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Management and survival trends for diffuse gliomas diagnosed at a single neurooncology center in China during 2000 to 2020

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Currently reported survival outcomes for gliomas exhibit significant variability and controversy. In this study, we aim to provide survival data in Chinese populations by conducting a retrospective analysis of management and survival trends in a large cohort of glioma patients from a single institute in China. A total of 1206 patients with newly diagnosed gliomas treated between 2000 and 2020 were enrolled, including 537 glioblastoma (WHO grade 4), 450 astrocytomas (grade 2/3) and 219 oligodendroglial tumors (grade 2/3). The estimated overall survival at 5 years was 18.9% for glioblastoma, 58.8% for astrocytomas, and 80.7% for oligodendroglial tumors, while median survival was 17.2 months, 82.8 months, and not reached, respectively. The survival trend has increased over the past decades for all types of gliomas. Additionally, similar survival trends were observed between grade 2 and 3 IDH-mutant gliomas. Rising trends were observed in patients undergoing postsurgical radiation and chemotherapy. Multivariate analysis identified adjuvant radiochemotherapy as an independent factor for better prognosis in glioblastoma and astrocytomas. In summary, despite its retrospective nature, this cohort of glioma patients exhibits favorable survival outcomes compared to global statistics, indicating a geographical disparity in glioma prognosis. The promotion of adjuvant chemoradiotherapy contributes to improved prognosis.

Keywords Gliomas, Real-world management, Survival trend, Prognostic factors

It has undergone major changes over the last decades in the diagnosis and treatment of diffuse gliomas, the most frequent type of primary malignant brain tumors in adulthood. The latest WHO classification of central nervous system tumors in 2021, has evolved from a histology-based system to a combination of morphological and molecular features. Adult diffuse gliomas are now categorized into three types: glioblastoma (GBM), IDH-wildtype (wt) (WHO grade 4); astrocytoma, IDH-mutant (mut) (WHO grade 2, 3 or 4); oligodendroglioma, IDH-mut and 1p/19q-codeleted (WHO grade 2 or 3)[1,2]. Maximal safe resection emphasizing a prior consideration for prevention of new neurological deficits is associated with improved outcome and thus recommended across all glioma entities[3,4]. Regarding adjuvant therapy, mature results of various perspective clinical trials provide important evidences for clinical practice[3].

The third cycle of the CONCORD program for global surveillance of cancer survival (CONCORD-3) includes more than 700,000 patients diagnosed with primary brain tumors during 2000–2014 in 59 countries. A comprehensive analysis on CONCORD-3 data found significant disparities in the survival rates of glioma patients across various countries and regions[5]. The prognosis of diffuse and anaplastic astrocytoma was more favorable in Europe than in Asia. In contrast, the survival of GBM is worse in Western populations. The 5-year survival rate ranged from 5 to 10% in the US and most European countries, while was 11–15% in several Asia-Pacific

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countries, including Australia, New Zealand, South Korea and Singapore. China exhibited the most favorable survival with nearly 17% at 5 years[5]. The poor prognosis for GBM in European and the US has also been reported by national cancer registries[6,7]. The EUROCARE study found that 5-year survival for GBM patients diagnosed from 2000 to 2007 in Europe was 6%[6]. The Central Brain Tumor Registry of the US (CBTRUS) reported a 5-year survival for GBM in the US in 2001–2019 of 6.7%[7]. However, the survival outcomes of Chinese patients with GBM are controversial. A multicenter large-scale retrospective study conducted by the Chinese Glioma Genome Atlas (CGGA) group reported that the estimated 5-year survival rate for Chinese population with GBM diagnosed between 2011 and 2017 was only 6.1%[8], which is significantly lower compared to the findings of CONCORD-3 study[5]. Potential reasons for these discrepancies include the underdeveloped tumor registration system in China, and the fact that most of selected Chinese registries might not be representative. Given the vastness of China territory and its diverse populations, we cannot rule out the possibility that a limited number of Chinese registries contributed to comparatively higher 5-year survival rates. It remains unclear whether a significant geographical disparity exists in glioma prognosis between the East and the West. Thus, we conducted a retrospective analysis on 1,206 patients with newly diagnosed diffuse gliomas treated at our center from 2000 to 2020. This analysis represents a large cohort from the Chinese population and aims to evaluate their prognosis in real-world conditions. The changes in treatment modalities and survival-related factors were also analyzed. The findings will provide crucial evidence to clarify the actual survival outcomes of gliomas in China and their differences compared to Western countries. The deeper understanding of the global epidemiology of brain tumors will aid in the development of more targeted and efficient regional health policies.

In addition, given that the distinction between WHO grade 2 and 3 gliomas based on cellularity and mitotic activity is vague and somewhat subjective, there are low concordance rates among neuropathologists[9]. Genetic alterations and lineage development are considered more predictive of glioma outcomes than tumor grading[10]. Therefore, in this study, we analyzed survival trends for gliomas primarily by tumor type than by grade.

Patients and methods

Patient inclusion and data collection

Adult patients, ranging from 15 to 90 years old, who received tumor resection and were newly diagnosed with brain diffuse gliomas at the Sun Yat-sen University Cancer Center (SYSUCC) between 2000 and 2020 were included for analysis. Biopsy cases were excluded. The patients were diagnosed according to the WHO classification of central nervous system brain tumors, using the pathological criteria applicable at the time, specifically the editions from 2000, 2007 and 2016[11–13].

Relevant clinical data, such as gender, age at diagnosis, date of operation, histological type and grade, molecular status, and information regarding radiotherapy and systemic treatment, were collected from the patients' medical records. Tumor location was determined, and the maximal diameter was measured using pre-operative MRI scans by experienced radiologists and neurosurgeons. IDH status was assessed using immunohistochemistry (IHC) with a R132H specific anti-IDH1 antibody, and Sanger sequencing methods. Chromatin 1p/19q deletion and EGFR amplification were assessed using fluorescence in situ hybridization (FISH). MGMT promoter methylation was detected using fluorogenic quantitative PCR. TERT promoter mutations was identified using Sanger sequencing. Next-generation sequencing was applied to confirm molecular alterations in certain cases. This study was performed in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of SYSUCC. Written informed consents were obtained from all patients for medical research; For participants below the age of 16, informed consent was obtained from their parents. No information leading to the identification of a participant would be published.

Treatment

Maximal safe resection is the principle of glioma surgery. Several modern techniques including electrophysiological monitoring, intraoperative ultrasound and fluorescence visualization help achieve this goal. Postsurgical radiation and chemotherapy are recommended for high-grade gliomas (HGGs, WHO grade 3–4) and low-grade gliomas (LGGs, WHO grade 2) with high risks to recur[3,4]. Radiotherapy was typically administered at a dose of 50–60 Gy within 6 weeks after surgery. Before the year 2005, nitrosourea-based chemotherapy (BCNU or CCNU combined with teniposide or etoposide) and platinum chemotherapy (cis-platinum combined with teniposide or etoposide) were major regimens for systemic treatment. From 2005 onwards, temozolomide (TMZ) begun to be utilized, and become the primary agent for both astrocytic and oligodendroglial tumors. Some patients with HGGs received interferon-alfa, dianhydrogalactitol or other new therapies because of participation in clinical trials[14,15].

Follow-up

Follow-up was performed through patient visits or telephone calls every 3 to 6 months according to the type of tumor until Jun 2023 or death. The OS was calculated as the duration from the date of first operation to death or the end of follow-up. Patients without follow-up data were excluded. Patients died within a month following tumor resection were also excluded due to the high possibility of surgical complications.

Statistical analysis

SPSS software version 26 (IBM Corp., Santa Monica, USA) and GraphPad Prism software version 9 (GraphPad Software Inc., La Jolla, USA) were applied for statistical analysis. Variables were compared using t-test or chi-squared tests. Survival rate were estimated using the Kaplan–Meier method and compare with log-rank tests. Multivariate Cox proportional-hazards regression were conducted for calculating hazard ratio (HR). A two-side *P* value less than 0.05 was considered statistically significance.

Results

Patient characteristics

A total of 1206 patients with diffuse gliomas, who had complete clinical data and available survival information, were included in this study. Among them, 537 were diagnosed with GBMs, 450 with astrocytomas, 161 with oligodendrogliomas and 58 with oligoastrocytomas. It has been demonstrated that most oligoastrocytomas can be reclassified as oligodendrogliomas by detecting molecular markers including IDH mutation and 1p/19q loss[16,17]. Therefore, we combined oligoastrocytomas and oligodendrogliomas as an entity of oligodendroglial tumors ($n=219$) for further analysis. Of the patients with astrocytomas, 251 were classified as WHO grade 2, while 199 were grade 3. As for oligodendroglial tumors, 101 were grade 2 and 118 were grade 3. Additionally, IDH status was available for 704 patients (68.6%), 1p/19q status for 749 patients (73.0%), MGMT status for 556 patients (46.1%), TERT promoter status for 359 patients (29.8%), EGFR amplification status for 226 patients (18.7%). Patient characteristics are summarized in Table 1. The median onset age was 53 years old (range 15–81) for patients with GBM, 38 years old (range 15–82) for patients with astrocytomas, and 42 years old (range 15–75) for patients with oligodendroglial tumors. Regarding both astrocytoma and oligodendroglial tumors, patients with WHO grade 2 and those with grade 3 exhibited similar age at diagnosis, and was significantly younger than GBM patients.

Clinical management and trends

As shown in Table 2, the medical records show that around 50% of the patients with HGG underwent a combined treatment with radiation and chemotherapy after tumor resection. Approximately 10–20% of patients received either radiotherapy or chemotherapy alone. For LGG patients, a lower proportion underwent combined radiochemotherapy, whereas a higher proportion received only one type of adjuvant therapy (Table 2).

Then, we analyzed the changes in the proportions of patients receiving postsurgical treatment (radiation and/or chemotherapy) over three time periods from 2000 to 2020, as illustrated in Fig. 1. Increased trends in the proportions were observed in patients with GBM and LGG. The increase in postsurgical treatment occurred mainly between the period of 2000–2006 and 2007–2013 for GBM, while between 2007 and 2013 and 2014–2020

Characteries (*n*/%)	Glioblastoma (WHO grade 4, $n=537$)*	Astrocytoma (WHO grade 2/3, $n=450$)*	Oligodendroglial tumors (WHO grade 2/3, $n=219$)*
Gender			
Male	316/ 58.8%	252/ 56%	117/ 53.4%
Female	221/ 41.2%	198/ 44%	102/ 46.6%
Age (years)			
15–39	123/ 22.9%	248/ 55.1%	93/ 42.5%
40–64	316/ 58.9%	182/ 40.4%	118/ 53.9%
65–90	98/ 18.2%	20/ 4.4%	8/ 3.6%
Tumor locations**			
Supratentorial lobes	411/ 76.5%	341/ 75.8%	174/ 79.5%
Supratentorial midline	109/ 20.3%	87/ 19.3%	43/ 19.6%
Subtentorial	17/ 3.2%	22/ 4.9%	2/ 0.9%
Maximal diameter (cm)			
<6	396/ 73.7%	309/ 68.7%	153/ 70.0%
≥6	121/ 22.6%	101/ 22.4%	62/ 28.3%
Not available	20/ 3.7%	40/ 8.9%	4/ 1.7%
WHO grade			
4	537/ 100%	0/ 0%	0/ 0%
3	0/ 0%	199/ 44.2%	118/ 53.9%
2	0/ 0%	251/ 55.8%	101/ 46.1%
IDH status			
Wild-type	323/ 60.1%	55/ 12.2%	14/ 6.4%
Mutant	32/ 5.9%	161/ 35.8%	119/ 54.3%
Not available	182/ 34.0%	234/ 52.0%	86/ 39.3%
MGMT promoter status			
Methylated	115/ 21.4%	98/ 21.8%	88/ 40.2%
Non-methylated	174/ 32.4%	69/ 15.3%	12/ 5.5%
Not available	248/ 46.2%	283/ 62.9%	119/ 54.3%

Table 1. Clinicopathological information of different subtypes of gliomas. *Gliomas were diagnosed according to the WHO classification of central nervous system brain tumors applicable at the time, specifically the editions from 2000, 2007 and 2016. **Supratentorial lobes include frontal, temporal, parietal and occipital lobes, while midline regions include insular lobes, corpus callosum, basal ganglia and thalamus.

	GBM ($n=537$)	AIII ($n=199$)	AII ($n=251$)	OIII ($n=118$)	OII ($n=101$)
Both radiation and chemotherapy	272 (50.7%)	94 (46.8%)	78 (31.1%)	67 (56.8%)	27 (26.5%)
Radiation or chemotherapy	56 (10.4%)	40 (20.4%)	73 (29.1%)	16 (13.6%)	35 (34.7%)
None or unknow	209 (38.9%)	65 (32.8%)	100 (39.8%)	35 (29.6%)	39 (38.6%)

Table 2. The treatment of patients with different subtypes of gliomas received. AIII: astrocytoma, WHO grade 3; AII: astrocytoma, WHO grade 2; OIII: Oligodendroglial tumors, WHO grade 3; OII: Oligodendroglial tumors, WHO grade 2.

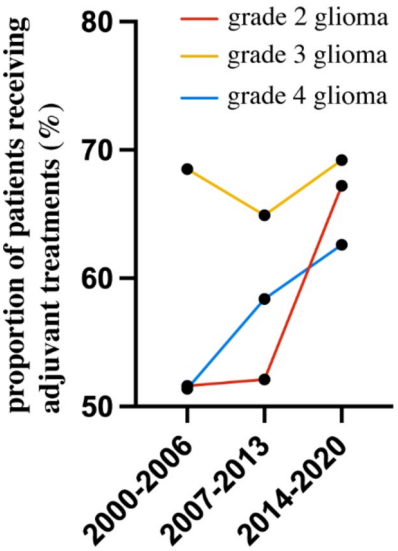

Fig. 1. Changes in the proportion of patients receiving postsurgical adjuvant treatments between 2000 and 2020.

for LGG. In contrast, for anaplastic gliomas (WHO grade 3), the proportion remained steady, ranging between 65.8% and 69.4%.

Survival outcomes and trends

Up to May 2023, 397 (73.9%) out of 537 patients with GBM, 200 (44.4%) out of 450 with astrocytomas and 47(21.5%) out of 219 with oligodendroglial tumors had died following a median follow-up of 61.0 months (range 1.8 to 178.8 months). Among patients diagnosed between 2000 and 2020, median OS was 17.2 (95% confidence interval [CI]: 15.6–19.0) months for GBM, 82.8 (95% CI: 68.2–97.4) months for astrocytomas, and not reached for oligodendroglial tumors (Fig. 2A). Kaplan-Meier estimate of the cumulative survival rate at 2 and 5 years was 37.8% and 18.9% for GBM, 78.0% and 58.8% for astrocytomas, and 87.8% and 80.7% for oligodendroglial tumors, respectively. There were remarkable improvements in survival for patients with astrocytomas and oligodendroglial tumors over a 20-year period from 2000 to 2020 (Fig. 2B and C). Additionally, we observed a trend of a slight increase in the 2-year survival rate for GBM patients, mainly between the 2000–2006 and 2007–2013 period. However, the longer-term survival at 5 years did not show significant differences, ranging between 14.1% and 20.6% (Fig. 2D).

When integrating molecular pathology, 334 patients were diagnosed with GBM IDH-wt, 186 were diagnosed with astrocytoma IDH-mut, 112 were diagnosed with oligodendroglioma IDH-mut 1p/19q-codeleted. The median OS for GBM IDH-wt was 17.0 (95% CI: 14.9–19.1) months, while survival rate was 35.6% at 2 years and 16.0% at 5 years. We also estimated the age-specific survival for patients with IDH-wt GBM. The median OS for elderly patients (65–90 years) was 12.1 (95% CI: 10.3–14.0) months, compared to 18.7 (95% CI: 16.6–20.7) months for adults aged 40–64 years, and 19.6 (95%CI: 9.8–29.3) months for young adults (15–39 years; Fig. 3A). Regarding to astrocytoma IDH-mut and oligodendroglioma IDH-mut 1p/19q-codeleted, median OS was not reached at the current follow-up. However, similar trends in survival were observed between grade 2 and grade 3 tumors in both the astrocytoma IDH-mut and oligodendroglioma IDH-mut 1p/19q-codeleted (Fig. 3C and D). The median OS for astrocytoma, IDH-mut, WHO grade 4 was 67.4 months. This was significantly worse than that of lower-grade astrocytoma (grade 2–3), but better than that of GBM, IDH-wt, WHO grade 4.

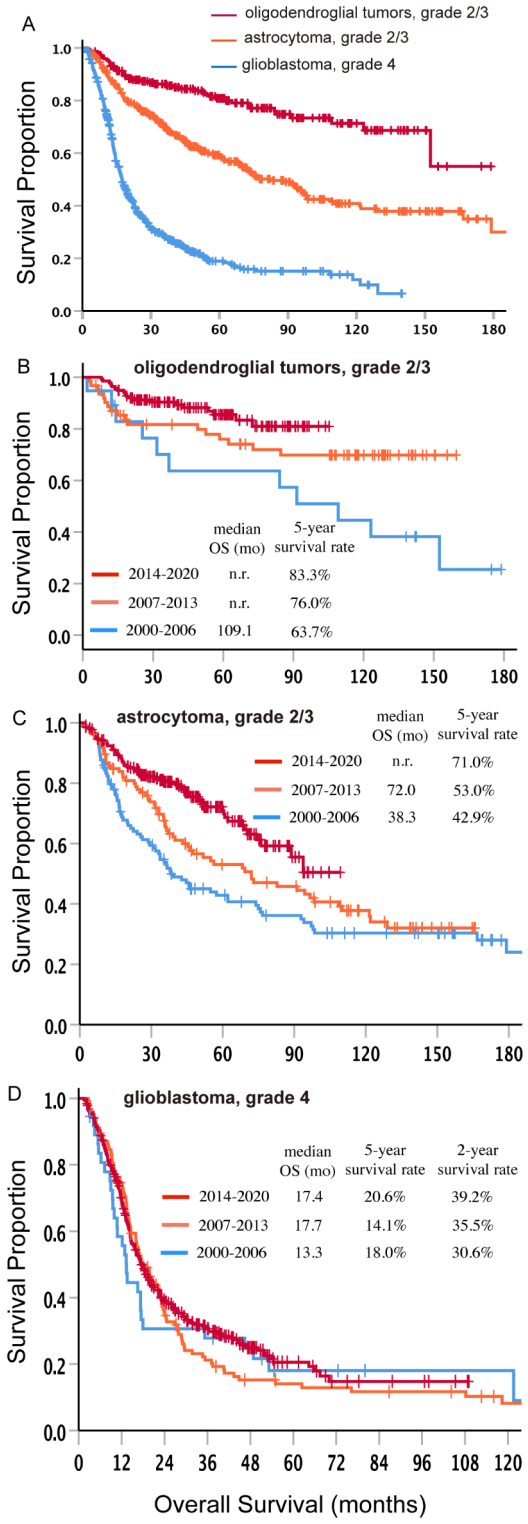

Fig. 2. Survival outcomes for different types of gliomas. (**A**) Comparison of survival among patients with glioblastoma, astrocytoma and oligodendroglial tumors. (**B-D**) Survival trends for oligodendroglial tumors (b), astrocytoma (c) and glioblastoma (d) from 2000 to 2020. OS, overall survival; n.r., not reached.

Prognostic factors in clinical practice

For both GBM and astrocytoma, older age, midline location, and wildtype IDH were independent risk factors, whereas postsurgical radiation and chemotherapy was an independent indicator for better survival (Table 3). Tumor with larger diameter (≥6 cm) and non-methylated MGMT indicated worse survival for patients with GBM, while higher tumor grade indicated unfavorable prognosis for patients with astrocytoma (Table 3). The

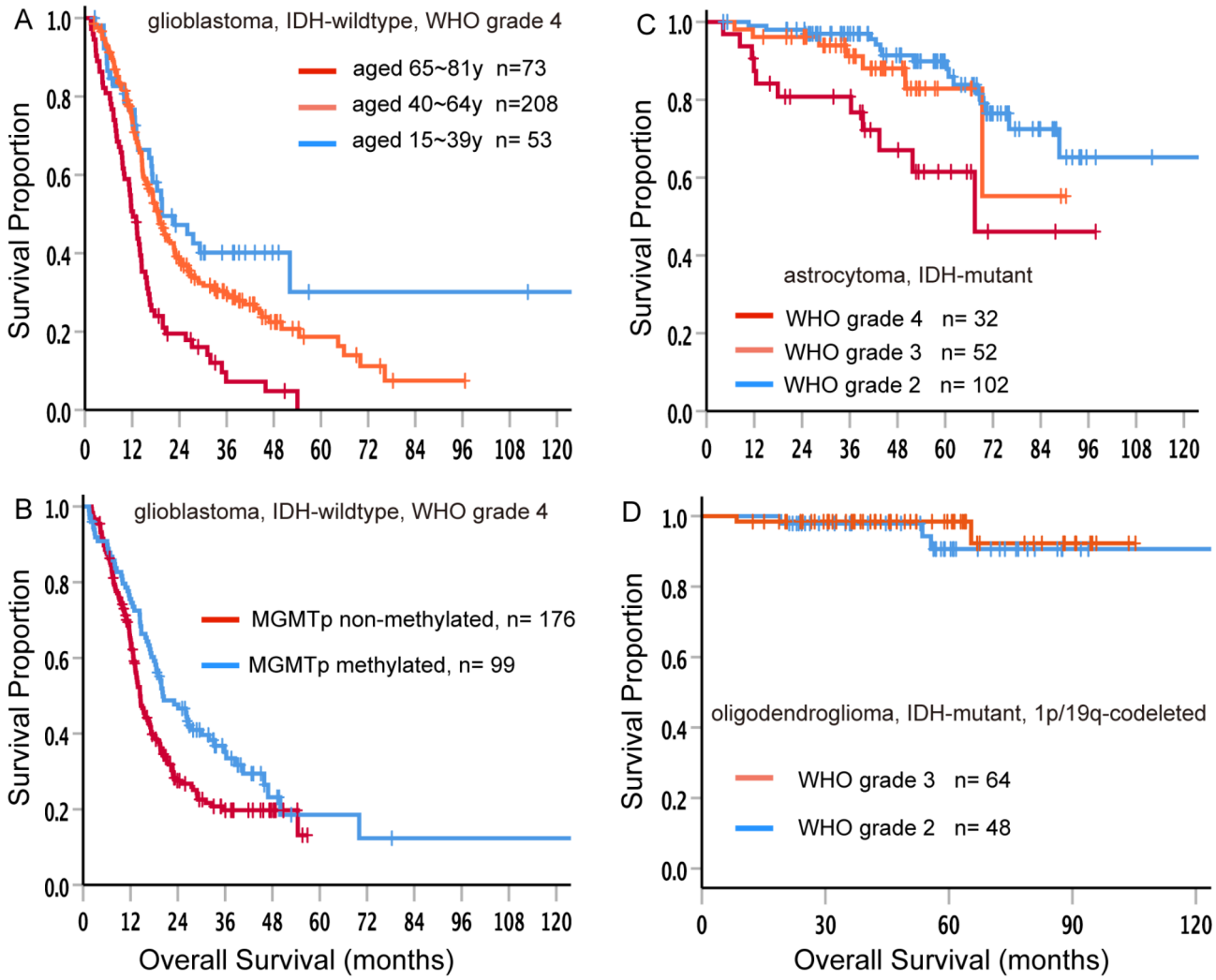

Fig. 3. Survival outcomes for different types of gliomas integrating molecular alterations. (**A**) Comparison of survival among glioblastoma patients from different age groups. (**B**) Comparison of survival for glioblastoma with and without MGMT promoter methylation. (**C**) Comparison of survival for astrocytoma with different malignant grades. (**D**) Comparison of survival for oligodendroglioma with different malignant grades.

median OS for IDH-wt GBM carrying methylated MGMT was 20.2 months (95% CI: 13.5–26.8), compared to 14.4 months (95% CI: 12.8–16.0; Fig. 3B) for those without methylated MGMT. In addition, patients with IDH-wt, MGMT-methylated GBM who received both radiation and chemotherapy exhibited a prolonged OS of median 23.0 months (95% CI: 15.0–31.0). Regarding to oligodendroglial tumors, age at diagnosis, tumor location and MGMT status, but not grade, size of tumor and treatment modality, were significantly associated with survival outcome (Table 3).

Discussion

This retrospective study explores the changes in the real-world treatment and survival trend in a large cohort of Chinese patients with newly diagnosed diffuse gliomas over the last couple of decades. GBM is the most common and lethal glioma type in adults. The results of several landmark clinical trials, primarily enrolling patients from western countries, have established a global consensus on the survival outcome of GBM patients who undergo standard treatment, including tumor resection, radiation and TMZ chemotherapy. The median OS in these trials ranged between 14.6 and 16.7 months, while the 2- and 5-year survival rate was around 30% and 10%, respectively[18–20]. However, conventional clinical trials employ strict criteria to enroll patients, such as age, performance status, history of chronic disease. These criteria cannot adequately reflect the actual effectiveness of treatment for a broader patient population in clinical practice. Genugten et al.[21] found that TMZ had less efficacy for GBM patents in the routine management, resulting in a survival benefit of only 18% at 2 years. Additionally, not all patients in the real-world setting receive the standard of care due to personal choice or financial difficulty. The worldwide epidemiological CONCORD-3 study[5] reveals that the net survival of GBM patients in the North America and Europe range from 10 to 24% at 2 years and 5 to10% at 5 years. These results indicate an inferior prognosis of GBM when compared to that of clinical trials. Consequently, assessment of

	HR	95% CI	*P*-value
GBM			
Gender (Female vs. Male)	0.87	0.70–1.08	0.208
Age (years)			
15–39	ref		
40–64	1.65	1.25–2.18	< 0.001
65–90	2.91	2.08–4.09	< 0.001
Tumor locations			
Supratentorial lobes	ref		
Supratentorial midline	1.43	1.11–1.85	0.006
Subtentorial	2.09	1.20–3.64	0.009
Maximal diameter (cm)			
<6	ref		
≥6	1.37	1.08–1.73	0.01
Not available	0.99	0.60–1.63	0.962
IDH status			
Wild-type	ref		
Mutant	0.42	0.22–0.78	0.009
Not available	1.16	0.83–1.61	0.39
MGMT promoter status			
Non-methylated	ref		
Methylated	0.43	0.23–0.81	< 0.001
Not available	0.87	0.57–1.12	0.20
Adjuvant treatment			
None or unknow	ref		
Radiation or chemotherapy	1.0	0.70–1.43	0.99
Both radio-chemotherapy	0.69	0.56–0.86	0.001
Astrocytomas			
Gender (Female vs. Male)	0.97	0.73–1.30	0.849
Age (years)			
15–39	ref		
40–64	2.04	1.50–2.77	< 0.001
65–90	5.31	3.02–9.34	< 0.001
Tumor locations			
Supratentorial lobes	ref		
Supratentorial midline	2.06	1.47–2.89	< 0.001
Subtentorial	0.90	0.47–1.74	0.754
Maximal diameter (cm)			
<6	ref		
≥6	1.14	0.81–1.60	0.445
Not available	0.86	0.52–1.43	0.561
WHO grade (3 vs. 2)	2.12	1.56–2.88	< 0.001
IDH status			
Wild-type	ref		
Mutant	0.22	0.13–0.38	< 0.001
Not available	0.72	0. 43-1.21	0.217
MGMT promoter status			
Non-methylated	ref		
Methylated	0.62	0.32–1.20	0.157
Not available	1.02	0.54–1.93	0.942
Adjuvant treatment			
None or unknow	ref		
Radiation or chemotherapy	0.76	0.53–1.08	0.128
Both radio-chemotherapy	0.60	0.43–0.86	0.004
Oligodendroglial tumors			
Gender (Female vs. Male)	1.48	0.76–2.88	0.225
Age (years)			
Continued			

	HR	95% CI	*P*-value
15–39	ref		
40–64	1.14	0.59–2.18	0.70
65–90	7.37	2.21–24.6	0.001
Tumor locations			
Supratentorial lobes	ref		
Supratentorial midline	4.73	2.43–9.18	<0.001
Subtentorial	63.9	10.7-381.2	<0.001
Maximal diameter (cm)			
<6	ref		
≥6	1.15	0.55–2.41	0.706
Not available	1.68	0.21–13.7	0.627
WHO grade (3 vs. 2)	1.48	0.76–2.88	0.255
MGMT promoter status			
Non-methylated	ref		
Methylated	0.09	0.02–0.49	0.006
Not available	0.91	0.25–3.29	0.891
Adjuvant treatment			
None or unknow	ref		
Radiation or chemotherapy	1.20	0.54–2.68	0.651
Both radio-chemotherapy	1.02	0.49–2.14	0.952

Table 3. Multivariate Cox regression analysis for diffuse gliomas. HR: hazard ratio; CI: confidence interval.

survival outcome in real-world conditions or at population level will provide deeper insight into the prognosis of diseases and implementation of clinical guidelines.

It is noteworthy that in CONCORD-3 study[5], the prognosis of GBM in the Chinese population is the highest globally with a 5-year survival rate of nearly 17%. Consistently, analysis of the data from a Chinese cancer registry network reveals a high survival rate (over 18% at 5 years) in patients diagnosed with primary malignant brain cancer, mainly GBM[22]. In our cohort, the estimated survival for histologically diagnosed GBM who received treatment between 2000 and 2020 was 37% at 2 years and 18.9% at 5 years. When integrating molecular pathology, the 5-year survival is 16.0% for GBM patients with wildtype IDH, while the median OS was 17 months. Additionally, a perspective study conducted by our team demonstrate that the median OS of GBM patients receiving standard treatments in our center exceeds 17 months[14]. These data indicate a relatively better prognosis for GBM in Chinese patients compared to global levels, and the results from western clinical trials. However, there are also conflicting reports. Two retrospective studies observed that the 5-year survival rate of Chinese patients with GBM was only between 6–9%[8,23]. The inherent limitation of retrospective studies and statistical bias may lead to such discrepancies in the observed survival of GBM. In addition to China, GBM patients from other Asian counties, including Japan, Korea and Singapore, also exhibit better survival rates compared to the worldwide average[5,24,25]. The CBTRUS and Surveillance, Epidemiology, and End Results registries (SEER) data also reveals that the survival of GBM was higher among patients with Asian ancestry than non-Hispanic Whites[26]. An additional interesting finding from a perspective randomized trial showed that Korean patients who underwent standard therapy plus tumor-treating fields (TTFs) had almost doubled the survival at 2 years compared to participants enrolled from the western countries[27]. These findings support a possibility of a better prognosis for GBM in the Asian population than in the western population[18–20]. It is well accepted that genetic alterations determine the evolution, progression and prognosis of tumors. Multiple genome-wide association studies (GWAS) have revealed single nucleotide polymorphisms (SNPs) associated with glioma susceptibility. Characteristics in cancer genomics is different between Asian-Pacific populations and Whites[28–30]. Additionally, a lower incidence of EGFR amplification in GBM has been observed in East Asian cohorts[31,32]. EGFR amplification is associated with a poor prognosis in GBM[33]. Older age at diagnosis is another risk factor for worse prognosis of GBM. A lower median age at diagnosis of GBM has been observed in East Asians, as well as Asian and Pacific Islander patients in the US (55–61 years) than in Whites (≥65 years)[25,28]. The median age of diagnosis of GBM in our cohort was 53 years old. The differences in onset age and genetic variance may be the reasons of the survival disparities of GBM between Asian and Western cohorts. The observed disparities in prognosis might also arise from the criteria used for pathological diagnosis and survival estimation. Therefore, developing a brain tumor-specific cancer registry system with unified standards in Asian countries is needed to better explain the regional disparities in outcome of gliomas.

The present study revealed that the estimated 5-year survival for astrocytoma and oligodendroglial tumors in the Chinese population was 58.5% and 80.7%, respectively, which is similar to the results of previous clinical trials[34–37].The procarbazine, lomustine and vincristine (PCV) regimen is recommended by US and European guidelines as the standard of care for oligodendroglial tumors[38,39]. However, procarbazine and lomustine have not been conveniently available in mainland China for an extended period. Due to its effectiveness in treating astrocytic tumors and its lower toxicity, TMZ has been widely used for oligodendroglial tumors in

China. In this cohort, the majority of patients with oligodendroglial tumors were also treated with TMZ rather than PCV. The survival outcomes of oligodendroglial tumors in this study provide real-world evidence for the satisfied effectiveness of TMZ chemotherapy. Randomized trials, including the NOA-04 and CODEL studies, are comparing the efficacy of TMZ with PCV for the treatment of oligodendroglial tumors[40,41]. However, recent results showed that first-line PCV/RT was associated with better OS outcomes compared with TMZ/RT in IDH-mut 1p/19q-codeleted grade 3 oligodendroglioma[42].

IDH status plays a crucial role in determining glioma diagnosis and prognosis. There is accumulating evidence that IDH-mut astrocytoma and oligodendroglioma, especially the latter, exhibit similar survival between grade 2 and 3 tumors[43,44]. To the best of our knowledge, we are the first to report similar survival trends in IDH-mut gliomas between WHO grade 2 and grade 3 in Chinese population. These findings would challenge the currently used clinical guidelines, which recommend different regimens based on tumor grading; specifically, postoperative adjuvant therapy is recommended for grade 3 gliomas, while grade 2 gliomas with low risks of recurrence do not require it. Reclassification and analyses of previous clinical trials according to current diagnostic criteria are necessary to provide updated guidance for glioma treatment. For IDH-wt gliomas, the completion of molecular testing is required for tumor classification, grading and prognostication. In histologically lower-grade gliomas with wildtype IDH, if chromosome 7 gains or 10 losses, or if EGFR amplification or TERT promoter mutation was positive, these tumors should be upgraded to molecular GBM[45]. Otherwise, pediatric-type diffuse gliomas should be differentiated.

In the present study, we observed a significant gain in the survival outcome of astrocytomas and oligodendroglial tumors during the period from 2000 to 2020, and a trend of a slight increase in the 2-year survival rate for GBM. The advancement of treatment pattern is the main reason for the improvement in survival of glioma. Regarding to GBM, the increased trend in survival was mainly between 2000 and 2006 and 2007–2013. In our cohort, there is an elevation in the proportion of GBM patients receiving TMZ chemotherapy since 2007, the year mainland China approved TMZ for treating GBM, indicating a positive impact on the prognosis of GBM in the Chinese population. Advancements in radiation therapy and surgical techniques are also crucial factors associated with enhanced prognosis. Moreover, multivariate and comparative analysis demonstrated postsurgical treatment as an independent prognostic factor for better survival in glioblastoma and astrocytomas. Although short-term survival has improved, we did not observe a significant increase in the 5-year survival rates for GBM patients in this study, suggesting that further widespread promotion of foundational treatment, including TMZ and TTFs, is essential for increasing survival at the population level. Additionally, there is a need to explore more effective treatment modalities, such as immunotherapy and molecular targeted individualized therapy, to improve long-term survival for GBM. A recent study demonstrates the safety and promising effectiveness of oncolytic virus therapy in treating progressive GBM[46], leading to its first approval for glioma treatment in Japan.

Due to its retrospective nature, this study has some limitations. First, the rate of loss to follow-up is relatively high among patients with LGG, potentially leading to an overestimation of their survival time. Second, the details of treatments could not be collected for all patients. For instance, the extent of tumor resection is not included in the statistics because postoperative MR examinations were not performed for a significant number of patients treated during the early period. Additionally, some patients did not follow standard of care. The interval between surgery and the initiation of adjuvant treatment may exceed guideline recommendations due to the suboptimal postoperative recovery of some patients. For patients tolerated to TMZ, they may receive chemotherapy beyond six cycles. The impact of these non-standard intervention on clinical outcomes remains unclear and need further investigation. Furthermore, findings of this study are based on Chinese populations and may not be fully generalizable to other populations due to potential ethnic and geographic variations.

In conclusion, our analysis of survival outcomes of a large cohort of Chinese patients with gliomas reveals that the prognosis for various subtypes of diffuse gliomas, particularly GBM, is among the most favorable compared to global levels. The 5-year survival rate was 16–19% for GBM. These findings indicate significant geographical disparities in glioma survival between the West and the East, which should be addressed in clinical consultations with Asian patients. Improved prognosis expectations may influence their treatment choices. We also observed an increased trend for patients receiving adjuvant radiochemotherapy over the past 20 years, that probably contributes to the survival gains in this cohort. This represents real-world evidence supporting the promotion of comprehensive treatment for gliomas in clinical practice. Additionally, molecular pathology is closely associated with glioma diagnosis and survival outcome. Reanalysis of previous clinical trials according to current diagnostic criteria is necessary to provide updated guidance for glioma treatment.

Data availability

The clinical data presented in this study has been uploaded onto the Research Data Deposit platform (www.researchdata.org.cn), with the approval RDD number as RDDA2024255949. The raw data of genomic sequencing generated in this study is deposited in the Genome Sequence Archive in National Genomics Data Center, China National Center for Bioinformation (https://ngdc.cncb.ac.cn/gsa-human), with the accession number as HRA001707. These data are available from the corresponding author on reasonable request.

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Author contributions

D.L. and Y.C. designed this study and wrote the first draft of the manuscript. T.W., X.J., C.K. and X.Z. collected and analyzed the clinical data. Y.L. and J.W. analyzed the data of neuro-imaging. J.Z. and K.S. collated the pathological reports. Q.Y., C.G., and Y.M. collated the data of chemotherapy. S.W. collated the data of radiotherapy. Z.C. supervised this study and revised the manuscript.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

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