Volumetric Analysis of Extent of Resection, Survival, and Surgical Outcomes for Insular Gliomas

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■ BACKGROUND: **Insular gliomas are challenging tumors to surgically resect owing to the anatomy surrounding them. This study evaluates the role of extent of resection (EOR) and molecular markers in surgical outcome and survival for insular gliomas.**

■ METHODS: **Seventy-four patients who had undergone initial resection for insular glioma by the same surgeon between 2006 and 2016 were analyzed. Low-grade gliomas (LGGs) (grade II) and high-grade gliomas (HGGs) (grade III/IV) were analyzed for the prognostic role of volumetric EOR and molecular markers in patient survival outcomes.**

■ RESULTS: **The cohort included 25 patients with LGGs (33.8%) and 49 patients with HGGs (66.2%). Median EOR was 91.7% (range, 10%—100%). New permanent postoperative deficits were found in 2.7% of patients. Patients with LGGs with ≥90% EOR had 5-year survival of 100%, and patients with <90% EOR had 5-year survival of 80%. Patients with HGGs with ≥90% EOR had 2-year survival of 83.7%, and patients with <90% EOR had 2-year survival of 43.8%. For LGGs, EOR was predictive of overall survival ($P = 0.017$), progression-free survival (PFS) ($P = 0.039$), and malignant PFS ($P = 0.014$), whereas 1p/19q codeletion was predictive of PFS ($P = 0.014$). For HGGs, EOR was predictive of overall survival ($P = 0.020$) and PFS ($P = 0.024$). Preoperative tumor volume most significantly affected EOR for insular gliomas ($R^2 = 0.053$, $P = 0.048$).**

■ CONCLUSIONS: **Extensive resections of insular gliomas can be achieved with low morbidity and can improve overall survival and PFS. In this series of LGGs, EOR was associated with longer malignant PFS, and 1p/19q codeletion was predictive of PFS.**

INTRODUCTION

Insular gliomas are the most common intrinsic tumor of the insular cortex and account for approximately 25% of all low-grade gliomas (LGGs) and 10% of all high-grade gliomas (HGGs).[1-3] Tumors in this cortical area are surrounded by eloquent brain that controls motor and language function. The vascular supply for the descending motor pathway also passes through the insular region.[4-6] Patients with insular tumors often present with devastating intractable epilepsy or motor dysphasia making it essential to properly treat these lesions.[7-10]

Owing to their deep location in the sylvian fissure and complex anatomy that surrounds the area, insular tumors are challenging tumors to resect.[7,11] The standard of care for insular gliomas includes a maximal safe resection followed by chemoradiation therapy.[12] Surgery in the insular region may require opening the sylvian fissure for insular exposure, which puts vital functional cortical areas, motor and language subcortical fibers, and vascular structures at risk in this region.[11,13] There is a high risk of neurologic deficits after resection of insular tumors given the proximity of

Key words
- Glioma
- High grade
- Insula
- Insular tumors
- Low grade
- Survival

Abbreviations and Acronyms
CI: Confidence interval
EOR: Extent of resection
HGG: High-grade glioma
HR: Hazard ratio
IDH: Isocitrate dehydrogenase
LGG: Low-grade glioma
MCA: Middle cerebral artery
MPFS: Malignant progression-free survival
MRI: Magnetic resonance imaging
OS: Overall survival
PFS: Progression-free survival

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the insula to vital vascular and neural structures, and severe speech and motor disorders can result in the postoperative period.[14]

Given the high risk of surgery, some authors have reported that insular tumors are inoperable and opt for stereotactic biopsies for diagnosis followed by chemotherapy and/or radiotherapy as an alternative treatment.[2,15-17] However, other authors have reported favorable results with insular tumor resections using specialized microsurgical techniques and an understanding of the insular anatomy.[12,16,18-21] Despite the high risks of surgery in the insular region, there are limited studies that evaluate the role of the extent of resection (EOR), analyzed volumetrically, on patient outcomes and survival for insular gliomas.[22,23] Additionally, with an increasing understanding about glioma genetics and the role of genetics in prognosis for LGGs (isocitrate dehydrogenase 1/2 [IDH1/2] mutation and 1p/19q codeletion), no previous volumetric analysis for insular gliomas have accounted for these variables when evaluating the role of EOR in patient survival outcome.[24] In this study, we present a cohort of insular gliomas operated by a single surgeon at a single center and evaluate the role of EOR and molecular markers in patient outcome and survival.

MATERIALS AND METHODS

Patient Selection

The university institutional review board approved this study. Seventy-four consecutive patients with insular gliomas resected for the first time by a single surgeon between January 2006 and July 2016 were prospectively collected and retrospectively reviewed. Patients were ≥18 years old. Pathology assessment of the tumor was based on World Health Organization guidelines. Patients with gliomatosis cerebri were not included in this study. Clinical data were collected from the patient chart review.

Surgical Approach

A transcortical approach was used for all insular tumors. The location and side of the hemisphere of the tumor determined whether the tumor was resected under general anesthesia (45 cases) or by awake craniotomy (29 cases). Our method for awake anesthesia has been previously described.[25] After the craniotomy was performed and dura mater opened, cortical and subcortical sensorimotor mapping was conducted. Once functional regions were identified, corticectomies above and below the sylvian fissure in noneloquent regions were made allowing for tumor resection around the sylvian vessels. Cortical mapping of the medial border of the tumor was also conducted if needed to identify the internal capsule. The goal of all surgeries in this cohort was for a safe, 100% total resection; however, tumor invasion into areas deemed eloquent for motor, sensory, or language areas by intraoperative cortical or subcortical mapping or extensive involvement of the middle cerebral artery (MCA) within the tumor limited the EOR.

Patient Outcome Data

Patients were examined preoperatively, immediately postoperatively, and during follow-up visits by the senior surgeon (A.Q.-H.). Neurologic deficits were determined by identifying new or worsening deficits related to motor, sensory, or language function. Outpatient examinations were conducted at 1 month, 6 months, and then annually following surgery. Transient deficits were considered new or worsening neurologic deficits after surgery that resolved before the 6-month follow-up clinic visit. Permanent deficits were neurologic deficits that persisted beyond the 6-month follow-up clinic visit. The length of hospitalization was calculated based on the duration of hospital stay from the day of surgery until the day of discharge.

Survival data, including overall survival (OS), progression-free survival (PFS), and malignant progression-free survival (MPFS), were also analyzed. OS was the time between initial surgery and death. PFS was the time from initial surgery to unequivocal demonstration of tumor regrowth on follow-up imaging. MPFS was defined as cases in which grade II gliomas, determined from pathology from the initial surgery, were found to transform into a higher grade lesion via histopathology from a subsequent resection or biopsy or enhancement from follow-up imaging. Patients with no tumor progression were censored as of their last documented imaging date.

Tumor Volumetric Analysis

The preoperative tumor volume was determined by using T1-weighted magnetic resonance imaging (MRI) with gadolinium contrast or T2-weighted and fluid attenuated inversion recovery MRI (1.5- to 3-mm axial cuts) depending on the tumor type. The OsiriX software (Pixmeo SARL, Bernex, Switzerland) was used to quantify tumor volume by 2 clinicians with neuroscience and radiology training who were blinded to the patient information, as we have previously described.[25-28] If the interobserver volume difference was large, a third clinician, also blinded to the cohorts, would evaluate the volumes, and the mean volume was determined from the 2 similarly calculated volumes. The postoperative tumor volume was calculated using the images obtained from MRI studies performed 48 hours after surgery, in the same manner as the preoperative imaging. The EOR was calculated with the following equation: (preoperative − postoperative tumor volume)/preoperative tumor volume.

Statistical Analysis

Univariate statistics were conducted to produce descriptive statistics that were reported as number of patient subjects and percent for categorical variables, median and range for continuous nonparametric variables, and mean and SD for continuous parametric variables. Kaplan-Meier curves were used to generate OS, PFS, and MPFS for all patients. The Kaplan-Meier curves plotted EOR and OS or PFS, using ≥90%, 70%–89%, and <70% EOR groups to maintain consistency with previous insular glioma studies.[23,29] For MPFS, EOR for the Kaplan-Meier curve was divided into ≥90% and <90%, as this has been a common grouping when assessing the impact of EOR.[12] Differences were assessed for statistical significance using the log-rank test. A univariate Cox proportional hazards model was used to determine predictors of survival curves. For survival risk factors, variables that had a P value <0.15 on the univariate analysis were entered into the multivariate analysis. The multivariate Cox proportional hazards model required a P value <0.05 for significance to be achieved. EOR was treated as a continuous variable in the Cox proportional hazards models to determine if it predicted OS, PFS, and MPFS. A linear regression was used to evaluate variables