

# Survival Rate Analysis Of Patients With Advanced Ovarian Cancer Treated According To Different Protocols

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## Citation

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## Abstract

**PURPOSE:** Certain indications point out that application of systemic chemotherapy prior to radical surgery can influence the length of remission period as well as overall survival. Aim of this paper is to analyse progression-free survival and overall survival rates of patients with advanced ovarian carcinoma primary treated according to different therapeutical procedures: by systemic chemotherapy after which underwent cytoreductive surgery and those treated by radical surgery and received chemotherapy and to compare survival data.

**PATIENTS AND METHODS:** This study included 168 patients with advanced ovarian carcinoma. Patients were divided in four groups. First group of patients underwent systemic chemotherapy prior to radical surgery. Patients of second and third group first had radical surgery followed by chemotherapy; after chemotherapy, patients from the second group underwent cytoreductive surgery. Patients from the fourth group were treated with systemic chemotherapy only. Progression-free survival and overall survival rate were calculated according to Kaplan-Meier method. Log Rank test was used to compare survival rates.

**RESULTS:** The longest progression-free survival (28 months) and overall survival rate (43 months) was recorded for patients subjected to radical surgery after systemic chemotherapy. Their survival was significantly better ( $p < 0.01$ ) than survival of patients who first underwent radical surgery after which chemotherapy was applied and especially better than survival of patients who were administered chemotherapy only ( $p < 0.0001$ ) since their survival data was the worst (6 months progression-free and 14 months overall).

**CONCLUSION:** Application of systemic chemotherapy prior to radical surgery has been proven efficient in treatment and survival of patients with advanced ovarian carcinoma.

## INTRODUCTION

Possible survival assessment of ovarian carcinoma patients is very complex and requires analysis of a great number of factors which can influence survival. The most important factors are disease stadium, age and residual tumour after laparotomy, histopathological type and clinical stage of the disease [1]. Each of these factors influence patient survival in a certain way, and their analysis is a complex issue which is still a very frequent focus of interest of scientists around the world. Surgical cytoreduction is the key factor influencing survival of patients with advanced ovarian carcinoma. Nevertheless, it is not always possible to perform surgical cytoreduction due to numerous possible complications [2, 3]. This is why in recent years various references often include discussions about when radical surgery should be applied and when systemic chemotherapy should be used, i.e. which is the optimal moment for radical surgical treatment of patients with advanced ovarian

carcinoma [4]. The role of systemic chemotherapy prior to radical surgery becomes even more important when taken into account that it facilitates subsequent performance of optimal radical cytoreduction, which is still the key factor influencing the survival data, coupled with the possibility of intraoperative intraperitoneal application of chemotherapy drugs which, according to the most recent research, treatment doubles survival length [5, 6].

## OBJECTIVE

To analyse progression-free survival and the overall survival rates of patients with advanced ovarian carcinoma treated according to different protocols: by systemic chemotherapy before radical surgery, by radical surgery after which received chemotherapy and cytoreductive surgery and to compare survival data.

## PATIENTS AND METHODS

This study included 168 patients with advanced ovarian carcinoma who were treated and subjected to surgery in University Clinic for Obstetrics and Gynaecology "Narodni Front" in Belgrade in the period 2007-2010. The research was organized as a prospective study. Patients were divided in four groups. First group of patients underwent systemic chemotherapy prior to radical surgery (27 patients). Second group of patients was first treated with radical surgery after which they were treated with chemotherapy; after chemotherapy, patients from this group underwent citoreductive surgery (19 patients). Third group of patients was treated with radical surgery after which they were treated with chemotherapy but citoreductive surgery was not done (89 patients). Patients from the fourth group were treated with systemic chemotherapy only (33 patients). The decision whether to start treatment by radical surgery i.e. whether to continue radical surgical procedure or to start treatment by application of systemic chemotherapy after histological diagnostics done during biopsy depended on the assessment of intraoperative findings performed by the surgeon. In these cases, surgeon was a gynaecologist with vast experience in oncological surgery and the assessment was based on prediction of intraoperative and postoperative complications which could prolong postoperative recovery period and postpone systemic chemotherapy until complete recovery.

All patients were affected by histopathologically diagnosed serous ovarian carcinoma. Histopathological diagnostics was based on biopsy findings (for patients from first and fourth group) and on radical surgery findings (for patients from second and third group). All patients were administered chemotherapy with Taxol and Carboplatin. Their condition was evaluated in three-month intervals. Patients from the first, second and third group were 57 years old (in average) while patients from the fourth group were significantly older (63 years old in average). Statistical analysis has shown that patients from the fourth group were significantly older, both from patients of the first group ( $t=2.539 \Rightarrow p<0.05$ ) as well as from the patients of second and third group ( $t=2.999 \Rightarrow p<0.01$ ).

Progression-free survival and overall survival rate were calculated according to Kaplan-Mayer method. Log Rang test was used to compare survival rates of the four groups.

## RESULTS

Patients were divided in four groups.

Group 1. After biopsy and histopathological verification of

cancer type, patients from this group were first administered systemic chemotherapy after which radical surgery was performed. It included total abdominal hysterectomy with bilateral adnexectomy, omentectomy and maximum tumor cytoreduction. Patient average age for the first group was 57. This group comprised of 27 patients.

Group 2. Patients from the second group were first subjected to radical surgery according to advanced ovarian carcinoma protocol, after which they were administered systemic chemotherapy. After chemotherapy they were surgically treated again, that is, citoreductive surgery (reexploration with maximum tumor cytoreduction) was performed. Average age of second group patients was 57. This group comprised of 19 patients.

Group 3. Patients from the third group were subjected to radical surgery according to advanced ovarian carcinoma protocol, after which they were administered systemic chemotherapy. Average age of third group patients was 57. This group consisted of 89 patients.

Group 4. Patients from the fourth group were subjected to tumor biopsy only as means of histopathological diagnostics, after which systemic chemotherapy was administered. Average age of fourth group patients was 63. This group consisted of 33 patients.

Statistical analysis has shown that patients from the fourth group were significantly older, both from patients of the first group ( $t=2.539 \Rightarrow p<0.05$ ) as well as from the patients of second and third group ( $t=2.999 \Rightarrow p<0.01$ ).

### Progression-Free Survival Analysis

Progression-free survival of patients who were initially administered systemic chemotherapy followed by radical surgery (first group) equalled 28 months.

Progression-free survival of patients who were initially subjected to radical surgery followed by chemotherapy and citoreductive surgery (second group) equalled 13 months.

Progression-free survival of patients who were initially subjected to radical surgery followed by systemic chemotherapy but not subjected to citoreductive surgery (third group) equalled 24 months.

Progression-free survival of patients who were treated by systemic chemotherapy only and not subjected to radical surgery (fourth group) equalled 6 months.

Results have shown that the period before disease progression was the longest for patients who were first administered systemic chemotherapy which was followed by radical surgery (first group) i.e. the remission period lasted 28 months.

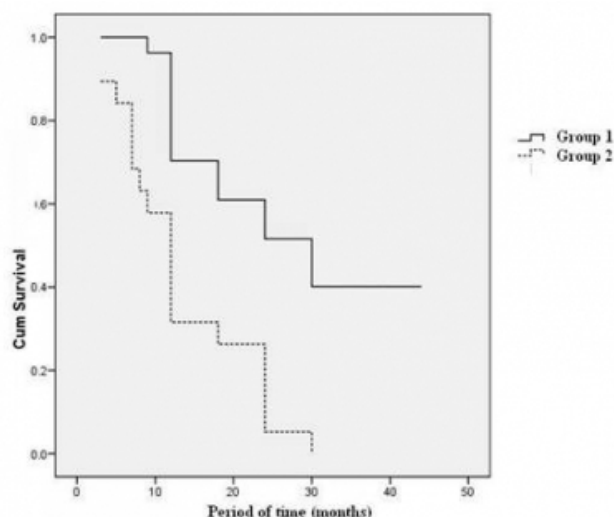
Progression-free survival of patients who were subjected to radical surgery followed by systemic chemotherapy equalled 24 months as compared to patients who were subjected to radical surgery followed by chemotherapy after which citoreductive surgery was performed. Remission period for the latter equalled 13 months.

Remission period was the shortest in patients who did not undergo radical surgery (fourth group). In these cases, remission occurred after only 6 months.

Statistic analysis used to compare progression-free survival data of patients who were first administered chemotherapy after which radical surgery was performed with that of patients who underwent radical surgery first after which they were administered chemotherapy determined the existence of a statistically highly significant difference in survival between the two groups of patients ( $X^2=16.260 \Rightarrow p<0.0001$ ). Remission period for patients first treated with systemic chemotherapy followed by radical surgery was significantly longer, as shown in Figure 1 (please refer to Figure 1).

**Figure 1**

Progression-free survival curve for patients who were first administered systemic chemotherapy after which they were subjected to radical surgery (group 1) and patients who first underwent radical surgery followed by systemic chemotherapy (group 2).



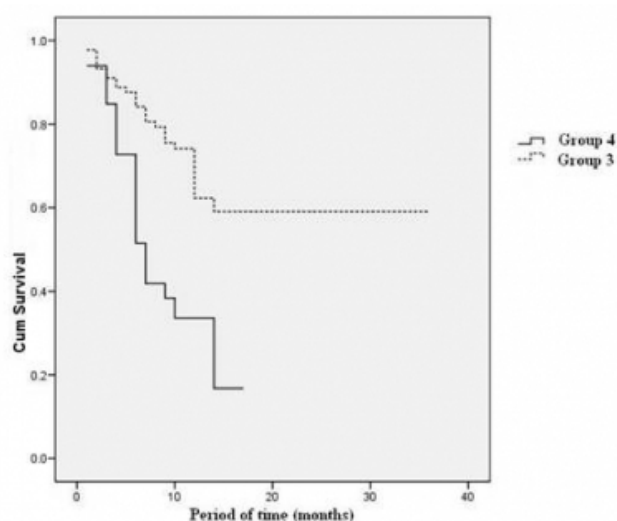
Statistic analysis of progression-free survival data of patients who were treated with systemic chemotherapy only and patients who underwent radical surgery first after which they were administered systemic chemotherapy determined the existence of a statistically highly significant difference in progression-free survival between the two groups of patients ( $X^2=17.515 \Rightarrow p<0.0001$ ). Remission period for patients

who were subjected to radical surgery was significantly longer.

Progression-free survival of patients treated with systemic chemotherapy (group 4) and those subjected to radical surgery followed by systemic chemotherapy (group 3) is represented in Figure 2 (please refer to Figure 2).

**Figure 2**

Progression-free survival for patients who were administered systemic chemotherapy (group 4) and patients who underwent radical surgery followed by systemic chemotherapy (group 3).

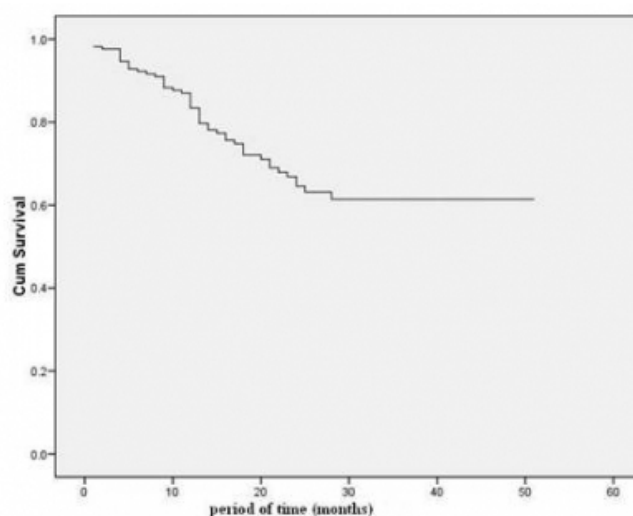


## Overall Survival Analysis

Average survival of all patients included in this research equalled 36 months (please refer to Figure 3).

**Figure 3**

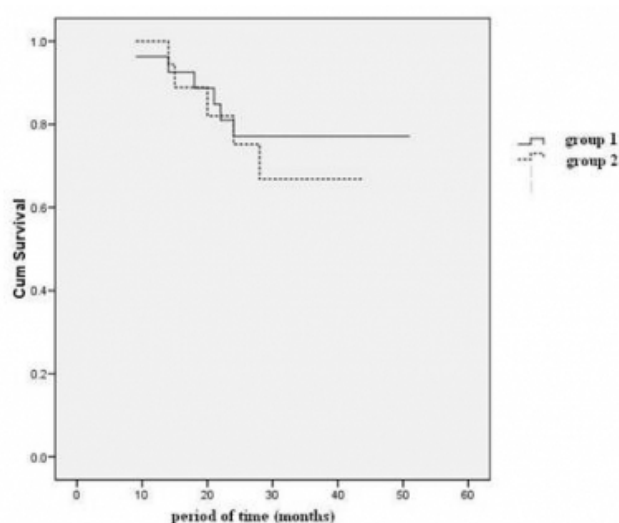
Survival curve for patients diagnosed and treated from ovarian carcinoma in the period 2007 - 2010.



However, analysis of survival data of patients from each group separately has lead to the following conclusions. Overall survival of patients treated with systemic chemotherapy followed by radical surgery (group 1) equalled 43 months. The survival of these patients was the longest when compared to all patients analysed. Overall survival of patients who were first subjected to radical surgery after which they were administered systemic chemotherapy, including both patients who were later subjected to citoreductive surgery and those not subjected to citoreductive surgery (second and third group of patients) equalled 36 months. The poorest survival was recorded for patients treated with systemic chemotherapy only, without radical surgery (group four). Their overall survival equalled only 14 months. However, comparison of overall survival between patients who were first administered systemic chemotherapy after which radical surgery was performed and patients who were first subjected to radical surgery after which systemic chemotherapy was administered (first and second group) using the Log Rank test has concluded that there is no statistically significant difference between survivals of analysed groups ( $X^2=0.277 \Rightarrow p>0.05$ ). A small clinical significance, nevertheless, does exist (please refer to Figure 4).

**Figure 4**

Overall survival curve for patients treated with systemic chemotherapy followed by radical surgery (group 1) and patients subjected to radical surgery followed by systemic chemotherapy (group 2).

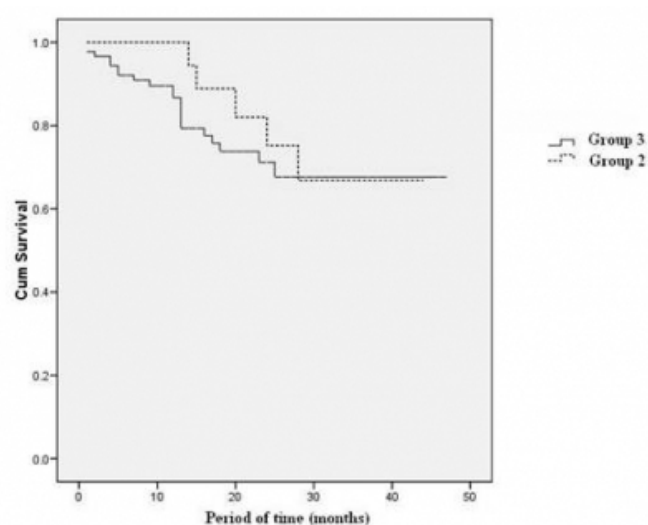


Overall survival of patients who were first subjected to radical surgery after which systemic chemotherapy was

administered (including both patients who underwent citoreductive surgery after chemotherapy and those who were not subjected to citoreductive surgery) equalled 36 months. Statistically significant difference in survival of patients from observed groups was not determined ( $X^2=0.356 \Rightarrow p>0.05$ ). Citoreductive surgery performed after radical surgery and after application of systemic chemotherapy has no influence on the overall survival (please refer to Figure 5).

**Figure 5**

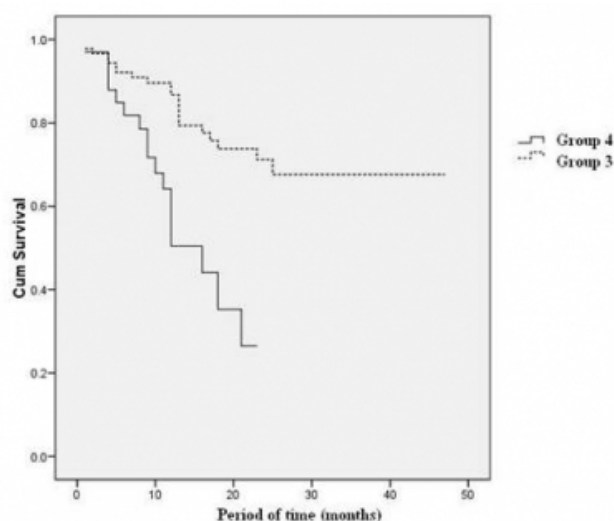
Overall survival curve after radical surgery and systemic chemotherapy for patients who were/were not subjected to citoreductive surgery (group 2 and group 3).



The poorest survival (14 months) was recorded for patients who were not subjected to radical surgery, i.e. who were treated only with systemic chemotherapy. Statistical analysis has confirmed the existence of highly statistically significant difference in survival of patients treated with systemic chemotherapy only and those patients who were subjected to radical surgery followed by systemic chemotherapy ( $X^2=15.245 \Rightarrow p<0.0001$ ).

**Figure 6**

Overall survival curve for patients treated with systemic chemotherapy only (group 4) and patients subjected to radical surgery followed by chemotherapy (group 3).



Results have shown that patients who were administered systemic chemotherapy prior to radical surgery had the longest progression-free survival as well as the longest overall survival (28 and 43 months respectively).

The poorest survival was recorded for those patients who were not subjected to radical surgery at all (6 months progression-free and 14 months overall).

Cytoreductive surgery performed after radical surgery and systemic chemotherapy has no influence on the length of the overall survival but does influence the length of the progression-free period, which is longer for patients who were not subjected to cytoreductive surgery.

## DISCUSSION

Even though radical surgery with maximum cytoreduction still represents the primary method of treatment of advanced ovarian carcinoma, the role of chemotherapy is obvious. Application of new therapy modalities with Platinum (Taxol Carboplatin etc.) has been proven very efficient in treatment and control of ovarian carcinoma [5, 7]. It has been noted that ovarian carcinoma respond very well to systemic chemotherapy, which can lead to «transformation» from inoperable into operable state [8].

Considering the fact that surgical cytoreduction is the key factor influencing the survival, the significance of adequate and timely application of radical surgery becomes obvious

[9, 10].

This research has shown that both progression-free survival and the overall survival are significantly longer for patients who were primarily treated with systemic chemotherapy which was then followed by radical surgery. The research has also shown that performance of cytoreductive surgery on patients who were subjected to radical surgery followed by systemic chemotherapy has no effect on the overall survival but does affect the length of the progression-free period, which is shorter for patients who were subjected to cytoreductive surgery. Patients treated with systemic chemotherapy only and were not subjected to radical surgery had the poorest overall survival as well as the shortest progression-free period.

Application of systemic chemotherapy prior to radical surgical treatment has been proven to be a very efficient treatment of patients with advanced ovarian carcinoma.

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