen receptor polymorphisms might promote aggressive epithelial ovarian cancer biology[6].

This study aimed to assess the association between BMI and survival in Egyptian patients with epithelial ovarian cancer.

METHODS

This retrospective study was carried out on patients with epithelial ovarian cancer at the Oncology Department, Faculty of Medicine, Menoufia University. .

In the study period, from January 2011 to April 2014, a total of 87 patients were enrolled, but the clinical data completed only for 66 (76%) patients.

The collected data include patients' personal and clinical characteristics (age, performance status, weight, height, co-morbidities, parity and surgical interference), in addition to the disease characteristics, baseline investigations, treatment course, time to progression (TTP) and overall survival (OS).

Standing height was determined without shoes using Harpenden stadiometer (to the nearest 0.1 Cm).. Weight was measured using a digital scale (to the nearest 0.1 Kg) wearing light clothing and without shoes. BMI was calculated using the formula weight (in kilograms) divided by height (in meters) squared.

The World Health Organization classification of BMI[7] was used to classify patients as shown in Table 1.

Results were collected, tabulated and statistically analyzed by an IBM compatible personal computer with SPSS statistical package version 20 (IBM SPSS statistics for Windows, version 20.0, Armnok, NY: IBM Corp.).

Descriptive statistics were expressed in number (No), percentage (%), mean ($\bar{x}$) and standard deviation (SD). For quantitative variables, Student's *t*-test was used for comparison between two groups of normally distributed data, while Mann-Whitney's test was used in the case of abnormal distribution. ANOVA test was used for comparison of quantitative variables between more than two groups of normally distributed data with LSD test as post Hoc test; while Kruskal Wallis test was used for comparison of quantitative variables between more than two groups of abnormally distributed data with Tamhane's test as a post hoc test. The correlation between two continuous variables was tested using Pearson correlation for normally-distributed data and Spearman correlation for abnormally-distributed data. Chi-square test (χ^2) was used to study association between qualitative variables. Whenever any of the expected cells were less than five, Fischer's exact test was used. Kaplan-Meier method was used for survival analysis and Log rank was used to test the significance of difference in survival between groups.

RESULTS

The included 66 patients' age ranged from 23 to 73 years and their BMI ranged from 17.6 to 48.1. More than half of patients were obese (BMI ≥30). Patients' characteristics are shown in Table 2.

Disease characteristics are shown in Table 3. Serous adenocarcinoma was the commonest pathology among the studied group (80.3%). Fifty two patients (78.8%) had elevated tumor marker CA-125 at presentation.

Table 4 shows the relationship between some of the studied variables and BMI. The average BMI did not differ significantly according to any of these variables.

Thirty seven patients (56%) were followed up until death. The estimated median OS of the whole group of patients was 47 months (95%CI: 37.25 – 56.74).

Table 5 shows the relation between OS and some of the studied variables. Overall survival was significantly better in patients with platinum sensitive tumors, those who underwent surgery (at presentation or interval) and those with normal CA-125 level at presentation.

On comparing OS and TTP of patients with BMI ≤25 and patients with BMI >25, no statistically significant difference was obtained between the two groups (*p*-value = 0.93 for both). Kaplan Meier curve for OS and PFS in these two groups are shown in figures 1 and 2.

The estimated median OS of patients with a BMI ≤25 was 50 months (95%CI: 19.75 – 80.24) while that of those with a BMI >25 was 42 months (95% CI: 33.51 – 50.48).

The estimated median TTP of patients with a BMI ≤25 was 18 months (95%CI: 0 – 41.83) while that of those with a BMI >25 was 23 months (95% CI: 15.24 – 30.75).

There was no statistically significant difference between the different categories of BMI as regards to OS and TTP as shown in Table 6. Kaplan Meier curves showing OS and TTP in different BMI categories are shown in figures 3 and 4.

Table 1: The International Classification of adult underweight, overweight and obesity according to BMI[7].

Classification	BMI (kg/m²)
Underweight	<18.5
Normal range	18.5 – 24.99
Overweight	
Pre-obese	25 – 29.99
Obese	
Obese class I	30 – 34.99
Obese class II	35 – 39.99
Obese class III	≥ 40

Table 2: Patients' characteristics.

	Mean ±SD,	Range
Age (years)	52.19 ± 10.9	23 - 73
Weight (kg)	78.27 ± 20.16	39 - 125
Height (cm)	156.93 ± 6.36	145 - 178
Body mass index	31.75 ± 7.93	17.6 - 48.1
	No.	**%**
Parity		
Multipara	53	80.3
Nullipara	13	19.7
Co-morbidities		
Hypertension	10	15.2
Diabetes	5	7.6
Diabetes & hypertension	3	4.5
None	48	72.7
ECOG performance status		
0	22	33.3
1	33	50
2	10	15.2
3	1	1.5
Time of surgery		
Initial	35	53
Interval	16	24.2
None	15	27.7
Result of surgery		
Optimal	14	21.2
Suboptimal	37	56.1
Body mass index groups		
Underweight	3	4.5
Normal range	11	16.7
Pre-obese	17	25.8
Obesity class I	13	19.7
Obesity class II	8	12.1
Obesity class III	14	21.2

ECOG: *Eastern Cooperative Oncology Group*

Table 3: Disease characteristics.

	No.	%
Laterality		
Unilateral	33	50
Bilateral	33	50
Stage		
I	15	22.7
II	7	10.6
III	24	36.4
IV	20	30.3
Platinum sensitivity		
Sensitive	48	72.7
Resistant	18	27.3
Pathology subtype		
Serous adenocarcinoma	53	80.3
Mucinous adenocarcinoma	6	9.1
Endometroid	7	10.6
CA-125 initial level		
Normal	14	21.2
Elevated	52	78.8

Table 4: Comparison between different aspects of characteristics regarding BMI.

	BMI (Mean± SD)	P-value
Stage		
I	32.55 ± 7.37	0.54
II	30.48 ± 6.42	
III	30.90 ± 7.45	
IV	32.61 ± 0/59	
Platinum Sensitivity		
Sensitive	32.40 ± 7.58	0.27
Resistant	30.01 ± 8.78	
Pathological subtypes		
Serous adenocarcinoma	31.99 ± 7.59	0.82
Mucinous adenocarcinoma	31.23 ± 6.36	
Endometroid	30.35 ± 12.02	
CA-125 initial level		
Normal	32.93 ± 7.92	0.61
Elevated	31.43 ± 7.98	
Parity		
Multipara	32.72 ± 7.82	0.06
Nullipara	28.18 ± 7.38	
Co-morbidities		
Hypertension	33.11 ± 5.94	0.09
Diabetes	40.12 ± 7.65	
Hypertension & diabetes	32.86 ± 8.28	
None	30.53 ± 7.93	
Time of surgery		
Initial	32.10 ± 1.49	0.75
Interval	30.46 ± 5.55	
None	32.30 ± 8.09	

Table 5: Overall survival (OS) according to different risk factors.

	Estimated median OS	SE	95% CI	P-value
Platinum Sensitivity				
Sensitive	50	5.82	38.59 – 61.4	<0.001
Resistant	11	3.18	4.76 – 17.23	
Pathology				
Serous adenocarcinoma	39	4.30	30.57 – 47.42	0.09
Mucinous adenocarcinoma	-	-	-	
Endometroid	59	9.41	40.53 – 77.46	
Time of surgery				
Initial	49	5.15	38.9 – 59.1	<0.001
Interval	56	9.87	36.65 – 75.34	
None	11	1.93	7.21 – 14.78	
Stage				
I	71	28.57	15 – 127	0.60
II	42	11.08	20.27 – 63.72	
III	41	7.45	26.38 – 55.61	
IV	49	8.38	32.55 – 65.44	
Ca-125 initial level				
Normal	71	15.56	40.48 – 101.51	0.01
Elevated	41	3.25	34.62 – 47.37	

Table 6: Estimated overall survival and time to progression according to BMI.

	Overall survival (months)				Time to progression (months)			
	Median	SE	95% CI	P-value	Median	SE	95% CI	P-value
Underweight	59	0	---	0.87	8	1.63	4.79 – 11.2	0.58
Normal range	50	26	31.61 – 100.96		38	17.94	2.82 – 73.18	
Pre-obese	43	5.8	11.18 – 54.38		18	6.86	4.55 – 31.44	
Obesity class I	47	18.27	0 – 82.81		23	4.95	13.28 – 32.71	
Obesity class II	69	43.22	22.68 – 153.71		29	15.71	0 – 59.79	
Obesity class III	39	8.32	22.68 – 55.31		19	7.48	4.33 – 33.66	

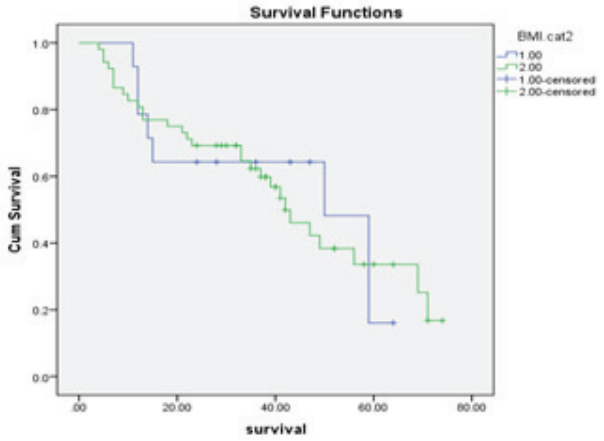

Figure. 1: Kaplan Meier curves showing overall survival of patients with BMI ≤25 and those with BMI >25

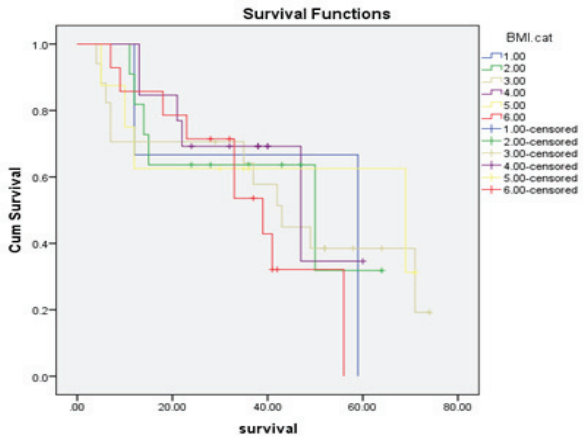

Figure. 3: Kaplan Meier curves showing overall survival of different BMI categories

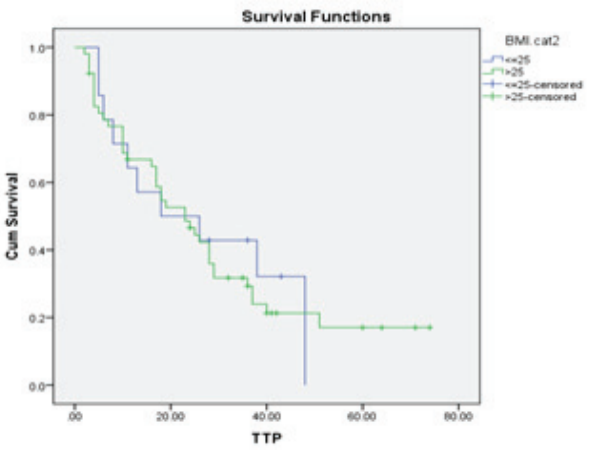

Figure. 2: Kaplan Meier curves showing time to progression of patients with BMI ≤25 and those with BMI >25

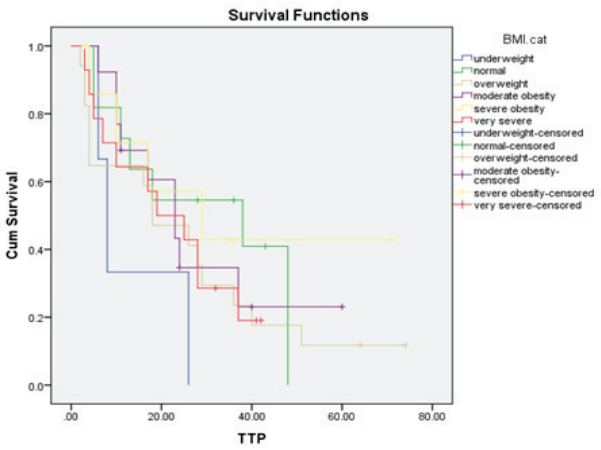

Figure. 4: Kaplan Meier curve showing time to progression of different BMI categories

DISCUSSION

Obesity is an established risk factor for ovarian cancer, and is associated with poor outcome in several tumors like breast cancer and colorectal cancer. However, the relation between obesity and ovarian cancer survival is less clear.

In this retrospective study, we found no statistically significant effect of being obese (≤25BMI) or non obese (BMI > 25) on OS in ovarian cancer patients. Alike, *Matthews et al*[8] found no difference in survival between patients with normal or abnormal BMI provided that complete surgical resection was done. Subsequently, he concluded that BMI was not the main issue; it was the possibility of resection. Also *Zhang et al*[9] found no statistically significant relation between BMI at diagnosis of ovarian cancer and patients' OS.

Our results are consistent with previous studies, whereas no association noted between ovarian cancer survival and being pre-obese or obese[8, 10 -12].

Till now, the adverse effect of obesity on ovarian cancer survival remains equivocal for BMI measured at the time of diagnosis, where *Bae et al*[13] reported that BMI does not influence the survival of advanced stage patients except in underweight patients, which may be related to cancer related cachexia.

Noteworthy, *Tyler et al* studied the impact of BMI on survival of younger patients with epithelial ovarian cancer and also found no association[15].

On the contrary, a recent large study which included the original data of 12,390 patients with ovarian carcinoma from 21 studies revealed that high BMI associated with an adverse effect on survival[16]. Such discrepancy in results may be attributed to the difference in sample size.

In our current study, no significant correlation obtained between BMI and TTP, consistent with previous studies, whereas *Skírnisdóttir* and *Sorbe*[11], *Barrett et al*[17] and *Hew et al*[18] found that TTP was identical in patients with elevated BMI and in those with normal BMI.

Regarding the pathological nature of the tumors and its relation to the BMI of the patients, our results showed an even distribution within the different BMI categories, which agrees with the results of *Bae et al*[13] and *Hew et al*[18].

Similarly, we found no significant association between BMI and the tumor stage in epithelial ovarian cancer patients. This concurs with the results of *Barrett et al*[17] and *Hew et al*[18]. In addition, no significant differences detected in the BMI according to parity, medical history, surgical optimality and initial CA-125, as reported by *Bae et al*[13].

The known prognostic factors in epithelial ovarian cancer (e.g., platinum sensitivity) did not correlate with BMI, as previously reported[18].

CONCLUSIONS

The prevalence of obesity among Egyptian patients with ovarian cancer is relatively high.

Although there is causal relationship between obesity and the development of epithelial ovarian cancers, no significant correlation obtained between BMI and OS and TTP among Egyptian patients. Similarly, there was no significant association between BMI and known prognostic factors in epithelial ovarian cancer.

The prognostic value of obesity remains a controversial issue with no consensus.

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