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Awake craniotomy versus craniotomy under general anesthesia for the surgical treatment of insular glioma: choices and outcomes

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ABSTRACT

Objective: To investigate differences in outcomes in patients who underwent surgery for insular glioma using an awake craniotomy (AC) vs. a craniotomy under general anesthesia (GA).

Methods: Data from patients treated at our hospital between 2005 and 2015 were analyzed retrospectively. The preoperative, intraoperative, postoperative, and longer term follow-up characteristics and outcomes of patients who underwent surgery for primary insular glioma using either an AC or GA were compared.

Results: Of the 52 identified patients, 24 had surgery using an AC and 28 had surgery under GA. The extent of resection was similar for the two anesthesia techniques: the median extent of resection was 61.4% (IQR: 37.8–74.3%) in the WHO grade <4 AC group vs. 50.5% (IQR: 35.0–71.2%) in the grade <4 GA group and 73.4% (IQR: 54.8–87.2%) in the grade 4 AC group vs. 88.6% (IQR: 61.2–93.0%) in the grade 4 GA group. Consistent with literature, there were more early neurological deficits after an AC, while the GA group showed more new late neurological deficits; however, these trends were not significant. Survival was similar between the two groups, with 100% 1- and 2-year survival in the grade <4 groups.

Conclusion: Our results showed that the extent of resection, neurological outcomes, and survival were similar using the two anesthesia techniques. Since AC is more challenging for the patient and for his or her caregiver after surgery, this finding has implications for clinical decision-making.

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Insula; glioma; awake craniotomy; general anesthesia; retrospective

Introduction

The insular cortex of the brain plays roles in a variety of important neurological processes, including somatosensory processing, gustation, balance, control of cardiovascular tone and language [1,2]. Neoplasms, and especially gliomas, may cause dysfunction of these processes [1]. Insular gliomas represent a substantial portion of all central nervous system neoplasms, with 25% of all low-grade gliomas and 10% of all high-grade gliomas found in the insula [3]. The estimated incidence rates are 0.34 per 100,000 person-years for low-grade insular gliomas and 0.41 per 100,000 person-years for high-grade insular gliomas [4].

Surgical resection of insular gliomas is challenging due to their close proximity to several eloquent cortical areas and other critical areas. In addition, the presence of critical vascular structures, especially branches of the middle cerebral artery, can further complicate the procedure [5,6]. Case series of insular glioma resections show similar results to other glioma resection according to postoperative cognitive function [7]. Furthermore, these studies show that radical resection can improve progression-free survival and overall survival [8–11].

Traditionally, neurosurgeons have had the option to resect or debulk an insular glioma either by performing a craniotomy under general anesthesia (GA) or by using an awake craniotomy (AC), which allows cortical and/or subcortical mapping [12]. The AC procedure was developed to allow greater resection with less risk of damaging eloquent cognitive brain functions [1,13–15]. There is limited evidence regarding the best anesthesia technique for resecting these insular tumors, and the number of patients in published articles is relatively low. This is likely due to the technical challenges of the procedure and the low incidence of the disease.

Many patients with insular tumors have been treated at our hospital during the last decade. The data from these patients were analyzed to gain a better understanding of this specific patient population and the differences in outcomes between the two anesthesia techniques. Our aim was to investigate the differences in survival,

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extent of resection (EOR), and neurological outcomes in patients who underwent surgery using AC vs. GA.

Methods

Patients

First, patients were identified who underwent a craniotomy under GA or using an AC for the resection or debulking of a primary insular glioma between 2005 and 2015. Patient information was retrieved from the electronic patient registry at our hospital. It is routine practice to ask neurosurgical patients at intake whether they will allow their data to be used anonymously for research. Informed consent for the use of all data was provided by all of the patients in this retrospective analysis. This study protocol was approved by the ethics board at our hospital (MEC 2013-090). The neurosurgeon consulted with the neuro-anesthesiologist and then chose which anesthesia technique to use for each patient. This clinical choice was investigated in this case series in which patients were retrospectively categorized into two groups, an AC group and a GA group. All gliomas were resected using a transsylvian approach. Data were extracted for the entire perioperative (pre-, intra-, and post-operative) period and for the follow-up period. All data were extracted by the first author, double-checked by the last author, and discussed with the co-authors. The use of the two anesthesia techniques over time was also analyzed.

Preoperative characteristics

The clinical characteristics at presentation and the tumor characteristics were determined in order to investigate the factors that may have influenced the choice of anesthesia technique. The following clinical characteristics were assessed: the presence of linguistic, motor, and sensory dysfunction; whether the patient had epilepsy; tumor size at MRI (calculated by volumetric analysis); dominant hemispheric localization; and glioma type. Although the tumor glioma type could only be confirmed histologically postoperatively, radiological presentation often clearly correlates with the pathological diagnosis, especially for glioblastoma multiforme (GBM) [16,17]. Therefore, the glioma type was used as a preoperative characteristic. The differences in these variables were analyzed between groups in order to assess which factors drove the clinical decision.

Intraoperative characteristics

The duration of the procedure, the amount of blood lost, and the EOR were compared between the two groups to investigate whether the anesthesia type influenced these factors. The duration of the procedure was determined according to the anesthesia time, which was defined as the time in hours between the time-out procedure (TOP) and sign-out/extubation/transport to the PACU and according to the surgical time, which was defined as the time in hours between the first incision and the last suture.

Volumetric analysis

Brainlab neuronavigation and planning software (version 3.0.0, BrainLAB, Feldkirchen, Germany) was used to define the borders of the tumor and to calculate its volume in order to assess the percentage of tumor that was removed. The volume was calculated both pre- and postoperatively using MRI scans that were performed as close to the surgical date as possible. In general, a T2-weighted or FLAIR MRI was used for low-grade gliomas and a T1-weighted MRI with contrast was used for high-grade gliomas. The radiology reports were used as a reference during each assessment to confirm the tumor location and borders. All tumor volumes were calculated in cubic centimeters. Cystic components were included in the total volume, but perifocal edema and intratumoral hemorrhages were not. Patients who did not have an MRI scan either pre- or postoperatively were excluded from the volume analysis.

Postoperative characteristics

The early postoperative characteristics were compared between the two groups by determining the mean lengths of hospital stay and the complications that occurred as a result of the procedure. The one- and two-year survival was determined for all patients, as was the five-year survival for patients who were operated on before September 2012. Survival data for patients that were not followed-up at our hospital were obtained by calling each patient's general practitioner.

Neurological outcome

The scale used by De Witt Hamer et al. [18] was used to compare neurological outcomes in the two groups. Data were retrieved on new-onset postoperative neurological deficits that were categorized as early (up to 3 months after surgery) and late (3 months or longer after surgery), and data on severe and non-severe deficits were retrieved as well. Deficits were categorized as severe when the patient's muscle strength was grade 1, 2, or to 3 on the Medical Research Council scale or aphasia, severe dysphasia, hemianopsia or a vegetative state was present. All other deficits were considered non-severe. A deficit was scored when it persisted for more than one postoperative day and the patient needed an intervention for the deficit.

Statistical analysis

The clinical outcomes of WHO grade 4 gliomas are worse than for other gliomas that have similar effects on neurocognitive function at presentation [11,19]; accordingly, grade 4 gliomas were analyzed separately. After comparing patients with grade <4 and grade 4 gliomas, the GA and AC groups were compared within the grade <4 and grade 4 groups.

Normally distributed continuous variables were compared using independent sample *t*-tests. Non-normally distributed non-nominal variables were compared using the Mann–Whitney *U* test and the exact significance was reported, while nominal variables were compared using Chi-squared (χ^2) and Fisher's exact test when any of the categories had an expected count less than 5. To assess neurological outcomes, the proportion of patients presenting with an early or late deficit and the proportion who suffered from a severe early or late deficit were calculated. Neurological outcomes were presented with 95% CIs. Because survival and EOR were not normally distributed, 95% CIs were not reported for these outcome measures. The EOR was calculated by subtracting the preoperative tumor volume by the postoperative volume and dividing the result by the preoperative tumor volume.

To deal with missing data, only available data were analyzed. However, the percentages are based on the whole group, including missing cases. Because multiple hypothesis testing was performed, an α-level of 0.01 was considered statistically significant; this was estimated by the Bonferroni correction technique [20]. Furthermore, a *p*-value below 0.05 was seen as a trend toward significance and is discussed as such. The statistical analysis was performed using IBM SPSS Statistics 21 (IBM Corp., 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.).

Results

Data were retrieved for 52 patients; of these, 24 patients were treated with an AC, and 28 patients were treated using a craniotomy under GA. Over time, there was a trend toward using AC less often and using GA more often in our hospital (Figure 1).

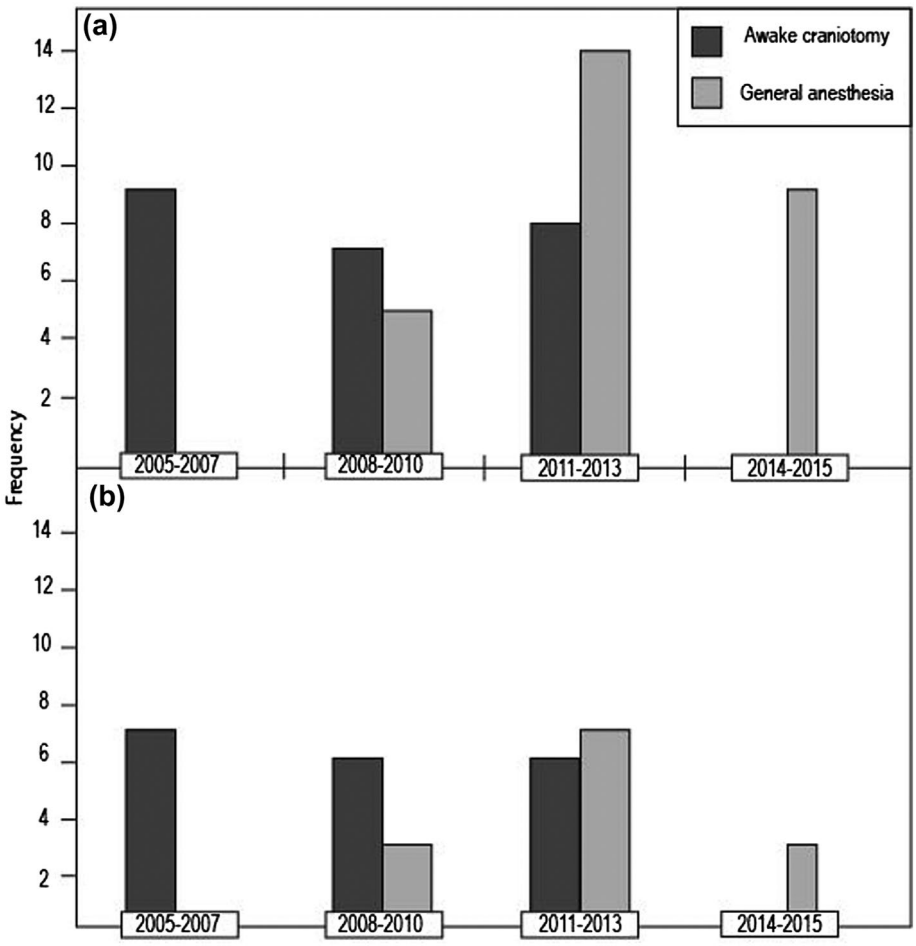

Figure 1. The frequency distribution of the performed techniques over time.
Notes: The bar graph shows the frequency of the procedures in the four indicated time periods. There was a decrease over time in the use of awake craniotomy, resulting in greater use of the general anesthesia procedure. Panel **a** shows the data for all surgeries, and panel **b** shows the data from surgeries for grade <4 gliomas.

Patient characteristics

The groups were similar for all descriptive variables except age (Table 1). The mean age was 55.2 ± 16.0 years for patients in the grade 4 GA group vs. 41.9 ± 10.5 years for patients in the grade <4 GA group (p = 0.017; 95% CI: 2.6–24.0 years). There were no significant differences in age between the patients in the two anesthesia groups.

Variables that could influence the choice to use AC versus GA

Table 2 shows an overview of the variables that could influence the choice to use AC vs. GA.

Clinical presentation

There were no significant differences in linguistic and motor dysfunction between the AC and GA groups. There was a trend toward statistical significance for differences in sensory dysfunction at presentation according to tumor grade in the GA group: 3 (23.1%) patients in the grade <4 GA group suffered from sensory dysfunction vs. 9 (60.0%) patients in the grade 4 GA group (p = 0.049). There was also a trend toward statistical significance for differences in epilepsy according to tumor grade in the GA group: 8 (53.3%) patients in the grade 4 GA group suffered from epilepsy vs. 12 (92.3%) patients in the grade <4 GA group (p = 0.038).

The tumor size was similar in the two groups for both grade <4 tumors and for grade 4 tumors. There was a trend toward statistical significance for differences in tumor size according to tumor grade in the GA group: 54.6 ± 25.4 cm^3 in the grade <4 GA group vs. 96.5 ± 59 cm^3 in the grade 4 GA group (p = 0.02); the difference was 41.9 cm^3; 95% CI: 7.0–76.8 cm^3. The tumors were more often localized in the dominant hemisphere in the grade <4 AC group than in the grade <4 GA group: 17 (89.5%) vs. 8 (61.5%) (p = 0.021). No such trend toward significance was found in the grade 4 groups in terms of localization in the dominant hemisphere. However, there was a significant difference in the glioma type in the GA group vs. the AC group. Specifically, astrocytomas were mostly resected using GA, while oligodendrogliomas were all resected using an AC. GBM was more often treated under GA. The p-value was <0.001 for these differences.

Table 1. Characteristics of the 52 patients who underwent primary resection for insular glioma at the Erasmus University Medical Center 2005–2015.

	Awake craniotomy (AC)		General anesthesia (GA)	
Variable	WHO grade <4 n = 19	WHO grade 4 n = 5	WHO grade <4 n = 13	WHO grade 4 n = 15
Age at surgery in years, mean ± SD	41.1 ± 11.8	41.5 ± 6.3	41.9 ± 10.5	55.2 ± 16.0
Male, n (%)	16 (84.2%)	4 (80%)	8 (61.5%)	10 (66.7%)
Weight in kg, mean ± SD	86.5 ± 12.3	79.6 ± 11.8	85.5 ± 20.9	88.7 ± 14.6
Height in m, mean ± SD	1.80 ± 0.08	1.83 ± 0.05	1.80 ± 0.12	1.80 ± 0.12
BMI in kg/m^2, mean ± SD	26.1 ± 2.97	23.8 ± 2.8	26.1 ± 4.11	27.8 ± 5.8
Right handed, n (%)	14 (73.7%)	5 (100%)	10 (76.9%)	11 (73.3%)

Notes: There was only one significant difference between any of the groups (grade 4 vs. grade <4 within the AC and GA groups or AC vs. GA within the grade 4 and grade <4 groups). That difference was for age, which was significantly different (p = 0.017) between the grade 4 GA group and the grade <4 GA group (95% CI: 2.6–24.0 years).

Intraoperative and postoperative characteristics

Table 3 shows the intraoperative and postoperative characteristics of the patients in the GA and AC groups.

Surgical duration

There was a trend toward significance for differences in anesthesia time in the GA group according to tumor grade: the anesthesia time was 6.4 ± 1.2 h for the grade <4 GA group and 5.0 ± 2.1 h for the grade 4 GA group (p = 0.036; mean difference, 1.4 h; 95% CI: 0.10–2.8 h). Post-hoc analysis showed a trend toward significance regarding the duration of anesthesia induction and preparation of the patient in the GA group: the time between the TOP and the incision was 1.2 ± 0.13 h for patients in the grade <4 GA group vs. 0.99 ± 0.24 h for patients in the grade <4 GA group (p = 0.02; mean difference, 0.19 h; 95% CI: 0.032–0.34 h).

Surgical characteristics

The intraoperative blood loss was higher in the grade <4 AC group, which showed a mean blood loss of 584 ± 214 ml vs. 307 ± 188 ml in the grade <4 GA group (p = 0.001; mean difference, 277 ml; 95% CI: 127–427 ml). There was no difference in blood loss between the grade 4 GA group vs. the grade 4 AC group or between the grade 4 and the grade <4 glioma groups within the two groups. Even though blood loss was greater in the grade <4 AC group, none of the patients received a blood transfusion. The EOR was similar in the grade <4 groups and in the grade 4 groups, but the EOR in the grade 4 GA group was significantly higher than in the grade <4 GA group: 82.4% (IQR: 60.1–92.8%) in the grade 4 group, and 50.5% (IQR: 35.0–71.2%) in the grade <4 group (p = 0.003) (Figure 2). One patient was excluded from the analysis because a postoperative MRI scan was not available, as the patient had pneumonia and was in the intensive care unit for 20 days. An MRI has not been performed in the ICU.

Table 2. Preoperative clinical characteristics of the 52 patients who underwent primary resection for insular glioma at the Erasmus University Medical Center 2005–2015.

	Awake craniotomy (AC)		General anesthesia (GA)		*P*-value for AC vs. GA		*P*-value for WHO grade <4 vs. grade 4	
Variable	WHO grade <4 *n* = 19	WHO grade 4 *n* = 5	WHO grade <4 *n* = 13	WHO grade 4 *n* = 15	WHO grade <4	WHO grade 4	AC	GA
Clinical presentation								
Linguistic dysfunction, *n* (%)	11 (57.9%)	4 (80%)	3 (23.1%)	7 (46.7%)	n.s.	n.s.	n.s.	n.s.
Motor dysfunction, *n* (%)	6 (31.6%)	2 (40.0%)	5 (38.5%)	5 (33.3%)	n.s.	n.s.	n.s.	n.s.
Sensory dysfunction, *n* (%)	8 (42.1%)	3 (60.0%)	3 (23.1%)	9 (60.0%)	n.s.	n.s.	n.s.	0.049
Epilepsy, *n* (%)	11 (57.9%)	3 (60%)	12 (92.3%)	8 (53.3%)	n.s.	n.s.	n.s.	0.038
Tumor size at presentation in cm^3, mean ± SD	61.2 ± 24.5	107.2 ± 62.1	54.6 ± 25.4	96.5 ± 59	n.s.	n.s.	n.s.	0.02
Tumor in dominant hemisphere, *n* (%)	17 (89.5%)	4 (80%)	8 (61.5%)	5 (33.3%)	0.021	n.s.	n.s.	n.s.
Histological classification, *n* (%)								
Astrocytoma	6 (31.6%)	–	13 (100%)	–	0.001	–	<0.001	<0.001
Oligodendroglioma	10 (52.6%)	–	0 (0%)	–				
Mixed	3 (15.8%)	–	0 (0%)	–				
Glioblastoma	–	5 (100%)	–	15 (100%)				

Table 3. Intraoperative and postoperative characteristics of the surgeries for primary insular glioma.

	Awake craniotomy (AC)		General anesthesia (GA)		*P*-value for AC vs. GA		*P*-value for WHO grade <4 vs. grade 4	
Variable	WHO grade <4 *n* = 19	WHO grade 4 *n* = 5	WHO grade <4 *n* = 13	WHO grade 4 *n* = 15	WHO grade <4	WHO grade 4	AC	GA
Anesthesia time in hours, mean ± SD	5.6 ± 1.2	5.0 ± 0.8	6.4 ± 1.2	5.0 ± 2.1	n.s.	n.s.	n.s.	0.036
Surgical time in hours, mean ± SD	4.2 ± 1.1	3.6 ± 0.6	5.0 ± 1.1	3.8 ± 1.9	n.s.	n.s.	n.s.	n.s.
Blood lost in ml, mean ± SD	584 ± 214	860 ± 456	307 ± 188	436 ± 373	0.001	n.s.	n.s.	n.s.
Length of hospital stay in days, median (IQR)	7 (6–9)	9 (8–12)	9 (7–11)	7 (6–13)	n.s.	n.s.	n.s.	n.s.

Postoperative characteristics

The length of hospital stay was similar in the AC and GA groups. Table 4 shows the complications. The one-, two-, and five-year survival rates were higher in the grade <4 groups than in the grade 4 groups. No difference between AC and GA was found according to one-, two-, and five-year survival (Figure 3). The five-year survival time could be determined for the AC group, but some information was missing for the GA group.

Neurological outcome

Early onset deficits developed in 67% (95% CI: 46–88%) of the patients in the AC group and in 57% (95% CI: 37–77%) of the patients in the GA group. Severe early onset deficits developed in 25% (95% CI: 6–44%) of the patients in the AC group and in 11% (95% CI: 0–24%) of the patients in the GA group. Late onset deficits developed in 48% (95% CI 26–70%) of the patients in the GA group and in 33% (95% CI: 10–56%) of the patients in the AC group. Severe late onset deficits developed in 12% (95% CI: 0–27%) of patients in the GA group and in 5% (95% CI: 0–17%) of the patients in the AC group. None of the differences between the groups were significant. The groups were too small to analyze differences between grade 4 and grade <4 groups (Figure 4).

Summary

To summarize, a total of 52 patients underwent primary insular glioma resection at our hospital. This retrospective case series analysis found that over the course of the study period, the GA procedure was used more often than the AC procedure. Astrocytomas and GBMs were more often treated under GA, while oligodendrogliomas were more often treated using AC. Intraoperative blood

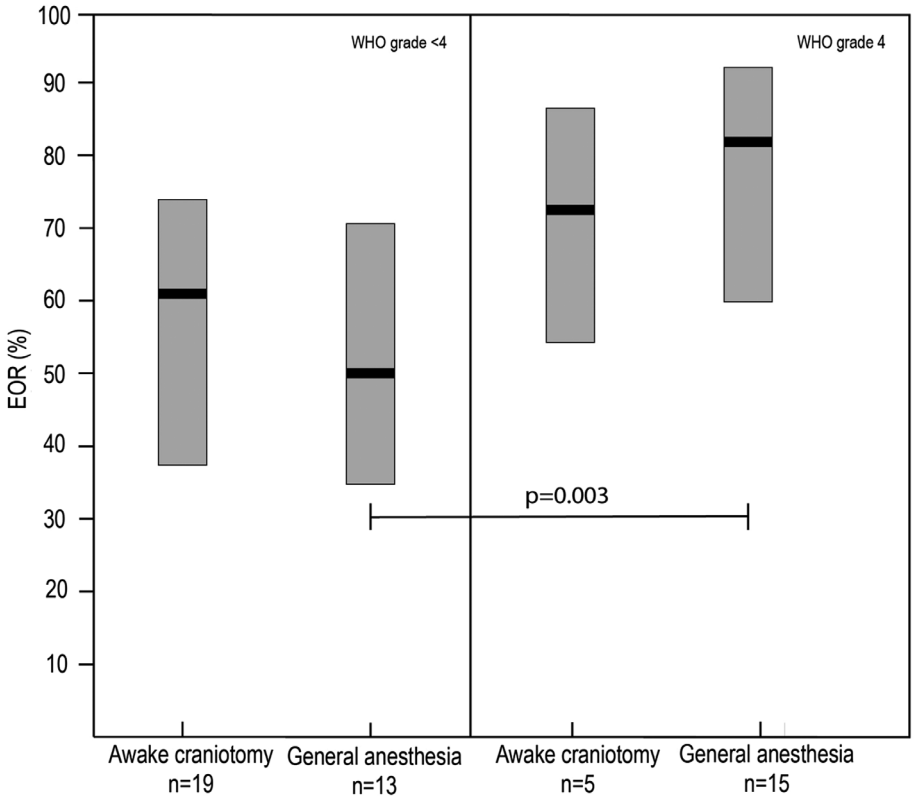

Figure 2. A box plot shows the median extent of resection (EOR) and the 1st and 3rd quartiles for each group of patients.
Note: The grade 4 patient groups had a larger extent of resection, and this difference was significant between the grade <4 and grade 4 GA groups ($p = 0.002$).

Table 4. Summary of the surgical complications that occurred after surgical resection and before discharge in the 52 patients who underwent primary resection for insular glioma at the Erasmus University Medical Center 2005–2015.

	Awake craniotomy ($n = 24$)	General anesthesia ($n = 28$)	Total n
Complication			
Postoperative insult	1	1	2
Periorbital edema	3	0	3
Atelectasis	0	1	1
Postoperative hemorrhage	2*	0	2
Headache	1	2	3
Hyperglycemia	1	1	1
Nausea	1	1	2
Pulmonary embolism	0	1	1
Urinary tract infection	1	0	1
Pneumonia	0	1	1

*1 patient underwent a recraniotomy.

loss was greater in patients with grade <4 tumors in the AC group than in the GA group. The EOR was similar between the AC and GA groups, but the mean EOR was greater in the grade 4 GA group than in the grade <4 GA group. The one-, two-, and five-year mortality was similar between the AC and GA groups, but patients with grade 4 gliomas had worse survival than those with grade <4 tumors. New early deficits were more prevalent in the AC group, and new late deficits were more prevalent in the GA group, but the differences were not significant.

Discussion

This retrospective analysis of patients with insular gliomas who were treated by an AC or by a craniotomy under GA was performed to gain insights into the effects of these two techniques on the patients, especially on EOR, survival, and neurological outcome.

Choice of anesthesia technique

In the later part of the investigated period, the GA technique was preferred over the AC technique because the GA procedure is less challenging for the patient and has advantages for the doctors. GA was also preferred for grade 4 gliomas, which more often present perivascularly and with adhesions to the M2 and M3 branches of the middle cerebral artery [21]. Pressure on these branches is painful for AC patients, so GA is typically used for grade 4 gliomas. The neurosurgeons at our hospital found that surgeries performed using AC were often quite long; the patients became fatigued, reducing the advantages of performing an awake surgery. Since craniotomy under GA showed good results, neurosurgeons who became comfortable resecting these tumors more often opted to use GA. However, AC was still preferred for patients with frontal opercular extension, especially when the dominant frontal operculum was involved and the patients presented with speech problems following an epileptic insult. Indeed, patients were more often treated with an AC if they presented

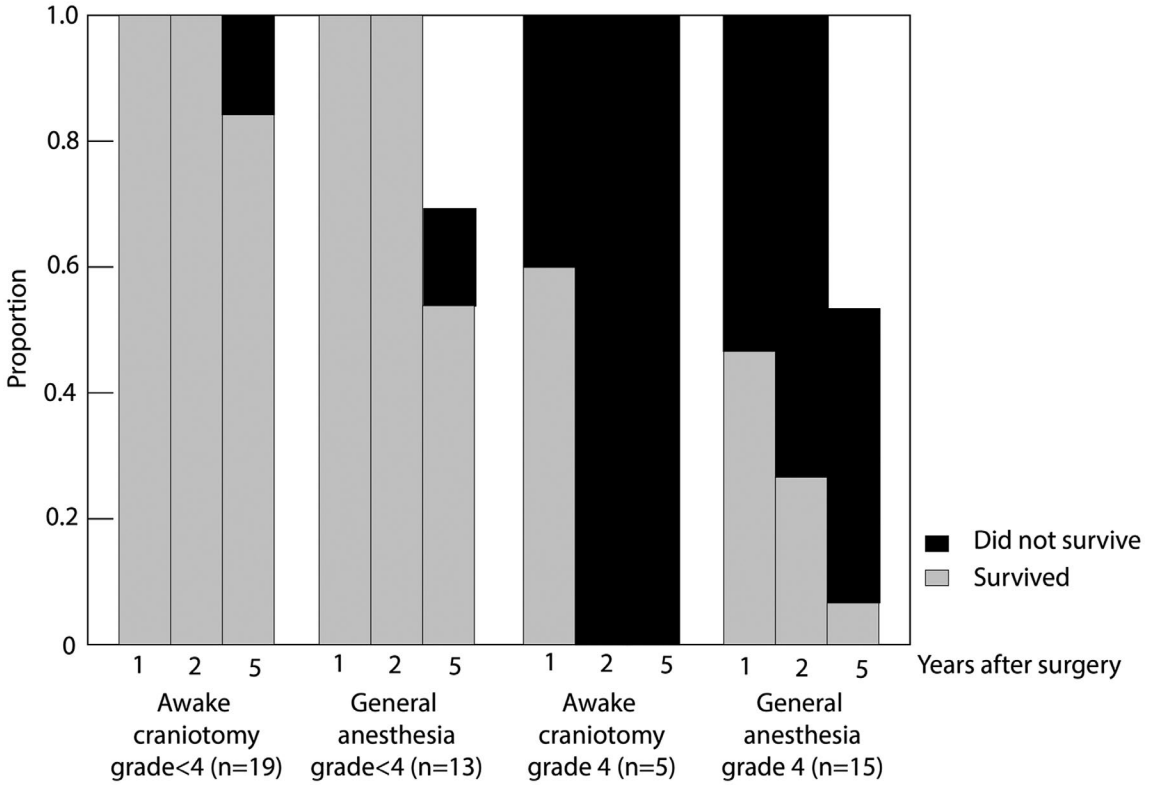

Figure 3. A bar graph shows the proportion of patients who were alive one, two, and five years after surgery.
Note: In the general anesthesia (GA) group, information on five-year survival was not available for 4 (30.8%) patients in the grade <4 GA group or for 7 (46.7%) patients in the grade 4 GA group.

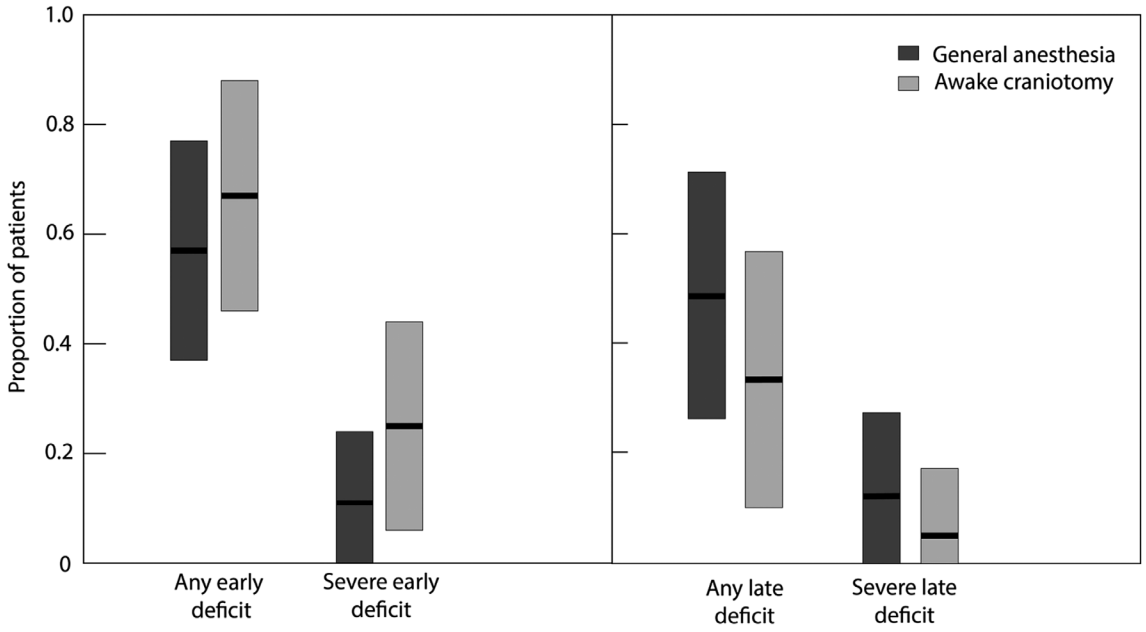

Figure 4. A box plot shows the proportions and 95% confidence intervals of patients with newly developed, any early, severe early, any late, or severe late neurological deficits.
Notes: More early neurological deficits were seen in the awake craniotomy group, while more late neurological deficits were seen in the general anesthesia group. This trend was seen for any deficits and for severe deficits, but none of the differences reached statistical significance.

with a tumor localized in their dominant hemisphere. Note that linguistic dysfunction as a symptom did not differ significantly between the groups. Because linguistic function resides mostly in the dominant hemisphere [22], AC may have been chosen for these patients to allow resection while ensuring clear demarcation of the functional language area in order to preserve this function [23].

Oligodendrogliomas were more often operated on using AC, and astrocytomas more often resected under

GA. This is most likely because oligodendrogliomas are more often located in the frontal operculum than astrocytomas; therefore, AC is more often used for these tumors. A study on the use of AC for the resection of tumors in eloquent areas showed that all tumors had an oligodendrogliomal component [24].

Outcomes

The EOR was similar using AC and GA, but the EOR was smaller within the GA group for grade <4 tumors than for grade 4 tumors. This group also had a larger preoperative tumor volume, and this might explain the higher EOR. Since the edges of the tumor are the most difficult to resect, a larger tumor with a smaller surface area-to-volume ratio, could result in a higher EOR. In addition, GBMs with central necrosis are easier to distinguish from normal brain tissue than are low grade gliomas, allowing easier resection without the need to map the region. In the literature, the median EOR for insular gliomas varies from 83.4 to 86.2% [7,10,23]. However, only Lang et al. reported the EOR for the non-glioblastoma group separately (median EOR, 86%) [5]. However, it seemed that in this study, the population that presented with grade <4 tumors mainly had small diffuse tumors that were hard to resect. Diffuseness was not measured, so it cannot be compared to reports in the literature, but tumor size was measured. The mean tumor size was 61.2 cm^3 in the AC group and 54.6 cm^3 in the GA group, which contrasts with, for example, the mean tumor size of 107.7 cm^3 reported in the study by Alimohamadi et al. [23].

The neurological outcomes observed in our population suggested that the AC results in fewer late neurological deficits than the GA technique, although the difference was not significant. For a power of 80%, a sample size of 49 per group would be needed to find the same difference in the occurrence of early deficits, as in the study by De Witt Hamer et al. ($\alpha = 0.01$) [18]. For a power of 80%, a sample size of 1953 per group would be needed to detect the same difference in late deficits using the same assumptions. These larger sample sizes may not be attainable for this rare disease. Nevertheless, the trends of more early onset neurological deficits after AC and more late onset neurological deficits after GA are consistent with the literature [18]. De Witt Hamer et al. hypothesized that an AC enables more extended resection and more tumor control, resulting in the preservation of neurological functions that can be mapped at the cost of early transient neurological deficits.

Differences in 1- and 2-year mortality were not observed between the two anesthesia groups. GA was preferred for the treatment of astrocytomas, which have a worse survival prognosis than oligodendrogliomas [11,25]. This apparent contradiction is explained by the small sample size in this study. Furthermore, the literature suggests that survival curves start to diverge after more than two years. Since most GA procedures were performed in the second half of the study period, data were not available for some patients for the five-year survival analysis, and conclusions regarding five-year survival cannot be drawn. Our results indicated that one and two years after surgery for insular glioma, there were no differences in survival using AC vs. GA.

Other findings

In the GA group, patients in the grade <4 group were younger than patients in the grade 4 group and more often presented with epilepsy. These findings can be explained by differences in the pathogenesis of primary and secondary GBM. Primary GBMs are most likely derived from neurological progenitor cells, while secondary GBMs are most likely derived from dedifferentiated glial cells [26]. Primary GBMs are more frequently diagnosed and often express wild type isocitrate dehydrogenase 1 or 2 (IDH1/2); in contrast, 73–88% of the patients with secondary GBMs express mutated IDH1 or IDH2 [26]. The epidemiological distribution of IDH1/2 mutations, which are associated with epilepsy, in the types of GBMs could explain the lower frequency of epilepsy in the grade 4 group in our population. It is more likely that this group mostly had primary GBMs that expressed wild type IDH1/2, which would explain the lower prevalence of epilepsy in the grade 4 group than in the grade <4 group [27]. Since epilepsy is a symptom that can be suggestive of brain tumors, secondary GBMs might be diagnosed in an earlier stage, e.g. as an astrocytoma, which could explain the lower prevalence of secondary GBMs as well as the younger age at which they are diagnosed [26].

Intraoperatively, blood loss was greater in the grade <4 AC group than in the grade <4 GA group. This can be explained by the higher mean arterial blood pressure in awake patients. There was no indication that this results in a clinically relevant difference in outcome.

The anesthesia time was longer in the grade <4 GA group than in the grade 4 GA group. The 1.4-h difference between the groups could not be explained by the subanalysis, which showed a difference of 0.2 h between the induction and preparation time between the grade <4 GA group and the grade 4 GA group. The difference between these groups cannot be fully explained. However, it can be more difficult to determine the borders of an insular LGG than the borders of an HGG, and therefore for this step may take longer when treating insular LGGs.

Limitations

This study had some limitations. First, this was a retrospective, single-center study of a disease that has a low incidence, so a larger sample size was not available. Some real differences may have been missed because of the size of the study. However, the sample size was comparable to or even larger than studies that have been published previously by other groups. Because the insula is a relatively

common location for gliomas [3] and because insular gliomas have distinctive clinical features [10], this patient population is worth analyzing. Considering the low incidence of insular glioma, this study contributes to the existing body of knowledge about these patients.

Second, patients with WHO grade 4 glioma were compared with patients with grade <4 glioma, but it could be argued that WHO grade 3 and 4 groups should have been compared with WHO grade 1 and 2 groups. In this study, patients were divided based on similar clinical presentation and survival, but other authors have frequently grouped patients with grade 3 glioma with patients with grade 4 glioma [7]. However, the grade 4 group in this study was large enough to merit its own group, especially considering the distinctive clinical features of GBMs.

Finally, there are some limitations due to the retrospective design of the study, and additional prospective studies are needed to validate these observations. The advantage of our approach is that it provides a starting point for further study of additional research questions. For example, these results suggest that the value of AC for patients who present with linguistic dysfunction should be investigated further, as should the possible clinical relevance of higher blood loss during AC vs. GA.

Notably, there is an alternative technique that can be used to protect motor function in which the cortical processes are mapped using motor evoked potentials while the patient is under GA [28]. However, this technique was not performed at our hospital before 2015, so it is not discussed in this case series. It may be interesting to evaluate tumor extension into the temporal or frontal operculum as well as tumor extension medially beyond the lenticulostriate perforators; however, the subgroups were too small to draw any conclusions.

Use of the transcortical approach for the resection of this type of tumor is another technique that is not performed in our hospital, even though it may provide greater exposure of the insula and therefore might facilitate a greater EOR [29]. However, in our experience, this technique is not in widespread use, plus it should be critically evaluated as it involves the use of an approach through healthy brain tissue.

Conclusion

AC was used more often for the resection of dominant hemispheric tumors and oligodendrogliomas, while GA was used more often for astrocytomas and GBMs. However, both anesthesia techniques resulted in similar EORs, similar neurological outcomes, and similar one- and two-year survival in patients with similar tumor grades. Therefore, the added value of the more challenging AC procedure should be carefully considered for each patient. Prospective studies are needed to further evaluate the relative value of these techniques.

Disclosure statement

The authors report no conflicts of interest.

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