# Survival Analysis of Ovarian Cancer Patients based on Age at The Dr. Wahidin Sudirohusodo Makassar Hospital in 2014-2018

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## Abstract

**Background.** Generally, a younger age at diagnosis indicates a better prognosis, with younger women having an average survival of at least 2 years longer than older women. It is estimated that in young women the disease is diagnosed more quickly in the early stages when compared to older women.

**Method.** A cohort retrospective study. This research was conducted at the Dr. Wahidin Sudirohusodo Makassar Hospital by taking the medical records of ovarian cancer patients from January 2014 to December 2018. The study subjects were 263 patients. The Kaplan-Meier method was used to estimate survival rate and Cox Regression to investigate the effect of variable.

**Results.** The survival of ovarian cancer patients within 30 months is 78%. Ovarian cancer patients who survived to the 30th month based on age ≤ 60 years were 79% whereas > 60 years to 30th month none had survived with an HR score of 2.74 (95% CI: 1.09-6.88 ). Multivariate analysis HR values were obtained for age 2.65 (95% CI: 1,07-6,52) after being controlled by stage, and performance status.

**Conclusion.** Age affects the survival of ovarian cancer patients. Patients aged> 60 years are more at risk of dying compared to patients aged ≤ 60 years

***Keywords:*** *ovarian cancer, survival, age*

## Introduction

Globally, the incidence of ovarian cancer was 6.6 per 100,000 population, while the mortality rate was 3.9 per 100,000 population with 300,000 new cases. Based on the same source, the incidence and mortality of ovarian cancer in Asia ranks ninth for cancer diseases suffered by women of all ages. The same situation is also found in Indonesia. Ovarian cancer is still the top ten causes of cancer deaths in women of all ages, with a total of 7,842 or 4.34%.[1]

Ovarian cancer is known as "The Silent Killer". Although the incidence of ovarian cancer is not as high as the incidence of breast and cervical cancer, especially in developing countries, the lethality rate is very high.[2] Ovarian cancer contribute for 2.5% of all malignancies among women. Most cases of ovarian cancer (60-70%) are found at an advanced stage so the treatment results are not as expected. This is due to the absence of specific symptoms (symptomless) in the initial state and the discovery of an approved method of early detection so that the survival rate of patients is low.[3]

For all types of ovarian cancer and ovarian cancer stage under the SEER (Surveillance, Epidemiology and End Results Program) of 2018, the five-year relative survival rate was 47%.[4] If ovarian cancer was discovered and treated before the cancer had spread beyond the ovaries (Stage 1A and 1B), the five-year relative survival rate was 95%. However, only 15% of all ovarian cancers are found in the early stages.[5]

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There are many factors that influence the survival rate of ovarian cancer patients. Various factors such as age, grade, FIGO stage, residual disease, CA125, performance status, the presence and absence of ascites, histology, albumin, alkaline phosphatase, race, and various molecular markers are considered to be important prognostic factors affecting the survival of ovarian cancer.[6] The prognosis factors according to Holschneider and Barek (2000) that consistently influence the survival of ovarian cancer patients are stage, tumor histology, grade, age, tumor residues, and ascites.[7]

The age of patient are important prognostic factors in influencing survival rates. It is estimated that in younger age women are more likely to be diagnosed early in the stage than in older women. Also therapy in young women is more aggressive than therapy for the elderly.[8]

The highest age of ovarian cancer is 55-64. The average age at which women are diagnosed is 63, which means that half of women are younger than 63 when diagnosed with ovarian cancer and half are older. The average age of ovarian cancer death is 70.[9] Compared to stages, young women with ovarian cancer are more likely to survive than older women because older women are likely to be in the end stage. Women with stage III-IV ovarian cancer aged 45 years compared to those aged 85 and above are only 8% resistant.[10] Research from Chan (2006) found that overall survival rates of patients with age groups <30, 30-60, and> 60 years, respectively, were 78.8%, 8.8%, and 35.5%.[11] Therefore, the purpose of this study was to determine survival of ovarian cancer patients based on age at the Dr. Wahidin Sudirohusodo Makassar Hospital in 2014-2018.

## Method

The design of this study is a retrospective cohort study. This research was conducted at the Dr. Wahidin Sudirohusodo Makassar Hospital obtained medical records of ovarian cancer patients from January 2014 to December 2018 in the hospital information system. The results of the total sample count were obtained in 86 cohort subjects, the minimum sample size in this study was 172. However, in this study we would exclude all ovarian cancer patients who met the inclusion and exclusion criteria. The inclusion criteria were patients with new cases of ovarian cancer and who were receiving treatment only at the Dr. Wahidin Sudirohusodo Makassar Hospital. Exclusion criteria are patients whose medical records are incomplete. The independent variable of study was age. The dependent variable was the survival of ovarian cancer patients. The variables of the covariate were marital status, stage, grade, ascites, albumin, treatment compliance, and performance status. Univariate analysis to see the frequency distribution, the proportion of each variable. To determine survival rate of ovarian cancer patients using the Kaplan Meier test and Log Rank Test. Cox regression analysis is used to investigate the effect of variable.

## Results

During this study, a total of 263 patients were studied during the period January 2014 - December 2018. Of the 263 patients event (died) 26 (9.89%) and 237 censored patients (90.11). Patients aged ≤ 60 years were 226 (85.93%) and> 60 years 37 (14.07%). Ovarian cancer patients with marital status were 240 (91.25%) and unmarried 23 (8.75%).

It is known that most ovarian cancer patients who come for treatment in the end stage are 141 (53.61%), while patients with early stages are 122 (46.39%). Patients who had moderate and poor grade were 193 (73.38%), while patients with high grade were 70 (26.62%). Patients who had ascites were 179 (68.06%) and patients who did not have ascites 84 (31.94%). Patients with albumin levels <3.6 g / dl were 191 (72.62%) and patients whose albumin levels were ≥ 3.6 g/dl were 72 (27.38%). Patients with good performance status were 248 (94.30%) and patients with weak performance status were 15 (5.70%). Obedient patients were 257 (97.72%) and non-compliant patients were 6 (2.28%).

The survival rate of ovarian cancer patients within 30 months is 78% with an average survival rate of ovarian cancer patients for 8 months. Based on Figure 1, it was found that ovarian cancer patients who survived to the 30th month based on the age of ≤ 60 years by 79% while> 60 years to the 30th month none had survived with an HR value of 3.82 (95% CI: 95% 1.36-9.51).

**Table 1. Frequency Distribution of Ovarian Cancer Patients in RSUP Dr. Wahidin Sudirohusodo Makassar in 2014-2018**

| Variables | Total | | Aged ≤ 60 years | | Aged > 60 years | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| Patient Status | | | | | | |
| Sensor | 237 | 90,11 | 207 | 87,34 | 30 | 12,66 |
| Event | 26 | 9,89 | 19 | 73,08 | 7 | 26,92 |
| Stage | | | | | | |
| Early Stage | 122 | 46,39 | 107 | 87,70 | 15 | 12,30 |
| End Stage | 141 | 53,61 | 119 | 84,40 | 22 | 15,60 |
| Marital Status | | | | | | |
| Married | 240 | 91,25 | 203 | 84,54 | 37 | 15,42 |
| Unmarried | 23 | 8,75 | 23 | 100 | - | - |
| Treatment Compliance | | | | | | |
| Obedient | 257 | 97,72 | 220 | 85,60 | 37 | 14,40 |
| Non-compliant | 6 | 2,28 | 6 | 100 | - | - |
| Grade | | | | | | |
| High | 70 | 26,62 | 65 | 92,86 | 5 | 7,14 |
| Moderate and low | 193 | 73,38 | 161 | 83,42 | 32 | 16,54 |
| Ascites | | | | | | |
| No | 84 | 31,94 | 74 | 88,10 | 10 | 11,90 |
| Yes | 179 | 68,06 | 152 | 84,92 | 27 | 15,08 |
| Albumin Level | | | | | | |
| < 3,6 g/dl | 191 | 72,62 | 64 | 88,89 | 8 | 11,11 |
| ≥ 3,6 g/dl | 72 | 27,38 | 162 | 84,82 | 29 | 15,18 |
| Performance Status | | | | | | |
| Good | 248 | 94,30 | 214 | 86,29 | 34 | 13,71 |
| Weak | 15 | 5,70 | 12 | 80 | 3 | 20 |

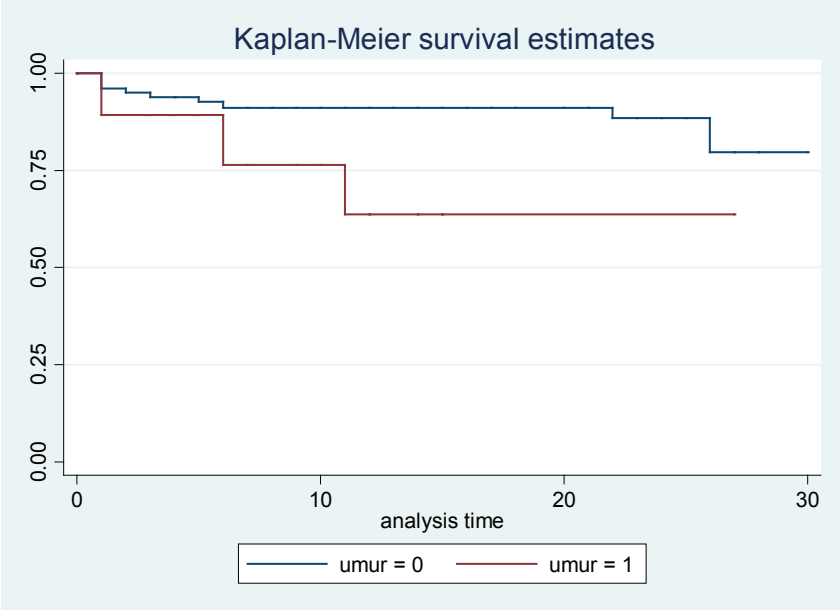


**Figure 1. Kaplan Meier's Curve for the Survival of Ovarian Cancer Patients by Age**

**Table 2. Multivariate Final Models Effects of Age on the Survival of Ovarian Cancer Patients**

| variables | Coef B | HR | 95% CI | p value |
|---|---|---|---|---|
| Age | 0,973 | 2,65 | 1,07-6,52 | 0,032 |
| Stage | 0,726 | 2,07 | 0,82-5,22 | 0,132 |
| Performance Status | 2,539 | 12,68 | 5,67-28,32 | 0,000 |

In the bivariate results, the HR value for age was 3.82 (95% CI 1.36-9.51; p <0.0010). This study also conducted stratification analysis to see the variables that interacted, but the results were no interactions and there were confounding on stage, marital status, grade, and performance status. After conducting stratification analysis, all variables were entered then proceed to multivariate analysis and HR values were obtained for age 2.74 (95% CI: 1.09-6.88) after being controlled by marital status, stage, ascites, grade, albumin levels, treatment compliance and performance status. When entering multivariate analysis before entering final modeling, there is no interactions or counfounding were found. From table 2, we get the final model of patients aged> 60 years who have a risk of 2.65 times death compared to patients aged ≤ 60 years after being controlled by variables of stage and performance status.

## Discussion

Based on the results of this study conducted at the Dr. Wahidin Sudirohusodo Makassar Hospital with a total of 263 patients, the cumulative probability of survival of ovarian cancer patients was 79% for 30 months. Events (died) occur more frequently in ovarian cancer patients with end-stage (53.61%) compared to ovarian cancer patients with early-stage (46.39%). This survival rate is higher than the Junita Sari study (2008) at Dharmais Cancer Hospital for 36 months by 51%.[12] Research by Aneta et al. (2018) in Podkarpacie province 51.2% .[13] This difference in survival occurred because in this study the lost to follow-up was included in the risk population, as well as differences in sample size, data capture and other factors in each study.

From the results of the analysis found that ovarian cancer patients who survived to the 30th month based on

age ≤ 60 years by 79% while> 60 years to 30th month no one had survived. On average ovarian cancer patients aged ≤ 60 years can survive for 9 months while ovarian cancer patients aged> 60 years can only survive for 5 months. This result is not much different from the results of Chan et al's study where the survival rate of ovarian cancer patients aged <60 years by 84.8% while different for ages> 60 years which obtained by 77.1%.[14] But these results are different from Junita (2007) results in which the survival rate for patients aged ≤ 49 years by 64%, in the 50 to 59 years age group by 34% while those aged ≥ 60 years by only 23% for 3 years.[12] Research conducted by Aneta et al. (2018) also states that as a woman gets older at the time of diagnosis, her survival will decrease. Comparing patient survival in groups> 65 years with women 45-65 years for 3 years by 24.2% .[13] This result may differ due to age category. Although a cut-off age of 60 years has commonly been used, the age criteria have differed among previous studies.

Past research about age as a prognostic factor is very important. Generally, a younger age at diagnosis indicates a better prognosis, with women younger than 65 years having at least 2 years longer median survival compared to women older than 65 years; older women also have an increased risk of recurrence and death. Age remains an independent prognostic factor after controlling for common confounding factors, such as performance status and medical comorbidities. Younger-aged women tend to have less invasive and well differentiated cancers and fewer comorbidities compared to older counterparts, yielding a more favorable overall prognosis.[15] Some studies also find that young women with early-stage ovarian cancer and with good differentiated tumors have good survival higher than older women. However, another study found that age was not the only prognosis factor after adjusting for other variables such as the stage and grade of the disease.[14]

In multivariate analysis it is known that patients aged> 60 years have a risk of 2.65 times of death compared with patients aged ≤ 60 years after being controlled by variable stage and performance status. In contrast to research by Chan et al. where patients> 60 years old have a risk of 1.96 times death compared to patients aged <60 years after being controlled with stage, grade, and citology.[14]

In this study it is also known that staging and general condition affect the survival of ovarian cancer patients. The survival rate of ovarian cancer patients decreases with increasing stage of the disease.[15] Diagnosis of ovarian cancer is often delayed due to lack of early examination and specific symptoms. Only about 25% of women diagnosed with ovarian cancer occur in stage 1.[17] Late diagnosis affects cancer treatment, making it more difficult to effectively fight cancer.[16] Better performance status generally provide greater tolerance for various therapeutic modalities, from surgery to chemotherapy, and might motivate the adoption of more aggressive treatment plans by doctors. Several studies support this reason and confirm the significance of prognosis independent of performance status.[15]

Elderly patients with ovarian cancer may benefit from a multidisciplinary approach, including a comprehensive evaluation by a gynecologist, oncologist, nurse and pharmacist. Comprehensive geriatric assessments have been shown to be able to predict morbidity and mortality in elderly cancer patients.[18] However, the high heterogeneity of elderly patients means that it is not feasible to make treatment decisions based on age alone, and a more objective assessment is required.[19]

Weaknesses in this study are that researchers cannot control the state and quality of data that have been done by others in the past and the research can only rely on secondary data that is already in incomplete medical record records where the possibility of errors in recording or available data is not appropriate with what is needed in research. For this reason, better records are needed for ovarian cancer patients.

## Conclusions and Recommendations

From this study it was concluded that age affects the survival of ovarian cancer patients. Patients aged> 60 years are more at risk of dying compared to patients aged ≤ 60 years. It is recommended to do research with more samples to be able to prove other factors that influence the survival of ovarian cancer patients. The research can be continued with different outcomes, categorizing different variables, and including several characteristic variables such as economics.

**Ethical Considerations:** This Study was approved by Faculty of Public Health University of Indonesia Ethics Committee (No. 370/UN2.F10/PPM.00.02/2019).

**Competing Interest:** The authors declared that no competing interest exist.

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## References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians. 2018 Nov;68(6):394-424.
2. Siegel R, DeSantis C, Virgo K, Stein K, Mariotto A, Smith T, Cooper D, Gansler T, Lerro C, Fedewa S, Lin C. Cancer treatment and survivorship statistics, 2012. CA: a cancer journal for clinicians. 2012 Jul;62(4):220-41.
3. Torre LA, Trabert B, DeSantis CE, Miller KD, Samimi G, Runowicz CD, Gaudet MM, Jemal A, Siegel RL. Ovarian cancer statistics, 2018. CA: a cancer journal for clinicians. 2018 Jul;68(4):284-96.
4. SEER. *Cancer Stat Facts: Ovarian Cancer*. National Cancer Institute: Surveillance, Epidemiology, and End Results Program. 2018. Available At: https://seer.cancer.gov/statfacts/html/ovary.html
5. Canadian Cancer Society. *Prognosis and Survival in Ovarian Cancer*. 2018. Available at: https://www.cancer.ca/en/cancer-information/cancer-type/ovarian/prognosis-and-survival/?region=on
6. Clark TG, Stewart ME, Altman DG, Gabra H, Smyth JF. A prognostic model for ovarian cancer. British journal of cancer. 2001 Oct;85(7):944.
7. Berek, JS. *Epithelial Ovarian Cancer*. Chapter 11. 1996. Williams & Wilkins. Baltimore.
8. Aziez, M.F, Andrijono, Saifuddin, AB. Buku Acuan Nasional: Onkologi Ginekologi. 2006. Jakarta: Yayasan Bina Pustaka Sarwono Prawirihardjo.
9. NCI. *Understanding Ovarian Cancer*. Society of Gynecology Oncology. 2015.
10. Ries LA. Ovarian cancer: survival and treatment differences by age. Cancer. 1993 Jan 15;71(S2):524-9.
11. Chan JK, Urban R, Cheung MK, Osann K, Husain A, Teng NN, Kapp DS, Berek JS, Leiserowitz GS. Ovarian cancer in younger vs older women: a population-based analysis. British journal of cancer. 2006 Nov;95(10):1314.
12. Junita SU. Kajian Epidemiologi Ketahanan Hidup 3 Dan 5 Tahun Penderita Kanker Ovarium Epithelial Pengaruh Stadium RSKD Jakarta Tahun 1993-2005. 2008. Depok: Universitas Indonesia
13. Radziszewska AU, Karczmarek-Borowska B, Wójcik S, Kluz T. Survival rates among women with ovarian cancers diagnosed in the area of Podkarpacie province in the years 1990–2015. Contemporary Oncology. 2018;22(3):151.
14. Chan JK, Tian C, Monk BJ, Herzog T, Kapp DS, Bell J, Young RC. Prognostic factors for high□risk early□stage epithelial ovarian cancer: A Gynecologic Oncology Group study. Cancer. 2008 May 15;112(10):2202-10.
15. Ezzati M, Abdullah A, Shariftabrizi A, Hou J, Kopf M, Stedman JK, Samuelson R, Shahabi S. Recent advancements in prognostic factors of epithelial ovarian carcinoma. International scholarly research notices. 2014;2014.
16. Sihombing M, Sirait AM. Angka ketahanan hidup penderita kanker ovarium di RS Dr. Cipto Mangunkusumo Jakarta. Maj Kedokt Indon. 2007;57(10):346-52.
17. Badgwell D, Bast Jr RC. Early detection of ovarian cancer. Disease markers. 2007;23(5-6):397-410.
18. Extermann M, Hurria A. Comprehensive geriatric assessment for older patients with cancer. Journal of Clinical Oncology. 2007 May 10;25(14):1824-31.
19. Yoshikawa K, Fukuda T, Uemura R, Matsubara H, Wada T, Kawanishi M, Tasaka R, Kasai M, Hashiguchi Y, Ichimura T, Yasui T. Agerelated differences in prognosis and prognostic factors among patients with epithelial ovarian cancer. Molecular and clinical oncology. 2018 Sep 1;9(3):329-34.