Thalamus tumor prognosis; systematic review

Abstract

Introduction: Thalamic tumors can occur in all aging groups, however the children and adolescents are reported as the high risk aging groups. In this systematic review we aimed to investigate the prognosis of thalamic tumors with various histology and different aging groups.

Methods: PubMed was searched for English language articles that studied the prognosis of patients with thalamic lesions regarding the survival and mortality of patients. Inclusion criteria were all the cohort and retrospective studies that included only patients with thalamus tumors. Articles that studied involvement of other parts despite the thalamus or those that included patients with secondary thalamus tumors were excluded.

Results: totally 15 articles were included in this systematic review. The prognosis value of tumor histology, extend of resection, and patients’ age is extracted from the included articles. Results are presented as survival duration and overall survival rate of patients.

Discussion: Although thalamic tumors are difficult to be operated, it is possible to be resected without mortality and morbidity. Factors including histological type of tumor, extent of resection, and presenting age can affect the prognosis of the thalamic tumors.

Conclusion: The prognosis of thalamus tumors is mainly related to tumor type. Benign thalamic tumors have shown favorable outcome regarding the survival duration.

Keywords: thalamus tumor, histology, prognosis
Introduction
Primarily thalamic tumors are rare and involve almost 1 to 5% of all types of brain tumors (1). These tumors types are not easily operated due to their deep seated and midline location which make their management challenging. Differentiating the primarily originating thalamic tumors from secondary invading thalamic lesions is difficult. Various clinical presentations are proposed for thalamic tumors including motor weakness, increased intracranial pressure, sensory deficits, seizures, and sometimes with mental deterioration and personality changes. Several factors can affect the initial accurate diagnosis and estimation of the disease prognosis including variability in exact location in the thalamus, histological type, extent of resection, bilaterality, and presenting age.
Because of the histologically vital location of these tumors they were known inoperable tumor types, however today literature propose the association between the extent of the resection and patients survival (2).
The first reported excision of the thalamic tumors was in 1932 performed by Cushing, following this partially resection of the thalamic lesion, radiation performed and patient survived for 13 years.
Development of new imaging modalities, surgical types and approaches, and surgical devices has facilitated the accessibility to deep-seated tumors(3). Despite these technological progress the exact and the most optimum treatment modality of thalamic lesions is under investigation.
In this systematic review, we focused on the articles included patients with thalamic tumors to investigate the effect of prognostic factors on patients survival and mortality rate.

Method
PubMed was searched to retrieve the relevant articles we the purpose of this systematic review. The selected search strategy was as follow: thalamus AND tumor. The inclusion criteria were all the English language articles which studied the prognosis of patients with
primarily unilateral or bilateral thalamic tumor. No time limitation was used in our searching strategy. All the case reports, non-English articles, and those which studied the prognosis of patients with secondary thalamic lesions were excluded from our search criteria. The flow chart of the included articles in this systematic review is provided in Figure 1.

**Figure 1.** Flow chart of the included articles

**Results**

Based on our search strategy, a total of 15 articles were included in our study. Detailed information regarding the patients characteristics, treatment, histology of the tumor, and patients survival rate are provided in Table1. Information regarding the quality of the included articles (type of study and follow up duration) are also detailed in Table1. In some retrospective articles the exact follow up duration is not mentioned for each patients and only information regarding the survival duration or disease free duration were mentioned in the article.
Table1. Detailed information of articles studied the prognosis of patients with thalamus tumors

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients</th>
<th>Treatment</th>
<th>Histopathological findings</th>
<th>Survival and Mortality</th>
<th>Study type-Follow-up duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kramm, 2011, (5)</td>
<td>N:31 Age: mean 10.8</td>
<td>Sub TR:5 PR:11 Biopsy:15</td>
<td>HGG</td>
<td>5-year EFS%±SD: 7.3±5 5-year OS%±SD: 7.4±5.1</td>
<td>Retrospective, NA</td>
</tr>
<tr>
<td>Menon, 2010, (6)</td>
<td>BTT:9 Primary BTT:7 Secondary BTT:2 M/F:3/6 Age: 14.6 yrs</td>
<td>CSF diversion and endoscopic biopsy:7 R:8</td>
<td>Grade II fibrillary astrocytoma: 6</td>
<td>3/9 (33.3%): 1-5 yrs (average 2.3 yrs) Symptoms free duration: 4/9(44.4%):9.5 M (progressive disease on last follow up) Death:2 with secondary BTT</td>
<td>Retrospective, minimum of 1 year follow up</td>
</tr>
<tr>
<td>Author</td>
<td>N: M/F: Age</td>
<td>Procedures</td>
<td>Pathology</td>
<td>Outcome</td>
<td>Follow-up</td>
</tr>
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<td>-----------------</td>
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<tr>
<td>Fernandes, 2006</td>
<td>14/9, 8.1 yrs</td>
<td>Sub TR:2, TR:2, Biopsy:3, CT:2, RT+CT:6</td>
<td>Pilocytic A:5, Oligo:7, Glioblastomas:2</td>
<td>Overall survival rate: 3yrs(5/13(38%)) Pilocytic A: 100% survival rate: 4/4 Oligo: 14% survival rate: 1/7 Glioblastomas 0% survival rate: 0/2</td>
<td>Retrospective, 2-124M</td>
</tr>
<tr>
<td>Albright, 2004</td>
<td>19, median 8 yrs</td>
<td>TR:6, Sub TR:10</td>
<td>Low grade glioms: 7 High grade glioma: 12</td>
<td>Survival rate All low-grade tumors: 2-12 yrs high-grade tumors: 9 died within 2 yrs 3 survived 2, 3, and 16 yrs</td>
<td>Retrospective, NA</td>
</tr>
<tr>
<td>Ozek, 2002</td>
<td>19/10/8, range: 2-16 yrs</td>
<td>TR:16</td>
<td>Low grade astrocytoma: 10 High grade astrocytoma: 3 Ependymoma: 2 PNET: 2 Ganglioglioma: 1</td>
<td>All benign tumors are alive within 24 M 6 malignant tumor died within 3-24 M</td>
<td>Retrospective, 24M</td>
</tr>
<tr>
<td>Krouwer, 1995</td>
<td>57, mean 22 yrs</td>
<td>NO OP:14, Biopsy: 37 Sub TR:6, RT:20, RT+CT:18, CT:2 hyperfractionated, RT:17</td>
<td>Astrocytoma: 14 Anaplastic astrocytoma: 25 Glioblastoma multiforme: 2</td>
<td>median time to tumor progression: 47 W median survival: 73 W 1-, 2-, 3-, and 5-year survival rates were 67%, 35%, 24%, and 20%</td>
<td>Retrospective, -</td>
</tr>
<tr>
<td>Reardon, 1998</td>
<td>36, median 10 yrs</td>
<td>-</td>
<td>Low-grade tumors: 24 high-grade tumors: 12</td>
<td>All cases: 4-year progression-free survival: 28% OS: 37% Low-grade tumors: 4-year PFS: 36% OS: 52% High grade tumors:</td>
<td>Retrospective, median follow-up of 4.3 years</td>
</tr>
<tr>
<td>Study</td>
<td>N</td>
<td>M/F</td>
<td>Age</td>
<td>UTT</td>
<td>BTT</td>
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<tr>
<td>Cuccia, 1997(14)</td>
<td>26</td>
<td>20/6</td>
<td>mean 8.5 yrs</td>
<td>Anaplastic:</td>
<td>Biopsy</td>
</tr>
<tr>
<td>Villarejo, 1994(16)</td>
<td>8</td>
<td>F/M</td>
<td>3-9 yrs</td>
<td>TR:</td>
<td>7</td>
</tr>
<tr>
<td>Beks, 1987, (17)</td>
<td>27</td>
<td>13/14</td>
<td>mean 25.5 yrs</td>
<td>No OP:</td>
<td>4</td>
</tr>
<tr>
<td>Bernstein, 1984, (18)</td>
<td>60</td>
<td>M/F</td>
<td>5-18 yrs</td>
<td>No OP:</td>
<td>16</td>
</tr>
</tbody>
</table>

Discussion

Thalamic tumors are located deeply within vital brain sites and conventional procedures are reported to be associated with high mortality and morbidity rate. Regardless of type of thalamic tumor, they are proposed to be associated with poor prognosis. Stereotactic techniques have been progressed over decades due to sequential improvements in computer software, operating equipment, and surgical experience. These techniques are proposed as safe procedures for completely resecting deep-seated lesions, such as thalamic tumors.

Thalamic lesions are difficult types to be resected; thalamic tumors in only two out of 14 cases studied by Fernandez et al could be totally resected, one was followed by the overall survival of the patient (9). Berstein et al found no statistical difference in the rate of survival between patients with low-grade lesions that are resectable compared with those with biopsied tumors (18).

Various factors including variability in exact location in the thalamus, histological type, extent of resection, bilaterality, and presenting age can affect the prognosis of the thalamic tumors.

Total of 17 patients with histopathologically proven malignant tumor, which were partially resected, showed survival duration of 1 to 30 months. Based on the reported survival rate, extent of resection in patients with malignant thalamic tumor is not significantly related to the patients survival rate. According to the obtained results, Bilginer et al recommended subtotal or total resection as the main goal in thalamic surgeries (4).

The surgery of patients with bilateral involvement of thalamus is difficult and will be limited to biopsy and Cerebrospinal fluid diversion procedures; biopsies prior to adjuvant therapies are usually recommended for patients with thalamic lesions. Based on the information revealed by investigating patients with bilateral thalamic in the study of Menon et al, radiotherapy following biopsy is still recommended (6). Complete surgical resection via
stereotactic technique is proposed as the optimum initial treatment for pilocytic astrocytomas in thalamus. According to Moshel et al most of the small residual tumors do not progress and are stable; so further surgery or adjuvant therapy are not recommended following stability of residual tumors. They proposed radiation therapies following initial operation for those with inoperable tumors or with recurrent and progressive pilocytic tumors. Removing the tumors with volumetric stereotactic resection has shown beneficial effects on decreasing the tumor progress and recurrence rate and improves the patients long term quality of life. They eventually proposed volumetric stereotactic resection with favorable long-term prognosis without adjuvant chemotheraphy and/or radiation therapy (7). In the study of Berstein et al. no significant relation was obtained in survival rate of patients with radiation therapy compared with those without radiation therapy (18). In the study of Beks et al stereotactic biopsy sampling was proposed as the treatment of choice (17). Open biopsy has shown prognostically favorable results following univariate Cox proportional-hazards analysis (12).

**Tumor type**

It is proposed that resection of some types of thalamic tumors can be achieved with low mortality rate which is dependent on the histological type and pathological grade of tumor. Bilateral thalamic tumors are known as rare type of thalamic tumors which have almost symmetrical enlargement of both thalamic nuclei. This type of thalamic tumor reveals poor prognosis regarding the survival rate of patients. There is low number of studies on the prognosis of this tumor type. The prognostic value of bilateral thalamic tumors is investigated in the study of Bilginer et al which was associated with low survival rate of patients (4). Two patients included in the study of Menon et al with secondary bilateral thalamic tumor rapidly deteriorated and succumbed to their illness; they proposed poor prognosis of patients with secondary thalamic tumors regarding the survival rate (6). Bithalamic involvement negatively affected the progression free survival and overall survival of patients with low grade tumors
investigated in the study of Reardon et al (13). They eventually proposed bithalamic involvement as a poor prognostic factor among patients with low grade thalamic lesions.

In the study performed by Bilginer et al, patients at the age of 3-10 years old who had malignant thalamic tumor revealed lower survival rated compared with those with benign tumor. This lower survival duration was also observed for 11-19 years old patients with malignant tumor compared with benign types (4).

In one study various types of thalamic lesion were compared regarding the prognostic level including: pilocytic astrocytomas, oligodendrogliomas, and glioblastomas (9) according to their results pilocytic astrocytomas is associated with favorable prognosis compared with two other types. On the other hand, high grade oligodendrogliomas were accompanied with considerably low prognosis; 6/7 patients died within 24 months of follow-up (9). This poor prognosis of oligodendrogliomas, and glioblastomas is confirmed in other studies (13, 15, 18, 19). In the study performed by Cuccia et al, despite all influential factors on survival and mortality rate of patients, histology of tumor type is proposed as the main prognostic factor which should be diagnosed and taken into account at first; the dependency of survival rate on histologic subtype of tumor is confirmed by other researches (11, 14). Based on the series of Nishio et al, 2 patients with pilocytic astrocytoma revealed survival duration of 11 to 16 years, however 5/7 cases with fibrillary astrocytoma showed survival time of 3 years following initial diagnosis (15).

It can be concluded that complete resection, with no residual tumor visible on postoperative MR images, correlates with survival in children with low-grade astrocytomas, however extent of resection (>90%) seems to correlate with survival in children with high-grade gliomas. Krouwer et al, proposed histological diagnosis of astrocytoma as a prognostically favorable factor based on univariate Cox proportional-hazards analysis (12).
Age

Age is proposed as a prognostic factor which might influence the treatment outcome in patients with thalamic tumors.

Some studied investigated the prognosis of patients’ age on their survival rate. According to age distribution in one recent study, the survival rate for group 1 (3–10 years) was 13 months and group 2 (11–19 years) was 18 months for histologically proved malignant tumors (4). They proposed patients age as an imperative factor mainly in cases with malignant tumors. Some other studied suggested better prognosis for patients at younger ages compared with older cases. In the study of Nishio et al, all the patients older 26 years old died within 3 years however 5/11 patients younger than 25 years old survived for 2-16 years (15). In that article, 2/3 cases at younger ages with low grade fibrillary astrocytoma survived for 4 and 11 years, however 4 adults with low grade thalamic tumor died within 36 months (15). They suggested different biological behavior for thalamic tumors in adults compared with younger patients. Krouwer et al suggested younger age (< 18 years old) as favorable prognostic factor according to univariate Cox proportional-hazards analysis (12). In the study of Reardon et al no significant relation was obtained regarding the age at diagnosis with overall survival; this result was also obtained by Puget et al (8, 13). However, Puget et al proposed as association between younger age and the higher incidence of benign thalamic tumor (8).

Conclusion

Although thalamic tumors are difficult to be operated, it is possible to be resected without mortality and morbidity. According to the included studies, the prognosis of thalamic lesions is associated with the histological subtype of the tumor. High grade gliomas showed poor prognosis which can be due to resection complications, low response to radiation and chemotherapy.
References


