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Nomogram for Predicting Individual Survival After Recurrence of Advanced-Stage, High-Grade Ovarian Carcinoma

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For a list of Gynecologic Oncology Group member institutions who participated in the primary treatment studies, see Appendix 1 online at http://links.lww.com/xxx.

Abstract

Objective: To analyze clinical prognostic factors for survival after recurrence of high grade, advanced stage ovarian–peritoneal–tubal carcinoma and to develop a nomogram to predict individual survival after recurrence.

Methods: We retrospectively analyzed patients treated on multicenter Gynecologic Oncology Group protocols for stage III and IV ovarian–peritoneal–tubal carcinoma who underwent primary debulking surgery, received chemotherapy with paclitaxel and a platinum compound, and subsequently developed recurrence. Prognostic factors affecting survival were identified and used to develop a nomogram, which was both internally and externally validated.

Results: There were 4,739 patients included in this analysis, of which, 84% had stage III and 16% had stage IV ovarian carcinoma. At a median follow-up of 88.8 months (95% CI: 86.2-92.0 months), the vast majority of patients (89.4%) had died in follow-up. The median survival after recurrence was 21.4 months (95% CI 20.5 −21.9 months). Time to recurrence after initial chemotherapy, clear cell or mucinous histology, performance status, stage IV disease, and age were significant variables used to develop a nomogram for survival after recurrence, which had a concordance index of 0.67. The time to recurrence alone accounted for 85% of the prognostic information. Similar results were found for patients who underwent second look laparotomy and had a complete pathologic response or received intraperitoneal chemotherapy.

Discussion: For individuals with advanced stage ovarian carcinoma who recur after standard first-line therapy, estimated survivals after recurrence are closely related to the time to recurrence after chemotherapy and prognostic variables can be used to predict subsequent survival.

Precis:

After advanced-stage ovarian carcinoma recurs, prognostic variables including time to recurrence, patient age, performance status, histology, and stage accurately predict subsequent survival.

INTRODUCTION

Based on two landmark phase III trials[1,2], and after FDA approval in December of 1992[3], the combination of a cisplatin and paclitaxel was quickly adopted as the standard first-line therapy for ovarian carcinoma. Randomized trials have since confirmed the therapeutic equivalence of the substitution of paclitaxel with docetaxel[4] or cisplatin with the less toxic carboplatin[5,6], as such the combination of platinum compound and taxane remains the standard first-line therapy. This has been affirmed by two intergroup consensus statements, although research in altered dosing, schedule, and method of delivery of these chemotherapy agents continues.[7,8] While up to 80% of patients with advanced (stage III&IV) ovarian carcinoma achieve a complete response to first line therapy with paclitaxel and a platinum compound, the long-term prognosis for an individual patient remains unpredictable. The risk of recurrence and death is related to stage, with 68% of advanced stage III or IV patients expected to die with 10 years of surveillance.[9] However, other prognostic factors including tumor histology, patient age and performance status have been recognized.[10]

Even in early stage disease (I and II), survival after recurrence may approximate that of advanced disease after recurrence. Ahmed et al. reported the outcome of stage I ovarian

carcinoma patients who were observed without chemotherapy.[11] Following recurrence, the median survival was similar to patients who presented with advanced stage disease, with a 5 year disease-free survival of 42%. Chan et al. evaluated survival after recurrence of stage I and II ovarian carcinoma after comprehensive staging and adjuvant chemotherapy. The median survival after recurrence was similar to patients with advanced stage disease who recurred. Patients with longer (>24 months) treatment-free interval had, after relapse therapy, a longer median survival of 35 months compared to 10 months in those who recurred ≤24 months (p=0.003).[12]

From 1989-1991, three pivotal papers identified the platinum treatment-free interval as a critical predictor of response to second-line therapy.[13-15] These papers identified patients progressing on therapy or within 6 months of completing therapy as having the worst prognosis. These studies did not address survival and little has been written about the expected duration of survival after recurrence. Von Gruenigen et al reported that the length of initial remission time significantly affected survival (p<0.01).[16] However, specific survival estimates based on initial progression-free survival were not reported.

Due to the large number of patients with high grade advanced stage ovarian–peritoneal–tubal carcinoma who were treated with the combination of a platinum compound and paclitaxel in Gynecologic Oncology Group (GOG) trials, we sought to analyze clinical prognostic factors for survival after recurrence and to develop a nomogram to predict individual survival after recurrence. A validated nomogram would provide an objective framework for determining survival, improve counseling about individualized prognosis and potentially influence treatment recommendations.

METHODS

We retrospectively analyzed patients treated on GOG trials 111, 114, 132, 152, 158, 162, 172, and 182, which were conducted from April 1992 to September 2004.[1, 6, 17-22] (Table 1) GOG trials 114, 158, and 172 included patients with optimal (≤ 1.0 cm residual) stage III disease while other trials such as GOG 111, 132, 152, and 162 included patients with suboptimal (>1.0 cm residual) stage III and IV disease. GOG trial 182 included both optimal and suboptimal stage III and IV ovarian carcinoma patients. The results of these trials have been reported previously. All patients gave written informed consent prior to study entry in compliance with all local IRB and federal guidelines. Consistent with GOG/NRG guidelines, approval for the study was obtained by the ancillary data committee. All patients underwent primary cytoreductive surgery and were treated with a combination of paclitaxel and a platinum compound per protocol guidelines. Post chemotherapy maintenance was not utilized in any of these trials. Tumors from all patients underwent central pathologic review for confirmation of histology and tumor grade. Women with grade 1 serous carcinoma (a surrogate for low-grade serous disease) were excluded from this analysis.[23] Among the 7,651 patients enrolled in these trials, 2912 patients were excluded from analysis. These exclusions, not mutually exclusive, included patients without recurrence (N=1343), initial chemotherapy regimen without paclitaxel (N=913), patients with grade 1 tumors (N=886) and patients deemed ineligible and excluded from the original protocol (N=378).

Categorical variables were compared by the Pearson chi-square test,[24] and continuous variables by the Wilcoxon–Mann–Whitney test.[25] Survival was estimated using the Kaplan–Meier method.[26] The Cox proportional hazards model was used to evaluate independent prognostic factors as well as to estimate their covariate-adjusted effects on overall survival (OS).[27] The nonlinearity of the effect of continuous variables was assessed using restricted cubic splines. All statistical tests were two-tailed with the significance level set at α=0.05. Statistical analyses were performed using the R programming language and environment.[28]

Prognostic variables including patient age, performance status (measure of independent functionality), race, residual tumor size, International Federation of Gynecology and Obstetrics (FIGO) stage, tumor histology and grade were used to create a nomogram to predict OS. Starting from a full Cox model for OS containing all prognostic factors, we removed factors not meeting a certain maximum-likelihood threshold by fast backward elimination and kept the resulting model as the basis for the nomogram.[29] To account for differences in treatment and evaluation for recurrence among protocols not otherwise accounted for in the available data, we included protocol enrollment as a stratification variable in the models. Validation of each nomogram included three procedures. First, model discrimination was measured quantitatively with the concordance index, which is similar to the area under the receiver operating characteristic (ROC) curve but for censored data.[30] Bootstrapping (a method of repetitive resampling for calculating bias in certain estimators) provided a relatively unbiased estimate of the concordance index.[31] Second, calibration was assessed through grouping patients by their nomogram-predicted probabilities, then comparing the group mean with the actual Kaplan–Meier estimate of OS; bootstrapping was again used for bias correction. Third, we calculated the concordance index of the nomogram model for an external validation data set, the control arm (chemotherapy only) of GOG 218.[32,33]

In order to assess time to recurrence as a predictor of survival in our nomogram model, we fitted an additional survival model with time to recurrence as its only covariate. The adequacy index of time to recurrence for predicting survival is then the ratio of the −2 log likelihood ratio of the subset model, and the −2 log likelihood ratio of the full model, i.e. $A = LR_{\text{subset}}/LR_{\text{full}}$.[34] If the adequacy index $A = 1$, then the subset contains all the predictive information of the entire set of covariates; if $A = 0$, then it contains no predictive information.

RESULTS

Four thousand seven hundred and thirty-nine patients with high grade ovarian carcinoma who received paclitaxel and a platinum compound and recurred after first-line chemotherapy were included in this analysis. Their demographics are presented in Table 2. Eighty-four percent of patients had stage III and 16% had stage IV ovarian carcinoma. The percentages of patients that had no gross residual disease, gross residual disease (≤ 1.0 cm) and gross residual disease (> 1.0 cm); were 20.2%, 44.5% and 35.2%, respectively. The median progression free survival was 15.0 months (95% CI 14.7 −15.3 months). At a median follow-up of 88.8 months (95% CI: 86.2-92.0 months), the vast majority of patients (89.4%) had

died in follow-up. Figure 1 shows that the median survival after recurrence was 21.4 months (95% CI 20.5-21.9 months).

The median survival after recurrence stratified by time to recurrence is presented in Table 3. For almost every subsequent 3-month interval starting with < 6 months, patients whose time to recurrence fell in that interval had longer median survival than the previous interval's patients. The survival differences among the shortest and longest interval groups were significantly different (log-rank test $p < 0.001$). Figure 2 plots a restricted cubic spline fit of impact of time to recurrence on overall survival in the nomogram model. This figure shows the partial effects plot of log time to recurrence on the log hazard ratio. Note that the risk of death decreases with increasing time to recurrence, more quickly for the shorter intervals: for example, a change of time to recurrence from 3 months to 6 months corresponds to a hazard ratio of 0.83, or a 17% decrease in the risk of death with the additional 3 months; and a change of time to recurrence from 30 to 33 months corresponds to HR= 0.91, a 9% decrease in the risk of death.

The strong significance of time to recurrence also holds in the covariate-adjusted Cox survival model of the nomogram. Following recurrence, time to recurrence after chemotherapy, performance status, histology, residual disease, stage, and age were significant variables used to develop a nomogram for survival after recurrence.

The "adequacy index" for time to recurrence alone was A= 0.85, which means time to recurrence accounted for 85% of the prognostic information, with the other factors accounting for much less. In decreasing order of significance were residual disease, performance status, histology, stage and age, which had adequacy indices of 0.092, 0.060, 0.059, 0.037, and 0.031, respectively.

Two important variables in treatment during the study period included the routine use of second-look laparotomy (in a model with fewer patients, since we could not assess complete response for all) and the use of intraperitoneal chemotherapy. One thousand three hundred and forty-two patients underwent second-look laparotomy after a complete clinical response (absence of disease by physical and radiologic exams and biochemical markers). A pathologic complete response (no pathologic evidence of persistent disease on surgical specimens) was documented in 920 patients (68.5%) while 422 had persistent disease. Patients with a complete pathologic response were statistically younger (p=0.003) and had more favorable histology (more frequent endometrioid and less frequent clear cell–mucinous histology). Two hundred and eighty-seven patients (6.1%) in the trials received intraperitoneal chemotherapy. Intraperitoneal chemotherapy patients were statistically younger (p=0.02), had only stage III disease and more frequently had residual disease measuring less than 1 cm. Neither surgical pathologic complete response at second look laparotomy or prior intraperitoneal therapy was associated with survival after recurrence, p=0.129 and 0.714, respectively.

A nomogram for predicting survival after recurrence was developed from prognostic factors that remained significant after fast backward elimination. The survival after recurrence nomogram (Figure 3) has a bootstrap-corrected concordance index of 0.67 and is well-

calibrated (Figure 4 on line only). Testing the model against an independent validation data set with similar patients, the control arm of GOG-0218 (whose patient characteristics and survival curve are given in Table 4 and Figure 5, respectively on line only), resulted in a concordance index of 0.65, very close to the bootstrap-corrected value.

DISCUSSION

Because data on recurrence and survival in a specific carcinoma are aggregated, oncologists are only able to provide median survival estimates for patients with a recurrence. In the current analysis, median survival after recurrence is 21.4 months with a range of 9.8 months to 48.5 months. Aggregate survival data does not provide adequate information for either the medical providers or patients regarding individual expected survival durations. To address this deficit, we retrospectively evaluated prognostic factors after recurrence for patients with advanced stage ovarian carcinoma to allow us to predict individual survival durations. While time to recurrence has long been recognized as a factor predictive of response to second-line platinum-based therapy, little has been published on its effect on survival.[13-16] We found time to recurrence was the most significant factor affecting survival accounting for approximately 85% of the prognostic information in our model. With each three-month increment in time to recurrence, discrete median survivals were observed. Most significant was the fact that the 95% confidence interval around the median survival was very close to the median value and varied by less than 10%.

Residual disease, histology and performance status were the next most significant factors affecting survival after recurrence (with adequacy indices of 0.092, 0.060, and 0.059, respectively). While clear cell ovarian and mucinous tumors more frequently present with early stage disease and have an improved survival, the opposite is true when they are diagnosed at a more advanced disease stage. In a previous GOG study of patients with stage III disease, Winter et al. reported a poorer progression free survival and overall survival for these histologies after first-line therapy with a platinum compound and paclitaxel.[10] Clear cell tumors have increased expression of ERCC1 (a nuclear excision repair protein involved in repair of platinum induced DNA damage) and are more chemotherapy resistant when compared to serous and endometrioid histologies.[35] Advanced stage tumors of mucinous histology have the worst prognosis of any epithelial ovarian tumor after standard therapy with a platinum and paclitaxel.[10] Advanced age and poorer performance status has previously been associated with increased mortality in stage III disease.[10] Since medical comorbidity data was not collected in these studies, the possibility that advanced age is a surrogate for medical comorbidity must be considered. In our study, performance status was more significant than age with adequacy indices of 0.060 and 0.031, respectively. Lastly, residual disease was more significant than stage with adequacy indices of 0.092 and 0.037, respectively. These clinical prognostic factors identified allowed us to develop a nomogram for survival after recurrence. This was well calibrated and reflects its predictive value. Two important treatment variations during the duration of our study were the use of routine second-look laparotomy and intraperitoneal chemotherapy. Neither of these treatment variations affected the model for survival after recurrence.

Cress et al. evaluated the characteristics of long-term survivors with epithelial ovarian carcinoma from the California Tumor Registry.[36] Younger age, early stage, low grade and non-serous histologies were significant predictors of long-term survival. The improvement in non-serous histologies in their study is related to their earlier stage at diagnosis. However, long-term survival also occurred in women with high risk carcinoma. Germline BRCA and other homologous DNA repair mutations such as PALB2, BRIP1, RAD51C and RAD51D mutations are identified in 20 percent of ovarian carcinoma patients.[37] These homologous DNA repair mutations have been associated with improved response to primary chemotherapy with prolonged progression-free and overall survival.[38]

One of the purposes of this analysis was to better understand the prognosis for patients with recurrent ovarian carcinoma. While the survival for the primary “platinum resistant” patient has been well defined, the survival for patients who “platinum sensitive” is more variable.[39] In the current study, the 95% confidence interval of survival was 8.3-10.9 months for platinum resistant patients and 9.1-48.5 months for platinum sensitive patients. This is likely due to the fact that the primary platinum resistant patient is less likely to have a BRCA mutation. Alsop et al. reported patients carrying BRCA1 or 2 mutations were less likely to have disease progression within 6 months of the end of primary treatment, 14.9% compared with 31.7% for those not carrying mutations, $p < 0.0001$.[40] In our study, 8.8% of patients recurred within 6 months while 91.2% patients recurred >6 months.

Strengths of this study are the large number of patients treated prospectively on NCI sponsored trials. Eligibility for these trials was clearly specified, pathology was confirmed for all patients by a central pathologic slide review and chemotherapy doses and dose modifications were strictly outlined. Additionally, the date of recurrence as well as the date of death was prospectively collected. An additional strength is a long duration of follow-up, with 89 percent of patients eventually succumbing to their disease.

Weaknesses of the study are the lack of clinical information at recurrence including the patient’s performance status, the volume of disease and the presence of symptoms at recurrence. Additionally, second-line and subsequent therapies were not uniformly recorded and, therefore, not analyzed. However, the uniformity of patient outcomes by time to recurrence, after correction for tumor histology and patient age, suggest very similar treatment or the lack of impact of variable treatments. Additional weaknesses of the study include the lack of data on germline or somatic BRCA mutations and other molecular analyses, either prospectively or retrospectively. Germline BRCA testing aids in identifying a patient population that is highly sensitive to platinum compounds and that has an improved progression free and overall survival.[37] In addition to searching for germline mutations, molecular profiling of the tumors from the patients in the studies was not performed.[41] While the Gynecologic Oncology Group did develop a tissue repository in 1992, tumor tissue banking was optional. Tissue was archived from only 7.6% of patients included in the studies in this analysis. Since time to recurrence is such a predominant factor in subsequent survival, time to recurrence is, in effect, a phenotype of the cancer genome. Additionally, dose dense paclitaxel has demonstrated some advantages to every 3 week dosing.[42] To date, the GOG has performed two randomized trials that utilized a weekly dose dense paclitaxel; however, neither had been published when this analysis was approved and, therefore, were

not available for ancillary analysis. The trials in this analysis were conducted before bevacizumab or PARP inhibitors were FDA approved for platinum sensitive recurrent ovarian cancer and these have been shown to improve survival by 4.9 and 4.7 months, respectively.[43,44] Lastly, the nomogram and validation of the nomogram was performed on patients who were participating in clinical trials. It is possible that their outcome is the result of patient selection including a superior performance status and the findings would need to be validated in a patient population outside a clinical trial.

In summary, while little is known about a patient's prognosis after a complete response to primary chemotherapy, survival after recurrence can be predicted based on time to recurrence and other prognostic variables.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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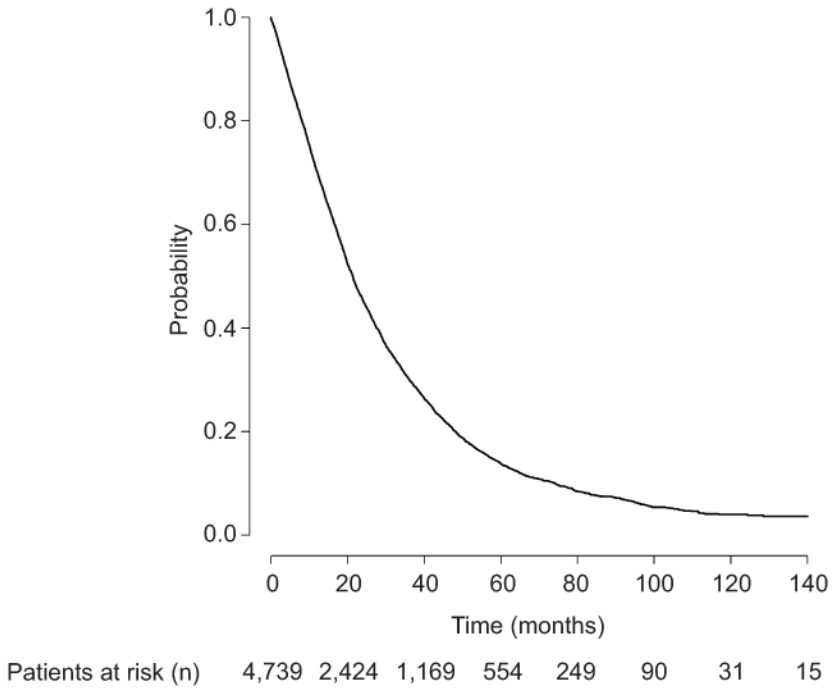

Figure 1.

Kaplan–Meier overall survival after recurrence. Figures below months indicate median survival: 21.4 months.

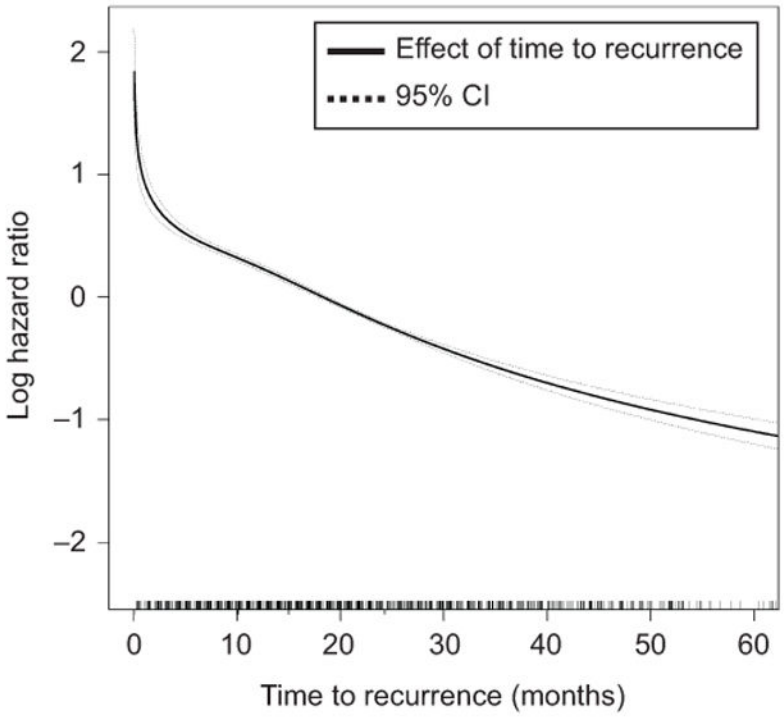

Figure 2.

Restricted cubic spline fit of effects of time to recurrence on overall survival. This figure shows the partial effects plot of log time to recurrence on the log hazard ratio. Note that the risk of death decreases with increasing time to recurrence more quickly for shorter intervals.

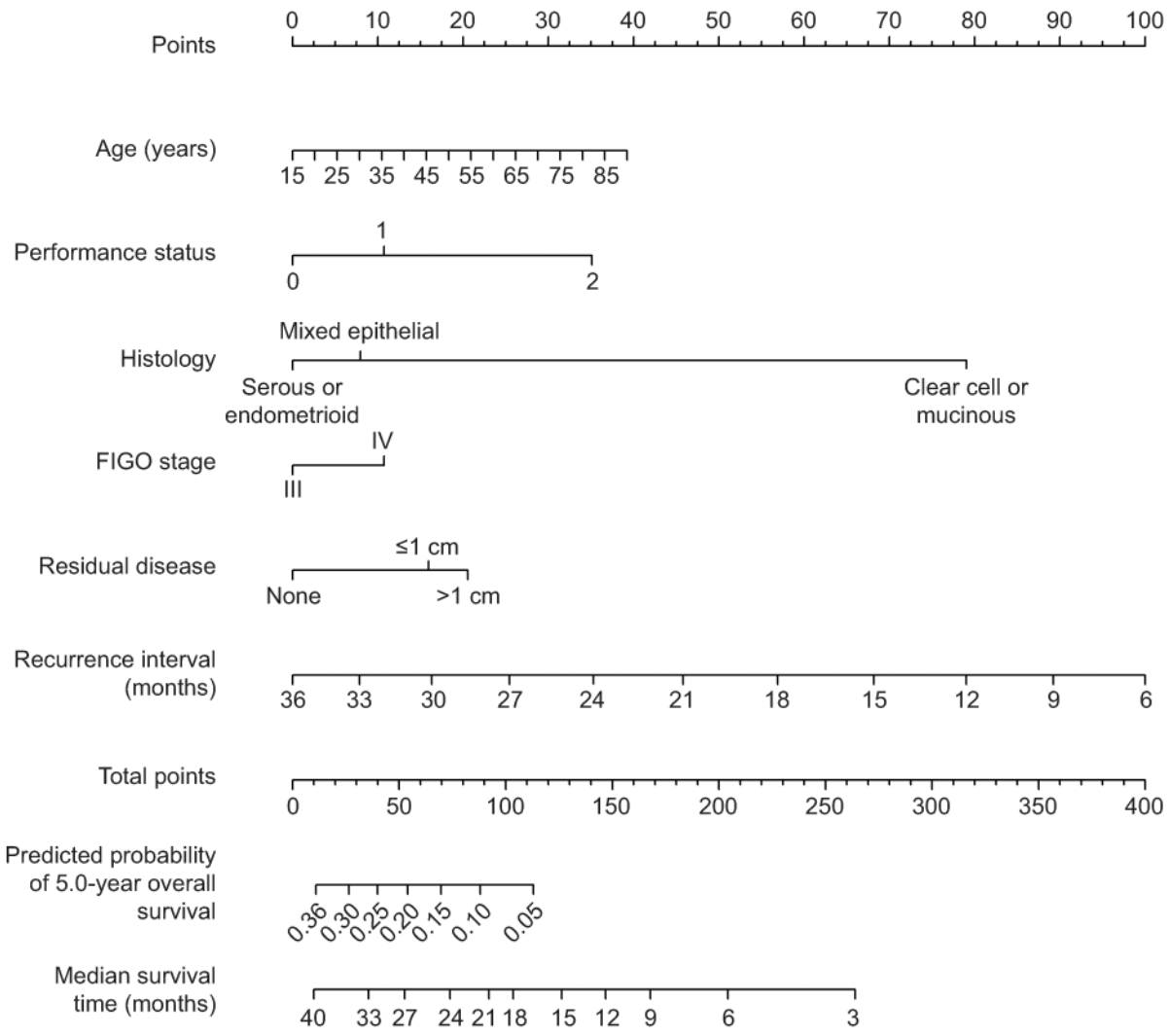

Figure 3.

Nomogram for predicting median survival time after recurrence. To use, find the patient's recurrence interval on the recurrence axis, then draw a straight line upward to the points axis to determine how many points toward death the patient receives for her recurrence interval. Do this again for the other axes, each time drawing a straight line upward toward the points axis. Sum the points received for each predictor and find the sum on the total points axis. Draw a straight line down to the median-survival axis to find the patient's median survival time after recurrence of ovarian cancer. FIGO, International Federation of Gynecology and Obstetrics.

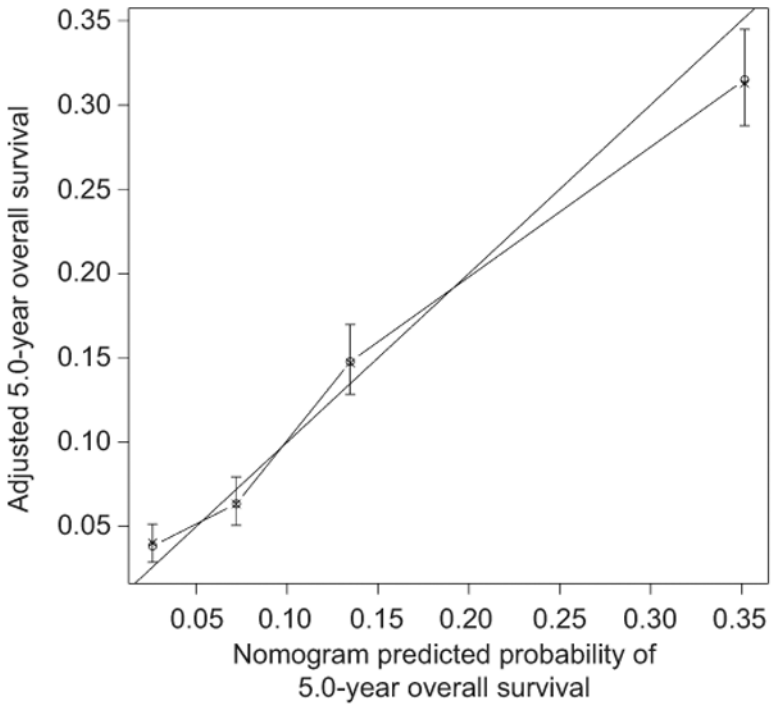

Figure 4.

Calibration curve for the overall survival nomogram model. The *dotted line* represents an ideal nomogram and the *solid line* represents the observed nomogram. The vertical bars indicate 95% CIs and the *open circles* represent bias-corrected estimates.

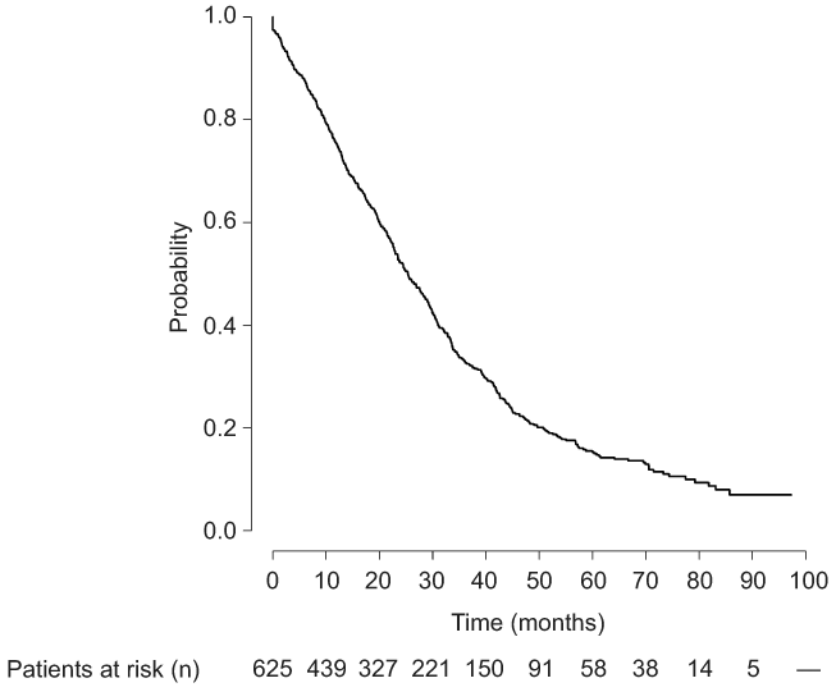

Figure 5.
Kaplan–Meier overall survival after recurrence for the Gynecologic Oncology Group-218 validation cohort. Median survival: 25.4 months (95% CI, 23.0–28.3 months).

Table 1.

Gynecologic Oncology Group First-Line Trials in Ovarian Cancer

Protocol (Year Published)	Protocol Regimen	Patient Population	PFS (mo)	OS (mo)
GOG-111 (1996)	IV cisplatin/IV paclitaxel×6 cycles vs IV cisplatin/IV cyclophosphamide×6 cycles	Suboptimal stage III greater than 1 cm and IV (n=410)	18 (*P*<.001) 13	38 (*P*=.001) 24
GOG-114 (2001)	High-dose IV carboplatin×2 cycles IP cisplatin, IV paclitaxel×6 cycles vs IV cisplatin/IV paclitaxel×6 cycles	Optimal stage III less than 1 cm (n=462)	28 (*P*=.01) 22	63 (*P*=.05) 52
GOG-132 (2000)	High-dose cisplatin×6 cycles vs High-dose IV paclitaxel×6 courses vs IV cisplatin/IV paclitaxel×6 cycles	Suboptimal stage III greater than 1 cm and IV (n=648)	16.4 (*P*=.002) 10.8 14.1	30.2 (*P*=.310) 25.9 26.3
GOG-152 (2004)	IV cisplatin/IV paclitaxel×6 with SCS vs IV cisplatin/IV paclitaxel×6	Suboptimal stage III greater than 1 cm and IV (n = 550)	10.5 (*P*=NS) 10.7	33.9 (*P*=NS) 33.7
GOG-158 (2003)	IV carboplatin/IV paclitaxel×6 cycles vs IV cisplatin/IV paclitaxel×6 cycles	Optimal stage III less than 1 cm (n=792)	20.7 (*P*=NS) 19.4	57.4 (*P*=NS) 48.7
GOG-162 (2007)	IV cisplatin/IV paclitaxel 24 hours×6 cycles vs IV cisplatin/IV paclitaxel 96 hours×6 cycles	Suboptimal stage III greater than 1 cm and IV	12.4 (*P*=NS) 12.6	29.9 (*P*=NS) 30.5
GOG-172 (2006)	IP cisplatin 100 mg/M2/IV paclitaxel/IP paclitaxel day 8×6 cycles vs IV carboplatin/IV paclitaxel×6 cycles	Optimal stage III less than 1 cm (n=415)	23.8 (*P*=.05) 18.3	65.6 (*P*=.03) 49.7
GOG-182 (2009)	IV carboplatin/IV paclitaxel/IV gemcitabine×8 cycles vs IV carboplatin/IV paclitaxel/IV PLD every other×8 cycles vs IV carboplatin/IV topotecan×4 cycles followed by IV carboplatin/IV paclitaxel×4 cycles vs IV carboplatin/IV gemcitabine×4 cycles followed by IV carboplatin/IV paclitaxel×4 cycles vs IV carboplatin/IV paclitaxel×8 cycles	Incompletely resected stage III–IV (n=4,312)	(*P*=NS) (*P*=NS) (*P*=NS) (*P*=NS) 16 mo	(*P*=NS) (*P*=NS) (*P*=NS) (*P*=NS) (*P*=NS) 44.1 mo
GOG-218 (2011)	IV carboplatin/IV paclitaxel/IV placebo×6 cycles followed by placebo for 1 y vs IV carboplatin/IV paclitaxel/IV bevacizumab×6 cycles followed by placebo for 1 y vs IV carboplatin/IV paclitaxel/IV bevacizumab×6 cycles followed by bevacizumab for 1 y	Incompletely resected stage III–IV (n = 1,873)	10.3 (*P*<.001) 11.2 14.1	(*P*=NS)

PFS, progression-free survival; OS, overall survival; GOG, Gynecologic Oncology Group; IV, intravenous; IP, intraperitoneal; NS, not significant; PLD, pegylated liposomal doxorubicin; SCS, secondary cytoreductive surgery.

Table 2:

Eligible Patient Demographics and Clinical Characteristics (*N*=4739)

	N	
Age $_{years}$	4739	50.7 58.8 66.4
Performance status	4734	
0		44.0% (2082)
1		47.7% (2260)
2		8.3% (392)
Histology	4739	
serous		81.2% (3849)
mixed epithelial		6.2% (295)
endometrioid		6.3% (299)
clear-cell/mucinous		2.2% (106)
other		4.0% (190)
FIGO stage	4733	
III		84% (3975)
IV		16% (758)
Tumor grade (differentiation)	4739	
2		39.1% (1853)
3		60.9% (2886)
Residual disease classification	4739	
No gross residual		20.2% (959)
Gross residual ≤ 1 cm		44.5% (2111)
Gross residual > 1 cm		35.2% (1669)
Regimen	4739	
IV		93.9% (4452)
IP		6.1% (287)
GOG protocol	4739	
GOG-0111		3.0% (140)
GOG-0114		6.7% (316)
GOG-0132		6.5% (308)
GOG-0152		2.4% (113)
GOG-0158		12.3% (582)
GOG-0162		4.7% (222)
GOG-0172		5.7% (269)
GOG-0182		58.9% (2789)
Complete pathologic response	1342	
no		31.4% (422)
yes		68.6% (920)
Primary recurrence site	2179	
pelvis		30.7% (669)
lung		6.1% (132)

	N
abdomen	57.6% (1256)
vagina	5.6% (122)

a b c represent the lower quartile *a*, the median *b*, and the upper quartile *c* for continuous variables.

N is the number of non–missing values. Numbers after percents are frequencies.

Table 3:

Kaplan–Meier Overall Survival Following Recurrence Based on Time to Recurrence

Time to recurrence (months)	*N*	events	median (95% CI)
≤6.0	417	405	9.8 (8.3–10.9)
6.0–9.0	485	474	10.3 (9.1–11.7)
9.0–12.0	757	737	13.7 (12.5–15.1)
12.0–15.0	711	679	20.3 (19.1–21.7)
15.0–18.0	554	525	23.6 (21.9–25.7)
18.0–21.0	345	307	29.4 (26.3–32.5)
21.0–24.0	264	231	32.6 (28.1–37.0)
24.0–27.0	189	170	36.5 (31.4–40.7)
27.0–30.0	160	130	35.3 (31.5–41.1)
30.0–33.0	137	106	38.4 (32.1–46.3)
33.0–36.0	125	103	35.7 (26.7–43.0)
≥36.0	595	369	44.8 (41.2–48.5)

Table 4:

Patient Characteristics for GOG-0218 Validation Cohort (*N* = 625)

	N	
Age $_{years}$	625	51.7 60.3 67.1
Performance status	625	
0		49.4% (309)
1		44.2% (276)
2		6.4% (40)
Histology	625	
mixed epithelial		4.0% (25)
clear-cell/mucinous		2.9% (18)
other		93.1% (582)
FIGO stage	625	
III		75.4% (471)
IV		24.6% (154)
Residual disease > 1 cm	625	
yes		64.8% (405)
no		35.2% (220)

a b c represent the lower quartile *a*, the median *b*, and the upper quartile *c* for continuous variables.

N is the number of non–missing values.

Numbers after percents are frequencies.