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RESEARCH

What surgical approach for left-sided eloquent glioblastoma: biopsy, resection under general anesthesia or awake craniotomy?

Clémentine Gallet[1] · Anne Clavreul[1,2] · Xavier Morandi[3,4] · Matthieu Delion[1] · Nolwenn Madec[1,5] · Philippe Menei[1,2] · Jean-Michel Lemée[1,2]

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Abstract

Purpose Neurosurgeons use three main surgical approaches for left-sided glioblastoma (GB) in eloquent areas: biopsy, tumor resection under general anesthesia (GA), and awake craniotomy (AC) with brain mapping for maximal safe resection. We performed a retrospective study of functional and survival outcomes for left-sided eloquent GB, comparing these surgical approaches.

Methods We included 87 patients with primary left-sided eloquent GB from two centers, one performing AC and the other biopsy or resection under GA. We assessed Karnofsky performance score (KPS), language and motor deficits one month after surgery, progression-free survival (PFS) and overall survival (OS).

Results The 87 patients had a median PFS of 8.6 months [95% CI: 7.3–11.6] and a median OS of 20.2 months [17-3-24.4], with no significant differences between the three surgical approaches. One month after surgery, functional outcomes for language were similar for all approaches, but motor function was poorer in the biopsy group than in other patients. The proportion of patients with a KPS score > 80 was higher in the resection with AC group than in the other patients at this timepoint.

Conclusion We detected no real benefit of a resection with AC over resection under GA for left-sided eloquent GB in terms of survival or functional outcomes for language. However, given the poorer motor function of biopsy patients, resection with AC should be proposed, when possible, to patients ineligible for surgical resection under GA, to improve functional outcomes and patient autonomy.

Keywords Awake craniotomy · Glioblastoma · Functional outcomes · Survival

Abbreviations

AC	awake craniotomy
EOR	extent of resection
GA	general anesthesia
GB	glioblastoma
GTR	gross total resection
KPS	Karnofsky performance score
PFS	progression-free survival
STR	subtotal resection

✉ Jean-Michel Lemée
JMLemee@chu-angers.fr

1 Département de Neurochirurgie, CHU Angers, 4 rue Larrey, 49 933 Angers Cedex 9, Angers, France

2 Université d'Angers, Inserm UMR 1307, CNRS UMR 6075, Nantes Université, CRCI2NA Angers, France

3 Département de Neurochirurgie, CHU Rennes, Rennes, France

4 Laboratoire d'Anatomie et d'Organogenèse, Faculté de Médecine, CHU Rennes, Rennes, France

5 Les Capucins, centre de rééducation et réadaptation fonctionnelle adulte et pédiatrique, Angers, France

Introduction

Brain tumors occur at all ages, from infancy to old age [1]. Glioblastoma (GB) is the most common malignant primary brain tumor, with the worst prognosis [2]. The current standard of care is maximal surgical resection followed by radiotherapy plus concomitant and adjuvant temozolomide (TMZ) [3]. Even with this aggressive treatment, median overall survival (OS) is about 15 months, and recurrence and a fatal outcome generally occur [2].

Surgery is the first-line treatment, and the aim is to achieve a resection with the best oncofunctional compromise [4–9]. However, GB surgery is challenging for tumors located in or near eloquent areas. In such cases, neurosurgeons adopt several different surgical approaches [10, 11], limitation of the intervention to a biopsy, resection limited to the tumor under general anesthesia (GA), or awake craniotomy (AC) with brain mapping, for maximal safe resection.

AC allows the neurosurgeon to identify "eloquent areas", the removal of which would result in neurological impairment, by cortical and subcortical electrostimulation on an awake, participating patient. AC has been widely used to identify language areas, which are located in the left hemisphere in more than 90% of the population [12, 13]. More recently, additional cognitive functions, such as facial or emotion recognition, which map to the right hemisphere, have also been monitored [14, 15]. AC is now considered the gold standard for slow-growing lesions, such as low-grade glioma (LGG). It induces functional reshaping through plasticity [16], but its real benefits for fast-growing lesions, such as GB remain unclear. Several studies have addressed this question [17–24]. For example, Moiraghi et al. [21] found that AC allowed larger resections than surgery under GA, with a positive impact on survival in carefully selected GB adult patients. One limitation of these studies is that they report data only from their own centers. Comparisons of patients from a single neurosurgical department lead to the constitution of cohorts with different clinical and radiological characteristics corresponding to the criteria for deciding between biopsy, surgical resection under GA or with AC.

As a means of overcoming this limitation, we designed a retrospective comparative two-center study, performed at two neurosurgery departments in France managing left-sided eloquent GB with different surgical approaches. Neurosurgery department A performs AC with brain mapping control, particularly for areas involve in language and motor activities, whereas neurosurgery department B performs stereotactic biopsy or resection under GA. A homogeneous group suitable for comparisons was constructed by including only primary isocitrate dehydrogenase (IDH)-wildtype GB patients treated postoperatively with the Stupp adjuvant protocol. Furthermore, patients from neurosurgery department B were reviewed blindly by two senior neurosurgeons from neurosurgery department A with experience in AC on brain tumors, to assess their eligibility for AC procedures. The aim of this retrospective study was to compare the functional and survival outcomes of patients with left-sided eloquent GB between the three different types of surgical management.

Methods

Study population

The inclusion period extended from January 2015 to October 2020. We selected all patients who had undergone surgical procedures (resection or biopsy) in neurosurgery department B satisfying the following criteria: (1) newly diagnosed left supratentorial GB, (2) negative immunohistochemical staining for IDH1-R132H, (3) one month of follow-up data available and, (4) first-line treatment according to the Stupp protocol. The decision for biopsy or resection was made on a case-by-case basis between the different care team members, considering the tumor's size, location relative to functional brain areas as well as patient's age and clinical status. The same criteria were applied to patients undergoing surgical resection with AC in neurosurgery department A, except that only GB patients in whom language and/or motor brain mapping was performed were included. Patients selected from neurosurgery department B were reviewed blindly by two senior neurosurgeons from neurosurgery department A to assess their eligibility for AC procedures. Patients considered ineligible for surgical resection during AC were excluded. The following exclusion criteria were used: (1) the GB was located far from eloquent areas, (2) oncological resection was not possible with an acceptable benefit-to-risk ratio and, (3) clinical and/or demographic criteria excluding AC, such as old age, preoperative deficits, particularly major language impairments not resolved by corticosteroid treatment ruling out language mapping, or emergency surgery. Patients were grouped by surgical approach: biopsy under GA ("Biopsy_GA"), resection under GA ("Resection_GA"), resection during AC ("Resection_AC").

For this retrospective study, French legislation required only authorization from the French National Data Protection Authority (CNIL; authorization no. ar22-0064v0/no. 1,476,342) and the non-objection of patients to use of their personal data.

Functional status

Karnofsky performance score (KPS) and motor and language deficits and were noted retrospectively from medical records before surgery and one month after surgery. We focused on this time point rather than the immediate postoperative period (48–72 h) during which there is a risk of edema-related deficits, or three months after surgery, to exclude deficits related to tumor progression or adjuvant chemoradiotherapy. Motor and language deficits were classified as previously described [17] (Table 1). Deficits were considered new if they first appeared after surgery.

Table 1 Demographic and clinical characteristics of patients with left-sided eloquent GB treated by three surgical approaches: stereotactic biopsy under GA, resection under GA or resection during AC. All patients had IDH wild-type GB

Language deficits were stratified into four grades (extrapolated from the adult NIHSS scale [25]): 0, no aphasia/normal; 1, mild-to-moderate aphasia (comprehension clinically adequate but spontaneous speech non-fluent, with marked word-finding difficulties, semantic, or phonemic paraphasia); 2, severe aphasia (patient difficult to understand due to reduced language and/or a difficulties with comprehension); and 3, mute, global aphasia

Motor deficits were classified according to the modified McCormick scale [26]: 0, no deficit; 1, mild deficit (almost normal limb use, with patients able to walk, but an impairment of fine movements of the upper limb); 2, moderate deficit (movement possible with external aid); and 3, severe deficit (limited function, dependent)

	Biopsy_GA	Resection_GA	Resection_AC	*P*-value
Number	14 (100%)	37 (100%)	36 (100%)	
Age (years)				0.027*
• Median (range)	55 (47–72)	61 (37–71)	62 (24–79)	
• ≤ 60	12 (86%)	17 (46%)	17 (47%)	
• > 60	2 (14%)	20 (54%)	19 (53%)	
Sex				0.134
• Male	6 (43%)	27 (73%)	23 (64%)	
• Female	8 (57%)	10 (27%)	13 (36%)	
Extent of tumor				0.109
• Unilobar	13 (93%)	28 (76%)	23 (64%)	
- Frontal	8 (57%)	8 (22%)	10 (28%)	
- Occipital	0 (0%)	1 (3%)	1 (3%)	
- Parietal	3 (21%)	3 (8%)	7 (19%)	
- Temporal	2 (14%)	16 (43%)	5 (14%)	
• Multilobar	1 (7%)	9 (24%)	13 (36%)	
EOR				
• STR	NA	18 (49%)	18 (50%)	1.000
• GTR	NA	19 (51%)	18 (50%)	
Preoperative language deficits				0.255
• 0	10 (71%)	23 (62%)	20 (56%)	
• 1	3 (21%)	13 (35%)	16 (44%)	
• 2	1 (7%)	0 (0%)	0 (0%)	
• 3	0 (0%)	1 (3%)	0 (0%)	
Preoperative motor deficits				
• 0	9 (64%)	32 (86%)	33 (92%)	0.075
• 1	2 (14%)	3 (8%)	3 (8%)	
• 2	2 (14%)	2 (5%)	0 (0%)	
• 3	1 (7%)	0 (0%)	0 (0%)	
Postoperative language deficits_1 month				0.099
• 0	8 (57%)	26 (70%)	18 (50%)	
• 1	5 (36%)	11 (30%)	18 (50%)	
• 2	1 (7%)	0 (0%)	0 (0%)	
• 3	0 (0%)	0 (0%)	0 (0%)	
Postoperative motor deficits_1 month				
• 0	4 (29%)	33 (89%)	31 (86%)	< 0.001*
• 1	5 (36%)	2 (5%)	3 (8%)	
• 2	4 (29%)	0 (0%)	2 (6%)	
• 3	1 (7%)	2 (5%)	0 (0%)	
KPS_1 month				
• ≤ 80	9 (64%)	17 (46%)	8 (22%)	0.003*
• > 80	3 (21%)	18 (49%)	28 (78%)	
• Unknown	2 (14%)	2 (5%)	0 (0%)	
Stupp protocol				0.085
• Incomplete	10 (71%)	16 (43%)	25 (69%)	
• Complete	3 (21%)	18 (49%)	11 (31%)	

Table 1 (continued)

	Biopsy_GA	Resection_GA	Resection_AC	*P*-value
• Unknown	1 (7%)	3 (8%)	0 (0%)	
Survival outcomes				
PFS				0.285
• Median (months) [95% CI]	7.8 [6.4–24.5]	11.6 [8.6–17.2]	7.3 [6.1–11.7]	
• PFS-12 rate (%) [95% CI]	21.4 [7.9–58.4]	43.2 [29.9–62.3]	29.1 [17.0-49.8]	
OS				0.650
• Median (months) [95% CI]	21.8 [10.9-NA]	23.4 [17.6–36.7]	17.5 [15.2–34.7]	
• OS-36 rate (%) [95% CI]	24.2 [8.1–72.7]	28.3 [16.0-50.1]	22.2 [11.3–43.7]	

Abbreviations: EOR, extent of resection for first surgery, GTR, gross total resection (90–100%); KPS, Karnofsky performance score; OS, overall survival from first surgery; OS-36, survival rate 36 months after first surgery; PFS, progression-free survival from first surgery; PFS-12, progression-free survival rate 12 months after first surgery; STR, subtotal resection ($<90\%$)

AC technique, EOR, Stupp protocol and survival analysis

AC was performed as previously described [17, 25] (Supplementary data). EOR was recorded by the surgeon or was determined from a postoperative MRI scan performed within 48 h of surgery by a neuroradiologist. EOR was classified as gross total (GTR; 90–100%) or subtotal (STR; < 90%). The Stupp protocol was considered complete if TMZ chemoradiotherapy and six cycles of adjuvant TMZ were performed, and incomplete if TMZ was discontinued during the radiotherapy or consolidation phase. PFS was defined as the time from surgery to first clinical and/or tumoral progression, according to the RANO criteria [26]. OS was calculated from the date of initial surgery until the date of last follow-up or death. Patients alive at last follow-up were censored.

Statistical analyses

Data were analyzed in R v4.1.0 (https://www.r-project.org). Differences between groups were assessed in overall Chi-squared or Fisher's exact tests for categorical data. P-values were adjusted by the Benjamini-Hochberg method for multiple testing. A multivariate logistic regression analysis was performed to identify significant independent predictors of postoperative deficits one month after surgery. Univariate Cox regression analysis was performed with the covariates of all patients, to identify factors associated with OS. Variables with crude p-values <0.25 in univariate analysis were included in multivariate Cox regression analysis unless correlated with each other. Survival curves were plotted according to the Kaplan-Meier method and compared in log-rank tests. Values of $p<0.05$ were considered statistically significant.

Results

Characteristics of GB patients

We included 87 left-sided IDH-wildtype GB patients in total, 36 of whom underwent AC in neurosurgery department A, the other 51 undergoing surgery under GA, including 14 who underwent biopsy only, in neurosurgery department B. Demographic and tumor characteristics are presented in Table 1. The groups differed significantly for patient age ($p=0.027$) with more patients under 60 years of age in the "Biopsy_GA" group (86%), than in the "Resection_GA" (46%) (post hoc $p=0.047$) and "Resection_AC" (47%) (post hoc $p=0.047$) groups. Other variables, including sex, tumor extent, EOR and complete Stupp protocol did not differ significantly between groups (Table 1). No early postoperative complications that could have affected the neurologic recovery were observed, except for one patient in the "Resection_AC" group in whom evacuation of a brain parenchymal hematoma was required.

Functional status

Language deficits. Before surgery, language deficits did not differ between groups ($p=0.255$) (Table 1). One month after surgery, there was also no significant difference in language deficits between groups ($p=0.099$) (Table 1). In the "Biopsy_GA" group, seven patients (50%) remained asymptomatic one month after stereotactic biopsy, and three (21%) retained their preoperative language deficits (Fig. 1A). Functional language status had deteriorated by this time point in three patients (21%), with the acquisition of new grade 1 language deficits, and had improved in one patient (7%). In the "Resection_GA" group, 19 patients (51%) remained asymptomatic one month after surgery and seven (19%) retained their preoperative language deficits. Functional language status had deteriorated in four patients (11%), with the acquisition of new grade 1 language deficits

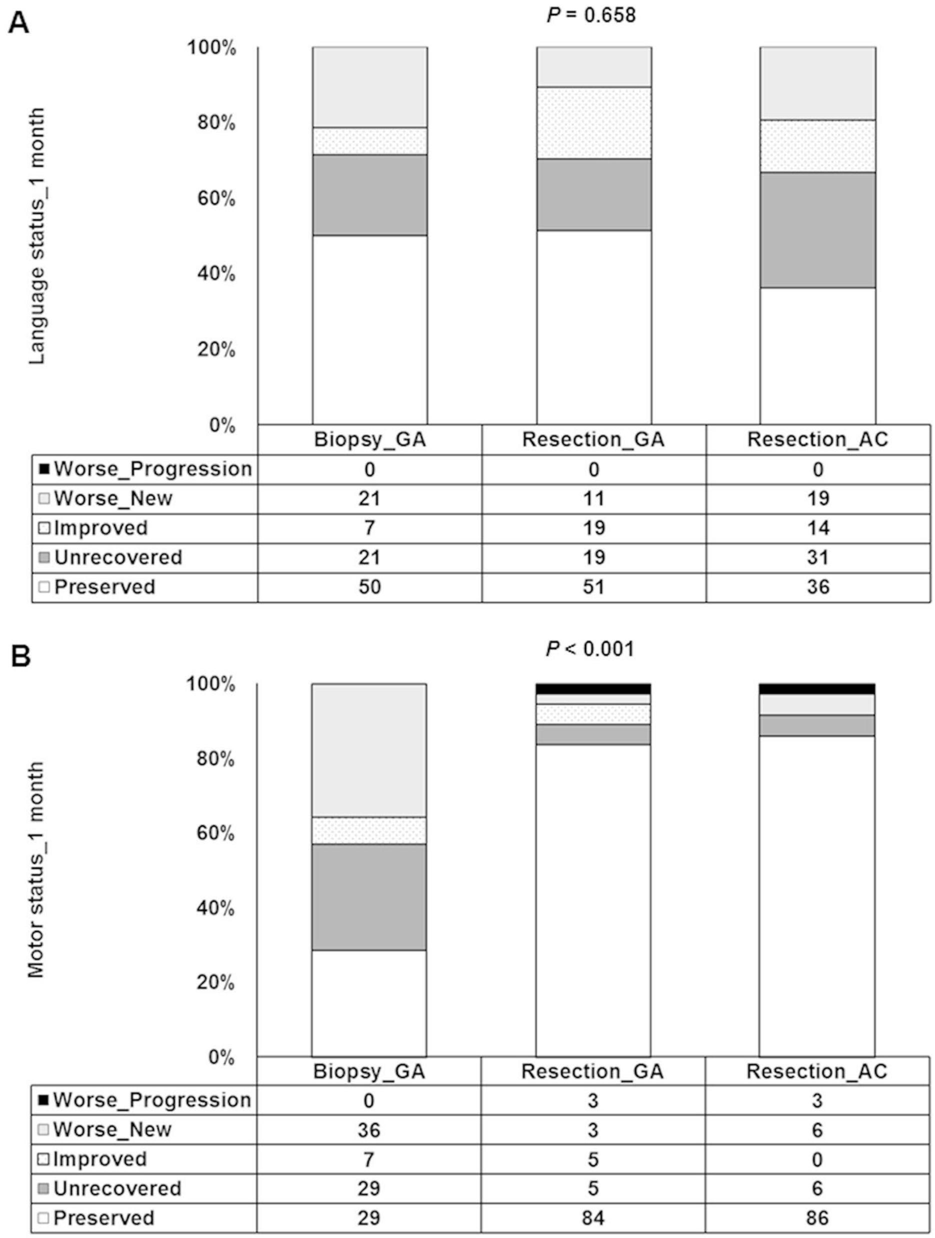

Fig. 1 Functional outcomes in patients with left-sided eloquent GB one month after stereotactic biopsy under GA, resection under GA or resection during AC: (A) Functional language outcome and (B) functional motor outcome. Four outcome levels were defined: preserved (patients remaining asymptomatic), unrecovered (patients retaining their preoperative deficits), improved (patients with an improvement of preoperative deficits) and, worse (patients whose functional status has deteriorated, with the acquisition of new motor and/or language deficits or a worsening of their preoperative deficits)

and had improved in seven patients (19%). In the "Resection_AC" group", 13 patients (36%) remained asymptomatic one month after surgery and 11 (31%) retained their preoperative language deficits. Functional language status had deteriorated in seven patients (19%), with the acquisition of new grade 1 language deficits and had improved in five patients (14%).

Motor deficits. Before surgery, motor deficits did not differ between groups ($p = 0.075$, respectively) but they differed significantly one month after surgery ($p < 0.001$) (Table 1). Motor deficits were significantly worse in the "Biopsy_GA" group than in the "Resection_GA" (post hoc $p < 0.001$) and "Resection_AC" (post hoc $p < 0.001$) groups. Motor deficits did not differ significantly between the "Resection_GA" and "Resection_AC" groups (post hoc $p = 0.352$). Four patients in the "Biopsy_GA" group (29%) remained asymptomatic one month after stereotactic biopsy and four patients (29%) retained their preoperative motor deficits (Fig. 1B). Functional motor status had deteriorated by this time point in five patients (36%), with the acquisition of new mild-to-moderate motor deficits and, had improved in one patient (7%). In the "Resection_GA" group, 31 patients (84%) remained asymptomatic one month after surgery and two (5%) retained their preoperative motor deficits. Functional motor status had deteriorated in two patients (5%), with the acquisition of new severe motor deficits in one and

Table 2 Multivariate logistic regression analysis to identify factors predictive of postoperative deficits in patients with left-sided eloquent GB one month after stereotactic biopsy under GA, resection under GA or resection during AC CI, confidence interval; OR, odds ratio

Variable	OR	95% CI	*P*-value
Age (>60 years)	1.22	[0.43–3.54]	0.709
Sex (female)	0.56	[0.17–1.67]	0.305
Preoperative deficits (with)	5.44	[1.99–16.35]	0.001*
Extent of tumor (multilobar)	1.05	[0.33–3.30]	0.937
Surgical approach			
• Biopsy_GA	1		
• Resection_GA	0.02	[0.00–0.16]	0.001*
• Resection_AC	0.07	[0.00–0.48]	0.021*

a worsening of preoperative motor deficits in the other. Two patients (5%) displayed an improvement of preoperative motor deficits, passing from mild-to-moderate deficits to no deficit. In the "Resection_AC" group, 31 patients (86%) remained asymptomatic one month after surgery and two (6%) retained their preoperative motor deficits. Functional motor status had deteriorated in three patients (8%), with the acquisition of new mild-to-moderate motor deficits in two patients and a worsening of preoperative motor deficits in one. No improvement of motor functions was observed.

Postoperative KPS. One month after surgery, the proportion of GB patients with a KPS > 80 was higher in the "Resection_AC" group than in the "Biopsy_GA" (post hoc $p = 0.005$) and "Resection_GA" (post hoc $p = 0.039$) groups (Table 1). KPS score did not differ significantly between the "Biopsy_GA" and "Resection_GA" groups (post hoc $p = 0.179$).

Predictive factors for functional outcome. Multivariate logistic regression analysis was performed to identify factors predictive of deficits one month after surgery. Two independent risk factors were identified: the presence of preoperative deficits ($p = 0.001$) and stereotactic biopsy under GA ($p = 0.001$ vs. resection under GA and $p = 0.021$ vs. resection during AC) (Table 2). Sex and tumor extent had no significant impact on the incidence of postoperative language and/or motor deficits (Table 2).

Survival outcomes

The 87 patients had a median PFS of 8.6 months [95% CI: 7.3–11.6] and a median OS of 20.2 months [17.3–24.4] with no significant difference in PFS between the three groups ($p = 0.285$) (Fig. 2 A). Median PFS was 7.8 months [95% CI [6.2–24.5] in the "Biopsy_GA" group, 11.6 months [95% CI: 8.6–17.2] in the "Resection_GA" group and 7.3 months [95% CI: 6.1–11.7] in the "Resection_AC" group. OS did not differ significantly between the three groups either ($p = 0.650$) (Fig. 2B). Median OS was 21.8 months [95% CI: 10.9-NA] in the "Biopsy_GA" group, 23.4 months [95% CI: 17.6–36.7] in the "Resection_GA" group and 17.5 months [95% CI: 15.2–34.7] in the "Resection_AC" group.

Three variables were associated with a shorter OS in univariate analysis: presence of preoperative deficits

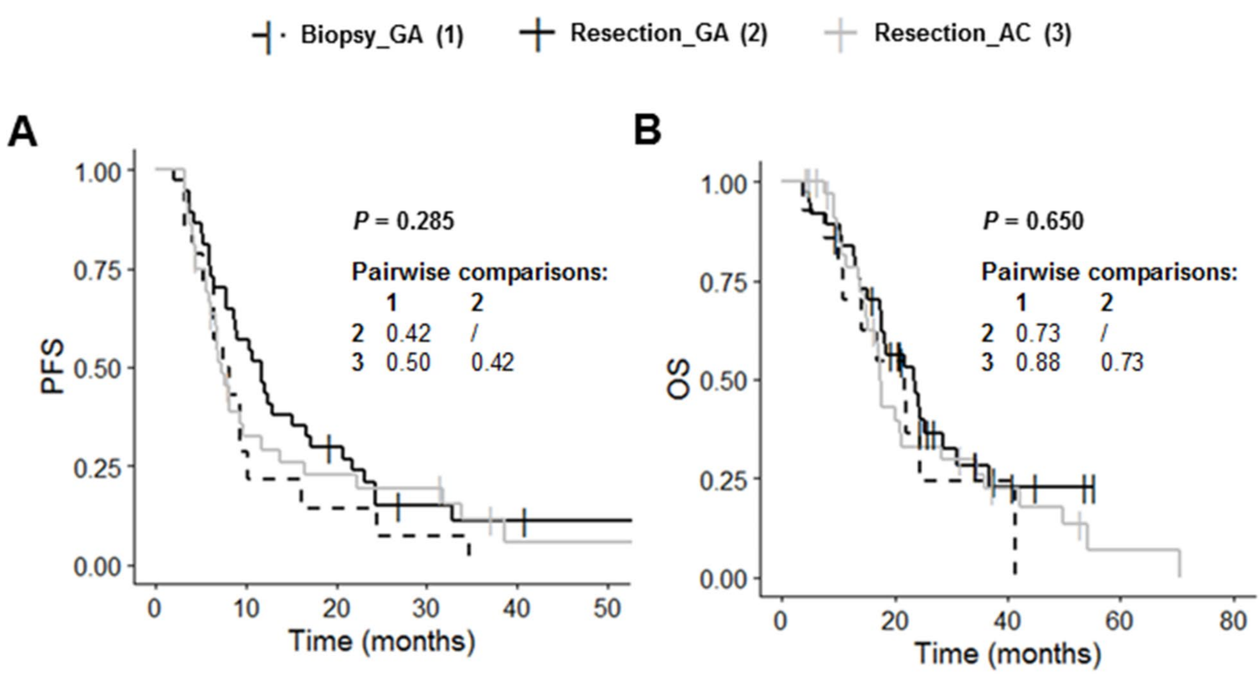

Fig. 2 Kaplan-Meier curves for the survival of patients with left-sided eloquent GB stratified by three surgical approaches: biopsy under GA, resection under GA and resection during AC (A: PFS; B: OS). Abbreviations: PFS, progression-free survival; OS, overall survival

Table 3 Univariate and multivariate Cox regression analyses of factors associated with OS in patients with left-sided eloquent GB undergoing three types of surgery: biopsy under GA, resection under GA or resection during AC. Abbreviations: CI, confidence interval; KPS, Karnofsky performance score; OR, odds ratio

	Univariate analysis			Multivariate analysis		
Variables	**OR**	**95% CI**	***P*-value**	**OR**	**95% CI**	***P*-value**
Age (> 61 years)	0.67	[0.40–1.12]	0.126	1.10	[0.62–1.96]	0.736
Sex (female)	0.78	[0.46–1.33]	0.364			
Tumor extent (multilobar)	0.77	[0.44–1.34]	0.348			
Preoperative deficits (with)	1.71	[1.03–2.83]	0.039*	1.67	[0.97–2.89]	0.066
Postoperative deficits (with)	1.72	[1.03–2.86]	0.037*	1.09	[0.60–1.99]	0.780
Postoperative KPS (> 80%)	0.64	[0.38–1.09]	0.099	0.91	[0.50–1.65]	0.756
Surgical approach						
• Biopsy_GA	1					
• Resection_GA	0.76	[0.37–1.59]	0.470			
• Resection_AC	0.96	[0.46–1.99]	0.905			
Stupp protocol (complete)	0.23	[0.12–0.41]	< 0.001*	0.23	[0.12–0.46]	< 0.001*

($p = 0.039$), presence of postoperative deficits one month after surgery ($p = 0.037$) and incomplete Stupp protocol ($p < 0.001$). We identified one variable as independently associated with shorter OS in multivariate analysis: incomplete Stupp protocol ($p < 0.001$) (Table 3). Preoperative deficits tended to be independent prognostic factors for OS ($p = 0.066$).

Discussion

Neurosurgeons use several different surgical approaches to treat GB located in or near eloquent areas, as illustrated by the two neurosurgery departments participating in this retrospective study. Department A performs resection with AC for all cases of left-sided eloquent GB, whereas department B favors stereotactic biopsy or resection limited to the tumor under GA. No study has yet determined whether left-sided GB in or near eloquent areas is best resected, or whether surgical intervention should be limited to biopsy. In general, resection is recommended over biopsy for patients in good clinical condition, but care is required to ensure that surgery does not worsen the patient's neurological status [27–31].

Here, we analyzed functional language and motor status one month after surgery by one of three approaches: biopsy under GA, resection under GA or resection during AC. Functional language outcomes were similar for all three approaches, but functional motor status was worse in patients who underwent stereotactic biopsy than in other groups. The rate of new motor deficits was high in the biopsy groups (36%), possibly due to a higher proportion of patients having frontal GB. Consistent with previous findings [17, 32–34], stereotactic biopsy and the presence of preoperative deficits were found to be independent risk factors for the presence of postoperative deficits.

Resection during AC is generally favored over resection under GA as a means of achieving maximal resection while preserving functional outcomes. However, we observed no positive impact of AC on EOR, with complete resection achieved in about 50% of patients in both surgical research conditions. This result is not consistent with previous findings reporting the more frequent achievement of maximal lesion removal by AC than by surgery under GA [18, 20, 21, 35–38]. The identification of critical and non-critical areas by mapping in awake patients is thought to increase safety, by enabling the neurosurgeon to optimize resections that would necessarily have been more conservative under GA to prevent the generation of permanent postoperative deficits. However, grossly abnormal tissue can retain function and therefore cannot be safely resected, resulting in incomplete EOR during AC [39, 40]. The use of fluorescence-guided surgery at neurosurgery department B (in 43% of cases in this study) may also have improved EOR under GA [41].

Resection during AC also conferred no advantage over resection under GA in terms of the recovery and preservation of language and motor functions. Zigiotto et al. [24] also found no difference in cognitive functions, including language functions, between patients undergoing surgery under GA and during AC. We observed new language deficits in about 15% of patients with both surgical approaches, and these deficits were mild to moderate. New motor deficits were less frequent, occurring in about 4% of patients. They were mild in all but one case, a patient undergoing surgery under GA who presented severe motor deficits. The induction of new postoperative deficits is not uncommon after AC [17]. It was reported that the functional identification of the motor cortex and the corticospinal tract becomes almost complete with the mapping technique; however, it was less than 60% success for the language area and the language-related fibers detection reflecting the true diversity and in vivo patterns of cortical language organization

[42]. Despite the success in identifying the motor areas with AC, motor deficits cannot be completely avoided with this surgical approach. Combined application of intraoperative voluntary movement during AC and transcortical motor evoked potential (MEP) monitoring could be useful for resection and prediction of postoperative motor function in patients with gliomas within or close to motor-related areas [43]. MEP monitoring for intraoperative assessment of the motor cortex should also be considered for surgical resection under GA if surgery is close to the motor cortex [44].

The proportion of patients with a postoperative KPS > 80 was higher in the resection during AC group. KPS score is widely used to predict the autonomy of patients with brain tumors. This result, consistent with previous findings [20, 22], indicates that, despite the lack of significant difference in functional language and motor status between GB patients undergoing resection under GA and during AC, resection during AC may result in a better general performance status for daily activities.

Several studies have indicated that postoperative neurological deficits after surgery are predictive of poor survival in GB patients [29, 30]. However, although stereotactic biopsy was found to be an independent risk for postoperative deficits, we found no significant difference in PFS or OS between patients with left-sided eloquent GB patients undergoing biopsy under GA, resection under GA or resection during AC. An OS of about 20 months was observed for GB patients undergoing these three types of surgical intervention, a value typical for GB patients in the Stupp era [3, 18, 27, 32]. This result conflicts with other studies reporting an association between maximal tumor resection and better OS [45–47] and indicating that AC can improve OS in GB patients [20, 21, 24]. This discrepancy may be partly explained by the homogeneous nature of the retrospective series of GB patients studied here (primary GB, IDH-wildtype, Stupp regimen for first-line treatment) and the results being obtained at two centers. Previous studies comparing survival outcomes for GB patients undergoing surgery in AC and GA conditions were performed in a single neurosurgery department. This introduces a significant bias in the constitution of cohorts because the center may have proposed surgical resection under GA as the default intervention for tumors located in eloquent areas for which AC was considered not to be feasible with an acceptable benefit-to-risk ratio. We also found no significant difference in PFS and in OS between patients with left-sided eloquent GB undergoing biopsy under GA, resection under GA or resection during AC based on data for patients included in the French GB biobank [48], (supplementary data). It was not possible to assess functional outcomes in this cohort because the postoperative deficits at one and three months of follow-up were not recorded on the electronic case report forms.

Limitations

One of the limitations of this study is its retrospective design, which may introduce several unavoidable biases. Another limitation is the lack of a rigorously validated quantitative, semi-automated volumetric analysis tool for measuring preoperative tumor volume and residual volume. Furthermore, the prognosis of GB is known to be influenced by O(6)-methylguanine methyltransferase promoter methylation status, but information about this marker was lacking. It was also not possible to compare pre- and postoperative KPS because of the large number of missing data for preoperative KPS. Furthermore, predictive factors for functional and survival outcomes should be interpreted with caution, given the small sample size. Health-related quality of life (HRQoL) and patient and family satisfaction were not evaluated here, but should be investigated in future studies. One study [49] reported that an early deterioration of HRQoL after surgery is an independent factor strongly associated with poor survival in patients with GB.

Conclusion

Here, we observe no real benefit of resection during AC over resection under GA for left-sided eloquent GB, in terms of survival and functional outcomes, but AC may be better for preserving patient autonomy. Given the worse motor functional status of biopsy patients, resection with AC should be proposed, when possible, to patients considered ineligible for surgical resection under GA, to improve functional outcome. The prospective multicenter, randomized controlled trial comparing different surgical approaches for GB in critical locations conducted by Gerritsen et al. [50] may help to confirm this improvement.

Supplementary information The online version contains supplementary material available at https://doi.org/10.1007/s11060-022-04163-9.

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Author contributions All authors contributed to study conception and design. The data were collected and analyzed by Clémentine Gallet, Anne Clavreul and Jean-Michel Lemée. The first draft of the manuscript was written by Clémentine Gallet and all the authors commented on intermediate versions of the manuscript. All the authors have read and approved the final manuscript.

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Declarations

Conflict of interest None.

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