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Long-term clinical and seizure outcomes of insular gliomas via trans-opercular approach

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ABSTRACT

Objective: To report long-term clinical and seizure outcomes of patients who were operated upon insular gliomas via trans-opercular approach.
Patients and Methods: Since 2010, surgical resection of insular gliomas was performed via trans-opercular approach by our group. Clinical, surgical and follow-up results were analyzed retrospectively.
Results: The majority were low-grade (81.8%) and among them oligodendroglioma was the most common (n = 8). Half of the patients underwent awake craniotomy with cortical electrical stimulation and total removal was achieved in 6 patients. Long-term follow-up showed the majority of patients (90.9 %) were completely seizure free. Only one patient showed slight paresis on one upper extremity at the long-term follow-up.
Conclusions: Trans-opercular approach for insular gliomas is safe and maximal resection with minimal neurological deficits is possible. Use of ultrasonic aspirator and neuronavigation make surgery safer. Surgery-related complication is very rare. Future studies should contain larger number of patient and long-term follow-up in order to provide more accurate data.

1. Introduction

The insula, 5th lobe, is hidden in the depth of the sylvian fissure and covered by three opercula: frontal, temporal, and parietal. It has close relationship with one of the most important vasculature of the brain, the middle cerebral artery (MCA) and its branches. Furthermore, important white matter fiber tracts course underneath. All these anatomical features make the insula untouchable structure for many years when it is involved by space-occupying lesions. Since it has sensorimotor, cognitive, and emotional functions, surgical approaches can result in severe neurological deficits.

After seminal work by Yasargil [1], it became possible to touch the insula with acceptable neurological deficits and as surgical experience increases and different approaches are developed, clinical and cognitive outcomes improved. Recent developments in neuronavigation and magnetic resonance imaging technologies (MRI), use of cerebral electrical stimulation (awake craniotomy), and development of neuropsychological testing led us to understand functions of the insula and made surgery safe. Another important issue for both patients and neurosurgeons is that insula is a part of the limbic and paralimbic systems and can involve in seizure development. Thus, not only for clinical outcome but also seizure outcome is also utmost importance since continuous seizure decreases quality of life (QoL) significantly [2].

Gliomas, particularly low-grade gliomas (LGG), are the most common tumors involving the insula, accounts for almost 30%, followed by high-grade gliomas (HGG) which is almost 10 percent [3]. Surgery for gliomas in the insula is challenging because of its complex anatomical location mentioned above. Two main surgical approaches have been performed: trans-sylvian and trans-opercular. The choice of surgical approach is mainly depended upon the experience of surgical team and results of two approaches have been published in the literature [4–6].

The aim of this paper is *not* to compare the two approaches, rather we want to present our results in patient with insular gliomas operated via trans-opercular approach which has been extensively used by Olivier [7] in Montreal, Canada and Duffau [8] in Montpellier, France. Since 2010, our team has changed surgical strategy from trans-sylvian

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[4] to trans-opercular approach in glioma surgery with respect to insula and insulo-opercular regions.

2. Materials and methods

This retrospective clinical study included patients who admitted our clinic and operated on insular gliomas between 2010 and 2016. Clinical symptoms, especially presenting symptoms and neurological examinations including use of anti-epileptic drugs (AED) were noted. As a first step, MRI of the head is obtained from all patients. Routinely, neuropsychological testing was performed in order to specify dominant side for memory and speech. Neuronavigation was used in all patients and awake craniotomy with cortical and subcortical electrical stimulation was performed in patients who were able to tolerate awake surgery. Trans-opercular approach with subpial/endopial resections was the choice of surgery. After surgery MRI within the first 72 h was performed in order to detect extent of resection (EOR) and all were followed-up regular with interval. Clinical and seizure outcomes were noted and seizure outcome was evaluated by Engel classification [9] which was dichotomized as Class I (completely seizure free) versus Class II–IV (not completely seizure free). Depending on the histopathological diagnosis, grade-III and -IV gliomas were sent to radiation therapy for further treatment. Patients and/or their next of kin were informed about possible complications of surgery and after getting signed informed consent, surgery was performed. Our local ethics committee informed us that there is no need to have approval because of its retrospective nature. Thus we did not get official approval from the local ethics committee for this study. All patients were followed-up at least 1 year after surgery.

We used a commercially available statistical software package (SPSS version 15.0 Inc., Chicago, Illinois, USA) for all statistical analyses. The mean ± standard deviation was calculated for each parameter. The independent samples *t*-test and chi-square test were used for appropriate comparisons. Differences were considered statistically significant if $p < 0.05$.

2.1. Surgical considerations

In all cases, the borders of tumor were initially delineated via neuronavigation. For the tumors with frontal or temporal extensions, initial resection of lobar involvement guided the surgical approach to the superior or inferior part of the insular tumor. For pure insular tumors, on the other hand, frontal and/or temporal opercula was used for cortical windowing according to the area of tumoral extension (frontal corridor for tumors mainly in the superior half and temporal corridor for the inferior half). In awake patients, non-essential areas as the site of entry was determined by functional mapping (speech areas on the dominant side and motor areas on dominant/nondominant sides) using direct electrical stimulation (DES). In cases under general anesthesia, pars triangularis and orbitalis of inferior frontal gyrus, and/or anterior portion of superior temporal gyrus were used for transcortical approach (dominant/nondominant sides) as they are assumed less critical to interfere with associative tracts.

The limits of resection were identified mainly by cortical and subcortical DES and navigation in awake patients. Since techniques of awake craniotomy has been published in the literature extensively, we will not go into detail here. Under general anesthesia, the deep limits of resection were mostly determined by neuro-navigation and surgeon's experience based on the consistency of tumor, color change of lenticular nuclei and according to some common landmarks as the base of periinsular sulci and lateral lenticulostriate arteries. Moreover, subpial resection which aids to follow the limits of periinsular sulci and stay in secure margins was the technique of choice in all cases.

Table 1
Clinical characteristics of 22 patients *before surgery* reported in this study.

Factor	Value (n/%)
Age (years)	*46.18 ± 13.8*
Sex (M/F)	11/11; 50/50
Dominant hand (R/L)	22/0; 100/0
Presenting signs or symptom	
● Seizure	15/68.2
●Headache + seizure	4/18.2
● Headache	*2/9.1*
● Paresis on extremities	1/4.5
Mean seizure frequency/week	4.5 ± 8.5
Mean age at seizure onset (years)	43.4 ± 12.2
Number of anti-epileptic drug (mean)	0.95 ± 0.48

F: Female; L: Left; M: Male; R: Right.

3. Results

3.1. Clinical characteristics before surgery

Table 1 summarizes clinical features of 22 patients operated on insular gliomas via trans-opercular approach. There is no sex predilection and age ranged from 26 to 73 years. The main presenting symptom was seizure as expected in this region and neurological examinations showed 5 patients had neurological deficits: slight facial paralysis in 3 and paresis on the extremities in two. Generally, seizure started late and duration from the first symptom to surgery was almost 4 months. All except 3 were on AED, most of which was started by other institutions before seen by us. Every patient had MRI early after surgery which is generally within 72 h of resection in order to evaluate EOR and time interval for clinical follow-up with head MRI was performed depending on the grade of tumor.

3.2. Radiological and surgical characteristics

Table 2 shows summary of radiological and surgical findings of the patients. On radiological examinations head MRI showed right side was commonly involved however; no statistical significant difference was found regarding the side of involvement (χ^2 test; p = 0.67). There was generally opercular involvement in addition to the insula and pure insular involvement is rare. No significant differences among localization of gliomas in this region was found (χ^2 test; p = 0.17). In all surgeries, neuronavigation was used and although cortical electrical stimulation was planned for all patients but we were able to perform it in 50% because mainly of two reasons: one is that some patients did not want to have awake craniotomy and the other reason is that some could not tolerate and we had communication problems. Trans-opercular approach with asleep-awake-asleep anesthesia if needed was preferred. The surgical technique did not change according to the dominance of hemisphere. Inferior frontal or superior temporal gyrus is the

Table 2
Radiological and surgical characteristics of 22 patients reported in this study.

Factor	Value (n/%)
Side of tumor (R/L)	12/10; 54.5/45.5
Localization	
● Temporo-insular	8/36.4
● Fronto-insular	8/36.4
● Insular	4/18.2
● Fronto-temporo-insular	2/9.1
Anesthesiology (awake/general)	11/11; 50/50
Early MRI (total/gross total removal)	6/16; 27.3/72.7
Progression of residue on late MRI (yes/no)	4/18; 18.2/81.8

L: Left; MRI: Magnetic resonance imaging; R: Right.
Early MRI explains head MRI within 72 h of surgery.
Gross total removal denoted removal of tumor ≥90%.