EJGO European Journal of Gynaecological Oncology

Original Research

Advanced stage ovarian cancer survival in Jakarta

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Summary

Objective: Ovarian cancer is one of most common cancers among women and has high mortality rate. In Indonesia, most patients initially present with advanced stage disease. Several factors contribute to ovarian cancer survival rate. Here, we evaluate factors that contributed to ovarian cancer survival rate in our medical center. *Materials and Methods:* This is a retrospective study reporting on 128 advanced stage ovarian cancer cases in Dr. Cipto Mangunkusumo Central General Hospital, a national reference and teaching hospital in Jakarta, Indonesia. Patients were treated with cytoreductive surgery and chemotherapy, and followed for a five-year period. Univariate and multivariate survival analyses were performed to investigate the impact of age, parity, residual tumor, chemotherapy regimen, and lymph nodal status on overall survival. *Results:* In 51.6% of patients, surgery failed to achieve optimal debulking. The overall two and four year post-diagnosis survival rates were 28.7% and 9.4%, respectively. Uni-variate analysis revealed patient age, stage, histopathology, residual tumor, chemotherapy administration, but not the regimen and treatment completeness, impact patient survival. Multivariate analysis showed cancer stage (HR = 1.3, p = 0.04), and chemotherapy (HR = 2.8, p = 0.01) affected survival rate. *Conclusion:* Advanced stage ovarian cancer has a poor survival rate, especially in older patients. In this study, the only factors that impacted patient survival were cancer stage and adjuvant chemotherapy. Complex cytoreductive surgery in advanced stage ovarian cancer should also be performed to improve patient survival.

Key words: Advanced stage ovarian cancer; Survival rate; Residual tumor; Cytoreductive surgery; Chemotherapy; Histopathology.

Introduction

Yearly, ovarian cancer accounts for 295,414 new cases and 184,799 death worldwide [1]. In Indonesia, ovarian cancer is the third most commonly cancer diagnosed among women, and most are diagnosed in an advanced cancer stage [2, 3]. Worldwide, ovarian cancer represents only 7.0% of all cancers diagnosed in females, but the mortality rate is 58.9% [3]. Survival epidemiology is important for us as a Key Performance Indicator (KPI) of gynecologic cancer services and to guide information given to the patient during counseling. Improvements in cytoreductive surgery and chemotherapy have led to improved survival for ovarian cancer patients. Patients with optimal cytoreductive surgery have a median 10 years survival of 62% [4]. Moreover, several factors such as age, stage, and histopathology contribute to patient survival [4, 5]. Given the general lack of data concerning ovarian cancer survival in Indonesia, we evaluated patient survival and factors that contribute to disease survival in this country.

Materials and Methods

This is a retrospective cohort study using data retrieved from medical records of Dr. Cipto Mangunkusumo National Central General Hospital in Jakarta, Indonesia. Patients who received a diagnosis of advanced ovarian cancer from January 1, 2012 until December 31, 2016 were enrolled in this study. Surgical staging and grading followed the International Federation of Gynecology and Obstetrics (FIGO) standards. The inclusion criteria were: 1) Epithelial ovarian cancer Stages IIIB, IIIC, IVA, and IVB according to FIGO classification; 2) patients underwent cytoreductive surgery following diagnosis. Patients without histopathological results and those with non-primary ovarian cancer were excluded from this study.

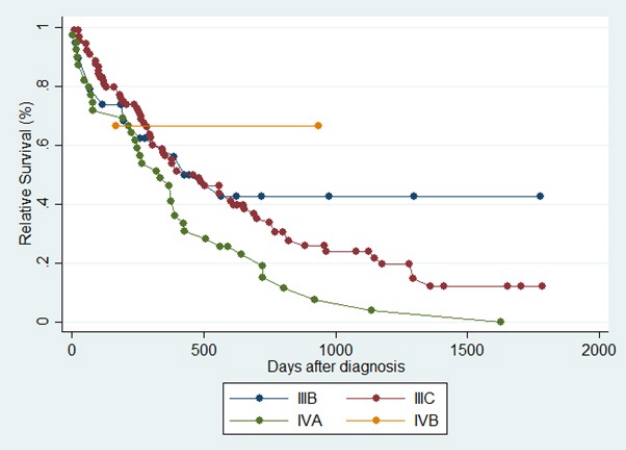

Figure 1. — Four-year relative survival by stage.

For statistical analysis, variables regarding patient characteristics were recorded in the following manner: 1) age, less than 50 years old or more than equal 50 years old; 2) parity; 3) clinical stage; 4) histopathological type; 5) cell

Eur. J. Gynaecol. Oncol. - ISSN: 0392-2936
41, n. 4, 2020
doi: 10.31083/j.ejgo.2020.04.5295

Table 1. — *Descriptive Ovarian Cancer Patient Characteristics.*

Characteristics	Patients n = 128 (%)
Age (y)	
< 50	78 (43.3)
≥ 50	50 (56.7)
Parity	
Nuliparity	37 (28.9)
Primiparity	50 (39.0)
Multiparity	41 (32.1)
Cancer Stage	
IIIB	17 (13.2)
IIIC	74 (57.8)
IVA	35 (27.3)
IVB	2 (1.7)
Residual tumor	
< 1 cm	62 (48.4)
≥ 1 cm	66 (51.6)
Differentiation	
1	40 (31.2)
2	34 (26.6)
3	54 (42.2)
Lymph Node Involvement	
Positive	42 (67.1)
Negative	86 (32.9)
Histology	
Serous	57 (44.5)
Mucinous	20 (15.6)
Endometrioid	16 (12.5)
Clear cell	22 (17.2)
Others	13 (10.2)
Chemotherapy	
Received	100 (78.1)
Not given	28 (21.8)
Complete treatment	
Yes	76 (59.3)
No	52 (40.7)
Chemotherapy Regimen	
Carboplatin and Paclitaxel	62 (48.4)
Carboplatin Cyclopospamide	66 (51.6)

differentiation; 6) lymph node involvement; 7) intervention types (*i.e.*, received chemotherapy or not), 8) chemotherapy regimen (carboplatin and paclitaxel, or carboplatin and cyclophosphamide), 9) residual tumor noted as follows: i) residual tumor smaller than 1 cm; ii) residual tumor larger than 2 cm; 10) complete treatment, patient who underwent cytoreductive surgery followed with six completed cycles of adjuvant chemotherapy.

Data were analyzed using STATA. Kaplan Meier tests were used to determine patient survival rates, while multivariate analysis was used to determine prognostic factors, logistic regression analysis was also performed where indicated. Overall survival was measured in all cases, survival curves were plotted using the Kaplan-Meier method, and results included the log-rank test. The Cox proportional hazards regression model was used for univariate and multivariable analyses. Significant variables from the univariate analysis were included in the multivariable model. Differences were considered statistically significant at $p < 0.05$.

This study was approved by the ethics committee of Dr. Cipto Mangunkusumo National Central General Hospital. Patient medical record confidentiality was maintained in accordance with applicable medical ethical standards.

Results

We collected data on 128 advanced stage ovarian cancer patients diagnosed between January 1, 2012 and December 31, 2016. The majority of patients were ≤ 50-years-old (43.3%), primipara (39.0%), Stage IIIC (57.8%), serous histotype (44.5%), received chemotherapy (78.1%), and completed chemotherapy (59.3%). Optimal cytoreduction was achieved in 48.4% of the patients. Chemotherapy regimen was not given to 28 (21.8%) patients, due to patient refusal, inadequate performance status, and perioperative death. Patient characteristics are shown in Table 1.

Median overall survival rate was 388 days (1 year, 3 weeks, 1 day). The shortest survival rate was one day (peri operative death) and the longest survival rate was four years, ten months. Overall survival rates, across all stages, for two and four years post-diagnosis were 28.7% and 9.4%, respectively (Table 2). Four year relative survival analysis is shown in Figure 1. Log rank analysis with chisquare analysis determined factors which significantly correlated with patient survival. These were age, stage, histotype, residual tumor, and chemotherapy administration (but not the specific regimen and treatment completeness) (Table 2). Cox multivariate modeling determined the significant factors were cancer stage (Hazard Ratio (HR) = 1.3, *p*-value 0.04), and whether the patient received chemotherapy (HR = 2.8, *p*-value 0.01) (Table 3).

Discussion

Advanced stage ovarian cancer has a poor overall survival rate [4, 6]. Most advanced stage ovarian cancer patients who achieve clinical remission will experience disease relapse, disease progression, or death within five years [4]. Indeed, it is estimated that five year survival rates for patients with advanced ovarian cancer are 30% [4]. Patients in our medical center did not survive for five years after initial diagnosis and several factors contributed to this observation. Most patients were more than 50 years old, which is a poor prognostic factor [7]. Other factors contributing to poor prognosis in our patient population were high grade tumor differentiation and residual tumor burden after surgery [8, 9]. Moreover, while individual patient conditions also exacerbated survival, multivariate analysis revealed that the factor which most significantly improved patient survival the administration of chemotherapy.

Table 2. — *Survival rate of advanced stage ovarian cancer patients (days)*

Factors	Survival Rate After Diagnosis*		*p* value+
	2 years	4 years	
All	28.7 (0.20-0.37)	9.4 (0.03-0.18)	
Age at diagnosis			0.003
< 50	30.1 (0.21-0.39)	9.9 (0.04-0.19)	
≥ 50	0	0	
Parity			0.29
Nulliparity	17.9 (0. 06-0.34)	0	
Primiparity	31.7 (0.18-0.45)	0	
Multiparity	27.3 (0.14-0.42)	24.2 (0.11-0.38)	
Cancer Stage			0.02
IIIB	41.3 (0.16-0.64)	41.3 (0.16-0.64)	
IIIC	31.1 (0.20-0.42)	11.5 (0.04-0.23)	
IVA	11.2 (0. 03-0.25)	0	
IVB	50 (0.006-0.94)	0	
Histotype			0.03
Serous	41.7 (0.27-0.55)	17.4 (0.06-0.32)	
Others	17.6 (0.09-0.28)	3.6 (0.03-0.14)	
Differentiation			0.39
Grade I	27.8 (0.14-0.43)	7.7 (0.006-0.27)	
Grade II	24.7 (0.11-0.40)	4.4 (0.003-0.17)	
Grade III	26.9 (0.14-0.40)	16.7 (0.05-0.31)	
Residual tumor			< 0.001
< 1 cm	18.2 (0.09-0.29)	4.2 (0.0045-0.1)	
≥ 1 cm	37.1 (0.25-0.48)	14.8 (0.05-0.29)	
Lymph Node Involvement			0.17
Positive	35.4 (0.19-0.51)	10.2 (0.01-0.27)	
Negative	24.3 (0.17-0.35)	10.2 (0.03- 0.20)	
Chemotherapy			< 0.001
Given	36.5 (0.26-0.46)	12.0 (0.04-0.22)	
Not Given	0	0	
Complete Treatment			< 0.001
Yes	40.1 (0.28-0.51)	10.9 (0.04-0.51)	
No	9.6 (0.03-0.20)	7.2 (0.02-0.17)	
Chemotherapy Regiment			0.29
Carboplatin-pacliaxel	29.3 (0.17-0.42)	0	
Carboplatin Cyclophospamide	25.6 (0.15-0.35)	10.2 (0.03-0.20)	

**Data are % (95% confidence interval); + log rank test*

A prognostic factor which can be modified is optimal cytoreductive surgery. However, our analysis showed residual tumor burden was only significant using univariate analysis but not with multivariate analysis. Nevertheless, successful cytoreductive surgery improves patient survival [10] and advanced-stage ovarian cancer and patient's age decreased successfully with cytoreductive surgery [10].

It is important that complex cytoreductive surgery is performed by a team, in order to remove as much as possible tumor mass. However, not all patients will benefit an extensive cytoreductive surgical approach, especially older patients as older patients tend to have other comorbidities affecting intraoperative safety and postoperative recovery [10]. We should able to weigh and review the target of surgery and next management steps to the patient.

This retrospective study lacks patient follow up. This factor is one of problems that we have encountered in cancer management at our medical center. Factors that were not included in our study, but which contribute to patient compliance, were patient educational level, socio-economic status, and patient address not in Jakarta. Poor follow up also affected survival analysis in this study. This is the first study from Dr. Cipto Mangunkusumo National Central General Hospital to report ovarian cancer survival. There remain improvements that need to be established to accurately report survival, such as patient's performance status, and enrich our understanding of comorbidities that affect survival especially in older ovarian cancer patients.

Table 3. — *Estimated Hazard Ratio of Epithelial Ovarian cancer*

Variable	Adjusted HR	95% CI HR	P value
Age	1.4	0.62-3.3	0.3
Parity	0.8	0.61-1.06	0.13
Histology	1.3	0.85-2.1	0.19
Differentiation	1.03	0.82-1.3	0.44
Cancer stage	1.3	1.00-1.9	0.04
Residual tumor	0.8	0.5-1.3	0.52
Lymph node involvement	0.73	0.46-1.16	0.19
Complete treatment	1.5	0.88-2.6	0.12
Receive chemotherapy	2.8	1.2-6.4	0.01
Chemotherapy regimen	0.79	0.45-1.37	0.4

Conclusion

Advanced stage ovarian cancer has poor survival rate, especially in older patients. In this study, the only factors that impact patient survival were cancer stage and chemotherapy. Complex cytoreductive surgery in advanced stage ovarian cancer should be performed to improve cancer tumor mass removal and improve patient survival.

Acknowledgements

The authors did not receive any spesific grant from funding agencies in the public, commercial, or non-profit sectors. We thank the Department of Obstetrics and Gynecology, Cipto Mangunkusumo National Central Hospital and Faculty of Medicine, Universitas Indonesia for the opportunity given in writing this manuscript.

Conflict of interest

The authors declare no conflict of interest in preparing this article.

Submitted: June 19, 2019
Accepted: September 19, 2019
Published: August 15, 2020

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