Transsylvian Insular Glioma Surgery: New Classification System, Clinical Outcome in a Consecutive Series of 79 Cases

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Received, April 22, 2020.
Accepted, December 11, 2020.

BACKGROUND: Surgery of insular glial tumors remains a challenge because of high incidence of postoperative neurological deterioration and the complex anatomy of the insular region.

OBJECTIVE: To explore the prognostic role of our and Berger-Sanai classifications on the extent of resection (EOR) and clinical outcome.

METHODS: From 2012 to 2017, a transsylvian removal of insular glial tumors was performed in 79 patients. The EOR was assessed depending on magnetic resonance imaging scans performed in the first 48 h after surgery.

RESULTS: The EOR ≥90% was achieved in 30 (38%) cases and <90% in 49 (62.0%) cases. In the early postoperative period, the new neurological deficit was observed in 31 (39.2%) patients, and in 5 patients (6.3%), it persisted up to 3 mo.

We proposed a classification of insular gliomas based on its volumetric and anatomical characteristics. A statistically significant differences were found between proposed classes in tumor volume before and after surgery ($P < .001$), EOR ($P = .02$), rate of epileptic seizures before the surgical treatment ($P = .04$), and the incidence of persistent postoperative complications ($P = .03$).

In the logistic regression model, tumor location in zone II (Berger-Sanai classification) was the predictor significantly related to less likely EOR of ≥90% and the maximum rate of residual tumor detection ($P = .02$).

CONCLUSION: The proposed classification of the insular gliomas was an independent predictor of the EOR and persistent postoperative neurological deficit. According to Berger-Sanai classification, zone II was a predictor of less EOR through the transsylvian approach.

KEY WORDS: Insular glioma surgery, Outcome, Transsylvian approach, Oncology, Classification

Operative Neurosurgery 0:1–0, 2021 DOI: 10.1093/ons/opab051

Despite the evident progress in neurosurgery, resection of insular gliomas still remains challenging considering a high degree of incidence of postoperative neurological deterioration.[1-4] This is associated particularly with the complexity of the surgical anatomy of the insular region. Many eloquent structures, including uncinate, arcuate, inferior fronto-occipital fascicules, and corticospinal tract, are located in a close proximity to the insular lobe. The branches of the middle cerebral artery (MCA) and the lenticulostriate arteries (LSAs) embrace the insular lobe and make its surgical anatomy more complex.

ABBREVIATIONS: APS, anterior perforated substance; **EOR,** extent of resection; **HGG,** high-grade glioma; **IDH,** isocitrate dehydrogenase; **KPS,** Karnofsky Performance Score; **LGG,** low-grade glioma; **LSA,** lenticulostriate artery

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Three main approaches can be used to the tumors of the insular lobe: transsylvian, transcortical, and combined transcortical-transsylvian approach.[3,5]

The recent studies showed that the selection of a surgical approach is still controversial regarding to safety and adequate exposure for maximum tumor resection.[2,3,5,6]

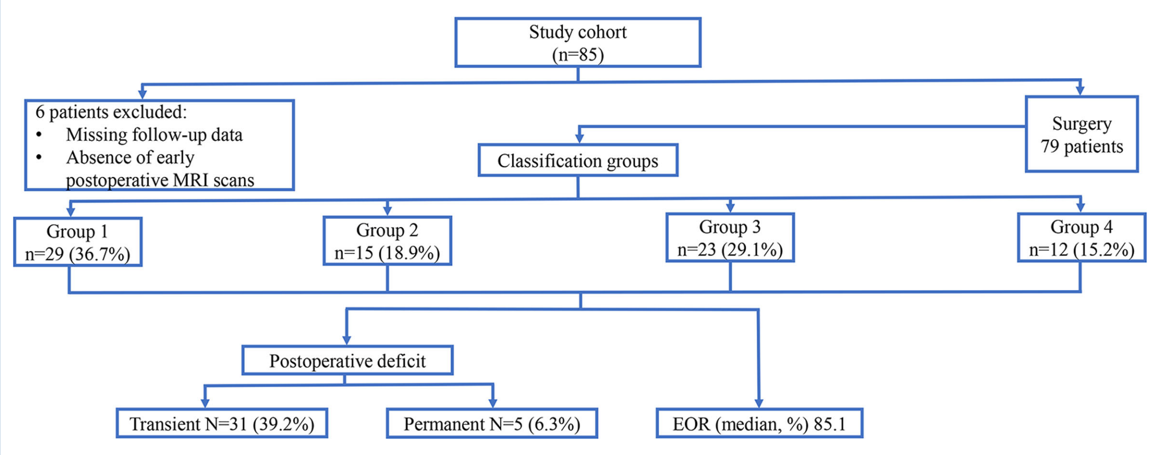


FIGURE 1. *Patient flowchart.*

There are several classification systems of tumors of the insular lobe.[7-9] It has to be mentioned that the prognostic value of Berger-Sanai tumor classification system was applied to patients operated only via the transcortical approach.[6,8,10] Up to date, there is no prognostic evidence regarding to application of Berger-Sanai tumor classification system to the insular gliomas operated through transsylvian approach.

In this prospective study, we report our experience of insular tumor resection via transsylvian approach and explore the prognostic role of our classification system and Berger-Sanai classification system.

METHODS

Patient Population

Between June 2012 and March 2017, 85 adult patients underwent surgical resection of insular tumors (Figure 1). All operations were performed by the first author. Six patients were excluded from our study because of the missing follow-up data or absence of early postoperative magnetic resonance imaging (MRI) scans (in the first 48 h). This study was approved by the Ethics Board of our hospital. Informed consent was obtained in all cases.

The final group of patients consisted of 39 males and 40 females aged from 20 to 67 yr (median: 39.7). In 49 patients, the tumor was located in the left hemisphere and in 30 patients in the right.

The histological type of tumor was classified according to the WHO classifications.[11,12] Prevailed patients with low-grade gliomas (LGG) (Table).

Patients who underwent radio or chemotherapy before surgery were not included in the current study. Two patients underwent stereotactic biopsy before admission to our hospital.

Clinical Assessment and Instrumental Examination

All patients underwent neurological examination before and after surgery on the first and seventh days. Neurological examination was also performed in every 3 mo during the follow-up period. The emergence of new neurological deficits and deterioration of existing ones (motor, speech, or sensory functions) were registered as postoperative complications. The neurological deficit was considered as permanent if it was persistent after 3 mo.

In all cases, the preoperative MRI scans were obtained using scanner HDxt 3.0T (GE Healthcare, Chicago, Illinois). The MRI protocol included T1, T1 + C, T2, fluid-attenuated inversion-recovery (FLAIR), and diffusion-weighted images (DWI).

Volumetric Analysis

Segmentation and volume measurements were performed pre- and postoperatively in the axial plane on Advantage Windows workstation (AW Volume Share 5; GE Healthcare).

The extent of tumor resection (EOR) was evaluated on MRI scans performed during the 48 h after surgery. The EOR of LGG was evaluated on T2 and FLAIR sequences and the EOR of high-grade glioma (HGG) on contrast-enhanced T1 images. Evaluation was performed by 2 neuro-radiologists independently.

Surgical Data

In all cases, transsylvian approach was used for exposure of the insular lobe. In 2 cases, resection of the operculum was necessary. All surgeries were performed without brain retractors under the microscope OPMI NC-4 with application of MARI device.[13]

Intraoperative Electrophysiological Monitoring

Evoked motor potential monitoring (Nicolet Viking Select device; Natus) was conducted in all cases.[14] Two methods for brain stimulation were used: transcranial and direct cortical stimulation.

Two patients (2.5%) underwent awake surgery. In both patients, tumors were located in close proximity to the speech associative fibers and cortical areas.

Adjuvant Therapy

In the postoperative period, radiation therapy was performed in 30 (37%) patients, 31 (39%) patients underwent radiation and

TABLE. Characteristics of 79 Patients With Insular Gliomas According to a Proposed Classification

Characteristics	All	Group 1	Group 2	Group 3	Group 4	*P* value
Number of patients	79	29	15	23	12	
Age (median\range)	39.7 (20-67)	38 (26-61)	41 (24-58)	39 (20-61)	43 (28-67)	$P = .24$
Sex (male)	39	11	11	11	6	$P = .42$
Sex (female)	40	18	4	12	6	
Left side	49	8	9	13	6	
Right side	30	21	6	10	6	
Preoperative KPS (median)	88	89	88	89	85	$P = .09$
Preoperative KPS (range)	60 to 100	80 to 100	80 to 100	70 to 100	60 to 100	
Seizure	58	17	10	21	10	**$P = .04$**
Histopathology						
Ganglioglioma	1	–	–	1	–	
Oligodendroglioma	3	2	–	–	1	
Diffuse Astrocytoma	41	16	7	13	5	
Oligoastrocytoma	8	2	3	2	1	
Anaplastic astrocytoma	8	3	2	3	–	
Anaplastic Oligodendroglioma	–	–	–	–	–	
Glioblastoma	15	6	3	3	3	
Anaplastic oligoastrocytoma	3	–	–	1	2	
IDH1 mutation status						$P = .61$
Mutation	53	18	4	16	8	
Wild-type	26	11	11	7	4	
1p19q status						$P = .11$
Codeletion	10	3	2	1	4	
Intact	69	26	13	22	8	
Extent of resection						**$P = .02$**
≥90%	30	16	4	4	6	
70% to 89%	34	8	8	13	5	
<70%	15	5	3	6	1	
Median	85.1	90.4	80.4	77.0	87.5	
Preoperative tumor volume, cm^3						**$P < .001$**
Median	56.6	36.8	77.2	54.7	82.1	
Range	5.77 to 207	5.8 to 207	16.1 to 178	8 to 121	33.1 to 154	
Postoperative tumor volume, cm^3						$P < .01$
Median	6.72	2.7	10.4	8.2	6.1	
Range	0 to 55	0 to 23	0 to 55	1.2 to 50.4	0 to 34.6	
Postop deficit						
Transient deficit	31	11	5	9	6	$P = .21$
Motor deficit	8	1	2	3	2	
Language deficit	13	6	3	2	2	
Sensory disturbance	0	0	0	0	0	
Visual field disturbance	0	0	0	0	0	
Motor and language deficit	10	4	0	4	2	
Permanent deficit	5	0	0	3	2	**$P = .03$**
Motor deficit	4	0	0	3	1	
Language deficit	1	0	0	0	1	
Postoperative KPS (median)	82.8	84	84	79.1	83.9	$P = .31$
Postoperative KPS (range)	40 to 100	70 to 100	70 to 100	40 to 100	50 to 100	
Radiation therapy	61	21	13	19	8	
Chemotherapy	32	12	7	9	5	

Boldface values are statistically significant.

chemotherapy, 1 (1.3%) patient underwent chemotherapy alone, and in 17 (21%) patients, no radiation and/or chemotherapy was performed.

Follow-up

The median follow-up period was 37.4 mo (range 11.9-70.6 mo).

Statistical Data Analysis

Statistical analysis was conducted using the R programming language and environment (version 3.2.1). The chi-square test and Fisher exact test were performed to compare the distributions of categorical variables. The differences in continuous variables were evaluated with the Mann-Whitney and Kruskal-Wallis tests. The multivariate analysis was performed using the logistic regression model. The results of the statistical tests were considered significant with $P < .05$.

RESULTS

Clinical Presentation

The leading clinical manifestations of insular tumors were epileptic seizures in 58 (73%) patients (Table).

Different types of aphasia were observed in 4 (5%) patients with left insular tumors. Motor disorders of moderate degree were observed in 3 (3.8%) patients and paresthesia in 1 (1.3%) patient. Signs of intracranial pressure (papilledema) were revealed in 1 (1.3%) patient.

Tumor Classification

At our hospital, we have been using the volumetric-anatomic classification of insular tumors proposed by authors for 8 yr. It combines elements of both the Berger-Sanai scheme and the Yasargil classification scheme, but it is based on volumetric-anatomical principles.

Depending on the insular tumor extension relative to the surrounding anatomic structures, we identified the following groups of patients (Figure 2).

For group 1, the tumor was located only in the insular lobe and did not extend beyond its borders (peri-insular sulci and the limen insula), and the medial border was the basal ganglia and LSA in 29 (36.7%) patients.

For group 2, most of the tumor volume was located in the insula (more than 50% of the tumor volume) but with an extension to the adjacent lobes (temporal and/or frontal lobes) in 15 (18.9%) cases.

For group 3, most of the tumor volume was located in the insula (more than 50%), but with an extension medially, spreading on the anterior perforated substance (APS), and in some cases, up to subcallosal area, including LSA in 23 (29.1%) patients.

For group 4, most of the tumor volume was located outside the insular lobe (the tumor volume within the insula comprised less than 50% of the total tumor volume, according to volumetric analysis) in 12 (15.2%) patients.

According to Berger-Sanai[8] classification, the following tumor distributions were revealed: zone I in 4 (5%), zone II in 2 (2.5%), zone III in 2 (2.5%), zone IV in 1 (1.3%), zones I + II in 1 (1.3%), zones I + IV in 9 (11.4%), zones II + III in 4 (5%), zones III + IV in 1 (1.3%), and giant (tumor extension to all zones) in 55 patients (69.7%).

According to the Yasargil classification, following tumor distributions were revealed: type 3A in 41 (51.9%) patients, type 3B in 6 (7.6%) patients, type 5A in 19 (24%) cases, and type 5B in 13 (16.5%) cases.

Tumor Resection

Transsylvian approach without intersecting superficial middle cerebral veins was performed in 70 (88.6%) cases, and in 9 (11.4%) cases, small bridging veins were sacrificed.

During the dissection of the Sylvian fissure, damage of the MCA branches was not observed in any cases (Figure 3). Tumor resection was initiated between M2 segments of the MCA at the anterior part of the insula. The M1 segment of the MCA together with proximal LSAs up to the APS was separated from the tumor and preserved (Video).

Extent of Tumor Removal—Volumetric Analysis

The median tumor volume measured before surgery was 56.6 cm^3 (7.9-207 cm^3).

According to MRI data, performed in the postoperative period (48 h), the EOR $\geq$90% was achieved in 30 (38%) cases and $<$90% in 49 (62.0%) cases. In 34 (43.2%) patients, EOR was 70% to 90% and less than 70% in 15 (18.9%) patients. The highest EOR was observed in group 1 (median 90.4%) and in group 4 (median 87.5%). The smallest EOR was observed in group 3 (median 77%).

The median residual tumor volume was 6.72 cm^3 (0-55 cm^3).

Using our classification, a statistically significant association was revealed between the EOR and tumor location ($P = .02$). In a univariate analysis, no statistically significant relationship was revealed between the EOR and the Berger-Sanai zones ($P = .41$) and Yasargil grades ($P = .17$).

However, in the logistic regression model, tumor location in zone II (Berger-Sanai classification) was related to the EOR of more than 90%.

We analyzed the fact of residual tumor detection according to postoperative MRI scans in a group of 55 patients (69.7%) in which the tumor occupied all insular zones according to the Berger-Sanai classification. Most often, the residual tumor in the postoperative images was revealed in zone II (40%; $P = .02$).

Morbidity Profile

In the early postoperative period (24 h), new neurological deficit was observed in 31 (39.2%) patients: in 8 patients (10.1%), motor impairment; in 13 (16.5%), only speech disorders; and 10 (12.7%) patients had speech and movement disorders (Table). Among patients with speech disorders, 4 patients had a severe impairment, 6 had moderate, and 13 had mild disability.

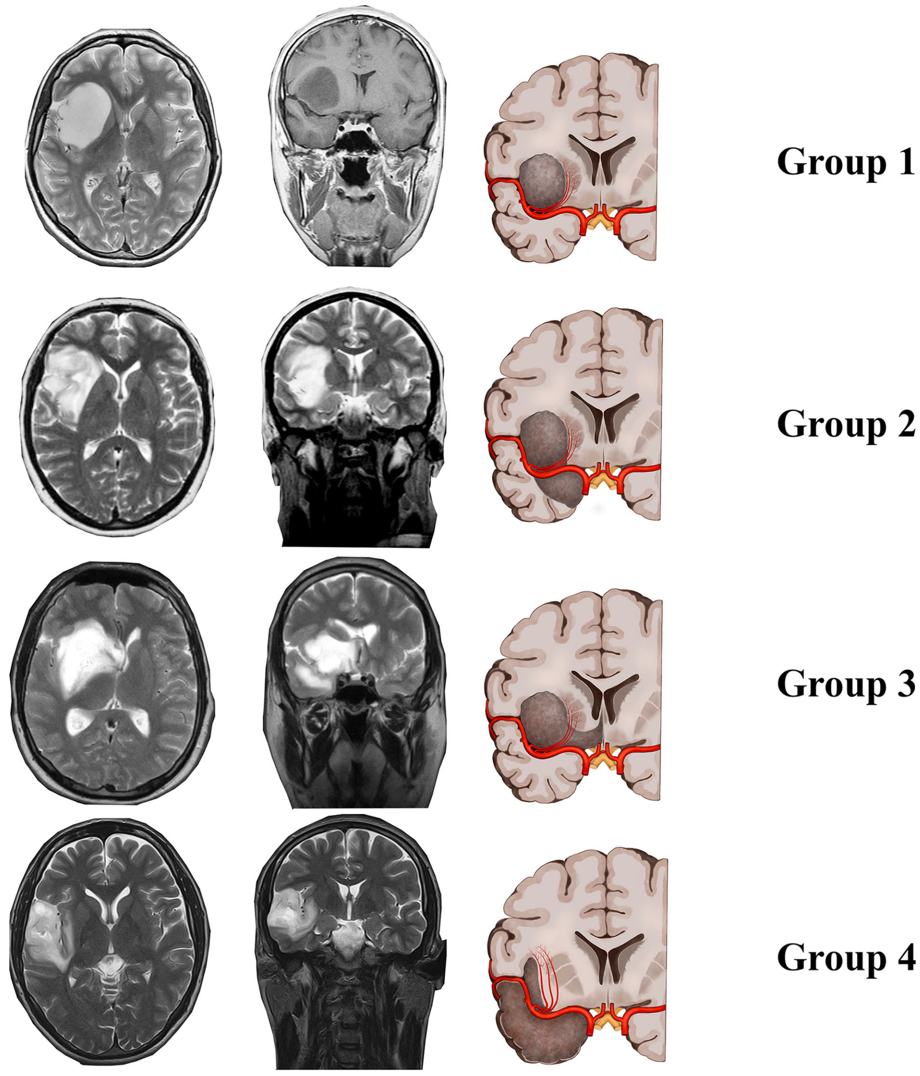


FIGURE 2. *Four types of insular tumor extension according to the classification presented in the article.*

Out of 18 (22.8%) patients with motor deficit, mild hemiparesis was observed in 5 (6.3%) patients, moderate in 2 (2.5%), and severe in 8 (10.1%) cases. An isolated central facial nerve palsy was observed in 3 (3.8%) patients.

In the early postoperative period, clinically manifested vasospasm was observed in 1 (1.9%) patient.[15] Increased systolic linear blood flow velocity up to 140 to 150 cm/s without clinical manifestation was revealed in 11 (17.7%) patients.

Follow-up

Persistent neurological deficit was evaluated 3 mo after surgical treatment and was observed in 5 (6.3%) patients: 1 patient (1.3%) with speech disorders and 4 patients (5.1%) with motor deficits.

Engel IA and IB classes included 40 (50.6%) patients 6 mo after surgical treatment.

Statistical Analysis of Differences Between Classes According to the Proposed Classification

There were statistically significant differences in preoperative and postoperative tumor volume depending on the proposed classes ($P < .001$ and $P < .01$, respectively); the maximum degree of tumor resection was more likely to be achieved in group 1, less likely in group 3 ($P = .02$); the rate of epileptic seizures before surgical treatment prevailed in group 4 ($P = .04$); and the incidence of persistent postoperative complications was higher in group 3 ($P = .03$) (Table).

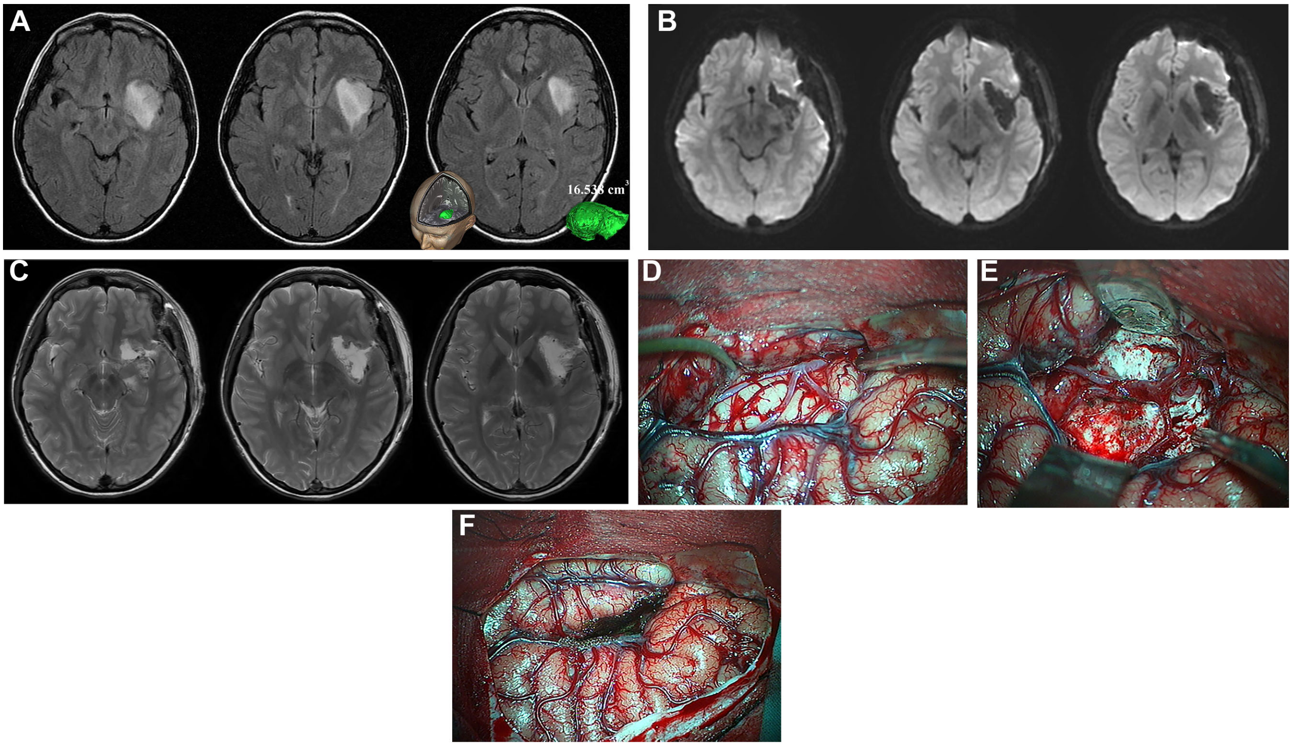


FIGURE 3. *The clinical example of the left insular lobe tumor removal (group 1, Berger-Sanai Giant, Yasargil classification 3A).* **A**, *The MRI scan (FLAIR) reveals an insular lobe tumor with a hyperintensive MR signal. Tumor volume before surgery was 16.538 cm^3.* **B** *and* **C**, *Postoperative MRI scans (DWI: 3 scans and T2: 3 scans).* **D-F**, *Three intraoperative photos demonstrating consecutive stages of tumor removal. A wide dissection of the Sylvian fissure. The tumor of the insular lobe is exposed with the M2 segments of the MCA lying on the superficial surface of the tumor. The view of the surgical wound after the resection of the tumor.*

The following indicators such as Karnofsky Performance Score (KPS) before and after surgery, age, gender, complications in the early postoperative period, the presence of the isocitrate dehydrogenase 1 (IDH1) mutation, and 1p19q status were not statistically significantly different between the groups proposed by authors' classification system.

DISCUSSION

Currently, there is a unanimous opinion that the first line of the treatment of the insular gliomas, despite the complex anatomy of the area, is microsurgical removal.[1,16]

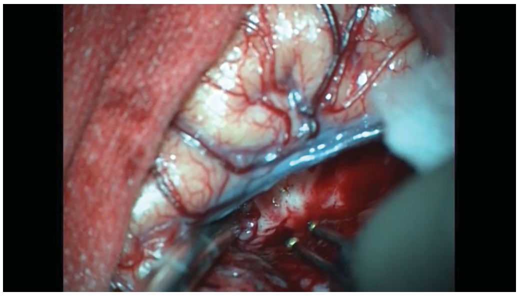
Surgical manipulation in some areas of the brain is limited because of the high risk of postoperative complications and morbidity of patients. But at the same time, the EOR (both LGG and HGG) directly correlates with the survival time of patients.[8,17-22]

Surgical Approaches to the Insular Lobe and Clinical Outcome

There is no consensus about the optimal surgical approach to the insular lobe. A large amount of publications about insular lobe surgery, starting with the pioneering work of Yasargil et al,[9] advocated transsylvian approach.[23-26] Later on, the development of modern methods of electrophysiological monitoring led to the predominance of transcortical approach for insular tumor removal.[6,10,27,28]

The main advantage of transcortical approach is a larger operating window and space for manipulation, which was also confirmed by the results of anatomical investigation, in which these 2 approaches were compared.[29-31] This advantage is provided by resection of the functionally "nonsignificant" brain tissue under the control of electrophysiological methods.[8] However, in white matter of the fronto-parietal operculum, the associative fibers of the superior longitudinal fasciculus III are located,[30] Broca's area in the dominant hemisphere and the motor area of the facial muscles (temporary central facial paresis reaches up to 9.3%[8] after transcortical approach).

In the nearest future, it will still be a matter of dispute whether the rate of postoperative neurological deficit depends on the surgical approach to the insular lobe because it is a difficult task to compare the results of known series performed in different hospitals by different surgeons. Only in 2 articles, Simon et al[32] and Przybylowski et al[5] compared transsylvian and transcortical



VIDEO. *Removal of the tumor of the insula via transsylvian approach.*

approaches and revealed that the rate of postoperative neurological complications did not depend on the approach to the insular lobe.

According to our results, in the early postoperative period a new neurological deficit was observed in 31 (39.2%) cases and persistent neurological deficit was observed in 5 (6.3%) patients. In other known works, the persistent neurological deficit rate ranged from 2.7% to 20%.[6-9,24-26,32-35]

Insular Tumor Classification Systems

Insular tumors can be classified as a very diverse group of tumors because they may spread beyond insular borders or within the different parts of the insular lobe itself. To date, a few classifications were developed.[8,9,27,36]

Sanai et al[8] demonstrated that EOR via transcortical approach depends on tumor location. Maximal resection was achieved when tumor was located within zone I and zone IV and minimal resection within zone II. Also, tumor location was an independent predictor of early postoperative neurological deficit, which developed more often when tumor size was giant or the tumor was located in zone I. Late deficit did not depend on tumor location.[10]

The maximum EOR in our series of patients was observed in the group 1, which was probably due to the possibility of determining periinsular sulci in this group of patients when using the transsylvian approach.

Persistent neurological deficit was more often observed in the group 3. This is possibly due to more frequent damage of the LSAs in this group because they are located inside the tumor.

For the first time, we performed analysis of correlation between tumor location (based on Berger-Sanai classification) and EOR via transsylvian approach. The location of the tumor in zone II had a significant impact on EOR (more than 90%). This fact can be explained by proximity of cortico-spinal tract to this region and deeper surgical corridor through Sylvian fissure in this zone.

In our opinion, attributing the group 4 patients to "insular gliomas" is somewhat disputable. In fact, many tumors of frontal or temporal lobe with minimal insular involvement were classified as "insular gliomas." In some cases, temporal or frontal lobectomy can be performed while the insular part of the tumor remains intact (eg, in group 4, the median EOR was 87.5%). Probably, we should reassess insular tumor classification and base it according to the tumor volume within the insular lobe (volumetric analysis). In our hospital, volumetrically anatomic classification of the insular tumors has been used for 8 yr by now. We believe that only patients from groups 1, 2, and 3 should be included into EOR analysis and that only this kind of tumors can be classified as "insular tumors."

Limitations

The overall number of patients was 79, and number of patients within groups varied significantly. Moreover, complication rate greatly depends on neurosurgeon's experience and skills, which makes any attempt of comparing similar studies challenging.

CONCLUSION

The proposed classification of insular lobe tumors makes it possible to predict the extent of tumor resection and expected permanent neurological deficit.

Funding

This study did not receive any funding or financial support.

Disclosures

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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