Risk Factors for Early Hydrocephalus on Post Unilateral Thalamic Tumor Resection

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Objective: The outcome of surgical treatment for thalamic tumors is poor. Hydrocephalus is one of the most frequent postoperative complications after unilateral thalamic tumor resection. This study examined the relationship between surgical approaches, pathological grade, image characteristics, preoperative complications, extent of resection, and incidence of postoperative hydrocephalus.

Methods: The study retrospectively reviewed clinical data from 80 patients who underwent resection of thalamic tumors between 2015 and 2021. Data on patient survival and disease progression status were obtained retrospectively to calculate overall survival (OS) and progression free survival (PFS).

Results: No patients died during the perioperative period and two patients suffered postoperative coma. Tumors were totally resected in 44 cases (55 %), subtotally resected in 21 cases (26.25 %), and partially resected in 15 cases (18.75 %). Thirty-five cases of hydrocephalus occurred within 1 month after operation (43.75 %). Surgical approaches associated with hydrocephalus were as follows: hydrocephalus occurred in seven cases after trans-frontal lateral ventricle approach for tumor resection (62.9 %), in 17 cases after through parieto-occipital transventricular approach tumor resection (43.58 %), and in one case after trans-frontal lateral ventricle approach for tumor resection + third ventriculostomy (7.1 %). Postoperative muscle strength decrease occurred in 41 patients (51.25 %). Longer PFS and OS were correlated with degree of resection in patients with thalamic glioblastoma (P < 0.05) and had no relationship with hydrocephalus.

Conclusion: Surgical treatment of thalamic tumors is an effective therapeutic method. The incidence of postoperative hydrocephalus is not associated with tumor size, degree of tumor enhancement, peritumoral edema, tumor invasion, midline crossing, and pathological grade. The incidence of postoperative hydrocephalus was higher in patients with preoperative hydrocephalus and low resection degree, and lower in patients with endoscopic third ventriculostomy. The risk of early postoperative hydrocephalus in thalamic tumors is high. Intraoperative third ventriculostomy could reduce the incidence of early postoperative hydrocephalus. PFS and OS were longer in patients with thalamic glioblastoma with a high resection degree (P < 0.05) and were not associated with hydrocephalus.

Keywords: thalamic tumors, hydrocephalus, therapeutic method, surgery, OS, PFS
INTRODUCTION

Thalamic tumors account for 5% of all brain tumors. The main pathological type is glioma, with lower proportions of lymphoma, cavernous angioma, and inflammatory lesions (1–3). The pathological grade of thalamic glioma is low in pediatric patients and high in adults (4). The thalamus is located in the center of brain and connected with the hypothalamus, ventriculus tertius, lateral ventricles, basal ganglia, and aqueduct of the midbrain. As a result, surgery on the thalamus is technically difficult and associated with a high risk of postoperative complications, leading to unfavorable prognosis: high mortality and disability rate. Recent advances in neuroimaging and surgical techniques have made surgical resection of thalamic tumors feasible and have reduced the morbidity which associated with this approach (5–7). Surgical resection combined with adjunct therapies, such as radiotherapy and chemotherapy, improves overall survival (OS) (6, 7). However the incidence of postoperative complications such as limb dysfunction and hydrocephalus as well as the high cost remain challenging (6, 8, 9). Hydrocephalus is a common preoperative and postoperative complication during thalamic tumor surgery (10–12). At present, ventriculoperitoneal shunt surgery and third ventriculostomy are commonly used methods to avoid postoperative hydrocephalus (10–12). However, there are very few reports about the risk factors of hydrocephalus after thalamic surgery. So, we conducted the research of the risk factors of postoperative hydrocephalus to reduce the incidence of postoperative hydrocephalus and improve the prognosis and quality of life for thalamic tumor patients. Therefore, tumor resection needs to be extensive following standard treatments to reduce the incidence of postoperative hydrocephalus.

We performed a retrospective review of patients treated at our department for thalamic tumors in the last 6 years. We report our experience to address the following questions: the risk factors of early hydrocephalus after thalamic tumor resection and the effects of the surgical approach and surgical treatment strategy on early postoperative hydrocephalus. We also examined possible treatments to prolong OS and reduce postoperative hydrocephalus to improve mobility and motility.

MATERIALS AND METHODS

Clinical Materials

We retrospectively reviewed 80 patients with thalamic tumors treated by tumor resection at Sanbo Brain Hospital, Capital Medical University, between January 1st 2015 and January 30th 2021. All cases in the research achieved surgical resection, and cases with stereotactic biopsy were not included in this research. The data included demographics, presenting symptoms, imaging characteristics, tumor extent, histology, treatment received, and follow-up (Table 1).

Radiological Profiles

All patients underwent preoperative magnetic resonance imaging (MRI) (Table 2). The pre-operative MRI sequences included enhancement T1 weighted, T1 weighted, T2 weighted and flair imaging. Part of the patients achieved SWI and DTI imaging pre-operatively. SWI imaging examination can help to judge the deep veins around the tumor and protect these important structures intra-operatively. DTI imaging can help to judge the relationship between fiber

| Characteristics |  
|-----------------|----------|
| Ages | Median 33, Range 1–65 |
| Sex | Male 43, Female 37 |
| Initial case | 78 |
| Recurrent cases | 2 |
| Tumor site | Right 43, Left 37 |
| Preoperative maximum tumor diameter (mm) | Median 42, Range 12–78 |
| Preoperative Karnofsky Performance Status scores | Median 70, Range 20–90 |
| Symptoms and signs | Intracranial hypertension 38, Motor disturbance 15, Sensory dysfunction 4, Dizziness 11, Visual disturbance 4, Others 5 |

| Characteristics | N (%) |
|-----------------|-------|
| Tumor location |  
| Confining to the thalamus 21 (26.25%)  
| Invading the surrounding structures 59 (73.75%) (brainstem, basal ganglia, contralateral thalamus) |
| Maximum tumor diameter (mm) | Median 42, Range 12–78 |
| Cystic change | Yes 23 (28.75%), No 57 (71.25%) |
| Enhancement in imaging |  
| Homogeneous enhancement 11 (13.75%), Partial enhancement 57 (72.25%), Without enhancement 12 (15.00%) |
| Peritumoral edema | Yes 21 (26.25%), No 59 (73.75%) |
| Preoperative hydrocephalus | Yes 64 (80.00%), No 16 (20.00%) |
FIGURE 1 | Preoperative and postoperative imaging of thalamic malignant tumor resection with trans-frontal lateral ventricle approach. (A-C) display: Axial, sagittal, and coronal enhanced MRI of malignant tumors of the left thalamus. The main body of the tumor is located in the thalamus, pushing the surrounding normal structure, supratentorial lateral ventricle expansion, and the third ventricle pushing to the right. (D,E) display: The bundle of fibers passing through the left thalamus is destroyed and pushed by the tumor. (F) The deep cerebral vein (great cerebral vein) is located at the ventral and posterior side of the tumor and is pushed to the right by the tumor. (G-I) display: MRI images obtained after thalamic tumor resection via the trans-frontal lateral ventricle approach. The images show that the volume of ventricles did not increase or expand after total tumor resection.

bundle and tumor pre-operatively, and therefore reduce postoperative complications.

Treatment
Three microsurgery approaches were used according to the location of the tumor in the thalamus and surrounding structures.

If the main body of thalamic lesions is located in the thalamus and does not invade the lateral structure of the thalamus widely enough, we applied surgical resection through unilateral trans-cortical lateral ventricle approach. The patient was in supine position with head raised 30°. The frontal cortex site during the operation is located 2.5 cm in front of the coronal suture and 1 cm beside the midline. The diameter of the cortical ostomy is about 2.5 cm and the depth of the ostomy is about 3 cm. In most cases, the top of the thalamic tumor could be observed outside the choroid plexus of the lateral ventricle. If thalamic lesions invade the lateral structure of thalamus and grow posterolateral, we adopt surgical resection through parieto-occipital transventricular approach. The patient was placed in lateral position, and the incision
Preoperative and postoperative imaging of thalamic malignant tumor resection with left trans-frontal lateral ventricle approach + third ventriculostomy.

(A-C) display: Axial, sagittal and coronal enhanced MRI of malignant tumors of the left thalamus. MRI shows that the main body of the tumor was located in the left thalamus, invading the third ventricle, the right thalamus, the supratentorial lateral ventricle, and the expansion of the third ventricle. (D-F) display: MRI of thalamic tumor resection with left trans-frontal lateral ventricle approach + third ventriculostomy. The images show that the tumor was completely removed, and the volume of the lateral ventricle did not increase and expand. The position indicated by the blue arrow (†) in e is the leak at the bottom of the third ventricle.

center was located in the trigone of lateral ventricle. The body surface projection of the cortical ostomy was 7 cm beside the midline and 3 cm above the transverse sinus. The diameter of the cortical ostomy is 2.5–3 cm, and the depth is about 3 cm. With this ostomy the tumor could be sufficiently exposed.

Tumor resection was performed via trans-frontal lateral ventricle approach for tumor resection in 27 cases (33.75%) (Figure 1), trans-frontal lateral ventricle approach for tumor resection plus third ventriculostomy™ in 14 cases (17.5%) (Figures 2, 3), and 1 through parieto-occipital transventricular approach tumor resection in 39 cases (48.75%) (Figure 4).

Patients with glioma diagnosed by postoperative pathology received chemotherapy and radiotherapy. The Stupp strategy was used in Class WHO IV (13).

Follow Up
All follow-up MRI studies were performed at 1 month post-surgery, and then every 3–6 months. OS and the progression-free survival (PFS) data were calculated from the 1st day after operation. Disease progression was defined as symptom worsening. Tumor recurrence was evaluated by MRI or magnetic resonance spectroscopy (MRS). The post-operative MRI sequences included T1 weighted, T2 weighted, enhanced T1 weighted and Flair imaging. Whether the ventricle was enlarged and whether there was hydrocephalus were observed. Some post-operatively patients underwent cerebrospinal fluid cine sequences. The sequence used for cerebrospinal fluid flow sequences examination is cerebrospinal fluid phase contrast sequence (CF-PCA, CSF-QF sequence). MRI examination was performed using the Netherlands Philips Archieva 1.5T MR imaging system. RANO standard was used as the evaluation standard of treatment response of high-grade glioma. Post-operative MRI was performed to evaluate the surgical effect, whether the tumor recurred, whether the residual tumor volume increased, and whether new lesions appeared in other locations. MRS can help to distinguish tumor recurrence and radiation necrosis. Within 1 month and 3 months post-operatively, all patients achieved MRI to evaluate whether the tumor recurred and the effect of the followed treatment (such as chemotherapy and radiotherapy). Follow-up MRI was performed once every 6 months for benign tumors and every 3 months for malignant tumors. Follow-up time was to the end of life. The timing of follow-up MRI was of course adapted to possible modifications of clinical conditions. If hydrocephalus occurs in the early stage after surgery, ventriculoperitoneal shunt will be performed. We use Medtronic adjustable pressure shunt tube, and the initial
value of pressure valve after shunt is 2.5 kpa, Subsequently, the pressure would be adjusted according to whether the patient had intracranial hypertension symptoms. There were no complications of infection and shunt tube dependent syndrome after shunt operation. If the postoperative imaging data showed that the ventricle was enlarged (it may be because there was hydrocephalus before the operation, resulting in the decrease of brain compliance, or incomplete obstruction after the operation. The ventricle size would not be improved after the operation), while the patient had no symptoms of high intracranial pressure, it would continue to be observed. For early hydrocephalus, the postoperative follow-up time continued until the case died.

**Statistical Analysis**

SPSS 22.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Kaplan–Meier curves were used to calculate
OS and PFS. Multivariate analysis was performed by the log-rank test. Correlations were made using multivariate analysis according to the Kaplan–Meier method. The level of significance (p) was 0.05 for all tests.

RESULTS
Extent of Surgical Resection
All the 80 cases underwent surgery. All patients survived during the perioperative period. We independently reviewed the preoperative and postoperative MRI data to determine the extent of tumor resection. The extent of resection was divided into gross total resection (90–100% removal; 44 cases), subtotal resection (80–90% removal; 21 cases), and partial resection (<80% removal; 15 cases) based on the intraoperative findings and postoperative MRIs (14). The volume of tumor was measured by “miplatform ZFP viewer” software. All radiological data, including pre-operative and post-operative data, were drawn directly from the peri-surgical reports and we invited a neuro-pathologist to check the validity. The neuro-radiologist was blinded to the results of pathological examination, surgical methods and clinical conditions. The neuro-radiologist have more than 10 years of image reading experience. Factors including tumor volume (unit: mm3), tumor location, scope, peritumoral edema, cystic change, calcification, peritumoral edema, deep vein, fiber bundle imaging Cine imaging of cerebrospinal fluid were evaluated. Besides whether there was hydrocephalus and distant metastasis were also evaluated.

Histopathology
The pathological diagnoses of the 80 patients were as follows: 54 patients had glioblastoma (WHO IV), six had anaplastic astrocytoma (WHO III), seven were WHO II, one had diffuse large B lymphoma, one germinoma, one embryonal tumor of the central nervous system, and 10 had benign tumors. There were 10 cases of benign entities, i.e., five cases of cavernous hemangioma, one case of pilocytic astrocytoma, one case of brain abscess, one case of arachnoid cyst, one case of pilocytic hemangioma, and one case of epidermoid cyst.

Treatment Outcomes
There were 35 cases (43.75%) of hydrocephalus at 1 month after operation. Among them, hydrocephalus occurred in seven cases after trans-frontal lateral ventricle approach for tumor resection (62.9%), in 17 cases after through parieto-occipital transventricular approach tumor resection (43.58%), and in one case after trans-frontal lateral ventricle approach for tumor resection + third ventriculostomy (7.1%) (Table 3).

FIGURE 4 | Preoperative and postoperative imaging of thalamic malignant tumor resection with through parieto-occipital transventricular approach (A-C) display: Axial, sagittal and coronal enhanced MRI of malignant tumors of the right thalamus. The MRI shows that the main body of the tumor was located in the right thalamus; the supratentorial lateral ventricle and third ventricle were dilated. (D-F) display: MRI of thalamic tumor resection with the right lateral ventricular triangle approach. The images show total resection of the tumor; the volume of the lateral ventricle after surgical resection of the thalamic lesion did not expand.
The risk factors correlated with hydrocephalus were determined by multivariate analysis ($P < 0.05$) (Tables 4, 5). Hydrocephalus after unilateral thalamic space-occupying surgery is related to whether hydrocephalus is present before surgery, the degree of tumor resection, and whether third ventriculostomy is performed. Intraoperative third ventriculostomy can significantly reduce the symptoms of postoperative short-term hydrocephalus. The more extensive the surgical resection, the lower the risk of early postoperative hydrocephalus. If the patient has complications of hydrocephalus before the operation, the risk of hydrocephalus early after surgery is high.

The early occurrence of hydrocephalus after unilateral thalamic space-occupying surgery is not correlated with tumor volume, benign or malignant lesions, tumor image enhancement degree, peritumoral edema, invasion, tumor crossing midline, or pathological grade.

**Survival Analysis**

The survival time of thalamic glioblastoma is shorter than the other tumors with low malignancy. Glioblastoma accounts for the majority of cases in this research, Therefore, the prognosis of other tumors has not been systematically analyzed. In the glioblastoma group, hydrocephalus developing short-term after tumor resection (within 1 month) was not correlated with OS (Figure 5A) or PFS (Figure 5B) rate.

The glioblastoma group was divided into two subgroups, patients whose resection degree $\geq 80\%$ and patients whose resection degree $< 80\%$. The results showed that resection degree $\geq 80\%$ improved OS (Figure 5C) and PFS (Figure 5D).

There is no dead case among all the benign cases, and only one case of cavernous hemangioma had hydrocephalus complications early after operation.

**DISCUSSION**

There are many surgical approaches to remove thalamic tumors, Several trans-midline approaches have been reported in the literatures for thalamus tumors (e.g., the interhemispheric transparaterminal gyrus approach described by Kumar and the transcalsosal interforniceal approach described by Graziano) (14, 15).

There is really no large-scale clinical comparison between transcortical approach and transcalsosal interfornix approach to show which approach is better, but we choose trans-cortical approaches mainly from the following points.

Compared to these reported approaches, the trans-cortical approach we chose contains the following advantages:

For unilateral thalamic lesions the tran-scorical approach could supply better surgical corridor, while the trans-midline approaches is suitable for lesions invading bilateral thalamus. Besides, as the fiber bundles of the corpus callosum are relatively dense, retraction of the corpus callosum would be more difficult and generate more injury.

| Surgical approach                                    | Number of cases | Number of postoperative hydrocephalus |
|------------------------------------------------------|-----------------|--------------------------------------|
|                                                      | $N$ (%)         | $N$ (%)                              |
| Trans-frontal lateral ventricle approach plus third ventriculostomy | 14 (17.50%) | 1 (7.14%)                             |
| Trans-frontal lateral ventricle approach             | 27 (33.75%) | 17 (62.96%)                           |
| Through parieto-occipital transventricular approach  | 39 (48.75%) | 17 (43.59%)                           |

| Factor                                              | OR   | 95% CI   | $P$-value |
|-----------------------------------------------------|------|----------|-----------|
| Third ventriculostomy (Yes/No)                      | 0.076| 0.008-0.690| 0.022     |
| Degree of tumor resection                           | 0.459| 0.213-0.991| 0.047     |
| Tumor volume                                        | 1.008| 0.996-1.020| 0.246     |
| Enhancement in imaging                              | 0.830| 0.284-2.419| 0.732     |
| Tumor crossing midline                              | 0.324| 0.050-2.110| 0.238     |
| Peritumoral edema                                   | 1.231| 0.342-4.426| 0.750     |
| Benign and malignant tumor                          | 2.232| 0.272-18.295| 0.454     |
| Preoperative hydrocephalus                          | 7.534| 1.367-41.519| 0.020     |

Graziano proposed a novel approach: contractual antior inter hemispheric transitional gyrus approach (15). This approach is beneficial to the protection of corticospinal tracts. However, it also needs to cut a section of corpus callosum. In addition, this surgical channel will pass through many important structures, such as anterior communicating arteries, both A2 anterior cerebral arteries; Lastly, if the thalamic tumor grows to the top of the thalamus, the surgical field of vision may be poor.
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FIGURE 5 | (A) Correlation of overall survival after tumor resection with early hydrocephalus in the glioblastoma group (green line: no hydrocephalus in the early postoperative period; blue line: hydrocephalus in the early postoperative period). The results showed that there was no correlation between early postoperative hydrocephalus and overall survival rate; p = 0.31. (B) Correlation between progression-free survival after tumor resection and early hydrocephalus in the glioblastoma group (green line: no hydrocephalus in the early postoperative period; blue line: hydrocephalus in the early postoperative period). The results show that there was no correlation between early postoperative hydrocephalus and progression-free survival rate; p = 0.44. (C) Correlation between tumor resection degree and overall survival rate in the glioblastoma group (green line: resection degree ≥80%; blue line: resection degree <80%). The results showed that full resection of lesions improved the overall survival rate (OS); p = 0.048. (D) Correlation between tumor resection degree and progression free survival rate in the glioblastoma group (green line: resection degree ≥80%; blue line: resection degree <80%). The results showed that full resection of lesions improved the total progression free survival (PFS); p = 0.043.

when dealing with the superior part of the tumor through this approach.

Postoperative hydrocephalus leads to a decline in the patient’s consciousness and increases the potential risk of hernia cerebri, which is life-threatening in severe cases. For postoperative hydrocephalus of the thalamus, a lateral ventricular puncture and external drainage may increase the risk of infection, and a lateral ventricular peritoneal shunt increases the medical burden. Therefore, it is important to analyze the risk factors related to hydrocephalus after thalamic tumor resection and reduce the risk of postoperative hydrocephalus.

To analyze the risk factors of postoperative hydrocephalus in thalamic lesions, we can clarify the problems according to our research results. First of all, we should clarify a question: what is the mechanism of hydrocephalus caused by thalamic space occupying lesions (Figure 6). Second, we need a clear view that the causes of hydrocephalus after thalamic space occupying surgery may be caused by the following reasons (1). The lesion was not completely resected, and the midbrain aqueduct was still blocked. (2) Scar formation around the upper end of the midbrain aqueduct after the operation. (3) The tumor recurred after the operation or continued to grow after partial resection.

Why is there a high risk of hydrocephalus after thalamic tumor resection with trans-frontal lateral ventricle approach in this group of cases? The reason is that the tumor body of the
The special location of thalamic tumors can make resection difficult. Their treatment and the role of aggressive surgical resection have been a matter of debate for the last two decades (9, 16–20). Advances in neuroimaging and surgical techniques have made surgical resection of thalamic tumors feasible. Surgical resection in combination with adjunct therapies, such as radiotherapy and chemotherapy, based on the histological characteristics of the tumor has been suggested by many publications (7–9, 13, 16–26). However, postoperative complications such as limb dysfunction and hydrocephalus remain challenging (6, 8, 9, 27). Solving these problems is important to improve mobility and motility.

Postoperative hydrocephalus may lead to coma and cerebral hernia, which are life-threatening. Treatment of hydrocephalus may further cause infection and is associated with a high cost. Therefore, decreasing the incidence of postoperative hydrocephalus is important.

Postoperative hydrocephalus may be caused by incomplete resection, scar contracture, anastomotic stenosis, and the tumor type. Patients with a trans-frontal lateral ventricle approach are prone to postoperative hydrocephalus. The tumor in this group is located near the midline, compressing the midbrain aqueduct and third ventricle. Scar contracture and anastomotic stenosis often occur after surgery. Tumors from patients who undergo through parieto-occipital transventricular approach are located laterally from the thalamus, away from the midbrain aqueduct and third ventricle. This location is associated with a low incidence of hydrocephalus. The third ventriculostomy bypasses fluid despite compression of the midbrain aqueduct, which decreases the risk of hydrocephalus. Gross total resection relieves the compression of the midbrain aqueduct to reduce the incidence of hydrocephalus. Preoperative hydrocephalus is associated with high intracranial pressure, which affects the ability of the choroid plexus to absorb cerebrospinal fluid, thus increasing the risk of postoperative hydrocephalus despite tumor resection.

**CONCLUSION**

Surgical treatment of thalamic tumors is an effective therapeutic method. The incidence of postoperative hydrocephalus is
not associated with factors including tumor size, degree of tumor enhancement, peritumoral edema, tumor invasion, midline crossing, and pathological grade. The incidence of postoperative hydrocephalus is higher in patients with preoperative hydrocephalus and low resection degree, meanwhile patients with third ventriculostomy got lower postoperative hydrocephalus risk. Besides, the risk of early postoperative hydrocephalus in thalamic tumors is high. Intraoperative triple ventriculostomy can reduce the incidence of early postoperative hydrocephalus. PFS and OS are longer in thalamic glioblastoma cases with a high resection degree.

**DATA AVAILABILITY STATEMENT**

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

**ETHICS STATEMENT**

The studies involving human participants were reviewed and approved by Ethics Committee of Sanbo Brain Hospital. Written informed consent for publication was obtained from all participants. Written informed consent to participate in this study was provided by the participants’ legal guardian/next of kin. Written informed consent was obtained from the individual(s), and minor(s)’ legal guardian/next of kin, for the publication of any potentially identifiable images or data included in this article.

**AUTHOR CONTRIBUTIONS**

XZ designed the study. LZ and CW collected data and revised the manuscript for important intellectual content. LZ analyzed the data and wrote the article. All authors have read and approved the final manuscript.

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