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Long term follow-up and outcomes in adult patients with thalamic gliomas

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ABSTRACT

Objectives: To investigate the optimal treatment and prognosis of thalamic glioma in adult patients.
Patients and methods: We retrospectively analyzed the adult patients with thalamic glioma admitted to our hospital from May 2005 to September 2016. Patients were divided into two groups according to their treatment: surgery-based combined treatment and intensity modulated radiation therapy (IMRT)-based treatment. Univariate chi-square test and multivariate logistic regression were used to identify independent factors for the treatment modality. A log-rank test, adjusting for propensity score, was used to compare the overall survival (OS) and progression-free survival (PFS) of patients between the two groups.
Results: Fifty-eight adult patients with thalamic gliomas were included in the analysis. Of them, 31 were treated with surgery-based treatment, and 27 were treated with IMRT-based treatment. The overall survival (OS) and progression-free survival (PFS) of patients between the two groups were not significantly different (median OS 16.0 (range 1.0–163.0) months vs. 10.0 (range 1.0–118.0) months, $p = 0.344$ and median PFS 10.0 (range 1.0–163.0) months vs. 6.0 (range 1.0–118.0) months, $p = 0.464$, respectively) even after adjusting for potential confounding factors.
Conclusions: The OS and PFS of adult patients with thalamic glioma were not significantly different between patients in the surgical group and in the IMRT group. IMRT might be an acceptable alternative to surgery for adult patients with unresectable thalamic glioma.

1. Introduction

The treatment of thalamic glioma is controversial due to the high morbidity and mortality associated with surgical resection of this deeply located tumor. Previous studies from us and others have discussed the effectiveness of surgical resection of thalamic gliomas in children [1–9] or in patients from all age groups [10–14], while it was seldom discussed in only adult patients or in comparison of the effectiveness between different treatment modalities. It is still uncertain which treatment modality is more beneficial to the prognosis of adult patients with thalamic glioma and what subgroup might benefit from a radical surgical procedure or from radiotherapy, such as intensity modulated radiation therapy (IMRT), combined with or without chemotherapy.

Therefore, in the present study, we retrospectively studied a cohort of adult patients with thalamic gliomas admitted to our hospital over an 11-year period. The aims of this study were to examine which treatment modality, surgical resection-based treatment or IMRT-based treatment, is beneficial for patient prognosis and whether IMRT-based treatment is an acceptable alternative therapy for unresectable thalamic glioma.

2. Patients and methods

2.1. Patient enrollment

Adult patients (age ≥ 18) who were newly diagnosed with primary thalamic gliomas at Huashan Hospital according to brain MRI between May 2005 and September 2016 were enrolled in this study. Patients who received radiotherapy before enrollment were ruled out of the final analysis. Brain Magnetic Resonance Spectroscopy (MRS) was used to determine whether the thalamic lesion was malignant. If a malignant tumor was highly suspected, treating physician then made a

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comprehensive evaluation for performance status, health condition and brain images of the patient, and decided which treatment modality was used according to the following indications:

Surgical indications: 1) patients who had poor performance status; 2) tumor had an obvious mass effect on MRI, including severe brain edema; 3) tumor was indiscrete and enhanced well on contrasted MRI; and 4) tumor vaguely enhanced or non-enhanced on contrasted MRI but with well-defined margins on T2-weighted or T2 flair MRI.

Biopsy + IMRT indications: 1) patients who had poor cardio-pulmonary function and could not be able to tolerate radical surgery; 2) tumor blood supply was not abundant on CT perfusion imaging and was expected to had low risk of bleeding following biopsy; 3) tumors that were diffuse, multifocal or involving the posterior limb of the internal capsule were generally considered for a biopsy.

The study was approved by the Huashan hospital ethics committee. All methods were performed in accordance with the relevant guidelines and regulations. Informed consent was obtained from all participants or their legal guardians before treatment.

2.2. Data collection and definition

The symptoms, signs and neurological status were examined before and after treatment (within 2 weeks) and included raised intracranial pressure (ICP) (such as headaches, nausea, vomiting or papilloedema), motor deficits, ataxia, dyspraxia, tremor, facial paralysis, seizures, dysphasia, sensory dysfunction (such as numbness, hypoalgesia or hyperalgesia of the limbs), visual disturbance (including diplopia, oculomotor defects, blurred or impaired vision) and mental changes (including apathy, somnolence, fatigue and memory impairment). The patients' performance status was assessed using the Karnofsky Performance Scale (KPS), with scores ranging from 0 (dead) to 100 (normal or no complaints). The handedness of the patients was evaluated before operation. Complications or adverse events included high fever, electrolyte disturbances, intracerebral hemorrhage, and new onset of motor deficits (transient and permanent motor deficits), apathy, dysphasia and acute radiation-induced cerebral edema or necrosis.

Other data collected included age, gender, symptom duration before admission, brain magnetic resonance imaging (MRI) findings (including tumor location, volume, edema, hydrocephalus, extension to adjacent structure and tumor enhancement), surgical approaches, extent of tumor resection, ventriculoperitoneal (VP) shunt, ventricular reservoir implant surgery, histopathology and molecular pathology findings (p53, histone 3 K27M mutation, MGMT, EGFR, Ki67, IDH1) by immunohistopathology. The histopathological diagnosis was based on the classification system of central nervous system set out by the World Health Organization (WHO) classification system. Follow up neurological and radiological examinations were performed immediately, two weeks and three months after surgery, and then every six months. The outcome was evaluated by OS and PFS. PFS was calculated from the date of diagnosis to the date that an unambiguous increase in tumor size was radiologically proven or the date of death in patients who had not been diagnosed with progression of disease. OS was measured from the date of diagnosis to the date of death or the last follow-up date on which the patient was reported to be alive.

2.3. Treatment

Adult patients were classified into surgical group and IMRT group according to treatment modality. Patients in the surgical group received surgical-based combination therapy, including tumor resection with or without three-dimensional conformal radiotherapy (3DCRT) and/or chemotherapy. Patients in the IMRT group underwent stereotactic biopsy before receiving IMRT-based combined treatment, including IMRT with or without chemotherapy.

Table 1
Baseline clinical characteristics of adult patients with thalamic glioma.

	Surgical group (n = 31)	IMRT group (n = 27)	OR (95% CI)	p value
Gender male[a]	20 (64.5)	15 (55.6)	1.46 (0.53 − 4.15)	0.593
Age[b]	40.3 ± 13.9	37.1 ± 13.8	t = 0.872	0.387
Duration before admission (month)[c]	1.0 [0.5 − 3.0]	1.0 [1.0 − 4.0]	U = 336.0	0.197
Initial symptoms[a]				
Raised ICP	19 (61.3)	14 (51.9)	1.47 (0.55 − 4.08)	0.596
Motor deficits	10 (32.3)	6 (22.2)	1.67 (0.49 − 5.94)	0.557
Sensory dysfunction	11 (35.5)	11 (40.7)	0.80 (0.28 − 2.26)	0.788
Visual disturbance	7 (22.6)	7 (25.9)	0.83 (0.25 − 2.74)	> 0.999
Dysphasia	1 (3.2)	3 (11.1)	0.27 (0.02 − 1.93)	0.329
Mental changes	9 (29.0)	7 (25.9)	1.17 (0.37 − 3.61)	> 0.999
Seizures	2 (6.5)	2 (7.4)	0.86 (0.13 − 5.83)	> 0.999
Ataxia/ dyspraxia/ tremor	2 (6.5)	0 (0)	4.66 (0.21 − 101.5)	0.494
Facial paralysis	2 (6.5)	1 (3.7)	1.79 (0.15 − 20.95)	> 0.999
KPS[c]	70 [60 − 80]	80 [80 − 90]	U = 230.5	0.002
MRI findings[a]				
Location				0.380
Right	12 (38.7)	12 (44.4)	0.79 (0.28 − 2.25)	0.790
Left	18 (58.1)	12 (44.4)	1.73 (0.61 − 4.91)	0.430
Bilateral	1 (3.2)	3 (11.2)	0.27 (0.03 − 2.73)	0.329
Edema	21 (67.7)	16 (59.3)	1.44 (0.50 − 4.31)	0.588
Hydrocephalus	16 (51.6)	13 (48.1)	1.15 (0.41 − 3.23)	> 0.999
Tumor extension	23 (74.2)	19 (70.4)	1.21(0.38 − 3.84)	0.776
Enhancement	25 (80.6)	18 (66.7)	2.08 (0.63 − 6.90)	0.247
Volume[b] (ml)	21.8 ± 14.8	25.4 ± 14.7	t = 0.941	0.351

IMRT, intensity modulated radiation therapy; OR, odds ratio; CI, confidence interval; ICP, intracranial pressure; KPS, Karnofsky Performance Scale; MRI, magnetic resonance imaging. [a] Data are compared by Chi-square test or Fisher's exact test and results are showed as number (%). [b] Data are compared by Student's t-test and results are showed as mean ± standard deviation (SD). [c] Data are compared by Mann–Whitney U test and results are showed as medians and interquartile ranges [IQR].

2.3.1. Surgery

Surgical approaches were classified into two categories, interhemispheric middle line approach and trans-cortical approach, based on the specific location of the tumor and its direction of growth. The former mainly included a trans-corpus callosal approach, while the latter included a trans-superior parietal approach, a trans-frontal approach and a trans-sylvian approach. Surgical procedures were performed under general anesthesia, and the anatomy of the tumor was assessed using intraoperative 3-D navigational MRI that was rigidly registered to the StealthStation neuro-navigator (Medtronic Surgical Technologies, Louisville, CO.). DTI examination was performed for all surgical patients before operations. To prevent injury to the corticospinal tracts, reconstructed corticospinal tracts acquired by pre-surgical DTI on the same side as the tumor were also registered to the StealthStation intraoperative neuro-navigator.

2.3.2. Imrt

Patients were treated with either 45 − 50 Gy (for WHO grade II glioma, administered in 25 fractions of 1.8–2.0 Gy each for five days per week over a period of 5 weeks) or 54 − 60 Gy (for WHO grade III–IV glioma, administered in 30 fractions of 1.8–2.0 Gy each for five days per week over a period of 6 weeks) prescribed to the International Commission of Radiological Units and Measurements reference point using a single phase IMRT technique in the IMRT group or the 3DCRT technique in the surgical group.

Table 2
Treatment, histopathology and outcome information of adult patients with thalamic glioma.

	Surgical group (n = 31)	IMRT group (n = 27)	OR (95% CI)	p value
Surgical details				
Surgical approaches[a]		NA	/	/
Trans-corpus callosal	16 (51.6)	NA	/	/
Trans-superior parietal	6 (19.4)	NA	/	/
Trans-frontal	5 (16.1)	NA	/	/
Trans-sylvian	4 (12.9)	NA	/	/
Extent of resectioin[a]				
Gross Total Resection (100%)	1 (3.2)	NA	/	/
Subtotal resection (70 − 99%)	23 (74.2)	NA	/	/
Partial resection (< 70%)	7 (22.6)	NA	/	/
Ventriculo-peritoneal shunt[a]	8 (25.8)	11 (40.7)	0.51 (0.16 − 1.54)	0.270
Ventricular reservoir implantation[a]	15 (48.3)	2 (7.4)	11.72 (2.36 − 58.24)	0.001
Adjuvant therapy[a]				
Chemotherapy	24 (77.4)	16 (59.3)	2.36 (0.75 − 7.37)	0.163
Radiochemotherapy	22 (71.0)	16 (59.3)	1.68 (0.56 − 5.01)	0.413
Molecular markers[a]				
p53 mutation	18 (58.1)	20 (74.1)	0.48 (0.16 − 1.48)	0.271
H3 K27M mutation, n = 31/25 [c]	17 (54.8)	21 (77.8)	0.23 (0.06 − 0.83)	0.024
MGMT, n = 23/23 [c]	17 (73.9)	14 (60.9)	1.82 (0.52 − 6.37)	0.530
EGFR, n = 10/19 [c]	5 (50.0)	10 (52.6)	0.90 (0.19 − 4.17)	> 0.999
IDH1, n = 15/17 [c]	0 (0)	0 (0)	/	/
Ki-67[b]	8 [5.0 − 20.0]	5 [2.0 − 10.0]	U = 304.0	0.073
Histopathology[a]				0.046
Diffuse astrocytoma	5 (16.1)	9 (33.3)	0.38 (0.11 − 1.34)	0.218
Anaplastic oligodendroglioma	0 (0)	2 (7.4)	0.16 (0.01 − 3.53)	0.212
Anaplastic astrocytoma	13 (41.9)	12 (44.4)	0.90 (0.32 − 2.56)	0.847
Glioblastoma multiforme	13 (41.9)	4 (14.8)	4.15 (1.16 − 14.92)	0.042
WHO classification				0.057
WHO grade I	0 (0)	0 (0)	/	/
WHO grade II	5 (16.1)	9 (33.3)	0.38 (0.11 − 1.34)	0.218
WHO grade III	13 (41.9)	14 (51.9)	0.67 (0.24 − 1.90)	0.598
WHO grade IV	13 (41.9)	4 (14.8)	4.15 (1.16 − 14.92)	0.042
Post-treatment symptoms[a]				0.031
Improvement	18 (58.1)	7 (25.9)	3.96 (1.29 − 12.10)	0.018
Not change	4 (12.9)	10 (37.0)	0.25 (0.07 − .093)	0.063
Deterioration	9 (29.0)	10 (37.0)	0.70 (0.23 − 2.09)	0.582
Complications/adverse events[a]	13 (41.9)	10 (37.0)	1.23 (0.43 − 3.54)	0.791
High fever	9 (29.0)	1 (3.7)	10.64 (1.25 − 90.64)	0.014
Electrolyte disturbances	2 (6.5)	0 (0)	4.66 (0.21 − 101.50)	0.494
Intracerebral hemorrhage	3 (9.7)	0 (0)	6.75 (0.33 − 136.90)	0.241
Transient motor deficits	5 (16.1)	3 (11.1)	1.54 (0.33 − 7.14)	0.712
Permanent motor deficits	3 (9.7)	0 (0)	6.75 (0.33 − 136.90)	0.241
Apathy	6 (19.4)	4 (14.8)	1.38 (0.35 − 5.52)	0.737
Dysphasia	3 (9.7)	3 (11.1)	0.86 (0.16 − 4.65)	> 0.999
Radiation-induced cerebral edema/necrosis	/	10 (37.0)	/	/
Survival[a]				
One-year PFS	13 (41.9)	8 (29.6)	1.72 (0.58 − 5.11)	0.415
Two-year PFS	5 (16.1)	3 (11.1)	1.54 (0.33 − 7.14)	0.712
One-year OS	19 (61.3)	10 (37.0)	2.69(0.93 − 7.80)	0.114
Two-year OS	9 (29.0)	6 (22.2)	1.43 (0.43 − 4.72)	0.765

IMRT, intensity modulated radiation therapy; OR, odds ratio; CI, confidence interval; NA, not applicable; H3, histone 3; MGMT, O6-methylguanine-DNA methyltransferase; EGFR, epidermal growth factor receptor; IDH1, isocitrate dehydrogenase 1; n, number; WHO, World Health Organization; PFS, progression-free survival; OS, overall survival. [a] Data are compared by Chi-square test or Fisher's exact test and results are showed as number (%). [b] Data are compared by Mann–Whitney *U* test and results are showed as medians and interquartile ranges [IQR]. [c] The number of patients who tested H3 K27 M mutation was 56 (31 in surgical group and 25 in IMRT group), MGMT was 46 (23 in surgical group and 23 in IMRT group), EGFR was 29 (10 in surgical group and 19 in IMRT group) and IDH1 was 32 (15 in surgical group and 17 in IMRT group).

2.3.3. Chemotherapy

The Stupp protocol was used in both groups of patients [15].

Tumor resection analysis. The tumor volumes (cm3) were measured using pre- and postoperative imaging by a single experienced neurosurgeon who was blinded for surgical approaches. The extent of tumor resection, determined by surgery record or comparison of pre- and postoperative contrast-enhancing T1-weighted MRI or T2-weighted MRI for tumors that could not be enhanced, was calculated using the following formula: (pre-operative tumor volume − postoperative tumor volume)/pre-operative tumor volume. Each resection was then graded as a gross total resection (GTR, 100%), subtotal resection (STR, 70 − 99%) and a partial resection (PR, < 70%).

2.4. Follow-up evaluation

Follow-up information was obtained from radiotherapy records, hospital charts, referring physicians and the patient, or occasionally from the patient's relatives through interviews performed at outpatient clinics or over the telephone by physicians.

2.5. Statistics analysis

All statistical analyses were performed using STATA software (version 12.0; STATA Corporation, College Station, TX). Descriptive data are expressed as n (%), means ± standard deviation or medians and interquartile range. The χ^2 test or Fisher's exact test was used for the

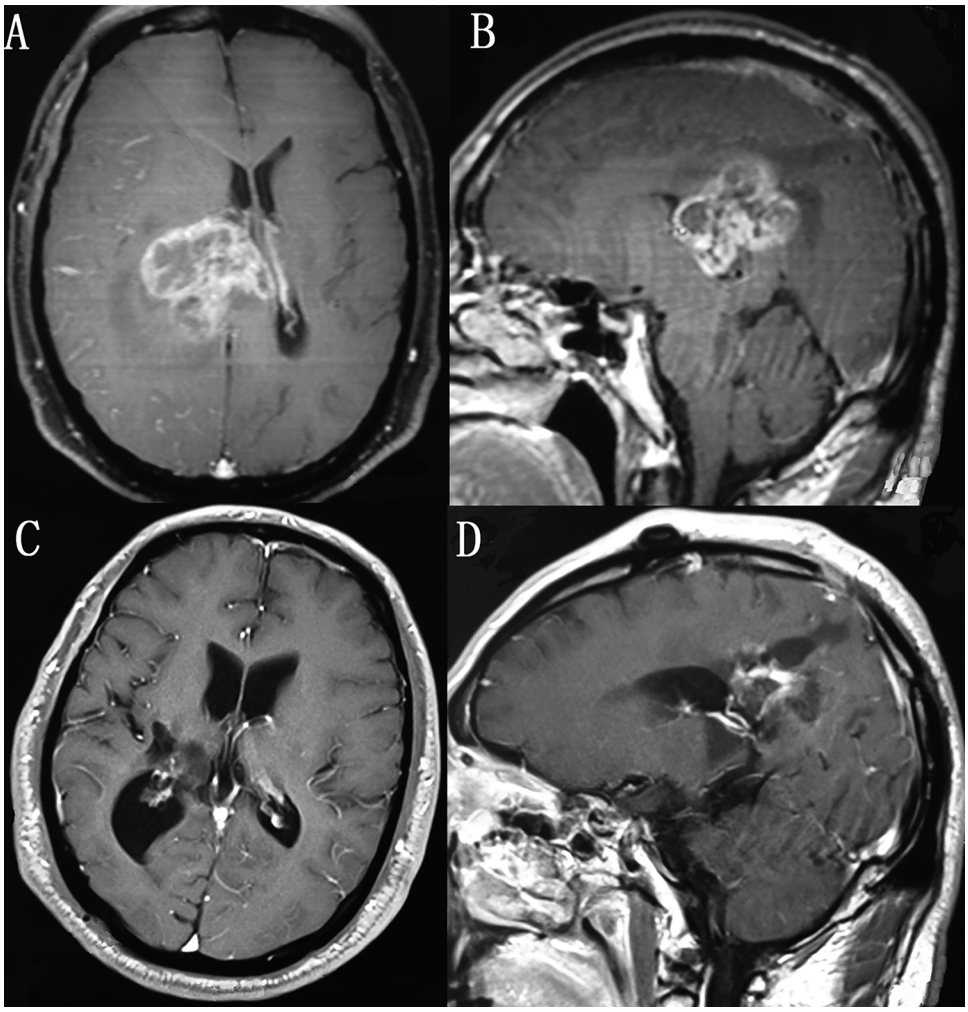

Fig. 1. This 50-year-old male patient presented with intermittent headache associated with a left upper limb tremor. Axial (A) and sagittal (B) contrast T1-weighted MRI revealed an enhanced right thalamic tumor. The tumor was removed via the right trans-superior parietal lobule approach. The histopathological diagnosis was diffuse astrocytoma, WHO grade II. Ventricular reservoir implantation was performed during tumor resection in order to drain necrotic tissue contained cerebrospinal fluid in a short period after surgery and to drain the cerebrospinal fluid in case of obstructive hydrocephalus. This patient also received adjuvant chemo-radiotherapy. Axial (C) and sagittal (D) contrast T1-weighted MRI demonstrating no tumor recurrence two years after tumor resection. This patient was still alive with well self-care ability of daily life at last follow-up. MRI, magnetic resonance imaging; WHO, World Health Organization.

comparison of categorical variables between surgical and IMRT groups. The results are reported as odds ratio (OR) with a 95% confidence interval (CI). Normally and non-normally distributed continuous variables were compared with Student's *t*-test and the Mann–Whitney *U* test, respectively.

Multivariate logistic regression was performed to investigate independent factors for the treatment modality. The backward mode with a p value threshold of 0.5 for elimination was used for logistic regression. A propensity score, which represented the predicted probability of having undergone tumor resection, was calculated using variables ($p < 0.1$) that were determined previously by logistic regression. The propensity score was used to adjust potential confounding factors between the two groups. Survival curves were based on Kaplan–Meier estimates with the use of a log-rank test to compare survival distributions.

3. Results

3.1. Clinical characteristics

Between May 2005 and September 2016, a total of 65 adult patients (age ≥ 18) were newly diagnosed with primary thalamic gliomas at Huashan Hospital. Among them, seven patients were ruled out because of pre-surgical radiotherapy, and finally 58 patients entered into the final analysis (31 underwent tumor resection and 27 underwent IMRT). The date of the last follow-up was December 2019. Their baseline clinical characteristics were list in Table 1. Treatment information, post-treatment symptoms, histopathology results and outcome are listed in Table 2. The representative cases in surgical and IMRT group were presented in Fig. 1 and 2, respectively.

3.2. Propensity score matching (PSM)

The baseline clinical characteristics that differed ($p < 0.50$) between the surgical and IMRT groups and age were entered into a multivariable logistic model to predict independent factors of treatment modality for thalamic glioma, and the predicted probability (propensity score) of being subjected to surgical resection was then calculated to adjust the selection bias and confounding factors (Table 3).

Finally, preoperative KPS (adjusted OR, 0.90; 95% CI, 0.83 − 0.96; p = 0.003) and enhancement on contrast MRI (adjusted OR, 4.12; 95% CI, 0.77 − 22.05; $p = 0.098$) (both variables had a p value < 0.1) were included in the PSM test. The baseline clinical characteristics of adult patients with thalamic glioma after PSM are listed in Table 4.

3.3. Relationship between treatment modality and OS and PFS

The median OS and PFS time were 11.5 months (range 1.0–163.0 months) and 7.0 months (range 1.0–163.0 months), respectively, for all adult patients with thalamic gliomas in this cohort, and 3 patients were still alive at the last follow-up: two in the surgical group and one in the IMRT group. The median OS and PFS for patients in the surgical group was 16.0 months (range 1.0–163.0 months) and 10.0 months (range 1.0–163.0 months), respectively, and 10.0 months (range 1.0–118.0 months) and 6.0 months (range 1.0–118.0 months), respectively, in the IMRT group.

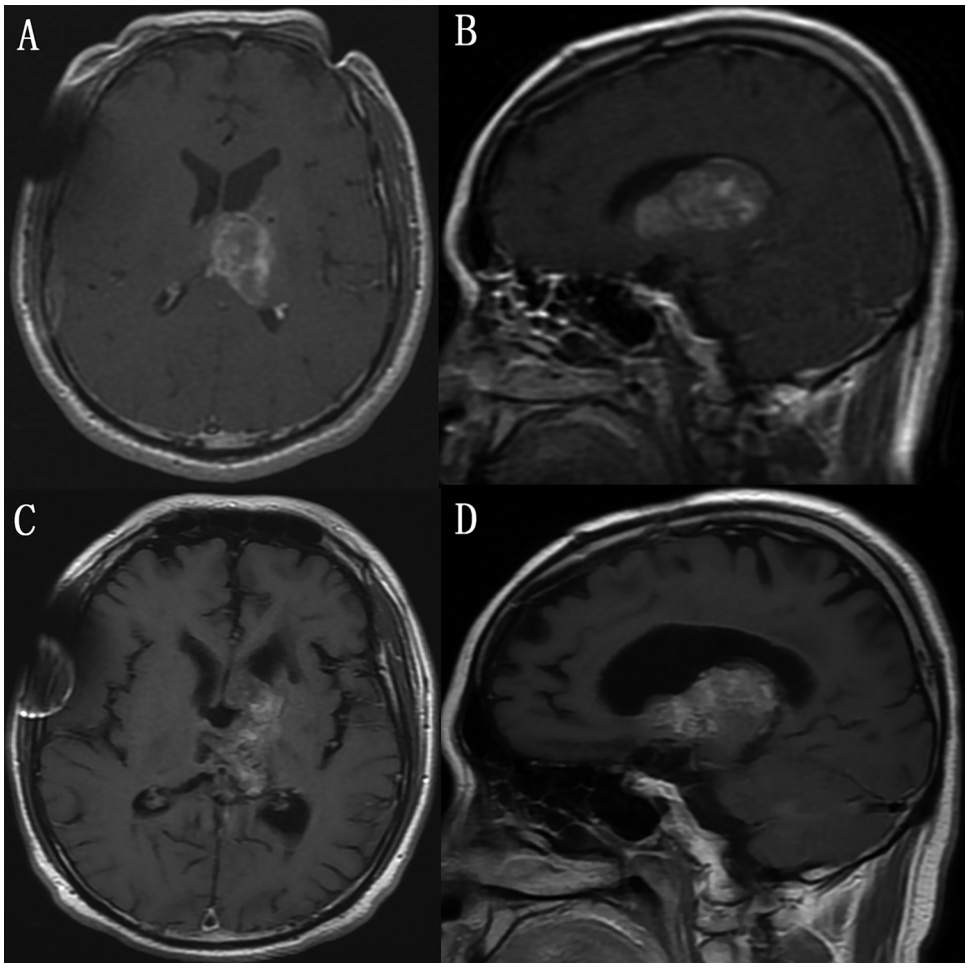

Fig. 2. This 49-year-old male patient discovered his left thalamic tumor fortuitously in physical examination (head CT) four years before admission to our hospital, when he had no symptoms and did not receive any medical treatment. Two years later, he suffered progressive headache and received Cyber Knife Stereotactic Radiation Therapy and 10 courses of temozolomide chemotherapy, during which ventriculoperitoneal shunt was performed because of obstructive hydrocephalus. Four years after initial discovery of the tumor, this patient came to our hospital. Axial (A) and sagittal (B) contrast T1-weighted MRI revealed an enhanced left thalamic tumor. He received IMRT treatment and temozolomide chemotherapy after tumor biopsy. The histopathological diagnosis was anaplastic astrocytoma, WHO grade III. Four and a half years later, axial (C) and sagittal (D) contrast T1-weighted MRI revealed that the tumor had shrunk and no recurrence was observed. This patient was still alive with well self-care ability of daily life at 118 months following surgery. CT, computed tomography; MRI, magnetic resonance imaging; IMRT, intensity modulated radiation therapy; WHO, World Health Organization.

Table 3
Independent predictors of treatment modality.

	Adjusted OR (95% CI)	p Value
Age	1.03 (0.98 – 1.09)	0.210
Duration before admission	0.90 (0.78 – 1.05)	0.197
Dysphasia	0.30 (0.02 – 4.06)	0.362
Ataxia/dyspraxia/tremor	/	/
KPS	0.90 (0.83 – 0.96)	0.003
Location	0.49 (0.15 – 1.57)	0.229
Enhancement	4.12 (0.77 – 22.05)	0.098
Volume	0.99 (0.94 – 1.03)	0.557

OR, odds ratio; CI, confidence interval; ICP, intracranial pressure; KPS, Karnofsky Performance Scale.

Patients in the surgical group are more likely to have a higher rate of one-year OS than patients in the IMRT group. The differences of OS and PFS between different treatment modalities were not statistically significant ($p = 0.344$ and $p = 0.464$, log-rank test, Fig. 3A and B). In addition, the differences of OS and PFS between the surgical and IMRT group were still not statistically significant ($p = 0.576$ and $p = 0.648$, log-rank test, Fig. 3C and D) after adjusting the selection bias and confounding factors by PSM.

4. Discussion

Thalamic gliomas account for 1–5% of brain tumors and are more common in children and adolescents than that in adults [7,10,16,17]. It is reported that only 1% of adult intracranial tumors primarily occurred in the thalamic region [18]. Although treatments for children with thalamic glioma have been described [1–9], studies that focus only on adult patients are rare.

The median or mean survival of patients with thalamic gliomas ranged from 12 to 120 months in different studies [3–5,13]. The one- and two-year OS ranged from 53.8%–80% and 20.7%–65%, respectively [3,13,17]. However, previous studies reported patients with thalamic gliomas were only based on groups of children [3–9,17,19], or groups that spanned all age groups [10,13] or reported on a series of patients including cases not only with thalamic tumors but also with brainstem tumors [13], which made interpretation of their findings less convincing. Moreover, there is some evidence suggesting that thalamic gliomas in adults respond poorer to surgical resection than gliomas in children younger than 18 years of age and thus adult patients have shorter survival times than children [10,13,16,20]. Therefore, it is necessary to compare the survival data of this series with the data only from adult patients included in the previous studies.

The median OS and PFS of adult patients with thalamic glioma from the previous studies ranged from 6 to 20 months and 5.3–10.75 months respectively. This is generally similar to our study, in which median OS and PFS are 11.5 months and 7.0 months, respectively, for all adult patients with thalamic gliomas, regardless of the treatment modality. However, the discrepancies in the baseline characteristics between the surgical and IMRT groups may result in bias in patient selection and survival analysis. Therefore, to minimize this bias, a propensity score, which was calculated using variables that had p value < 0.1 (pre-operative KPS and tumor enhancement) in the logistic regression to predict the treatment of surgical resection, was entered into the predictive model to adjust for potential confounding. The results showed that tumor resection indeed prolonged patient OS and PFS; however, the

Table 4
Baseline clinical characteristics of adult patients with thalamic glioma after propensity score matching (PSM).

	Surgical group (n = 21)	IMRT group (n = 21)	OR (95% CI)	p value
Gender male[a]	13 (61.9)	10 (47.6)	1.79 (0.57 – 6.21)	0.536
Age[b]	38.1 ± 14.9	37.5 ± 13.5	t = 0.130	0.897
Duration before admission (month)[c]	0.5 [0.3 – 2.5]	1.0 [1.0 – 3.0]	U = 156.0	0.103
Initial symptoms[a]				
Raised ICP	12 (57.1)	15 (71.4)	0.53 (0.17 – 1.86)	0.520
Motor deficits	6 (28.6)	3 (14.3)	2.40 (0.57 – 9.73)	0.454
Sensory dysfunction	7 (33.3)	8 (38.1)	0.81 (0.22 – 2.87)	> 0.999
Visual disturbance	4 (19.0)	6 (28.6)	0.59 (0.16 – 2.21)	0.719
Dysphasia	1 (4.8)	0 (0)	3.15 (0.12 – 81.74)	> 0.999
Mental changes	5 (23.8)	5 (23.8)	1.00 (0.24 – 4.14)	> 0.999
Seizures	1 (4.8)	0 (0)	3.15 (0.12 – 81.74)	> 0.999
Ataxia/dyspraxia/tremor	2 (9.6)	0 (0)	5.51 (0.25 – 122.10)	0.488
Facial paralysis	2 (9.6)	1 (4.8)	2.11 (0.18 – 25.17)	> 0.999
KPS[c]	80 [70 – 90]	80 [80 – 90]	U = 173.5	0.225
MRI findings[a]				
Location				0.317
Right	9 (42.9)	8 (38.1)	1.22 (0.35 – 4.19)	> 0.999
Left	12 (57.1)	10 (47.6)	1.47 (0.43 – 4.95)	0.758
Bilateral	0 (0)	3 (14.3)	0.12 (0.01 – 2.54)	0.232
Edema	15 (71.4)	14 (66.7)	1.25 (0.34 – 4.64)	> 0.999
Hydrocephalus	10 (47.6)	11 (52.4)	0.83 (0.25 – 2.78)	> 0.999
Tumor extension	14 (66.7)	14 (66.7)	1.00 (0.28 – 3.61)	> 0.999
Enhancement	17 (81.0)	15 (76.2)	1.70 (0.40 – 7.20)	0.719
Volume[b] (ml)	21.5 ± 15.9	27.9 ± 15.1	t = 1.338	0.188
WHO classification				0.320
WHO grade I	0 (0)	0 (0)	/	/
WHO grade II	3 (14.3)	7 (33.3)	0.33 (0.07 – 1.53)	0.277
WHO grade III	11 (55.3)	10 (74.6)	1.21 (0.36 – 4.06)	> 0.999
WHO grade IV	7 (33.3)	4 (19.0)	2.13 (0.47 – 7.42)	0.484

IMRT, intensity modulated radiation therapy; OR, odds ratio; CI, confidence interval; ICP, intracranial pressure; KPS, Karnofsky Performance Scale; MRI, magnetic resonance imaging. [a] Data are compared by Chi-square test or Fisher's exact test and results are showed as number (%). [b] Data are compared by Student's *t*-test and results are showed as mean ± standard deviation (SD). [c] Data are compared by Mann–Whitney *U* test and results are showed as medians and interquartile ranges [IQR].

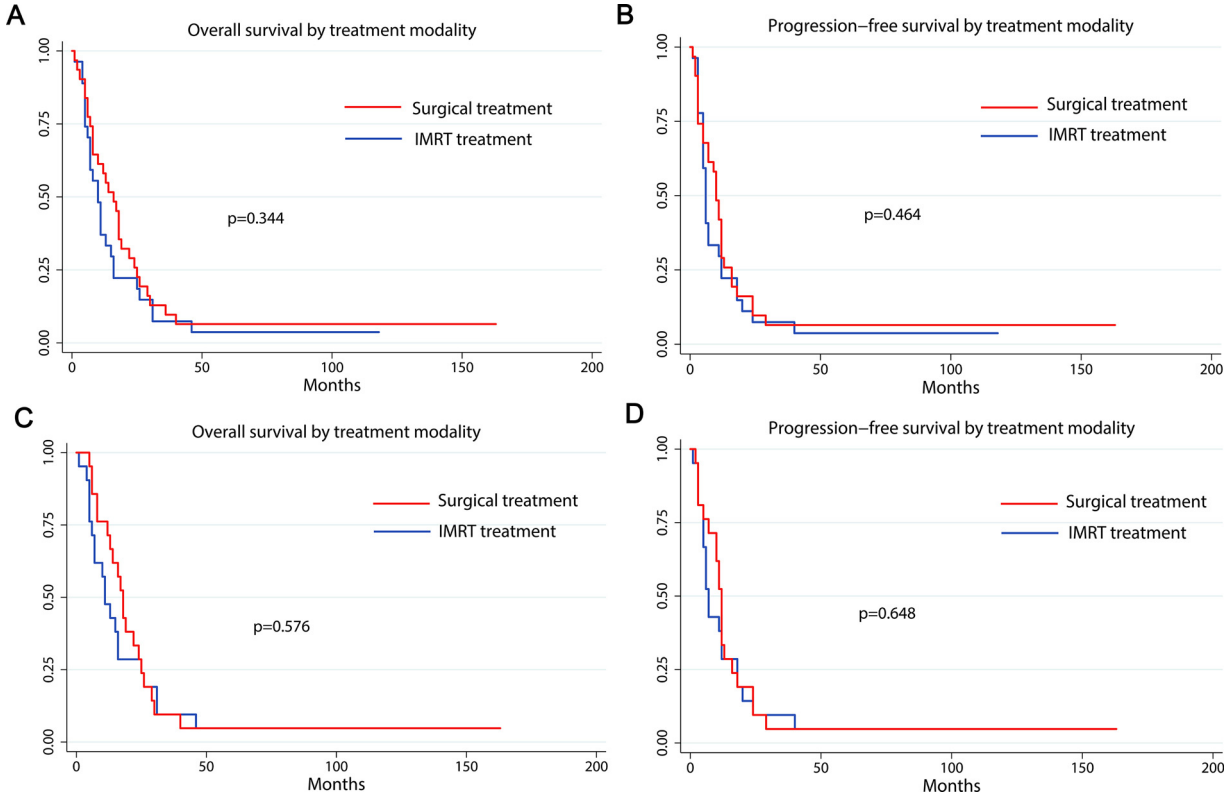

Fig. 3. Overall survival (A) and progression-free survival (B) of adult patients who underwent surgical based combinational treatment versus those who underwent IMRT-based combinational treatment. After adjusting the selection bias and confounding factors by propensity score matching, the differences of overall survival (C) and progression-free survival (D) between the surgical and IMRT groups were still not statistically significant. IMRT, intensity modulated radiation therapy.

differences did not reach statistical significance ($p < 0.05$), even after adjusting confounding factors, compared with patients in the IMRT group.

Previous studies of ours and of other authors have suggested that the GTR is associated with prolonged OS of patients with thalamic glioma [2,5,8,10–12,14,21–23]. In the present study, the rate of STR (76.3%) was relatively higher compared with that in previous studies (18.2–80.0% for adult patients), and the GTR rate (5.3%) was relatively lower than that in those studies (0–73.3% for adult patients). This probably reduced the positive impact of surgery on the survival of patients, narrowing the differences in OS and PFS of patients between the surgical and IMRT groups.

It is challenging to surgically remove thalamic glioma, since it is deeply located in the brain and adjacent to vital functional area. There was a high rate of post-operative complications reported by previous studies [5,6,11,14,16,20]. Although surgical resection is the first choice for the treatment of thalamic glioma, it is necessary to find an effective and feasible alternative treatment to surgery, especially for tumor that is not capable of being surgically removed or for patients of advanced age and/or with complications. IMRT technique is gaining widespread acceptance in the treatment of malignant tumor, including high grade and unresectable glioma. It is proven to be superior to conventional 3DCRT with better target coverage irrespective of intracranial tumor location and simultaneously reduced radiation to the surrounding normal brain tissue, which make patients more tolerant to IMRT treatment than to 3DCRT [24,25]. In this study, patients in IMRT group had lower rate of complications and adverse events than those in surgical group (Table 2). This suggested that patients had a well tolerance to IMRT treatment, and it was safe for adult patients with thalamic glioma to receive IMRT treatment. In addition, since surgical resection did not statistically significantly prolong the OS and PFS of patients compared with IMRT treatment, we considered that IMRT therapy might be an effective and safe alternative treatment for thalamic glioma.

In the previous studies, there were only three that reported the relationship between tumor molecular features and the outcome of adult patients with thalamic gliomas [26–28]. *H3F3A* K27M mutation is frequently observed in diffuse midline glioma, such as thalamic glioma, and is considered as a biomarker for high-grade glioma. Aihara et al. found that thalamic gliomas from young adults, such as those from children and adolescents, frequently harbored the *H3F3A* K27M mutation. However, *H3F3A* K27 M mutation and *MGMT* methylation in thalamic gliomas were not determinants of OS and PFS in adult patients [27]. Similar results were also reported by Jie Feng et al., whose study found that although the *H3F3A* K27 M mutation was frequently observed in the adult brainstem and thalamic gliomas, this mutation tended to be associated with a poorer prognosis only in brainstem gliomas but not in thalamic gliomas [26].

5. Conclusion

In this study, we found that there were no statistically significant differences in OS and PFS between patients in the surgical group and the IMRT group. IMRT might be an effective and safe alternative treatment for thalamic glioma, especially for unresectable thalamic glioma or for patients of advanced age and/or with complications.

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CRediT authorship contribution statement

Zhiqi Li: Conceptualization, Methodology, Investigation, Formal analysis, Data curation, Writing - original draft. **Hanfeng Wu:** Conceptualization, Methodology, Investigation, Data curation. **Biwu Wu:** Conceptualization, Methodology, Investigation, Data curation, Resources. **Jiaying Lyu:** Methodology, Formal analysis, Validation, Visualization. **Yikui Liu:** Data curation, Resources. **Chao Tang:** Resources, Validation. **Wei Hua:** Resources, Validation. **Shukun Hu:** Supervision. **Yang Wang:** Conceptualization, Data curation, Supervision. **Yi Zhang:** Conceptualization, Methodology, Writing - review & editing, Data curation, Supervision.

Declaration of Competing Interest

The authors declare no competing interests.

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