Clinical Characteristics and Prognostic Outcomes of Spinal Cord Gliomas with Intracranial Metastasis: An Integrated Analysis Based on Individual Cases

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OBJECTIVE: **To characterize the clinicopathological features and identify survival predictors in rare spinal cord gliomas (SCGs) with intracranial metastasis (IM), with the goal of guiding clinical decision-making and optimizing management strategies.**

METHODS: **A retrospective analysis was conducted on 62 histopathologically verified SCGs (12 low-grade and 50 high-grade) with IM based on published cases and case series. Survival outcomes were analyzed using Kaplan-Meier methods with time-dependent variables. Kaplan-Meier analysis was used to evaluate survival patterns, and Cox proportional hazards regression was applied to identify prognostic factors associated with survival outcomes.**

RESULTS: **Univariate analysis showed symptom duration and extent of resection significantly affected diagnosis-to-intracranial metastasis (DTIM) (extent of resection as an independent factor, $P < 0.05$). Overall survival analysis demonstrated that the IM site, pathology type, and intracranial metastasis-to-outcome (IMTO) significantly influenced patient prognosis ($P < 0.05$). Multivariate analysis confirmed DTIM and IMTO as independent predictors of overall survival ($P < 0.05$).**

CONCLUSIONS: **Maximal safe resection with adjuvant therapy remains of paramount importance. Extending the DTIM and IMTO through tailored therapeutic strategies significantly enhances survival outcomes in patients with SCGs complicated by IM.**

Key words
- High-grade spinal cord glioma (HGSG)
- Low-grade spinal cord glioma (LGSG)
- Intracranial metastasis (IM)
- Prognostic factors

Abbreviations and Acronyms
CT: Chemotherapy
DTIM: Diagnosis-to-IM interval
GBM: Glioblastoma
GTR: Gross total resection
HGSG: High-grade Spinal cord glioma
IM: Intracranial metastasis
IMTO: IM-to-outcome interval
LGSG: Low-grade spinal cord glioma
OS: Overall survival
PR: Partial resection
RT: Radiotherapy
SCGs: Spinal cord gliomas
STR: Subtotal resection

INTRODUCTION

Compared with intracranial gliomas, primary tumors originating from the spinal cord, such as spinal cord gliomas (SCGs), are relatively rare.[1-4] SCGs, which account for the majority of intramedullary spinal tumors, commonly present with symptoms such as back pain, lower limb weakness, and sensory abnormalities, distinguishing them from their intracranial counterparts, whereas intracranial gliomas often manifest with symptoms related to increased intracranial pressure or focal neurological deficits.[2,5] Although most diffuse gliomas exhibit a propensity to progress to higher grades or recur locally (either in situ or adjacent to the primary site) following surgical resection, distant metastasis remains a rare event.[6,7] To date, the majority of reported cases of distant metastasis, including those from intracranial gliomas or SCGs, have been reported in case reports or small case series. A prior review summarized the clinical features and survival outcomes of patients with metastases originating from intracranial glioblastoma (GBM) multiforme.[8] However, studies specifically addressing the clinical characteristics, treatment, and prognosis of SCGs with intracranial metastasis (IM) are scarce. Therefore, we conducted an integrated analysis of 62 reported cases of SCGs with IM to

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elucidate their clinical characteristics and optimize management strategies.

MATERIALS AND METHODS

Patient Population

Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, a systematic search was conducted to identify English-language articles from PubMed, Medline, and Web of Science, as well as comprehensive searches of Chinese databases, including CNKI (China National Knowledge Infrastructure) and Wanfang Database, for reports on SCGs with IM. A total of 62 cases with available clinical and survival data were extracted from 41 articles published between 1981 and 2024.[7,9-48] Search terms included: "spinal cord gliomas," "spinal cord astrocytoma," "spinal cord glioblastoma," "intracranial dissemination," "intracranial metastasis," "glioma," "astrocytoma," "gliosarcoma," "spinal cord neoplasms," and "brain neoplasms/secondary." Reference lists of included articles were also screened to identify additional relevant studies. The inclusion criteria for the study were as follows: 1) English-language articles involving primary gliomas at all levels of the spinal cord; 2) non-English-language articles if the abstract contained relevant information; and 3) availability of patient baseline characteristics and survival data. Articles with incomplete survival data, duplicate cases, or insufficient clinical details were excluded. Of the 62 reported cases, 41 studies from 1981 to 2024 were ultimately selected for detailed analysis. A flowchart depicting the study selection and inclusion process is presented in Figure 1.

Data Collection and Extraction

Data extraction from studies that met the inclusion criteria was independently performed by four authors (J.L., T.C., Y.Z., W.M.) and

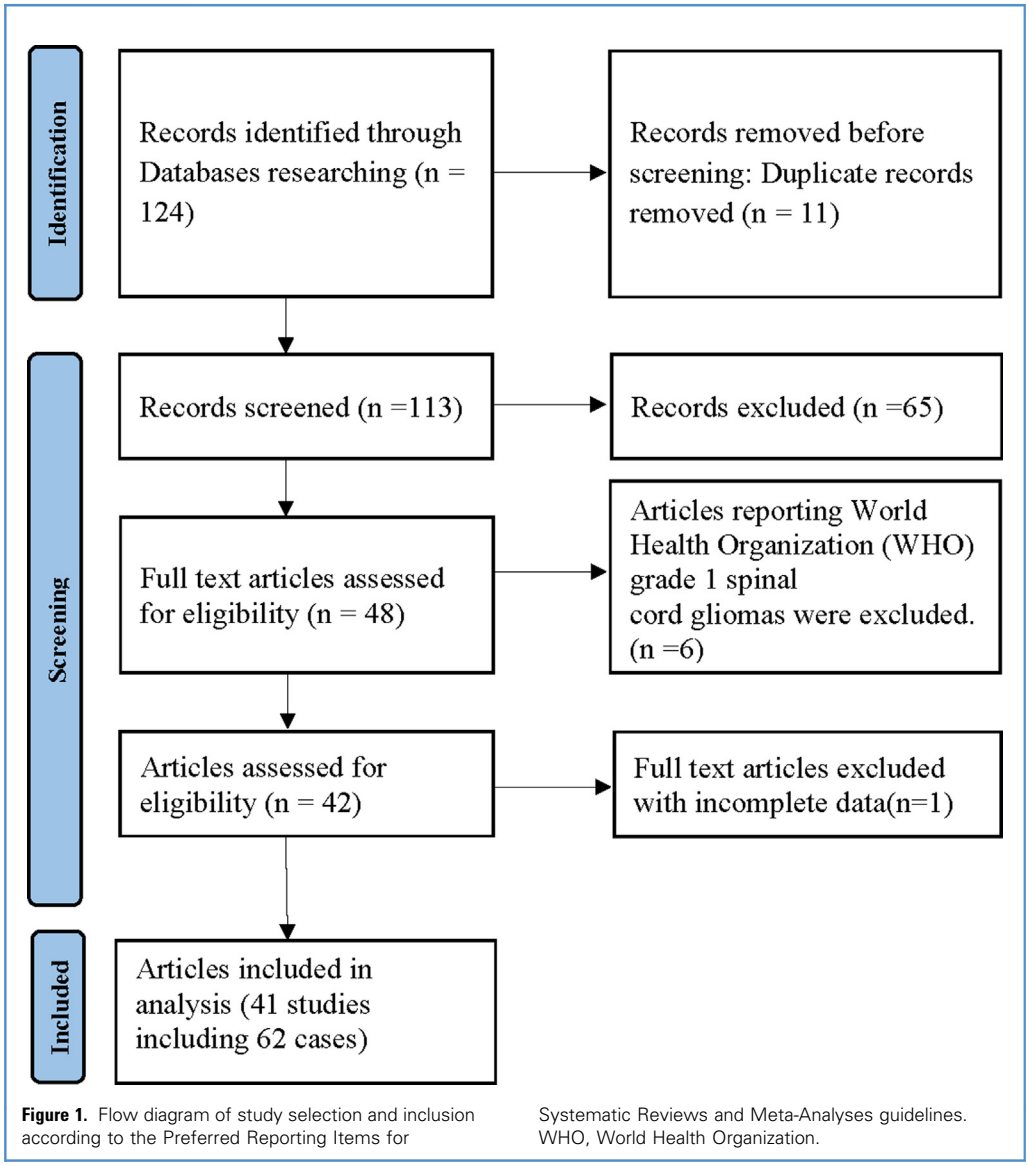

Figure 1. Flow diagram of study selection and inclusion according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. WHO, World Health Organization.

subsequently verified by three investigators (J.L., T.R., X.N.). Missing data were either not explicitly reported in the original articles or could not be differentiated from other available data. Clinical and radiological characteristics, details of surgical and adjuvant therapies, survival rates, and other relevant data were systematically extracted from the eligible articles. Extent of resection (EOR) was classified according to the percentage of tumor removed during surgery, as reported in the original studies: biopsy, partial resection (PR), subtotal resection (STR), or gross total resection (GTR). Adjuvant therapies, including radiotherapy (RT) and chemotherapy (CT), were identified from the literature. Patients with low-grade spinal cord glioma (LGSG) and high-grade spinal cord glioma (HGSG) were stratified into two subgroups based on median age; symptom duration was likewise categorized using a cutoff of $\leq$3 months versus >3 months. Due to distinct biological behavior, prognosis, and treatment approaches, grade 1 gliomas were excluded from analysis. Included cases were classified according to the World Health Organization (WHO) glioma grading system as low grade (WHO grade 2) or high grade (WHO grades 3 and 4). The diagnosis-to-intracranial metastasis (DTIM) interval was defined as the duration from initial histopathological diagnosis to the first radiological detection of IM, and the intracranial metastasis-to-outcome (IMTO) interval was defined as the period from IM detection to the occurrence of primary endpoint events, including death or last follow-up. Overall survival (OS) was defined as time from spinal glioma diagnosis to endpoint event or last follow-up. Differences in DTIM interval, IMTO interval, and OS were compared between LGSG and HGSG cohorts. Studies published between 1981 and 2024 were included to achieve comprehensive representation of this rare entity. While notable progress has been made in glioma classification and treatment strategies over this interval, advances in the classification of SCGs remain limited. Given the scarcity of spinal cord glioma cases with IM, the inclusion of earlier studies was necessary to enhance data availability. Stratified subgroup analyses were conducted to address differences in glioma grading and therapeutic approaches.

Data Synthesis and Quality Assessment

Primary outcomes assessed included demographics, clinical characteristics, treatment modalities, and patient outcomes. The level of evidence was evaluated according to the 2011 Oxford Centre for Evidence-Based Medicine guidelines.[49] Meta-analysis was not performed due to the predominance of included studies being level IV or V evidence. Risk of bias for each study was independently appraised by two authors (J.L., X.N.) using the Joanna Briggs Institute critical appraisal checklists.[50]

Statistical Analysis

Continuous variables are presented as medians (quartiles) and were compared via nonparametric tests. The relationships between categorical variables were evaluated via Fisher's exact test or the chi-square test. The impact of variables on OS and DTIM was calculated via Kaplan–Meier analysis, and differences between the subgroups were assessed via the log-rank test. The random forest method was used to impute missing values for variables where the missing values accounted for less than 5% of the total count. Statistical analyses were performed via SPSS software (version 24, SPSS Inc., Chicago) and R (version 4.2.2, http://www.R-project.org) software.

RESULTS

Study Selection

The study selection process was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, as illustrated in Figure 1. An initial literature search identified 124 articles, of which 41 studies met the predefined inclusion criteria, comprising a total of 62 patients. Of these, 8 publications were case series involving 29 patients, and 33 were case reports involving 33 patients. According to established criteria, case series and case reports were categorized as Level IV and Level V evidence, respectively (Table 1). Rigorous quality assessment demonstrated a uniformly low risk of bias across all included studies (Supplementary Tables).

Patient Demographics and Clinical Characteristics

A total of 62 patients (34 males, 28 females) with SCGs with IM were identified and included in this study. The median age was 16.0 years (range, 2.5–61) in the LGSG cohort and 20.0 years (range, 4–67) in the HGSG cohort (Tables 1 and 2). Symptoms duration ranged from 0.3 to 108 months, with median symptom durations of 3.0 and 2.0 months in the LGSG and HGSG groups, respectively. Tumor location analysis revealed that spinal gliomas were found in the cervical, thoracic, and lumbar segments in 18 (29.0%), 31 (50.0%), and 11 (17.7%) patients, respectively. Notably, distinct segmental distributions were observed between groups: in the LGSG cohort, 50.0% of tumors were cervical, 33.3% thoracic, and 16.7% lumbar; in contrast, HGSG cases were predominantly thoracic (54.0%), followed by cervical (24.0%) and lumbar (18.0%) regions. Although cervical involvement was more frequent in LGSG, while thoracic distribution predominated in HGSG, these differences were not statistically significant ($P = 0.312$). Two patients exhibited tumor spread across both thoracic and lumbar segments. Overall, 50.0% of tumors were located in the thoracic segment, and 55.6% involved three or more spinal segments (42.9% in LGSG vs. 57.9% in HGSG). High-grade gliomas demonstrated increased propensity for multisegment involvement. GBM accounted for 31/62 (50.0%) cases; notably, 31/50 (62.0%) of the HGSG group were diagnosed as GBM. With regard to metastatic spread, 2 (18.2%) patients in the LGSG group and 10 (27.8%) in the HGSG group developed supratentorial metastases. Similarly, infratentorial metastases occurred in 2 (18.2%) LGSG and 12 (33.3%) HGSG patients. Approximately 25.5% of tumors metastasized to the supratentorial region; the most frequent metastatic pattern involved concurrent supratentorial and infratentorial sites, observed in 44.7% of cases (Table 2). The median DTIM was 3.0 months in the LGSG group and 6.0 months in the HGSG group. In addition, the median IMTO was 5.0 months in both groups. Median OS was 17.7 months for LGSG and 12.0 months for HGSG. Detailed demographics and clinical characteristics are summarized in Tables 1 and 2.

Surgery and Adjuvant Therapy

Among all patients, 20 (39.2%) patients underwent GTR or STR, 12 (23.5%) underwent PR, and 19 (37.3%) underwent biopsy. In the LGSG group, 1 (8.3%) patient underwent GTR, 4 (33.3%) patients

Table 1. Details of the Clinical Features, Outcomes, and Evidence Levels (2011 Oxford Centre for Evidence-Based Medicine) of Patients with Spinal Cord Gliomas with Intracranial Metastasis

Studies	Study Design—Level of Evidence	Age (Years)	Gender	Duration (Month)	Spinal Site	IM Site	Pathology	WHO Grade	Spinal Surgery	RT	CT	DTIM	IMTO	Survival	Outcome
Darbari et al. 2022	Retrospective series—IV	20	M	1	T6-8	NA	GBM	4	STR	Yes	Yes	NA	NA	12	Dead
		24	M	4	T4-11	NA	GBM	4	STR	Yes	Yes	NA	NA	7	Dead
		16	M	3	C5-6	NA	GBM	4	STR	Yes	Yes	NA	NA	14	Dead
Marco Del Pont et al. 2021	Case report—V	32	F	NA	C6-T2	Sup.	AE	3	GTR	Yes	NA	24	NA	NA	Alive
Yang et al. 2020	Case report—V	12	F	6	T10-S2	NA	GBM	4	STR	Yes	Yes	8	1	9	Alive
Kumar et al. 2019	Case report—V	4	M	0.8	C2-T8	Inf.	GBM	4	Biopsy	Yes	Yes	4	0	4	Dead
Jayachandran et al. 2019	Case report—V	31	M	6	T10	Inf.	GBM	4	GTR	Yes	Yes	7	10	17	Alive
Inoue et al. 2018	Retrospective series—IV	61	M	3	T12	NA	DA	2	Biopsy	NA	NA	NA	NA	18.4	Dead
		43	F	5	T11	NA	AA	3	Biopsy	NA	NA	NA	NA	25.4	Dead
		15	F	1	T3-4	NA	GBM	4	No	NA	NA	NA	NA	8.2	Dead
		67	M	10	T11	NA	AA	3	Biopsy	NA	NA	NA	NA	37.4	Dead
		53	M	12	T11-12	NA	GBM	4	PR	NA	NA	NA	NA	32.8	Dead
		43	F	12	T7-9	NA	AA	3	Biopsy	NA	NA	NA	NA	19.9	Dead
Yan et al. 2017	Case report—V	10	M	0.7	T11-L1	Sup. + Inf.	GBM	4	GTR	Yes	Yes	10	4	14	Dead
Nunn et al. 2017	Case report—V	31	M	0.7	T9-CM	NA	GBM	4	STR	Yes	Yes	6	8	14	Dead
Kokkalis et al. 2016	Case report—V	12	M	2	T4-8	Sup.	GBM	4	GTR	Yes	Yes	16	4	20	Dead
Derinkuyu et al. 2015	Case report—V	9	F	NA	T8-10	Sup.	GBM	4	NA	Yes	Yes	0	8	8	Dead
Morais et al. 2013	Case report—V	19	M	1	T6-11	Sup.	GBM	4	PR	Yes	Yes	6	15	21	Dead
Mori et al. 2012	Case report—V	10	F	0.5	CM	Sup. + Inf.	GBM	4	Biopsy	Yes	Yes	0	14	14	Dead
Saidha et al. 2012	Case report—V	50	F	2	C2-7	Inf.	AA	3	Biopsy	No	No	0	5	7	Dead
Schlereth et al. 2012	Case report — V	63	M	0.75	T6-7	Sup.	AA	3	Biopsy	Yes	Yes	14	0.5	14.5	Dead
Kataria et al. 2011	Case report—V	15	F	3	T11-L1	Inf.	AA	3	PR	Yes	No	3	0	3	Dead
Kim et al. 2011	Retrospective series—IV	16	F	NA	T12-L1	Sup. + Inf.	GBM	4	Biopsy	Yes	Yes	7	5	12	Dead
		48	M	NA	T11-12	Sup. + Inf.	GBM	4	Biopsy	Yes	Yes	10	6	16	Dead
Jeong et al. 2010	Case report—V	22	M	7	T3-11	Inf.	AA	3	PR	Yes	No	4	7	11	Dead
D'Haene et al. 2009	Case report—V	57	M	2	T7-8	Inf.	LGG	2	Biopsy	Yes	Yes	0	2.5	2.5	Dead
Matsumoto et al. 2008	Case report—V	21	M	1	C3-5	Inf.	GBM	4	STR	Yes	Yes	22	4	26	Dead

Battaglia et al. 2007	Case report—V	11	M	NA	T4-5	Sup. + Inf.	GBM	4	GTR	Yes	Yes	3	3	6	Dead
Ramirez et al. 2007	Case report—V	22	M	6	C5-7	Sup. + Inf.	AO	3	PR	Yes	Yes	19	3	22	Dead
Marchan et al. 2007	Case report—V	50	M	NA	T11	Inf.	GBM	4	Biopsy	Yes	Yes	3	69	72	Dead
Schuurmans et al. 2006	Case report—V	29	F	4	C3-6	Inf.	AE	3	STR	Yes	No	24	NA	NA	Alive
Stecco et al. 2005	Case report—V	14	M	24	T12-L1	Inf.	GBM	4	STR	No	No	9	NA	NA	Dead
Caroli et al. 2005	Case report—V	6	M	4	T9-11	Inf.	GBM	4	STR	Yes	Yes	4	5	9	Dead
Medhkour et al. 2005	Case report—V	20	M	1	T12-L1	Sup. + Inf.	GBM	4	STR	Yes	No	6	4	10	Dead
Perilongo et al. 2002	Retrospective series—IV	7	M	3	C5-6	Sup. + Inf.	LGG	2	PR	NA	NA	3	6	9	Dead
		3.3	F	1	C7-T5	Sup. + Inf.	LGG	2	Biopsy	NA	NA	3	3	108	Dead
Yamashita et al. 2001	Case report—V	43	F	NA	T7-9	Sup. + Inf.	AA	3	Biopsy	Yes	Yes	2	21	23	Dead
Klepstad et al. 2001	Case report—V	12	F	12	C1-7	Inf.	GBM	4	PR	No	No	0	4	4	Dead
Strik et al. 2001	Case report—V	31	F	1	T10-11	Sup. + Inf.	GBM	4	STR	Yes	No	8	6	14	Dead
Claus et al. 1995	Case report—V	41	M	108	L4-5	Sup. + Inf.	A	2	PR	Yes	No	28	0	28	Dead
Gajjar et al. 1995	Retrospective series—IV	13	M	NA	C	Sup. + Inf.	DA	2	Biopsy	Yes	Yes	NA	NA	15	Alive
		5	F	NA	T	Sup. + Inf.	DA	2	Biopsy	Yes	Yes	NA	NA	91	Alive
Umezu et al. 1992	Case report—V	40	M	5	C2-5	Sup. + Inf.	A	2	PR	Yes	No	7	0	7	Dead
Asano et al. 1990	Case report—V	23	F	1	T11-12	Sup. + Inf.	GBM	4	PR	Yes	No	7	18	25	Dead
Cohen et al. 1989	Retrospective series—IV	27	F	5	C	Inf.	AA	3	NA	NA	NA	NA	NA	4	Dead
		20	F	13	C	Inf.	AA	3	NA	NA	NA	NA	NA	7	Dead
		17	F	1	T	Inf.	GBM	4	NA	Yes	NA	NA	NA	10	Dead
		16	F	10	L	Inf.	GBM	4	NA	Yes	NA	NA	NA	6	Dead
		15	M	2	L	Sup. + Inf.	AA	3	NA	NA	NA	NA	NA	17	Dead
		14	M	9	L	NA	GBM	4	NA	Yes	NA	NA	NA	4	Dead
		14	F	1	L	Sup. + Inf.	AA	3	NA	NA	NA	NA	NA	28	Dead
		10	F	1	C	NA	GBM	4	NA	Yes	NA	NA	NA	5	Dead
		9	M	0.5	C	NA	GBM	4	NA	Yes	NA	NA	NA	1	Dead
Bell et al. 1988	Retrospective series—IV	13	M	2	T2-6	Sup. + Inf.	AA	3	STR	Yes	Yes	2	10	12	Dead
		2.5	M	12	C	Inf.	A	2	Removal	No	No	12	5	17	Dead
		3	M	NA	C2-7	Inf.	DA	2	GTR	Yes	No	16	30	46	Alive
Kendrick et al. 1987	Case report—V	41	F	NA	T	NA	GBM	4	PR	NA	NA	0	0.5	0.5	Dead

IM, intracranial metastasis; CM, conus medullaris; Inf., infratentorial; Sup., supratentorial; C, cervical; T, thoracic; L, lumbar; AO, anaplastic oligodendroglioma; AE, anaplastic ependymomas; AA, anaplastic astrocytoma; DA, diffuse astrocytoma; A, astrocytoma; GBM, glioblastomas; LGG, low-grade glioma; GTR, gross total resection; STR, subtotal resection; PR, partial resection; DTIM, diagnosis-to-IM interval; IMTO, IM-to-outcome interval; NA, not available; CT, chemotherapy; RT, radiotherapy; WHO, World Health Organization.

Continues

Table 1. Continued

Studies	Study Design—Level of Evidence	Age (Years)	Gender	Duration (Month)	Spinal Site	IM Site	Pathology	WHO Grade	Spinal Surgery	RT	CT	DTIM	IMTO	Survival	Outcome
Johnson et al. 1987	Case report—V	8	F	3	T11-L3	Inf.	AA	3	STR	Yes	No	4	10	14	Dead
Sarabia et al. 1986	Case report—V	54	M	24	L1	Sup. + Inf.	AA	3	STR	Yes	No	6	0	6	Dead
Hely et al. 1985	Retrospective series—IV	38	F	1.5	T	Sup.	A	3	Biopsy	Yes	No	NA	1	7	Dead
		19	F	3	L	Sup. + Inf.	A	2	Biopsy	Yes	No	1	27	28	Dead
Simonati et al. 1981	Case report—V	19	F	0.3	T	Sup.	DA	2	Biopsy	Yes	No	0	0.5	0.5	Dead

IM, intracranial metastasis; CM, conus medullaris; Inf., infratentorial; Sup., supratentorial; C, cervical; T, thoracic; L, lumbar; AO, anaplastic oligodendroglioma; AE, anaplastic ependymomas; AA, anaplastic astrocytoma; DA, diffuse astrocytoma; A, astrocytoma; GBM, glioblastomas; LGG, low-grade glioma; GTR, gross total resection; STR, subtotal resection; PR, partial resection; DTIM, diagnosis-to-IM interval; IMTO, IM-to-outcome interval; NA, not available; CT, chemotherapy; RT, radiotherapy; WHO, World Health Organization.

underwent PR, and 7 (58.3%) patients underwent biopsy. A significant difference in the proportion of surgical interventions was observed between the LGSG and HGSG groups ($P < 0.05$) (Table 2).

RT was administered to 9 (90%) LGSG patients and 37 (92.5%) HGSG patients. Chemotherapy was provided to 5 (45.5%) patients in the LGSG group and 22 (64.7%) patients in the HGSG group. Concurrent chemoradiotherapy was delivered to 4 LGSG patients and 22 HGSG patients. Notably, in the LGSG cohort, the proportion receiving RT (90.0%) was significantly higher than that receiving CT (45.5%), while in the HGSG group, the rates of RT and CT were 92.5% and 64.7%, respectively. Furthermore, concurrent chemoradiotherapy was utilized in 15.4% of LGSG patients and 84.6% of HGSG patients (Table 2). Importantly, patients who underwent tumor biopsy followed by CT and RT demonstrated improved survival outcomes (Figure 4A–C).

Survival Outcomes and Prognostic Analysis

With respect to the factors affecting DTIM, both symptom duration and the EOR were found to significantly influence IM. Patients who underwent GTR or STR experienced a significantly longer DTIM compared to those receiving PR or biopsy. Additionally, patients presenting with symptoms for less than 3 months exhibited shorter DTIMs ($P < 0.05$). Regression analysis further identified EOR as an independent determinant of DTIM ($P < 0.05$) (Tables 3 and 4; Figure 2). Kaplan–Meier analysis was utilized to evaluate the impact of various factors on OS in patients with IM. Univariate regression analysis revealed that age, sex, symptom duration, spinal tumor location, spinal glioma infiltration, EOR, CT, and RT did not demonstrate significant differences between subgroups ($P > 0.05$) (Figure 3A-B; Figure 4A-C). Notably, patients who received RT or CT tended to have numerically longer OS compared to those who did not (Table 3). However, the IM site, pathological type, DTIM, and IMTO were all significantly associated with OS (Table 3; Figure 3A-F). Multivariable regression analysis confirmed DTIM (hazard ratio = 4.952, 95% confidence interval [1.633–15.015], $P = 0.005$) and IMTO (hazard ratio = 4.968, 95% confidence interval [1.697–14.542], $P = 0.003$) as independent prognostic factors for OS in patients with IM ($P < 0.05$) (Table 4; Figure 3 A-F).

DISCUSSION

Metastatic dissemination in intracranial and SCGs predominantly occurs in high-grade variants, such as GBM, owing to their marked invasiveness.[7] Chamberlain et al.[51] retrospectively analyzed 80 patients with GBM and demonstrated that recurrence and metastasis patterns were associated with the initial cranial imaging findings. In that cohort, 87.5% of recurrences were local, 6.25% distant, 3.75% multifocal, and 2.5% diffuse. Irrespective of tumor subtype, metastasis generally marks the terminal stage of disease and is associated with poor survival outcomes. Spinal cord gliomas with IM are exceptionally rare in clinical practice, most frequently reported in case studies or small series. Survival outcomes are as unfavorable as those of patients with intracranial gliomas with metastasis.[8,12] In the present study, we examined the clinical characteristics,

Table 2. Summary of Demographics and Clinical Features of Patients with Intracranial Metastasis

Characteristics	Total (n = 62)	LGSG (n = 12)	HGSG (n = 50)	*P* Value
Age (years)	19 (12.0–38.5)	16 (3.7–40.8)	20 (12.8–33.5)	0.261
Male (%)	34 (54.8)	8 (66.7)	26 (52.0)	0.359
Duration of symptoms (months)	3 (1.0–6.0)	3 (1.5–8.5)	2 (1.0–6.3)	0.706
Spinal tumor location (%)				0.312
C	18 (29.0)	6 (50.0)	12 (24.0)	
T	31 (50.0)	4 (33.3)	27 (54.0)	
L	11 (17.7)	2 (16.7)	9 (18.0)	
T + L	2 (3.2)	0	2 (4.0)	
Spinal glioma infiltration ≥3 segments (%)	25/45 (55.6)	3/7 (42.9)	22/38 (57.9)	0.462
Spinal glioma grade (%)				**<0.001**
2 (DA/A/LGG)	12 (19.4)	12 (100.0)	-	
3 (AA/AO/AE)	19 (30.6)	-	19 (38.0)	
4 (GBM)	31 (50.0)	-	31 (62.0)	
IM site (%)		-		0.349
Supratentorial	12/47 (25.5)	2/11 (18.2)	10/36 (27.8)	
Infratentorial	14/47 (29.8)	2/11 (18.2)	12/36 (33.3)	
Combined	21/47 (44.7)	7/11 (63.6)	14/36 (38.9)	
Extent of resection (%)				**0.042**
GTR/STR	20/51 (39.2)	1 (8.3)	19/39 (48.7)	
PR	12/51 (23.5)	4 (33.3)	8/39 (20.5)	
Biopsy	19/51 (37.3)	7 (58.3)	12/39 (30.8)	
RT yes (%)	46/50 (92.0)	9/10 (90.0)	37/40 (92.5)	0.794
CT yes (%)	27/45 (60.0)	5/11 (45.5)	22/34 (64.7)	0.257
Combined adjuvant therapy (%)	26 (41.9)	4 (15.4)	22 (84.6)	0.102
DTIM (months)	6 (2.0–10.0)	3 (0.5–14.0)	6 (2.5–9.5)	0.763
IMTO (months)	5 (2.5–10.0)	5 (0.25–28.5)	5 (3.0–10.0)	0.961
Overall survival (months)	14 (7.0–21.0)	17.7 (7.5–41.5)	12 (7.0–19.9)	0.134
Dead (%)	55 (88.7)	9 (75.0)	46 (92.0)	0.095

The bold *P* value underlines the statistically significant outcome measure.
C, cervical; T, thoracic; L, lumbar; DA, diffuse astrocytoma; A, astrocytoma; GBM, glioblastomas; IM, intracranial metastasis; LGG, low-grade glioma; AO, anaplastic oligodendroglioma; AE, anaplastic ependymomas; AA, anaplastic astrocytoma; GTR, gross total resection; STR, subtotal resection; PR, partial resection; RT, radiotherapy; CT, chemotherapy; DTIM, diagnosis-to-IM interval; IMTO, IM-to-outcome interval; LGSG, low-grade spinal cord glioma; HGSG, high-grade spinal cord glioma.

management, and prognostic outcomes of patients with SCGs with IM.

Prognostic Factors Affecting DTIM

IM from SCGs is rare and can occur across all age groups and glioma grades. Our findings regarding the impact of sex, symptom duration, and EOR on DTIM are consistent with previous studies. Brown et al.,[52] demonstrated that more extensive tumor resection prolongs progression-free survival, while Li et al.,[53] emphasized the prognostic significance of symptom duration in gliomas. In the present analysis, sex, symptom duration, and EOR were all found to significantly influence DTIM; age, tumor site, infiltration, and IM site did not exhibit significant effects. The lack of association between age and IM is in line with findings by Inoue et al.,[54] whereas the relationship between symptom duration and tumor progression has similarly been highlighted by Li et al.,[53] and Niu et al.,[55] studies. Multivariate analysis identified EOR as an independent factor affecting DTIM (**Tables 3** and **4**, **Figure 2A** and **B**). The DTIM varied by surgical modality—from shortest to longest—for biopsy, PR, and gross/subtotal resection (GTR/STR), respectively. This finding is consistent with that of Brown et al.,[52] who found that more

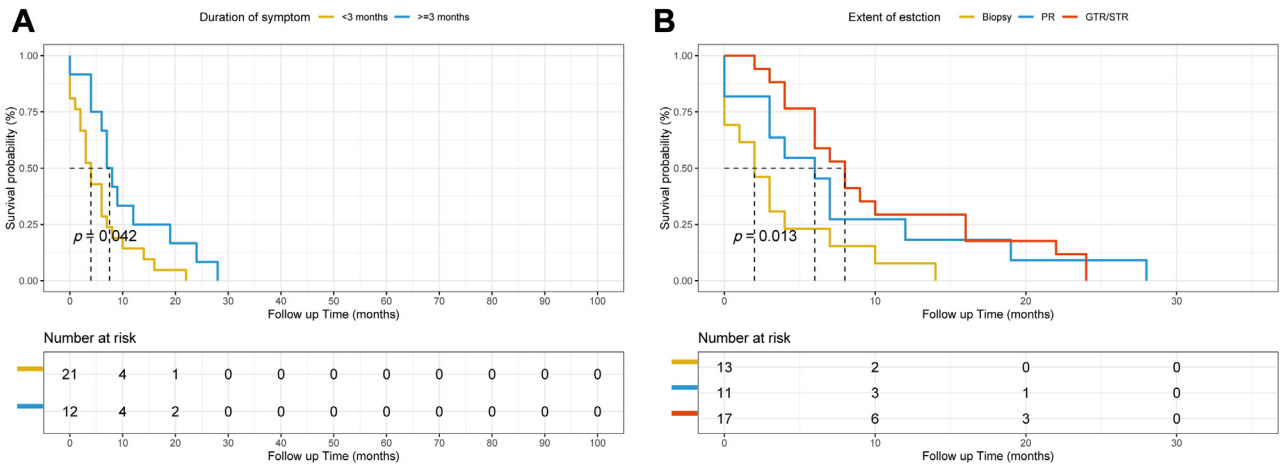

Figure 2. K-M analysis was used to determine the impact of variables on the DTIM in patients with spinal cord gliomas with intracranial metastasis. The Kaplan-Meier survival curves were stratified by the duration of symptoms (**A**) and extent of resection (**B**), respectively. DTIM refers to initial histological confirmation to first radiological detection of intracranial metastasis. DTIM, diagnosis-to-intracranial metastasis; GTR, gross total resection; STR, subtotal resection; PR, partial resection; K-M, Kaplan-Meier.

extensive resection significantly reduced the risk of tumor progression at both 6 months and 1 year in a pooled analysis of 41,117 GBM patients from 37 studies. Although the biological behavior of gliomas may vary by age—as seen in supratentorial gliomas—analysis in our cohort revealed no significant age effect on IM, which again agrees with Inoue et al.,[54] Similar to supratentorial gliomas, the biological behavior of SCGs may differ across different age groups.[54] The interval between symptom onset and diagnosis may reflect tumor aggressiveness. In an investigation involving 40 adults with brainstem glioma, Li et al.,[53] in a study of 40 adults with brainstem glioma, reported that patients with symptoms lasting more than 2 months experienced longer progression-free survival and a more favorable prognosis, suggesting that symptom duration may indicate tumor progression rate. Shorter symptom duration was associated with more aggressive disease and poorer prognosis. In our cohort, the median DTIM was shorter in the LGSG group, whereas the period was more extensive, indirectly reflecting the inconsistent sensitivity of LGSG to treatment. Some tumors may undergo malignant transformation, which is a significant factor contributing to the IM of LGSG. Compared with that of HGSG with metastasis, the median symptom duration of LGSG was longer, which delayed its diagnosis (**Table 2**). As LGSGs progress, they are prone to malignant transformation, increasing the risk of IM and leading to a shorter DTIM. This underscores the importance of early detection and intervention in LGSG with intracranial dissemination.

Prognostic Factors Affecting OS

The biological characteristics and genetic profiles of gliomas differ markedly between low-grade and high-grade tumors, resulting in varied clinical management strategies and prognostic outcomes. Compared to LGSG, HGSG are generally associated with a poor prognosis, shorter survival, and more rapid progression. This study revealed sex disparities among LGSG and HGSG patients, which is consistent with findings reported in most glioma subtypes.[2,3,56] The duration of symptoms, defined as the interval from symptom onset to diagnosis, may serve as an indicator of tumor progression. Previous studies have identified symptom duration as an important prognostic indicator of OS in midline gliomas, including thalamic gliomas.[55,57] Notably, patients with symptoms persisting longer than six months have been shown to achieve better outcomes.[56] However, in the present study, Cox regression analysis between subgroups based on the duration of symptoms in patients with spinal gliomas and IM revealed no significant difference in the prognostic analysis between LGSG and HGSG.

Gliomas with fewer segments tended to exhibit less neurologic impairment than those with multiple segments did, which was significantly associated with a better prognosis. Larger and more invasive tumors carry a heightened risk of postoperative neurological deficits and present greater surgical challenges, collectively contributing to unfavorable outcomes in patients with multisegmental gliomas. These findings are in agreement with previous reports by Sun et al.,[58] and Lacroix et al.,[59] which emphasized the aggressive nature and poor prognosis associated with gliomas spanning multiple spinal segments. The majority of spinal gliomas are situated in the cervicothoracic segment.[58,60-62] Indeed, spinal gliomas with IM are commonly detected at the cervicothoracic segment, particularly the thoracic segment. Kaplan–Meier analysis identified tumor grade, IM site, and the IMTO as significant prognostic factors for OS (**Figure 3**). Surgical resection remains the gold standard treatment for patients with spinal gliomas and related intracranial metastases, with EOR serving as a key prognostic indicator. Maximal resection, particularly for cerebral and midline gliomas, is typically associated with improved survival outcomes.[57,59] However, the impact of EOR may differ between low-grade and high-grade

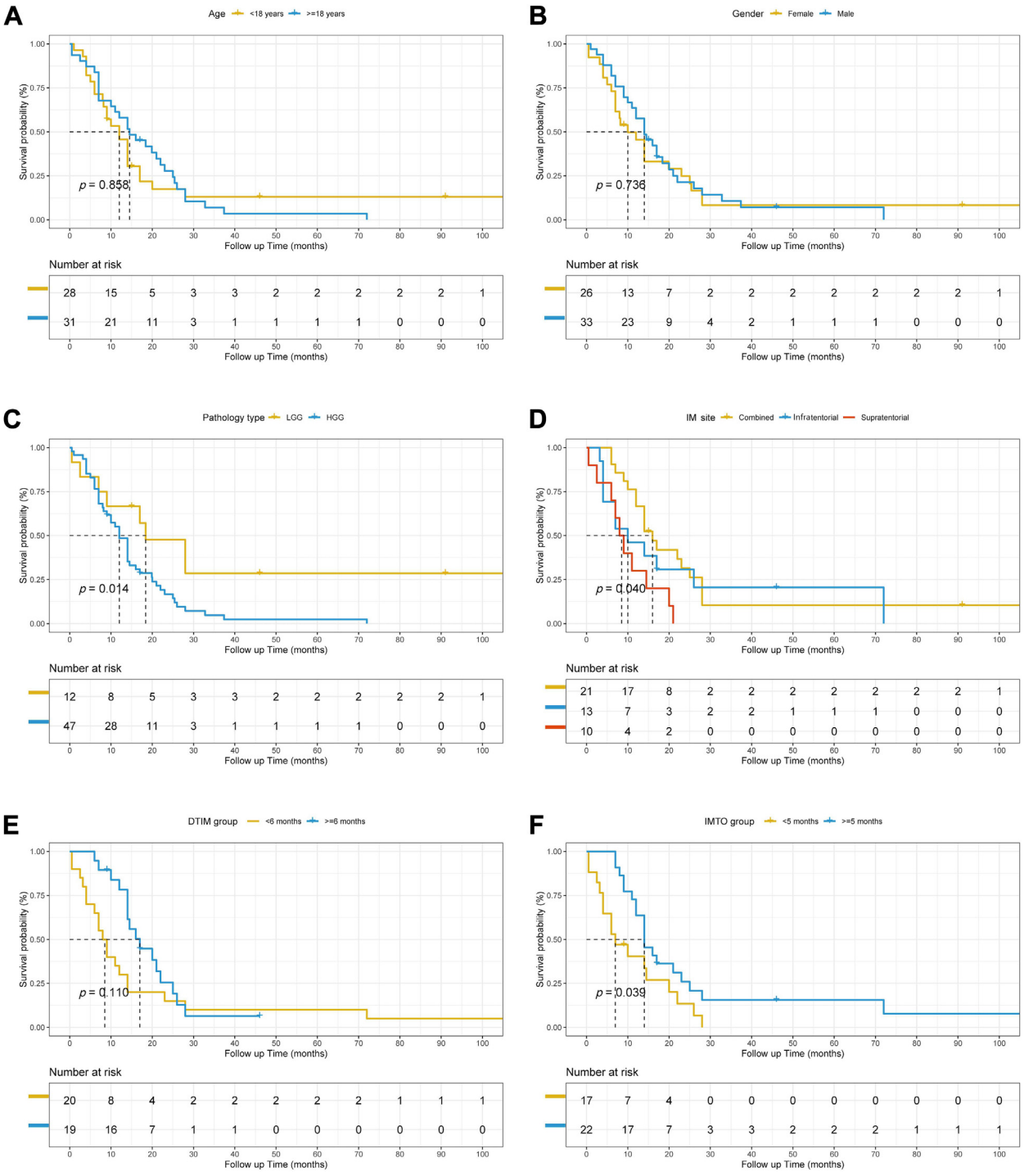

Figure 3. K-M analysis was used to determine the impact of variables on OS in patients with spinal cord gliomas with intracranial metastasis. K-M survival curves stratified by age (**A**) and sex (**B**), respectively. (**C**) Kaplan-Meier survival curve stratified by pathology type ($P < 0.05$). (**D**) Kaplan-Meier survival curve stratified by metastasis site ($P < 0.05$). (**E**) Kaplan-Meier survival curve stratified by DTIM ($P > 0.05$). (**F**) Kaplan-Meier survival curve stratified by IMTO ($P < 0.05$). OS, overall survival; DTIM, diagnosis-to-intracranial metastasis; IMTO, intracranial metastasis-to-outcome; HGG, high-grade glioma; LGG, low-grade glioma; IM, intracranial metastasis; K-M, Kaplan-Meier.

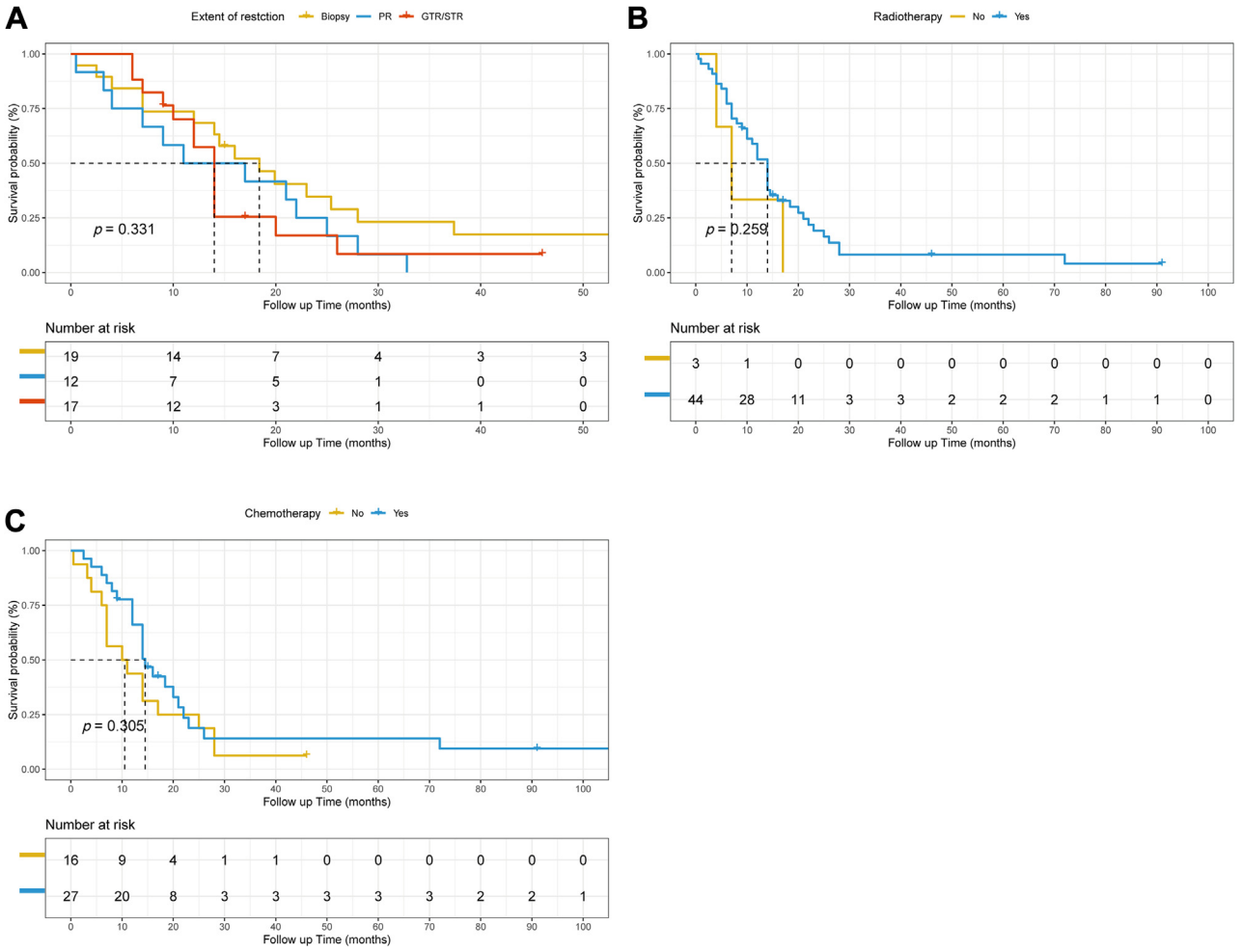

Figure 4. Kaplan-Meier analysis was used to determine the impact of treatment on the OS of patients with spinal cord gliomas with intracranial metastasis. Kaplan-Meier survival curves stratified by the extent of resection (**A**), radiotherapy (**B**), and chemotherapy (**C**) (all $P > 0.05$). OS, overall survival; GTR, gross total resection; STR, subtotal resection; PR, partial resection.

gliomas and warrants further investigation. The importance of EOR in improving survival has been demonstrated in studies by Constantini et al.,[63] and Wolff et al.,[64] while the survival benefits of RT and CT have been reported in studies by Subhas et al.,[62] and Liu et al.,[65] Although RT and CT were not identified as independent prognostic factors in the present study, their established role in prolonging survival should not be overlooked. Constantini et al.[63] reviewed 164 cases of spinal gliomas, reporting that radical surgical resection led to better outcomes for low-grade tumors but yielded inconclusive results for high-grade cases, highlighting the need for further validation—a finding partially in line with our results. The optimal EOR for patients with SCGs remains controversial. For example, some studies on pediatric HGG of the spinal cord concluded that patients who underwent GTR had better survival rates than those who did not undergo GTR.[64] However, others, another review on primary spinal GBM revealed that maximal resection does not prolong survival.[66] In this study, patients who underwent GTR or STR within a specific period had superior prognoses compared with those who underwent PR or biopsy. Interestingly, patients who underwent biopsy tended to have comparatively better long-term clinical outcomes (**Figure 4** A and B), a finding that contrasts with the intracranial glioma paradigm, where maximal safe resection is associated with prolonged survival.[67-69] Owing to incomplete data on the surgical modality for intracranial lesions and the limited sample size, the effects of treatments for intracranial lesions on survival outcomes remain unknown. Furthermore, these conclusions require further validation. Due to limited data regarding surgical approaches for intracranial lesions and the small sample size, the effects of treatments for intracranial disease on survival outcomes remain unclear and require further study.

Although RT and CT were not identified as independent prognostic factors for OS in this study, patients who received RT

Table 3. Univariate Analysis for the Time From Diagnosis to IM and Overall Survival

	DTIM (Months)		OS (Months)	
Variable	**Median (Q1-Q3)**	***P* Value**	**Median (Q1-Q3)**	***P* Value**
Age		0.498		0.264
< 18 years	4.0 (3.0, 8.8)		11.0 (6.0, 15.5)	
≥ 18 years	6.0 (2.0, 11.0)		14.5 (7.0, 24.0)	
Gender		**0.015**		0.302
Male	2.5 (1.0, 7.0)		14.0 (9.0, 20.0)	
Female	2.5 (4.0, 12.5)		9.5 (6.3, 22.2)	
Duration of symptoms (median)		**0.037**		0.935
≤3 months	4.0 (2.0, 7.0)		14.0 (7.3, 18.1)	
>3 months	7.5 (5.5, 13.75)		9.0 (6.5, 21.0)	
Spinal tumor location		0.447		0.809
C	9.5 (3.0, 19.8)		8.0 (4.8, 18.2)	
T	4.0 (2.0, 7.0)		14.0 (8.1, 20.5)	
L	6.0 (3.5, 7.5)		14.0 (7.0, 25.3)	
T + L	6.0 (5.0, 7.0)		11.5 (10.3, 12.8)	
Spinal glioma infiltration		0.684		0.389
<3 segments	7.0 (3.8, 8.8)		14.5 (9.5, 25.2)	
≥3 segments	5.0 (3.0, 14.5)		12.0 (7.5, 20.5)	
IM site		0.992		0.067
Supratentorial	4.0 (1.0, 15.0)		8.5 (6.3, 13.6)	
Infratentorial	4.0 (3.0, 10.5)		10.0 (4.0, 17.0)	
Combined	6.0 (3.0, 8.0)		15.0 (12.0, 25.0)	
Spinal glioma grade		0.746		0.136
LGG	3.0 (1.0, 12.0)		17.7 (8.5, 32.5)	
HGG	6.0 (3.0, 9.0)		12.0 (7.0, 18.45)	
Extent of resection		**0.010**		0.430
GTR/STR	8.0 (6.0, 16.0)		14.0 (9.0, 16.0)	
PR	6.0 (3.0, 9.5)		14.0 (6.3, 22.8)	
Biopsy	2.0 (0, 4.0)		16.0 (9.5, 26.7)	
RT		0.515		0.445
Yes	6.0 (3.0, 10.0)		13.0 (7.0, 18.8)	
No	4.5 (0, 9.8)		7.0 (5.5, 12.0)	
CT		0.955		0.208
Yes	6.0 (3.0, 10.0)		14.0 (10.5, 20.5)	
No	6.0 (2.2, 8.8)		10.5 (6.8, 19.0)	
DTIM (median)		-		**0.013**
<6 months	-	-	8.5 (4.0, 14.0)	

Bold values indicate statistically significant differences between comparison groups ($P < 0.05$).

HGG, high-grade glioma; LGG, low-grade glioma; IM, intracranial metastasis; GTR, gross total resection; STR, subtotal resection; PR, partial resection; C, cervical; T, thoracic; L, lumbar; RT, radiotherapy; CT, chemotherapy; DTIM, diagnosis-to-IM interval; IMTO, IM-to-outcome interval; OS, overall survival.

Continues

Table 3. Continued

	DTIM (Months)		OS (Months)	
Variable	**Median (Q1-Q3)**	***P* Value**	**Median (Q1-Q3)**	***P* Value**
≥6 months	-	-	16.0 (13.0, 21.5)	
IMTO (median)		0.273		**0.020**
<5 months	6.0 (3.0, 14.0)		7.0 (4.0, 14.5)	
≥5 months	4.0 (2.0, 7.0)		14.0 (11.3, 22.5)	

Bold values indicate statistically significant differences between comparison groups ($P < 0.05$).
HGG, high-grade glioma; LGG, low-grade glioma; IM, intracranial metastasis; GTR, gross total resection; STR, subtotal resection; PR, partial resection; C, cervical; T, thoracic; L, lumbar; RT, radiotherapy; CT, chemotherapy; DTIM, diagnosis-to-IM interval; IMTO, IM-to-outcome interval; OS, overall survival.

and CT exhibited prolonged survival, consistent with previous reports.[59,70] Subhas K et al.[62] retrospectively analyzed 128 patients with HGSG and found that postoperative RT and CT significantly improved patient prognosis and survival outcomes. While the precise role of adjuvant therapies in glioma remains to be fully established, current evidence suggests they may confer survival benefits, particularly in high-grade cases.[70] Prior studies have emphasized that postoperative RT provides an OS advantage in high-grade spinal gliomas, especially in pediatric patients.[61,65] RT may deliver short-term improvements in clinical and radiographic outcomes, prolonging survival in a minority of patients with high-grade glioma.[62] In the present study, despite not being identified as an independent prognostic indicators, RT appeared to enhance survival outcomes (Figure 4B-C). In addition, the combination of surgical resection and RT improved survival compared to radiation alone.[71] Determining optimal therapeutic regimens will require further investigation with larger, more contemporary cohorts. This study also found that extensive spinal cord involvement was linked to poorer therapeutic effects, likely due to the aggressive nature of gliomas. Notably, significant differences in OS were observed among metastases involving different spinal cord segments, potentially attributable to symptom variation across brain regions and differing compensatory mechanisms. Variations in efficacy may be attributed to variations in the blood-spinal cord and blood–brain barrier functions.[72] Importantly, DTIM and IMTO were

Table 4. Multivariate Cox Regression Analyses for DTIM and OS

	DTIM			OS		
Variables	**HR**	**95% CI**	***P* Value**	**HR**	**95% CI**	***P* Value**
Duration of symptoms (≤3/>3 months)	1.677	0.680—4.137	0.262	-	-	-
Extent of resection				-	-	-
GTR/STR	-	-	**Reference**	-	-	-
PR	1.198	0.488—2.940	0.693	-	-	-
Biopsy	2.780	1.100—7.022	**0.031**	-	-	-
Spinal glioma pathology (LGG/HGG)				0.507	0.181—1.418	0.195
DTIM (<6/≥6 months)	-	-	-	4.952	1.633—15.015	**0.005**
IMTO (<5/≥5 months)	-	-	-	4.968	1.697—14.542	**0.003**
IM site						
Supratentorial				-	-	**Reference**
Infratentorial				0.402	0.140—1.152	0.090
Combined				0.549	0.220—1.367	0.198

Bold values indicate statistically significant differences between comparison groups ($P < 0.05$).
GTR, gross total resection; STR, subtotal resection; PR, partial resection; HGG, high-grade glioma; LGG, low-grade glioma; DTIM, diagnosis-to-IM interval; IMTO, IM-to-outcome interval; IM, intracranial metastasis; OS, overall survival; HR, hazard ratio; CI, confidence interval.

identified as independent prognostic factors for OS, aligning with previous research.

In this study, EOR was identified as an independent prognostic factor for DTIM, which itself was independently associated with OS. These findings suggest that EOR has a significant impact on OS and that RT and CT may also play important roles in improving treatment efficacy. For patients with SCGs, maximum safe resection should be pursued when feasible, as it can enhance survival and optimize treatment outcomes. Clinically, routine MRI surveillance is recommended for early detection of metastasis in patients with spinal cord glioma, enabling timely diagnosis and intervention.

Limitations

Several limitations of this study warrant consideration. First, its retrospective design and relatively small sample size may introduce selection and publication biases, potentially compromising statistical power. Incomplete data precluded a comprehensive assessment of survival outcomes across subgroups, and subgroup analyses stratified by tumor grade or EOR were not feasible due to limited case numbers. The broad time span of included studies (1981–2024) also introduces methodological heterogeneity, given the evolution of diagnostic criteria, treatment modalities, and reporting standards over time. Furthermore, reliance on case reports and case series may contribute to publication bias, as cases with negative or inconclusive outcomes are less often reported. In light of ongoing advances in glioma classification and treatment, future research should prioritize more contemporary patient cohorts to better inform prognosis and therapeutic efficacy.

CONCLUSIONS

Spinal gliomas with IM are extremely rare malignancies. This study comprehensively characterized their clinical characteristics and survival outcomes and identified independent prognostic factors, including DTIM and IMTO, thereby contributing to a deeper understanding of the features of the condition and offering valuable insights for optimizing patient management. Maximal safe resection, complemented by adjuvant therapy, remains essential for improving survival outcomes. Given the rarity and complexity of these tumors, future research should focus on larger, contemporary cohorts to refine treatment strategies. Overall, this study enhances current understanding and provides a clinical framework for managing patients with SCGs and IM.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Jiaoming Li: Conceptualization, Data curation, Formal analysis, Investigation, Writing — original draft, Writing — review & editing, Project administration. **Tao Chang:** Data curation, Formal analysis, Methodology, Software. **Yan Zeng:** Data curation, Resources, Software. **Weichao Ma:** Project administration, Resources. **Jingsong Liu:** Conceptualization, Supervision. **Tianjian Ren:** Supervision, Writing — original draft. **Xiaodong Niu:** Conceptualization, Software, Supervision, Writing — review & editing, Methodology.

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