



Original Contribution

AGE BASED PROGNOSIS FOR EARLY EPITHELIAL OVARIAN CANCER

N. Lazarov*, L. Lazarov, S. Lazarov

Department of Obstetrics & Gynecology, Obstetrics & Gynecology Clinic, University Hospital,
Trakia University, Stara Zagora, Bulgaria

ABSTRACT

OBJECTIVE: To analyze the role of the age as a prognostic factor for women with early epithelial ovarian cancer. **MATERIAL:** The medical records of 254 female patients with ovarian cancer (stage I- II) were investigated. The exploration time was 12 years (2000- 2012). **METHODS:** We used: Operative method, Descriptive analysis, Correlative analysis, Variation analysis, Graphic analysis, Kaplan – Mayer analysis, Covariate analysis, Chi – square – analysis, Log rank test.

RESULTS: The highest overall survival (o. s.) have women < 40 years of age (96.6 %), and the lowest – women >70 years (57% o. s.). Women between 45 and 50 y. o. a. have second poorest overall and progression free survival ($p < 0.0001$). **CONCLUSIONS:** Female patients with epithelial ovarian cancer, stage I - II, younger than 40 years, that are optimally treated, have much better chance to survive (12 times) than the older patients with the same disease (HR = 11.5691, 95% CI, 5.8408 to 22.9154, $p < 0.01$). Women older than 70 years, as well as female between 40 and 50 years of age are at a very high risk for disease specific death ($p = 0.0001$).

Key words: age, prognostic factor, prognosis, early, epithelial, ovarian cancer, carcinoma

INTRODUCTION

All tendencies in the Medical science and in particular in the Oncology are driven in three main directions:

1. Developing new regimen of administration and /or combinations of already known therapeutics
2. Discovering and developing of new experimental types of therapy (immunotherapy, gene therapy, viral therapy, stem cell therapy etc.).
3. Early detection of the cancer through improvement of diagnostics and screening methods

Management of epithelial ovarian cancer makes no exception. Because of the significant difference of survival between the early and advance stages of EOC, and until the medical

science finds a proper cure for this disease, the main goal will remain the early detection of ovarian cancer. That is the reason why we are investigating prognostic factors for early stages of epithelial ovarian cancer (EOC I – II stage).

Age at the time of diagnosis is one of the most important prognostic factors, taken under consideration when it comes to survival of female patients with early EOC.

OBJECTIVE

To analyze the role of the age as a prognostic factor for women with early epithelial ovarian cancer.

MATERIAL

For the purpose of the research, we've used the database of two district oncology centers of the cities of Bourgas and Stara Zagora, Bulgaria. The medical records of 254 female patients with ovarian cancer (stage I- II) were investigated. The women were registered and underwent surgery during the period 2000 – 2005. The exploration time was 12 years (2000- 2012). All

*Correspondence to: Nikolai L Lazarov, MD, PhD,
Address: M. M. Kusev blv.# 69, Stara Zagora,
Bulgaria, E-mail: n.lazaroff@gmail.com
Cell phone: 00359 884 26 92 02

of the patients were surgically staged, and have histo- pathological result for morphology type and degree of differentiation (grade) of the tumor. The youngest woman in the research was 12 and the oldest – 84 years old.

METHODS

The information has been collected, using investigation paper form, which we preliminarily created, than imported in a table manner and processed with statistical package MedCalc 12.2.1.0. We used: Descriptive analysis, Correlative analysis, Variation analysis, Graphic analysis, Kaplan

– Mayer analysis, Covariate analysis, Chi – square – analysis.

RESULTS

To the including criteria responded 215 of 254 female patients. The other 39 patients were removed from the research because of: insufficient data (n = 17), non- epithelial origin of the tumor (n=15), and reason of death, other than the investigated disease (n=7). The mean age of diagnosis is 53.4 years. The patients has been split into 6 age groups: under 40 years, 40 – 45years, 45 – 50 years, 50 – 60 years, 60 – 70 years and >70 years of age (**Table 1**).

Table 1. Count of patients with early EOC distributed by age groups.

AGE GROUPS (years)	COUNT	%
1. <40 y.	32	14,9%
2. 40– 45y.	22	10,2%
3. 45– 50y.	33	15,3%
4. 50– 60y.	59	27,4%
5. 60– 70y.	41	19,1%
6. >70y.	28	13,0%
Sum	215	100.0%

Most of the patients are in Group 4, between 50 and 60 years of age, with **27%** (n=59), followed by the sum of Group 2 and Group 3 with **25.6%** (n=55). More than a half of the patients in our study (**n=114**) are members of those three groups. It appears that women between 40 and 60 years of age are exposed to a biggest risk and consequently considered as a risk group for developing epithelial ovarian cancer. It could be due to the unstable hormonal levels of climax and menopause. Women that are entering this age period should be specifically and regularly examined (pelvic exam, vaginal ultrasound and Ca – 125 levels) in order to exclude the presence of EOC.

In order to analyze the age as a prognostic factor for patients with early EOC we have to inspect the overall survival and the progression free survival, as well as five – year survival of the different age groups.

As expected the highest overall survival (o. s.) showed the group of women < 40 years of age (96.6 % till the end of the period of investigation), and the lowest – the group >70 years (57% o. s. on the 5-th. postoperative year).

The curves of the other 4 age groups are declining with biggest intensity during the first 4 years. The lowest level of them reaches the 4-th group (45 – 50 years of age) with 70 % overall survival on the 4-th year, and stays the lowest till the end of evaluation period reaching 65%. Next in row is the curve of the 4-th group with 80 % o. s. on the 4-th year and 68% o. s. at the end of the period. What makes an impression here is the better o. s. of the 5-th group, compared to 3-rd and 4-th groups. It appears that according to age factor, considering the overall survival, the poorest prognosis is for the women over 70 years, followed by those between 40 and 45 years (Age group 3).

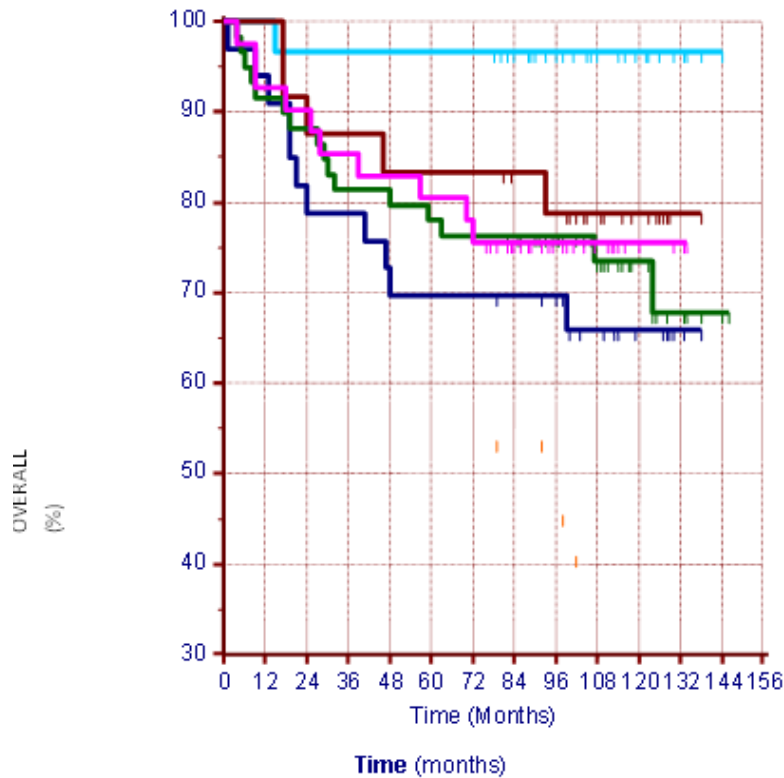


Figure 1. Influence of the age on the overall survival

Interesting fact is the lack of change of the overall survival levels between the fourth and the

eight postoperative years. That means that women, who survived 4 years, should be alive at least another four years.

Table 2. Overall survival of patients with early EOC (stage I-II) by age groups

	AGE GROUPS						
	1 (<40y.)	2 (40–45y.)	3 (45–50y.)	4 (50–60y.)	5 (60-70y.)	6 (>70y.)	
ALIVE	31	17	22	43	31	11	155 (72,1%)
DECEASED	1	5	11	16	10	17	60 (27,9%)
ALL	32 (14,9%)	22 (11,2%)	33 (15,3%)	59 (27,4%)	41 (19,1%)	28 (13,0%)	215
OVERALL SURVIVAL	96.9%	77.3%	66.7%	72.9%	75.6%	39.3%	72.1%

Even combining the patients from groups 2 and 3 group in one (Age 40- 50 years), in order to

make the age intervals equal (10 years for each group) the correlations of the graphics are not significantly different (**Figure 2**).

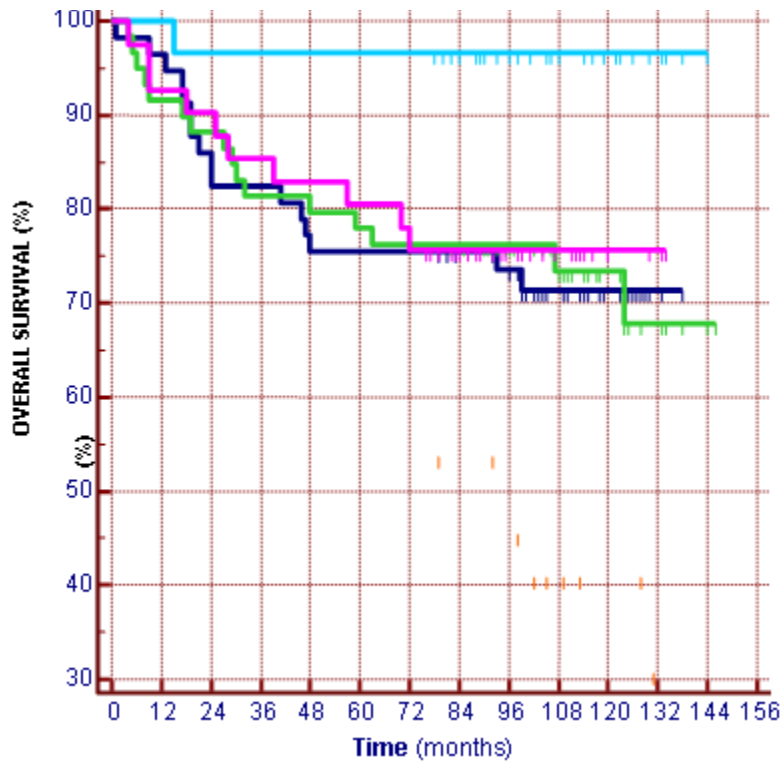


Figure 2. Influence of the age on the overall survival 2

The new, combined Group2 also shows a tendency of poor prognosis (o. s.70%). Once again Group5 has a better overall survival than Group 2 and Group 4 to the end of the 6-th year, after that the three groups are maintaining similar percentage o. s. (around 75%) to the 8-th

year, and again Group 2 becomes with the lowest from the three (p = 0.0001).

We have deliberately divided the 5-th decade into two groups because of the intensive hormonal changes of the period. Overall survival is shown on **Table 3 and Figure 3**.

Table 3. Overall survival by age groups 2

	AGE GROUPS 2					ALL
	1 <40	2+3 40- 50	4 50 - 60	5 60 – 70	6 >70	
ALIVE	31	39	43	31	11	155 (72,1%)
DECEASED	1	16	16	10	17	60 (27,9%)
ALL	32 (14,9%)	55 (25,6%)	59 (27,4%)	41 (19,1%)	28 (13,0%)	215 (100%)
OVERALL SURVIVAL	96.9%	70.9%	72.8%	75.6%	39.3%	72.1%

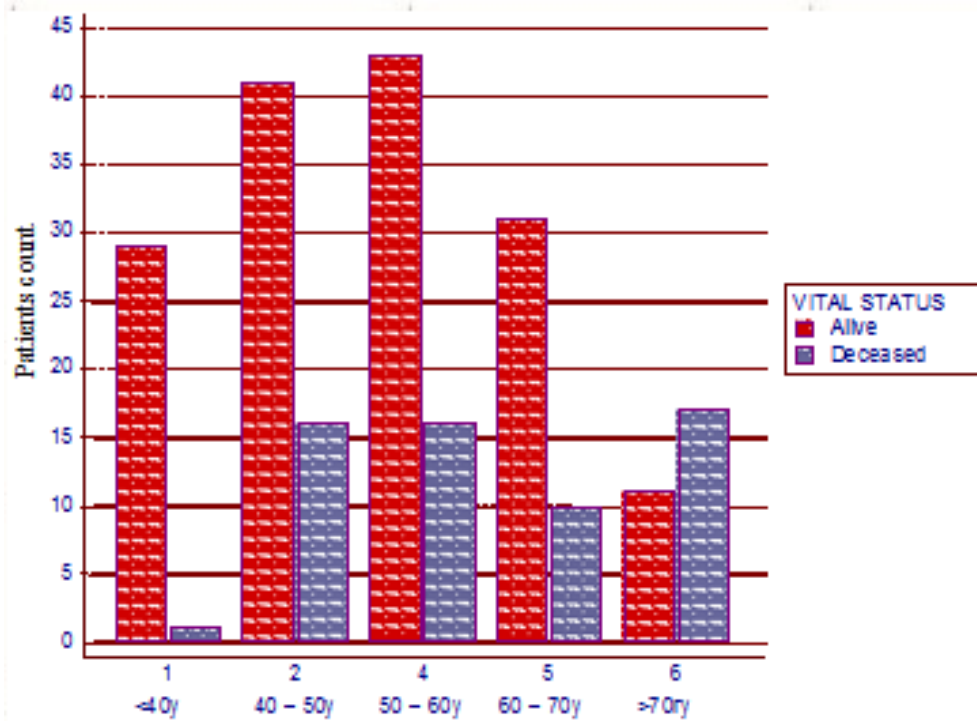


Figure 3. Overall survival by age groups 2

The correlations of the progression free survival (p. f. s.) of these age groups are similar to the o. s.

investigated event here is the relapse of the disease and the other quantity is the time, measured in months.

The Kaplan – Maier analysis illustrates the relations of the different age groups. The

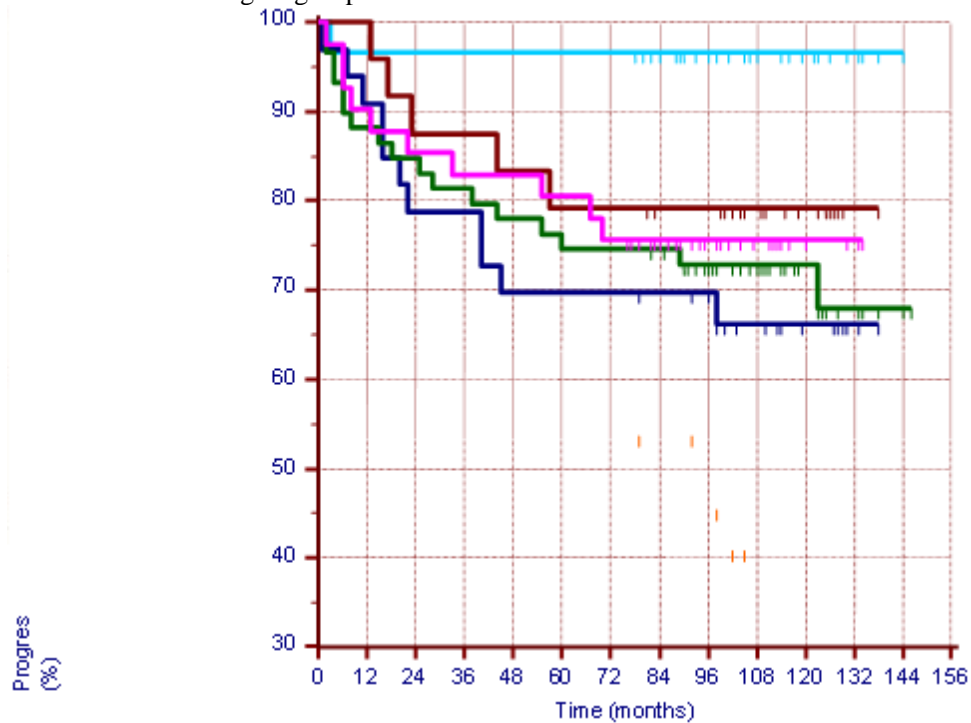


Figure 4. Influence of the age on progression free survival

Once again Group 6 holds the lowest values, followed by Group 3(40 – 45 y. o. a). This can be easily distinguished after the end of the third postoperative year (36 months).

The highest progression free survival has the group of women under 40 y. o. a. The clearest difference between this group and the other

groups appear at the beginning of the second postoperative year.

FIVE-YEAR SURVIVAL

Although the five– year survival does not mean healing, it is still an important point for orientation of how effective the treatment is. **Table 4** represents the impact of the age on 5-year survival.

Table 4. 5-year survival by age groups

	AGE GROUPS					ALL
	1 <40	2+3 40- 50	4 50 – 60	5 60 - 70	6 >70	
ALIVE	31	40	46	33	16	166 (77,2%)
DECEASED	1	15	13	8	12	49 (22,8%)
ALL	32 (14,0%)	55 (25,6%)	59 (27,4%)	41 (19,1%)	28 (13,0%)	215
5-YEARS SURVIVAL	96.9%	72.7%	78%	80%	57.1%	77.2%

When it comes to 5-year survival, with the poorest prognosis are again women at 70 and older (57.1%), followed by the largest age group in our research – patients, 40 to 50 years of age. The analysis of the age as a prognostic factor for patients with early EOC (stage I- II) has

pointed a border age of 40years. Patients under this age, with early stage of EOC that are optimally treated have much better chance of healing (96% o. s.) than the older patients ((sum. 67.3%) (**Figure 5**).

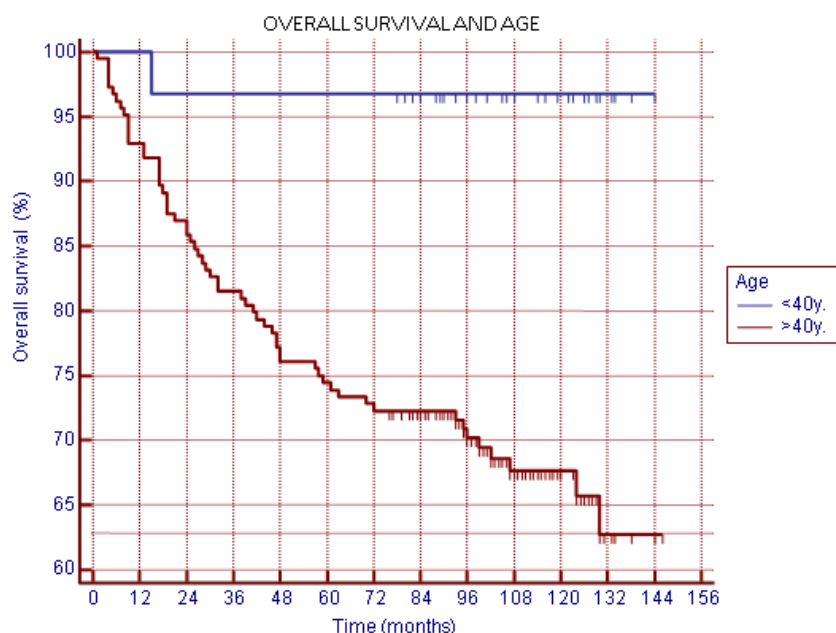


Figure 5. Overall survival and age

The hazard of death from EOC for patients at the age of 40 and older is nearly 12 times greater (HR = 11.5691, 95% CI, 5.8408 до 22.9154, p <0.01) than the other group.

DISCUSSION

Many authors share the prognostic importance of age for women with ovarian cancer. Multivariate analysis by K. Bertelsen et al. in 1993 (1) showed that age, stage, residual tumor, histologic grade and adjuvant treatment had prognostic value. In a research in 2003 S. Tingulstad et al. (2), using Cox multivariable regression analysis report age at the diagnosis as one of the three independent prognostic factors. The data of our research corresponds with the data of Tate Thigpen 1993(3) and H.A.A.M. Maas et al.(4) 2004 that women > 70 y. o. a. exhibited significantly poorer survival than those younger. The overall and disease free survival do not proportionally decline with increased age as Carol L. Kosary wrote in 1994(5). Our results show that females in age group 45 – 50 y. o. a. represent a high risk- group for morbidity and mortality of ovarian cancer. Most probably, the low survival rates in this group are due to the unstable hormonal levels of the phases of climax (hyperestrogen phase and hypergonadotropine phase), that are associated with intensive proliferation and mitotic activity of the superficial epithelium of the ovary.

CONCLUSIONS

1. Women between 40 and 60 years of age are exposed to a biggest risk and consequently considered as a risk group for developing epithelial ovarian cancer.
2. Female patients with epithelial ovarian cancer, stage I - II, younger than 40 years, that are optimally treated, have much better chance to survive (12 times) than the older patients with the same disease (HR =

LAZAROV N., et al.

11.5691, 95% CI, 5.8408 до 22.9154, p <0.01).

3. The highest risk for disease specific death have the women older than 70 years, followed by female patients between 40 and 50 years of age (p = 0.0001).

REFERENCE

1. K. Bertelsen, B. Hølund, J.E. Andersen, K. Nielsen, I. Strøyer, P. Ladehoff, Prognostic factors and adjuvant treatment in early epithelial ovarian cancer, *International Journal of Gynecological Cancer*, 3, 4, 211–218, July/August 1993.
2. Tingulstad, Solveig MD; Skjeldestad, Finn Egil MD, PhD; Halvorsen, Tore B. MD, PhD; Hagen, Bjørn MD, PhD, Survival and Prognostic Factors in Patients With Ovarian Cancer, *Obstetrics & Gynecology*: - 101 - 5, Part 1 - 885–891, May 2003.
3. Tate Thigpen, Mark F. Brady, George A. Omura M.D, William T. Creasman, William P. Mcguire, William J. Hoskins, Stephen Williams, Age as a prognostic factor in ovarian carcinoma: The gynecologic oncology group experience, *Cancer* 71, Supplement S2, 606–614, 15 January 1993.
4. H.A.A.M. Maas, R.F.P.M. Kruitwagen, V.E.P.P. Lemmens, S.H. Goey, M.L.G. Janssen-Heijnen, The influence of age and co-morbidity on treatment and prognosis of ovarian cancer: a population-based study, *Gynecologic Oncology*: 97,1, 104–109, 2005
5. Carol L. Kosary, Figo stage, histology, histologic grade, age and race as prognostic factors in determining survival for cancers of the female gynecological system: An analysis of 1973-87 SEER cases of cancers of the endometrium, cervix, ovary, vulva, and vagina, *Seminars in Surgical Oncology*, 10, 1, 31–46, January/February 1994.