Original Article

Surgery in High-Grade Insular Tumors: Oncological and Seizure Outcomes from 41 Consecutive Patients

Abstract

Background: Insular high-grade gliomas are uncommon and constitute approximately 10% of all intracranial high-grade gliomas. Several publications in the recent years have thrown substantial light in the understanding of insular low-grade gliomas. However, there is a paucity of information concerning the spectrum of high-grade lesions affecting the insula, the mode of presentation vis-à-vis low-grade gliomas, and the survival rates to modern therapy. **Aims and Objectives:** We aim to highlight various clinical patterns, histo-pathological spectrum and the survival rates in patients with high-grade insular lesions. Also, we explore the factors that govern favourable outcomes. **Materials and Methods:** A retrospective study of 41 patients operated for high-grade insular tumors at our institute between March 2010 to December 2018 was done to evaluate the clinico-radiological features, surgical nuances, survival rates and seizure outcomes. **Results:** Raised intracranial pressure was the most frequent clinical presentation (*n*=28/41, 68.3%). Nearly 60% of the patients (*n*=25) had involvement of all four Berger-Sanai zones. The high-grade tumors encountered in our series were: glioblastoma (*n*=15), gliosarcoma (*n*=3), and embryonal tumor, not otherwise specified in 3 patients, while 21 patients had grade 3 astrocytoma. 33 out of 41 patients (80.5%) in our study showed excellent seizure control (ILAE grade 1A) at follow-up. Clinical presentation with seizures (P = 0.01, HR=0.3), WHO grade IV histopathology (P = 0.04, HR=3.7) and development of recurrence (P = 0.05, HR=5.5) were found to be independent predictors of OS. **Conclusion:** Insular high-grade gliomas are commoner than thought and nearly half of these are grade IV tumors (51%). A presentation with seizures may indicate precursor low-grade gliomas and portend a better survival. A maximum "safe" surgical resection, keeping the postoperative quality of life in mind, should be the goal.

Keywords: *Factors, glioblastoma, high-grade glioma, insular lobe, outcome, surgery, survival*

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Introduction

Insula is an anatomically and functionally complex area. Gliomas in the insula have long been considered irresectable. This precept primarily stemmed from the high degree of functionality of this area and perhaps more importantly, the devastating consequences resulting from iatrogenic injury to the critical adjoining neurovascular structures.[1-3] Therefore, earlier attempts at surgery were met with unacceptable complications. A questionable benefit of tumor resection over a much safer strategy of biopsy and adjuvant therapy perhaps also contributed to the surgical nihilism.[1-3]

Over the years, however, things have changed dramatically. The importance of the extent of tumor resection on the progression-free as well as overall survival (OS), irrespective of the grade of the tumor, has been proven by many studies.[3-7] In addition, advances in the functional neuroimaging, intraoperative neuromonitoring tools, and increasing experience of surgery in this area have made us believe that insular surgery can be performed with acceptable morbidity. This has provided a great impetus for neurosurgical oncologists to attempt resection of these tumors with the right mix of caution and aggression nowadays.

Insular gliomas constitute 25% of all intracranial low-grade gliomas.[8] However, the proportion of high-grade gliomas are relatively less (an estimated incidence of 10% of all intracranial high-grade gliomas). A large number of publications in recent years have thrown substantial light in the understanding of insular low-grade

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gliomas.[9,10] However, we do not find many publications focusing only on the high-grade gliomas in this location. Most of the articles tend to combine the low grade and the high-grade insular gliomas while deriving the results. Therefore, there is a paucity of information concerning the spectrum of high-grade lesions affecting the insula, the mode of presentation vis-à-vis low-grade gliomas, and the survival rates to modern therapy.

The present article focuses on insular high-grade tumors to highlight:

1. Patterns of clinical presentation
2. The spectrum of high-grade lesions affecting the insula and
3. Determine the overall and progression free survival (PFS) of these lesions to the modern multimodality treatment.

We additionally aimed to explore the factors that govern favorable outcomes to the treatment strategies.

Materials and Methods

Patient details

This was a retrospective study of patients operated for insular tumors at our institute between March 2010 and December 2018. Among a total of 110 insular gliomas operated in this period, 41 patients were found to have high grade tumors (37.3%). This included high grade gliomas (WHO Grade III and IV) and embryonal tumor.

In addition to their clinical presentations, the performance status was determined in each of these cases using the Karnofsky's performance score (KPS). KPS was re-assessed at the time of discharge and successive follow-ups. The preoperative KPS scores were grouped into "poor KPS" group if KPS was <80 and "good KPS" group with KPS 80 or more.

Radiological evaluation

Computed tomography (CT) and contrast-enhanced magnetic resonance imaging (MRI) of the head was performed in all patients. Maximal tumor dimension was used as a measurement of the tumor size. We classified the tumor extent in our cases according to the Yasargil's classification for insular gliomas.[11] Within the insula, the tumor extent and location was categorized as per the Berger-Sanai zones.[12]

Surgical treatment and postoperative care

We reviewed the operative records for surgical details such as – type of approach, and the extent of excision. All the patients underwent craniotomy and excision of the tumor under general anesthesia or awake craniotomy (n = 2). We used neuro-navigation in 6 (14.6%) of our later cases for designing skin flap and tailoring the size of the craniotomy. Intraoperative ultrasonography was used in some of these patients to localize the tumor as well as for resection control (n = 4, 9.8%). In the latter five patients, intraoperative monitoring (a combination of motor evoked potential, cortical, and subcortical stimulation) was used. Only 2 of these patients underwent tumor excision using sodium fluorescence in this study. We recorded postoperative complications and their management. A contrast-enhanced CT head was done in the immediate postoperative period to rule out any surgical cavity hematoma formation.

Postoperative care

An immediate postoperative contrast-enhanced CT scan was done in all of these patients to have an idea of the extent of excision and to rule out any iatrogenic complications. A contrast-enhanced MRI after 3 months was done in all cases to assess the extent of surgical resection, as a part of the radiotherapy planning and dose volume estimation. Near-total resection (NTR) was defined as more than 90% of tumor excision as seen on postoperative MRI. Subtotal resection (STR) was defined as incomplete (50%–90%) resection of the tumor, while partial excision was defined as <50% tumor excision. The intent of surgery was maximal safe resection in all cases and surgery for a simple biopsy was not performed in any case.

Adjuvant therapy

Postoperatively, all high-grade (WHO Grade III and IV) glioma patients were advised adjuvant therapy in the form of irradiation (45–60 Gy in 30 fractions, 1.6–2 Gy/fraction) and chemotherapy in the form of oral temozolomide as per the Stupp *et al*. study.[13]

Histological examination

All surgical specimens were thoroughly evaluated histo-pathologically and graded according to the WHO classification of CNS tumors.[14] In some of these patients, immunohistochemistry was performed with glial fibrillary acidic protein staining and proliferation index estimation (Ki 67 index). After revision of the WHO classification in 2016 and adoption of the molecular markers in our institute, 7 patients also underwent molecular marker study for IDH, p53 and ATRX mutations (17%). Due to the lack of facility, MGMT promoter methylation was not performed in this series.

Follow-up

We obtained the follow-up data through outpatient department visits or telephonic interviews. Follow-up data included changes in the preoperative symptoms, seizure control as per ILAE and Engel grades, overall and PFS.[15]

The interval between surgery and death was considered as OS, while the time duration between surgery and clinico-radiological disease progression was defined as PFS. We defined progression as an increase in the size of the residual (at least 25% of the postoperative MRI) or appearance of new lesions in the event of a gross total tumor excision with or without clinical worsening.

Statistical analysis was performed using SPSS software version 24 (IBM Corp, Chicago, Illinois, USA). The survival analysis was done using the Kaplan–Meier method and the factors were analyzed using a Cox regression analysis, and cases lost to follow-up were excluded from the survival analysis.

Results

Patient characteristics

The mean patient age in our study group was 41.27 years (range 4–72 years), and the majority of our patients were males (male:female = 4.1:1).

The average duration of symptoms was 7.06 months (range 1 week–36 months). Twenty-two patients (53.7%) presented within 3 months of the onset of symptoms. Clinical features of raised intracranial pressure (ICP) such as holocranial headache (n = 28, 68.3%) and projectile vomiting (n = 10, 24.4%) were the most common presenting complaints in our patients. Among these, one patient presented with painless progressive deterioration of vision secondary to raised ICP. Seizures (n = 24, 58.5%) and motor deficits (n = 17, 41.5%) were the next most frequent modes of clinical presentation. Other unusual presenting complaints included impairment of memory (n = 6, 14.6%) and alteration of behavior (n = 6, 14.6%). Patient demographics and clinical details are summarized in Table 1.

Table 1: Demographic details and modes of clinical presentation of our patient group

Description	Number of patients (n=41), n (%)
Demographics	
Mean age±SD (years)	41.27±15.36
Median age (range)	40 (4-72)
Gender	
Male	33 (80.5)
Female	8 (19.5)
Mean duration of presenting symptoms (months)	7.06±10.96
Follow up duration (months), mean±SD	18.39±23.44
Clinical presentation	
Sensorium	
Conscious, oriented	27 (65.9)
Disoriented	12 (29.3)
Unable to follow commands	2 (4.9)
Features of raised ICP	
Headache	28 (68.3)
Vomiting	10 (24.4)
Papilledema	19 (46.3)
FND	
Motor deficits	17 (41.5)
Speech involvement	1 (2.4)
Both	7 (17.1)
Seizures	24 (58.5)
Focal aware	10 (24.4)
Focal with impaired awareness	10 (24.4)
Generalized	4 (9.8)
Others	
Impaired memory	6 (14.6)
Altered behaviour	6 (14.6)

SD – Standard deviation; ICP – Intracranial pressure; FND – Focal neurological deficits

Radiological data

Majority of the patients in our series had left-sided tumors (n = 24, 58.5%). Thirty-three (80.5%) patients had large-sized insular tumors (size >4 cm) with 19 (46.3%) of them showing displacement of the middle cerebral artery due to the tumor. Nearly half of our patients had temporal pole involvement (Yasargil's type 5B; n = 20, 48.8%). The details of anatomical involvement of the insula as per the Berger-Sanai zones have been summarized in Table 2.

Surgical and histopathological data

The majority (n = 39, 95.1%) of patients were operated under general anesthesia, while awake craniotomy was utilized in two patients only. We used "Trans-cortical" approach in 28 (68.3%) patients, and "trans-sylvian" approach was utilized in 13 (31.7%) patients for tumor excision. We were able to achieve NTR of the tumor in 23 patients (56.1%), while 18 patients (43.9%) had

Table 2: A summary of various radiological parameters of in our study

Description	Number of patients (n=41), n (%)
Radiological parameters	
Laterality	
Right	17 (41.5)
Left	24 (58.5)
Tumor size (cm)	
More than 4	33 (80.5)
<4	8 (19.5)
MCA shift	19 (46.3)
Exophytic component	3 (7.3)
Location (as per BS zones)	
I + II	2 (4.9)
II + III	2 (4.9)
I + II + III	5 (12.2)
II + III + IV	7 (17.1)
All	25 (61)
Yasargil's classification	
3A	1 (2.4)
3B	9 (22)
5A	11 (26.8)
5B	20 (48.8)
Contrast enhancement	
Homogeneous	3 (7.3)
Heterogenous	25 (61)
No enhancement	13 (31.7)

MCA – Middle cerebral artery; BS: Berger-sanai

STR with evidence of residual lesion on the immediate postoperative imaging.

Histopathologically, 20 patients (48.8%) were found to have WHO Grade III gliomas and 21 patients (51.2%) had Grade IV tumors, respectively. Among the Grade III tumors, we found 15 cases of anaplastic astrocytoma, 4 cases of anaplastic oligoastrocytoma, and 1 case of anaplastic oligodendroglioma. The high-grade tumors encountered in our series were: glioblastoma (n = 15), gliosarcoma (n = 3), and embryonal tumor, not otherwise specified in three patients. Surgical details and histopathology results, including molecular data, are shown in Table 3.

Immediate surgical outcome

Perioperative mortality was noted in two patients (4.9%), – one patient had poor preoperative Glasgow Coma Scale ($E_1V_tM_2$), and the second patient developed cerebrospinal fluid (CSF) leak with meningitis. Major postoperative complications observed in 4 of the 39 remaining patients (10.2%) and included: surgical cavity hematoma which required evacuation (n = 1, 2.4%), persistent new motor deficits (n = 3, 7.3%), and motor aphasia (n = 1, 2.4%). Minor complications (n = 7, 18%) included transient neurological deficits (n = 7, 17.1%), wound-related complications such as pseudomeningocele formation (n = 4, 9.8%), CSF leak (n = 2, 4.9%), and wound infection (n = 2, 4.9%). While pseudomeningocele resolved with conservative management in all the patients, infected wounds were surgically debrided. While other less frequently encountered complications were deep vein thrombosis (n = 1, 2.4%) and lower respiratory infection (n = 1, 2.4%).

Postoperatively, adjuvant chemoradiation therapy was advised to all patients. However, only 28 (68.3%) patients completed the prescribed adjuvant therapy. Survival (OS and PFS) analysis was compared between patients who received postoperative chemo-radiation versus those who did not. Patients who received adjuvant therapy showed significantly (log-rank test, P = 0.001) longer OS (45.9 ± 8.1 months vs. 1.3 ± 0.5 months). Eight patients in the adjuvant therapy group had developed tumor recurrence versus no tumor recurrence observed in patients who did not take chemoradiation. This finding most probably occurred as a result of significantly short OS in this group of patients.

Table 3: Operative details and histopathological distribution of our cases

Description	Number of patients (n=41), n (%)
Operative details	
Anesthesia	
GA	39 (95.1)
Awake	2 (4.9)
Approach	
Transopercular	28 (68.3)
Transylvian	13 (31.7)
EOR	
Near total	23 (56.1)
Subtotal	18 (43.9)
Other	
Lobectomy (yes/no)	28/13
Resurgery	14 (34.1)
WHO grade	
Grade III	20 (48.8)
AA	15
AOA	4
AODG	1
Grade IV	21 (51.2)
GBM	15
GS	3
PNET	2
ATRT	1
Adjuvant therapy	
Radiotherapy	28 (68.3)
Chemotherapy	28 (68.3)

GA – General anesthesia; EOR – Extent of resection; AA – Anaplastic astrocytoma; AOA – Anaplastic oligoastrocytoma; AODG – Anaplastic oligodendroglioma; GBM – Glioblastoma; GS – Gliosarcoma; PNET – Primitive neuroectodermal tumor; ATRT – Atypical teratoid rhabdoid tumor

Table 4: A summary of various clinical outcome parameters in our study

Description	Number of patients (n=41), n (%)
Functional status	
Preoperative KPS, median (range)	80 (20-90)
KPS at discharge, median (range)	80 (30-90)
Seizure outcome	
Engel grade	
1A	33 (80.5)
1C	2 (4.9)
2B	3 (7.3)
2C	1 (2.4)
ILAE grade	
1A	33 (80.5)
3	6 (14.6)
Antiepileptic drugs	
Monotherapy	24 (58.5)
Two or more AEDs	17 (41.5)
Survival outcome	
Survived	14 (34.1)
Died	25 (61)
Within 3 months	14 (56)
3-6 months	3 (12)
Beyond 6 months	8 (32)
Lost to follow-up	2 (4.9)

KPS – Karnofsky's performance score; AED – Antiepileptic drugs

Long term seizure outcome

The average duration of follow-up in our series was 18.4 months, ranging from 1 to 88 months. 33 out of 41 patients (80.5%) in our study showed excellent seizure control (ILAE Grade 1A) at the time of follow-up [Table 4].

Survival outcomes

A total of 25 patients (61%) died in our study, including two perioperative mortalities. Twelve patients (29%) died within 3 months of surgery. Three patients (12%) died between 3 and 6 months, while 8 (32%) deaths occurred beyond 6 months of surgery.

The mean OS time was found to be 32.2 ± 6.5 months. The OS rate at 12 months and 18 months of follow-up was 72.2% and 54.2% in Grade III and 42.9% and 19% in Grade IV tumors, respectively. Patients with Grade III tumors showed a significant (log-rank test, P = 0.001) longer OS (50.4 ± 7.7 months) as compared to those with Grade 4 tumors (11.5 ± 4.9 months) [Chart 1]. No significant difference (log-rank test, P = 0.31) was noticed in OS between oligohistology and nonoligo histology subgroups in WHO Grade III patients. Among the Grade IV tumors, we observed a much longer survival in glioblastoma multiforme/gliosarcoma subgroup (88 months) versus embryonal tumors subgroup (20.5 months); however, it did not reach statistical significance (log-rank test, P = 0.168).

During the follow-up, eight patients (19.5%) developed tumor recurrence. The mean PFS was 42.9 ± 4.78 months and PFS rate at 1 year, 2 years and 3 years was 100%, 95.5%, and 32.2%, respectively. We found no significant difference in PFS across WHO Grade 3 versus Grade 4 tumors (log-rank test, P = 0.9). All were re-operated [Chart 2].

Cox regression analysis was done to assess the effect of various factors on survival. It revealed that clinical presentation with seizures (P = 0.01, Hazard Ratio (HR) = 0.3), WHO Grade IV histopathology (P = 0.04, HR = 3.7), and development of recurrence (P = 0.05, HR = 5.5) were independent predictors of OS. Whereas, age, gender, the clinical presentation with raised ICP, baseline KPS, size of the tumor, and extent of resection had no significant effect on patient survival. However, none of the factors were found to affect the PFS significantly.

Discussion

Insula represents one of the most complex areas of the brain. The anatomical and functional complexities of the insula as well as the peri-insular area have been a significant reason for it being considered a "no man's land" for years. The things have, however changed drastically over the last couple of decades.

The insular region harbors 1/4th of low-grade gliomas and about 10% of high-grade gliomas affecting the CNS.[8] As compared with the existing data, we have observed a higher percentage (n = 38/110, 34.5%) of high-grade gliomas affecting the insular region operated at our center. Recently, several studies have been published on insular gliomas and their surgical excision.[12,16-18] These studies have shown that maximal excision of these tumors is possible with acceptable complications and that the extent of excision remains the most crucial factor in determining the survival outcomes. A review of previous publications suggests that the authors either focus on the low-grade gliomas only or they tend to analyze both low- and high-grade gliomas in their analysis. One of the reasons for the lack of a specific analysis of insular high-grade gliomas and other malignant lesions could be the relative rarity of these lesions. With increasing experience with these lesions, neurosurgeons all over the world will be involved in managing the high-grade insular tumors and information on these tumors, including their survival outcome, will be extremely useful to the neurosurgical community. Therefore, our study assumes significance in this regard.

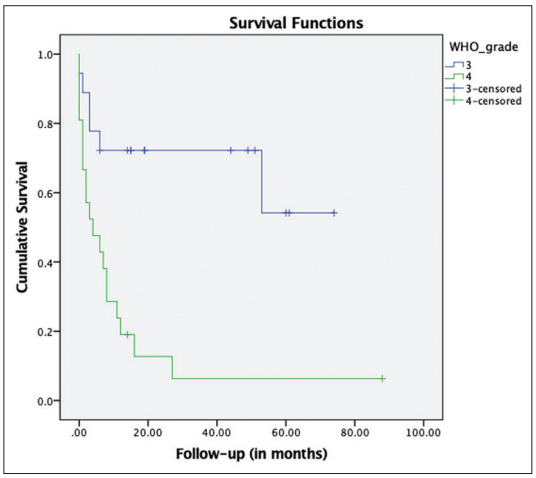

Chart 1: Kaplan–Meier survival curves comparing the overall survival between Grade 3 and Grade 4 tumors

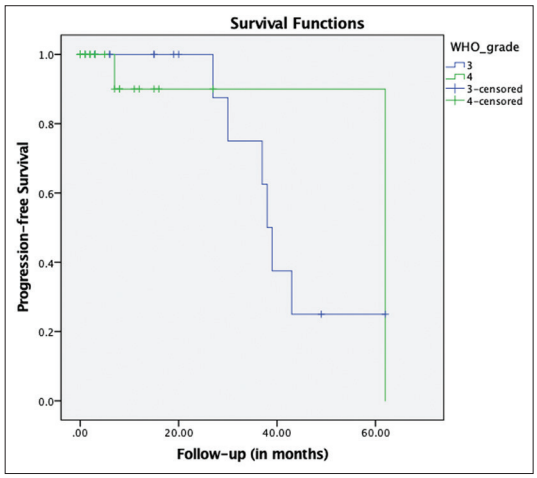

Chart 2: A comparative analysis of progression-free survival between Grade 3 and Grade 4 tumors

While our study was comparable to others in terms of median age at the time of diagnosis, a higher predilection among males (male:female = 4.1:1) was noticed. Seizures are noted to be the most frequent clinical presentation by other authors previously, but holocranial headache was found to be the most common mode of presentation in our study.[12,16-18] This could again be explained by the inclusion of only high-grade lesions in our study. Infiltrative nature of the high grade lesions, pronounced peritumoral edema and a high proportion of sizeable tumors (>4 cm, *n* = 33, 80%) in this study led to raised ICP in our study compared to the previous studies.[12,16-18] Interestingly, findings from the present study also support the observation that involvement of the left side of the brain is found slightly more frequent than the right.

Several classification systems for insular tumors have been proposed based on the anatomical extent of the tumor, lobar involvement, putamen involvement, displacement of corticospinal tracts, and lenticulostriate vessels.[12,16,19,20] As per the most popular Berger-Sanai zonal classification, previous studies have reported zone 1 to be the most frequent site of tumor location in the insular region.[12,17,18] Due to a higher number of large-sized tumors in our series, 25 patients (61%) had tumor involvement of all four zones at the time of presentation. Similar to Sanai *et al*.'s study, we did not find any statistically significant correlation in the relative zonal distribution when compared in terms of location of the tumor-right versus left, histopathological grade – Grade III versus Grade IV, the extent of resection-STR versus NTR and survival outcome.[12]

We have also utilized Yasargil's classification system in our study – Type 5 B was the most common (*n* = 20, 48.8%) subtype encountered and type 3 A was least frequent (*n* = 1, 2.4%). Similar to BS zonal distribution, there was no significant difference among various Yasargil's subtypes in this study.

Owing to the large-sized tumors and associated peritumoral edema, brain bulge was noticed intraoperatively in 30 patients in this study. This observation had crucial importance in our approach to surgical management. At first, awake craniotomy could be done in only two cases, and second, transcortical window technique was done more frequently (*n* = 28, 68.3%) as it was very difficult to open the Sylvian fissure in these patients. In a few cases (*n* = 7, 17.1%), the tumor involvement and edema were so extensive that it mandated a temporal lobectomy first.

Despite recent advancements in modern neurosurgical practice, insular tumors pose significant challenges to the surgeon. A common consensus remains to be agreed upon regarding a safe and effective surgical approach to the insula.[21] On one hand, the trans-cortical approach provides easy and direct access to the insular tumor lying beneath, it provides limited access to the tumors in limen insulae and runs the risk of neurological deficits. A transylvian approach, on the other hand, provides proximal early identification of the insular vasculature but becomes highly tricky in the distal part of the sylvian fissure with limited access to BS zone II.

Extent of resection (EOR) has been established to be an independent predictor of survival in CNS tumors.[5-7] However, due to the anatomical complexity of the insula and high surgical expertise required, achieving a gross-total tumor excision remains a challenging goal to achieve. On the other hand, a subtotal resection is sometimes attempted intentionally to safeguard the lenticulo-striate vessels and internal capsule at the medial surgical extent. Therefore, a STR or NTR for insular tumors is a more frequent "safely achievable" oncosurgical goal. That said, we do agree with numerous publications that support better survival outcomes with increasing extent of excision. The risk associated with aggressive surgical excision of these lesions is obvious and thus needs a tailoring of the surgery. Duffau has suggested this be done under continuous intraoperative neuromonitoring to safeguard adjoining functional areas.[3] This concept of function guided resection has become very popular. Other tools such as intraoperative MRI, intraoperative ultrasonography, and fluorescence-guided resection have also become popular. While we do not have intra-operative MRI at our center, we have used intraoperative ultrasonography, intraoperative neuromonitoring and sodium fluorescence in our latter patients. Their advantages are well proven but getting used to them, incorporating them in the routine surgical practice has to be gradual, as we experienced in our latter cases. However, we believe that a good extent of excision can still be performed using the normal anatomical landmarks, being aware of the "danger zones" and following the color/texture of the tumor. In this regard, surgery for high grade lesions may be more advantageous than the low-grade gliomas.

We observed that the OS in these patients was pretty impressive, with nearly 32 months of OS. The recurrence rate was 20%, which we agree may be an underestimation. We found that a presentation with seizures appeared a favorable factor for the OS, indicating that these patients probably had indolent tumors. We also observed that those who completed the adjuvant therapy also had a better survival. On the other hand, those who developed a recurrence and those who had Grade IV histology fared worse, understandably as both situations predicted an aggressive tumor biology. We did not find the extent of excision a significant factor, unlike most other studies.[5-7,22,23] It could be because of a lack of stringent application of the criteria to assess the extent of excision in this study, unlike other studies. We however need to understand that in the absence of all the gadgets that are at our disposal at the moment, it is better to end up with a sub total excision that err on the side of aggressive resection

and producing neurological deficits. It becomes even more important in the light of recent literature which establishes residual tumor volume as a more accurate prognostic parameter in comparison to the extent of resection.[24-26]

In addition to the advantages with respect to the oncological outcome, we were able to achieve a good (ILAE 1A) seizure control in the majority (n = 33, 80.5%) of our patients. More than half (n = 24, 58.5%) of our patients have maintained seizure control using a single anti-epileptic drug. This was despite the fact that the extent of excision in this series was not very high. In this regard, we concur with the Duffau group that a transcortical approach has a better seizure outcome that the transylvian approach.[27]

There were some important limitations in our series which include retrospective data collection, small sample size and incomplete molecular profile information. Small sample size is a difficult problem in these tumors unless a multi-institutional collaboration is done. Perhaps due to this rarity, previous publications on insular gliomas have combined the low and high grade tumors to derive conclusions. The aim was however to highlight specifically the features of high-grade insular lesions, hence the small sample size. In the modern era, molecular characterization of gliomas is an indispensable part. However, we have to realize that acquisition of these molecular marker kits and expertise will take place slowly at centers in the developing countries, whereas neurosurgeons have continued to resort to surgery for these lesions for years. Due to the limited number of molecular studies performed, we could not perform a statistical analysis of these cases. Volumetric analysis of the tumor could yield a better and quantitative assessment of a residual or recurrent lesion and this has been considered very important in recent publications.[17,24,25] This was again due to the lack of necessary software and expertise. Moreover, a limited infrastructure in overloaded centers may not allow such measurements in all cases in centers like ours. Despite these limitations, our study demonstrates that high grade lesions of the insula are more common than previously estimated and a reasonably good outcome is possible with standard surgical techniques, supplemented by adjuvant chemoradiation. Our study has also shed light on the possible factors that may affect the OS in these patients.

Conclusion

Insular high-grade gliomas are commoner than thought and nearly half of these are Grade IV in histology (51%). Clinical presentation with seizures and completion of adjuvant therapy portend a better prognosis, whereas Grade IV histology and development of recurrence adversely affect the survival. A maximum "safe" surgical resection, keeping the postoperative quality of life in mind, should be the goal in managing these tumors of the insula. With this attempt, the OS may be in the tune of 32 months with a PFS of 43 months. Interestingly, we could observe an excellent seizure outcome in 80% of these patients.

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Conflicts of interest

There are no conflicts of interest.

References

1. Lang FF, Olansen NE, DeMonte F, Gokaslan ZL, Holland EC, Kalhorn C, *et al*. Surgical resection of intrinsic insular tumors: Complication avoidance. J Neurosurg 2001;95:638-50.
2. Das KK, Singh S, Deora H, Khatri D, Mehrotra A, Srivastava AK, *et al*. Microsurgical excision of giant dominant lobe insular cavernoma presenting acutely: Sometimes you win, sometimes you learn. Interdiscip Neurosurg Adv Tech Case Manag 2019;18:100475.
3. Duffau H. Surgery of insular gliomas. Prog Neurol Surg 2018;30:173-85.
4. Deora H, Das KK, Jaiswal A, Behari S. Letter to the Editor. Tumor extension determines approach in insular gliomas. J Neurosurg 2019:1-2. [doi: 10.3171/2019.5.JNS191308].
5. Brown TJ, Brennan MC, Li M, Church EW, Brandmeir NJ, Rakszawski KL, *et al*. Association of the extent of resection with survival in glioblastoma: A systematic review and meta-analysis. JAMA Oncol 2016;2:1460-9.
6. Khan I, Waqas M, Shamim MS. Role of intra-operative MRI (iMRI) in improving extent of resection and survival in patients with glioblastoma multiforme. J Pak Med Assoc 2017;67:1121-3.
7. Li YM, Suki D, Hess K, Sawaya R. The influence of maximum safe resection of glioblastoma on survival in 1229 patients: Can we do better than gross-total resection? J Neurosurg 2016;124:977-88.
8. Duffau H, Capelle L. Preferential brain locations of low-grade gliomas. Cancer 2004;100:2622-6.
9. Zhou C, Wang Y, Liu X, Liang Y, Fan Z, Jiang T, *et al*. Molecular profiles for insular low-grade gliomas with putamen involvement. J Neurooncol 2018;138:659-66.
10. Tang C, Zhang ZY, Chen LC, Sun Z, Zhang Y, Qin Z, *et al*. Subgroup characteristics of insular low-grade glioma based on clinical and molecular analysis of 42 cases. J Neurooncol 2016;126:499-507.
11. Velasquez C, Caballero H, Vazquez-Barquero A, Vega M, Rial JC, Carcedo-Barrio MC, *et al*. Insular gliomas with exophytic extension to the sylvian cistern: A glioma growth pattern that has gone previously unnoticed. World Neurosurg 2016;87:200-6.
12. Sanai N, Polley MY, Berger MS. Insular glioma resection: assessment of patient morbidity, survival, and tumor progression. J Neurosurg 2010;112:1-9.
13. Stupp R, Mason WP, van den Bent MJ, Weller M, Fisher B, Taphoorn MJ, *et al*. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Engl J Med 2005;352:987-96.
14. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, *et al*. The 2016 World Health Organization classification of tumors of the central nervous system: A summary. Acta Neuropathol 2016;131:803-20.
15. Durnford AJ, Rodgers W, Kirkham FJ, Mullee MA, Whitney A, Prevett M, *et al*. Very good inter-rater reliability of engel and ILAE epilepsy surgery outcome classifications in a series of 76 patients. Seizure 2011;20:809-12.
16. Panigrahi M, Chandrasekhar YB, Vooturi S, Ram GA, Rammohan VS. Surgical resection of insular gliomas and roles of functional magnetic resonance imaging and diffusion

tensor imaging tractography-single surgeon experience. World Neurosurg 2017;98:587-93.
17. Eseonu CI, ReFaey K, Garcia O, Raghuraman G, Quinones-Hinojosa A. Volumetric analysis of extent of resection, survival, and surgical outcomes for insular gliomas. World Neurosurg 2017;103:265-74.
18. Wang Y, Wang Y, Fan X, Li S, Liu X, Wang J, *et al*. Putamen involvement and survival outcomes in patients with insular low-grade gliomas. J Neurosurg 2017;126:1788-94.
19. Moshel YA, Marcus JD, Parker EC, Kelly PJ. Resection of insular gliomas: The importance of lenticulostriate artery position. J Neurosurg 2008;109:825-34.
20. Yaşargil MG, von Ammon K, Cavazos E, Doczi T, Reeves JD, Roth P. Tumours of the limbic and paralimbic systems. Acta Neurochir (Wien) 1992;118:40-52.
21. Hervey-Jumper SL, Berger MS. Insular glioma surgery: An evolution of thought and practice. J Neurosurg 2019;130:9-16.
22. Khatri D, Jaiswal A, Das KK, Pandey S, Bhaisora K, Kumar R. Health-related quality of life after surgery in supratentorial gliomas. Neurol India 2019;67:467-75.
23. Sanai N, Polley MY, McDermott MW, Parsa AT, Berger MS. An extent of resection threshold for newly diagnosed glioblastomas. J Neurosurg 2011;115:3-8.
24. Grabowski MM, Recinos PF, Nowacki AS, Schroeder JL, Angelov L, Barnett GH, *et al*. Residual tumor volume versus extent of resection: Predictors of survival after surgery for glioblastoma. J Neurosurg 2014;121:1115-23.
25. Xing Y, Wang X. Which parameter is more important for the prognosis of new-onset adult glioblastoma: Residual tumor volume or extent of resection? World Neurosurg 2018;116:e444-51.
26. Chaichana KL, Cabrera-Aldana EE, Jusue-Torres I, Wijesekera O, Olivi A, Rahman M, *et al*. When gross total resection of a glioblastoma is possible, how much resection should be achieved? World Neurosurg 2014;82:e257-65.
27. Michaud K, Duffau H. Surgery of insular and paralimbic diffuse low-grade gliomas: Technical considerations. J Neurooncol 2016;130:289-98.