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ORIGINAL ARTICLE

Assessment of outcome of Ovarian Cancer Treatment; Retrospective cohort study

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ABSTRACT

Background: When it comes to women with malignant gynecological tumor diagnosis, ovarian cancer (OC) is the most prevalent cause of death. Generally, it ranks as the fifth most common cause of mortality for females.

Objectives: The present study aimed to study the epidemiological characteristics and treatment outcomes of OC cases in the Clinical Oncology and Nuclear Medicine Department at Zagazig University Hospitals.

Methods: This retrospective cohort study targeted seven years from January 2015 to December 2021 and was conducted on 160 medical files of patients with OC from the Clinical Oncology and Nuclear Medicine Department, Zagazig University hospitals. The data of pathological and epidemiological characters and their outcomes were studied.

Results: 66.9% of the studied patients had surgery upfront. The most frequent surgery types were TAH + BSO + Surgical staging (38.3%), TAH+BSO (29.4%), and Fertility-sparing surgery was reported in 7.9% of the cases. Regarding primary chemotherapy (95.6%) of patients had Primary chemotherapy as follows (٢.5%) Neoadjuvant treatment only, (45%) Adjuvant only, (23.7%) had neoadjuvant and adjuvant, (4.4%) Definitive, and (20%) Palliative treatment. Regarding Hormonal treatment ; (6.9%) of patients had Hormonal treatment as follows (1.9%) Adjuvant, (1.3%) Definitive, and (3.7%) salvage for Recurrence. There was a highly significant decrease in all Survival parameters (Local recurrence Free Survival, Regional recurrence Free Survival, Distant metastasis Free Survival, Disease-Free Survival, Progression Free Survival, and Overall survival) as regards an increase in age, Advanced disease & stage and ECOG PS 3, increase in Stage, and Epithelial tumors ($p < 0.01$ respectively). The mean survival time (MST) was significantly reduced in the advanced disease group compared to other clinical presentation groups. MST was significantly reduced in the ECOG-3 group compared to other ECOG PS groups. MST was significantly reduced in the distant metastasis group compared to other extension of disease groups. MST was significantly reduced in the stage IV group compared to other histopathology stage groups. MST was significantly reduced in the serious adverse effects group compared to the no serious adverse effects group.

Conclusion: This study demonstrates that age as an important epidemiological factor, histopathological finding assessment, surgical status, radiological, location, grading, tumor morphology, treatment, outcome, recurrence of tumor, disease-free survival, and overall survival that was collected from patient archives in Clinical Oncology and nuclear medicine department in Zagazig University Hospitals. Therefore, this data can provide preliminary information for upcoming research.

Keywords: treatment, Ovarian cancer, cohort study.

INTRODUCTION

Ovarian cancer (OC) is the primary cause of death among cases diagnosed with gynecological cancer. In addition, it is the fifth leading etiology of death among females [1]. The four most common histological types of epithelial OC are clear cell, endometrioid, serous, and mucinous tumor. Seromucinous and Brenner [2] .

OC is linked to factors related to ovulation, including progesterone, estrogens, and gonadotropin-releasing hormones (GnRHs) [3]. High concentrations of GnRHs throughout ovulation may enhance epithelial proliferation and tumor formation. Furthermore, there is a relationship between OC and the concentrations of estrogen, which vary throughout ovulation [4].

A variety of factors affected the prognosis for people with OC. Good prognostic factors affecting overall survival (OS) are the absence of ascites, parity histopathological type other than clear, or mucinous cells, favorable performance status, early-stage disease, well-differentiated tumor, smaller residual tumor volume following primary surgery, and smaller disease volume before surgical removal [5].

OC is diagnosed and treated using a multimodal strategy, which generally includes surgical and systemic therapy with monoclonal antibodies, chemotherapy, and targeted treatments. Therapeutic techniques for OC are based on the histologic type, stage, and grade of the illness, and usually include combined chemotherapy and surgery [6,7].

The present work aimed to study the epidemiological data and treatment and its outcome of OC patients in the Clinical Oncology and Nuclear Medicine Department at Zagazig University Hospitals.

METHODS

Patients:

This retrospective cohort study targeting seven years from January 2015 to December 2021 and conducted on 160 medical files of patients with OC from the Clinical Oncology and Nuclear Medicine Department, Zagazig University Hospitals, and files with missed data were excluded. The data on pathological and epidemiological characters and their outcomes were collected from 160 cases. The study was conducted after approval of the Institutional Research Board (IRB), Faculty of Medicine, Zagazig University was obtained. Total anonymity of the collected data was maintained throughout the study. The research was conducted under the World Medical Association's Code of Ethics (Helsinki Declaration) for human research.

METHODS

All demographic data, surgical status, location, recurrence, histopathological types, and grades, tumor morphology, treatment, outcome, OS, and disease-free survival have been obtained from case archives at Zagazig University Hospital's Clinical Oncology and Nuclear Medicine Department.

Statistical Analysis:

Data analysis was done with MedCalc version 20 (MedCalc, Ostend, Belgium). Parametric numerical data is represented by mean, standard deviation (± SD), and range. Non-parametric numerical data is represented by median and inter-quartile range (IQR)—the frequency and percentage of non-numerical data. The Mann-Whitney's Test (U test) was used to analyze the statistical significance of the difference in a non-parametric variable between two research groups. The chi-square test was used to examine the relationship between two qualitative variables. The log-rank test (Kaplan-Meier survival curve) was used to assess the statistical significance of the difference between 2 survival curves over time between the two study groups. P-values < 0.05 were considered significant.

RESULTS

The mean age of all cases was (51.5 ± 13) years. Regarding basic clinical data; (86.9%)

of patients were Multipara, (18.8%) had Oral contraceptives, (0.6%) had HRT, and (12.5%) had a Cancer family history. The types of family history and clinical symptoms, signs, and histopathology are presented in Table (1).

Regarding different treatment modalities 66.9% of the studied patients had surgery upfront **(2.5%) of patients** had Neoadjuvant Chemotherapy only, (45%) of patients had Adjuvant Chemotherapy only,(23.7%)had neoadjuvant and adjuvant chemotherapy, (4.4%) definitive and (20%) of patients had Palliative Chemotherapy, and (6.9%) of patients had Hormonal treatment. The types of hormonal and their response, chemotherapy, and toxicity were presented in Table (2).

Regarding the Best Overall Response, Pathological response and Outcome data are presented in Table (3).

Regarding histopathological data; there was a highly significant increase in Stage, and Epithelial tumors were associated with increase mortality rate, in the mortality group; compared to the survived group ($p < 0.01$) (Table 4).

Regarding chemotherapy data, there was a highly significant elevation in Primary chemotherapy, in the mortality group; compared to the survived group ($p < 0.001$). Highly significant increase in Palliative Chemotherapy, Palliative toxicity, Adherence to Palliative, Palliative Interruption, and Hospital admission in the mortality group; compared to survived group ($p < 0.05$). There was a highly significant reduction in total carbo dose, Adjuvant Chemotherapy, in the mortality group; compared to the survived group ($p < 0.05$ respectively). (Table 5).

Concerning the outcome data, there was a highly significant decrease in all Survival parameters, in the mortality group; compared to the survived group ($p < 0.01$ respectively). There was a highly significant reduction in the best overall response, and pathological response, in the mortality group; compared to the survived group ($p< 0.05$). There was a highly significant elevation in distant relapse, and progression, in the mortality group; compared to survived group ($p< 0.05$) (Table 6).

The mean survival time (MST) was significantly decreased in the advanced disease group (38 months); compared to other clinical Presentation groups ($p < 0.0001$). The MST was markedly decreased in the ECOG-3 group (22 months); compared to other ECOG PS groups ($p < 0.0001$). The mean survival time was markedly decreased in the Distant metastasis group (17 months); compared to other Extension of disease groups ($p < 0.0001$). The MST was markedly decreased in the Stage IV group (17 months); compared to other histopathology Stage groups ($p < 0.0001$). The MST was markedly decreased in epithelial and mesenchymal tumor groups (54 and 24 months); compared to other histopathology groups ($p = 0.022$). The MST was markedly increased in neoadjuvant and adjuvant chemotherapy groups (54 and 79 months); compared to other chemotherapy timing groups ($p < 0.0001$). (Table 7).

Table 1: Basic clinical data , symptoms and signs and histopathology among 160 ovarian cancer patients:

Variables		Frequency (%) / Mean ± SD
Age (years)		51.5 ± 13
Multipara	+ve	139 (86.9%)
Oral contraceptive	+ve	30 (18.8%)
HRT	+ve	1 (0.6%)
Cancer family history	+ve	20 (12.5%)
Type of family history cancer	None	140 (87.5%)
	Brain	1 (0.6%)
	Breast	10 (6.2%)
	Colorectal	2 (1.3%)
	Endometrial	1 (0.6%)
	HCC	2 (1.3%)
	Ovarian	3 (1.9%)
	RCC	1 (0.6%)
Weight loss	+ve	20 (12.5%)
Bloating	+ve	10 (6.2%)
Vague abdominal discomfort	+ve	140 (87.5%)
Altered bowel habit	+ve	72 (45%)
Backache	+ve	17 (10.6%)
Nausea & Vomiting	+ve	23 (14.4%)
Vaginal bleeding	+ve	20 (12.5%)
Adnexal mass	+ve	93 (58.1%)
Ascites	+ve	60 (37.5%)
Pleural effusion	+ve	17 (10.6%)
Bowel obstruction	+ve	7 (4.4%)
Hydronephrosis	+ve	7 (4.4%)
Staging at diagnosis	Early disease	57 (35.6%)
	Advanced disease	103 (64.4%)
ECOG PS	0	0 (0%)
	1	85 (53.1%)
	2	66 (41.2%)
	3	9 (5.6%)
Histopathology	Epithelial tumours	137 (85.6%)
	Non epithelial tumours	23 (14.4)
Non epithelial tumors		

Variables		Frequency (%) / Mean ± SD
	Mesenchymal tumours	2 (1.3%)
	Mixed epithelial-mesenchymal	6 (3.7%)
	Sex cord-stromal tumours	8 (5%)
	Mixed sex cord-stromal tumours	0 (0%)
	Germ cell tumours	5 (3.1%)
	Monodermal teratoma and somatic-type tumours	1 (0.6%)
	Germ cell -sex cord-stromal tumours	1 (0.6%)
	Miscellaneous tumours	0 (0%)
	Mesothelial tumours	0 (0%)
Epithelial tumour type	Serous	95 (69.3%)
	Mucinous	26 (19%)
	Endometrioid	13 (9.5%)
	Clear	1 (0.7%)
	Brenner	1 (0.7%)
	Seromucinous	1 (0.7%)

Hormone replacement therapy (HRT). Hepatocellular Carcinoma (HCC). Renal cell carcinoma (RCC), Eastern Cooperative Oncology Group (ECOG). Performance status (PS)

Table 2: Treatment modalities among 160 ovarian cancer patients

Variable		(N=127)^	
		No.	%
Timing of surgery	Upfront	85(66.9%)	
	Post-neoadjuvant	42 (33.1%)	
Type of surgery	TAH+BSO	36 (28.3%)	
	TAH+BSO & Surgical staging	50 (39.4%)	
	Fertility sparing surgery	9 (7.1%)	
	Fertility sparing surgery & Surgical staging	1 (0.8%)	
	Primary Optimal Debulking	4 (3.1%)	
	Primary Suboptimal Debulking	7 (5.5%)	
	Interval debulking	19 (15.0%)	
	TAH + Omental biopsy + Peritoneal lavage	1 (0.8%)	
Neoadjuvant Chemotherapy	+ve	(%٢٦,٢) ٤٢	
	_ve	(%٧٣,٧) ١١٨	
Neoadjuvant Chemotherapy	Taxol+Carbo (3w)	(%١٩,٤) ٣١	
	Taxol+Carbo (w)	(%١,٩) ٣	

Variable		(N=127)^	
		No.	%
regimen	Taxol (w) + Carbo (3w)	٦	(%٣,٧)
	Single agent carboplatin	١	(%٠,٦)
	BEP	١	(%٠,٦)
	Total taxol dose (mg)	٢٥٣,٧ ± ٧٣,٣	
	Total carbo dose (mg)	٤٥٠ ± ١٠٢	
	NAC toxicity	٢٤	(%١٥)
	Adherence to NAC	٣٦	(%٢٢,٥)
	NAC Interruption	٦	(%٣,٧٥)
	Hospital admission (NAC)	٢	(%١,٣)
Adjuvant Chemotherapy	+Ve	١١٠	(%٦٨,٧)
	_ve	٥٠	(%٣١,٢)
Adjuvant Chemotherapy regimen	Taxol+Carbo (3w)	٧٧	(%٤٨,١)
	Taxol+Carbo(w)	٥	(%٣,١)
	Taxol(w)+Carbo(3w)	١٢	(%٧,٥)
	FOLFOX	١	(%٠,٦)
	BEP	٣	(%١,٩)
	EP	١	(%٠,٦)
	Holoxan+adria	٢	(%١,٣)
	Holoxan+vepsid	٤	(%٢,٥)
	Gemzar platinol	١	(%٠,٦)
	Gemzar carboplatin	١	(%٠,٦)
	Endoxan platinol	١	(%٠,٦)
	Platinol vepsid	١	(%٠,٦)
	Adria carboplatin	١	(%٠,٦)
	Total taxol dose (mg)	٢٧٧,٢ ± ١٠٢,٦	
	Total carbo dose (mg)	٤٥٧,٤ ± ١٠١,٦	
	AC toxicity	٨٦	(%٥٣,٧٥)
	Adherence to AC	٩٠	(%٥٦,٢٥)
	AC Interruption	١٠	(%٦,٢٥)
	Hospital admission (AC)	٢٠	(%١٢,٥)
Palliative Chemotherapy	+Ve	٣٢	(%٢٠)
	_ve	١٢٨	(%٨٠)
Palliative Chemotherapy Regimen	Taxol+Carbo (3w)	٢٥	(%١٥,٦)
	Taxol+Carbo(w)	٤	(%٢,٥)
	Taxol(w)+Carbo(3w)	١	(%٠,٦)
	XELOX	١	(%٠,٦)
	Holoxan –vepside	١	(%٠,٦)

Variable		(N=127)^	
		No.	%
	Total taxol dose (mg)	٦٤,٧ ± ٢٦٧,٥	
	Total carbo dose (mg)	١١٠,٦ ± ٤٣٣,٩	
	Palliative toxicity	(%١٨,٧٥) ٣٠	
	Adherence to Palliative	(%١٥,٦) ٢٥	
	Palliative Interruption	(%٤,٣٧) ٧	
	Hospital admission (Palliative)	(%٧,٥) ١٢	
	Hormonal treatment		
Hormonal ttt	+ve _ve	(%٦,٩) ١١ (%٩٣,١) ١٤٩	
Hormonal ttt timing	Adjuvant	(%١,٩) ٣	
	Definitive	(%١,٣) ٢	
	Recurrence ttt	(%٣,٧) ٦	
Hormonal agent	No	(%٩٣,١) ١٤٩	
	Tamoxifen	(%١,٩) ٣	
	Anastrozole	(%١,٩) ٣	
	Letrozole	(%٣,١) ٥	
Response to hormonal	CR	(%٠) ٠	
	PR	(%٠,٦) ١	
	SD	(%١,٩) ٣	
	PD	(%٣,١) ٥	
	Not applicable	(%١,٣) ٢	

Bleomycin, etoposide and platinum (BEP). Neoadjuvant Chemotherapy (NAC). Adjuvant Chemotherapy (AC)

Table (3): Outcome data among 160 ovarian cancer patients:

Variables		Frequency (%) / Mean ± SD
Best Overall Response	CR	(%٦١,٢) ٩٨
	PR	(%٩,٤) ١٥
	SD	(%٢٠,٦) ٣٣
	PD	(%٨,٨) ١٤
	Not applicable	(%٠) ٠
Pathological response	No known neoadjuvant ttt	(%٥٢,٥) ٨٤
	Minimal response (CRS 1)	(%٧,٥) ١٢
	Moderate response (CRS 2)	(%٨,٨) ١٤
	Marked response (CRS 3)	(%١٠) ١٦
Local recurrence		(%٢٧,٥) ٤٤
Local recurrence Free Survival (months)		٢٤,٦ ± ٢٧,٣
Regional recurrence		(%٢١,٢) ٣٤
Regional recurrence Free Survival (months)		٢٣,٦ ± ٢٩,٥

Variables	Frequency (%) / Mean ± SD
Distant relapse	(%٢٦,٩) ٤٣
Distant metastasis Free Survival (months)	٢٢,٣ ± ٢٧,٤
Relapse	(%٣٥) ٥٦
Disease Free Survival (months)	٢١ ± ٢٧,٤
Progression	(%٧٥,٦) ١٢١
Progression Free Survival (months)	٢,٣ ± ١٩,٩
Mortality	(%٦٥) ١٠٤
Overall survival (months)	٢٨,٨ ± ٤٠

Table 4: Comparison between the 2 groups as regards Histopathology data using Chi square test:

Variable		Mortality group (104)	Survived group (56)	Chi square test
				P value
Stage	Stage I	19 (18.3%)	34 (60.7%)	< 0.0001**
	Stage II	3 (2.9%)	1 (1.8%)	
	Stage III	53 (51%)	21 (37.5%)	
	Stage IV	29 (27.9%)	0 (0%)	
Histopathology	Epithelial tumours	97 (93.3%)	40 (71.4%)	= 0.0022**
	Nonepithelial tumours	7 (6.7%)	16 (28.6%)	
	Mesenchymal tumours	2 (1.9%)	0 (0%)	
	Mixed epithelial-mesenchymal	2 (1.9%)	4 (7.1%)	
Non epithelial tumour type	Sex cord-stromal tumours	1 (1%)	7 (12.5%)	
	Mixed sex cord-stromal tumours	0 (0%)	0 (0%)	
	Germ cell tumours	2 (1.9%)	3 (5.4%)	
	Monodermal teratoma	0 (0%)	1 (1.8%)	
	Germ cell -sex cord-stromal tumours	0 (0%)	1 (1.8%)	
	Miscellaneous tumours	0 (0%)	0 (0%)	
	Mesothelial tumours	0 (0%)	0 (0%)	
Epithelial tumour type	Serous	70 (72.2%)	25 (62.5%)	= 0.3034
	Mucinous	17 (17.5%)	9 (22.5%)	
	Endometrioid	9 (9.3%)	4 (10%)	
	Clear	1 (1%)	0 (0%)	
	Brenner	0 (0%)	1 (2.5%)	
	Seromucinous	0 (0%)	1 (2.5%)	
	Undifferentiated	0 (0%)	0 (0%)	

Table 5: Comparison between the 2 groups as regards treatment, neoadjuvant, adjuvant, and palliative Chemotherapy

Variable		Mortality group (104)	Survived group (56)	Student's t test
		Mean ± SD	Mean ± SD	P value
Total taxol dose (mg)		248.6 ± 77.4	262.8 ± 67.3	= 0.570
Total carbo dose (mg)		450 ± 103.9	450 ± 101.9	= 1.000
Variable		Mortality group (104)	Survived group (56)	Chi square test
				P value
Neoadjuvant chemotherapy				
Neoadjuvant Chemotherapy	+ve	27 (26%)	15 (26.8%)	= 0.9103
NAC toxicity	+ve	17 (16.3%)	7 (12.5%)	= 0.5171
Adherence to NAC	+ve	22 (21.2%)	14 (25%)	= 0.5796
NAC Interruption	+ve	4 (3.8%)	2 (3.5%)	= 0.9332
Hospital admission (NAC)	+ve	1 (1%)	1 (1.8%)	= 0.6555
Adjuvant chemotherapy				
Adjuvant Chemotherapy	+ve	62 (59.6%)	48 (85.7%)	= 0.0007**
AC toxicity	+ve	60 (57.7%)	26(46.43%)	= 0.4504
Adherence to AC	+ve	54 (52%)	36 (64.3%)	= 0.4323
AC Interruption	+ve	7 (6.73%)	3(5.36%)	= 0.7480
Hospital admission (AC)	+ve	51 (49%)	10 (17.9%)	= 0.0001**
Palliative chemotherapy				
Palliative Chemotherapy	+ve	٣٢ (٣٠.8%)	0 (0%)	< 0.0001**
Palliative toxicity	+ve	30 (28.8%)	0 (0%)	< 0.0001**
Adherence to Palliative	+ve	25 (24%)	0 (0%)	= 0.0004**
Palliative Interruption	+ve	7(6.7%)	0 (0%)	= 0.049**
Hospital admission	+ve	12 (11.5%)	0 (0%)	= 0.008**
Treatment data				
Primary chemotherapy	+ve	102 (98.1%)	51 (91.1%)	= 0.039*
Chemotherapy timing	No	2 (1.9%)	5 (8.9%)	< 0.0001**
	Neoadjuvant only	2 (1.9%)	2 (3.6%)	
	Adjuvant only	37 (35.6%)	35 (62.5%)	
	Neoadjuvant and adjuvant	25 (24%)	13 (23.2%)	
	Definitive	6 (5.8%)	1 (1.8%)	
	Palliative	32 (30.8%)	0(0%)	
Response to Chemotherapy (CT)	CR	9 (8.7%)	7 (12.5%)	= 0.8784
	PR	9 (8.7%)	5 (8.9%)	
	SD	9 (8.7%)	4 (7.1%)	
	PD	0 (0%)	0 (0%)	
	Not applicable	77 (74%)	40 (71.4%)	

Table 6: Comparison between the 2 groups as regards Outcome data

Variable		Mortality group (104)	Survived group (56)	Student's t test
		Mean ± SD	Mean ± SD	P value
Local recurrence Free Survival (months)		20.4 ± 20	40 ± 26	< 0.001**
Regional recurrence Free Survival (months)		23 ± 19	41.5 ± 26.2	< 0.001**
Distant metastasis Free Survival (months)		20 ± 18.4	41 ± 22.5	< 0.001**
Disease Free Survival (months)		21.6 ± 17.5	38.2 ± 22.9	< 0.001**
Progression Free Survival (months)		10.3 ± 10	37.8 ± 29.4	< 0.001**
Overall survival (months)		30.3 ± 24.6	58.1 ± 27.4	< 0.001**
Variable		Mortality group (104)	Survived group (56)	Chi square test
				P value
Best Overall Response	CR	44 (42.3%)	54 (96.4%)	< 0.0001**
	PR	14 (13.5%)	1 (1.8%)	
	SD	32 (30.8%)	1 (1.8%)	
	PD	14 (13.5%)	0 (0%)	
	Not applicable	0 (0%)	0 (0%)	
Pathological response	No known	45 (43.3%)	39 (69.6%)	= 0.0004**
	(CRS 1)	9 (8.7%)	3 (5.4%)	
	(CRS 2)	9 (8.7%)	5 (8.9%)	
	(CRS 3)	9 (8.7%)	7 (12.5%)	
Local recurrence	+ve	29 (27.9%)	15 (26.8%)	= 0.8823
Regional recurrence	+ve	23 (22.1%)	11 (19.6%)	= 0.7162
Distant relapse	+ve	34 (32.7%)	9 (16.1%)	= 0.024*
Relapse	+ve	36 (34.6%)	20 (35.7%)	= 0.8898
Progression	+ve	98 (94.2%)	23 (41.1%)	< 0.0001**

Table 7: Mean survival time of each Clinical Presentation, ECOG PS, extension of disease, staging, histopathology, and chemotherapy timing groups:

Factor		**Mean ± SE**	**Log-rank test**
Staging at diagnosis	Early disease	98.192±8.245	**P < 0.0001****
	Advanced disease	**38.259**±3.795	
	Overall	**59.707±4.642**	
ECOG PS	ECOG-1	87.017±6.852	**P < 0.0001****
	ECOG-2	27.382±2.345	
	ECOG-3	**22.667±5.379**	
	Overall	**59.707±4.642**	
Extension of disease	Limited to ovaries	98.538±8.507	**P < 0.0001****
	Pelvic extension	56.500±10.109	
	Abdominal extension	47.161±5.267	
	Distant metastasis	**17.690±1.318**	
	Overall	**59.707±4.642**	
Histopathology stage	Stage I	99.116±8.456	**P < 0.0001****
	Stage II	56.500±10.109	
	Stage III	46.137±5.188	
	Stage IV	**17.690±1.318**	

Factor		Mean ± SE	Log-rank test
	Overall	**59.707±4.642**	
Histopathology	**Epithelial tumours**	**54.006±4.633**	**P = 0.022***
	Mesenchymal tumours	**24.500±10.5**	
	Mixed epithelial-mesenchymal	72.667±10.956	
	Sex cord-stromal tumours	86.667±10.070	
	Mixed sex cord-stromal tumours	0±0	
	Germ cell tumours	60.4±12.929	
	Monodermal teratoma and somatic-type tumours	36±0	
	Germ cell -sex cord-stromal tumours	50±0	
	Miscellaneous tumours	0±0	
	Mesothelial tumours	0±0	
	Overall	**59.707±4.642**	
Chemotherapy timing	No	65±3.775	**P < 0.0001****
	Neoadjuvant only	**54±9.950**	
	Adjuvant only	**79.954±7.136**	
	Neoadjuvant and adjuvant	42.519±4.457	
	Definitive	19.286±2.569	
	Palliative	18.031±1.338	
	Overall	**59.707±4.642**	

DISCUSSION

In 2020, OC accounted for 3.4% of newly diagnosed cases of cancer and 4.7% of cancer-related mortality in women globally [8]. By 2040, the global prevalence is anticipated to rise by 37%, with 428,966 new cases and a considerable increase in mortality. It is the seventh most prevalent cancer among women and the ninth most lethal disease globally, consequently being the most deadly gynecological cancer [9].

Our study was conducted on 160 patients with OCs. Our study aimed to study treatment and its outcome in OC cases.

The current findings demonstrated that the mean age of all cases was (51.5 ± 13) years. (86.9%) of patients were Multipara, (18.8%) had Oral contraceptives, (0.6%) had HRT, and (12.5%) had a Cancer family history.

Regarding the type of family history of cancer; (0.6%) of patients had a history of brain cancer, (6.2%) had a history of breast cancer, (1.3%) had a history of colorectal cancer, (0.6%) had a history of endometrial cancer, (1.3%) had a history of HCC cancer, (1.9%) had a history of OC, and (0.6%) had a history of RCC cancer.

Our results were supported by Tufan et al. [10] who aimed for a retrospective assessment of epidemiologic and prognostic characteristics of cases with epithelial OC (EO), and find out the variables that affect OS, they reported that the study comprised 149 individuals with malignant EOCs. The mean age was 52.8 ± 13 years. The majority of the cases were multipara (85.9%).

Along with our results, Meena et al. [11] who aimed to evaluate therapeutic and outcome patterns in EOC, reported that 663 cases with OC were conducted in their study, with a mean age of 50 (±12.85) years, multiparous reported in (92.05%). Otherwise, they reported that (12.9%) with contraception use, (3.46 %) with a family history of malignancy.

Also, Sindiani et al. [12] who aimed to investigate the pathological, clinical, and

operative features of primary EOC, reported that their study comprised 59 cases with primary EOC, with a median age of 54.5 years (range 27-74).

Similarly, Andreou et al. [13] who aimed to evaluate the parameters linked to OS and progression-free survival (PFS) among individuals with OC, reported that 106 cases participated in their investigation, with a median age of 58 years at the time of diagnosis.

While, Chi et al. [14] who aimed to assess the prognostic factors in advanced epithelial ovarian carcinoma, they reported that among 282 patients there were 146(51.7%) patients with a family history of cancer

Regarding Clinical symptoms and signs; we found that (12.5%) of patients had Weight loss, (6.2%) had Bloating, (87.5%) had Vague abdominal discomfort, (45%) had Altered bowel habits, (10.6%) had Backache, (14.4%) had Nausea & Vomiting, (58.1%) had Adnexal mass, (37.5%) had Ascites, (10.6%) had Pleural effusion, (4.4%) had a Bowel obstruction, (12.5%) had Vaginal bleeding, and (4.4%) had Hydronephrosis. Regarding stage at diagnosis; (35.6%) of patients had Early disease, and (64.4%) had advanced disease. Regarding ECOG PS; (53.1%) of patients had ECOG-1, (41.2%) had ECOG-2, and (5.6%) had ECOG-3.

Our results were supported by Dilley et al. [15] who aimed to evaluate OC symptoms and routes to diagnosis and survival, they reported that among women diagnosed with primary tubo-OC, weight loss was reported in (11.7%) of the studied patients. Otherwise, reported that abdominal or pelvic discomfort/pain was reported in (39.5%), increased abdominal size/bloating was reported in (39.2%), change in bowel habit was reported in (20%), vaginal bleeding was reported in (7.7%), nausea was reported in (5.1%), early-stage patients found in (88.5%) and late-stage patients reported in (84%).

On the other hand, Sindiani et al. [12] assumed that distension was reported in 19 (32.2%) of the studied patients, abdominal pain in 30 (50.1%), post-menopausal bleeding in 9 (15.3%), ascites or pleural effusion in 14 (23.7%).

Also, Tufan et al. [10] reported that abdominal distension was reported in 88 (59.1%) of the studied patients, abdominal pain in 31 (20.8%) and vaginal bleeding in 14 (9.4%) of the studied patients.

Furthermore, Meena et al. [11] reported that (ECOG) ≤ 1 was reported in 474 (71.4%) of the studied patients and (ECOG) ≥ 2 was reported in 189 (28.5%).

Regarding Histopathology, (85.6%) of patients had Epithelial tumors, (1.3%) had Mesenchymal tumors, (3.7%) had mixed epithelial-mesenchymal, (5%) had Sex cord-stromal tumors, (3.1%) had Germ cell tumors, (0.6%) had Monodermal teratoma and somatic-type tumors and Germ cell -sex cord-stromal tumors. Regarding Epithelial tumor type, (69.3%) of patients had Serous epithelial tumors, (19%) had Mucinous epithelial tumors, (9.5%) had Endometrioid epithelial tumors, (0.7%) had Clear, Brenner, and Seromucinous epithelial tumors.

This came in accordance with Sindiani et al. [12] who reported thatHigh-grade serous was reported in 43 (72.9%) of the studied patients. Otherwise, Clear cell was reported in 4 (6.8%), Mucinous in 3 (5.1%), Endometrioid in 2 (3.3%), Transitional in 1 (1.7%) and Carcinosarcoma in 1 (As well, Chi et al. [14] who reported that the most common Epithelial tumor type was Serous type, among 282 patients, Serous type reported in 199 of the studied patients, Endometrioid in 46, Clear cell in 19, Mucinous in 10 and Mixed in 8 of the studied patients.

Similarly, Kim et al**.** [16], who aimed to analyze the clinicopathologic characteristics of epithelial ovarian cancer and evaluated the prognostic factors that have an impact

on survival of the patients with epithelial ovarian cancer, reported that a total of 147 patients with epithelial ovarian cancer were included in their study, the histopathologic distribution of all the patients was as follows serous type was reported in (57.1%) of the studied patients, mixed type in (3.4%), mucinous type in (15.0%). Otherwise, endometrioid type was reported in (15.0%) and clear cell type (9.5%).

While, Kehoe et al,[17] reported that among 474 patients, regarding histology there were 6 (1%) Mucinous, 16 (3%) endometroid, and 17 (4%) clear cell

Furthermore, Wong et al,[18] who aimed to assess the incidence and mortality of ovarian cancer, and the survival patterns of invasive epithelial ovarian carcinoma in Hong Kong, reported that Sex-cord stromal tumors were reported in (1.1%) of the studied patients and Germ cell tumors was reported in (5.9%) of the studied patients.

Regarding Treatment data; our results showed that (95.6%) of patients had Primary chemotherapy, with (2.5%) had Neoadjuvant treatment, (45%) had Adjuvant treatment, (23.7%) had neoadjuvant and adjuvant, (4.4%) had Definitive treatment, and (20%) had Palliative treatment. Regarding Response to Chemotherapy; (10%) of patients had CR, (8.8%) had PR, and (8.1%) had SD. Regarding Neoadjuvant Chemotherapy; (26.2%) of patients had Neoadjuvant Chemotherapy, with (19.4%) having Taxol+Carbo (3w), (1.9%) had Taxol+Carbo (w), (3.7%) had Taxol (w) + Carbo (3w), with average taxol dose was (253.7 ± 73.3) mg, and average carbo dose was (450 ± 102) mg. Regarding Neoadjuvant Chemotherapy toxicity; (15%) of patients had NAC toxicity, (22.5%) were adherent to NAC, (3.75%) had NAC Interruption, and (1.3%) had Hospital admission. Regarding Adjuvant Chemotherapy; (68.7%) of patients had Adjuvant Chemotherapy, with (48.1%) had Taxol+Carbo (3w), (3.1%) had Taxol+Carbo (w), (7.5%) had Taxol (w) + Carbo (3w), with average taxol dose was (277.2 ± 102.6) mg, and average carbo dose was (457.4 ± 101.6) mg. Regarding Adjuvant Chemotherapy toxicity; (53.75%) of patients had AC toxicity, (56.25%) were adherent to AC, (6.25%) had AC Interruption, and (12.5%) had Hospital admission.

Regarding Palliative Chemotherapy; (20%) of patients had Palliative Chemotherapy, with (15.6%) had Taxol+Carbo (3w), (2.5%) had Taxol+Carbo (w), (0.6%) had Taxol (w) + Carbo (3w), with average taxol dose was (267.5 ± 64.7) mg, and average carbo dose was (433.9 ± 110.6) mg. Regarding Palliative Chemotherapy toxicity; (18.75%) of patients had Palliative toxicity, (15.6%) were adherent to Palliative, (4.37%) had Palliative Interruption, and (7.5%) had Hospital admission.

Our results are in line with Chi et al. [14] who reported that among 282 patients, the primary chemotherapeutic regimens were given to 272 (96.4%) of the studied patients.

Also, Meena et al. [11] reported that regarding Chemotherapy response among 311 patients, Stable disease was reported in 31 (9.9%) of the studied patients, and Palliative treatment was used in 81 (12.2%) of the studied patients. Otherwise, they reported that complete response was reported in 90 (28.9%) of the studied patients, Partial response in 155 (49.8%), and Progressive disease in 35 (11.2%).

On the other hand, Kehoe et al. [17] reported that among 550 women with ovarian cancer, there were 274(49.8%) took neoadjuvant chemotherapy.

As well, Kehoe et al. [19] reported that among 474 patients there were 274 (52.1%) took primary chemotherapy, there were 63 (23%) received Carboplatin monotherapy and 210 (77%) received Carboplatin plus paclitaxel.

In addition, Inciura et al. [20] who aimed to compare the impact of the adjuvant and neoadjuvant chemotherapy regimens on the clinical outcomes in patients with advanced ovarian cancer, reported that 574 patients with advanced ovarian cancer, there were 213(37.1%) Neoadjuvant chemotherapy, 361(62.8%) Adjuvant chemotherapy

Furthermore, Dabi et al. [21] reported that 44 (67.7%) of the studied patients received platinum and 40 (61.5%) received taxane.

Regarding Hormonal ttt; our findings revealed that (6.9%) of patients had Hormonal ttt,

(1.9%) had Adjuvant, (1.3%) had Definitive, and (3.7%) had Recurrence treatment. Regarding Hormonal agents; (1.9%) of patients had Tamoxifen and Anastrozole, while (3.1%) had Letrozole. Regarding Response to hormonal treatment; (0%) of patients had CR, (0.6%) had PR, (1.9%) had SD, and (3.1%) had PD. Regarding Adverse effects; (98.1%) of patients had no serious Adverse effects, and (59.4%) had Serious Adverse effects.

Regarding Best Overall Response, (61.2%) of patients had CR, (9.4%) had PR, (20.6%) had SD, (8.8%) had PD. Regarding the Pathological response; (7.5%) of patients had a Minimal response, (8.8%) had a moderate response, and (10%) had a Marked response.

Our results disagree with Okunade et al. [22] who aimed to evaluate risk predictors of early recurrence in women with epithelial ovarian cancer in Lagos, Nigeria., they reported that 81 cases of ovarian cancer, over one half (54.5%) of the recurrence occurred within 12-months of treatment

Also, Dabi et al. [21] reported that in the neo-adjuvant chemotherapy–group, there were 28 (30.8%) had complications.

Regarding Outcome data; our current study showed that (27.5%) of patients had Local recurrence, with average Local recurrence Free Survival of (27.3 ± 24.6) months, (21.2%) had Regional recurrence, with average Regional recurrence Free Survival of (29.5 ± 23.6) months, (26.9%) had Distant relapse, with average Distant metastasis Free Survival of (27.4 ± 22.3) months, (35%) had Relapse, with average Disease-Free Survival of (27.4 ± 21) months, (75.6%) had Progression, with average Progression-Free Survival of (19.9 ± 2.3) months, and (65%) suffered Mortality, with average Overall survival of (40 ± 28.8) months. A comparative study between the 2 groups revealed; a highly significant decrease in all Survival parameters (Local recurrence Survival, Regional recurrence Survival, Distant metastasis Survival, Disease-Free Survival, Progression Free Survival, and Overall survival), in the mortality group; compared to the survived group ($p < 0.01$ respectively).

Our results agreed with Okunade et al. [23] who reported that the median OS (overall survival) was 24 months. Otherwise, they reported that 63 (75.9%) of the studied patients had recurrence within 2 years and death within 2 years was reported in 29 (34.9%).

Our results show a Highly significant increase in stage and epithelial tumors, in the mortality group; compared to the survived group ($p< 0.01$).

Furthermore, Okunade et al. [23] reported that in the death group, there were 17 (32.1%) histotype 2 and 12 (40.0%) histotype 1. There were 12 (29.3%) serum CA125 > 370 U/mL, in the non-death group, there were 36 (67.9%) histotype 2 and 18 (60.0%) histotype 1, there were 29 (70.7%) had serum CA125 > 370 U/mL.

Our results showed a non-significant difference concerning response to chemotherapy ($p > 0.05$). A non-significant difference was detected as regards neoadjuvant chemotherapy ($p > 0.05$).

The current results showed a highly significant elevation in hospital admission in the mortality group ($p< 0.05$). Highly significant reduction in total carbo dose adjuvant chemotherapy in the mortality group; compared to the survived group ($p < 0.05$ respectively). Highly significant increase in palliative chemotherapy, palliative toxicity, adherence to palliative, palliative interruption, and hospital admission, in the mortality group ($p < 0.05$ respectively).

The current results agreed with Okunade et al. [23] who reported that in the death group there were 16 (44.4%) of the studied patients used neoadjuvant chemotherapy, in the non-death group , there were 20 (55.6%) used of the studied patient's neoadjuvant chemotherapy

While Chang et al. [24] reported that the administration of adjuvant chemotherapy did not substantially affect OS ($p = 0.102$).

The present findings revealed a highly significant reduction in all survival parameters, in the mortality group; compared to survived group ($p< 0.01$). Our results showed that there was a highly significant reduction in the best overall response, and pathological response, in the mortality group;

compared to the survived group (p< 0.05). Highly significant elevation in distant relapse, and progression, in the mortality group; compared to the survived group (p< 0.05).

Our results are in line with Winter III et al. [25] who reported that GOG performance status is significantly related to mortality.

Similarly, Assayag et al. [26] concluded that ECOG PS was a significant predictor of overall survival.

Our results showed that MST was markedly reduced in the advanced disease group (38 months); compared to other clinical presentation groups (p < 0.0001). MST was significantly reduced in the ECOG-3 group (22 months); compared to other ECOG PS groups (p < 0.0001). MST was significantly reduced in the distant metastasis group (17 months); compared to other extension of disease groups (p < 0.0001). MST was significantly reduced in the stage IV group (17 months); compared to other histopathology stage groups (p < 0.0001).

Along with our results, Tufan et al. [10] showed that the MST was markedly decreased in the Stage IV group compared to other histopathology stage groups (p<0.001). As well, Meena et al. [11] showed that lower stage of disease significantly related to favorable survival

Furthermore, Okunade et al. [23] assumed that the FIGO stage (early, advanced) of the tumor was associated with survival outcomes. In addition, Dilley et al. [15] demonstrated that the advanced stage is significantly associated with increased mortality

On the other hand, von Gruenigen & Green [27] reported that there was no significant relation between histopathology stage and duration of survival time.

Our findings revealed that the MST was markedly decreased in epithelial and mesenchymal tumor groups (54 and 24 months); compared to other histopathology groups (p = 0.022). The MST was markedly increased in neoadjuvant and adjuvant Chemotherapy groups (54 and 79 months); compared to other chemotherapy timing groups (p < 0.0001).

This came in accordance with Onal et al. [28] who aimed to assess prognostic factors in advanced EOC. They showed that adjuvant chemotherapies were independent variable related to longer survival (p=0.04). Also, Kehoe et al. [19] reported that neoadjuvant chemotherapy was associated with less early mortality. Furthermore, von Gruenigen & Green [27] reported that cases with a shorter survival time demonstrated a tendency toward greater chemotherapy throughout their final three months of life (P=0.057). However, Inciura et al. [20] reported that the application of neoadjuvant chemotherapy, compared to adjuvant chemotherapy, did not influence the OS and progression-free survival.

CONCLUSION

Despite the high frequency of OCs in Egypt, there are few studies have been conducted to evaluate the distribution of OCs based on clinic-epidemiological characteristics. This study demonstrates important demographic data, histopathological assessment, surgical status, radiological, location, grading, tumor morphology, treatment, outcome, recurrence of tumor, disease-free survival, and OS that was collected from patient archives in the Clinical Oncology and nuclear medicine department in Zagazig University Hospitals. Therefore, this data can provide preliminary information for upcoming research.

This study recommended implementing an OCs registry to collect descriptive and survival epidemiological data to follow their incidence and effect on the national health system.

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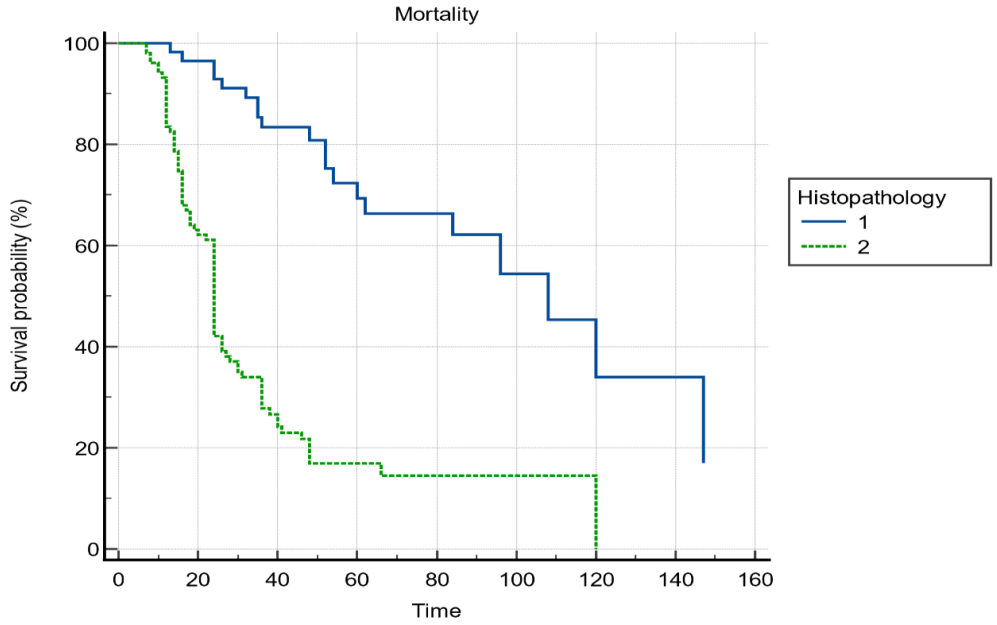

Figure s1: Kaplan-Meier survival curve of Clinical Presentation survivor groups.

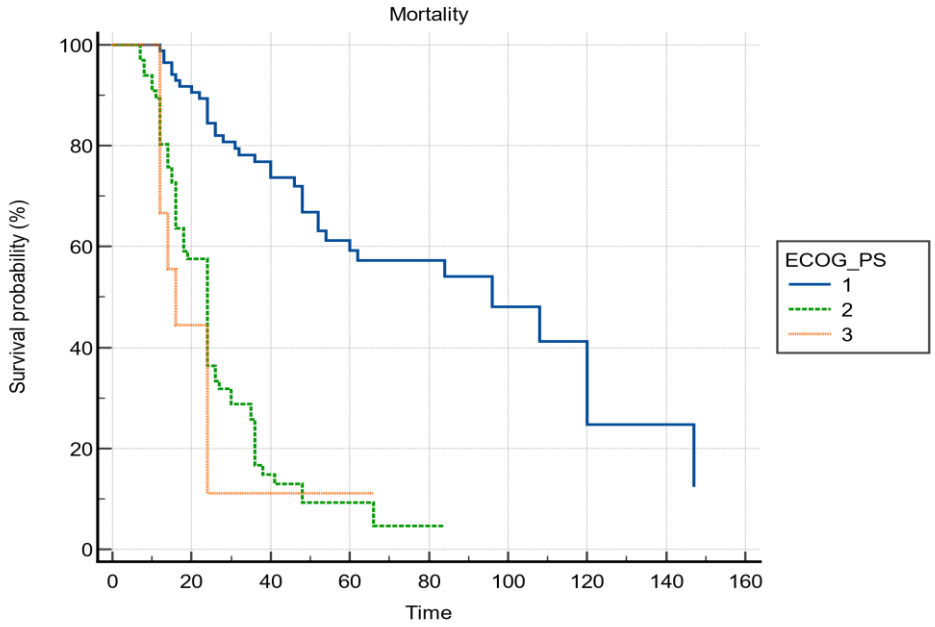

Figure S1: Kaplan-Meier survival curve of ECOG PS survivor groups.

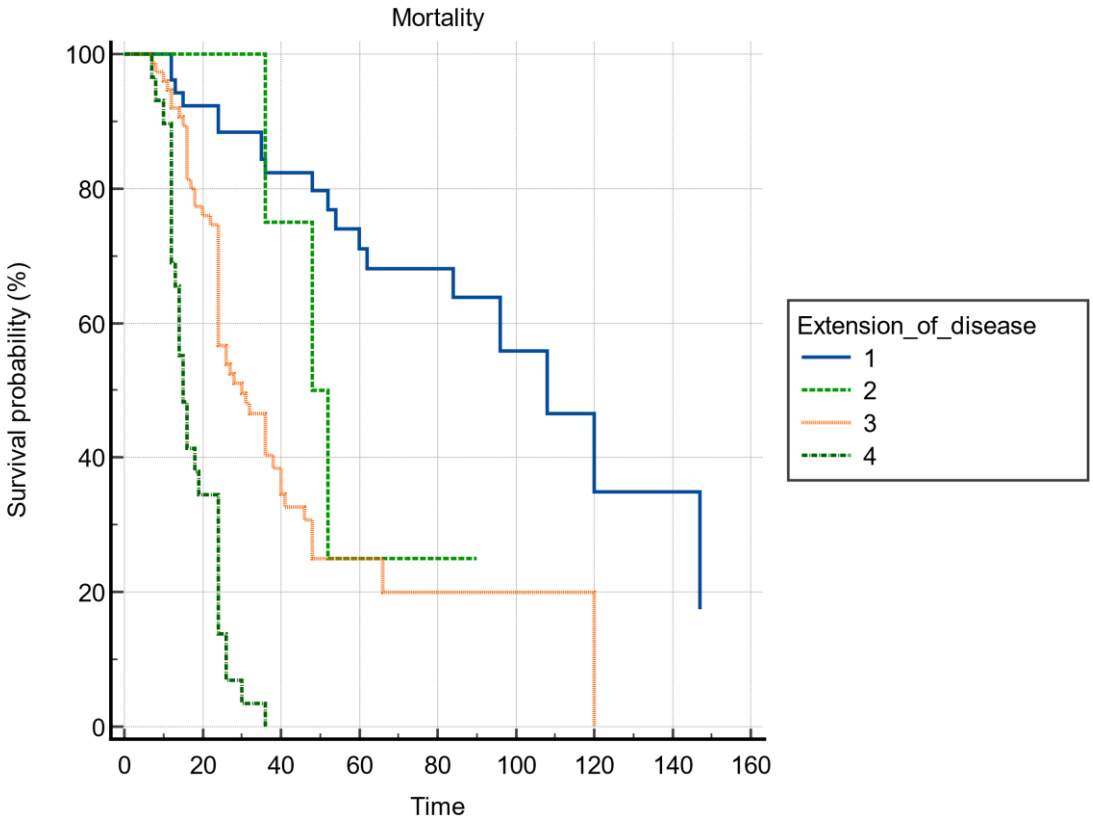

Figure S2: Kaplan-Meier survival curve of Extension of disease survivor groups.

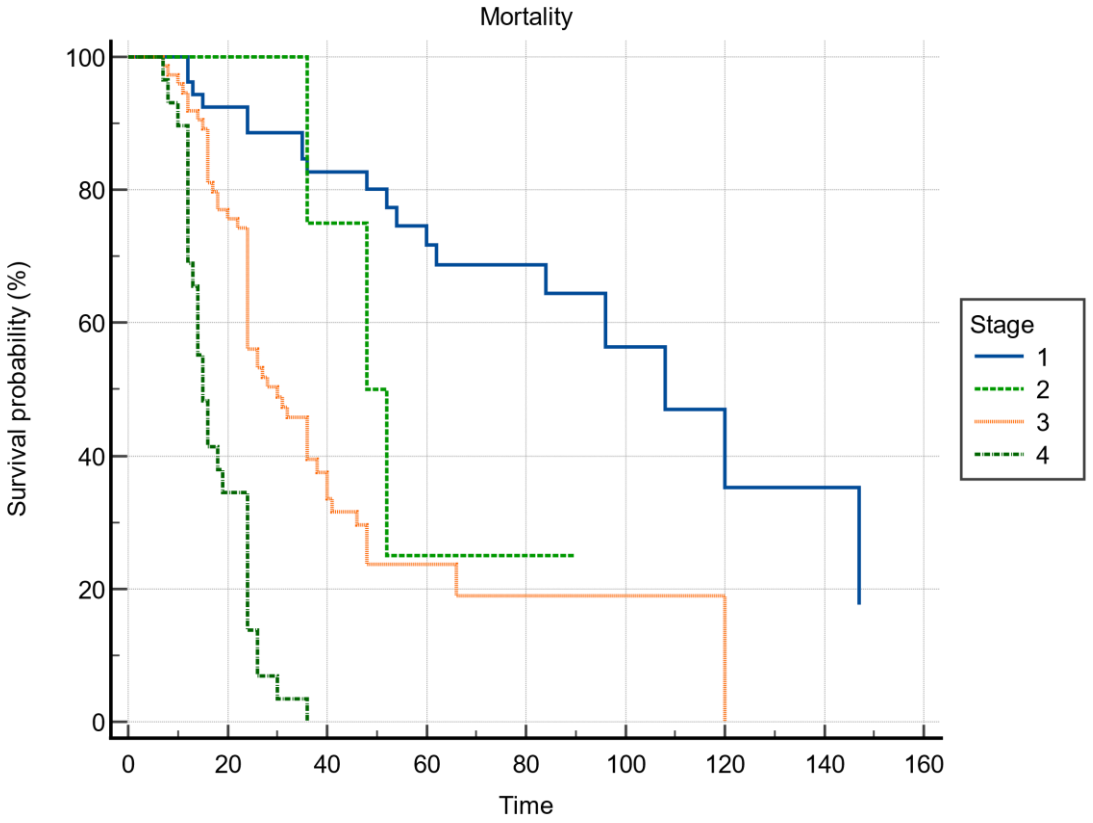

Figure S3: Kaplan-Meier survival curve of Histopathology Stage survivor groups.

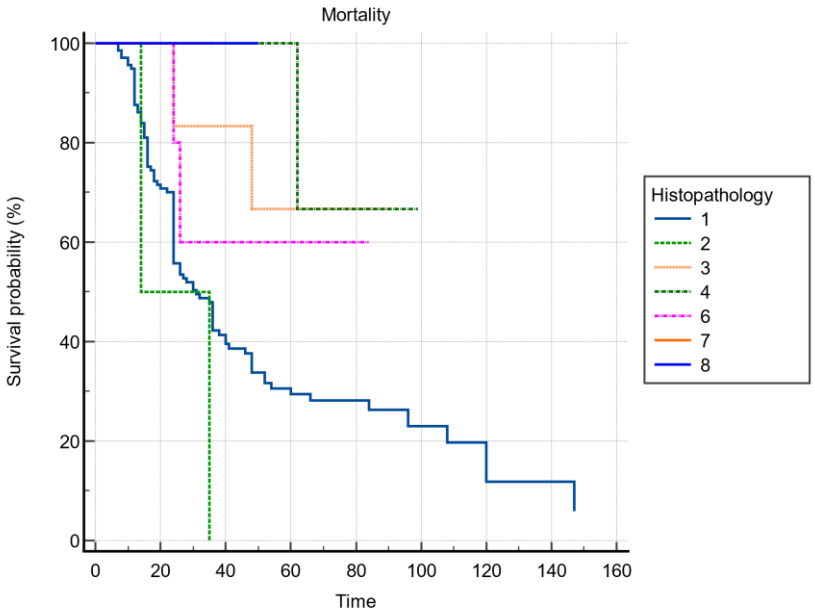

Figure S4: Kaplan-Meier survival curve of Histopathology survivor groups.

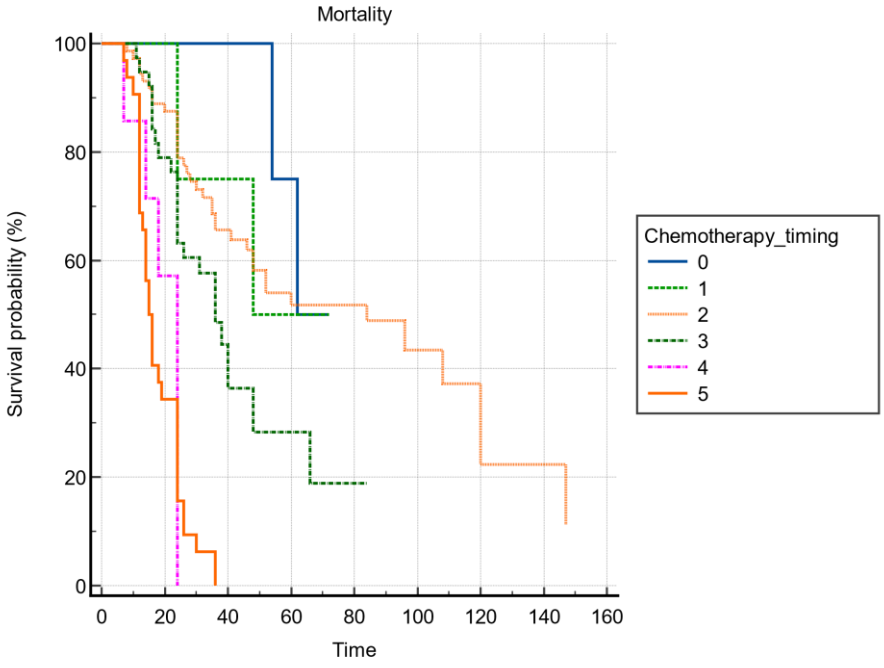

Figure S5: Kaplan-Meier survival curve of Chemotherapy timing survivor groups.

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