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Original Research

Characteristics of long-term survival in advanced stage ovarian cancer: a nationwide cohort in the Netherlands

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Abstract

Objective: Despite optimal treatment with debulking surgery and chemotherapy, the majority of patients with advanced stage epithelial ovarian cancer (EOC) die within five years. Survival beyond eight years is rare and the mechanisms that lead to such favorable outcomes are incompletely understood. We aimed to identify characteristics associated with long-term survival (LTS) in a population-based cohort of patients with advanced stage EOC. **Methods**: Patients with advanced stage (FIGO IIB-IV) EOC diagnosed between 2008 and 2012 were identified from the Netherlands Cancer Registry. LTS was defined as survival for more than eight years after diagnosis, based on 20% survival within this cohort. Patient, tumor, and treatment characteristics were analyzed using multivariable logistic regression to find predictors for LTS. **Results**: We identified 2744 eligible patients of whom 571 were long-term survivors (survival longer than eight years). Younger age, lower tumor stage, low-grade histology, FIGO IV based on extra-abdominal lymph node compared to pleural metastasis, primary debulking surgery vs neo-adjuvant chemotherapy followed by interval debulking surgery, residual disease less than one cm or no macroscopic disease, and ascites less than 100 mL were associated with LTS. Furthermore, less than six chemotherapy cycles compared to six, and carboplatin plus paclitaxel combined with other chemotherapy agents compared to carboplatin plus paclitaxel, were associated with a lower odds of LTS. **Conclusion**: Characteristics of the tumor, patient and treatment play a substantial role in respect to the prognosis of advanced stage EOC, and can assist in the prediction of LTS.

Keywords: Long-term survivor; Epithelial ovarian cancer; Prognostic factors; Cancer survivors

1. Introduction

Epithelial ovarian cancer (EOC) is the most common type of ovarian cancer and accounts for approximately three percent of all cancer types in women in the Netherlands. Among all gynecological cancers, EOC is the leading cause of cancer related death in Western countries [1,2]. Most women present with advanced stage disease and have a high risk of disease recurrence and death [3]. Despite the knowledge gained about prognostic factors and treatment enhancements, patients continue to show poor survival [4,5]. Nevertheless, 15% of women with advanced stage EOC survive for more than 10 years [6–8]. Several studies have attempted to evaluate these so-called 'long-term survivors', yet the underlying mechanism responsible for this extraordinary survival remains poorly understood [6–12].

Comparisons of treatment with primary debulking surgery (PDS) versus neo-adjuvant chemotherapy followed by interval debulking surgery (NACT-IDS), the extent of residual disease after surgery and tumour characteristics such as stage and differentiation grade have often been studied in association with long-term survival (LTS) [6–12]. However, chemotherapy characteristics, including drug class and number of cycles, but also tumour characteristics such as number and localization of metastasis, have been studied to a lesser extent. A better understanding of patient and treatment characteristics associated with LTS could help predict patient prognosis and stratify patient populations in future trials. Therefore, this study aimed to evaluate the association between LTS and tumor, patient and treatment characteristics in a population-based cohort from the Netherlands.

2. Materials and methods

2.1 Study population

Patient data were extracted from the Netherlands Cancer Registry (NCR); a nationwide registry comprising of data from all malignancies in the Netherlands since 1989. Clinical data (e.g., tumor-, treatment- and patient- characteristics) are retrieved from hospital files by dedicated clerks. Data on vital status and date of death are obtained from the municipal population registration. Patients diagnosed with advanced stage (FIGO IIB-IV) EOC between January 01, 2008 and February 01, 2012, and undergoing NACT-IDS or PDS were selected (**Supplementary Fig. 1**).

2.2 Definitions

Tumors were staged based on FIGO staging (2014) [13]. Tumor histotypes were classified as serous (high or low-grade), mucinous, endometrioid, clear cell, or other. Histotypes were based on the International Classification of Diseases for Oncology 3rd edition (ICD-O-3) (**Supplementary Table 1**) [14]. Chemotherapy regimens were classified as: carboplatin and paclitaxel (standard regimen), carboplatin and paclitaxel combined with one or more other chemotherapy agents (excluding biological agents, such as bevacizumab), carboplatin regimens without paclitaxel, and platinum-free regimens. Outcome of debulking surgery was defined as complete when no macroscopic lesions were present, optimal if the residual tumor was less than one cm, and suboptimal if the residual tumor was one cm or more. Distant metastases, related to FIGO IV, were divided into groups based on localization as: pleural malignant effusion, parenchymal, extra-abdominal lymph node, and "other" if there were metastases in multiple categories. Comorbidity was determined using the Charlson comorbidity index (CCI) [15]. Ascites was calculated as the sum of the preoperative paracentesis and yielded perioperative amounts. Pretreatment CA-125 levels were used, levels that were determined later than eight weeks prior to the start of the treatment were excluded ($n = 87$).

2.3 Outcomes

LTS was defined as the time between diagnosis and death at more than eight years, based on 20% survival. Vital status, dead or alive, was extracted from the municipal population register and last checked on February 1, 2020. To investigate the influence of several characteristics on overall survival, subanalyses were performed. Overall survival (OS) was calculated as the interval between the date of diagnosis and death. If the patients were alive, the date of the last check at the municipal population register was used, and patients were right-censored thereafter.

2.4 Statistical analysis

Baseline distributions were reviewed and summarized using descriptive statistics. Clinical characteristics of long-term survivors and patients who died within eight years after diagnosis were compared using Fisher's exact and Chi square tests for categorical variables, and *t*-test and Wilcoxon rank sum tests for continuous variables. Univariable and multivariable logistic regression analyses were performed to assess characteristics associated with LTS. Multiple imputation was used to adjust for missing log CA-125, omental cake, differentiation grade, and ascites. Twenty multiple imputed datasets were created; incomplete variables were imputed under a fully conditional specification. The parameters of substantive interest were separately estimated for each imputed dataset and combined using Rubin's rules. In subanalysis, the influence of histology on OS was depicted using Kaplan-Meier curves and assessed using multivariable Cox regression. The influence on survival within the first year after diagnosis and after five years was assessed by right censoring and left truncation, respectively. $p < 0.05$ were considered statistically significant. All statistical analyses were performed using STATA software, version 14.1 (STATA, College Station, TX; Computing Resource Center, Santa Monica, CA, USA).

3. Results

3.1 Baseline

A total of 2744 patients were enrolled (**Supplementary Fig. 1**), of which 571 (20.8%) survived for more than eight years, and 1616 (79.2%) died within eight years (Table 1). Minimum follow-up time was one day, and maximum was 12 years and 30 days. Long-term survivors were younger, had less comorbidities, presented with favorable tumor characteristics (non-serous histology and a lower tumor stage, grading, and number of distant metastases), and had fewer surgical complications than patients who died in eight years. Long-term survivors less frequently presented with more than 100 mL ascites or omental cake, and had lower levels of pretreatment CA-125 levels.

Descriptive analysis of treatment (Table 2) showed that long-term survivors more frequently received PDS (71.1% vs 45.4%), a complete debulking (56.9% vs 37.9%), regular carboplatin-paclitaxel combination chemotherapy (91.6% vs 85.0%), six chemotherapy cycles (83.7% vs 67.4%), optimal dose intensity (74.3% vs 66.2%) and less frequently less than six cycles (5.3% vs 13.2%) or more than six cycles (8.6% vs 17.3%) than patients who died within eight years.

Univariable analysis (Table 3) demonstrated a significant association between LTS and treatment type, residual disease, histotype, age, FIGO stage, number of distant metastases, differentiation grade, CCI, the presence of omental cake, more than 100 mL ascites, and CA-125. Furthermore, univariable analyses of therapy characteristics (Table 4) exhibited a significant relationship between LTS and chemotherapy regimen, number of cycles, and dose reduction.

Table 1. Baseline characteristics.

Characteristics	Dead ≤8 years (n = 2173)	%	Alive >8 years (n = 571)	%	p
Age, mean (SD)	64.5 (11.1)		60.3 (11.2)		<0.001
Stage					<0.001
FIGO II*	124	5.7	157	27.5	
FIGO III	1504	69.2	348	60.9	
FIGO IV	545	25.1	66	11.6	
Omental cake					<0.001
yes	1009	46.4	128	22.4	
Unknown	227	10.4	89	15.6	
Number of metastases**					<0.001
0	1628	74.9	505	88.4	
1	426	19.6	57	10.0	
2	99	4.6	8	1.4	
3	17	0.8	0	0.0	
4	3	0.1	1	0.2	
Localization of metastases					
Malignant pleural effusion	231	42.4	18	27.3	0.005
Lymphnodes	68	12.5	18	27.3	
Visceral	169	31.0	22	33.3	
Other	77	14.1	8	12.1	
Morphology					<0.001
High-grade serous	1693	77.9	363	63.6	
Low-grade serous	84	3.9	43	7.5	
Mucinous	61	2.8	24	4.2	
Endometrioid	115	5.3	77	13.5	
Clear cell	84	3.9	30	5.3	
Others	136	6.3	34	6.0	
Differentiation grade					<0.001
Grade I	102	4.7	67	11.7	
Grade II	353	16.2	89	15.6	
Grade III	1193	54.9	299	52.4	
Unknown	525	24.2	116	20.3	
Ascites					<0.001
<100 mL	897	41.3	265	46.4	
≥100 mL	794	36.5	127	22.2	
Unknown	482	22.2	179	31.3	
log CA-125, median(IQR)	6.45 (5.46–7.43)		5.81 (4.85–7.14)		<0.001
CA-125					<0.001
0–35	52	2.4	38	6.7	
>35	1685	77.5	391	68.5	
Unknown	436	20.1	142	24.9	
Charlson comorbidity index					0.004
Charlson 0	1504	69.2	431	75.5	
Charlson 1–2	549	25.3	111	19.4	
Charlson ≥3	47	2.2	7	1.2	
Unknown	73	3.4	22	3.9	
Surgical complication					0.040
yes	635	29.2	142	24.9	

*Consisting of FIGO IIB and IIC.

**Number of localizations of distant (FIGO IV) metastases.

Table 2. Therapy characteristics.

Characteristics	Dead ≤8 years (n = 2173)	%	Alive >8 years (n = 571)	%	p
Therapy					
PDS	986	45.4	406	71.1	<0.001
NACT	1187	54.6	165	28.9	
Residual tumor status					<0.001
Suboptimal	383	17.6	18	3.1	
Optimal	841	38.7	149	26.1	
Complete	823	37.9	325	56.9	
Unknown	126	5.8	79	13.8	
Chemotherapy regimen					
Carboplatin and paclitaxel	1846	85.0	523	91.6	0.021
Carboplatin and paclitaxel combined with ≥1 other chemotherapy agents	94	4.3	11	1.9	
Carboplatin based	104	4.8	21	3.7	
Platinum free	27	1.2	8	1.4	
Unknown	102	4.7	8	1.4	
Number of cycles					
<6 cycles	286	13.2	30	5.3	<0.001
6 cycles	1465	67.4	478	83.7	
>6 cycles	376	17.3	49	8.6	
Unknown	46	2.1	14	2.5	
Reduction in chemotherapy dose					<0.001
Yes	696	32.0	133	23.3	
Unknown	38	1.7	14	2.5	
Chemotherapy interrupted					0.48
Interrupted/postponed	291	13.4	70	12.3	
Chemotherapy medium stopped					
One medium stopped	149	6.9	30	5.3	0.17

Abbreviations: PDS, Primary debulking surgery; NACT, neoadjuvant chemotherapy.

3.2 Multivariable analyses, influence of patient and tumor characteristics

Multivariable analyses (Table 3) demonstrated that, after correction for confounders, higher age, NACT-IDS, FIGO stages III and IV, a higher differentiation grade, and more than 100 mL ascites remained associated with lower odds of LTS. Complete and optimal debulking were associated with a higher odds of LTS compared with suboptimal debulking. The same accounted for complete debulking vs optimal debulking (odds ratio [OR], 1.91; 95% confidence interval [CI], 1.52–2.42; $p < 0.001$) (data not shown). FIGO stage IV, based on extra-abdominal lymph node metastases, showed higher odds of LTS than malignant pleural effusion (OR, 3.21; 95% CI, 1.49–6.93; p = 0.003) (Table 5).

Subanalysis showed a time-dependent survival pattern in histotype (**Supplementary Fig. 2**). In multivariable Cox regression, an inferior survival for non-serous histotypes was observed in the first year compared to high-grade serous (mucinous: hazard ratio [HR], 4.77; 95% CI, 3.19–7.14; $p < 0.001$; endometrioid: HR, 1.67; 95% CI, 1.05–2.64; p = 0.030; and clear cell: HR, 2.09; 95% CI, 1.27–3.45; p = 0.004) (**Supplementary Table 2**). However, after five years, a superior survival was observed for low-grade serous and clear cell cases compared to high-grade serous (clear cell: HR, 0.51; 95% CI, 0.26–0.99; p = 0.049) (low-grade serous: HR, 0.56; 95% CI, 0.32–0.96; p = 0.035).

3.3 Multivariable analyses, influence of therapy characteristics

Multivariable analyses of therapy characteristics (Table 4) showed that after correction for confounders and number of chemotherapy cycles, administration of carboplatin and paclitaxel combined with other chemotherapy agents remained associated with lower odds of LTS than the standard regimen. Patients receiving less than six cycles had significantly lower odds of LTS than patients receiving six. Reduction in chemotherapy dose had a non-significant influence on LTS than standard chemotherapy after correction for confounders (data not shown).

As stated in the statistical methodology, multiple imputation was performed for missing log CA-125, presence of omental cake, differentiation grade, and more than 100 mL of ascites. The percentage of missing values across the imputed variables varied between 12% (omental cake) and 24% (ascites). For comparison, all multivariable analyses performed on the complete cases showed no significant difference in OR or HR.

Table 3. Logistic regression analysis exploring factors associated with long-term survival.

Characteristics	Univariable analysis			Multivariable analysis*		
	Odds Ratio	(95% CI)	*p*	Odds Ratio	(95% CI)	*p*
Age, continuous	0.97	(0.96–0.98)	<0.001	0.97	(0.96–0.98)	<0.001
Treatment						
PDS	Ref			Ref		
NACT	0.34	(0.28–0.41)	<0.001	0.45	(0.35–0.57)	<0.001
Residual disease						
Suboptimal	Ref			Ref		
Optimal	3.77	(2.28–6.24)	<0.001	3.16	(1.89–5.30)	<0.001
Complete	8.40	(5.15–13.71)	<0.001	6.05	(3.64–10.06)	<0.001
FIGO stage						
Stage II**	Ref			Ref		
Stage III	0.18	(0.14–0.24)	<0.001	0.32	(0.23–0.45)	<0.001
Stage IV	0.10	(0.07–0.14)	<0.001	0.21	(0.14–0.32)	<0.001
Omental cake, present*	0.35	(0.27–0.45)	<0.001	-		-
Number of metastases	0.47	(0.38–0.59)	<0.001	-		-
Morphology				-		-
High-grade serous	Ref					
Low-grade serous	2.38	(1.63–3.51)	<0.001			
Mucinous	1.83	(1.13–2.98)	0.014			
Endometrioid	3.12	(2.29–4.25)	<0.001			
Clear cell	1.67	(1.08–2.57)	0.021			
Other	1.17	(0.79–1.73)	0.443			
Differentiation grade*						
Grade I	Ref			Ref		
Grade II	0.38	(0.26–0.56)	<0.001	0.50	(0.32–0.80)	0.003
Grade III	0.38	(0.27–0.53)	<0.001	0.60	(0.40–0.89)	0.011
Ascites, ≥100 mL*	0.54	(0.4–0.68)	<0.001	0.62	(0.48–0.81)	0.023
Log CA-125*	0.80	(0.75–0.86)	<0.001	-		-
CA-125, categorized						
≤35	Ref			-		
>35	0.32	(0.21–0.49)	<0.001			
Charlson index				-		-
Charlson <1	Ref					
Charlson 1–2	0.71	(0.56–0.89)	0.003			
Charlson ≥3	0.52	(0.23–1.16)	0.109			
Surgical complications, yes	0.80	(0.65–0.99)	0.040	-		-

All covariates added in the multivariable model are depicted; age, treatment type, residual disease, FIGO and differentiation grade and ascites.

Abbreviations: Ref, reference; PDS, Primary debulking surgery; NACT, neoadjuvant chemotherapy.

*Multiple imputation.

** Consisting of stage IIb and IIc.

4. Discussion

In this study, the association between extensive patient, tumor and treatment characteristics, and LTS was studied in a large population-based cohort of 2744 patients with advanced stage EOC. The analyses suggested that 20% of the women survived for more than eight years and that there were significant associations between LTS and younger age, favorable tumor characteristics (lower tumor stage and differentiation grade, and extra-abdominal lymph node vs pleural metastases), treatment characteristics (positive influence of PDS and less residual disease), less than 100 mL ascites, and chemotherapy characteristics (negative influence of less than six cycles and a positive influence of standard chemotherapy regimen).

Table 4. Logistic regression analysis exploring treatment characteristics associated with long-term survival.

Characteristics	Univariable analysis			Multivariable analysis*		
	Odds Ratio	(95% CI)	*p*	Odds Ratio	(95% CI)	*p*
Chemotherapy subgroups						
Carboplatin and paclitaxel	Ref			Ref		
Carboplatin and paclitaxel combined with ≥1 other chemotherapy agents	0.41	(0.22–0.78)	0.006	0.46	(0.22–0.99)**	0.047
Carboplatin based	0.71	(0.44–1.15)	0.166	0.63	(0.34–1.17)**	0.146
Platinum free	1.05	(0.47–2.32)	0.912	1.25	(0.44–3.56)**	0.675
Number of cycles						
6 cycles	Ref			Ref		
<6 cycles	0.32	(0.22–0.47)	<0.001	0.47	(0.27–0.82)***	0.008
>6 cycles	0.40	(0.29–0.55)	<0.001	0.82	(0.58–1.16)***	0.266
Reduction in chemotherapy						
No	Ref			-		
Yes	0.65	(0.52–0.80)	<0.001	-		

Abbreviations: Ref, reference.

*Multiple imputation.

**Adjusted for morphology, FIGO, age, residual disease and amount chemo cycles.

***Adjusted for morphology, FIGO, age, residual disease and chemotherapy regime.

Table 5. Logistic regression analysis exploring localization of distant (FIGO IV related) metastases associated with long-term survival.

Characteristics	Univariable analysis (*n* = 611)			Multivariable analysis* (*n* = 611)		
	Odds Ratio	(95% CI)	*p*	Odds Ratio	(95% CI)	*p*
Metastases localization						
Pleural malignant effusion	Ref			Ref		
Lymph nodes**	3.40	(1.68–6.89)	0.001	3.21	(1.49–6.93)	0.003
Parenchymal	1.67	(0.87–3.21)	0.124	1.73	(0.85–3.52)	0.127
Other	1.33	(0.56–3.19)	0.518	1.47	(0.57–3.78)	0.424

* Adjusted for age, differentiation grade, therapy and residual disease.

** Extra-abdominal lymph node.

Abbreviations: Ref, reference.

Multiple studies have highlighted tumor and clinical characteristics associated with LTS, but have shown inconsistencies [6–12]. Most studies included patients treated before 2007 and were restricted to a demographic region [6–10,12]. Frequently studied were patients' age, and tumor stage, histology and grade, yet many therapy characteristics remained neglected. For instance, most studies only included patients who underwent PDS [8,10,12], while others provided little information regarding therapy type and residual disease [6,7]. Chemotherapy regimen and cycle numbers remain scarcely reported [8,12]. The NCR enabled us to collect complete LTS data, generating a nationwide cohort that is larger and more complete than most other studies.

Consistent with many other studies, we showed that younger age is associated with LTS [7,8,11]. As hypothesized, old age leads to higher overall and postoperative mortality in general and EOC-related complications in particular [16]. Also well described in other studies, our study confirmed that a higher FIGO stage and higher differentiation grade is associated with lower odds of LTS [7,8,17,18]. Also shown in this study is that extra-abdominal lymph node metastases were associated with higher odds of LTS than malignant pleural effusion, similar to other studies [19,20], suggesting that EOC with isolated distant extra-abdominal lymph node metastases may exhibit less aggressive behavior.

The influence of histological subtypes on the other hand is often debated. Non-serous histotypes are predominantly associated with LTS [7,17]. Consistent with other studies, we showed that high-grade serous tumors, when compared with low-grade and non-serous tumors, had lower odds of LTS in univariable, but not in multivariable analyses (with exception of 'others') [8,21]. However, subanalysis showed a time-dependent survival pattern of histotype, concordant with a previous study [22]. In the first year after diagnosis, an inferior OS was observed in non-serous histotypes compared with high-grade serous. But, after five years a superior OS was observed in low-grade serous and clear cell histotypes compared with high-grade

serous, and a non-inferior OS in the remaining histotypes. This could be explained by differences in treatment effectiveness. For instance, mucinous and clear cell histotypes initially respond poorly to platinum-based chemotherapy, while high-grade serous histotype initially responds well but develops a higher resistance in later years [23–25].

Studies have found significant associations between pretreatment or preoperative CA-125 levels and LTS [10, 26], while others have failed to find any such associations [21]. The present study showed that pretreatment CA-125 levels >35 U/mL were associated with lower odds of LTS in univariable analysis, but not in multivariable analysis. The correlation between CA-125 and stage, differentiation, ascites, and histology was observed in this study and recent reports; therefore, correcting for these factors could explain the change in odds [26]. Another frequently reported marker is ascites. This study indicates that more than 100 mL of ascites is significantly associated with lower odds of LTS, consistent with other studies [10–12]. Ascites is postulated to be a result of malignant cells spreading to serosal surfaces causing peritoneal effusion [27], which leads to abdominal distension, nausea, asphyxia, electrolyte disturbances, and negatively influences overall condition and prognosis [28].

The choice between PDS vs NACT-IDS is often debated. The importance of aiming for total macroscopic debulking surgery is widely accepted [29,30]. Consistent with this and other reports, the present study showed significantly higher odds of LTS in case of less residual disease [8–11,29]. Currently, the American Society of Clinical Oncology (ASCO) and the Society of Gynecologic Oncology (SGO) guidelines recommend PDS as the treatment of choice and advise considering NACT-IDS for patients with a high perioperative risk or a low likelihood of achieving complete or optimal debulking [31]. In concordance, our data showed that PDS resulted in a significantly higher odds of LTS. However, PDS is associated with a higher risk of postoperative complications compared to NACT-IDS [32], Therefore, NACT-IDS could be a preferable strategy in women who already have a higher perioperative risk, consistent with current guidelines [31].

The recommended chemotherapy regimen for treatment of advanced stage EOC is carboplatin and paclitaxel administered over six cycles [31,33]. This study showed that often neither the recommended regimen nor the advised number of cycles were administered. Consistent with the ASCO and SGO guidelines and other reports, the present study showed no significant benefit of administering more than six chemotherapy cycles [34,35]. Similarly, a lower odds of LTS was observed in patients who received less than six cycles than in those who received six. The present study also demonstrated a significantly lower odds of LTS when a third chemotherapy agent was included along with carboplatin and paclitaxel. Both the negative influence of less cycles and administration of additional agents can partially be explained by the observation that patients who do not respond well, and presumably have a worse survival, are more likely to discontinue therapy or receive additional chemotherapy agents.

The present study is limited by the restrictions of a population-based cohort and its historical nature. The use of a population-based cohort, with many heterogeneities arising from different histotypes, stages, or treatment, provides benefits and challenges. Benefits are the extrapolating ability to real-life settings, and the diversity and completeness of the studied characteristics. A challenge is the high number of possible confounding factors. Treatment selection was based on the guidelines at the time of treatment and shared decision-making between doctors and patients. Furthermore, selection of treatment regimen and cycles were likely influenced by patient performance status, which might have induced confounding by indication. The outcomes of this study were from patients treated before the broad use of poly ADP ribose polymerase inhibitors (PARPi); therefore, the influence of PARPi on LTS has not been studied and further investigation is warranted. Survival was not associated with the year of diagnosis in our data, but changes in practice over time influencing survival must be considered. Moreover, LTS and OS characteristics were used rather than cancer-specific survival, possibly inducing a bias of death due to causes other than the disease itself. Due to the high mortality of EOC and the adjustment for patient characteristics, we hypothesize that this influence is minimal. Pretreatment serum CA-125 levels were measured at different times, and can therefore potentially affect the results, though only levels determined within eight weeks before starting treatment were included. Furthermore, it cannot be ignored that some confounders were not addressed. Finally, this study was restricted by the lack of a central pathological review.

5. Conclusions

This study supports previous studies hypothesizing that in advanced stage EOC, younger age, lower FIGO stage, lower differentiation grade, treatment type, less residual tumor and less ascites are associated with LTS. Furthermore, we showed that extra-abdominal lymph node metastases as the only distant metastatic site, chemotherapy regimen, and number of cycles are also associated with LTS. Characteristics of the tumor, patient, and treatment play a substantial role in prognosis; yet these characteristics, whether individual or combined, cannot accurately predict LTS in EOC. Therefore, more prospective research on molecular characteristics of EOC to accurately predict long-term survival is warranted.

Author contributions

LW conceived and designed the study, contributed to materials, analyzed the data and wrote the manuscript; KKV contributed to the analysis and revised

the manuscript; MA contributed to the materials, interpreted the data and revised the manuscript; HMH, GSS, and RFPMK interpreted and revised the manuscript. All authors have read and approved the manuscript.

Ethics approval and consent to participate

All research activities were approved by the institutional review board of the NCR (K19.074). The requested dataset was considered anonymous and the use is therefore exempt from ethics review board approval according to Dutch legislation.

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Conflict of interest

The authors declare no conflict of interest.

Supplementary material

Supplementary material associated with this article can be found, in the online version, at https://www.imrpress.com/journal/EJGO/43/1/10.31083/j.ejgo4301007.

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