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Impact of Extent of Resection and Surgical Approach on Outcomes of Insular Gliomas

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Abstract

Background: The surgical treatment of gliomas in the insular region is considered a challenge for neurosurgeons. The insular cortex represents only 2% of the whole cortex, but gliomas in this area reach up to 25% of all low-grade gliomas (LGG) and 10% of all high-grade gliomas (HGG).

Aim of Study: This study aimed to discuss the different modalities in the surgical management of insular gliomas to obtain favorable surgical outcomes (maximum resection with no deficits) and to identify the different variants affecting the outcomes.

Material and Methods: The data of 21 patients with insular gliomas who had surgery at our institute between August 2018 and August 2020 were retrospectively evaluated in this study. The obtained data included age, gender, preoperative and postoperative clinical conditions, radiological features, approach of surgery, extent of resection of the tumor, and histopathology.

Results: Based on the immediate postoperative clinical outcomes, six cases (28.6%) showed new neurological deficits. Moreover, 9 tumors (42.9%) were treated via the trans-sylvian approach and 12 (57.1%) via the transcortical approach. Awake craniotomy was performed in four cases (19%). Of all cases, six (28.6%) had an extent of resection (EOR) of <90%, five (23.8%) had an EOR of ≥90%, and ten (47.6%) underwent gross total removal.

Conclusion: Overall, a significant statistical correlation between the EOR and the pathological grade of the tumor was observed, but no statistical difference between the transcortical and trans-sylvian approaches in relation to the outcome or the extent of resection. Gliomas in zone 2 and gliomas extending via the superior limiting sulcus showed more postoperative deficits.

Key Words: *Insular – Gliomas – Trans-sylvian – Transcortical – Outcome.*

Introduction

THE surgical management of gliomas in insular region is considered to be a challenging surgical procedure for neurosurgeons **[1-3]**. This is because it is performed near the eloquent areas of language, motor pathways, medial and lateral lenticulostriate arteries, and areas responsible for sensory, motor, olfactory, memory, language, pain processing, affect, gustation, emotional, and cognitive functions **[2-5]**. The lenticulostriate arteries arising from the first division of the middle cerebral artery penetrate the anterior perforated substance to supply the internal capsule, corona radiata, putamen, globus pallidus, and caudate nucleus, so the surgery of insular gliomas carries the risk of injury to these complex vascular and neural structures that may result into postoperative neurological deficits and unacceptable morbidities **[5-7]**.

The insula was named as the "island of Reil" by the German neurologist J. C. Reil in 1908 **[5]**. It is a triangle-shaped cortex embedded in the sylvian fissure and covered by the temporal, frontal, and parietal opercula. It is enclosed by circular sulci (also called limiting sulci) that has anterior, posterior, and inferior parts. It is divided by the central sulcus into two parts: Anterior part and posterior part **[3,5]**.

The insular cortex represents only 2% of the whole cortex, **[8]** but gliomas in this area reach up to 25% of all low-grade gliomas (LGG) and 10% of all high-grade gliomas (HGG) **[2,3,9,10,11]**. The incidence rates are 0.34 per 100000 persons per year for LGG and 0.41 per 100000 persons per year for HGG **[9]**.

This study aims to discuss the different modalities in the surgical management of insular gliomas to obtain favorable surgical outcomes (maximum

List of Abbreviations:

EOR : Extent of resection.
GBM : Glioblastoma multiforme.
TC : Transcortical.
TS : Trans-sylvian.

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resection with no deficits) and to identify the different variants affecting the outcomes.

Material and Methods

This retrospective study was carried out after getting the approval from the institutional review board. A total of 21 cases with newly diagnosed insular gliomas who underwent surgery in our institute from August 2018 to August 2020 were included.

The available data including age, sex, and preoperative conditions (preoperative and postoperative state of consciousness, state of motor power, speech affection, and manifestation of increased intracranial pressure) were obtained, along with the available radiological data of the patients including the of the preoperative CT and MRI scan with contrast. Tumor side and location were recorded. Tumor location was classified into 4 zones (I, II, III, IV) [2] according to the Berger-Sanai classification, and tumor location was assigned to one or multiple zones.

Among the patients, the aim of surgery was maximal safe excision of tumor for mass effect relief, reduction of tumor size (cytoreduction), control of seizure, better survival and histopathological diagnosis with preservation of functional cortex, neural tissues and critical vessels for good functional outcomes. These surgeries were performed by a single surgeon.

Surgical approach was tailored individually according to clinical and radiological assessment of the case (as tumor proximity to the cortex, attacking the shortest distance to tumor epicenter). We preferred the trans-sylvian approach in gliomas located in anterior zones (1 and 4) as it is safer in sparing frontal operculum and Broca's area. We preferred the transcortical approach in gliomas involving the posterior zones (2 and 3) as it is safer to preserve functional areas and vascular structures. We also preferred the transcortical approach in giant gliomas involving 4 zones (1,2,3 and 4) as it provides more exposure to the glioma and give a better chance for increasing the EOR safely. Meticulous tumor excision was performed taking into consideration the texture of the lesion with its anatomical extension, preservations of lenticulostriate arteries without violating neural tissues medial to them. Accordingly, suspicious tissues especially if medially to the lenticulostriates, were preserved. Unfortunately, intraoperative neuromonitoring was not available in our institute due to financial issues.

With regard to the surgical data, the surgical outcomes of the transcortical or trans-sylvian approach and the mode of anesthesia (either under general anesthesia or awake surgery) and any intraoperative surgical complications were recorded.

The postoperative clinical conditions were recorded for all patients. A postoperative neurological deficit was indicated if a newly recorded neurological clinical deterioration or a completely new neurological deficit was observed. Postoperative images were also obtained. CT scans were performed immediate postoperative using General Electric® rightspeed (USA) and Siemens® Somatom Emotion (Germany). Furthermore, MRI was done one month after surgery for all our patients using the 1.5 T Siemens Magnetom Symphony Maestro Class, Syngo MR 2002B (Siemens Medical System Inc., Erlangen, Germany).

Extent of tumor removal was determined through intraoperative gross removal assessment and comparing the preoperative and postoperative images. The extent of tumor resection (EOR) was classified as gross total (100%), near-total ($\geq$90%), or subtotal (<90%).

Histopathological examination for each tumor was performed according to the 2016 WHO classification of the CNS tumors. Periodic follow-up of the patients was registered, adjuvant treatment was prescribed according to EOR, histopathology and follow up status of the tumors.

Statistical analysis:

Data were entered and statistically analyzed in the Statistical Package of Social Science Software program, version 25 (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) and presented using the mean and standard deviation for quantitative variables and frequency and percentage for qualitative ones. The comparison between groups for qualitative variables was performed using the chi-square test or Fisher's exact test, whereas the comparison for quantitative variables was conducted using the Mann-Whitney U test. p-values less than or equal to 0.05 were considered statistically significant.

Results

There were 21 patients in our study, 11 men (52.5%) and 10 women (47.6%). The patients' ages ranged from 23 to 70 years, with a mean of 46 years. Moreover, ten cases (47.6%) presented only with manifestations of increased intracranial pressure (persistent headache, blurring of vision), and one (4.8%) presented with a disturbed conscious level (GCS 14). Other presentations include motor weakness in seven patients (33.3%), seizures in four (19%), status epilepticus in one (4.8%), dysphasia in four (19%), and aphasia in one (4.8%) (Table 1).

Table (1): Description of all studied variables.

	Description (n=21) (%)
Age (years):	
Range	23-70
Mean ± SD	45±14.1
Sex:	
Male	11 (52.4)
Female	10 (47.6)
Zones:	
Single	4 (19)
Multiple	17 (81)
Zones:	
2	2 (9.5)
3	2 (9.5)
2 and 3	4 (19)
3 and 4	9 (43)
1, 2, 3, and 4	4 (19)
Side:	
Right	9 (42.9)
Left	12 (57.1)
Preoperative clinical data:	
↑ Intracranial pressure, intact	10 (47.6)
Weakness	7 (33.3)
Dysphasia	4 (19)
Fits	4 (19)
Aphasia	1 (4.8)
Status epilepticus	1 (4.8)
Disturbed conscious level	1 (4.8)
Approach:	
Transcortical (with general anesthesia)	9 (42.9)
Transcortical (awake)	3 (14.3)
Trans-sylvian (with general anesthesia)	8 (38.1)
Trans-sylvian (awake)	1 (4.8)
Approach:	
Transcortical	12 (57.1)
Trans-sylvian	9 (42.9)
EOR:	
Gross total	10 (47.6)
Near-total	5 (23.8)
Subtotal	6 (28.6)
Pathology:	
Glioblastoma multiform	10 (47.6)
Astrocytoma G I	1 (4.8)
Astrocytoma G II	3 (14.3)
Astrocytoma G III	5 (23.8)
Oligodendroglioma G III	2 (9.5)
Postoperative neurological deficit (outcome):	
Occurred	6 (28.6)
Not occurred	15 (71.4)

According to the classification of Berger-Sanai, 2 most of tumors in our study were present in multiple zones, wherein nine gliomas (43%) were located in zones 3 and 4, four gliomas (19%) were located in zones 2 and 3, and four gliomas (19%) were giant insular gliomas located in zones 1, 2, 3, and 4. Only 4 cases were limited to one zone, where two gliomas (9.5%) were in zone 2 and two gliomas (9.5%) were in zone 3. Moreover, 12 (57.1%) cases had tumors in the left side and 9 (42.9%) cases had tumors in the right side.

Table (2): Association of early new postoperative neurological deficits with other factors.

	Postoperative neurological deficit (outcome)		*p*-value
	+Ve n (%)	–Ve n (%)	
Age (years):			
Range	31-61	23-70	0.668
Mean ± SD	42.5±10.6	45.9±15.4	
Sex:			
Male	3 (27.3)	8 (72.7)	1.000
Female	3 (30)	7 (70)	
Zones:			
Single	2 (50)	2 (50)	0.544
Multiple	4 (23.5)	13 (76.5)	
Zones:			
2	2 (100)	0 (0)	0.089
3	0 (0)	2 (100)	
2 and 3	1 (25)	3 (75)	
3 and 4	1 (11.1)	8 (88.9)	
1, 2, 3, and 4	2 (50)	2 (50)	
Side:			
Right	2 (22.2)	7 (77.8)	0.659
Left	4 (33.3)	8 (66.7)	
Approach:			
Transcortical (with general anesthesia)	3 (33.3)	6 (66.7)	0.900
Transcortical (awake)	1 (33.3)	2 (66.7)	
Trans-sylvian (with general anesthesia)	2 (25)	6 (75)	
Trans-sylvian (awake)	0 (0)	1 (100)	
Approach:			
Transcortical	4 (33.3)	8 (66.7)	0.659
Trans-sylvian	2 (22.2)	7 (77.8)	
EOR:			
Gross total	3 (30)	7 (70)	0.880
Near-total	1 (20)	4 (80)	
Subtotal	2 (33.3)	4 (66.7)	
Pathology:			
Glioblastoma multiform	3 (30)	7 (70)	0.667
Astrocytoma GI	0 (0)	1 (100)	
Astrocytoma GII	0 (0)	3 (100)	
Astrocytoma GIII	2 (40)	3 (60)	
Oligodendroglioma GIII	1 (50)	1 (50)	

Immediate postoperative clinical outcome showed that there were 6 cases (28.6%) showed new neurological deficits in the form of motor weakness associated with dysphasia in 2 cases (one case the glioma was in zones 2,3 and the other case was giant glioma involving all zones 1,2,3 and 4), motor weakness associated with seizure in 1 case (the glioma was in zones 3,4), which was controlled by anticonvulsant therapy, and motor weakness alone in 2 cases (the glioma was in zone 2 in one case and giant glioma involving the 4 zones in the other case), and only dysphasia in 1 case (the glioma was in zone 2) (Table 2). Half of these morbidities improved within 3 months after surgery. No mortalities were recorded.

With regard to the approach of surgery, 9 tumors (42.9%) were treated via the trans-sylvian approach and 12 (57.1%) via the transcortical approach. Awake craniotomy was performed in four cases (19%). Moreover, six cases (28.6%) had an EOR of <90% (subtotal removal), five (23.8%) had an EOR of ≥90% (near-total removal), and ten (47.6%) had an EOR of 100% (gross total removal) (Table 3).

Table (3): Association of EOR with other factors.

	EOR			*p*-value
	Gross total n (%)	Near-total n (%)	Subtotal n (%)	
Zones:				
Single	3 (75)	0 (0)	1 (25)	0.372
Multiple	7 (41.2)	5 (29.4)	5 (29.4)	
Zone:				
2	2 (100)	0 (0)	0 (0)	0.192
3	1 (50)	0 (0)	1 (50)	
2 and 3	1 (25)	2 (50)	1 (25)	
3 and 4	6 (66.7)	2 (22.2)	1 (11.1)	
1, 2, 3, and 4	0 (0)	1 (25)	3 (75)	
Side:				
Right	5 (55.6)	1 (11.1)	3 (33.3)	0.497
Left	5 (41.7)	4 (33.3)	3 (25)	
Approach:				
Transcortical (with general anesthesia)	5 (55.6)	2 (22.2)	2 (22.2)	0.116
Transcortical (awake)	0 (0)	0 (0)	3 (100)	
Trans-sylvian (with general anesthesia)	4 (50)	3 (37.5)	1 (12.5)	
Trans-sylvian (awake)	1 (100)	0 (0)	0 (0)	
Approach:				
Transcortical	5 (41.7)	2 (16.70	5 (41.7)	0.288
Trans-sylvian	5 (55.6)	3 (33.3)	1 (11.1)	
Pathology:				
Glioblastoma multiform	8 (80)	2 (20)	0 (0)	0.024
Astrocytoma GI	0 (0)	0 (0)	1 (100)	
Astrocytoma GII	0 (0)	0 (0)	3 (100)	
Astrocytoma GIII	2 (40)	2 (40)	1 (20)	
Oligodendroglioma GIII	0 (0)	1 (50)	1 (50)	
Postoperative neurological deficit (outcome):				
Occurred	3 (50)	1 (16.7)	2 (33.3)	0.880
Not ocurred	7 (46.7)	4 (26.7)	4 (26.7)	

Based on the histopathological examination of the tumors, the most common histological grade was grade IV glioblastoma multiforme (GBM) in ten cases (47.6%), grade III anaplastic astrocytoma in five (23.8%), grade II astrocytoma in three (14.3%), grade III oligodendroglioma (anaplastic oligodendroglioma) in two (9.5%), and grade I astrocytoma in one (4.8%). 20 cases were referred to the oncologist to receive adjuvant therapy, 17 cases with high histological grades received adjuvant chemotherapy and radiotherapy, 3 cases with the grade II astrocytoma received radiotherapy and one case (grade I astrocytoma) was followed without adjuvant therapy. Follow-up period of these cases ranged from 6 months to 28 months (with mean of 12.76 months), during this time no tumor progression occurred to any case. No mortalities were recorded.

Discussion

The aim of the surgical treatment for insular gliomas is to maximize the EOR of the tumor with the least possible complications or postoperative deficits. Therefore, the surgical treatment of these tumors is always considered a challenge for neurosurgeons because it is usually performed near the eloquent cortical areas, motor and sensory pathways, areas of language, middle cerebral artery branches, and lenticulostriate arteries. In the last decades, neurosurgeons have been developing ideal techniques and strategies for the management of these tumors **[4,12,13]**. In this work, we discussed our experience in the management of insular gliomas and analyzed the surgical outcomes. We also reviewed the literatures and adopted effective methods to obtain better outcomes.

Classification of insular gliomas:

Several classification systems for insular gliomas were described in the literatures. The Berger-Sanai insular classification system was described by Sanai et al., wherein the insula is divided in the sagittal view by a horizontal line through the sylvian fissure that is crossed by a perpendicular plane at the level foramen of Monro. These two perpendicular lines divide the insula into four zones: zones 1 (anterior and superior), zone 2 (posterior and superior), zone 3 (posterior and inferior), and zone 4 (anterior and inferior). The tumor location may be limited to one zone, multiple zones, or all four zones (giant insular glioma) **[2,5,8]**.

In another classification system introduced by Yasargil et al., insular gliomas are classified depending on the pattern of white matter invasion: Type 3A (involving the insula only), Type 3B (invading the operculum), Type 5A (invading the orbitofrontal and/or temporopolar white matter), and Type 5B (invading the mesiotemporal area) **[1,8,14]**. In another classification system by Mandonnet et al., the insular gliomas are classified according to the extension of the glioma in the white matter tracts as the uncinate fasciculus, arcuate fasciculus, or inferior fronto-orbital fasciculus **[8,15,10]**.

The importance of studying these classification systems is to understand the developmental patterns of these gliomas. Therefore, some authors have classified insular gliomas according to their developmental patterns as follows: (1) Gliomas limited to the insular cortex, (2) Gliomas that progress through the anterior limiting sulcus, (3) Gliomas that progress through the inferior limiting sulcus, and (4) Gliomas that progress through the superior limiting sulcus **[16,10]**.

In this study, it was found that gliomas limited to zone 2 and gliomas extending via the superior limiting sulcus showed more postoperative deficits. Some authors report the same results especially in the dominant hemisphere **[1,17]**. This could be because the tumors in this zone were located beside the posterior limb of the internal capsule and the bifurcation of the superficial middle cerebral vein and related to the postcentral gyrus, supramarginal gyrus, Rolandic cortex, and long insular arteries **[1,17,10]**. Moreover, the arcuate fasciculus which is connecting Broca's area and Wernicke's area is located near the superior limiting sulcus **[16]**.

Approach of surgery:

With regard to the approach of surgery, no statistical difference was observed between the transcortical and trans-sylvian approaches in relation to the surgical outcome (postoperative new neurological deficits) or the EOR. This opinion was emphasized by the study conducted by Przybylowski et al., on 100 patients over 10 years **[18]**.

Based on the literatures, the ideal surgical approach to insular gliomas has not been established **[2]**. Numerous surgical approaches were described in the literatures, such as the transcortical and trans-sylvian approaches or the combination of both. Further research is needed to determine the optimal approach to safely obtain favorable surgical outcomes in the form of greater EOR **[2,11,19]**.

The disadvantages of the trans-sylvian approach include the need to sacrifice some sylvian bridging veins and it carries some risk in up to 30% of cases in some literatures [13]. It may also require marked retraction especially in giant tumors, which may result in ischemia, cortical injury, or edema [2,3,11,13].

However, it also has several advantages, such as providing sufficient exposure for the gliomas in the anterior zones (zones 1 and 4) and sparing the frontal operculum (pars triangularis, pars orbitalis, pars opercularis) and the Broca's area, which are responsible for the expression of speech especially in the dominant hemispheres [3]. Based on Safaee et al.'s findings, the trans-sylvian approach is safe and effective [3].

The advantages of the transcortical approach were also discussed in the literatures. The transcortical approach with cortical mapping helps to identify and preserve functional areas especially in gliomas located in the posterior zones (zones 2 and 3) and the vascular structures [3]. Benet et al. suggested that transcortical approach provides good tumor exposure and more surgical freedom and less risk of spasm of the sylvian vessels [19] Daffau et al. discussed the multistage approach for gliomas in the posterior insula and suggested that the functional remapping of the neural tissue will make the second attack safer [20].

Based on the findings of Sanai et al.'s study on 104 cases over 10 years, they suggested that the transcortical approach with cortical mapping is highly superior to the trans-sylvian approach, which they do not recommend [2]. Moreover, in Hameed et al.'s study on 255 cases over 6 years, they suggested that the transcortical approach with cortical and subcortical mapping helps to maximize the EOR safely in all insular zones [13].

Based on the recent studies, the transcortical approach with cortical mapping is preferred by many authors more than the trans-sylvian approach for the surgical management of insular gliomas especially gliomas in the posterior superior quadrant (zone 2) [2,3,11,13,18,19].

We believe that the surgical approach should be tailored to each specific lesion and chosen according to the surgeon's versatility and preference.

Extent of resection and factors limiting it:

In this study, six cases (28.6%) had an EOR of <90%, five (23.8%) had an EOR of ≥90%, and ten (47.6%) had EOR of 100%. A significant statistical correlation was observed between the EOR and the pathological grade. The higher the grade, the higher the EOR. Hameed et al., in their case series emphasized the same finding [13]. This is because the more aggressive approach was selected in high grade tumors. It is also usually associated with more preoperative deficits and has clear tumor boundaries.

In this study, no statistical correlation was observed between the EOR and the anatomical zone. On the other hand, other reports found that gliomas in the posterior zones had lesser EOR because they are in close proximity to eloquent areas and suggested that these areas should be preserved at the expense of the EOR [11,13].

Outcome (new postoperative neurological deficit):

In this study, it was found that gliomas in the posterior zones showed more morbidity, which is consistent with the findings of other studies [1,10,17,16].

Moreover, this study has six cases (28.6%) with new postoperative neurological deficits. Table (4) presents our results and the results of other related literatures (Table 4). In this table, only the new postoperative deficits and the deterioration of previous deficits immediate after surgery (not permanent deficits) were compared regardless the grade or location of the tumors in each study. In most of these studies, the early postoperative deficits improve with time and the percent of permanent deficits is very low. This could be due to some edema near eloquent areas or retraction injury.21 Transient early postoperative new deficits range in literatures from 10% to 59% [11].

Table (4): Review of literature of new postoperative deficits.

	Number of patients (n)	Early new postoperative deficits (n)
M. Yasargil et al., 1992 [14]	80	No data
J. Zentner et al., 1996 [22]	30	63
V. Vanaclocha et al., 1997 [23]	23	22
F. Lang et al., 2001 [24]	22	36
H. Duffau, 2009 [20]	51	59
M. Skrap et al., 2012 [25]	66	33.4
Kawaguchi et al., 2014 [12]	83	26.5
Alimohamadi et al., 2016 [21]	10	10
Chikezie et al., 2017 [11]	74	10.8
Our study	21	28.6

Conclusion:

In insular gliomas, maximizing the resection of the tumor with no new postoperative neurological deficits results in a favorable surgical outcome. Gliomas in zone 2 and gliomas extending via the superior limiting sulcus showed more postoperative deficits. Moreover, we found a significant statistical correlation between the EOR and the pathological grade of the tumor (the higher the grade, the higher the EOR). In this study, no statistical difference was observed between the transcortical and transsylvian approaches in relation to the outcome (postoperative new neurological deficits) or the EOR.

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تأثير حد الاستئصال والنهج الجراحى على نتائج حالات الأورام الدبقية فى الفص الجزيرى للمخ

فى حالات الأورام الدبقية فى الفص الجزيرى للمخ، يعتبر الاستئصال الأقصى للورم بدون حدوث عجز إضافى للمريض بعد الجراحة هو الخيار الأمثل، بالإضافة لاستنتاجنا إحصائياً وجود ارتباط إحصائى بين حد الاستئصال ودرجة نشاط الورم (كلما زاد النشاط زاد حد الاستئصال). فى دراستنا لم يوجد ارتباط إحصائى بين النهج الجراحى وحد الاستئصال أو حدوث عجز إضافى بعد الجراحة.