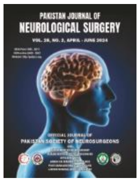

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Original Research

Awake Craniotomy Versus Surgery Under General Anaesthesia for Resection of Brain Tumour; A Systematic Review of Randomized Control Trials

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ABSTRACT

Objectives: To evaluate the clinical evidence on the comparison of results between an awake craniotomy and general anesthesia surgery for brain tumor removal.

Materials & Methods: A systematic literature search was carried out using the PubMed, Cochrane Library, EMBASE, and MEDLINE databases using key terms such as awake craniotomy, awake brain surgery, awake craniotomy, anesthesia craniotomy, asleep craniotomy, asleep brain surgery, and general anesthesia. The PICO (Participant, Intervention, Comparison, and Outcome) approach was used to extract the studies contrasting the impact of awake craniotomy versus general anesthesia on outcomes included in this systematic review. PRISMA guidelines were followed throughout.

Results: 102 records were identified out of which 8 were included in the final qualitative synthesis (2 RCTs, Cohort). All reported neurological impairments in both groups, except 2. Six studies indicated early language abnormalities and early motor deficiencies. Six studies indicated early language abnormalities and early motor deficiencies. The mean operation time of the General Anesthesia group was more than that of Awake Craniotomy. Awake craniotomy surgery was associated with an average reduction of 4 to 8 days in the hospital.

Conclusion: Under GA, AC (add abbreviations of these) offers a workable substitute for craniotomy for individuals with gliomas penetrating expressive areas; awake craniotomy with electrical stimulation is linked to improved long-term neurological and language abilities as well as a shorter hospital stay.

Keywords: Anaesthesia Management**.** Awake Craniotomy, General Anesthesia, Neurological function, Surgical Management, Tumor resection.

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INTRODUCTION

Among neurological problems among general populations, a wide number of participants are presented with brain metastatic cancer. The frequency of brain metastatic cancer lies from 10% to 30% among systematic cancers.[1] As the outcomes from these cancers improved with different surgical and pharmaceutical advancements, the mortalities and incidence increased too.[2] In the past, brain metastatic cancer patients had poor prognoses and were considered irreparable neurological problems which later led to death.[3] However, advancements in surgical procedures and aggressive treatment regimes resulted in better outcomes by increasing survival chances and overcoming symptoms.[4]

The surgical management of brain tumors has undergone significant advancements over the years, with Awake Craniotomy (AC) and Surgery under General Anesthesia (GA) emerging as two distinct approaches for the resection of brain tumors. The selection of the most appropriate surgical technique depends on several factors, including tumor location, patient characteristics, and surgical goals. Performing surgery while doing real-time neurological assessment and the patient is awake craniotomy while if the patient is in controlled unconsciousness during the surgery is surgery under general anesthesia.[5] During awake surgery, the neurological functions are preserved and also facilitate accurate tumor removal thus gaining popularity among neurosurgeons. This approach allows intraoperative mapping of eloquent brain regions, together with those liable for language and motor features, which can be particularly vital while managing tumors in near proximity to these regions. According to study results by Sacko et al. (2011), Awake Craniotomy turned into associated with notably better outcomes in phrases of the volume of resection and preservation of neurological function compared to Surgery under General Anesthesia.[6]

Contrarily, surgical procedure executed beneath standard anesthesia has the benefit of decreasing the affected person's soreness and anxiety in the course of the surgical process. Additionally, it allows the surgical group to work without being restrained by way of the patient's mobility, which can be difficult at some point during an awake craniotomy. Additionally, a regulated environment for airway protection and anesthesia management is provided by this technology. According to retrospective research by Lu et al, (2018), general anesthesia surgery was associated with faster operating times and fewer intraoperative complications than awake craniotomies. The unique clinical situation and patient characteristics must be carefully considered while choosing between these two strategies [2]. Zhou et al. (2020) did a retrospective research that revealed that preoperative neurological state, patient age, and tumor location were major factors affecting the decision between surgery under general anesthesia and awake craniotomy.[7]

This article will evaluate and compare the material on awake craniotomy vs general anesthesia surgery for the removal of brain tumors. By analyzing the benefits and drawbacks of each strategy, we want to provide doctors with a comprehensive overview that will enable them to make an educated choice when selecting the optimal surgical method based on the particular patient characteristics and desired surgical outcomes. The objective was to assess the clinical data comparing the outcomes of awake craniotomy versus general anesthesia surgery for the excision of brain tumors.

MATERIALS & METHODS

Data Sources and Searches

A comprehensive literature search was conducted using the PubMed, Cochrane Library, EMBASE, and MEDLINE databases, using the terms awake craniotomy, awake brain surgery, awake craniectomy, anesthesia craniectomy, asleep craniotomy, asleep brain surgery, and general anesthesia. We looked through previous RCTs and reviews cited for any potentially relevant papers that the database search had missed.

Study Selection

All Randomised Control Trials (RCTs) examining the efficacy of awake craniotomy and craniotomy under general anesthesia that were published in the English language satisfied the inclusion criteria for this systematic review. There were no restrictions on the subjects' ethnicity or the date of publication. Studies contrasting the impact of awake craniotomy versus general anesthesia on outcomes were included in this systematic review. The PICO (Participant, Intervention, Comparison, and Outcome) approach was used in these investigations. Studies comparing the effects of awake craniotomy vs surgery under anesthesia on outcomes in patients between the ages of 30 and 60 were included in this analysis using the PICO (Participant, Intervention, Comparison, and Outcome) framework. August 2023 was the earliest date taken into account. The list of unpublished articles omitted editorials, short communications, conference papers, reviews and meta-analyses, case reports, animal or in vitro studies, and comparisons with medical treatment.

Data Extraction

Our investigation was conducted using the PRISMA standards for reporting systematic reviews. Two reviewers independently extracted the data using a standardized extraction form. Less than 5% of the retrieved data were in disagreement between the two reviewers. When a consensus couldn't be achieved, a third reviewer was used instead. The data that was extracted included information on the patient population, procedure type, duration, length of hospital stay, baseline variables (age, sex), study design elements (type of surgery, number of patients per treatment), and outcome information (neurological deficits, surgery operation time, and length of hospital stay).

RESULTS

102 papers were discovered after a preliminary search using MEDLINE, EMBASE, CINAHIL, PubMed, and Google Scholar. As a result, 62 articles were screened; after duplicates were removed, 45 articles were left. After titles and abstracts were reviewed, 39 papers were disqualified because they didn't fit the criteria. After being determined to be eligible, 8 full-text publications were added to the qualitative synthesis. The research selection is depicted in Figure 1.

Characteristics of Studies

Six cohort studies and two RCTs were among the studies that were included. Table 1 provides a full description of the features of the included research. In four research, the awake craniotomy group had higher gliomas encroaching on or around eloquent regions, while seven studies found no difference in tumor locations between awake craniotomy and general anesthesia.

Neurological Deficits

With the exception of two investigations, all reported neurological impairments in both groups. Five studies each reported the rates of early and late neurological deficits. Six studies indicated early language abnormalities and early motor deficiencies. Five studies revealed average operation times and average hospital stays. The

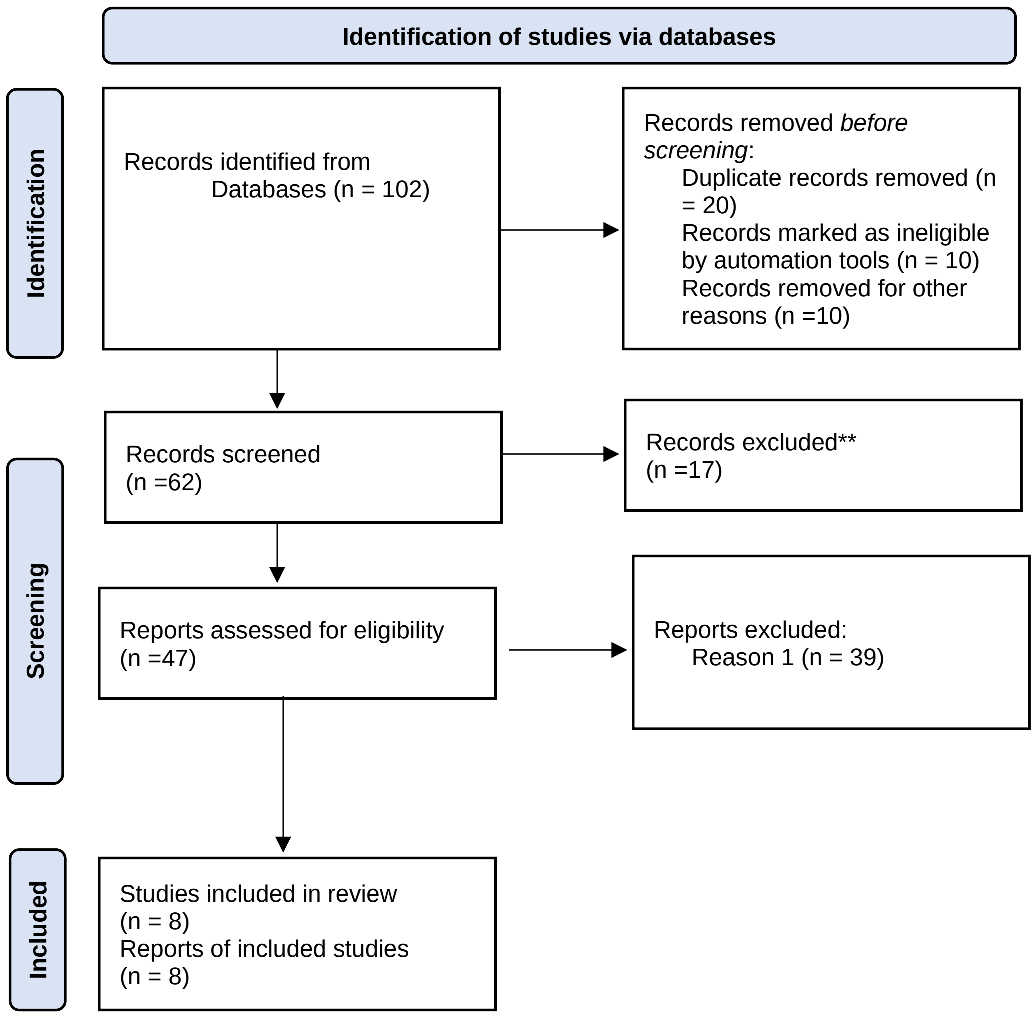

Figure 1: PRISMA flow chart.

Table 1: Summary of the baseline characteristics of 6 studies

Study Authors, References	Publication Year	Total Sample Size	Gender F/M		Allocation		Mean Age in Years		Tumor type	Study type
			AC	GA	AC	GA	AC	GA		
Gupta et al.[8]	2007	53	6/20	7/20	26	27	42.7	41.3	LGG metastases cavernoma	RCT
Sacko et al.[6]	2011	575	100/114	170/191	214	361	46.5	46	supratentorial mass lesions	Prospective study
Manninen et al.[9]	2002	107	23/27	32/25	50	57	53	58	supratentorial tumors	Prospective study
Chikezie et al.[10]	2017	58	8/19	12/19	27	31	49.1	50.3	Perirolandic Gliomas	RCT
Peraud et al.[11]	2004	14	5/6	1/2	11	3	31.1	33	Astrocytoma (WHO grade II)	Retrospective cohort
Tuominen et al.[12]	2013	40	9/11	9/11	20	20	44	43	Glioma	Retrospective cohort

Martino et al.[13]	2013	22	6/5	5/6	11	11	40.8	35.4	low-grade glioma	Retrospective cohort
Duffau et al.[14]	2005	222	44/56	67/55	100	122	38	36	low-grade gliomas	Retrospective cohort

RCT; randomize control trial, LGG; low grade glioma, AC; awake craniotomy, GA; general anesthesia

Table 2: Operative Characteristics Reported in Included Randomized Controlled Trials.

Study, Publication Year	Speech Deficit		Motor Deficit		Operation duration (min)		Quality of Tumor Removal %		Length of Hospitalization in days	
	AC	GA	AC	GA	AC	GA	AC	GA	AC	GA
Gupta et al.	18.7%	11.7%	NM	NM	196	182	10%	12%	6	<4
Sacko et al.	25%	22%	13%	24%	135	132	37%	52%	5	8
Manninen et al.	NM	NM	NM	NM	197	270	NM	NM	4	12
Chikezie et al	22.2%	22.6%	51.9%	61.3%	NM	NM	86.3%	79.6%	4	8
Peraud et al.	18.2%	33.3%	54.5%	100%	NM	NM	36.4%	100%	NM	NM
Tuominen et al.	15%	25%	10%	30%	285	195	50%	55%	NM	NM
Martino et al.	54.5%	45.5%	27.3%	36.4%	387	239	45%	0%	10	12
Duffau et al.	1.7%	9%	5.2%	8%	300	180	21.6%	6%	NM	NM

AC; awake craniotomy, GA; general anesthesia, NM; not mentioned

key findings of the eight included research are presented in Table 2.

Mean Operation Time

The mean operation time was reported in all studies except two studies.[4,11] The mean operation time was less in the patients with generalized anesthesia craniotomy surgery as compared to those who received awake craniotomy surgery.

Length of Hospital Stay

Out of 8 RCTs, three studies did not mention the length of hospital stay,[11-14] while the mean length of hospital stay ranged from 4 to 10 days in the awake craniotomy group and from 4 to 12 days in the general anesthesia group, according to other research, with awake craniotomy surgery being associated with an average reduction of 4 to 8 days in the hospital.

DISCUSSION

According to our findings, general anesthesia and awake craniotomy have the same postoperative linguistic and neurological impairment rates. Our research looked at whether awake craniotomy is better for patients' postoperative neurological functions than conventional general anesthesia. Even though awake craniotomy and direct electrical stimulation have a long history, the majority of earlier investigations were observational case series without a control group. The reported postoperative neurological impairments varied substantially throughout these trials. Serletis et al,[15] performed awake brain mapping on 511 patients, of which 78 instances (15.3%) experienced worsening neurological postoperative symptoms. In 29 cases (5.6%), this was a permanent occurrence. According to Berger et al,[16] the early neurological impairment occurred in 58 cases (9%) and the late neurological deficit occurred in 16 cases (3%), according to a retrospective assessment of 611 patients who underwent awake brain mapping.

We included two RCTs in this review. A potential bias is inevitable given the nature of awake craniotomy, which makes it impossible to blind the patient and the physician. For objective comparison to be possible, randomization is essential. Random allocation created by a computer was employed in the included RCT. Blinding might be implemented throughout the randomization procedure and postoperative follow-up examinations, albeit it was not done in this investigation. Participant selection bias was yet another potential prejudice. The majority of the studies we reviewed focused on gliomas, but a few also explored other disorders. Previous findings have consistently pointed to a positive connection between prognosis and the effectiveness of tumor resection.[14] The intriguing aspect of brain plasticity comes into play, allowing for the reorganization of the brain's functions in certain individuals with low-grade gliomas, and in some cases, even in those with high-grade gliomas. This phenomenon provides a window of opportunity for performing surgery on these patients months or even years after the initial procedure, potentially leading to complete tumor removal. This is particularly evident in cortical areas that aren't considered "primary" functional structures, where such reorganization is more feasible. While primary sensorimotor cortices exhibit less plasticity compared to secondary cortices, the potential for reorganization still exists. However, it's important to note that in our observations, we did not observe this kind of reorganization.

Previous research has indicated that there is a considerable range in the occurrence of neurological deficits following awake surgery, spanning from 4% to 23%. The differences in these percentages across various studies may, in part, be attributed to the duration of the follow-up period. In a study conducted by Bernstein et al., they identified new postoperative neurological impairments in 13% of patients, with persistent deficits observed in 4.5% of cases. Interestingly, their investigation revealed that patients undergoing surgery under local anesthesia (AC) had a lower incidence of long-term impairments, with only 6.5% experiencing such effects, as opposed to 17% of patients who underwent surgery under general anesthesia (GA).[15] However, in comparison to general anesthesia (GA), Gupta et al observed a higher incidence of postoperative neurological issues with awake craniotomy (AC). While only 11% of the GA group experienced new neurological abnormalities, the AC group showed a higher rate at 19%. In our recent study, the GA group exhibited a 16% occurrence of irreversible neurological impairments, whereas the AC group had a lower rate of 4.6%. It's worth noting that in our investigation, 11.4% of conscious patients (4 out of 35) did not exhibit postoperative impairment, but this did not consistently align with the absence of a response to electrical brain stimulation in expressive areas [8]. Nevertheless, we found that the lack of postoperative dysfunction doesn't necessarily mean there won't be a response to electrical brain stimulation in expressive areas. In our study, 11.4% of awake patients (4 out of 35) experienced temporary neurological deficits after surgery, even though stimulation results were negative. This contrasts with Bernstein et al.'s study, where 13.6% faced similar issues. The occurrence of temporary neurological deficits post-surgery, despite negative stimulation outcomes, underscores the complexity and nuances in predicting patient outcomes in this context.[17]

CONCLUSION

With AC as opposed to surgery under GA, patients with supratentorial lesions close to the eloquent cortex had improved neurological outcomes and achieved maximum tumor excision. Under GA, AC offers a workable substitute for craniotomy. For individuals with gliomas penetrating expressive areas, awake craniotomy with electrical stimulation is linked to improved long-term neurological and language abilities as well as a shorter hospital stay. Our review could offer the best level of proof to date to justify the use of awake language mapping, considering the potential ethical concerns in RCTs for awake craniotomy and general anesthesia.

Limitations

The absence of an appraisal of additional notable results is the main restriction. No studies examined changes in co-morbidities in detail. Neither study clarifies the methodology used to assess comorbidities. No inferences can be drawn about the duodenal switch method. The studies' extreme methodological heterogeneity made it impossible to perform a meta-analysis, which would have increased statistical power. None of the trials employed an expertise-based randomization methodology, which would have improved the outcomes of procedures that are not routinely performed in each center.

RECOMMENDATIONS

To provide reliable data on the comparison between awake craniotomy and general anesthesia for brain tumor removal, future research should focus on conducting more extensive randomized control studies. These studies should investigate reported neurological deficits, standardize awake craniotomy procedures, explore variations in results for specific patient subpopulations, examine long-term functional outcomes, conduct cost-benefit assessments, and explore patient preferences. With these initiatives in place, we can gain a better understanding of the subject matter and develop more personalized treatment plans.

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Additional Information

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Disclosures: The authors report no conflict of interest.

Ethical Review Board Approval: Ethical approval was not required for this systematic review as it did not involve primary data collection from human subjects. The review was conducted in accordance with PRISMA guidelines for systematic reviews and meta-analyses.

Human Subjects: This research did not involve direct interaction with human subjects as it is a systematic review of previously published studies.

Conflicts of Interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: All authors declare no conflicts of interest related to this work.

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Other Relationships: All authors declare that there are no other relationships or activities that could appear to have influenced the submitted work.

AUTHORS CONTRIBUTION

Sr.#	Author's Full Name	Intellectual Contribution to Paper in Terms of:
1.	Mahboob Khan	1. Study design and methodology.
2.	Abdul Hameed Khan	2. Paper writing.
3.	Farooq Sherzada	3. Data collection and calculations
4.	Abdul Basit Khan	4. Analysis of data and interpretation of results.
5.	Laila Ghaffar	5. Literature review and referencing.
6.	Nayab Orakzaki	6. Editing and quality insurer.