

## Original Article

Asleep-awake-asleep versus hypnosis for low-grade glioma surgery: long term follow-up outcome<sup>☆</sup>Nourou Dine Adeniran Bankole<sup>a,b,c,\*</sup>, Ulrick Sidney Kanmounye<sup>d</sup>, Abdessamad El Ouahabi<sup>b</sup>, Ilyess Zemmoura<sup>a,e</sup><sup>a</sup> CHRU de Tours, Neurosurgery Department, Tours, France<sup>b</sup> CHU Ibn Sina, Neurosurgery Department, Mohammed V University of Rabat, Morocco<sup>c</sup> Clinical Investigation Center (CIC), 1415, INSERM, CHRU de Tours, Tours, France<sup>d</sup> Research Department, Association of Future Africans Neurosurgeons, Yaoundé, Cameroon<sup>e</sup> UMR Inserm U1253, iBrain, University of Tours, Tours, France

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## ABSTRACT

**Background:** Hypnosis-aided craniotomy is a safe alternative to standard asleep-awake-asleep (AAA) surgery in glioma surgery. The impact of these two anesthetic methods on tumor prognosis has never been assessed.

**Objective:** This study aimed to evaluate the possible impact of the type of sedation (i.e., hypnosedation vs. standard sedation) on postoperative outcomes in awake surgery for gliomas.

**Methods:** Adult patients who underwent awake surgery for a diffuse glioma, excluding glioblastomas, between May 2011 and December 2019 at the authors' institution were included in the analysis. Pearson Chi-square, Fisher exact, and Mann-Whitney U tests were used for inferential analyses.

**Results:** Sixty-one (61) patients were included, thirty-one were female (50.8%), and the mean age was 41.8 years (SD = 11.88). Most patients had IDH mutated tumors (n = 51; 83.6%). Twenty-six patients (42.6%) were hypnosedated while 35 (57.4%) received standard AAA procedure. The overall median follow-up time was 48 months (range: 10 months-120 months). Our results did not identify any significant difference between both techniques in terms of extent of resection (sub-total resection >95% rates were 11.48% vs. 8.20%, OR = 2.2, 95% CI = 0.62–8.44; P = 0.34) and of overall survival (87.5% of patients in the AAA surgery group reach 9 years OS vs. 79% in the hypnosis cohort, CHR = 0.85, 95% CI = 0.12–6.04; P = 0.87).

**Conclusion:** Hypnosis for awake craniotomy is rarely proposed although it is a suitable alternative to standard sedation in awake craniotomy for LGGs, with similar results in terms of extent of resection or survival.

## 1. Introduction

Low-grade gliomas (LGG) are slow-growing tumors associated with a median survival time ranging from 4 to 13 years [1–3].

The prognosis of LGG improved over the last two decades. Two major factors may explain this improvement. First, is the development of awake surgery, which allows a greater extent of resection (EOR) while cognitive functions are better preserved. Second, is the advent of molecular biology and the better molecular classification of glial tumors, which allows clinicians to better adapt oncological treatments. The most

used molecular data is IDH mutation, which is associated with a better outcome [4].

The EOR has been for long known as a major prognostic factor in LGG. More recently, it has been demonstrated that the use of intra-operative direct brain electrical stimulation during awake surgery enables the surgeon to perform a resection according to functional boundaries, minimizing postoperative morbidity and therefore improving quality of life, which indirectly leads to a quantitative impact on the EOR [5].

The classical method to perform an awake craniotomy is the asleep-

**Abbreviation:** AAA, Asleep-awake-asleep; LGG, Low-grade gliomas; GBM, Glioblastoma; EOR, Extent of resection; OR, odd ratio; CHR, crude Hazard ratio.

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awake-asleep (AAA) technique [5]. Nonetheless, this anesthetic method might be contraindicated in some situations such as obesity or severe gastrointestinal reflux, or sometimes associated with a very long waking period or confusion and movements during the waking period. In a recent study [6], we demonstrated the reliability of hypnosis as an original alternative method for performing a craniotomy during awake surgery. In this previous work, although we did not demonstrate any superiority of hypnosis on the “classical” AAA method, which remains, in our opinion, the gold standard for resection of LGGs in young adults [6], we showed that hypnosis allowed an effective awake mapping for glioma resection with no negative psychological impact.

Our objective in this new study was to assess the possible impact of hypnosis on the oncological performance of awake surgery of LGG. Indeed, one could state that hypnosis may induce a modification of awake performances of the patient during cognitive tests administered during the fully awake period, i.e., the pre-resection cortical cartography and the intra-resection continuous tests. As a consequence, if hypnosis modifies the intra-operative performance of the patient, it could indirectly lead to a less effective tumor resection, and therefore a worst oncological issue. We reviewed the preoperative tumor characteristics, the residual tumor volume, post-operative course (clinical and radiological follow-up, oncological treatment), and survival data on our monocentric series of patients that had undergone awake surgery for a low-grade glioma, either with hypnosis or with AAA.

## 2. Methods

### 2.1. Ethics statement

The data collected during the study have been stored in a computer file following the law of the French Data Protection Act of January 6, 1978, amended in 2004. The study has been approved and adopted by the CNIL (CNIL N° 2023-028) and by the French national college of Neurosurgery Institutional review board (IRB N° 00011687) to which conform the different University Hospitals of this project. Patient consent procedure was always obtained in our department.

### 2.2. Study population

Between May 2011 and December 2019, all the patients who had undergone an awake craniotomy, either with hypnosis or with AAA procedure, for the resection of a presupposed LGG in our institution were included. All the patients who were diagnosed with a WHO grade IV glioma were excluded. We also excluded two cases of Papillary Glioneuronal Tumors (PGNT), one case of Dysembryoblastic Neuroepithelial Tumor (DNET), one case of Pleomorphic Xanthoastrocytomas Anaplastic (PXA).

Our series included 61 consecutive patients according to these criteria. Clinical, radiological, surgical, biological, treatment and survival data were collected retrospectively into a database.

### 2.3. Data acquisition and study outcome

Clinical patient information included age, gender, date of diagnosis, location of the tumor, date of surgery, preoperative tumor volume, post-operative residual tumor volume on 3- or 6-months postoperative MRI, histopathological diagnosis, molecular data, and long-term follow-up features. Of note, the sequelae were defined as permanent impairments after surgery (motor, language, visual, memory deficit, epilepsy). Our primary outcome was to assess the impact of hypnosis on the oncological performance of awake surgery of LGG. The secondary outcomes were to assess if the molecular profile, the preoperative tumoral volume, the residual tumor volume after surgery, and the EOR influenced the overall survival.

### 2.4. Brief description of hypnosedation

The rationale of using hypnosis sedation and its methodology was fully described by our team in a previous study [6]. Briefly, the only limitations for not choosing hypnosedation were either the availability of the anesthesiologist who practiced hypnosis, either the non hypnotizability of the patient, which could be tested a few weeks before surgery, or the patient’s wish not to undergo hypnosis (as it is not possible, fortunately, to force anyone to be hypnotized). Considering hypnosedation procedure, patients were positioned on a smooth foam mattress in a lateral decubitus. Hypnotic trance was induced by eye fixation, and was thereafter facilitated by a small dose of remifentanyl, after a peripheral catheter was placed. Throughout the trance, instructions were repeated: “lachez prise” (the French translation of “let go”), “faites confiance en vous-même” (trust yourself), “profitez des instants” (enjoy the moment). During hypnosis, the usual surgical steps that precede brain mapping were successively performed: local anesthesia of the skin, placement of the head clamp, skin asepsis, skin flap, opening of the skull, and then opening of the dura matter. The complete description of hypnosedation procedure is available in our previous study [6].

### 2.5. Methodology used to measure tumor volume

We used preoperative and postoperative (3–6 months after surgery) FLAIR MRI sequences to visualize tumors that all appeared as a hyperintense mass. We then used the open-source software ITKSNAP 3D Segmentation (v.3.4.0 US national institute of health) to semi-automatically segment the tumors (manual thresholding, manual placement of seeds in the regions of interest, 3D automatic expansion of the seeds, and manual correction of the segmentation obtained).

We empirically stratified the preoperative volume in three groups (<20 mL, 20–40 mL, and >40 mL), the residual tumor volume was stratified in two groups (<3cc and ≥3cc), and the EOR was also categorized as ≥95% or <95%.

### 2.6. Statistical analysis

Statistical analyses were performed with Excel and R-studio Rv. 4.2.3 (R Core Team). The Pearson Chi-square, Fisher exact, and Mann–Whitney U tests were used to evaluate correlations and associations. Data are presented as the mean  $\pm$  standard deviation. For all analyses, P-values < 0.05 were considered statistically significant. We used Kaplan Meier curves to analyze survival.

## 3. Results

Mean age of our population was 41.5 years (SD = 11.69). LGGs were usually limited to a single brain region (n = 44, 72.13%). Most tumors were located in the frontal (n = 46, 75.4%), temporal (n = 15, 24.6%), cingular (n = 13, 21.31%), and insular (n = 10, 16.4%) lobes (Table 1).

Forty-seven patients were classified WHO Grade II (78.7%) whereas 13 patients were classified WHO Grade III (21.3%). Fifty-one patients (83.6%) were diagnosed with a IDH mutated tumors, vs. 10 (16.4%) a IDH wild-type tumors. Preoperative tumor volume was >40 mL in 50.8% of patients (n = 31), and postoperative volume was ≥3 ml in 57.4% (n = 35). Median preoperative tumor volume was 45.13 ml (IQR = 42.19 ml) and median residual tumor volume was 3.8 ml (IQR = 13.12 ml). The median EOR was 85.7% (IQR = 19.26%); 49 patients had an EOR < 95% (80.32%). Thirty-eight patients (62.3%) were operated on once, and 23 (37.7%) underwent a redo surgery. The median time between the first surgery and the second surgery because of residual tumor progression was 3.5 years (IQR: 2,7) because of progression of residual tumor in functional area which not allow to achieve high extension rate (EOR < 95%) at the first time of surgery. Among them, 5 patients (8.2%) underwent three-time surgery with median time

**Table 1**  
Descriptive characteristics of patients.

Characteristic	Number of cases (Percentage)
Sex	
Female	31 (50.8)
Male	30 (49.2)
Number of brain regions invaded	
1	44 (72.1)
2	8 (13.1)
3	9 (14.8)
Location	
Frontal	46 (75.4)
Temporal	15 (24.59)
Insular	10 (16.39)
Parietal	5 (8.19)
Cingular	13 (21.31)
Occipital	2 (3.28)
Preoperative volume	
<20 mL	18 (29.5)
20–40 mL	12 (19.7)
>40 mL	31 (50.8)
Postoperative volume	
<3 mL	26 (42.6)
≥3 mL	35 (57.4)
Biomolecular profile	
IDH+	51 (83.6)
IDH+ 1p19q-	25 (41)
IDH+ 1p19q+	26 (42.6)
IDH-	10 (16.4)
Sedation	
Hypnosis	26 (42.6)
Standard	35 (57.4)

between the second time surgery of 2 years (IQR: 2.5).

Also, as sequelae, 13 patients (21.3%) presented seizures, 8 patients (13.1%) presented language deficit. We also found altered level of

consciousness in one patient (1.64%), disequilibrium in one patient (1.64%), dysexecutive syndrome in one patient (1.64%), and memory deficit in one patient (1.64%).

### 3.1. Overall survival in all population

The median follow-up time was 48 months (Range: 10–120 months), two patients were lost to follow-up (3.3%); they were in the AAA group.

The OS was respectively 98%, 94 %, and 83% at 2, 5 and 10 years (Fig. 1).

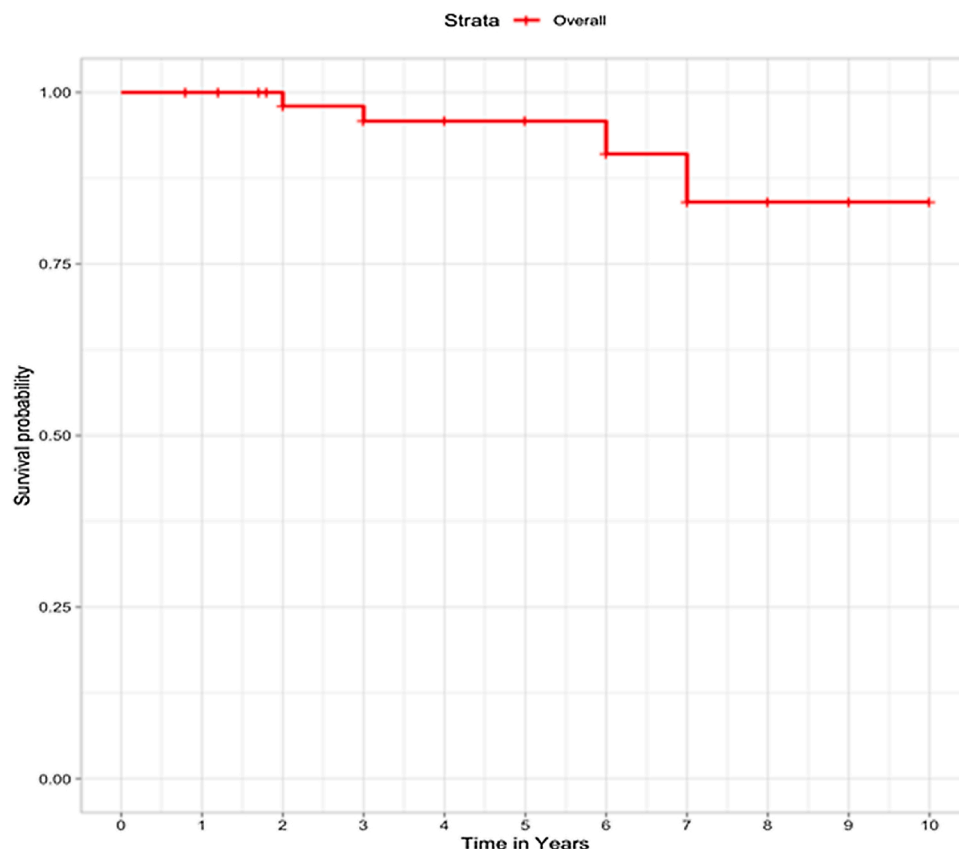
Four patients died of malignancy transformation respectively 2, 3, 6, and 7 years after surgery. All these deceased patients had a preoperative tumor volume >40 ml.

### 3.2. Prognostic factors in all population

The histological grade, 2 or 3 according to the WHO classification, did not influence significantly the OS. The 5 years OS were slightly better in patients with a WHO grade 2 gliomas than patients with a grade 3 (98% vs. 93% cHR = 1.46, 95% CI (0.15–14.18), Log Rank Test = 0.11, p = 0.7) (Fig. 2).

Regarding the molecular impact on the OS, patients with a glioma with IDH mutation and 1p19q codeletion (IDH+1p19q + patients) and, patients with IDH mutation but no 1p19q codeletion (IDH+1p19q- patients) had a longer overall survival than patients with no IDH mutation (IDH- patients), even though the difference was not statistically significant (100% of IDH+1p19q + patients and 94% of IDH+1p19q- patients reached 5 years OS versus 84% of IDH- patients; cHR = 0.66 95% CI = 0.06–7.39, P = 0.9) (Fig. 3).

The OS of patients with preoperative tumor volume <40 mL was significantly longer (100% reached 5 years and 9 years OS,) than patients with tumor volume > 40 ml (82% and 57% reached respectively 5



**Fig. 1.** Overall survival in the entire population.

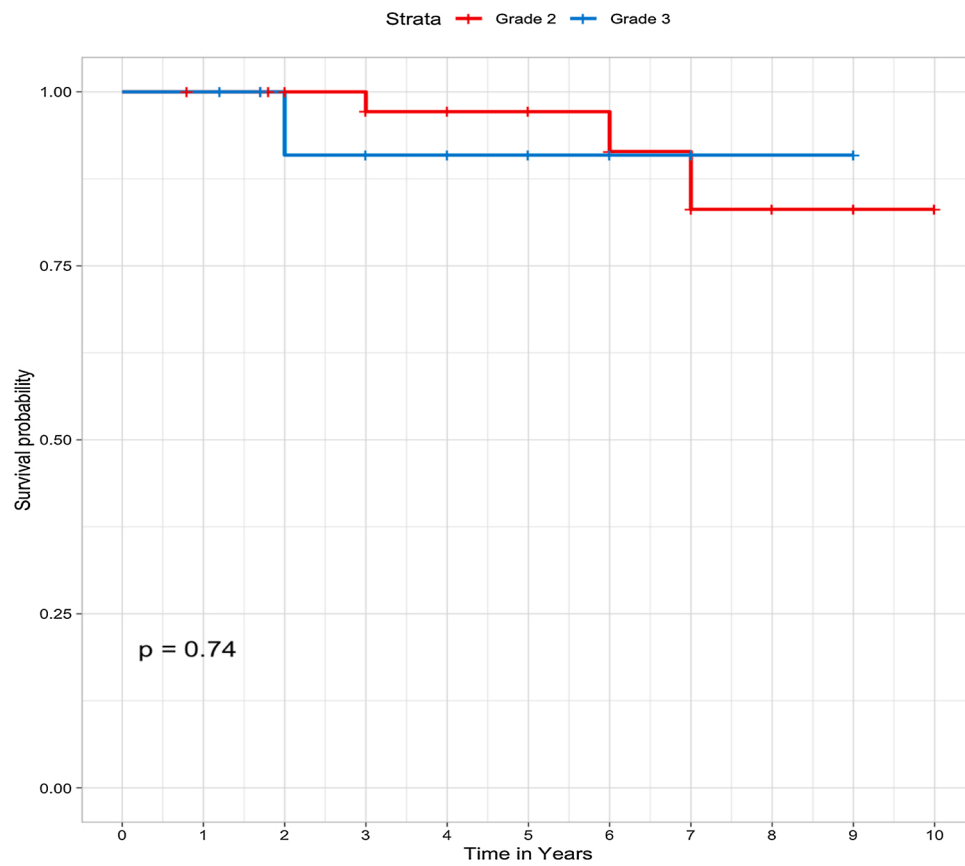


Fig. 2. Kaplan Meier survival curve comparing patients with WHO grade 2 vs. WHO grade 3 gliomas. WHO Grade 3, cHR = 1.46, 95% CI (0.15–14.18), Log Rank Test = 0.11,  $p = 0.7$ .

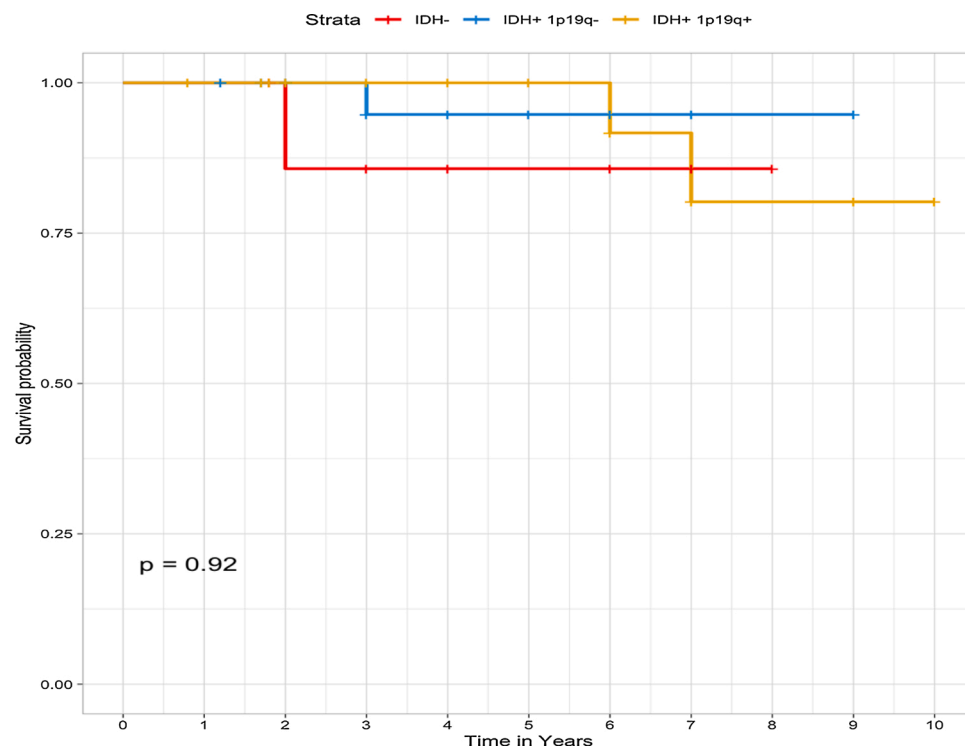


Fig. 3. Kaplan Meier survival curve according to IDH and 1p19q status. Log Rank Test = 0.17,  $p = 0.9$ , IDH+1p19q-, cHR = 0.58, (0.03-9.90),  $p = 0.70$ , IDH+1p19q+, cHR = 0.66, (0.06–7.39),  $p = 0.74$ .

years and 9 years OS,  $P = 0.037$ ) (Fig. 4).

In contrast the residual tumor volume did not influence significantly the OS (5 years and 9 years OS for patients with a residual tumor volume  $<3$  mL were reached respectively in 93% and 82 % while a residual tumor volume  $\geq 3$  mL was associated with a 5 years and 9 years OS in respectively 100% and 87.5%,  $cHR = 2.20, 95\% \text{ CI } (0.22-21.27)$   $P = 0.48$ ) (Fig. 5).

Also, the EOR did not significantly influence the OS rate. 94% and 87.5% of patients with an  $EOR \geq 95\%$  reached respectively 5 years and 9 years versus 100% and 75% of patients with an  $EOR < 95\%$  ( $cHR = 1.19$  95% CI 0.12–11.49;  $P = 0.88$ ) (Fig. 6).

### 3.3. Asleep-awake-asleep versus hypnosis

In Table 2, we present the comparative results between hypnosis and AAA. We found no statistical difference between the two groups. Twenty-six patients (42.6%) were hypnosedated while 35 (57.4%) received standard AAA. The hypnosis-aided surgery cohort had slightly more large tumor volumes  $>40$  ml (26.23% vs. 24.59%,  $OR = 0.27$ , 95% CI = 0.06–0.94;  $p = 0.11$ ) and the residual tumor volume tended to be smaller for the AAA group (14.75% of hypnosis-aided surgery residual tumors were  $<3$  ml vs. 27.87% for standard AAA surgery,  $OR = 0.56$ , 95% CI = 0.19–1.57,  $p = 0.28$ ) (Table 2). Also, patients experienced redo surgery wasn't significantly influenced, by the sedation technic whether hypnosis ( $n = 8, 13.1\%$ ) vs. AAA

( $n = 15, 24.6\%$ ),  $OR = 1.69, 95\% \text{ CI } = 0.59-5.08$ ;  $p = 0,38$  (Table 2).

Regarding the mortality rates, we found no difference between the hypnosis-aided ( $n = 2, 3.39\%$ ) and standard AAA surgery ( $n = 2, 3.39\%$ ),  $OR = 0.77$ , 95% CI 0.09–6.83,  $P = 0.81$ ) (Table 2).

### 3.4. Comparison of overall survival

Patients in the AAA group had similar survivals rate to those in the hypnosis group (97% and 87.5% of patient in the AAA group reached respectively 5- and 9-years OS versus 96% and 79% in the hypnosis group,  $cHR = 0.85$ , 95% CI = 0.12–6.04;  $P = 0.87$ ) (Fig. 7).

Multivariable analysis did not find any significant prognostic factor for OS.

## 4. Discussion

A small number of neuro-oncology centers practice hypnosedation due to the scarcity of the anesthetic skills and experience needed to perform hypnotherapy safely. We did not find evidence of a significant difference regarding residual tumor, EOR, as well OS between AAA and hypnosis. Concerning the whole cohort, regardless of the anesthetic method, patients with preoperative tumor volumes  $<40$  mL had significantly better 5-, and 9-years OS ( $P = 0.037$ ). IDH+1p19q+ and, IDH+1p19q- patients also had, as already demonstrated in the literature, a longer OS than IDH- tumor patients.

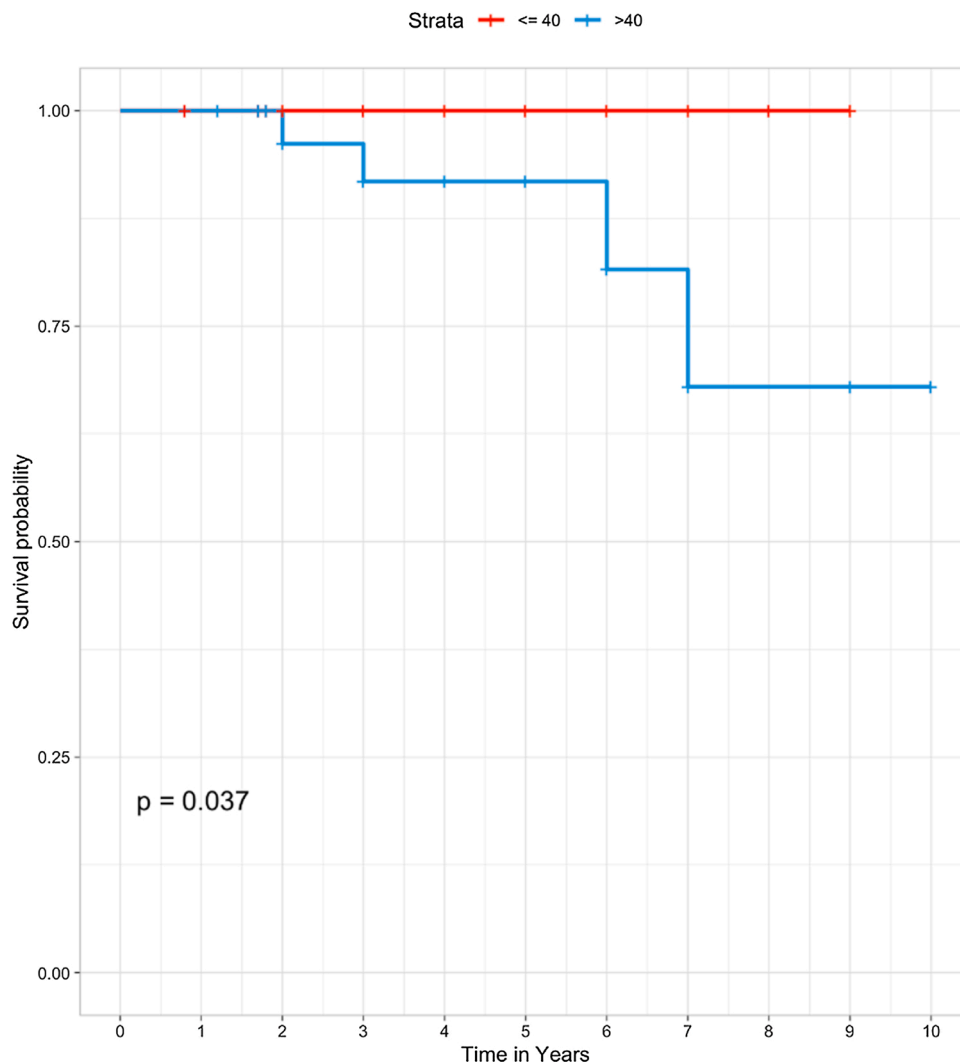


Fig. 4. Kaplan Meier survival curve according to preoperative tumor volume. Log Rank Test = 4.34 on 1 df,  $p = 0.04$ .

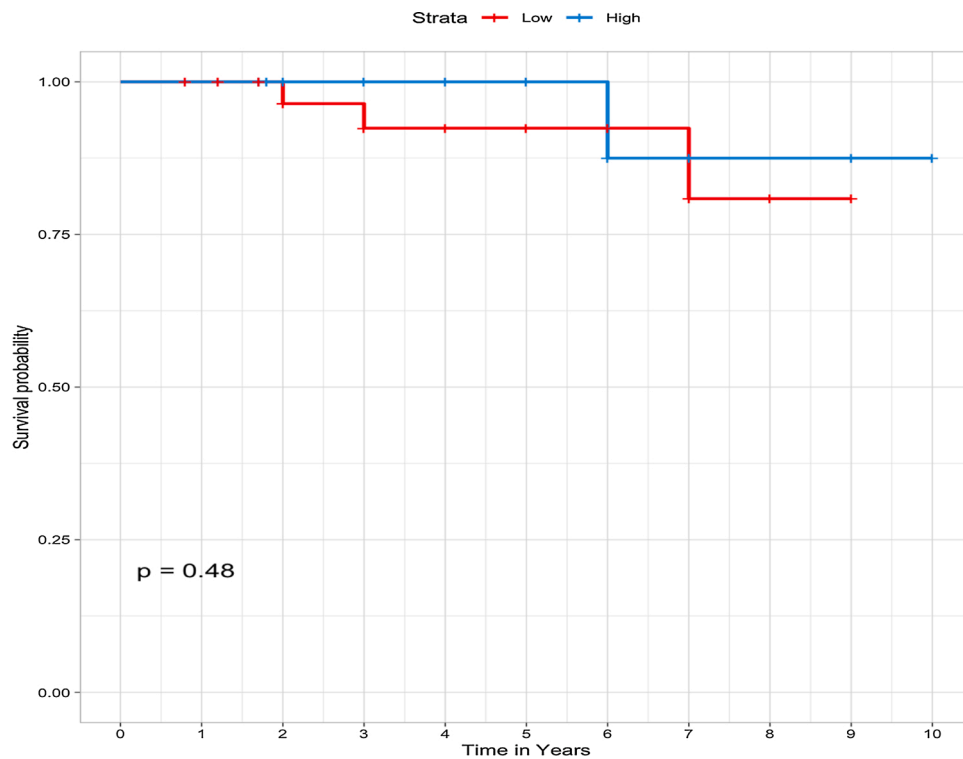


Fig. 5. Kaplan Meier survival curve disaggregated by Residual Volume postoperative. Low are define as < 3 mL and High as ≥3 mL High residual volume, cHR = 2.20, 95 % CI (0.22–21.27) P = 0.48.

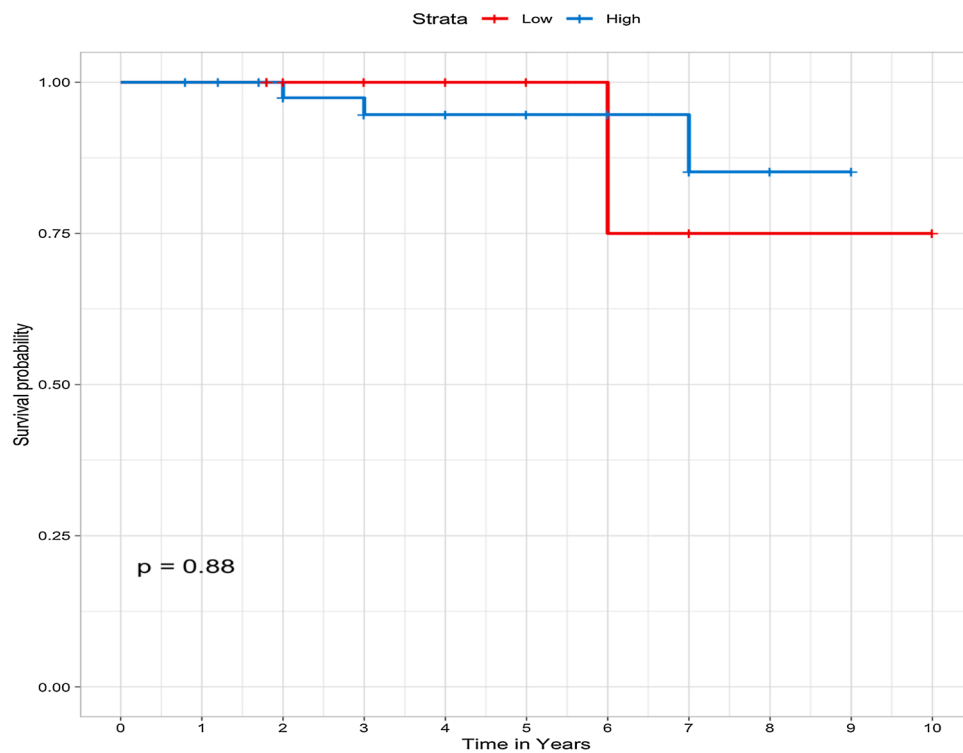


Fig. 6. Kaplan Meier survival curve according to the extent of resection (EOR). High is defined as EOR ≥ 95% and low as EOR < 95%. Log Rank Test = 0.2, p = 0.9, cHR = 1.19 (0.12, 11.49).

4.1. Asleep-awake-asleep (AAA) versus hypnosis

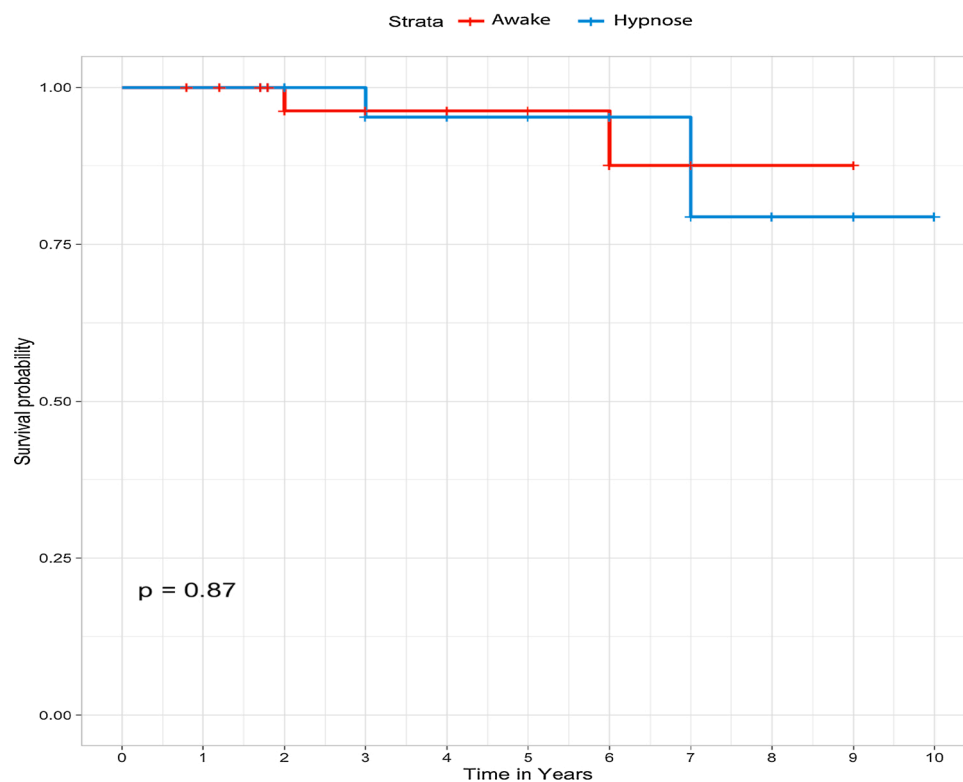
A lot of previous studies on LGG reported that awake surgery offers the best compromise between EOR and neurological cognitive

preservation, i.e., the best onco-functional balance between impact on survival prognosis and quality-of-life [7–10]. Recent studies explored alternative techniques to the classical AAA for awake craniotomy, as the AAA technique might sometimes be challenging for anesthesiologists.

**Table 2**  
Outcome comparison between hypnosis-aided and standard asleep-awake-asleep surgery for low-grade gliomas.

Variable	Hypnosis	Awake	OR	95% CI		p	Chi-square (p-value)
				Upper	Lower		
<b>Sex</b>							
Female	15 (24.59)	16 (26.23)	Reference				0,51
Male	11 (18.03)	19 (31.15)	1,62	0,59	4,59	0,35	
<b>Sequella</b>							
No	11 (18.03)	14 (22.95)	Reference				1,00
Yes	15 (24.59)	21 (34.43)	1,10	0,39	3,10	0,85	
<b>Status</b>							
Alive	24 (40.68)	31 (52.54)	Reference				1,00
Dead	2 (3.3)	2 (3.3)	0,77	0,09	6,83	0,81	
<b>Extent of Resection</b>							
≥95%	7 (11.48)	5 (8.20)	Reference				0,37
<95%	19 (31.15)	30 (49.18)	2,21	0,62	8,44	0,34	
<b>Molecular biology</b>							
IDH–	2 (3.28)	8 (13.11)	Reference				0,22
IDH+ 1p19q–	13 (21.31)	12 (19.67)	0,23	0,03	1,15	0,09	
IDH+ 1p19q+	11 (18.03)	15 (24.59)	0,34	0,05	1,70	0,22	
<b>WHO grade</b>							
Grade 2	22 (36.06)	26 (42.62)	Reference				0,77
Grade 3	4 (6.56)	9 (14.75)	1,45	0,43	5,35	0,55	
<b>Tumor volume</b>							
<20 mL	4 (6.56)	14 (22.95)	Reference				0,11
20–40 mL	6 (9.84)	6 (9.84)	0,29	0,05	1,35	0,12	
>40 ml	16 (26.23)	15 (24.59)	0,27	0,06	0,94	0,04	
<b>Residual volume</b>							
<3 mL	9 (14.75)	17 (27.87)	Reference				0,4
≥3 mL	17 (27.87)	18 (29.51)	0,56	0,19	1,57	0,28	
<b>Redo surgery</b>							
No	18 (29.51)	20 (32.79)	Reference				0,49
Yes	8 (13.11)	15 (24.59)	1,69	0,59	5,08	0,38	

P, OR P-value; OR, odds ratio.



**Fig. 7.** Kaplan Meier survival curve comparing the standard asleep-awake-asleep sedation cohort with the hypnosis cohort. Awake, cHR = 0.85, (0.12–6.04) Log Rank Test = 0.03, p = 0.9.



Our team proposed a method based on hypnosis and sedation without orotracheal intubation or laryngeal mask and showed that hypnosis was an effective and safe method for awake craniotomy [6]. Nonetheless, in this preliminary work, we did not assess the possible impact of hypnosis on oncological results.

Although we found in our series that the standard AAA surgery group had slightly better survival rate with those in the hypnosis cohort (97% and 87.5% of patient in the AAA surgery group reach respectively 5 years and 9 years OS versus 96% and 79% in hypnosis cohort,  $cHR = 0.85$ , 95% CI = 0.12–6.04;  $P = 0.87$ ), we did not find any statistical difference. On the other side, we noticed that the hypnosis-aided surgery cohort had slightly more patients with high tumor volumes >40 mL (26.23% vs. 24.59%, OR = 0.27, 95% CI = 0.06–0.94;  $P = 0.11$ ). Yet, it has already been demonstrated that preoperative larger tumor size is a negative prognostic factor of LGG [11]. Thus, we believe that the slight difference in OS obtained between AAA and hypnosis might be related to the preoperative volume rather than a direct negative impact of hypnosis on the oncological outcome. Furthermore, this data highlights that hypnosis is an effective anesthetic method, whatever the pre-operative volume.

Regarding the residual tumor volume, one should have the same consideration about the possible impact of preoperative tumor volume. Indeed, even though only 14.75% of hypnosis cases had a residual <3 mL, vs. 27.87% of AAA cases (OR = 0.56, 95% CI = 0.19–1.57,  $P = 0.28$ ), we believe these results have a direct connection to the higher preoperative tumor volume in the hypnosis group.

The only other study about hypnosis for awake craniotomy [6] had demonstrated the reliability of hypnosis as an original alternative method for performing a craniotomy. The authors reported that hypnosis does not suffer from the management of airways or the potentially long waking period, so that allows going ahead with the two limitations of the AAA method, and suggesting that hypnosis could be an interesting alternative option for awake surgery of older populations [6]. We believe that our results do not contradict these considerations, but should nevertheless lead to consider carefully hypnosis as a non-fully validated method that should be used preferentially in research protocols.

#### 4.2. Tumor volume

In a previous study, Duffau reported that when no signal abnormality was visible on control MRI (complete resection), patients had a significantly longer OS compared with patients having any residual abnormality [7]. It has also been demonstrated that tumor resection is associated with a better outcome than a biopsy [12].

In our study, we identified preoperative and postoperative tumors (6 months after surgery) on MRI 3D-T2 FLAIR sequence. We then calculated the preoperative and postoperative tumor volumes and the EOR using semi-automated segmentation. Then we stratified this data between the high EOR  $\geq 95\%$  and lower EOR < 95%. In another series of 190 DLGGs, Ius et al. showed that patients with an EOR  $\geq 90\%$  had an estimated 5-year OS of 93%, those with EOR between 70% and 89% had a 5-year OS of 84%, and those with EOR < 70% had a 5-year OS of 41% ( $p < 0.001$ ) [8]. In our series, 94% and 87.5% of patients with an EOR  $\geq 95\%$  reached respectively 5 years and 9 years versus 100% and 75% in patients with an EOR < 95%,  $cHR = 1.19$  95% CI 0.12–11.49;  $P = 0.88$ . Although we did not obtain a statistical difference, we can observe a clear tendency toward a better long-term OS for EOR  $\geq 95\%$ . We believe that it is the size of our sample that was not large enough to obtain a statistically significant P value. Multiple similar data have already been reported, demonstrating also the impact of preoperative tumor volume and of EOR on survival in LGG [9,10]. Our results confirm these already well-known prognostic factors, whatever the surgical method used for resection.

#### 4.3. Molecular profile

Mair et al. [13], reported in 2020 in a review that the prognosis of anaplastic astrocytoma patients without IDH mutation was significantly worse (median OS 19.4–20 months) compared to anaplastic astrocytoma with IDH mutation (median OS 65–81.1 months) [14,15]. In our series, 100% of the IDH+1p19q+ patients and 94% of IDH+1p19q- patients reached 5 years OS versus 84% in IDH- patients. Our findings are consistent with previous studies considering molecular prognostic factors of gliomas.

#### 4.4. Limitations

The main goal of our study was to assess the impact of hypnosis on oncological results of surgical resection of LGG. To better interpret our results, we collected the maximum amount of clinical, radiological, and molecular data, to try and limit the inherent methodological biases of this retrospective study.

The main limitations we identified are the retrospective collection of data and the small sample of patients in each group as only 35 AAA vs. 26 Hypnosis cases were studied. As a consequence, we can only, in this study, indirectly propose that hypnosis is valuable as an alternative technique to the standard AAA, because it offers the patient the same chance to obtain a good tumor resection, with preservation of cognitive function. But hypnosis was not superior, in any point, to AAA. In our opinion, it should be considered as an interesting alternative that anesthesiologists could propose if they face a theoretical contra-indication to AAA.

Nonetheless, one should consider that a strength of our study is, despite the small size of the sample, that all the patients have been treated by the same neurosurgical and neuro-oncological team, whatever the anesthetic method chosen (hypnosis or AAA), which may have limited the heterogeneity of the groups and the impact of surgical technique or oncological treatments, such as chemotherapy or radiotherapy, on OS.

Besides, as already mentioned, patients that were proposed hypnosedation do not differ from other patients, neither in any demographical characteristics, nor in terms of location, volume or type of tumor; the only limitations for not choosing hypnosedation were either the availability of the anesthesiologist who practiced hypnosis, either the non hypnotizability of the patient, or the patient's wish not to undergo hypnosis. This means that all the patients that were operated on using AAA had the same characteristics than those of the hypnosis group, except a psychological and/or cultural perception of hypnosis.

Finally, we did not find any other study in the literature about hypnosis for LGG to compare our results. This hypnosis method is indeed not yet widespread due to the low probability to have the opportunity to work in an institution with neuro-anesthesiologists both involved in awake surgery and in hypnosis.

#### 5. Conclusion

This study did not demonstrate the superiority of one method over the other. We encourage neurosurgical teams to use hypnosis for awake surgery under research protocols to obtain robust data that may help anesthesiologists to propose hypnosis in adequate situations, such as in patients with comorbidities that could contraindicate the classical AAA procedure. Hypnosedation is a suitable alternative to standard sedation in awake craniotomy for LGGs; however, it does not improve the quality of the surgical procedure, nor leads to a greater resection or longer OS. Tumor volumes, EOR, and molecular profile remain the best determinants of OS in diffuse gliomas.

#### Author contributions

All authors attest that they meet the current International Committee



of Medical Journal Editors (ICMJE) criteria for Authorship.

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### Conflicts of interest

The authors have no conflicting interest in this case report and any financial resources.

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