Clinical Characteristics and Overall Survival Prognostic Nomogram for Oligodendroglioma: A Surveillance, Epidemiology, and End Results Population-Based Analysis

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■ OBJECTIVE: **Oligodendroglioma is a rare primary malignant brain tumor that has highly variable clinical outcomes. The aim of this study was to investigate demographics, outcomes, and prognostic factors of all oligodendroglioma cases from the Surveillance, Epidemiology, and End Results database to build a clinical prognosis model to predict survival time of patients with oligodendroglioma.**

■ METHODS: **Cases diagnosed between 1975 and 2016 were selected from the Surveillance, Epidemiology, and End Results database. Age, sex, race, insurance, year of diagnosis, marital status, tumor location, tumor size, summary stage, surgery method, and use of radiotherapy and chemotherapy were evaluated with respect to overall survival by univariate and multivariate analysis. A nomogram predicting 5- and 10-year survival probability for oligodendroglioma was constructed and validated.**

■ RESULTS: **After data cleaning, 4568 patients with oligodendroglioma were included. At the time of last follow-up, mean survival times among grade II and grade III oligodendrogliomas were 74 and 39 months, respectively. In multivariate analysis, radiotherapy, age, tumor site, summary stage, and surgery demonstrated independent associations with survival in both cohorts. Race and radiotherapy demonstrated independent associations with survival in grade II oligodendroglioma. Sex and chemotherapy demonstrated independent associations with survival in grade III oligodendroglioma. Independent factors in either cohort were selected to build a clinical nomogram. The C-index for the nomogram was 0.738 (95% confidence interval 0.718–0.757). The calibration curves of 5- and 10-year survival rates showed good agreement between the nomogram predictions and actual observations.**

■ CONCLUSIONS: **This study was the first to develop a nomogram for predicting overall survival of patients with oligodendroglioma to help clinicians predict patient prognosis accurately and conduct further treatment.**

INTRODUCTION

Oligodendroglioma is a rare primary central nervous system tumor that originates from oligodendroglial precursor cells.[1] Oligodendroglioma accounts for 2%–5% of all primary central nervous system tumors, with an incidence of 1–2 cases per 1 million per year.[2] Oligodendrogliomas are diffusely infiltrative gliomas molecularly defined by *IDH* mutation and 1p/19q codeletion.[1] Oligodendroglioma is further stratified by World Health Organization (WHO) histological phenotype into low-grade well-differentiated WHO grade II oligodendroglioma and WHO grade III anaplastic oligodendroglioma.[3]

The outcome of oligodendroglioma varies greatly, and the identification of factors that improve prognosis remains a central tenet in the clinical practice of neurosurgical oncology.[4] Because of the rarity of the condition, scientific literature assessing prognostic factors in patients with oligodendroglioma is

Key words
- Nomogram
- Oligodendroglioma
- Prognosis
- SEER database

Abbreviations and Acronyms
CI: Confidence interval
GTR: Gross total resection
HR: Hazard ratio
OS: Overall survival
SEER: Surveillance, Epidemiology, and End Results
STR: Subtotal resection
WHO: World Health Organization

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minimal, and a single institution often lacks a sufficient patient cohort.[5] According to the 2020 National Comprehensive Cancer Network guidelines, the standard treatment for low-grade or high-grade gliomas is maximal safe resection followed by observation or adjuvant chemotherapy/radiotherapy.[6] However, there is not enough evidence to support this guideline, and recent studies on this topic came to different conclusions.[7,8] Therefore, population-based prognosis research and the establishment of a clinical prognosis model for the prediction of survival time would be of great importance.[9]

A nomogram is a multivariate visualization prediction model that can incorporate different variables affecting prognosis.[10] Nomograms have been widely constructed to quantify risk based on various important and independent prognostic factors for malignant tumors.[11,12] However, to our knowledge, no published literature has proposed a nomogram to predict the prognosis of patients with oligodendroglioma. Therefore, our study aimed to develop a nomogram that can be applied to individually assess survival time and to discuss different prognostic factors of patients with oligodendroglioma. In this study, retrospective data of 4568 patients with oligodendroglioma from the Surveillance, Epidemiology, and End Results (SEER) database were reviewed. Clinical characteristics and independent prognostic factors were analyzed, and a prognostic nomogram was then constructed and validated.

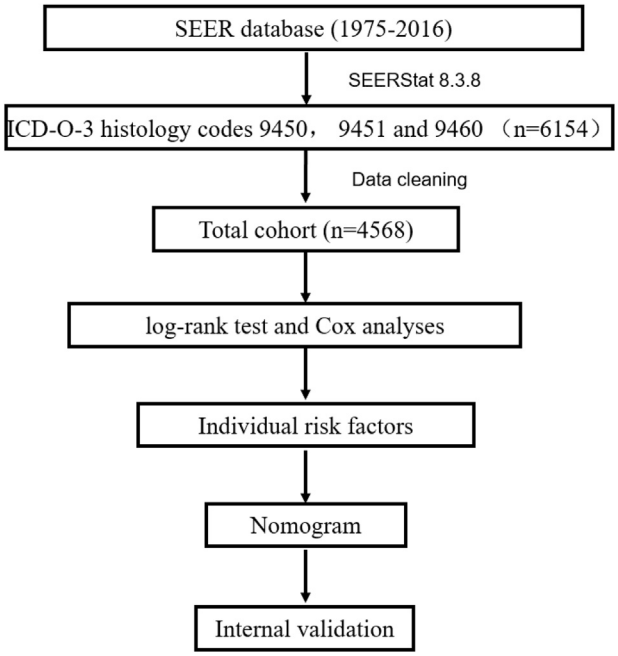

Figure 1. Flowchart of selection of patients with oligodendroglioma. SEER, Surveillance, Epidemiology, and End Results; ICD-O-3, *International Classification of Diseases for Oncology, Third Edition.*

MATERIALS AND METHODS

Data and Study Population

As this was a retrospective database study and no individual patient identifiable information was used, the hospital review board waived the need for informed consent. The SEER database (www.seer.cancer.gov) is the largest publicly available cancer dataset and covers approximately 30% of the total U.S. population from 18 areas of the United States.[13] The exact dataset we used for this analysis was SEER 18 Regs Custom Data (with additional treatment fields), Nov 2018 Sub (1975–2016 varying), released April 2019, based on the November 2018 submission.

All cases meeting the inclusion criteria were collected by SEER*Stat Version 8.3.8 (Surveillance Research Program, National Cancer Institute SEER*Stat software; seer.cancer.gov/seerstat). The inclusion criteria were as follows: pathologically diagnosed as oligodendroglioma (*International Classification of Diseases for Oncology, Third Edition* histology code 9450) or anaplastic oligodendroglioma (*International Classification of Diseases for Oncology, Third Edition* histology codes 9451 and 9460) in the brain; first malignant primary indicator, yes; site recode *International Classification of Diseases for Oncology, Third Edition*, brain; type of follow-up expected, active follow-up. Demographics and clinical characteristics were then collected.

Surgical records were coded as follows: gross total resection (GTR), code 30 or 55; subtotal resection (STR), code 20, 21 or 40; and no surgery (code 00) (7). Radiation records were coded as none/unknown, external beam radiation. Chemotherapy records were coded as none/unknown, yes. Patients without available treatment information were excluded from the data-cleaning process. The flow diagram is shown in **Figure 1**. The primary outcome was overall survival (OS), defined as the interval from diagnosis until death as a result of any cause.

Statistical Analysis

OS was compared using Kaplan-Meier models and univariate Cox proportional hazards analyses. Then possible prognostic variables from Kaplan-Meier survival curves and univariate Cox proportional hazards analyses were included in a multivariate Cox proportional hazards model to calculate hazard ratios (HRs). All analyses were conducted with IBM SPSS Version 23 (IBM Corporation, Armonk, New York, USA). Finally, based on the significant prognostic factors from the multivariate Cox proportional hazards analysis, a nomogram was formulated using the rms package Version 4.0.3 in R (R Core Team R: A language and environment for statistical computing. 2013. R Foundation for Statistical Computing, Vienna, Austria; www.R-project.org/) to obtain predicted survival probabilities at 5 and 10 years for patients with WHO grade II and patients with WHO grade III oligodendroglioma. Findings were considered statistically significant at P values <0.05.

RESULTS

Demographics, Tumor Factors, and Treatment Information

After data cleaning, we identified 3139 patients with WHO grade II oligodendroglioma and 1429 patients with WHO grade III oligodendroglioma. The demographics, tumor factors, and treatment information are given in **Table 1**. Diagnosis of oligodendroglioma

Table 1. Comparison of Demographics, Tumor Factors, and Treatment Information in Oligodendrogliomas

	Before Data Cleaning		After Data Cleaning	
Variable	**WHO Grade II**	**WHO Grade III**	**WHO Grade II**	**WHO Grade III**
Age, years				
0–19	338	43	204	28
20–39	1640	459	1182	368
40–49	1093	451	814	373
50–59	759	415	545	356
60–69	391	258	271	202
≥70	174	133	123	102
Race				
White	3817	1514	2754	1238
Black	223	85	163	67
Other	318	153	222	124
Unknown	37	7	0	0
Sex				
Male	2466	990	1741	797
Female	1929	769	1398	632
Year of diagnosis				
1975–1997	878	175	0	0
1998–2007	1880	796	1672	715
2008–2016	1637	788	1467	714
Insurance				
Uninsured	106	58	91	51
Insured	1438	655	1305	597
Any Medicaid	276	125	238	113
Unknown	2575	921	1505	668
Marital status at diagnosis				
Single	1319	395	937	316
Married	2473	1075	1768	878
Separated; divorced; widowed	439	229	308	185
Unknown	164	60	126	50
Reporting source				
Hospital inpatient/outpatient or clinic	4356	1733	3114	1406
Others	39	26	25	23
Primary site				
Frontal lobe	2302	931	1834	817
Temporal lobe	769	278	596	235
Parietal lobe	454	203	323	177
Occipital lobe	71	33	52	27

WHO, World Health Organization; NOS, not otherwise specified; STR, subtotal resection; GTR, gross total resection.

Continues

Table 1. Continued

	Before Data Cleaning		After Data Cleaning	
Variable	**WHO Grade II**	**WHO Grade III**	**WHO Grade II**	**WHO Grade III**
Overlapping lesion of brain	450	201	306	161
Ventricle	42	8	16	6
Brainstem	16	8	12	6
Brain, NOS	291	97	—	—
Tumor size, cm				
<3	424	133	386	120
3–6	1005	466	913	416
>6	336	279	304	267
Unknown	2630	881	1536	626
Grade				
Well differentiated	309	3	236	1
Moderately differentiated	1161	7	891	5
Poorly differentiated	150	4	88	2
Undifferentiated	217	1714	125	1404
Unknown	2558	31	1799	17
Laterality				
Left	1228	553	1105	506
Right	1291	534	1164	490
Not a paired site	1847	651	851	418
Paired site	29	21	19	15
Summary stage				
Localized	2975	1238	2681	1126
Regional	419	294	369	264
Distant	11	9	9	9
Unknown	990	218	80	30
Primary site surgery				
No surgery	552	157	474	128
STR	1612	799	1450	722
GTR	1293	616	1215	579
Surgery, NOS	60	12	—	—
Unknown	878	175	—	—
Reason no cancer-directed surgery				
Surgery performed	3664	1567	2665	1301
Not recommended	569	147	416	100
Recommended but not performed	132	40	52	26
Unknown	30	5	6	2

Continues

Table 1. Continued

	Before Data Cleaning		After Data Cleaning	
Variable	**WHO Grade II**	**WHO Grade III**	**WHO Grade II**	**WHO Grade III**
Radiation				
None/unknown	2581	512	2039	417
External beam radiation	1706	1188	1100	1012
Radiation, NOS	35	24	—	—
Unknown	73	35	—	—
Radiation sequence with surgery				
No radiation and/or surgery	2997	650	2241	484
Radiation before surgery	35	14	5	5
Radiation after surgery	1355	1083	889	929
Radiation before and after surgery	3	8	1	8
Sequence unknown	5	4	3	3
Chemotherapy				
No; unknown	3233	703	2193	498
Chemotherapy	1162	1056	946	931
Vital status				
Alive	2645	833	2154	745
Dead	1750	926	985	684
Death classification				
Alive or dead from cause other than cancer	2896	915	2293	805
Dead due to cancer	1438	815	808	602
Unknown	61	29	38	22
Total	4395	1759	3139	1429

WHO, World Health Organization; NOS, not otherwise specified; STR, subtotal resection; GTR, gross total resection.

in all patients occurred between 1998 and 2016. The median patient age at diagnosis was 42 years for WHO grade II oligodendroglioma and 49 years for WHO grade III oligodendroglioma. The proportions of White and Black patients in the 2 cohorts were very similar. In both cohorts, the incidence was slightly higher in male patients than in female patients, with 54.8% of WHO grade III tumors and 55.3% of WHO grade III tumors occurring in male patients. The most common site for both WHO grade II and WHO grade III tumors was the frontal lobe. Among patients with WHO grade II tumors, 447 (15.1%) did not undergo surgery, 1450 (46.1%) underwent STR, and 1215 (38.7%) underwent GTR. Among patients with WHO grade III tumors, 128 (8.9%) did not undergo surgery, 722 (50.5%) underwent STR, and 579 (40.5%) underwent GTR. There were 1100 (35.0%) patients with WHO grade II tumors and 1012 (70.8%) patients with WHO grade III tumors who received external beam radiation. There were 946 (30.1%) patients with WHO grade II tumors and 931 (65.1%) patients with WHO grade III tumors who received chemotherapy. At the time of last follow-up, the mean survival times among patients with WHO grade II oligodendroglioma and patients with WHO grade III oligodendroglioma were 74 months and 39 months, respectively.

OS and Prognostic Factors

Kaplan-Meier curves indicated that OS was significantly more favorable for WHO grade II oligodendroglioma than for WHO grade III oligodendroglioma (Figure 2). Univariate and multivariate Cox proportional hazards models of OS are presented in Table 2. Univariate Cox regression analysis revealed that age, sex, year of diagnosis, insurance, marital status, tumor site, tumor size, summary stage, surgery, radiotherapy, and

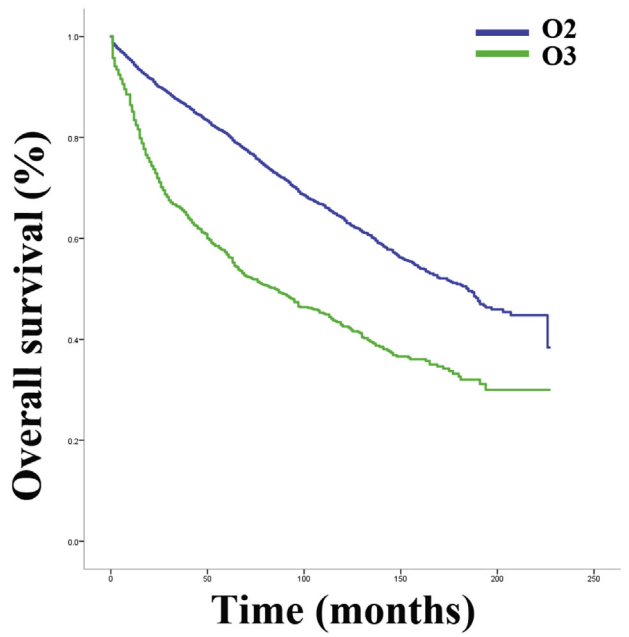

Figure 2. Kaplan-Meier curve showing the overall survival of patients with World Health Organization grade II and World Health Organization grade III oligodendrogliomas ($P = 0.000$). WHO, World Health Organization; O2, World Health Organization grade II oligodendroglioma; O3, World Health Organization grade III oligodendroglioma.

chemotherapy were significant factors for WHO grade II oligodendroglioma; age, race, year of diagnosis, insurance, marital status, tumor site, summary stage, surgery, radiotherapy, and chemotherapy were significant factors for WHO grade III oligodendroglioma.

Kaplan-Meier curves also indicated that surgery (Figure 3A and B), radiotherapy (Figure 3C and D), and chemotherapy (Figure 3E and F) were associated with OS in both WHO grade II oligodendroglioma and WHO grade III oligodendroglioma. Significant variables from univariate Cox regression analysis and Kaplan-Meier survival curves were further included in a multivariate Cox proportional hazards analysis. In the multivariate analysis, radiotherapy, age, tumor site, summary stage, and surgery all demonstrated independent associations with survival in both WHO grade II oligodendroglioma and WHO grade III oligodendroglioma. Race and radiotherapy demonstrated independent associations with survival in WHO grade II oligodendroglioma. Sex and chemotherapy demonstrated independent associations with survival in WHO grade III oligodendroglioma.

Nomogram for OS

The independent predictors from the multiple Cox proportional hazards analysis in either the WHO grade II oligodendroglioma or WHO grade III oligodendroglioma cohort were used to create a nomogram for predicting OS for patients with oligodendroglioma (Figure 4A). After summing the total scores of each predictor, the corresponding survival probability of each patient could be obtained. The C-index was 0.738 (95% confidence interval [CI] 0.718–0.757). The calibration curves of the 5- and 10-year survival rates showed good agreement between the nomogram predictions and actual observations (Figure 4B and C).

DISCUSSION

Accurate and effective prediction of prognosis is essential for both individualized treatment and guidelines.[14] Owing to the rarity of oligodendroglioma, studies have been challenging, and the SEER database offers an opportunity to perform studies of such rare diseases.[7,15] Our study of 4658 cases represents the largest retrospective study of oligodendroglioma in the literature to date and is the first to develop a nomogram for predicting OS of patients with oligodendroglioma.

Calibration plots were used to graphically evaluate the discriminative ability of the nomogram.[16] The nomogram in this study showed good discrimination in internal validation. The nomogram consists of 7 independent prognostic factors: age at diagnosis, cohort, tumor site, summary stage, surgery, chemotherapy, radiation, sex, and race. Younger age, low grade, frontal lobe location, localized stage, GTR, chemotherapy, female sex, and White race were associated with improved OS.

Similar to many previous studies,[14,17] age at diagnosis was found to be a significant predictor of survival of patients with oligodendroglioma in our study. Several studies found that tumor size was a significant predictor of OS for WHO grade II oligodendroglioma.[4,18] However, in our study, tumor size >5 mm was not independently associated with diminished OS in either WHO grade II or WHO grade III oligodendroglioma.

Surgery has been recognized as the most crucial treatment for oligodendroglioma.[7] In addition to obtaining pathological specimens, the goal of surgery is to remove as much of the tumor as is safely possible and to prevent high-grade transformation.[6] Kinslow et al.[7] reported that GTR was associated with improved OS in both WHO grade II oligodendroglioma (HR 0.74, 95% CI 0.58–0.95) and WHO grade III oligodendroglioma (HR 0.60, 95% CI 0.44–0.82), while STR fell short of significance. Our study also revealed that more complete resection of oligodendroglioma improves prognosis. However, Alattar et al.[8] reported that GTR was not associated with improved survival in patients with oligodendroglioma. These studies used older SEER data than those used in our study. The difference in the results reflects the development of surgery and postoperative management.[7]

The 2020 National Comprehensive Cancer Network guidelines (central nervous system cancers) removed postoperative radiotherapy for patients with low-grade glioma if they were <40 years old and underwent GTR.[6] However, Franceschi et al.[19] found that radiotherapy with or without chemotherapy, but not temozolomide alone, could extend progression-free survival for patients with WHO grade II oligodendroglioma. For WHO grade

Table 2. Univariate and Multivariate Cox Proportional Hazards Analysis Assessing Risk of Death in Patients with Oligodendrogliomas

	WHO Grade II		WHO Grade III	
Variable	**Univariate *P* Value (HR, 95% CI)**	**Multivariate *P* Value (HR, 95% CI)**	**Univariate *P* Value (HR, 95% CI)**	**Multivariate *P* Value (HR, 95% CI)**
Age, years				
0–19	Reference	Reference	Reference	Reference
20–39	0.000 (5.31, 2.98–9.47)	0.000 (2.19, 2.87–9.35)	0.394 (0.78, 0.44–1.38)	0.775 (1.09, 0.59–2.02)
40–49	0.000 (7.06, 3.95–12.61)	0.000 (6.50, 3.57–11.85)	0.633 (0.87, 0.49–1.53)	0.579 (1.19, 0.63–2.22)
50–59	0.000 (10.80, 6.03–19.34)	0.000 (10.17, 5.56–18.61)	0.338 (1.31, 0.75–2.31)	0.058 (1.83, 0.98–3.41)
60–69	0.000 (18.70, 10.35–33.77)	0.000 (18.18, 9.85–33.56)	0.001 (2.55, 1.44–4.52)	0.000 (3.70, 1.96–6.95)
≥70	0.000 (46.28, 25.31–84.62)	0.000 (44.49, 23.72–83.43)	0.000 (4.59, 2.55–8.27)	0.000 (5.77, 3.00–11.09)
Race				
White	Reference	—	Reference	Reference
Black	0.856 (0.97, 0.72–1.30)	—	0.003 (1.62, 1.18–2.21)	0.001 (1.70, 1.23–2.34)
Other	0.442 (1.09, 0.86–1.40)	—	0.327 (0.86, 0.65–1.15)	0.517 (0.90, 0.67–1.21)
Sex				
Male	Reference	Reference	Reference	Reference
Female	0.019 (0.85, 0.75–0.97)	0.020 (0.85, 0.75–0.97)	0.676 (0.96, 0.83–1.12)	—
Year of diagnosis				
1998–2007	Reference	Reference	Reference	Reference
2008–2016	0.010 (0.81, 0.69–0.95)	0.225 (0.83, 0.63–1.11)	0.000 (0.67, 0.57–0.80)	0.979 (1.00, 0.65–1.54)
Insurance				
Uninsured	Reference	Reference	Reference	Reference
Insured	0.235 (0.72, 0.42–1.23)	0.681 (0.89, 0.51–1.53)	0.115 (0.66, 0.40–1.10)	0.573 (0.85, 0.50–1.46)
Any Medicaid	0.013 (0.81, 0.69–0.95)	0.619 (1.16, 0.63–2.15)	0.000 (0.63, 0.52–0.75)	0.694 (1.13, 0.61–2.09)
Unknown	0.897 (0.97, 0.71–1.34)	0.907 (0.96, 0.54–1.71)	0.040 (0.69, 0.48–0.98)	0.343 (1.33, 0.73–2.43)
Marital status at diagnosis				
Single	Reference	Reference	Reference	Reference
Married	0.000 (1.54, 1.32–1.79)	0.098 (0.87, 0.73–1.02)	0.043 (1.22, 1.01–1.49)	0.964 (1.00, 0.81–1.24)
Separated; Divorced; Widowed	0.000 (1.77, 1.42–2.21)	0.195 (0.85, 0.67–1.08)	0.000 (1.57, 1.21–2.02)	0.619 (1.07, 0.81–1.41)
Unknown	0.015 (1.54, 1.09–2.20)	0.972 (1.00, 0.70–1.44)	0.714 (1.08, 0.69–1.69)	0.700 (0.81, 0.57–1.44)
Primary site				
Frontal lobe	Reference	Reference	Reference	Reference
Temporal lobe	0.000 (1.33, 1.14–1.56)	0.000 (1.47, 1.21–1.78)	0.000 (2.44, 2.00–2.96)	0.000 (2.24, 1.83–2.75)
Parietal lobe	0.866 (0.98, 0.73–1.22)	0.976 (1.00, 0.79–1.26)	0.000 (1.84, 1.47–2.31)	0.000 (1.70, 1.35–2.15)
Occipital lobe	0.740 (0.91, 0.55–1.51)	0.911 (0.97, 0.58–1.60)	0.004 (2.10, 1.27–3.48)	0.002 (2.27, 1.36–3.79)
Overlapping lesion of brain	0.000 (1.76, 1.46–2.13)	0.000 (1.47, 1.21–1.78)	0.000 (2.40, 1.92–3.00)	0.000 (2.10, 1.66–2.65)
Ventricle	0.401 (1.41, 0.63–3.16)	0.418 (1.82, 0.80–4.10)	0.000 (5.93, 2.44–14.40)	0.000 (8.30, 3.23–21.33)
Brainstem	0.682 (1.20, 0.49–2.90)	0.541 (1.32, 0.53–3.26)	0.000 (4.25, 1.89–9.56)	0.021 (2.88, 1.17–7.07)

WHO, World Health Organization; HR, hazard ratio; CI, confidence interval; STR, subtotal resection; GTR, gross total resection.

Continues

Table 2. Continued

Variable	WHO Grade II		WHO Grade III	
	Univariate *P* Value (HR, 95% CI)	Multivariate *P* Value (HR, 95% CI)	Univariate *P* Value (HR, 95% CI)	Multivariate *P* Value (HR, 95% CI)
Tumor size, cm				
<3	Reference	Reference	Reference	Reference
3–6	0.237 (1.17, 0.89–1.54)	0.681 (1.05, 0.80–1.39)	0.195 (0.81, 0.60–1.11)	—
>6	0.000 (1.77, 1.30–2.42)	0.314 (1.17, 0.85–1.62)	0.092 (0.75, 0.54–1.04)	—
Unknown	0.015 (1.36, 1.06–1.74)	0.378 (1.12, 0.86–1.46)	0.907 (1.01, 0.75–1.35)	—
Summary stage				
Localized	Reference	Reference	Reference	Reference
Regional	0.000 (2.16, 1.84–2.53)	0.000 (1.82, 1.53–2.17)	0.334 (1.09, 0.90–1.33)	0.034 (1.24, 1.01–1.52)
Distant	0.524 (1.57, 0.39–6.29)	0.904 (0.91, 0.22–3.71)	0.003 (2.91, 1.44–5.85)	0.002 (2.27, 1.54–6.95)
Unknown	0.041 (0.60, 0.37–0.98)	0.041 (0.60, 0.36–0.97)	0.236 (1.31, 0.83–2.08)	0.911 (0.97, 0.60–1.57)
Primary site surgery				
No surgery	Reference	Reference	Reference	Reference
STR	0.000 (0.78, 0.66–0.92)	0.400 (0.93, 0.78–1.10)	0.000 (0.55, 0.44–0.69)	0.003 (0.69, 0.54–0.88)
GTR	0.000 (0.55, 0.45–0.65)	0.022 (0.80, 0.66–0.96)	0.000 (0.43, 0.33–0.54)	0.001 (0.63, 0.48–0.82)
Radiation				
None/unknown	Reference	Reference	Reference	Reference
External beam radiation	0.000 (2.13, 1.88–2.41)	0.000 (1.57, 1.38–1.80)	0.044 (0.84, 0.72–0.99)	0.311 (0.91, 0.76–1.09)
Chemotherapy				
No; unknown	Reference	Reference	Reference	Reference
Chemotherapy	0.000 (1.44, 1.26–1.65)	0.116 (1.12, 0.97–1.29)	0.000 (0.56, 0.49–0.67)	0.000 (0.71, 0.60–0.84)

WHO, World Health Organization; HR, hazard ratio; CI, confidence interval; STR, subtotal resection; GTR, gross total resection.

III oligodendroglioma, Rusthoven et al.[20] reported no survival advantage with adjuvant radiotherapy (5-year OS: 50% with radiotherapy vs. 56% without radiotherapy, P = 0.277). Our study showed that there was no significant improvement in OS after external beam radiation for either WHO grade II or WHO grade III oligodendroglioma.

WHO grade III oligodendrogliomas are uniquely sensitive to chemotherapy.[5,21] The results from the RTOG 9402 and EORTC 26951 trials showed that procarbazine, lomustine, and vincristine plus radiotherapy may be an especially effective treatment for patients with 1p/19q codeletion anaplastic oligodendroglioma.[22,23] Early chemotherapy with procarbazine, lomustine, and vincristine, either before or after radiotherapy, appeared to improve the OS of patients with WHO grade III oligodendroglioma.[24] A phase 3 study showed that adjuvant temozolomide chemotherapy was associated with a significant survival benefit in patients with newly diagnosed non-codeletion anaplastic glioma (HR 0.91, 95% CI 0.76–1.09).[25] Although bevacizumab is frequently used in recurrent grade II and III gliomas without 1p/19q codeletion, the TAVAREC trial (NCT01164189) showed that the addition of bevacizumab to temozolomide did not improve OS.[26] Our study found that chemotherapy may be an independent favorable prognostic factor in patients with WHO grade III oligodendroglioma (HR 0.71, 95% CI 0.60–0.84). In patients with low-grade glioma, treatment with postradiation chemotherapy with procarbazine, lomustine, and vincristine was reported to be associated with longer OS.[27] However, our study showed no benefit from chemotherapy in WHO grade II oligodendroglioma (HR 1.12, 95% CI 0.97–1.29).

This study has a few important limitations. First, oligodendroglioma is increasingly defined by genetic abnormalities,[28] and the most recent guidelines released in 2016 demonstrated that *IDH* mutation and 1p/19q codeletion are both required for the diagnosis of oligodendroglioma.[3] Many oligodendroglioma

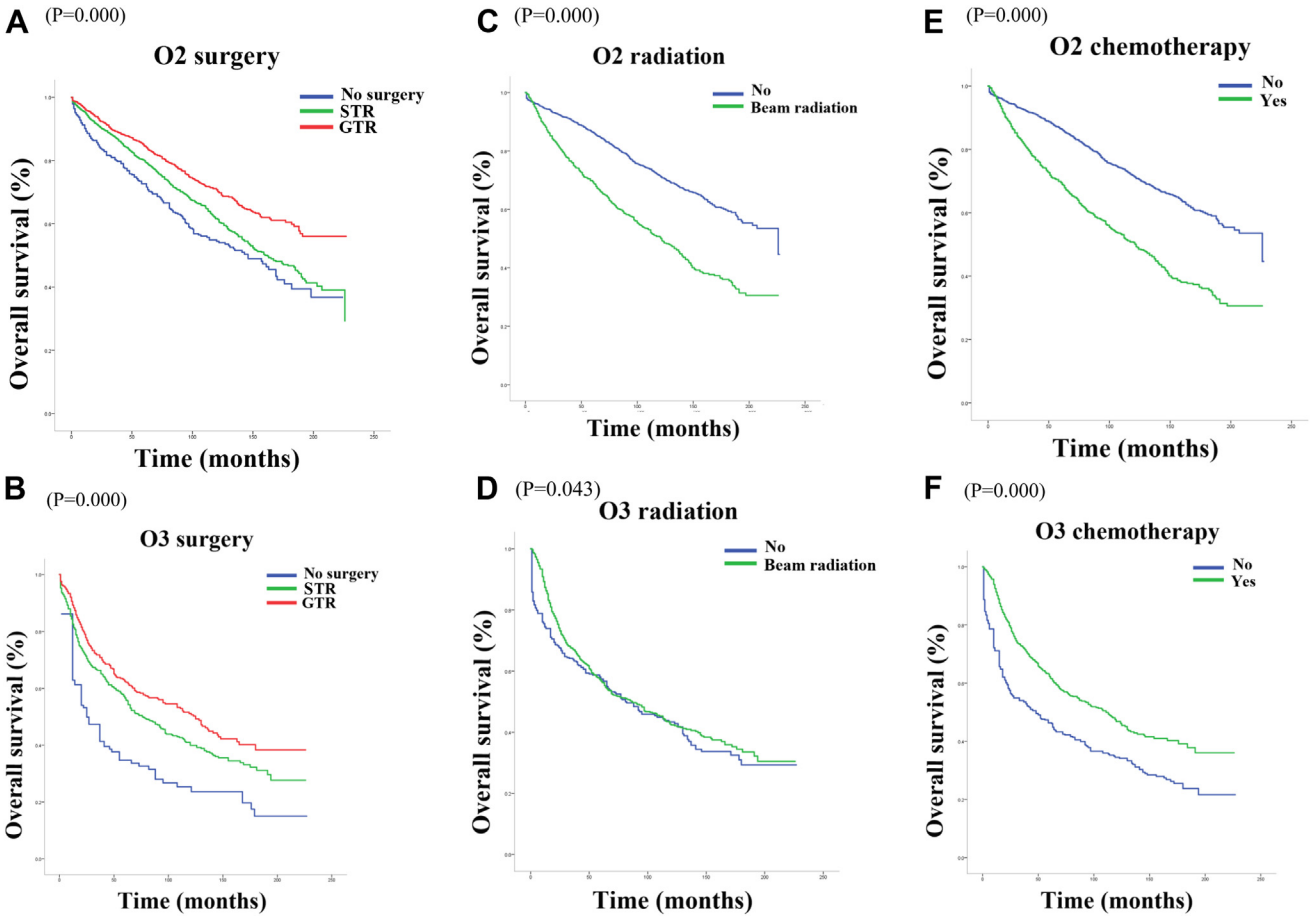

Figure 3. Kaplan-Meier curves comparing the influence of surgery (**A** and **B**), radiation (**C** and **D**), and chemotherapy (**E** and **F**) on overall survival of patients with World Health Organization grade II and World Health Organization grade III oligodendrogliomas. O2, World Health Organization grade II oligodendroglioma; O3, World Health Organization grade III oligodendroglioma; STR, subtotal resection; GTR, gross total resection.

diagnoses in this study were made purely on histological phenotype and might no longer be considered oligodendrogliomas under the current criteria. Second, many studies have determined that 1p/19q codeletion and the presence of an *IDH* mutation are strong favorable prognostic markers for OS.[29,30] However, genetic biomarker information is not available in the current SEER database. Third, the SEER database does not include many key clinical variables, such as radiation dose and chemotherapy information.[11] Finally, the present nomogram will require validation using other independent patient groups.

CONCLUSIONS

The present study represents the largest retrospective analysis to date of demographics, outcomes, and prognostic factors in oligodendroglioma. The nomogram established in our study objectively and accurately predicted the prognosis of patients with oligodendroglioma. Additional studies are required to verify our conclusions.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Liang Cao: Funding acquisition, Formal analysis, Data curation, Writing - original draft, final version of the manuscript. **Ping Rong:** Funding acquisition, final version of the manuscript. **Guannan Zhu:** Writing - review & editing, final version of the manuscript. **Aigang Xu:** Writing - review & editing, final version of the manuscript. **Si Chen:** Conceptualization, Methodology, Writing - review & editing, final version of the manuscript.

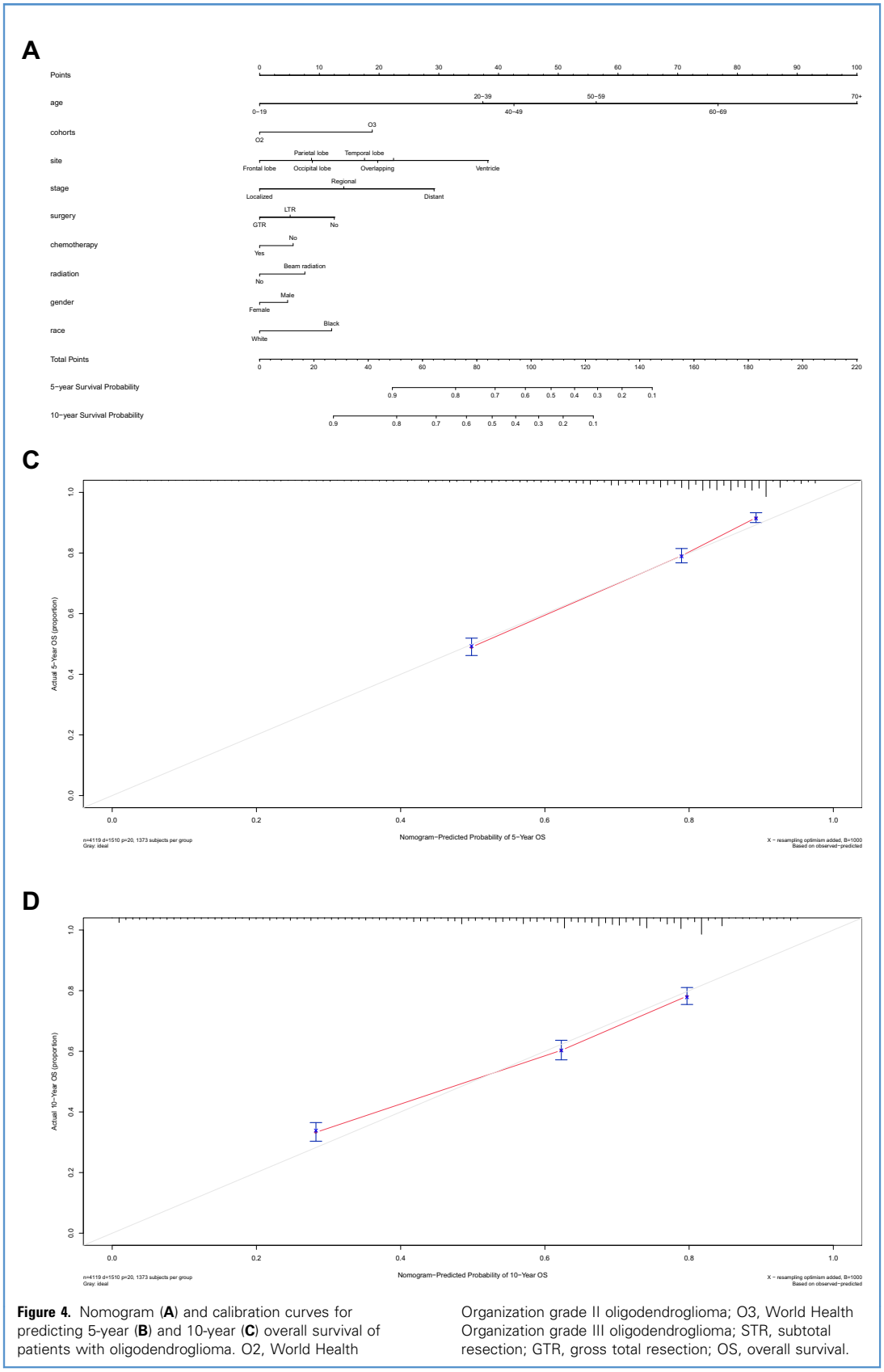

Figure 4. Nomogram (**A**) and calibration curves for predicting 5-year (**B**) and 10-year (**C**) overall survival of patients with oligodendroglioma. O2, World Health Organization grade II oligodendroglioma; O3, World Health Organization grade III oligodendroglioma; STR, subtotal resection; GTR, gross total resection; OS, overall survival.

REFERENCES

1. Penas-Prado M, Wu J, Cahill DP, et al. Proceedings of the Comprehensive Oncology Network Evaluating Rare CNS Tumors (NCI-CONNECT) Oligodendroglioma Workshop. *Neurooncol Adv*. 2020;2:vdz048.

2. Ostrom QT, Gittleman H, Truitt G, Boscia A, Kruchko C, Barnholtz-Sloan JS. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2011-2015. *Neuro Oncol*. 2018;20(suppl 4): iv1-iv86.

3. Louis DN, Perry A, Reifenberger G, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. *Acta Neuropathol*. 2016;131:803-820.

4. Lin DD, Deng XY, Zheng DD, et al. The effects of tumor size and postoperative radiotherapy for patients with adult low-grade (WHO grade II) infiltrative supratentorial astrocytoma/oligodendroglioma: a population-based and propensity score matched study. *Cancer Med*. 2018;7: 5973-5987.

5. Brandel MG, Alattar AA, Hirshman BR, et al. Survival trends of oligodendroglial tumor patients and associated clinical practice patterns: a SEER-based analysis. *J Neurooncol*. 2017;133:173-181.

6. Nabors LB, Portnow J, Ahluwalia M, et al. Central Nervous System Cancers, Version 3.2020, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2020;18:1537-1570.

7. Kinslow CJ, Garton ALA, Rae AI, et al. Extent of resection and survival for oligodendroglioma: a U.S. population-based study. *J Neurooncol*. 2019; 144:591-601.

8. Alattar AA, Brandel MG, Hirshman BR, et al. Oligodendroglioma resection: a Surveillance, Epidemiology, and End Results (SEER) analysis. *J Neurosurg*. 2018;128:1076-1083.

9. Liu S, Liu X, Xiao Y, Chen S, Zhuang W. Prognostic factors associated with survival in patients with anaplastic oligodendroglioma. *PLoS One*. 2019;14:e0211513.

10. Harrell FE Jr, Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. *Stat Med*. 1996;15: 361-387.

11. Zhao YY, Wan QS, Hao Z, Zhu HX, Xing ZL, Li MH. Clinical nomogram for predicting the survival of patients with cerebral anaplastic gliomas. *Medicine*. 2020;99:e19416.

12. Zhao YY, Chen SH, Hao Z, Zhu HX, Xing ZL, Li MH. A nomogram for predicting individual prognosis of patients with low-grade glioma. *World Neurosurg*. 2019;130:e605-e612.

13. Yolcu Y, Wahood W, Kerezoudis P, Alvi MA, Habermann EB, Bydon M. Primary central nervous system tumors: comparing two national cancer registries. *World Neurosurg*. 2019;128:e719-e731.

14. Wei RL, Zhang LW, Li JG, Yang FD, Xue YK, Wei XT. Behavior-oriented nomogram for the stratification of lower-grade gliomas to improve individualized treatment. *Front Oncol*. 2020;10: 538133.

15. Furst T, Hoffman H, Chin LS. All-cause and tumor-specific mortality trends in geriatric oligodendroglioma (OG) patients: A Surveillance, Epidemiology, and End Results (SEER) analysis. *J Clin Neurosci*. 2020;73:94-100.

16. Alba AC, Agoritsas T, Walsh M, et al. Discrimination and calibration of clinical prediction models: users' guides to the medical literature. *JAMA*. 2017;318:1377-1384.

17. Wang Z, Gao L, Guo X, et al. Development and validation of a nomogram with an autophagy-related gene signature for predicting survival in patients with glioblastoma. *Aging*. 2019;11: 12246-12269.

18. Chang EF, Clark A, Jensen RL, et al. Multi-institutional validation of the University of California at San Francisco Low-Grade Glioma Prognostic Scoring System. *J Neurosurg*. 2009;111: 203.

19. Franceschi E, Tosoni A, De Biase D, et al. Post-surgical approaches in low-grade oligodendroglioma: is chemotherapy alone still an option? *Oncologist*. 2019;24:664-670.

20. Rusthoven CG, Carlson JA, Waxweiler TV, et al. The impact of adjuvant radiation therapy for high-grade gliomas by histology in the United States population. *Int J Radiat Oncol Biol Phys*. 2014;90: 894-902.

21. Thomas AA, Abrey LE, Terziev R, et al. Multicenter phase II study of temozolomide and myeloablative chemotherapy with autologous stem cell transplant for newly diagnosed anaplastic oligodendroglioma. *Neuro Oncol*. 2017;19:1380-1390.

22. van den Bent MJ, Brandes AA, Taphoorn MJ, et al. Adjuvant procarbazine, lomustine, and vincristine chemotherapy in newly diagnosed anaplastic oligodendroglioma: long-term follow-up of EORTC Brain Tumor Group Study 26951. *J Clin Oncol*. 2013; 31:344-350.

23. Cairncross G, Wang M, Shaw E, et al. Phase III trial of chemoradiotherapy for anaplastic oligodendroglioma: long-term results of RTOG 9402. *J Clin Oncol*. 2013;31:337-343.

24. Lecavalier-Barsoum M, Quon H, Abdulkarim B. Adjuvant treatment of anaplastic oligodendrogliomas and oligoastrocytomas. *Cochrane Database Syst Rev*. 2014;2014:CD007104.

25. van den Bent MJ, Baumert B, Erridge SC, et al. Interim results from the CATNON trial (EORTC study 26053-22054) of treatment with concurrent and adjuvant temozolomide for 1p/19q non-co-deleted anaplastic glioma: a phase 3, randomised, open-label intergroup study. *Lancet*. 2017; 390:1645-1653.

26. Bent M, Klein M, Smits M, Reijneveld JC, French P. Final results of the EORTC Brain Tumor Group randomized phase II TAVAREC trial on temozolomide with or without bevacizumab in 1st recurrence grade II/III glioma without 1p/19q co-deletion. *J Clin Oncol*. 2017;35(15 suppl):2009.

27. Bell EH, Zhang P, Shaw EG, et al. Comprehensive genomic analysis in NRG Oncology/RTOG 9802: a Phase III trial of radiation versus radiation plus procarbazine, lomustine (CCNU), and vincristine in high-risk low-grade glioma. *J Clin Oncol*. 2020; 38:3407-3417.

28. Dubbink HJ, Atmodimedjo PN, Kros JM, et al. Molecular classification of anaplastic oligodendroglioma using next-generation sequencing: a report of the prospective randomized EORTC Brain Tumor Group 26951 phase III trial. *Neuro Oncol*. 2016;18:388-400.

29. Eckel-Passow JE, Lachance DH, Molinaro AM, et al. Glioma groups based on 1p/19q, IDH, and TERT promoter mutations in tumors. *N Engl J Med*. 2015;372:2499-2508.

30. Cairncross JG, Wang M, Jenkins RB, et al. Benefit from procarbazine, lomustine, and vincristine in oligodendroglial tumors is associated with mutation of IDH. *J Clin Oncol*. 2014;32:783-790.

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