Research Square

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Treatment Intensity and Initiation Timing in Elderly Patients With Extensive-Stage Small Cell Lung Cancer: A Large SEER-Based Survival Analysis and Prognostic Nomogram

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Abstract

Background: This study assessed how treatment intensity and timing affect survival in elderly extensive-stage small cell lung cancer (ES-SCLC) patients, explored survival heterogeneity across clinical subgroups, and built a prognostic nomogram for personalized risk stratification.

Methods: We extracted 7,053 patients aged ≥65 diagnosed with ES-SCLC (2010–2022) from the Surveillance, Epidemiology, and End Results (SEER) database . Propensity score matching (PSM) balanced baseline confounders across treatment intensity and timing groups. Kaplan-Meier and Cox models analyzed overall survival (OS) and cancer-specific survival (CSS). Independent predictors from the training cohort formed a nomogram validated internally.

Results: After PSM, patients receiving combined chemoradiotherapy had longer median OS than those receiving lower-intensity treatment (11.0 vs. 9.0 months; log-rank P < 0.001). Subgroup analyses showed that among patients with low metastatic burden, lower-intensity treatment was associated with worse survival compared with combined chemoradiotherapy (HR = 1.45, 95% CI: 1.38-1.53; P < 0.001), whereas no significant difference was observed among those with high metastatic burden (HR = 1.05, 95% CI: 0.88-1.25; P = 0.597). Treatment initiation at 30 days or later after diagnosis was associated with longer observed survival.

Conclusions: Chemoradiotherapy's survival advantage differs by metastatic burden in elderly ES-SCLC. High-burden patients obtain no obvious extra survival gain from intensive treatment, supporting individualized care for this frail group. Delayed treatment does not worsen survival. Our nomogram facilitates risk stratification and therapeutic consultation, though external validation is still needed.

Introduction

Small cell lung cancer (SCLC) is a highly aggressive neuroendocrine malignancy, accounting for approximately 15% of all lung cancer cases[1, 2]. At diagnosis, nearly two-thirds of patients are already diagnosed with extensive-stage disease (ES-SCLC), which is associated with poor prognosis[3]. Although the combination of immune checkpoint inhibitors and chemotherapy has become the standard first-line treatment for ES-SCLC in recent years[4], the overall clinical benefit remains limited, with only modest survival improvement of about two months[5], and a small proportion of patients achieving long-term survival[6]. Consolidative thoracic radiotherapy (TRT) and prophylactic cranial irradiation (PCI) may improve outcomes in selected patients[7], suggesting that carefully selected subgroups may benefit from multimodality treatment.

As the global population ages, the proportion of elderly patients with SCLC is steadily increasing[8–10]. However, older patients are often underrepresented in randomized clinical trials because of age-related organ dysfunction, comorbidity, frailty, and concerns about treatment tolerance. Consequently, the optimal treatment strategy for older patients with ES-SCLC remains uncertain[11]. In clinical practice, two issues are particularly relevant: how quickly treatment should be initiated and how intensive

treatment should be. Although the rapid growth kinetics of SCLC often support early intervention[12], older patients may require additional time for diagnostic clarification, staging, geriatric assessment, optimization of comorbidities, and multidisciplinary treatment planning. The survival implications of this interval remain unclear. Similarly, clinicians must balance treatment efficacy against toxicity and functional decline, particularly in frail patients[13]. Large-scale real-world data may therefore help clarify patterns of treatment and survival in this understudied population.

Baseline disease burden is another important determinant of prognosis in SCLC[14]. The conventional AJCC-TNM staging system, while useful, is relatively coarse in the context of ES-SCLC and fails to capture the prognostic heterogeneity between patients adequately. A practical metastatic burden classification may therefore help identify older patients who are more or less likely to benefit from intensive treatment.

In this study, we used a large SEER cohort to examine the associations of treatment intensity and treatment timing with OS and CSS in older patients with ES-SCLC. We further evaluated whether metastatic burden modified the association between treatment intensity and survival, and developed a prognostic nomogram to provide a reference for clinical diagnosis and treatment decision-making in elderly patients with ES-SCLC.

Methods

Population selection

Data for this retrospective cohort study were obtained from the Surveillance, Epidemiology, and End Results (SEER) database. We initially identified 70,489 patients diagnosed with SCLC between 2010 and 2022 and extracted demographic, clinicopathological, treatment, and survival information.

The inclusion criteria were as follows: (1) diagnosis between 2010 and 2022 and age ≥ 65 years; (2) histologically confirmed SCLC according to the International Classification of Diseases for Oncology, Third Edition (ICD-O-3) morphology codes 8002 and 8041–8045; and (3) extensive-stage disease, defined according to the SEER Combined Summary Stage as distant metastasis.

Patients were excluded if they had no pathological confirmation, a history of multiple primary malignancies, missing key baseline variables (including race, marital status, tumor size, or detailed metastatic site information), missing follow-up data, survival time shorter than 3 months, or prior surgical resection of the primary tumor. After applying these criteria, 7,053 eligible patients were included in the final analysis. The patient selection process is shown in Fig. 1. SEER data has been de-identified for all patient information, does not contain any patient identification information, and is publicly available. Therefore, our study does not require written informed consent from patients or approval from institutional ethics review committees.

Variables

The primary endpoints were overall survival (OS) and cancer-specific survival (CSS). Covariates were grouped into demographic characteristics, clinicopathological variables, and treatment-related factors.

Demographic variables included age (65–69, 70–74, 75–79, and ≥ 80 years), sex, race (White, Black, and other), and marital status.

Clinicopathological variables included tumor size (≤ 5 cm vs. >5 cm), histologic grade, and metastatic burden. Metastatic burden was defined according to the number of distinct metastatic sites recorded in SEER: patients with metastases involving three or more anatomical sites were classified as having high metastatic burden, whereas those with fewer than three involved sites were classified as having low metastatic burden.

Treatment-related variables included receipt of radiotherapy and chemotherapy. Treatment intensity was categorized as high intensity for patients receiving combined chemoradiotherapy and lower intensity for patients receiving chemotherapy alone, radiotherapy alone, or no documented antitumor treatment. Treatment timing was defined as the interval from diagnosis to initiation of treatment and categorized as early initiation (< 30 days) or delayed initiation (≥ 30 days).

Statistical analysis

All statistical analyses were performed using R software (version 4.5.2). Propensity score matching (PSM) was used to reduce baseline imbalances between treatment comparison groups. Survival outcomes were compared using Kaplan-Meier curves and log-rank tests. Patients were randomly divided into a training cohort and an internal validation cohort at a 7:3 ratio. Categorical variables were compared using chi-square tests. In the training cohort, univariate and multivariate Cox proportional hazards regression analyses were performed to identify independent prognostic factors, which were then used to construct a prognostic nomogram.

Model performance was evaluated using the concordance index (C-index) and time-dependent area under the receiver operating characteristic curve (AUC). Calibration curves were generated using 1,000 bootstrap resamples to assess agreement between predicted and observed outcomes. Decision curve analysis (DCA) was performed to estimate clinical net benefit. For risk stratification, a total risk score was calculated for each patient based on the nomogram. The optimal cutoff value was determined using the surv_cutpoint function in the R package survminer, and patients were classified into high-risk and low-risk groups. Survival differences between groups were assessed using Kaplan-Meier analysis and the log-rank test. All statistical tests were two-sided, and P values < 0.05 were considered statistically significant.

Results

Association between treatment intensity and survival

A 1:1 PSM analysis generated a balanced cohort of 6,388 patients, including 3,194 patients in each treatment intensity group. After matching, baseline covariates were well balanced, with standardized mean differences (SMDs) below 0.1. Kaplan-Meier analysis showed that patients receiving combined chemoradiotherapy had a longer median OS than those receiving lower-intensity treatment (11.0 months vs. 9.0 months; log-rank $P < 0.001$). A similar pattern was observed for CSS (Figs. 2A and B). Baseline characteristics are summarized in Table S1. Results before PSM are provided in Figure S1A -B and Table S2.

Association between treatment timing and survival

Before PSM, the early and delayed treatment groups differed in treatment intensity, age, marital status, and tumor size. After matching, baseline variables were well balanced between groups (all SMDs < 0.1), as shown in Table S3. Kaplan-Meier analysis showed longer median OS in the delayed initiation group than in the early initiation group (11.0 months vs. 9.0 months; $P < 0.001$) (Figs. 2C and D). Similar results were observed for CSS. These findings should be interpreted as associations rather than evidence that delaying treatment improves survival. Results before PSM are presented in Figure S1C-D and Table S4.

Prognostic model

Baseline characteristics of the training and validation cohorts

The 7,053 eligible patients were randomly divided into a training cohort (n = 4,938) and an internal validation cohort (n = 2,115). Baseline characteristics were balanced between cohorts, with no statistically significant differences in demographic, clinicopathological, or treatment-related variables (all $P > 0.05$), as shown in Table 1.

Table 1
Clinical and pathological characteristics of eligible elderly patients with ES-SCLC diagnosed between 2010 and 2022

Variables	Total (n = 7053)	Training set (n = 4938)	Validation set (n = 2115)	p
Treatment, n (%)				0.416
High intensity	3441 (48.79)	2393 (48.46)	1048 (49.55)	
Low intensity	3612 (51.21)	2545 (51.54)	1067 (50.45)	
Delayed treatment, n (%)				0.883
<30	4999 (70.88)	3503 (70.94)	1496 (70.73)	
≥30	2054 (29.12)	1435 (29.06)	619 (29.27)	
Sex, n (%)				0.112
Female	3505 (49.7)	2485 (50.32)	1020 (48.23)	
Male	3548 (50.3)	2453 (49.68)	1095 (51.77)	
Age, n (%)				0.294
65–69	2736 (38.79)	1898 (38.44)	838 (39.62)	
70–74	2158 (30.6)	1543 (31.25)	615 (29.08)	
75–79	1356 (19.23)	947 (19.18)	409 (19.34)	
≥80	803 (11.39)	550 (11.14)	253 (11.96)	
Marital, n (%)				0.106
Unmarried	3183 (45.13)	2260 (45.77)	923 (43.64)	
Married	3870 (54.87)	2678 (54.23)	1192 (56.36)	
Race, n (%)				0.699
White	6032 (85.52)	4231 (85.68)	1801 (85.15)	
Black	603 (8.55)	422 (8.55)	181 (8.56)	
Other	418 (5.93)	285 (5.77)	133 (6.29)	
Grade, n (%)				0.920
I-II	21 (0.3)	14 (0.28)	7 (0.33)	
III	680 (9.64)	470 (9.52)	210 (9.93)	
IV	849 (12.04)	599 (12.13)	250 (11.82)	

Variables	Total (n = 7053)	Training set (n = 4938)	Validation set (n = 2115)	p
Unknown	5503 (78.02)	3855 (78.07)	1648 (77.92)	
Tumor burden, n (%)				0.124
High burden	549 (7.78)	368 (7.45)	181 (8.56)	
Low burden	6504 (92.22)	4570 (92.55)	1934 (91.44)	
Tumor Size, n (%)				0.762
<=5	3716 (52.69)	2608 (52.81)	1108 (52.39)	
>5	3337 (47.31)	2330 (47.19)	1007 (47.61)	

Cox regression analyses for OS and CSS

Univariate and multivariate Cox proportional hazards regression analyses were performed to identify factors associated with OS and CSS. In univariate analyses, treatment intensity, treatment timing, sex, age, race, and metastatic burden were significantly associated with survival outcomes (all $P < 0.05$). Variables with statistical significance were included in multivariate Cox models. In the multivariate analysis for OS, lower-intensity treatment was associated with a higher risk of death (HR = 1.451, 95% CI: 1.366–1.541; $P < 0.001$). Male sex (HR = 1.158, 95% CI: 1.092–1.229) and older age (e.g.,≥80 vs. 65–69 years: HR = 1.313, 95% CI: 1.187–1.452) were also associated with poorer survival. In contrast, delayed treatment initiation (≥ 30 days) (HR = 0.778, 95% CI: 0.728–0.832), race other than White, and low metastatic burden (HR = 0.648, 95% CI: 0.580–0.725) were associated with lower mortality risk (Table 2). Similar findings were observed for CSS (Table S5).

Table 2
Univariate and multivariate analyses of OS in elderly patients with ES-SCLC

Variable	Univariate			Multivariate		
	HR	95%CI	*P*	HR	95%CI	*P*
Treatment						
High intensity	Ref			Ref		
Low intensity	1.457	1.372–1.546	< 0.001	1.451	1.366–1.541	< 0.001
Delayed treatment						
< 30	Ref			Ref		
≥ 30	0.813	0.761–0.869	< 0.001	0.778	0.728–0.832	< 0.001
Sex						
Female	Ref			Ref		
Male	1.182	1.114–1.254	< 0.001	1.158	1.092–1.229	< 0.001
Age						
65–69	Ref			Ref		
70–74	1.099	1.023–1.179	0.009	1.110	1.033–1.191	0.004
75–79	1.176	1.082–1.278	< 0.001	1.147	1.055–1.247	0.001
≥ 80	1.359	1.230–1.501	< 0.001	1.313	1.187–1.452	< 0.001
Marital						
Unmarried	Ref					
Married	0.971	0.915–1.030	0.322			
Race						
White	Ref			Ref		
Black	0.882	0.793–0.982	0.021	0.909	0.817–1.012	0.081
Other	0.894	0.784–1.019	0.094	0.891	0.781–1.016	0.086
Grade						
I-II	Ref					
III	1.026	0.603–1.748	0.924			
IV	1.132	0.666–1.925	0.646			

Variable	Univariate			Multivariate		
	HR	95%CI	*P*	HR	95%CI	*P*
Treatment						
Unknown	1.084	0.641–1.832	0.764			
Tumor burden						
High burden	Ref			Ref		
Low burden	0.625	0.559–0.698	< 0.001	0.648	0.580–0.725	< 0.001
Tumor Size						
≤ 5	Ref					
> 5	1.050	0.990–1.114	0.105			

Nomogram development

A prognostic nomogram was developed using independent prognostic factors identified in the multivariate Cox regression analysis, including treatment intensity, treatment timing, metastatic burden, age, and sex. By assigning weighted points to each variable, the model estimates individualized 1-, 3-, and 5-year OS and CSS probabilities in older patients with ES-SCLC (Fig. 2E and Figure S1E).

Time-dependent ROC analysis and calibration curves

Time-dependent ROC curves were generated to evaluate model discrimination over time. For OS, AUC values at 1, 3, and 5 years were 0.651, 0.715, and 0.735 in the training cohort and 0.627, 0.642, and 0.722 in the validation cohort, respectively (Figs. 2Fand G). For CSS, the corresponding AUC values were 0.651, 0.709, and 0.728 in the training cohort and 0.630, 0.633, and 0.695 in the validation cohort (Figure S1Fand G). Calibration curves for OS and CSS showed acceptable agreement between predicted and observed outcomes in both cohorts (Figs. 2H and I). DCA indicated a positive net benefit across clinically relevant threshold probabilities for 1-, 3-, and 5-year survival (Figs. 3A-F and Figure S2), supporting the potential utility of the model for risk stratification. The OS and CSS results are presented in separate panels within each figure to clarify endpoint-specific model performance.

Risk stratification and Kaplan–Meier survival analysis

Based on the total points generated from the nomogram, the optimal cutoff value was determined using X-tile software. Patients were classified into high-risk and low-risk groups. Kaplan-Meier analysis showed significant differences in OS and CSS between the two groups, with longer survival among patients in the low-risk group (Figs. 3G-J).

Subgroup and interaction analyses

Predefined subgroup analyses were performed to assess the robustness of associations between treatment intensity, treatment timing, and OS and to explore heterogeneity across clinical subgroups. The subgroup analysis for treatment intensity is shown in Fig. 4, and the subgroup analysis for treatment timing is shown in Fig. 5. Overall, lower-intensity treatment was associated with worse survival compared with combined chemoradiotherapy (HR = 1.41, 95% CI: 1.34–1.48; P < 0.001), and the survival benefit associated with combined chemoradiotherapy was generally consistent across most subgroups.

A significant interaction was observed for metastatic burden (P for interaction < 0.001; Fig. 4). Among patients with high metastatic burden, lower-intensity treatment was not associated with a statistically significant difference in survival compared with combined chemoradiotherapy (HR = 1.05, 95% CI: 0.88–1.25; P = 0.597). In contrast, among patients with low metastatic burden, lower-intensity treatment was associated with significantly worse survival compared with combined chemoradiotherapy (HR = 1.45, 95% CI: 1.38–1.53; P < 0.001). These findings suggest that metastatic burden may help identify older patients who are more likely to derive survival benefit from combined chemoradiotherapy. A significant interaction was also observed across age subgroups (P for interaction = 0.030), indicating that the magnitude of treatment benefit varied by age. No significant interactions were observed across subgroups defined by treatment timing, race, tumor grade, or tumor size (all P for interaction > 0.05).

For treatment timing, significant interaction effects were observed for histologic grade and primary tumor size (P for interaction = 0.044; Fig. 5). The association between delayed treatment initiation and better observed survival was particularly evident among patients with grade IV tumors (HR = 0.81, 95% CI: 0.71–0.95; P = 0.010). Patients with smaller tumors (≤ 5 cm) also showed a stronger association between delayed initiation and favorable survival (HR = 0.76, 95% CI: 0.71–0.82), whereas the association persisted with a smaller effect size among patients with tumors > 5 cm (HR = 0.86, 95% CI: 0.78–0.92). Across other predefined subgroups, including treatment intensity, sex, age, marital status, race, and metastatic burden, the association between delayed treatment initiation and survival was generally consistent (all P for interaction > 0.05).

Discussion

In this large SEER-based cohort of older patients with ES-SCLC, combined chemoradiotherapy was associated with longer OS and CSS compared with lower-intensity treatment. This finding is consistent with prior evidence supporting the role of multimodality treatment in selected patients with ES-SCLC[7, 15, 16]. However, older adults are more susceptible to treatment-related toxicity, functional decline, and competing risks of death, which may limit the net benefit of aggressive therapy[17, 18]. In real-world practice, treatment intensity often decreases with advancing age because of comorbidity, impaired organ function, frailty, and patient preference[19, 20]. Our findings suggest that treatment intensification may be beneficial for selected older patients, but that benefit is not uniform across all clinical subgroups.

In the present study, both multivariate Cox regression and subgroup analyses consistently highlighted the dominant role of high-intensity treatment in improving survival. However, this benefit was not

universal. Subgroup interaction analysis revealed that high-intensity treatment provided a significant survival advantage only in patients with low tumor burden, while no meaningful benefit was observed in those with high tumor burden (HR = 1.05, P = 0.597). This finding has important clinical implications, particularly for elderly patients, as high tumor burden often reflects more extensive metastatic disease and a poorer physiological reserve[14, 19, 21]. These factors are associated with frailty and reduced functional capacity, making elderly patients more susceptible to non-cancer-related mortality such as infections, cardiopulmonary failure, or other treatment-related complications[13, 22]. High-intensity treatment in these patients may exacerbate the risk of toxicities and fail to provide a clear survival benefit[19]. Furthermore, high tumor burden is associated with increased tumor mutational complexity and intrinsic therapeutic resistance, which may limit the effectiveness of standard cytotoxic treatments[23]. These findings suggest that in clinical practice, elderly patients with high tumor burden may be at risk of overtreatment if high-intensity therapies are pursued aggressively. A more de-escalated approach, taking into account the patient's frailty and tumor burden, may provide better outcomes, particularly for patients with limited physiological reserves.

Interestingly, this study identified a counterintuitive finding: patients who experienced a delay in treatment initiation (≥ 30 days from diagnosis) had significantly better survival outcomes than those who received early treatment (< 30 days) (multivariate HR = 0.778, P < 0.001). This does not suggest that delayed treatment itself confers a survival benefit but reflects confounding by indication in real-world practice. In routine clinical settings, patients requiring urgent treatment often present with aggressive disease, including manifestations like superior vena cava syndrome, severe respiratory failure, or brain metastases, which necessitate immediate, high-intensity interventions[24]. These patients tend to have a poor baseline prognosis. In contrast, elderly patients with indolent disease progression may benefit from delayed treatment, allowing for more thorough geriatric assessments, comprehensive staging, and multidisciplinary team (MDT) discussions to optimize treatment planning. Subgroup analyses further corroborated this interpretation. Delayed treatment showed a more pronounced survival benefit in patients with smaller tumors (≤ 5 cm; HR = 0.76), which is consistent with findings from recent studies. For example, Warrick et al. found that delayed initiation of immunotherapy in ES-SCLC did not compromise survival benefits[4], and studies on early-stage Non-SCLC have shown that postponing adjuvant chemotherapy to 3–4 months after surgery does not adversely affect long-term survival[25]. These studies suggest that, for clinically stable elderly patients, adequate time for evaluation and multidisciplinary decision-making may be more beneficial than starting treatment prematurely.

The AJCC-TNM staging system is widely used for prognostic assessment and treatment guidance[26]. However, it fails to account for important variables in elderly patients, such as functional status, comorbidities, and treatment tolerance. Existing prognostic models for ES-SCLC often include patients of all ages and do not account for the unique heterogeneity of elderly patients[27–30]. In this study, we developed and validated a visualized nomogram that integrates modifiable clinical variables, including treatment timing, intensity, and tumor burden. This nomogram demonstrated excellent predictive performance, with high discrimination and favorable clinical net benefit in predicting 1-, 3-, and 5-year OS and CSS. This model serves not only as a prognostic tool but also as a decision-support instrument that

enables clinicians to identify high-risk elderly patients and tailor treatment strategies based on individual characteristics such as frailty, functional status, and comorbidity. By incorporating these factors, clinicians can optimize treatment decisions, ensuring that elderly patients receive appropriate therapies that balance efficacy with treatment tolerance and minimize overtreatment.

Several limitations should be acknowledged. First, this was a retrospective analysis based on the SEER database, and residual confounding cannot be excluded despite PSM and multivariable adjustment. SEER does not provide detailed information on ECOG performance status, frailty, geriatric assessment, comorbidities, organ function, chemotherapy regimens, immune checkpoint inhibitor use, radiotherapy dose or field, treatment sequence, patient preference, or treatment-related adverse events. These unmeasured factors are highly relevant to treatment selection and survival in older adults with ES-SCLC. Second, treatment intensity was defined using available SEER treatment variables and therefore could not distinguish chemotherapy regimen, dose intensity, concurrent versus sequential chemoradiotherapy, consolidative thoracic radiotherapy, prophylactic cranial irradiation, or modern chemoimmunotherapy. Third, the nomogram was internally validated only; external validation in independent cohorts is needed before clinical application. Future studies integrating geriatric assessment, treatment toxicity, quality of life, and contemporary immunotherapy-era treatment patterns are warranted.

Conclusion

In conclusion, combined chemoradiotherapy was associated with improved survival among older patients with ES-SCLC, but the magnitude of benefit varied by metastatic burden. Patients with high metastatic burden did not show a clear incremental survival advantage from more intensive treatment in this real-world cohort, underscoring the need for individualized treatment decisions that consider disease burden, physiological reserve, and patient goals. Treatment initiation at 30 days or later was not associated with worse survival, although this association likely reflects clinical selection and should not be interpreted as a recommendation to delay therapy. The proposed nomogram may support risk stratification and shared decision-making, but external validation is required.

Declarations

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Ethics Statement

This study used de-identified publicly available data from the Surveillance, Epidemiology, and End Results (SEER) database. Ethics committee approval and informed consent were waived in accordance with institutional policy for research using public de-identified datasets. Clinical trial number: not applicable.

Data Availability

The data analyzed in this study are available from the SEER database, subject to SEER data-use policies and permissions.

Author Contributions

Huaying Zhang, Jun Li and Yajie Wang: conceptualization, data curation, formal analysis, writing - original draft. Quankai Dai, Yuandong Yu and Fengjun Cao: methodology, investigation, validation, and writing - review and editing. Yunyan Tai: supervision, project administration, and writing - review and editing. All authors approved the final manuscript.

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Figures

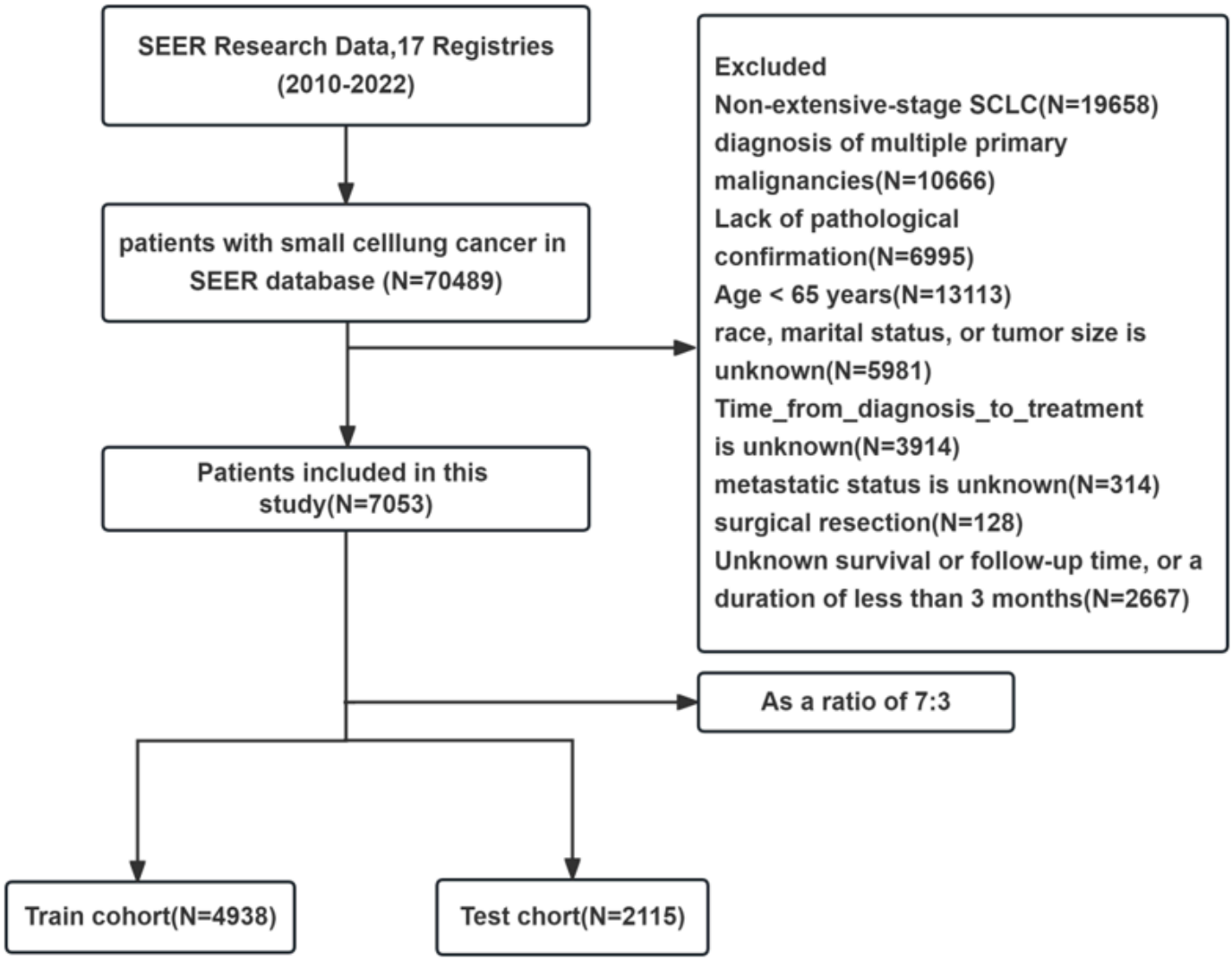


Figure 1

Flowchart showing the patient selection.

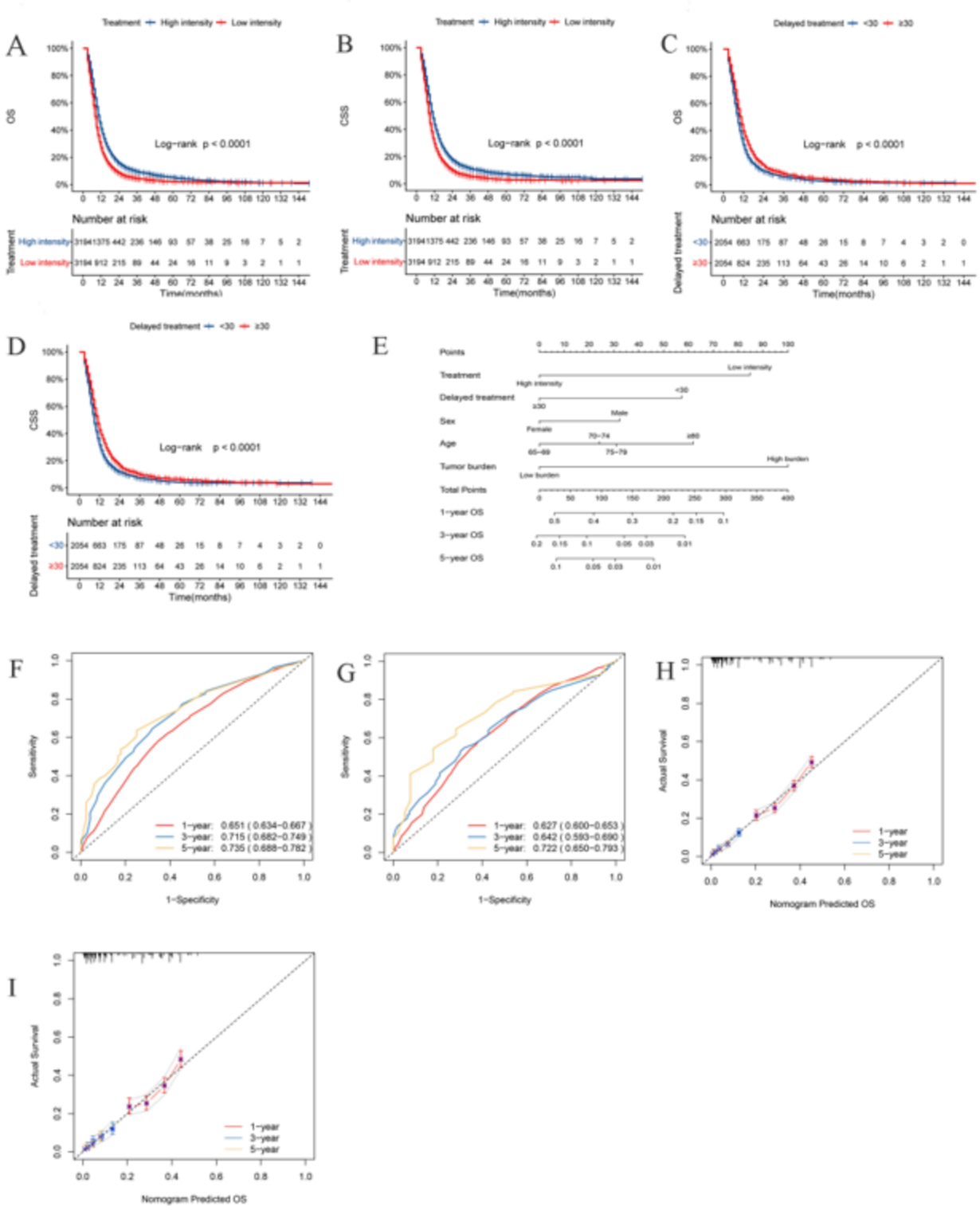


Figure 2

Survival stratification, prognostic model development, and validation for OS. (A-B) Kaplan-Meier curves for OS and CSS comparing treatment intensity groups (Chemoradiotherapy versus Lower-intensity treatment) after PSM. (C-D) Kaplan-Meier curves for OS and CSS comparing treatment timing groups (Early initiation [<30 days] versus Delayed initiation [≥30 days]). (E) Nomogram predicting 1-, 3-, and 5-

year OS. (F-G) Time-dependent ROC curves evaluating the discriminative ability of the nomogram for OS in the training and internal validation cohorts.

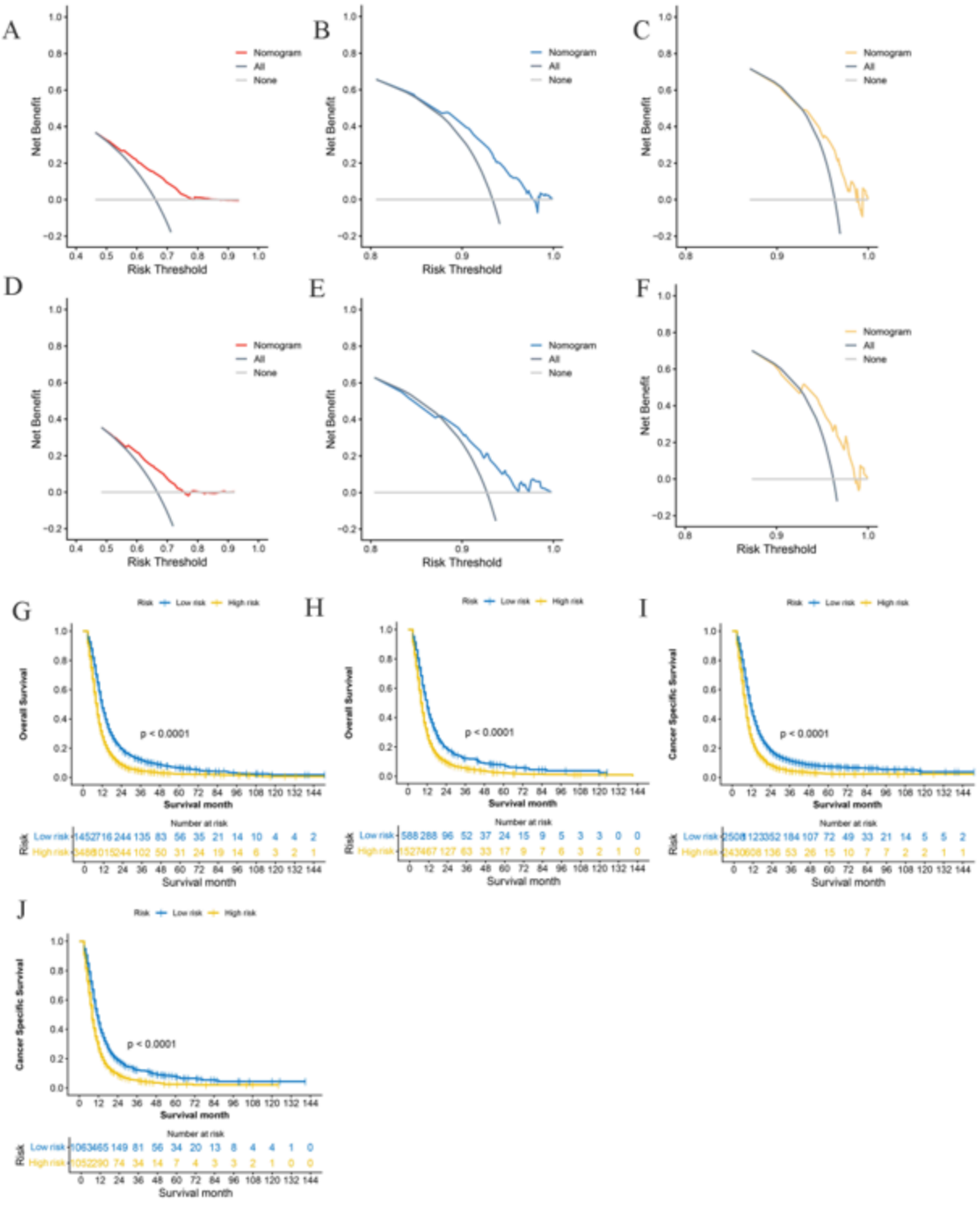


Figure 3

Clinical utility and risk stratification of the nomogram. (A-F) DCA showing the net benefit of the model for predicting 1-, 3-, and 5-year OS in the training (A-C) and validation (D-F) cohorts. (G-J) Kaplan-Meier

curves comparing OS and CSS between low-risk and high-risk groups in the training (G, I) and validation (H, J) sets.

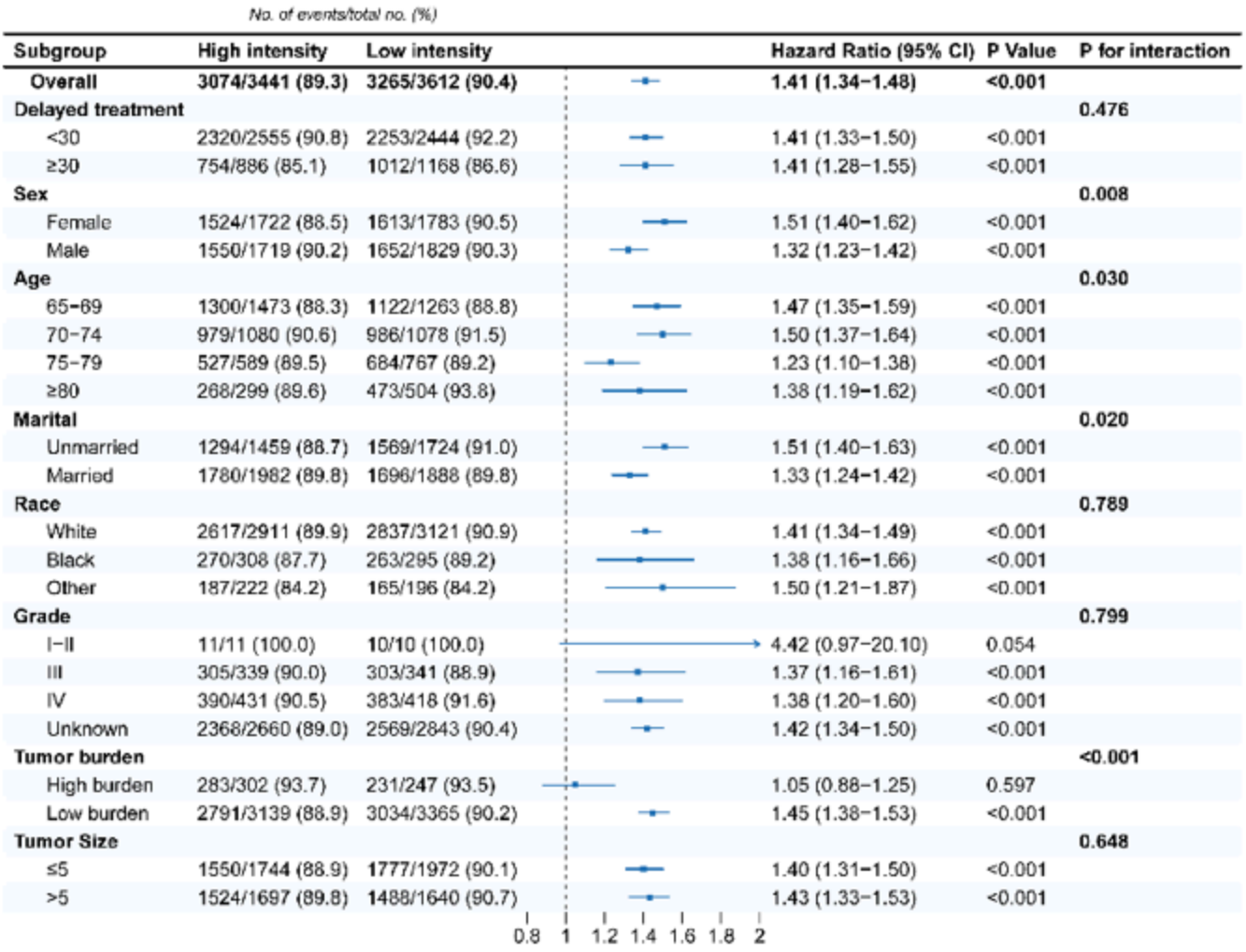


Figure 4

Subgroup analyses of treatment intensity effects on OS comparing lower-intensity treatment versus combined chemoradiotherapy.

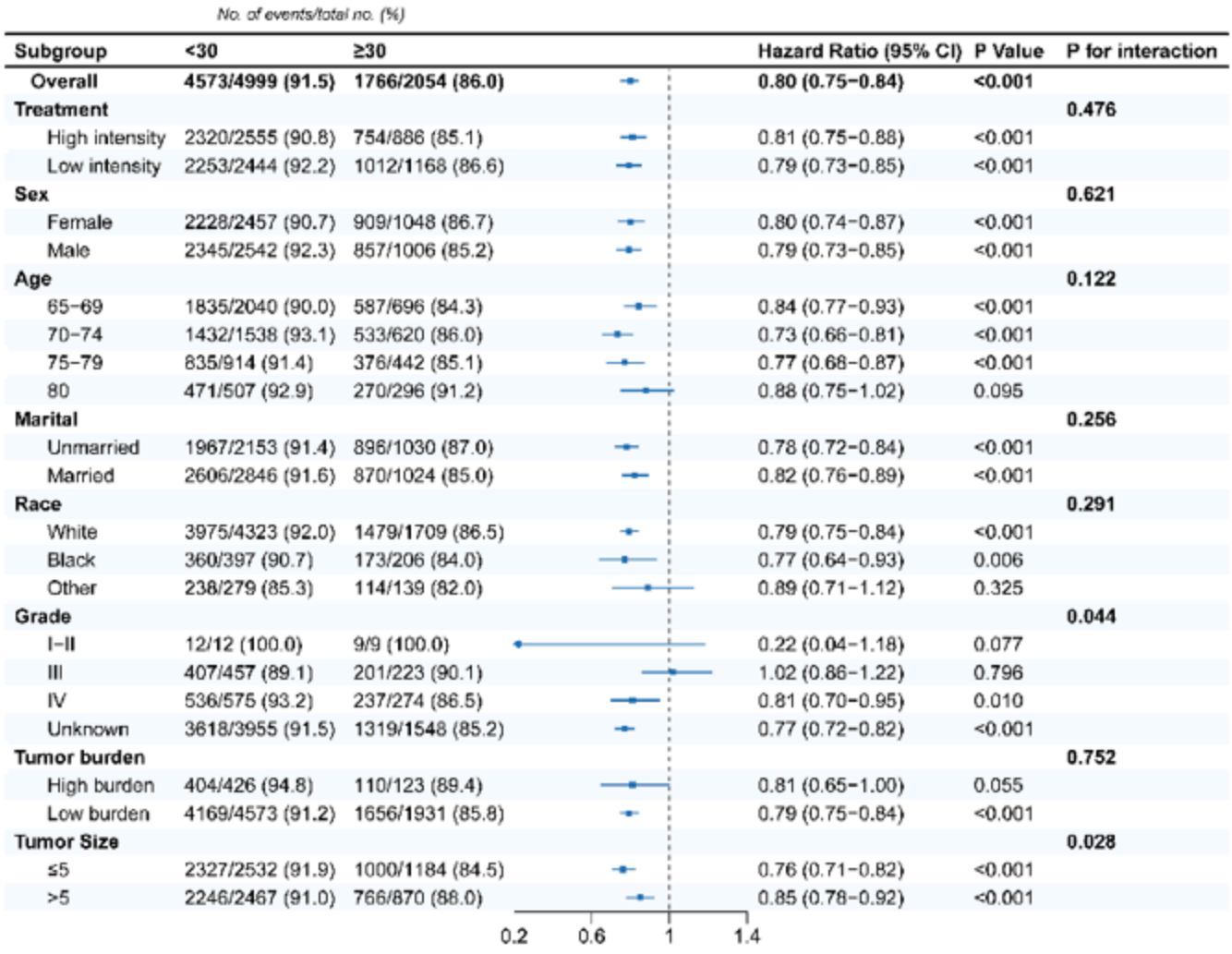


Figure 5

Subgroup analysis of OS comparing delayed (≥30 days) versus early (<30 days) treatment initiation.

Supplementary Files

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