Slovenian Medical Journal

Survival in patients with advanced staged epithelial ovarian cancer: is treatment with neoadjuvant chemotherapy more effective than primary debulking surgery?

Ocena preživetja bolnic z napredovalim epitelijskim rakom jajčnikov; ali je neoadjuvantna kemoterapija učinkovitejši način zdravljenja kot primarna citoreduktivna operacija?

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Abstract

Background: The aim of this research was to evaluate the superiority or non-inferiority of neoadjuvant chemotherapy (NACT) or primary debulking surgery (PDS) in the management of patients with advanced-stage epithelial ovarian carcinoma.

Methods: The study evaluated consecutive patients with advanced-stage (FIGO stage IIIC/IV) ovarian cancer treated at the Institute of Oncology institute Ljubljana from 01/01/ January 2005 to 31/12/ December 2015. The study tried to determine whether PDS and adjuvant chemotherapy compared to NACT and interval debulking surgery are equivalent management of patients with advanced epithelial ovarian cancer, in regard to overall survival (OS), 5-year survival, progression -free survival and resection rates.

Results: Three hundred and two women met the inclusion criteria, 84.1% (254/302) were treated with NACT and 15.9% (48/302) with PDS. Median age was 61 years (range 29–85). The median OS was lower in the NACT group compared to PDS group, i.e. 24 months and vs. 52 months, respectively. The PFS in NACT group was 9 months in NACT group and 19 months in PDS group. Five-year survival rate was 35% Iin patients treated with PDS 5-year survival rate was 35% and 15% in NACT group. In patients with complete gross resection treated with PDS median OS was 54 months compared to 36 months in patients treated with NACT and complete gross resection in IDS. Complete gross resection was achieved in 35.4% in PDS group and in 52.4% in NACT group.

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Key words: ovarian cancer; adjuvant chemotherapy; primary debulking surgery; interval debulking surgery; neoadjuvant chemotherapy

Ključne besede: rak jajčnikov; kemoterapija pred operacijo; primarna citoredukcija; odložena citoredukcija; kemoterapija po operaciji

Received / Prispelo: 18. 5. 2020 | **Accepted / Sprejeto:** 21. 7. 2021

Cite as / Citirajte kot: Merlo S, Pavlin T, Kovačević N. Survival in patients with advanced staged epithelial ovarian cancer: is treatment with neoadjuvant chemotherapy more effective than primary debulking surgery? Zdrav Vestn. 2022;91(1–2):3–13. **DOI:** https://doi.org/10.6016/ZdravVestn.3087

Conclusion: In this single institution analysis, the best survival outcomes were observed in patients who were treated with PDS followed by adjuvant chemotherapy. If the patient is not fit for the surgical procedure, NACT doubles the possibility to havefeasibility of complete gross resection. Despite higher rates of complete gross resection achieved after NACT, patients who were treated with PDS (complete gross resection or optimal surgery) had higher OS.

Izvleček

Izhodišča: Umrljivost zaradi raka jajčnikov je v svetu pomemben zdravstveni problem. Namen raziskave je bil primerjati uspešnost zdravljenja bolnic z napredovalim rakom jajčnikov z neoadjuvantno kemoterapijo pred operacijo ali s primarno citoreduktivno operacijo.

Metode: V retrospektivno raziskavo smo vključili bolnice, ki so bile zdravljene na Onkološkem inštitutu od januarja 2005 do decembra 2015 zaradi napredovalega epitelijskega raka jajčnikov (FIGO stadij IIIC/IV). Primerjali smo celokupno preživetje, petletno preživetje, obdobje brez ponovitve bolezni in uspešnost operacije glede na ostanek bolezni.

Rezultati: V raziskavo sta bili vključeni 302 bolnici, od katerih je 254 (84,1 %) bolnic prejelo kemoterapijo pred operacijo, 48 (15,9 %) pa jih je bilo zdravljenih s primarno citoreduktivno operacijo. Srednja starost preiskovank je bila 61 let (razpon 29–85 let). Celokupno preživetje bolnic in obdobje brez ponovitve bolezni v skupini, ki je prejela kemoterapijo pred operacijo, je bilo 24 in 9 mesecev ter 52 in 19 mesecev v skupini s primarno citoreduktivno operacijo. Pri bolnicah, zdravljenih s primarno citoredukcijo, je bilo petletno preživetje 35 %, pri bolnicah, zdravljenih s kemoterapijo pred operacijo, pa 15 %. V skupini s popolno primarno citoredukcijo, brez makroskopskega ostanka, in kemoterapijo po operaciji je bilo celokupno preživetje 54 mesecev, pri bolnicah, zdravljenih s kemoterapijo pred operacijo ter odloženo citoredukcijo brez makroskopskega ostanka pa 36 mesecev. Popolna primarna citoredukcija, brez makroskopskega ostanka, je bila narejena pri 35,4 % bolnic, po kemoterapiji pred operacijo pa se je popolna intervalna citoredukcija opravila pri 52,4 % operirank.

Zaključek: V raziskavi so imele najdaljše celokupno preživetje bolnice s popolno primarno citoredukcijo in kemoterapijo po operaciji. Če je bolnica prejela kemoterapijo pred operacijo, se je verjetnost popolne odložene citoredukcije brez makroskopskega ostanka povečala, vendar je bilo kljub temu celokupno preživetje krajše kot pri bolnicah s popolno ali optimalno primarno citoredukcijo.

1 Introduction

According to the Cancer Registry of the Republic of Slovenia, 156 women are diagnosed with ovarian cancer every year (15.0/100,000) and 147 (14.5/100,000) died in the period between 2012 and 2016. Ovarian cancer with its 2.9% is the 8th most common cancer among women (1).

Epithelial ovarian cancer is mostly detected at an advanced stage due to uncharacteristic symptoms resulting from tumour-related compression of adjacent organs, ascites, and lack of effective diagnostic examinations. According to the FIGO international staging system (Federation Internationale de Gynecologie et d'Obstetrique in French), two thirds of patients have stage III or IV (2,3).

In patients with advanced ovarian cancer, the disease recurs in 85% within the first two years after the completion of the post-surgical treatment and adjuvant chemotherapy. Thus, the five-year survival is only about 40% (2,4).

The basic treatment for ovarian cancer is primary debulking surgery and platinum- and taxane-based adjuvant chemotherapy. 70% of patients opt for such an approach to treatment (4,5). In patients who are not eligible for surgical treatment due to associated disease or age, the basic treatment is neoadjuvant chemotherapy, followed by delayed debulking surgery (6). The criteria for deciding on neoadjuvant chemotherapy are not clearly defined, but the latter method of treatment is chosen mainly in patients whose disease is so advanced that complete or at least optimal debulking surgery is not feasible at all (8,9).

The absence of macroscopic residual tumour after primary debulking surgery is the most important prognostic factor influencing the survival time. Studies have shown that primary debulking makes sense only in patients with a residual tumour of less than one cm in size (10,11). These findings raise the question of whether neoadjuvant chemotherapy followed by delayed debulking is as effective a treatment approach as primary debulking and adjuvant chemotherapy.

The aim of the study was to determine whether in patients with advanced ovarian epithelial cancer, treatment with primary debulking and adjuvant chemotherapy is comparable to neoadjuvant chemotherapy and delayed

debulking. We were interested in the overall survival, five-year survival, progression-free survival, and resection rates between groups.

2 Methods

2.1 Research plan and the patients

The retrospective study included 302 female patients with a histologically confirmed diagnosis of advanced epithelial ovarian cancer (FIGO stage IIIC/IV) who were treated at the Institute of Oncology between January 2005 and December 2015. This included a follow-up period of at least 60 months.

According to the primary treatment approach, the patients were divided into two groups. The first group included 254 (84.1%) patients who were treated with neoadjuvant chemotherapy (platinum- and paclitaxel-based) and delayed debulking. The second group included 48 (15.9%) patients with primary debulking surgery who received chemotherapy after surgery (3 cycles according to the same regimen as with the neoadjuvant chemotherapy). Histopathology was made by diagnostic laparoscopy or by core needle biopsy. Based on imaging examinations and the opinion of a gynaecologic oncologist, a decision was made on the type of treatment. The primary debulking surgery was opted for when it was estimated that complete or at least optimal debulking would be possible. Otherwise, neoadjuvant chemotherapy and delayed debulking were chosen. The tumour was assessed as unresectable if carcinomatosis of the intestinal serosa and/or mesentery was present or imaging showed that the tumour had spread to distant organs. The time window from the last neoadjuvant chemotherapy cycle to the delayed debulking surgery was 4-6 weeks, and the interval from primary debulking to the first adjuvant chemotherapy cycle was 3-4 weeks for all patients involved.

Progression-free survival was defined as the time from treatment completion to image-confirmed recurrence of the disease. An increase in the tumour marker CA-125 without clinical signs of disease recurrence was an indication for additional diagnosis by imaging. Overall survival was defined as the time from the diagnosis of ovarian cancer to death.

Success of a surgical procedure was assessed taking into account the residual tumour or the diameter of the largest lesion. In complete resection there was no macroscopic residual disease, in optimal resection the lesions were 1 cm or less, and in suboptimal resection the residual was greater than 1 cm.

Patients with a history of other malignancies, lower stage ovarian cancer (FIGO I to IIIB), histological diagnosis of non-epithelial ovarian cancer, and those who had previously received neoadjuvant chemotherapy were excluded from the study.

The research was approved by the Ethics Commission of the Institute of Oncology Ljubljana (consent number ERIDNPVO-0002/2020, dated 6 April 2019).

2.2 Statistical analysis

Statistical analysis was performed with the SPSS program, Version 26, Chicago, USA. Pearson's chi-square test was used where variables were arranged normally. If the variables were not distributed normally, a nonparametric Mann-Whitney U-test was used, and the median with the lowest and highest value was considered as the mean value. The overall survival and progression-free survival period were assessed using the Kaplan-Meier model. Values in both groups were compared with the log-rank test. $P<0.05$ assumed that the difference between the groups was statistically significant.

3 Results

From January 2005 to December 2015, 302 patients met the inclusion criteria. 254 patients were treated with neoadjuvant chemotherapy and 48 patients with primary debulking surgery. The baseline characteristics of the subjects presented in Table 1 were comparable between the two groups, except for age, pre-surgery ASA scores, performance assessment according to the World Health Organization (WHO), CA-125 values, and pre-surgery FIGO stage. The median duration of patient follow-up was 28 months (range, 0.5–170 months).

Overall survival in the neoadjuvant chemotherapy group was 24 months (95% CI: 20.5–27.4) and 52 months (95% CI: 43.2–60.7) in the group treated with primary debulking surgery ($p<0.001$).

The progression-free survival in the neoadjuvant chemotherapy group was 9 months (95% CI: 7.6–10.3) and in the primary debulking group it was 19 months (95% CI: 13.6 –24.4) ($p<0.001$).

Between 2005 and 2010, 163 patients with advanced epithelial ovarian cancer were treated at the Institute of Oncology Ljubljana, of which 30 were treated with primary debulking and adjuvant chemotherapy and 133 with neoadjuvant chemotherapy and delayed debulking. In 2011–2015, 139 patients were treated for advanced ovarian cancer, 18 with primary debulking surgery and adjuvant chemotherapy, and 121 with neoadjuvant

Table 1: Basic characteristics of patients (N=302).

Characteristics		Primary debulking (N=48)	Neoadjuvant chemotherapy (N=254)	p-value
Age (years)	Median	54,5	62.0	<0.001
	Range	38–85	29–84	
BMI (kg/m²)	Median	24.9	24.3	0.135
	Range	18.2–39.5	17.4–45.7	
Parity (number)	Median	2	2	0.049
	Range	0–4	0–6	
Menopause (years)	Median	50. 0	50.0	0.615
	Range	37–58	42–58	
ASA	1	16 (33.3%)	26 (10.2%)	<0.001
	2	24 (50.0%)	157 (61.8%)	
	3	8 (16.7%)	70 (27.6%)	
	4	0 (0%)	1 (0.4%)	
Performance status according to WHO	0	31 (64.6%)	92 (36.2%)	0.007
	1	13 (27.1%)	122 (48.0%)	
	2	4 (8.3%)	32 (12.6%)	
	3	0 (0%)	6 (2.4%)	
	4	0 (0%)	2 (0.8%)	
FIGO stage	IIIC	44 (91.7%)	176 (69.3%)	<0.001
	IV	4 (8.3%)	78 (30.7%)	
Histological type	Serous	43 (89.6%)	241 (94.9%)	0.251
	Endometrioid	4 (8.3%)	8 (3.1%)	
	Mucinous	1 (2.1%)	2 (0.8%)	
	Clear cell	0 (0.0%)	3 (1.2%)	
Neoadjuvant chemotherapy (125U/mL)	Median	287	892	0.008
	Schedule	34–5739	10–31481	
Surgical outcome	Complete resection	17 (35.4%)	133 (52.4%)	0.037
	Optimal resection (<1 cm)	14 (29.2%)	70 (27.6%)	
	Suboptimal resection (>1 cm)	17 (35.4%)	51 (20.1%)	

Legend: BMI – Body Mass Index; ASA – American Society of Anesthesiology; WHO – World Health Organisation; FIGO – *fr.* Federation Internationale de Gynecologie et d Obstetriques; CA – cancer antigen.

chemotherapy and delayed debulking. Overall survival and progression-free survival rates in 2005–2010 are shown in Table 2 and those in 2011–2015 are shown in Table 3. There is no statistically significant difference in overall survival and progression-free survival between 2005–2010 and 2011–2015 (Table 4).

The five-year survival of patients after primary debulking was 35% and after neoadjuvant chemotherapy

Table 2: Overall survival and progression-free survival (in months) between 2005 and 2010.

Period 2005–2010	Primary debulking (N=30)	Neoadjuvant chemotherapy (N=133)	p-value
Overall survival (months)	49 (95% CI: 26.1–71.8)	23 (95% CI: 18.7–27.2)	<0.001
Progression-free survival (months)	21 (95% CI: 12.6–29.3)	8 (95% CI: 6.3–9.6)	<0.001

Table 3: Overall survival and progression-free survival (in months) between 2011 and 2015.

Period 2005–2010	Primary debulking (N=18)	Neoadjuvant chemotherapy (N=121)	p-value
Overall survival (months)	52 (95% CI: 47.8–56.1)	27 (95% CI: 21.9–32.0)	0.014
Progression-free survival (months)	18 (95% CI: 6.2–29.7)	10 (95% CI: 7.6–12.3)	0.343

Table 4: Comparison of overall survival and progression-free survival in periods 2005–2010 and 2011–2015.

Period 2005–2010	Period 2005–2010 (N=163)	Period 2011–2015 (N=139)	p-value
Overall survival (months)	52 (95% CI: 43.5–62.2)	46 (95% CI: 32.1–51.6)	0.820
Progression-free survival (months)	19 (95% CI: 15.2–23.8)	16 (95% CI: 12.6–17.5)	0.851

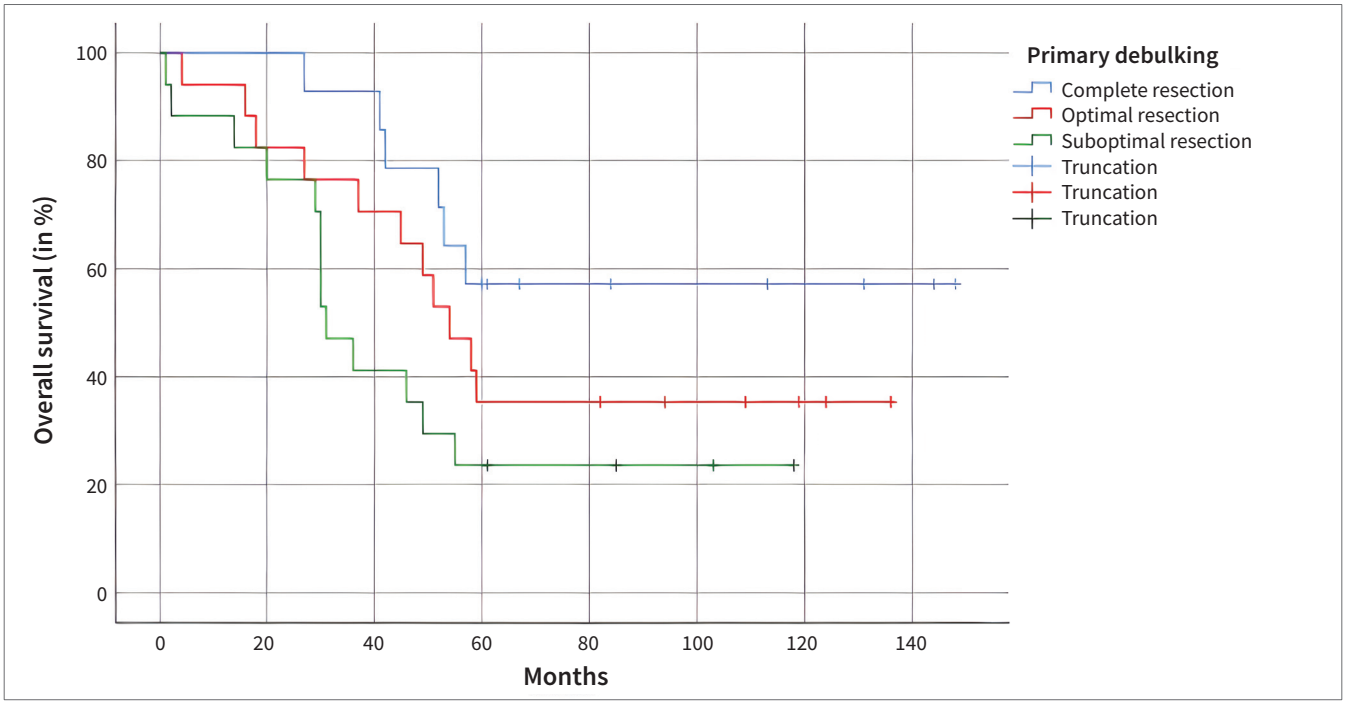

Figure 1: Overall survival in patients after primary debulking according to surgical outcome.

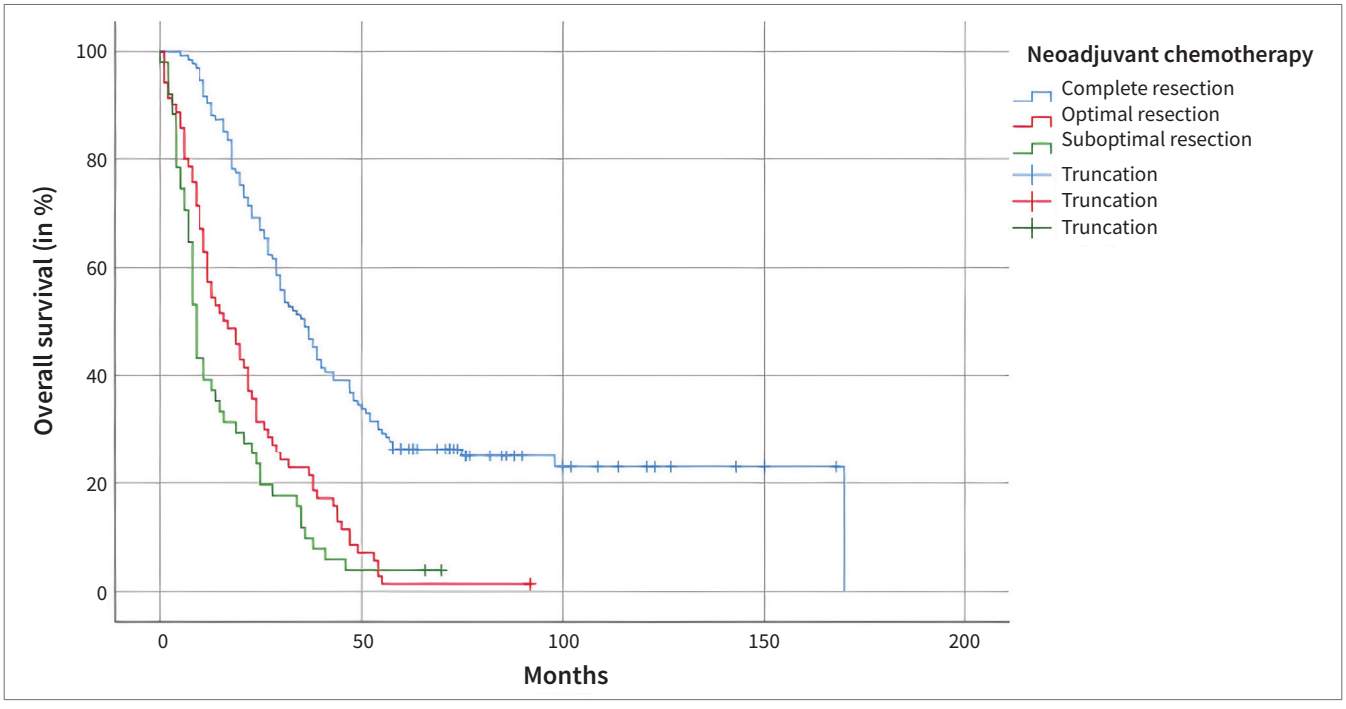

Figure 2: Overall survival in patients after neoadjuvant chemotherapy based on surgical outcome.

it was 15% (p<0.001). In the period between 2005 and 2010, the five-year survival rate in patients treated with primary debulking was 37% and in the period 2011–2015 it was 34% (p=0.786). Five-year survival in patients treated with neoadjuvant chemotherapy in 2005–2010 was 16% and in 2011–2015 it was 14% (p=0.754).

The longest overall survival was in patients treated with primary debulking in whom the surgical residual was 1 cm or less (p<0.001, Figures 1 and 2). Also, the longest progression-free survival was achieved in patients treated with primary complete debulking (p<0.001, Figures 3 and 4). The impact of different surgical outcomes

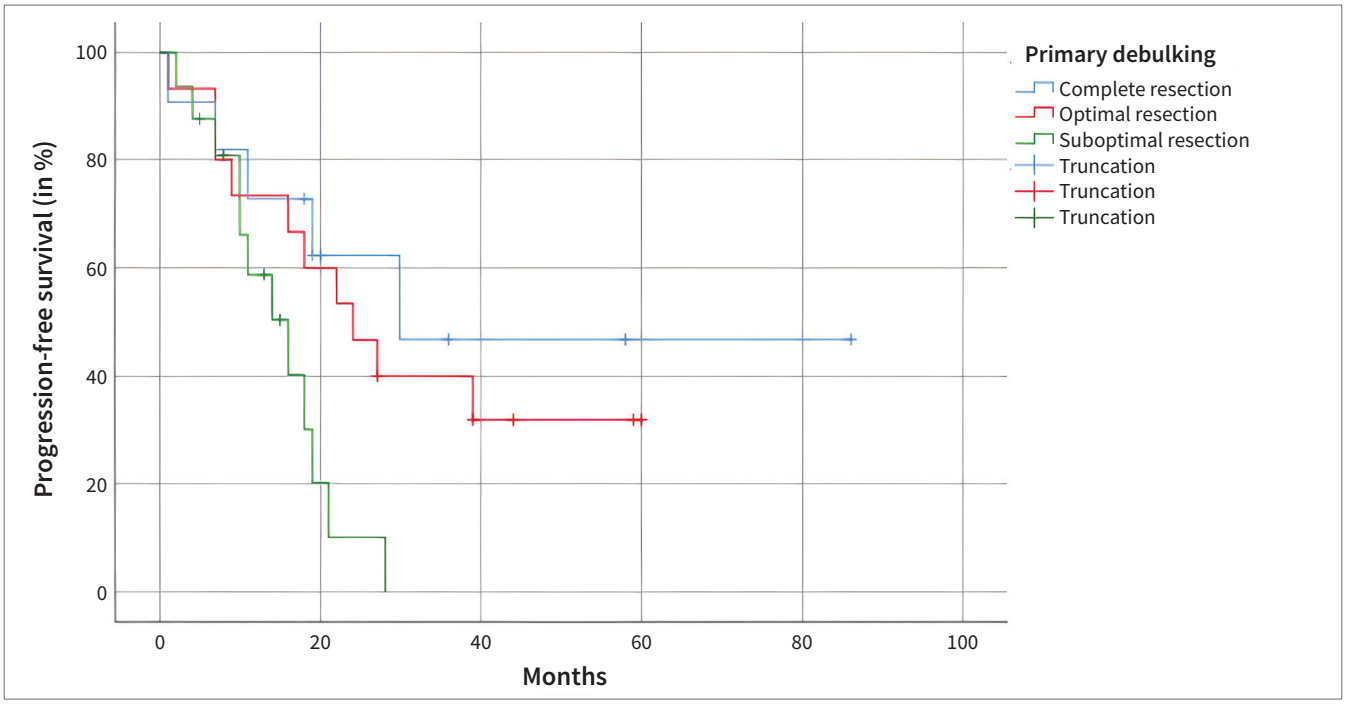

Figure 3: Progression-free survival in patients after primary debulking according to surgical outcome.

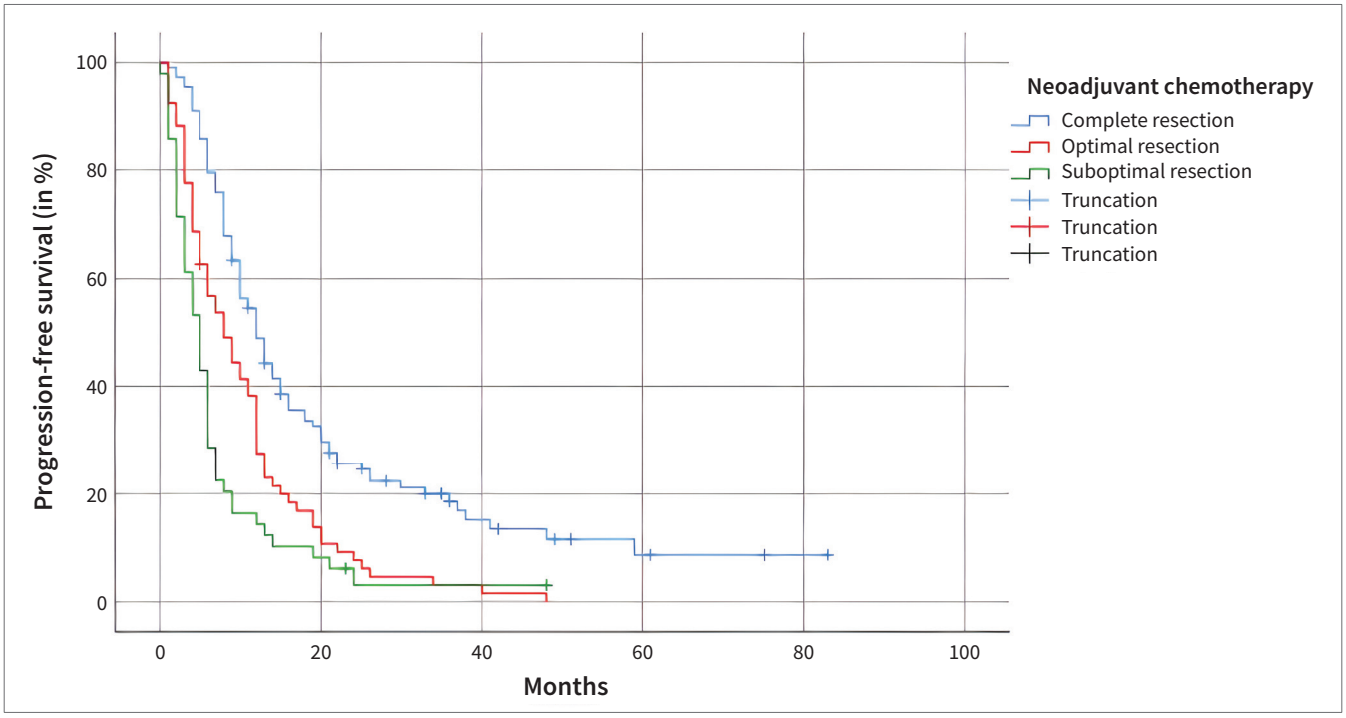

Figure 4: Progression-free survival in patients after neoadjuvant chemotherapy according to the surgical outcome.

on overall survival and on the progression-free survival is shown in Table 5.

Recurrence of the disease happened in 89.7% (271/302) of patients. The disease recurred in 87.5% (42/48) of patients treated with primary debulking and adjuvant chemotherapy and in 90.2% (229/254) of patients treated with neoadjuvant chemotherapy and delayed debulking (Table 6). Recurrence of the disease was treated with secondary debulking and second-line chemotherapy in 16.2% (44/271) of patients. The secondary second-line therapy only was introduced in 83.8% (227/271) of patients (Table 7).

The share of secondary debulking surgeries was higher in the group with primary debulking (42.9% compared to 11.4%, p<0.001).

Table 5: Overall survival and progression-free survival (in months) in different surgical outcomes in the group treated with primary debulking and neoadjuvant chemotherapy.

Surgical outcome		Primary debulking (N=48)	Neoadjuvant chemotherapy (N=254)	p-value
Overall survival (months)	Complete resection	54 (95% CI: 41.8 –66.1)	36 (95% CI: 30.0 –41.9)	<0.001
	Optimal resection (≤1 cm)	52 (95% CI: 33.3 –60.3)	16 (95% CI: 9.4 –22.5)	
	Suboptimal resection (>1 cm)	31 (95% CI: 25.3 –36.6)	9 (95% CI: 7.7–0.2)	
Progression-free survival (months)	Complete resection	24 (95% CI: 10.7–37.2)	13 (95% CI: 10.7–15.2)	<0.001
	Optimal resection (≤1 cm)	18 (95% CI: 9.4–25.3)	8 (95% CI: 6.4–9.5)	
	Suboptimal resection (>1 cm)	16 (95% CI: 8.4–23,5)	5 (95% CI: 3.4–6.5)	

Table 6: Disease recurrence in patients treated with primary debulking and in patients treated with neoadjuvant chemotherapy.

Ponovitev bolezni	Primary debulking (N=48)	Neoadjuvant chemotherapy (N=254)	p-value
Disease recurrence	6 (12.5%)	25 (9.8%)	0.578
Without recurrence of the disease	42 (87.5%)	229 (90.2%)	

Table 7: Method of treatment of recurrent disease in patients treated with primary debulking and in patients treated with neoadjuvant chemotherapy.

Recurrent disease treatment	Primary debulking (N=42)	Neoadjuvant chemotherapy (N=229)	p-value
Secondary debulking and second-line chemotherapy	18 (42.9%)	26 (11.4%)	<0.001
Second-line chemotherapy	24 (57.1%)	203 (88.6%)	

4 Discussion

The basic treatment for advanced ovarian cancer is primary debulking surgery and adjuvant platinum- and taxane-based chemotherapy. When complete or optimal removal of the tumour is not feasible due to metastases and/or infiltrative tumour growth, it is advisable to use neoadjuvant chemotherapy.

The results of the EORTC/NCIC and CHORUS trials showed comparable efficacy of neoadjuvant chemotherapy or primary debulking surgery. The overall survival of patients was comparable in both groups, but the proportion of optimal resections was higher in the group of subjects treated with neoadjuvant chemotherapy. The progression-free survival and overall survival for patients treated with primary debulking were 12 and 29 months in the EORTC/NCIC trial, compared with 12 and 30 months for the group of patients treated with neoadjuvant chemotherapy. In the CHORUS trial, the progression-free survival and overall survival were 11 and 23 months in primary debulking and 12 and 24 months in neoadjuvant chemotherapy. These data advocate neoadjuvant chemotherapy as a safe alternative to primary debulking (4,12).

At our facility, neoadjuvant chemotherapy was the treatment of choice for patients with advanced ovarian cancer because radical peritonectomies and upper abdominal surgeries were not routinely performed. It was also the treatment of choice for patients with associated diseases who were not suitable for more extensive surgical procedures.

The progression-free survival and overall survival for subjects treated with neoadjuvant chemotherapy in our study were 9 and 24 months, compared to 19 and 52 months in patients who had primary debulking surgery. Our results are in contrast to the results published in the EORTC/NCIC and CHORUS trials, but are comparable to the studies published by Mueller et al. (5). The reason for shorter overall survival and progression-free survival in patients receiving neoadjuvant chemotherapy was higher age, higher stage of the disease, higher CA-125 levels before surgery, and more prevalent disease compared to the group of patients treated with primary debulking.

The five-year survival was higher in the primary debulking group than in patients receiving neoadjuvant chemotherapy (35% and 15%, respectively). The same results in the study were published by Rosen (12): seven-year survival was lower in patients treated with neoadjuvant chemotherapy (8.6% vs. 41%; p<0.001), while May published a study on comparable five-year survival in the group treated with neoadjuvant chemotherapy and primary debulking (27% and 39%) (13).

The patients included in the analysis were primarily treated over an eleven-year period, which is a substantially long period in modern medicine in which the methods of diagnosis and treatment can change. According to the Cancer Registry, the five-year survival for patients with ovarian cancer in the period 2008–2012 was longer than in the period 2013–2017 (43.2% compared to 40.0%) (14). Our results did not show a statistically significant difference in the overall survival of patients treated in 2005–2010 compared to patients treated between 2011 and 2015 (52 and 46 months, p=0.820). There was also

no statistically significant difference between the progression-free survival in patients treated in 2005–2010 and those treated in 2011–2015 (19 and 16 months, p=0.851). There was no statistically significant difference in the five-year survival of patients treated with primary debulking in 2005–2010 compared to 2011–2015 (37% and 34%, p=0.786), or with neoadjuvant chemotherapy (16% and 14%, p=0.754). Despite advances in diagnostic procedures, more than half of ovarian cancer cases are still detected at an advanced stage. High mortality is primarily due to the high proportion of advanced cases in which the chances of survival are significantly lower than in the still limited disease (92% compared to 34%) (15).

In our study, we observed a statistically significant difference in surgical outcome in both groups of patients. Overall survival was longest in patients with complete primary debulking, namely 54 months. Overall survival in the neoadjuvant chemotherapy and delayed debulking group without macroscopic residual was 36 months. Bias was observed in the selection of patients for a specific type of treatment, as older patients with more advanced disease were more likely to be treated with neoadjuvant chemotherapy. Nevertheless, these patients had better survival rates than patients who underwent suboptimal primary debulking (overall survival was 31 months). The poorer survival in the group receiving neoadjuvant chemotherapy can be attributed to less favourable biological characteristics of the tumour and the intermittent discontinuation of cytostatics due to delayed debulking. This may have adversely affected tumour growth kinetics and contributed to the development of chemoresistance.

We also found statistically significant differences in the success of surgical resections between the two groups. Complete resection was achieved in 35.4% of patients who underwent primary debulking and in 52.4% of patients who received neoadjuvant chemotherapy. Many researchers believe that the feasibility of a complete resection is the most important factor in deciding on primary debulking. If complete resection cannot be achieved, neoadjuvant chemotherapy is advised (16-18). Despite the fact that the proportion of complete resections is statistically significantly higher in patients who received neoadjuvant chemotherapy, our study showed that overall survival and progression-free survival is longer in patients in whom at least optimal primary debulking can be achieved.

Complete debulking without a macroscopic residual was almost twice as likely to be achieved in patients who received neoadjuvant chemotherapy. Tumour marker CA-125, diagnostic imaging tests, age, disease stage, and associated diseases are indicators used to predict the success of primary surgery. Fagotti developed a prediction model for laparoscopy, which serves as a tool that can accurately evaluate the possibility of optimal debulking in patients with advanced ovarian cancer while not negatively affecting survival and not increasing morbidity (19).

In 75%–85% of patients with advanced epithelial ovarian cancer, the disease recurs within two years of stopping treatment (20). Patients are treated with secondary debulking and second-line chemotherapy or only with second-line chemotherapy (21,22). The results showed that the disease recurred in 89.7% of patients with advanced epithelial ovarian cancer. The disease recurred in 87.5% of patients treated with primary debulking and adjuvant chemotherapy and in 90.2% of patients treated with neoadjuvant chemotherapy and delayed debulking. In the case of recurrent disease, 16.2% of patients were treated with secondary debulking and second-line chemotherapy and 83.8% only with second-line chemotherapy. The share of secondary debulking was higher in the group with primary debulking. In a study published by Petrillo et al., 16.5% of patients underwent secondary debulking upon recurrence of the disease and received second-line chemotherapy. The proportion of secondary debulking did not depend on the patients' primary treatment (22). The lower proportion of secondary debulking in patients who were primarily treated with neoadjuvant chemotherapy can be attributed to a higher tumour burden and more extensive recurrence of the disease. Also, patients treated with neoadjuvant chemotherapy were older, had a higher stage of the disease, and poorer overall performance.

To determine the patients who were candidates for secondary debulking at recurrence of the disease, an assessment was made according to the AGO score (complete resection at first debulking, good patient performance, ascites, less than 500 mL) and the TIAN model (FIGO stage, residual size after primary debulking, progression-free survival, performance at recurrence, CA-125 levels at recurrence, ascites at recurrence of the disease) (23). In our institution, we opt for secondary debulking in patients with a recurrence of only one lesion and in whom, according to imaging tests, there is a high probability of complete debulking without a macroscopic residual. To the extent that these two criteria are not met, patients are candidates for second-line chemotherapy.

Preliminary results of the DESKTOP III trial showed a longer period without disease recurrence in patients

with recurrent disease previously treated with secondary debulking and second-line chemotherapy, compared with patients who received second-line chemotherapy alone (19.6 months vs. 14.0 months, p<0.001) (24). The GOG-213 trial showed no differences in overall survival and progression-free period in patients who relapsed and were treated with secondary debulking and second-line chemotherapy or with second-line chemotherapy alone (25).

The research was designed retrospectively, which is its limitation. There were no generally accepted criteria in our institution as to which patients are suitable for primary debulking and which for neoadjuvant chemotherapy. The choice of treatment depended on the clinical picture, laboratory results, imaging tests, diagnostic laparoscopy and the subjective assessment of the gynaecologic oncologist on the resectability of the tumour. The international ICON8 study proposes to postpone debulking for 4 to 6 weeks after the last cycle of neoadjuvant chemotherapy and adjuvant chemotherapy in the shortest possible time window after delayed debulking (26-28).

Remote metastases, poor performance and many complications during and after surgery in patients with advanced ovarian cancer are the reasons why we are increasingly opting for neoadjuvant chemotherapy and delayed debulking surgery (7,29). In our study, patients who received neoadjuvant chemotherapy represented a poorer group in terms of age, general performance, and stage of disease for disease outcome prediction.

5 Conclusion

The basic treatment for advanced ovarian cancer remains primary debulking and adjuvant chemotherapy, which should be offered as a treatment option to patients in whom at least optimal debulking can be performed. For other patients in whom optimal debulking is not feasible, or patients are not capable of more extensive surgery, we offer an alternative treatment with neoadjuvant chemotherapy and delayed debulking.

Conflict of interest

None declared.

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