

Usefulness of Awake Craniotomy for Low-grade Gliomas in Eloquent Areas

¹Dibya J Mahakul, ²Ashish Aggarwal, ³Amey R Savardekar, ⁴Hemant Bhagat, ⁵Chirag K Ahuja, ⁶Sunil K Gupta

ABSTRACT

The biggest dilemma in a neurosurgeon's mind while operating upon low-grade gliomas in eloquent areas is—how to achieve maximal tumor excision while preserving the neurological function. This aim is difficult to achieve once patient is under general anesthesia and hence, patient cooperation cannot be sought to know the neurological function. A novel method to overcome this hurdle is to excise gliomas (especially in eloquent areas) in awake stage while constantly seeking patient cooperation to know the corresponding neurological function. In this study, we operated 10 patients in awake stage and achieved reasonable tumor excision with no added deficits at 3 months follow-up. Hence, this technique achieves a compromise between oncological principle of maximal tumor excision while simultaneously following the neurosurgical principle of no new added deficits.

Keywords: Awake craniotomy, Excision, Gliomas, Tumor

How to cite this article: Mahakul DJ, Aggarwal A, Savardekar AR, Bhagat H, Ahuja CK, Gupta SK. Usefulness of Awake Craniotomy for Low-grade Gliomas in Eloquent Areas. *J Postgrad Med Edu Res* 2017;51(2):74-78.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

In adults, out of all primary brain tumors, 15% comprise low-grade gliomas (LGGs). These gliomas may behave in a benign manner having a long indolent course or sometimes they may progress rapidly or have malignant transformation. The average overall survival for these patients is approximately 6 years. Up to one-fourth of

patients may survive for couple of decades after diagnosis, which emphasizes the importance of maintaining an optimum quality of life (QoL) after tumor excision.

Several studies in recent era have demonstrated that greater extent of tumor resection is associated with an increased long-term survival.¹⁻³

However, the quest to maximally excise tumors, especially in eloquent areas, can lead to significant neurological impairments that have devastating consequences on the QoL and the survival of patient.⁴ These eloquent areas include left temporal and frontal lobes for speech and language, bilateral occipital lobes for vision, bilateral parietal lobes for sensation, bilateral motor lobes for movement, and subcortical structures, such as basal ganglia and internal capsule.⁵

Therefore, during tumor excision, a balance should be aimed for—between oncological principle of maximal tumor resection and neurosurgical principle of having no added deficits. One approach for achieving this aim is the technique of tumor excision in awake stage. This allows continuous real-time neurological monitoring during surgery and cessation of surgery once deficits start appearing.

The purpose of this study is to describe the results of awake craniotomy in patients where tumor was considered to have a high surgical risk, due to its location in eloquent area.

MATERIALS AND METHODS

Patients diagnosed to have a LGG in an eloquent area of the brain were included in this study. Preoperative evaluation included formal speech evaluation that consisted of naming, visual, auditory verb generation, and speech comprehension. Cognitive skill was tested using minimal state examination (MMSE).⁶ Preoperative focal neurological deficits in the form of paresis/sensory loss were evaluated and documented. Contrast-enhanced MRI (CEMRI) was done for every patient for tumor localization, disposition of peritumoral vessels, and relation with eloquent areas of the brain. Detailed informed consent was taken from every patient. After this evaluation, patients were taken up for surgery, i.e., craniotomy and tumor excision.

The awake craniotomy was conducted using sleep-awake technique. Patients received intravenous midazolam

¹Ex-Junior Resident, ^{2,3,5}Assistant Professor, ⁴Additional Professor
⁶Professor

¹Department of General Surgery, Postgraduate Institute of Medical Education and Research, Chandigarh, India

^{2,6}Department of Neurosurgery, Postgraduate Institute of Medical Education and Research, Chandigarh, India

³Department of Neurosurgery, National Institute of Mental Health and Neurosciences, Bengaluru, Karnataka, India

⁴Department of Anesthesia, Postgraduate Institute of Medical Education and Research, Chandigarh, India

⁵Department of Radiology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Corresponding Author: Ashish Aggarwal, Assistant Professor
Department of Neurosurgery, Postgraduate Institute of Medical Education and Research, Chandigarh, India, Phone: +911722756707, e-mail: aaggarwal_7@yahoo.com

(1–2 mg) and fentanyl (50–100 mcg). Further analgesia was achieved by propofol. An appropriate size laryngeal mask airway was inserted. Anesthesia was maintained with oxygen, nitrous oxide, and desflurane. Scalp nerve blocks were given with local anesthetics (0.5% bupivacaine) according to the location of the lesion. Anesthesia was monitored by using invasive blood pressure monitoring and by capnography. All patients received oxygen (3 L/min) through nasal prongs during surgery. Following craniotomy and reflection of dura mater, the anesthetic agents were stopped and laryngeal mask airway was removed. When the patient was conscious and responded to oral commands, the conscious sedation was maintained with dexmedetomidine infusion to near adequate depth using Ramsey sedation score.⁷ Tumor excision progressed and simultaneously patient was evaluated with respect to the task attributed to the particular brain area. Evaluation of performance was assessed by comparing accuracy and speed of response to the preoperative levels. If the patient developed deficit as compared to preoperative level, the surgery was stopped. After tumor resection was complete, the depth of sedation was increased and pain control medication (fentanyl) was started till the skin incision was closed. Patients were evaluated in the postoperative period with respect to any neurological deficit or development of seizure. The neurological status was again evaluated at discharge. A similar evaluation of performance was done at 3 months of follow-up. A repeat CEMRI was done at 3 months of follow-up to look for residual lesion. The QoL was assessed by a comprehensive neuropsychological questionnaire.⁸

RESULTS

Around 10 patients with glioma in eloquent areas of brain underwent awake craniotomy. The median age of the study group was 34 years with an age range of 26 to 48 years. There were 8 males.

All patients presented with seizures and headache. Four patients had mild hemiparesis, two had dysarthria, and one patient each had abnormal sensations in the limbs and abnormal wringing of the hands. All patients had their MMSE scores above the education adjusted cut-off score, with a maximum value of 29 in two patients and a minimum of 26. The CEMRI findings revealed intracranial space occupying lesions in the eloquent areas of brain, such as insular, fronto-opercular, posterior frontal, and frontotemporal regions on either of the sides (Table 1).

All patients underwent surgery for tumor resection in awake condition, as described in methodology. Total or near total excision was possible in 7 patients. In 3 patients, only subtotal excision could be achieved. Of these 3, 2 patients had increased deficit during the surgi-

Table 1: Details of site of tumor and suspected lesion on preoperative CEMRI

| Sl. no. | Region of brain | Side |
|---------|---|-------|
| 1 | Insular | Right |
| 2 | Fronto-opercular and insular | Right |
| 3 | Frontotemporal | Right |
| 4 | Fronto-opercular and insular | Left |
| 5 | Fronto-insular | Right |
| 6 | Fronto-opercular | Left |
| 7 | Posterior frontal | Left |
| 8 | Posterior frontal | Left |
| 9 | Fronto-opercular and insular | Left |
| 10 | Medial frontal with corpus callosal extension | Right |

cal procedure and therefore, resection had to be stopped. The tumor in third patient was located close to middle cerebral artery and hence, tumor had to be left *in situ*.

No intraoperative and perioperative anesthetic complications were noted in any patient. The deficits in the intraoperative and postoperative period were noted and compared with those in preoperative period. The average length of stay in hospital was 4 days.

Five patients had intraoperative worsening of neurological deficits which persisted in the immediate postoperative period. Out of these, three patients improved within a few days while two patients continued to have increased neurological deficit at discharge. Both these patients showed marked improvement in the follow-up period (Table 2).

Histopathology revealed a LGG (grade II) in six patients, three patients had anaplastic glioma (grade III) while one patient was reported as glioblastoma multiforme (grade IV)

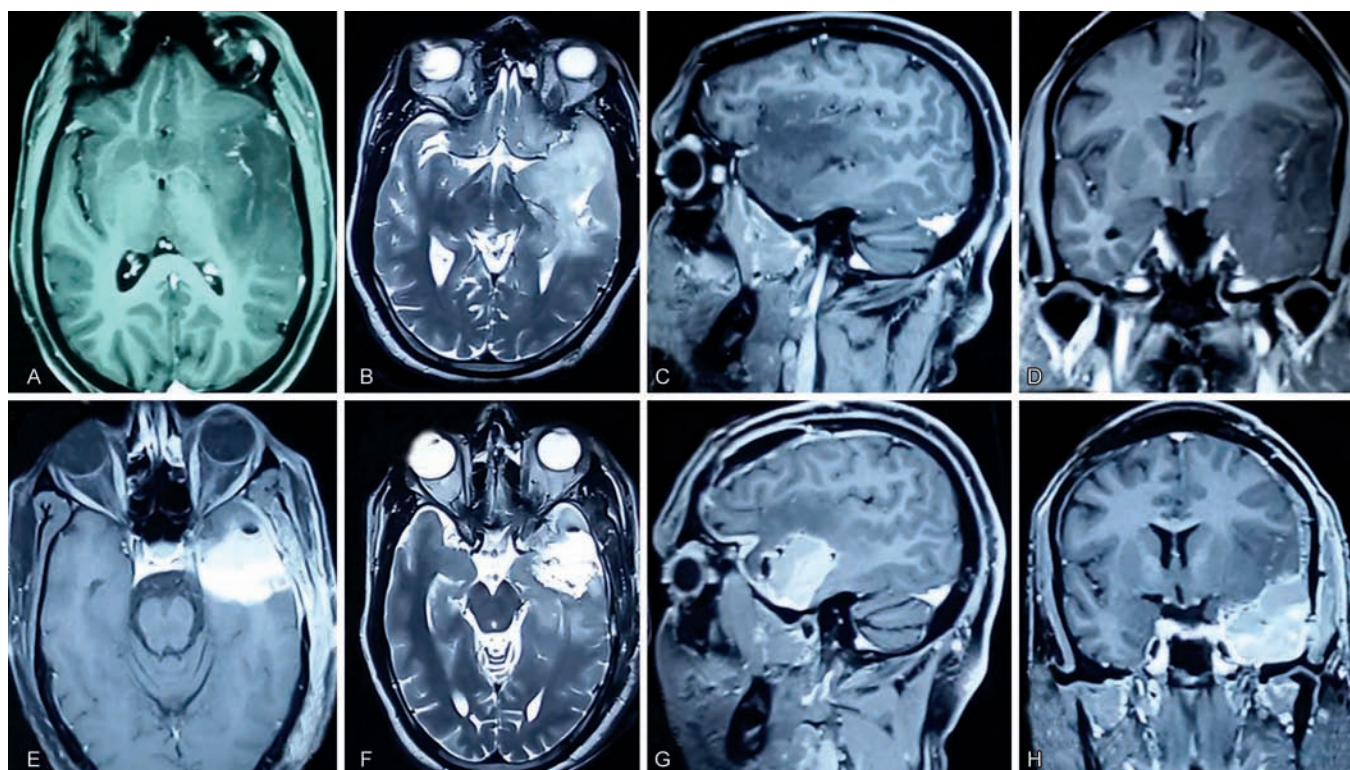
Three months after surgery, all patients were evaluated again and their MMSE, neurological deficit, were recorded. Mean value was 28 and there was mild improvement in MMSE score but this was statistically not significant. No patients had any residual neurological deficit. The two patients who had persistent deficits at time of discharge had also improved. The MRI demonstrated satisfactory tumor removal in 7 out of 10 patients (Figs 1A to H). All patients were seizure free at 3 months of follow-up and had occasional episodes of headache. Quality of life of all the patients, at 3 months indicated that all the patients had a satisfactory life and they have returned back to their social and professional lives.

DISCUSSION

Low-grade gliomas include various cell lineages of which WHO grade II tumors. Despite differences in histology, these tumors generally occur in young adults with a long-life expectancy.

Table 2: Description of neurological deficit at preoperative, intraoperative, immediate postoperative, and at discharge

| Sl. no. | Preoperative deficit | Intraoperative deficit | Immediate postoperative deficit | Deficit at discharge | Status of deficit at discharge as compared with preoperative period |
|---------|--|--|---|---|---|
| 1 | 1. Tingling in upper limb 2. Irrelevant talks | 1. Tingling in upper limb 2. Irrelevant talks | Nil | Nil | Decreased |
| 2 | 1. Left upper limb paresis 2. Dysarthria | 1. Left upper limb paresis 2. Dysarthria | 1. Left upper limb paresis 2. Dysarthria | 1. Left upper limb paresis 2. Dysarthria | Same |
| 3 | Wringing of hand | Nil | Nil | Nil | Decreased |
| 4 | 1. Right hemiparesis | 1. Right hemiparesis 2. Dysphonia | 1. Right hemiparesis 2. Dysphonia | 1. Right hemiparesis 2. Dysphonia | Increased |
| 5 | Nil | Mild left hemiparesis | Mild left hemiparesis | Nil | Same |
| 6 | Nil | Nil | Nil | Nil | Same |
| 7 | Right hemiparesis | Right hemiparesis | Right hemiparesis | Nil | Decreased |
| 8 | Nil | Left upper limb paresis | Left upper limb paresis | Nil | Same |
| 9 | Nil | Right hemiparesis | Right hemiparesis | Right hemiparesis | Increased |
| 10 | Left hemiparesis | Left hemiparesis | Left hemiparesis | Left hemiparesis | Decreased |



Figs 1A to H: Magnetic resonance imaging images A to D are preoperative and E to H are postoperative images: (A) Axial CEMRI T1 WI representing tumor in left frontotemporal and insular region; (B) axial T2 WI representing tumor; (C and D) sagittal and coronal CEMRI representing tumor; (E) axial CEMRI T1 WI; (F) axial T2 WI representing subtotal tumor removal. The bright signal is due to postoperative blood; and (G and H) sagittal and coronal CEMRI representing subtotal tumor excision

Although WHO grade II astrocytomas are slow growing,^{9,10} but the risk of malignant transformation and progression makes “complete” surgical removal a necessity to achieve better prognosis.^{11,12} Surgical biopsy or resection is recommended in almost all patients to establish the diagnosis since clinical and radiographic data are not definitive.¹³ Besides impending herniation, obstruction to cerebrospinal fluid flow, adequate seizure control and an attempt to delay adjuvant therapy¹³ are

other indications to opt for surgery in patients with LGG. However, surgery carries the risk of potentially increasing the neurological deficit, thus impairing the QoL. So, a balance between oncological principle and safe resection has to be achieved.

Awake craniotomy provides a safe and viable option to enhance the extent of tumor resection without deficits, resulting in a delay in malignant transformation and thus an increase in overall survival.¹⁴

In this method after craniotomy, tumor is excised in awake state. Patient is continuously asked to perform the task which is attributed to the area being operated upon (e.g., movement of a limb, speech, and visual perception, etc.). As soon as patient starts having deficit, further tumor excision is halted; thus minimizing the deficits.

The extent of tumor removal has a prognostic influence on the time interval to tumor progression, incidence of malignant degeneration, and period of survival.^{15,16}

Pereira et al¹⁷ by this method of awake craniotomy achieved a high tumor excision rate with low deficits. Their tumor excision rate was around 90%. Recovery from previous motor deficits was seen in 75% of patients, while intraoperative worsening of motor functions was observed in 8.9% of cases. Satisfaction and patient acceptance of the surgical procedure was seen in 89.9% of patients.

Duffau et al¹⁸ assessed the outcome of awake craniotomy in 24 patients with insular glioma. Despite language worsening in the immediate postoperative in 50%, all patients recovered to a normal neurological status within a span of 3 months. All patients returned to normal social and professional lives. The MRI revealed total or subtotal resections in 62.5% cases. At a mean follow-up of 3 years, 22 patients were alive suggesting that greater extent of tumor excision was accomplished without any added deficits.

Low et al¹⁹ analyzed their results of the outcome of awake craniotomy on 20 patients with brain tumor in eloquent cortex. Six patients (30%) had neurological deficit in postoperative period which subsequently improved in four patients. The degree of cytoreduction achieved was in the region of 80 to 90%.

In the present series, 5 patients out of 10 had worsening of neurological deficits, but at 3 months of follow-up, all of them improved with no added neurological deficit. Seizures were controlled in all patients. There was significant improvement in the MMSE scores ($p = 0.046$). All patients have returned back to their social lives.

There has been a duel between the principles of surgical oncology, to achieve greater resection of tumor and the neurosurgical principles of having no added deficits. Patients undergoing tumor excision in awake stage had an improved outcome including greater extent of resection and hence, longer progression free survival as compared with surgery under general anesthesia. And this was achieved without causing any added deficits. The ability of the neurosurgeons to achieve maximal tumor resection within the constraints of preserving optimal neurological functions, is greatly enhanced by this technique.

CONCLUSION

Awake craniotomy is a safe and effective option to achieve maximal tumor resection in patients with tumors near or

in the eloquent cortex of the brain. This technique not only increases the extent of the tumor resection, leading to a delay in malignant transformation and thus an increase in overall survival, but also has a relatively lower risk of postoperative neurological deficit and a shorter length of stay in hospital. In a cooperative patient, it is more acceptable than the conventional surgical procedures. Taking all the benefits of awake craniotomy into consideration, it should have an expanded role in brain tumor surgery regardless of the tumor location.

REFERENCES

- Berger MS, Deliganis AV, Dobbins J, Keles GE. The effect of extent of resection on recurrence in patients with low grade cerebral hemisphere gliomas. *Cancer* 1994 Sep 15;74(6): 1784-1791.
- Keles GE, Lamborn KR, Berger MS. Low grade hemispheric gliomas in adults: a critical review of extent of resection as a factor influencing outcome. *J Neurosurg* 2001 Nov;95(5): 735-745.
- Smith JS, Chang EF, Lamborn KR, Chang SM, Prados MD, Cha S, Tihan T, Vandenberg S, McDermott MW, Berger MS. Role of extent of resection in the long-term outcome of low grade hemispheric gliomas. *J Clin Oncol* 2008 Mar;26(8):1338-1345.
- Khu KJ, Doglietto F, Radovanovic I, Taleb F, Mendelsohn D, Zadeh G, Bernstein M. Patients' perceptions of awake and outpatient craniotomy for brain tumor: a qualitative study. *J Neurosurg* 2010 May;112(5):1056-1060.
- Chang EF, Clark A, Smith JS, Polley MY, Chang SM, Barbaro NM, Parsa AT, McDermott MW, Berger MS. Functional mapping-guided resection of low-grade gliomas in eloquent areas of brain: improvement of long-term survival. *J Neurosurg* 2011 Mar;114(3):566-573.
- Folstein MF, Folstein SE, McHugh PR. "Mini-mental status". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975 Nov;12(3):189-198.
- Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedation with alphaxalone-alphadolone. *Br Med J* 1974 Jun 22;2(5920):656-659.
- Saxena S, Chandiramani K, Bhargava R. WHOQOL-Hindi: a questionnaire for assessing quality of life in health care settings in India. *World Health Organization quality of life. Natl Med J India* 1998 Jul-Aug;11(4):160-165.
- Carincross JG, Laperriere NJ. Low-grade glioma to treat or not to treat? *Arch Neurol* 1989 Nov;46(11):1238-1239.
- Shaw EG. Low-grade glioma: to treat or not to treat? A radiation oncologist's viewpoint. *Arch Neurol* 1990 Oct; 47(10):1138-1140.
- Gunel M, Piepmeier JM. Management of low-grade gliomas. *Contemp Neurosurg* 1997;19(9):1-6.
- Karim AB, Maat B, Hatlevoll R, Menten J, Rutten EH, Thomas DG, Mascarenhas F, Horiot JC, Parvinen LM, van Reijn M, et al. A randomised trial on dose-response in radiation therapy of low-grade cerebral glioma: European organisation of research and treatment of cancer (EORTC) study 22844. *Int J Radiat Oncol Bio Phys* 1996 Oct 1;36(3):549-556.
- Berger, MS. Role of surgery in diagnosis and management in benign cerebral glioma. In: Apuzzo MLJ, editor. *Neurosurgical topics, Vol 2*. Park Ridge, Illinois: American Association of Neurological Surgeons;1995. p. 293-307.

14. Hayashi Y, Nakada M, Kinoshita M, Hamada J. Surgical strategies for nonenhancing slow-growing gliomas with special reference to functional reorganization: review with own experience. *Neurol Med Chir (Tokyo)* 2013;53(7):438-446.
15. Phillippon JH, Clemenceau SH, Fauchon FH, Foncin JF. Supratentorial low-grade astrocytomas in adults. *Neurosurgery* 1993 Apr;32(4):554-559.
16. Sanai N, Berger MS. Operative techniques for gliomas and the value of extent of resection. *Neurotherapeutics* 2009 Jul;6(3):478-486.
17. Pereira LC, Oliveira KM, L'Abbate GL, Sugai R, Ferreira JA, da Motta LA. Outcome of fully awake craniotomy for lesions near the eloquent cortex: analysis of a prospective surgical series of 79 supratentorial primary brain tumors with long follow-up. *Acta Neurochir (Wien)* 2009 Oct;151(10):1215-1230.
18. Duffau H, Moritz-Gasser S, Gatignol P. Functional outcome after language mapping for insular World Health Organization Grade II gliomas in the dominant hemisphere: experience with 24 patients. *Neurosurg Focus* 2009 Aug;27(2):E7.
19. Low D, Ng I, Ng WH. Awake craniotomy under local anaesthesia and monitored conscious sedation for resection of brain tumours in eloquent cortex--outcomes in 20 patients. *Ann Acad Med Singapore* 2007 May;36(5):326-331.