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Clinico-Epidemiological Study of Epithelial Ovarian Cancer Mansoura Experience

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Abstract: Background & objective: Ovarian cancer is the fifth most common cancer affecting women today. The aim of this retrospective study was to present the epidemiological, pathological, clinical characteristics of epithelial ovarian cancer patients treated at Clinical Oncology and Nuclear Medicine Department, Mansoura University Hospitals in the period between January 2009 and December 2013, with evaluation of progression free survival (PFS) overall survival (OS) and prognostic factors. Patients & methods: This is a retrospective study of epithelial ovarian carcinoma women treated at Clinical Oncology and Nuclear Medicine Department, Mansoura University Hospitals (in the period between January 2009 and December 2013). Data were analyzed after being collected from the patients' medical records. Clinical abstract sheets for all cases were designed. Results: The median age was 55 years (19 – 80 years), 58 patients (39.2%) were ECOG performance status (PS) 1, whereas, 50 patients (33.8%) were PS 0 at presentation. Ninety five patients (64.2%) were postmenopausal at presentation, serous cystadenocarcinoma was the predominant histopathologic type found in 94 patients (63.5%), followed by Endometrioid type (17.5%), 79 patients (53.4%) had stage III disease and 33 patients (22.3%) had stage IV disease. The majority of patients (99 patients 66.9%) had grade III tumors, 140 patients (94.6%) in the study underwent surgical treatment, optimal debulking was done in 85 patients (60.7%), while, suboptimal debulking was done in 55 patients (39.3%), the median overall survival was 49 months, while the median progression free survival was 18 months. Conclusion: the median age was 55 years old, serous carcinoma was the predominant histopathological type. Stage III and IV predominated. Most patients underwent initially surgery followed by adjuvant chemotherapy. The median overall survival & PFS were 49 & 18 months, respectively. Age, tumor histopathology, stage, grade and tumor residue after debulking surgery were significant independent prognostic factors for epithelial ovarian cancer.

Keywords: Ovarian Cancer, Epithelial Tumors, Clinicoepidemiologic Study, Prognostic Factors

1. Introduction

Ovarian cancer is the fifth most common cancer affecting women today, with an increasing rate, specifically in women aged ≥ 65 years [1]. Worldwide each year, more than 152,000 women died from this disease [2].

Ovarian cancer is considered to be the second most common gynecologic malignancy in developed countries, with an incidence of 9.4 per 100,000 women and a mortality rate of 5.1 per 100,000. Worldwide, among the gynecological malignancies, ovarian cancer is the leading cause of mortality in developed countries [3].

In developing countries, it is considered to be the third most common gynecologic malignancy, with an incidence of 5.0 per 100,000 and a mortality rate of 3.1 per 100,000. It is the most common cause of gynecologic cancer death, and the fifth leading cause of cancer death in women [4].

In Egypt, according to the National Population - Based Cancer Registry Program, ovarian carcinoma represents

4.12% of all female malignancies in the period between 2008 – 2011 [5].

Over 90% of ovarian tumours are epithelial ovarian cancer, less common histopathologies, include malignant germ cell neoplasms, carcinosarcomas (malignant mixed Müllerian tumors of the ovary) and sex cord-stromal tumors [2].

The major subtypes of epithelial ovarian cancer include: serous, mucinous, endometrioid, clear cell, and undifferentiated carcinoma [6].

Early diagnosis is very important to improve survival rates but symptoms of ovarian cancer may be non-specific, particularly in the early stages. In addition, there is no routine, simple test to accurately and reliably detect ovarian cancer in the general population. Approximately 70% of women with ovarian cancer are diagnosed at stage III or IV [7].

Primary treatment for ovarian cancer consists of surgical staging and cytoreduction, initial surgery should be a comprehensive staging laparotomy, including a total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO), followed in most patients by systemic chemotherapy, which involves a combination of a platinum and taxane-based chemotherapy (usually carboplatin and paclitaxel) [8].

The aim of this retrospective study was to present the epidemiological, pathological, clinical characteristics of epithelial ovarian cancer patients treated at Clinical Oncology and Nuclear Medicine Department, Mansoura University Hospitals in the period between January 2009 and December 2013, with evaluation of progression free survival (PFS) overall survival (OS) and prognostic factors.

2. Patients & Methods

This is a retrospective analysis of epithelial ovarian carcinoma women treated at Clinical Oncology and Nuclear Medicine Department, Mansoura University Hospitals (in the period between January 2009 and December 2013). Data were analysed after being collected from the patients' medical records.

Clinical abstract sheets for all cases were designed, and the following data were collected: age, ECOG performance status, menstrual status, tumor site, stage, histopathologic type, grade, treatment and tumor residue.

Statistical analysis:

Data were collected, coded, processed and analyzed using SPSS (statistical package for social sciences) version 16. Qualitative data were described using number and percent. Association between categorical variables was tested using Chi-square test ($\chi 2$).

Continuous variables were presented as mean ± SD (standard deviation) and Median (minimum - maximum). The two groups were compared with Student t test (parametric data) P-value considered significant if ≤ 0.05. The survival functions were tested using Kaplan-Meier and log rank test was used as a test of significance.

3. Results

This is a retrospective study which enrolled 148 patients with epithelial ovarian cancer treated at Clinical Oncology and Nuclear Medicine Department, Mansoura University Hospitals in the period between January 2009 and December 2013.

3.1. Patient Characteristics

Patients and tumor characteristics are shown in (table 1).

The median age was 55 years (19 – 80 years), with 78 patients (52.7%) were ≥ 55 years old, and 47.3% were < 55 years old.

Positive family history of ovarian, breast or colon cancers, in first degree relatives, was found in 18 patients (12.2%).

Fifty eight patients (39.2%) were ECOG performance status (PS) 1, whereas, 50 patients (33.8%) were PS 0 at presentation, while 35 patients (23.6%) were PS 2, and only 5 patients (3.4%) were PS 3.

Ninety five patients (64.2%) were postmenopausal at presentation, while 53 patients (35.8%) were premenopausal.

Most patients (80 patients) had bilateral disease (54.1%), and 43 patients (29.1%) had right ovarian cancer, while left ovarian cancer was encountered in 16.8% of cases (25 patients only).

This study showed serous cystadenocarcinoma predominance which was found in 94 patients (63.5%), followed by Endometrioid type (17.5%), then mucinous carcinoma constituted 9.5% and clear cell was found in 9.5% of patients.

Only 15 patients (10.1%) were diagnosed as stage I, whereas 21 patients (14.2%) had stage II disease, while 79 patients (53.4%) had stage III disease and 33 patients (22.3%) had stage IV disease at presentation.

The majority of cases (99 patients 66.9%) had grade III tumors, followed by grade 2 which constituted 24.3% and then grade 1 which constituted only 8.8%.

3.2. Treatment Modalities

As shown in table 2, 140 patients (94.6%) in the study underwent surgical treatment; 120 patients of them (85.7%) underwent early debulking, while 20 patients (14.3%) underwent interval debulking after neoadjuvant chemotherapy.

Optimal debulking was done to 85 patients (60.7%), while, suboptimal debulking was done to 55 patients (39.3%).

All patients received chemotherapy; 109 of them received paclitaxel-carboplatin regimen, and the others received other platinum based regimens.

Twenty eight patients received neoadjuvant chemotherapy.

3.3. Overall Survival and Progression Free Survival

After a median follow up period of 44 months, the median OS was 49 months with a range of (10 - 84 months) and 95% confidence interval, 43.5 to 54.5 months, while, the median progression free survival was 18 months (range 5 - 60 months and 95% CI, 16.6 to 19.4 months) figure 1 & 2.

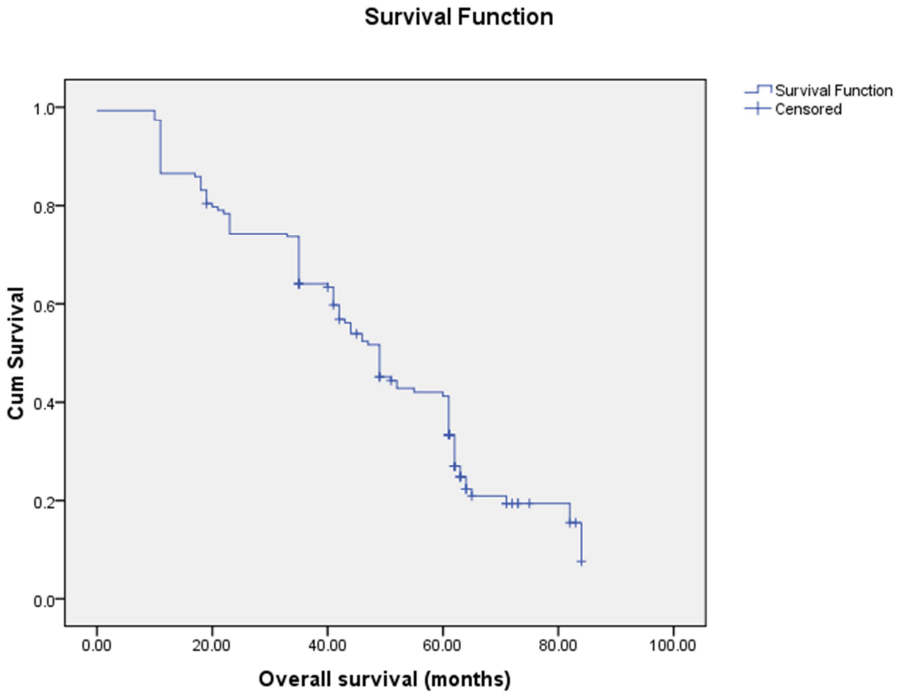

Figure 1. *Kaplan-Meier overall survival curve.*

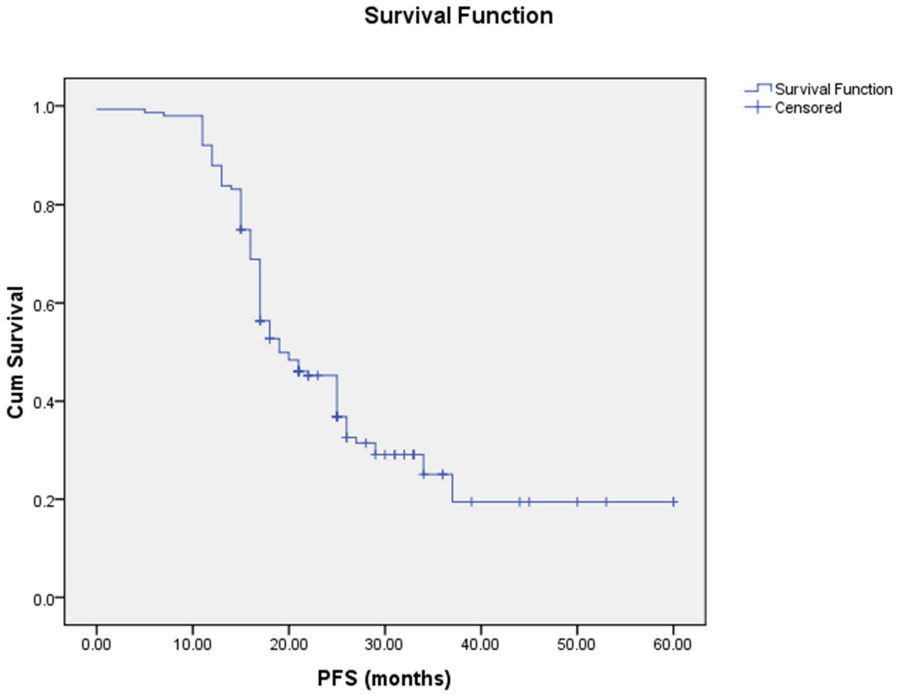

Figure 2. *Kaplan-Meier progression free survival curve.*

Table 1. *Patients and tumor characteristics.*

Characteristics	n= 148 No (%)
Age in years	
Median (minimum - maximum)	55 (19 - 80)
Age < 55 years	78 (52.7%)
Age ≥ 55 years	70 (47.3%)
Family history	
Positive family history	18 (12.2%)
Negative family history	130 (87.8%)
Presentation*	
Abdominal discomfort	110 (74.3%)
Abdominal distension	75 (50.7%)
Less common presentations	24 (16.2%)
ECOG performance status	
PS 0	50 (33.8%)
PS 1	58 (39.2%)
PS 2	35 (23.6%)
PS 3	5 (3.4%)

Characteristics	n= 148 No (%)
Menopausal status	
Premenopausal	53 (35.8%)
Postmenopausal	95 (64.2%)
Site of primary tumor	
Bilateral disease	80 (54.1%)
Right ovary	43 (29.1%)
Left ovary	25 (16.8%)
Histopathological types	
Serous type	94 (63.5%)
Endometrioid type	26 (17.5%)
Mucinous type	14 (9.5%)
Clear cell type	14 (9.5%)
Stage	
Stage I	15 (10.1%)
Stage II	21 (14.2%)
Stage III	79 (53.4%)
Stage IV	33 (22.3%)
Grade	
Grade 1	13 (8.8%)
Grade 2	36 (24.3%)
Grade 3	99 (66.9%)

Table 2. *Treatment modalities.*

Treatment analysis	No (%)
Surgical treatment	
Surgical treatment	140 (94.6%)
No surgery	8 (5.4%)
Surgical timing	
Early debulking	120/140 (85.7%)
Interval debulking	20/140 (14.3%)
Type of debulking surgery	
Optimal debulking	85/140 (60.7%)
Suboptimal debulking	55/140 (39.3%)
Chemotherapy treatment	
Adjuvant chemotherapy	120 (81.1%)
Neoadjuvant chemotherapy	28 (18.9%)

3.4. Correlation of Prognostic Factors with Survival

As shown in table 3, older age was associated with shorter OS and PFS (41 and 17 months respectively) versus (61 and 21 months) with younger age women, and this was statistically significant. We reported a higher overall survival in premenopausal than postmenopausal women (56 months versus 39 months respectively) (figure 3).

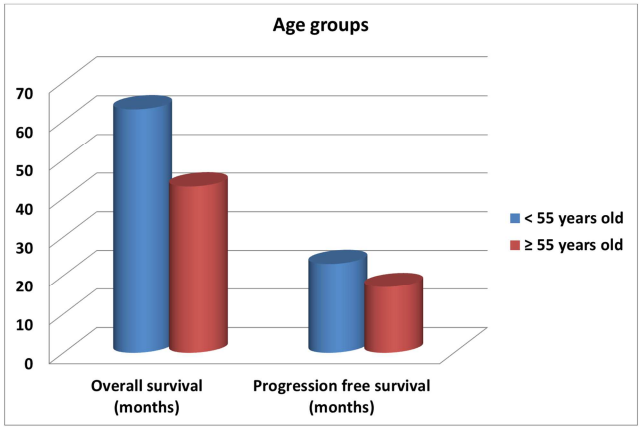

Figure 3. *Overall survival and progression free survival regarding age groups.*

Regarding tumor histopathology; patients with endometrioid type had longer overall survival (57 months) than those with serous type (46 months), patients with mucinous or clear cell types had shorter OS and PFS.

Based on tumor stage, early stages (stage I and II) had better overall survival (73 months and 63 months respectively), while, advanced stages (stage III and IV) expressed shorter overall survival 45 months and 17 months, respectively, and this was a statistically significant (figure 4, 5). Patients with high grade tumors either 2 or 3 were associated with decreased OS and PFS than those with grade 1 (figure 6).

The differences in OS and PFS between the optimal and suboptimal surgical debulking were evident, as OS and PFS with optimal debulking surgery were 61 months and 22 months respectively versus 36 months and 15 months respectively with suboptimal debulking (figure 7).

In the current study, by univariate analysis; age, tumor histopathology, stage, grade and tumor residual after debulking surgery were significant independent prognostic factors for survival, furthermore, tumor residual after debulking surgery was found to be the most significant factor that affected survival by multivariate analysis.

Table 3. *Prognostic factors affecting survival.*

Items	Overall survival		Progression free survival	
	Median (Range) in months	P value	Median (Range) in months	P value
Age groups				
< 55 years old	61 (10 – 84)	0.003*	21 (10 - 60)	0.001*
≥ 55 years old	41 (15 - 73)		17 (11 - 37)	
Menopausal status				
Premenopausal	56 (15 - 84)	0.001*	22 (10 - 60)	<0.001*
Postmenopausal	39 (10 - 75)		17 (11 - 39)	
Histopathological subtypes				
Serous type	46 (10 - 83)	< 0.001*	17 (10 - 55)	0.006*
Endometroid type	57 (15 - 84)		25 (19 - 60)	
Mucinous type	15 (12 - 44)		11 (5 - 23)	
Clear cell type	25 (11 - 38)		12 (10 - 30)	
Stage				
I	73 (55 - 84)	< 0.001*	36 (21 - 60)	< 0.001*
II	63 (36 - 65)		23 (17 - 36)	
III	45 (33 - 62)		18 (7 - 35)	
IV	17 (10 - 22)		12 (5 - 19)	

Items	Overall survival		Progression free survival	
	Median (Range) in months	P value	Median (Range) in months	P value
Grade				
1	65 (33 - 84)		30 (15 - 60)	
2	56 (20 - 75)	< 0.001*	23 (12 - 55)	< 0.001*
3	40 (10 - 60)		17 (10 - 37)	
Surgery				
Optimal debulking	61 (39 - 84)	< 0.001*	22 (12 - 60)	< 0.001*
Suboptimal debulking	36 (10 - 65)		15 (10 - 28)	

* P-value considered significant if ≤ 0.05.

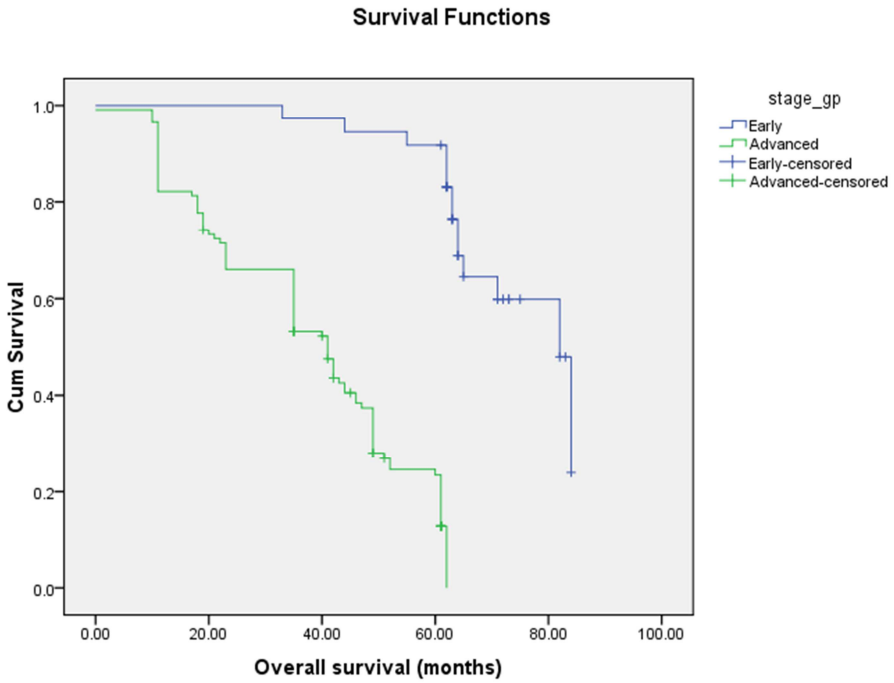

Figure 4. *Kaplan-Meier curve showing statistically significant correlation between overall survival and stage (early stages means I & II, while advanced means III & IV) (P < 0.001).*

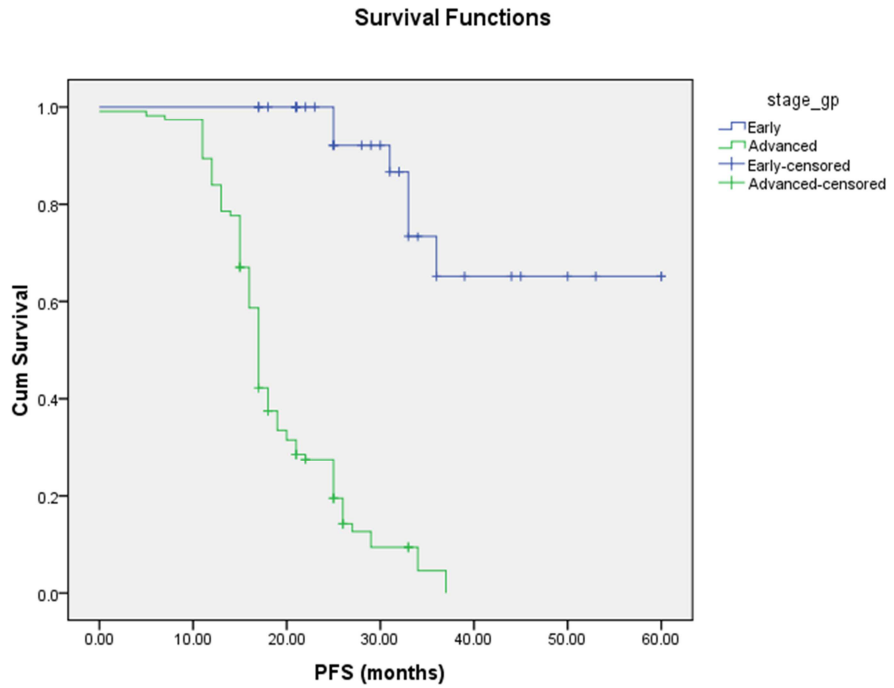

Figure 5. *Kaplan-Meier curve showing statistically significant correlation between progression free survival and stage (early stages means I & II, while advanced means III & IV) (P < 0.001).*

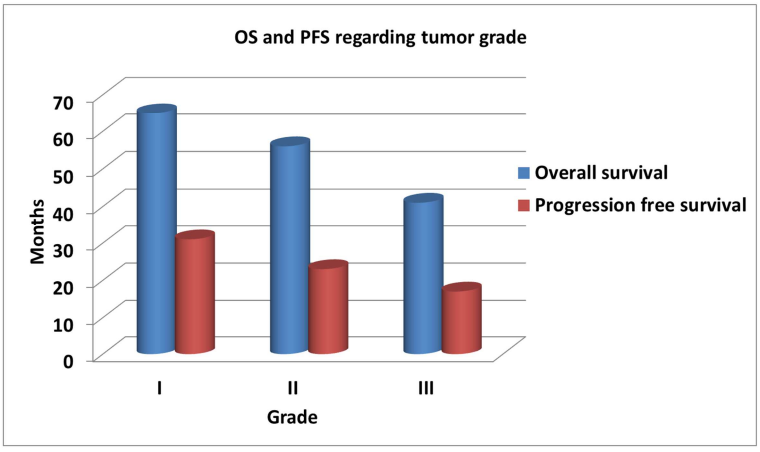

Figure 6. *Overall survival and progression free survival regarding tumor grade.*

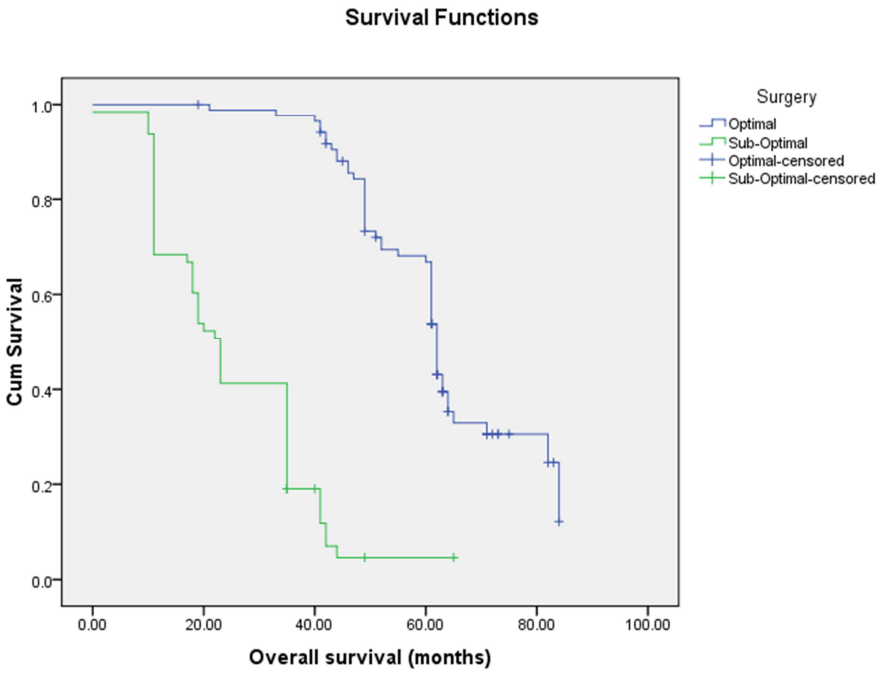

Figure 7. *Kaplan-Meier curve showing statistically significant correlation between overall survival and type of debulking surgery (P < 0.001).*

4. Discussion

This study is a retrospective clinico-epidemiological study that included 148 epithelial ovarian cancer patients treated at the Clinical Oncology & Nuclear Medicine Department, Mansoura University Hospital during the period from January 2009 up to December 2013.

In this study, the mean age was 53.8 ± 12.2 years which cope with *Abdel Aziz et al.* who reported a mean age of 53 years [9]; nearlythe same to a clinico-pathological study that was done in Iran, by *Karimi-Zarchi et al.,* who reported 53.87 ± 14.116 years mean age [10]. Additionally, it is very close to a retrospective study in Brazil which described a mean age of 54.6 years *[11]*.

Most of patients had advanced stage, stage III and IV were encountered in 75.7% of all patients, and this was very close to 78% reported by *Malik* [12], and 79.2% reported by *Mostafa et al.* [13], however, this percentage was lower than that (84.3%) described by *Abdel Aziz et al.* [9], and higher than that (56.2%) reported by *Paes et al* [11].

Among all patients, 91.2% of them had grade II and III disease which is in agreement with 90.5% and 88% reported by *Winter III et al.* [14] and *Nagle et al.*[15] respectively, however, *Abdel Aziz et al.* found that 80.7% of their patients were grade II and III [9], while, *Nassar* reported a percentage of 99.5%[16].

In this study, 85.7% of all patients were treated initially with surgery which is similar to an Egyptian study at Menoufia University, which reported 86.7% of their cases were treated with primary surgical treatment [9].

Sixty percent of the patients of this study underwent optimal debulking surgery (no residual or residual ≤ 1 cm). It is nearly close to 53% reported by Abdel Aziz et al. [9]. In a study evaluating surgery among 115 ovarian cancer patients (stages III and IV) in Netherlands, they found that only 45% of them had optimal surgery [17].

In the current study, the median OS was 49 months which is the same as in a Japanese study [18], additionally; it was very close to 45 months reported by an Egyptian study conducted by Abdel Aziz et al [9].

The median PFS was 18 months which was in agreement with 17 months described by Abdel Aziz et al [9] and Winter III et al [14]. Additionally, it was nearly the same as stated by du Bois et al.(17.9 months) [19]. Furthermore, PFS in different international studies ranged between 11 to 21 months which was in agreement with our result [20-22].

In this study, the 5 years overall survival for all patients was 37% which was found to be slightly lower than Baldwin et al., who reported 44% 5 years overall survival [23]. Wright et al. stated that 5-year OS for ovarian cancer patients increased from 27% in 1958–1962 to 49.7% in 1999 –2001 and increased to 50% for all stages of the disease in 2011 due to improvement of medical care [24].

In our sudy, there was a statistically significant correlation between OS, PFS, and age (p value= 0.003 and 0.001). The median overall survial for younger patients < 55 years was 61 months, while for ≥ 55 years was 41 months. An Egyptian study, reported a statistically significant correlation between OS and age (P = 0.039) [9].

In our study, a significant relation between OS, PFS, and stage was detected (p value = < 0.001). Median OS for stages I, II, III, and IV were 73, 63, 45, and 17 months, respectively; while, median PFS for stages I, II, III, and IV were 36, 23, 18, and 12 months, respectively. This was in agreement with a Abdel Aziz et al. [9] & Teramukai et al. [18], who reported also a statistically significant correlation between OS and stage (p value < 0.001).

Karimi-Zarchi et al. reported also a statistically significant correlation between OS and stage (p value = 0.0377), the mean OS for stage I was 84 months, while for stage IV it was only 10 months; and median OS for stages II and III were 67 and 48.7 months, respectively [10]. These results are very close to ours. Also a statistically significant correlation between both OS and PFS was expressed by a Brazilian retrospective study [11], and also by an Egyptian study, by Nassar et al [16].

In our study, there was a statistically significant correlation between OS, PFS, and tumor grade (p value = < 0.001). The median OS of histological tumor grade 1, 2, and 3 were 65, 56, and 40 months, respectively; while PFS were 30, 23, and 17 months, respectively. Similarly Abdel Aziz et al. reported a significant correlation between PFS and tumor grade (p value = 0.002) [9].

A statistically significant correlation between OS, PFS, and debulking surgery was detected in our study (p value = <0.001). The median overall and progression free survival for patients who had optimally debulked surgery were 61 months and 22 months respectively; while, the median overall and progression free survival for patients who had suboptimally debulked tumor were 36 months and 15 months respectively. Our results were nearly similar to an Egyptian retrospective study at Menoufia University which reported also a statistically significant correlation between OS, PFS, and debulking surgery (P value = 0.036 and 0.003, respectively) [9].

Furthermore, Teramukai et al [18], and Wei et al [25] reported a statistically significant correlation between OS, PFS, and debulking surgery (P < 0.001) which is similar to our results.

5. Conclusion

In this clinicoepidemiologic analysis, the median age was 55 years old, serous carcinoma was the predominant histopathological type. Stage III and IV predominated. Most patients underwent initially surgery followed by adjuvant chemotherapy. Paclitaxel- carboplatin regimen was the commonest chemotherapy used. The median overall survival & PFS were 49 & 18 months, respectively. Age, tumor histopathology, stage, grade and tumor residual after debulking surgery were significant independent prognostic factors for epithelial ovarian cancer. These findings were in accordance with the other national & international trials.

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