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Review Article

Risk factors and predictors of intraoperative seizures during awake craniotomy: A systematic review and meta-analysis

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ABSTRACT

Background: Awake craniotomy (AC) aims to minimize postoperative neurological complications while allowing maximum safe resection. Intraoperative seizures (IOSs) have been a reported complication during AC; however, literature delving into the predictors of IOS remains limited. Therefore, we planned a systematic review and meta-analysis of existing literature to explore predictors of IOS during AC.

Methods: From the inception until June 1, 2022, systematic searches of PubMed, Scopus, the Cochrane Library, CINAHL, and Cochrane's Central Register of Controlled Trials were conducted to look for published studies reporting IOS predictors during AC.

Results: We found 83 different studies in total; included were six studies with a total of 1815 patients, and 8.4% of them experienced IOSs. The mean age of included patients was 45.3 years, and 38% of the sample was female. Glioma was the most common diagnosis among the patients. A pooled random effect odds ratio (OR) of frontal lobe lesions was 2.42 (95% confidence intervals [CI]: 1.10–5.33, $P = 0.03$). Those with a pre-existing history of seizures had an OR of 1.80 (95% CI: 1.13–2.87, $P = 0.01$), and patients on antiepileptic drugs (AEDs) had a pooled OR of 2.47 (95% CI: 1.59–3.85, $P < 0.001$).

Conclusion: Patients with lesions of the frontal lobe, a prior history of seizures, and patients on AEDs are at higher risk of IOSs. These factors should be taken into consideration during the patient's preparation for an AC to avoid an intractable seizure and consequently a failed AC.

Keywords: Awake craniotomy, Intraoperative seizures, Meta-analysis, Systematic review

INTRODUCTION

The role of awake craniotomy (AC) in neurosurgery has gained much traction over the years due to a large body of evidence demonstrating its safety and efficacy in improving surgical outcomes for patients with a wide variety of pathologies, such as intra and extra-axial tumors, epilepsy, and even vascular neurosurgery.[13]

Historically, it has been practiced for millennia, as the treatment for epilepsy, as trepanation.[15] Bartholow published his first experience with electrical stimulation of the cortex in a human subject in 1874. Later scholars then worked towards mapping the cortex and eliciting specific motor responses to electrical stimulation of the corresponding cortical areas with the patient conscious and aware of their environment, eloquent areas of the cerebral hemispheres are stimulated to allow the surgeon to plan margins for resection with a reduced risk of compromising neurological function.[3,14] Certain neurological functions, such as speech, vision, cognition, or sound perception, are indispensable, and with constant feedback and reassurance during an AC, the surgery team is better aided in preserving essential sensory and motor function. Hence, the technique has allowed complex procedures on cortical areas that may have previously been deemed inoperable or would have resulted in a limited extent of resection.[14]

The anesthetist's approach varies depending on patient factors, and particular characteristics of the surgery such as type and length. Some ACs may be performed without sedating the patient in the "awake-awake-awake" method. A "conscious sedation" technique with monitored anesthesia care keeps the patient moderately sedated, to an extent where spontaneous breathing is maintained, reducing the incidence of effects such as hypotension, respiratory depression, and apnea. The anesthesia is then weaned off before cortical mapping and resumed before continuing with closure. On the other hand, a "sleep-awake sleep" technique uses an awake period of cortical mapping between two periods of complete sedation under general anesthesia (GA).[33] Orienting the patient to time, person, and place is important to get their cooperation during electrophysiologic cortical mapping. The patient must also be taught how they are expected to interact during the procedure.

Once the consciousness has been assessed by a designated member of the anesthesia team, cortical mapping begins with a reevaluation of higher mental function, specific to the marked brain area. The process of cortical mapping may extend over 3 hours and can be exhausting for the patient and care providers alike.[6] A cortical area is considered "eloquent" when neurostimulation leads to a motor twitch or loss of function, including a speech impediment.[16] There have been many efforts to improve patient satisfaction, particularly intraoperatively, to improve surgical outcomes.[29]

The benefits of the AC technique in tumor resection have been greatly discussed, with AC surgeries having shorter hospital stays (4 days vs. 9 days), and less frequent postoperative deficits (7% vs. 23%) in matched procedures done under GA.[5] However, it is important to understand that this procedure may not always be the best course of action. Besides patient and surgeon reluctance, other patient specific conditions may also be contraindications to the surgery. Upper airway obstructions, cognitive disorders, anxiety and agitation, the inability to remain still for long periods, or a history of seizures can all be relative contraindications. The location of the tumor and dural involvement may also require a craniotomy under GA.[41]

There are a few notable perioperative complications associated with an AC. Postoperative effects such as new motor and language defects may be found in the early postoperative period.[17] However, another study shows that after glioma resection, the number of patients with new persistent deficits drops from 14.0% immediately postoperatively to 1.6% at 6 months.[32] Intraoperative side effects include hypertension, hypotension, respiratory depression and desaturation, shivering, and brain swelling.[1,34] Exacerbation of existing asthma has also been observed in some patients.[1] The patient may also develop seizures, both intraoperatively and postoperatively.

Intraoperative seizures (IOSs) remain of particular interest as they can result in AC failure and significant morbidity. They may affect the ability to carry out further cortical mapping and monitoring of the patient. In cases where seizures do not resolve or convert to status epilepticus, emergency conversion to craniotomy under GA may be required.[24] Most patients experience focal motor or language seizures, while some may experience secondary generalized seizures.

The objective of our study is to explore factors associated with the development of IOS during awake craniotomies.

MATERIALS AND METHODS

The preferred reporting items for systematic reviews and meta-analyses (PRISMA) standards were used as a guideline for conducting this study.[20,21] The patient population, intervention, control, and outcome criteria were applied to create a focused question. This study was carried out successfully and adequately using the PRISMA checklist.[21] The study protocol was registered on PROSPERO (CRD42022362079), the registry for systematic reviews.

Search strategy

From the inception until June 1, 2022, we conducted a search of published literature using PubMed, Scopus, CINAHL, the Cochrane library, to identify studies reporting the risk factors of IOS during AC. The Medical Subject Headings database was used to search for relevant phrases, and the following free text terms were ultimately chosen as keywords: "Risk factors" OR "predictors" and "Intraoperative" and "Seizures" OR "Epilepsy" and "Awake Craniotomy." Furthermore, a search for gray literature was also performed. The search was restricted to the English language; the publishing date;

however, was not constrained. Pediatric focused literature and animal studies were filtered out. The detailed search strategies for each database can be found in the [supplementary file].

Study selection

There were case-control, cross-sectional, prospective, retrospective cohort, and randomized clinical trials (RCT) included in the study. For this analysis, only those studies were taken into consideration which were in English language, articles of sample size (n > 40), studies that reported human adult patients of age above 18, articles on AC inside the operating room, studies which reported IOS, and risk factors of IOS. We excluded publications other than English, articles on craniotomy under GA, research without assessments of IOS risk variables, case reports, review articles, editorials, letters to the editor, meeting abstracts, animal testing, *in vivo/in vitro* research, biological studies, publications without data extraction, and studies lacking full texts. Two authors of this study went through each article's title and abstract to eliminate studies that did not meet the criteria for inclusion. Independent reviews of the full texts of the remaining publications determined which research should be included in this meta-analysis. Conflicts were settled by peer discussion and eventual consensus.

Data extraction and outcome measures

The extraction of data was conducted using the data extraction for complex meta-analysis guide.[28] All the data were extracted on Excel and cross-checked by two authors independently. The conflicts were resolved by consensus or a third party. The following variables were collected from the included articles: Age and gender of the patient, year of publication, study design, study duration, sample size of the individual study, frequency of IOS, volume, grade, and location of the tumor, history of seizure and antiepileptic drug (AED) use, and outcome of each study.

Quality assessment

The Newcastle Ottawa quality assessment tool Newcastle-Ottawa scale (NOS) was used as reference to evaluate the collected papers' quality.[37] For selection, comparability, exposure, or outcome, depending on the research study design, each article was reviewed independently by two reviewers. Studies were deemed to be of acceptable quality if their total score was above 7, and disagreements among authors on the caliber of their studies were settled by discussion and agreement.

Statistical analysis

The statistical analysis of potential risk factors for IOS was conducted using the Cochrane Review Manager (RevMan 15). The mean difference (MD) reported with 95% confidence intervals (CI) was calculated for continuous variables. However, the OR with a 95% confidence level was used to analyze dichotomous variables. $P < 0.05$ was maintained as the level of significance for all analysis. Due to the diversity of the targeted population and length of included studies, a random effect model was used. In addition, when using meta-analysis to guide health-care decisions, the random-effects model is frequently favored. The I^2 statistic and Cochran Q-test were used to assess heterogeneity. If the I^2 statistic was >50% and the Q-test's $P < 0.10$, heterogeneity was deemed significant.

RESULTS

Our initial search strategy yielded 83 publications. Ten publications were read in full text after duplicates were removed and titles and abstracts were checked. Our meta-analysis ultimately comprised a total of six studies with 1815 participants. The thorough screening, eligibility evaluation, and inclusion procedure are displayed [Figure 1].[2,4,18,24,27,35] At both the title and abstract screening stage (Cohen's k = 0.71) and the full-text review stage (Cohen's k = 0.68), the study selection reliability of observers was significant.[7] Only one study was a prospective and cohort study, while the other five included studies were retrospective. Three studies received a score of 7, while one received a score of 8 and one scored the full 9 on the NOS, which is used to rate the quality of studies. The prospective study received a complete score of 6 on the NOS [Table 1].[37]

Table 2 presents the baseline characteristics and patient outcome of the included studies. There were 1815 patients in all, and 8.4% of them experienced IOSs. 14 patients required conversion of procedure to Craniotomy under GA as a consequence of IOSs. Mean patient age was 45.3 years, and almost 38% were women. About 93% of patients had been diagnosed with glioma. Of the lesions, 32% matched low-grade gliomas (LGG) and 53% matched high-GG (HGG); the grading of the other gliomas was not known. A total of 12 cases were craniotomies performed on metastatic lesions and lesions of radiation necrosis. The left hemisphere was involved in 64%, the right hemisphere showed involvement was seen in 35% and 52% of the patients had lesion in the frontal lobe. About 54% of the included patients had a history of seizures, and 29% were on AEDs.

All the included studies reported IOS in patients with a frontal lobe tumor, a history of seizure, and the use of AED, and these variables were statistically significant. A pooled random effect OR of frontal lobe tumors was 2.42 [95% CI: 1.10–5.33, $P = 0.03$; Figure 2a]. Study heterogeneity was considerable ($I^2 = 69\%$, $P = .007$). Patients with a history of seizures had a random effect OR of 1.80 [95% CI: 1.13–2.87, $P = 0.01$; Figure 2b] with heterogeneity of ($I^2 = 27\%$, $P = .023$).

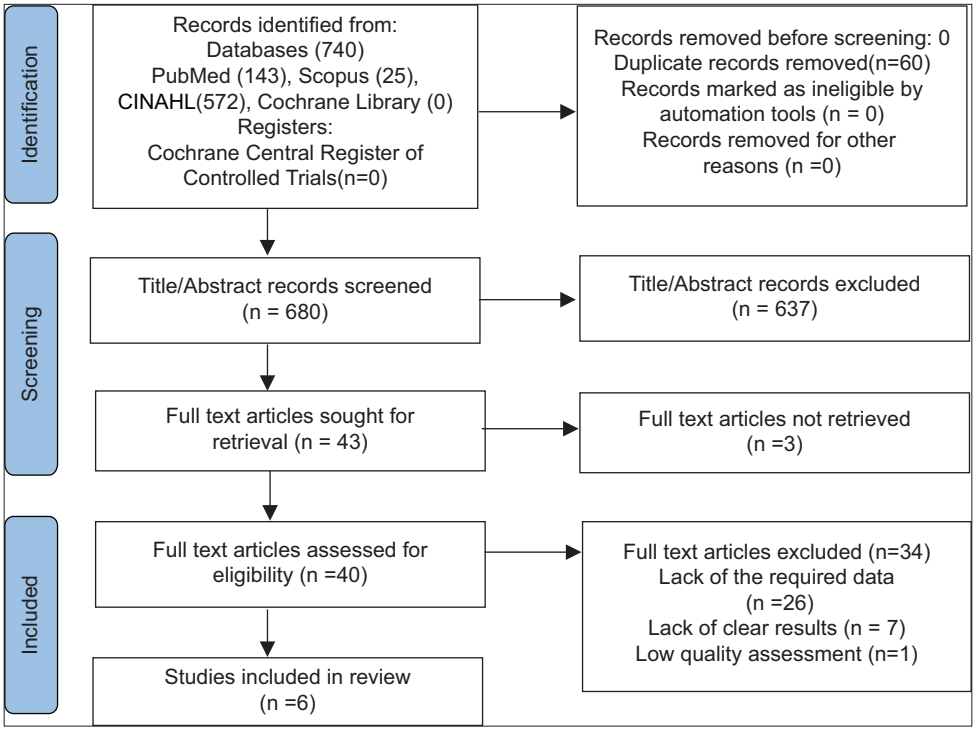

Figure 1: The preferred reporting items for systematic reviews and meta-analyses (PRISMA) 2020 diagram,[26] detailing the selection of studies to be included to assess the risk factors and predictors of intraoperative seizures during awake craniotomy. Cumulated Index to Nursing and Allied Health Literature (CINAHL); Number (n).

Table 1: Newcastle–Ottawa scale quality assessment table.

Study	Selection (4)	Comparability (2)	Exposure/Outcome (3)	Overall Star Rating (9)
Nossek *et al*. 2013[24]	☆☆☆☆	☆	☆☆☆	8
Paquin-Lanthier *et al*. 2021[27]	☆☆☆	☆☆	☆☆	7
Spena *et al*. 2019[35]	☆☆☆	☆	☆☆☆	7
Abecassis *et al*. 2021[2]	☆☆☆☆	☆☆	☆☆☆	9
Mamani *et al*. 2020[18]	☆☆☆	☆☆	☆☆	7
Boetto *et al*. 2015[4]	☆☆☆	☆	☆☆	6

Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses.[37] The table shows the score achieved (☆)by each study[24,27,35,2,18,4] out of the maximum possible score (provided in parentheses) for each category and the combined overall score. (Overall Star Rating) ☆ = 1 point.

Patients using AEDs had a significant random effect pooled OR of 2.47 [95% CI: 1.59–3.85, $P < 0.001$; Figure 2c] with heterogeneity ($I^2 = 27\%$, $P = 0.24$). Some of the variables that were not statistically significant were the gender of the patient; male patients (OR 0.66 [95% CI: 0.33–1.33, $P = 0.24$]), female patients (OR 1.52 [95% CI: 0.75–3.05, $P = 0.24$]), LGG (OR 1.50 [95% CI: 0.90–2.50, $P = 0.12$]), the volume of the tumor (MD −3.88 [95% CI: −15.43–7.67, $P = 0.51$]), right hemisphere tumors (OR 1.24 [95% CI: 0.87–1.79, $P = 0.24$]), and left hemisphere tumors (OR 0.82 [95% CI: 0.57–1.17, $P = 0.27$]). However, an association was seen with high-grade gliomas (OR 0.57 [95% CI: 0.38-0.85, $P= 0.005$] [Figures 2d-m]. The funnel plot analysis for each variable can be located in Figures 3a-m, providing a comprehensive evaluation of publications bias.

DISCUSSION

IOSs remain one of the commonly reported complications associated with AC.[19,31] A meta-analysis of 1019 patients presents IOSs as a 7% incidence (95% CI: 4–11).[22] Identifying patients at higher risk or predicting the occurrence of IOS could help reduce its incidence and improve patient selection. Much of the focus regarding the risk of seizures during AC

Table 2: Characteristics of included studies.

Study	Country	Study design	Duration of study	Sample size (*n*)	IOS (*n*)	No IOS (*n*)	Age (years)		Female (*n*)		History of Seizure (*n*)		Use of AED (*n*)		Frontal lobe tumors (*n*)		Outcome (Potential risk factors of IOS)
							IOS	No IOS	IOS	No IOS	IOS	No IOS	IOS	No IOS	IOS	No IOS	
Nossek *et al.* 2013[24]	Israel	Retrospective Case-control	2003–2011	477	60	417	45±14	52±16	27	70	37	155	19	73	51	237	Age, low grade gliomas, frontal lobe, history of seizure and use of AED
Paquin-Lanthier *et al.* 2021[27]	Canada	Retrospective Case-control	2006–2018	581	29	552	52±13	55.9±15.7	15	252	18	234	17	218	24	251	Intraoperative dexmedetomidine, Frontal lobe tumors, history of seizure and use of AED
Spena *et al.* 2019[35]	Italy	Retrospective Case-control	2010–2017	109	9	100	50±14	47±16	3	38	7	59	4	15	2	15	Anteriorly located tumors, Operated without intraoperative brain activity monitoring, and different patterns of stimulation for language and sensory-motor mapping
Abecassis *et al.* 2020[2]	US	Retrospective Case-control	2013–2018	229	35	194	50.2±12.9	48.6±17.1	15	89	20	117	17	76	18	114	*MGMT* promoter methylation
Mamani *et al.* 2020[18]	Mexico	Retrospective Case-control	2017–2019	45	7	38	36±16.29	45.55±14.36	1	11	5	28	6	27	5	19	Volume of the tumor
Boetto *et al.* 2015[4]	France	Prospective cohort	2009–2014	374	13	361	38±10	38±10.7	9	160	12	301	8	61	10	200	No statistically significant association was found between Age, gender, history of seizure, use of AED, location of tumor and grades of tumor

AED: Antiepileptic drugs, IOS: Intraoperative seizure, *n*: Number of patients, US: United States of America, MGMT: O6-methylguanine-DNA methyltransferase

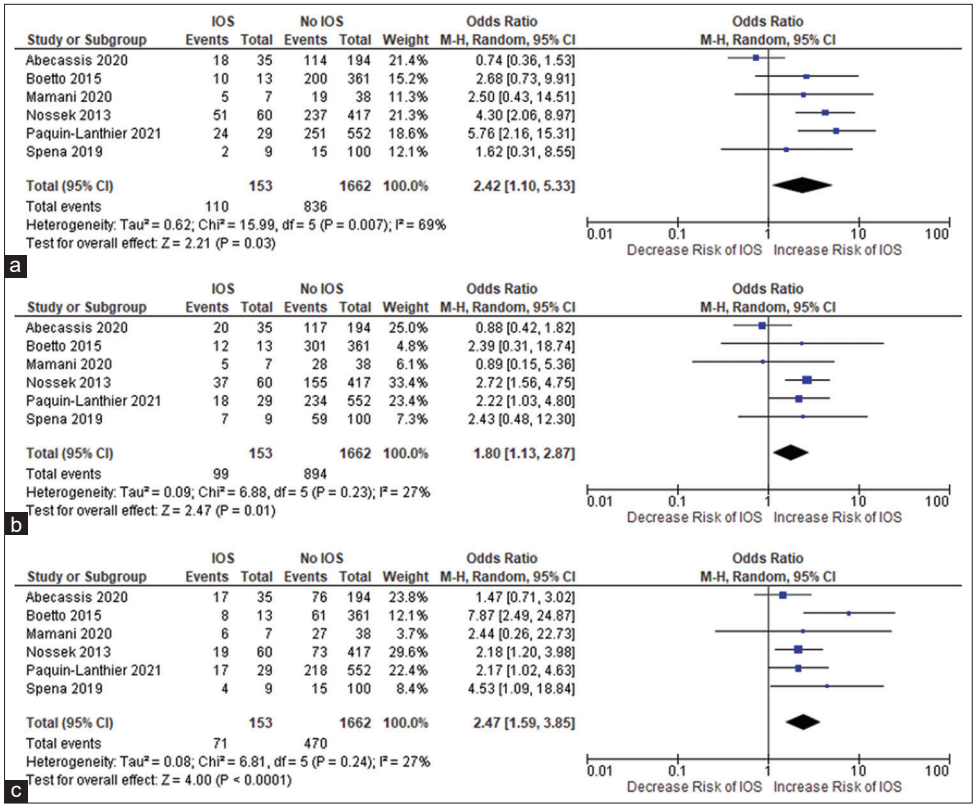

Figure 2: (a) Forest plot of pooled odds ratio (OR) of frontal lobe tumors. (b) Forest plot of pooled OR of history of seizure. (c) Forest plot of pooled OR of use of antiepileptic drug. IOS: Intraoperative Seizure(s), M-H: Mantel-Haenszel method to estimate pooled odds ratio, CI: Confidence Interval. Each blue quadrilateral and adjacent black line represent the study weight and Confidence interval respectively. The black diamond shape box represents the overall effect size.

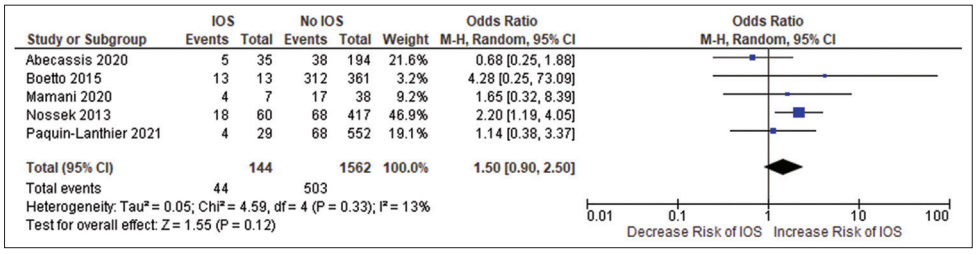

Figure 2d: Forest plot of pooled odds ratio of low-grade gliomas. IOS: Intraoperative Seizure(s), M-H: Mantel-Haenszel method to estimate pooled odds ratio, CI: Confidence Interval. Each blue quadrilateral and adjacent black line represent the study weight and Confidence interval respectively. The black diamond shape box represents the overall effect size.

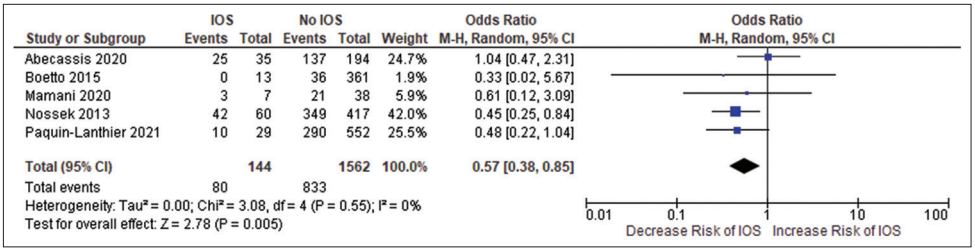

Figure 2e: Forest plot of pooled odds ratio of high-grade gliomas. IOS: Intraoperative Seizure(s), M-H: Mantel-Haenszel method to estimate pooled odds ratio, CI: Confidence Interval. Each blue quadrilateral and adjacent black line represent the study weight and Confidence interval respectively. The black diamond shape box represents the overall effect size.

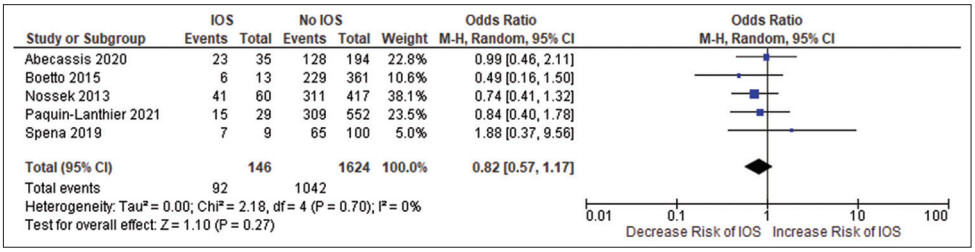

Figure 2f: Forest plot of pooled odds ratio of left hemisphere gliomas. IOS: Intraoperative Seizure(s), M-H: Mantel-Haenszel method to estimate pooled odds ratio, CI: Confidence Interval. Each blue quadrilateral and adjacent black line represent the study weight and Confidence interval respectively. The black diamond shape box represents the overall effect size.

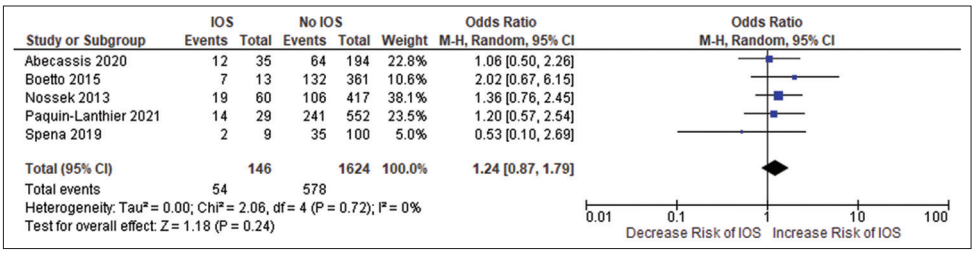

Figure 2g: Forest plot of pooled odds ratio of right hemisphere gliomas. IOS: Intraoperative Seizure(s), M-H: Mantel-Haenszel method to estimate pooled odds ratio, CI: Confidence Interval. Each blue quadrilateral and adjacent black line represent the study weight and Confidence interval respectively. The black diamond shape box represents the overall effect size.

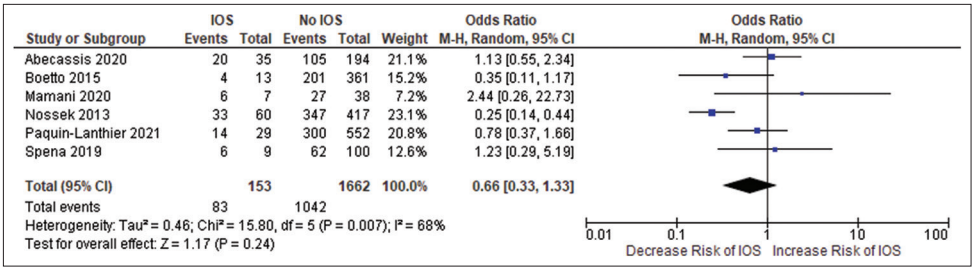

Figure 2h: Forest plot of pooled odds ratio of male gender. IOS: Intraoperative Seizure(s), M-H: Mantel-Haenszel method to estimate pooled odds ratio, CI: Confidence Interval. Each blue quadrilateral and adjacent black line represent the study weight and Confidence interval respectively. The black diamond shape box represents the overall effect size.

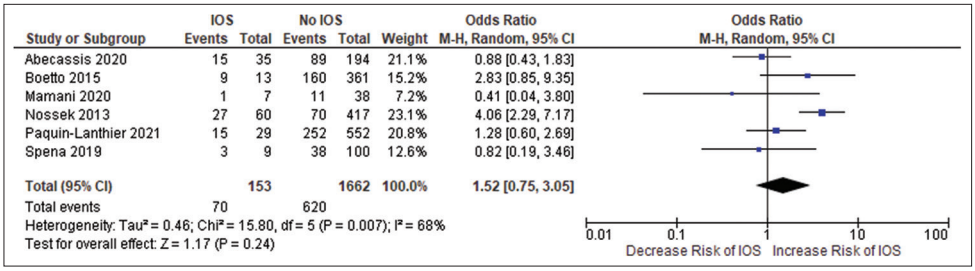

Figure 2i: Forest plot of pooled odds ratio of female gender. IOS: Intraoperative Seizure(s), M-H: Mantel-Haenszel method to estimate pooled odds ratio, CI: Confidence Interval. Each blue quadrilateral and adjacent black line represent the study weight and Confidence interval respectively. The black diamond shape box represents the overall effect size.

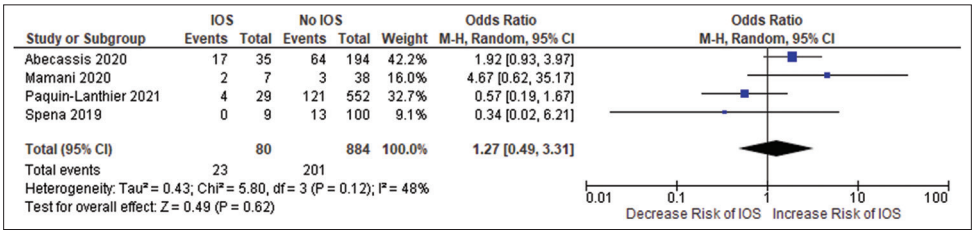

Figure 2j: Forest plot of pooled odds ratio of parietal lobe tumor. IOS: Intraoperative Seizure(s), M-H: Mantel-Haenszel method to estimate pooled odds ratio, CI: Confidence Interval. Each blue quadrilateral and adjacent black line represent the study weight and Confidence interval respectively. The black diamond shape box represents the overall effect size.

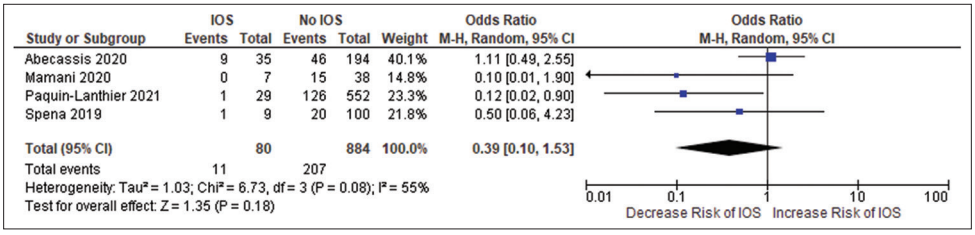

Figure 2k: Forest plot of pooled odds ratio of temporal lobe tumor. IOS: Intraoperative Seizure(s), M-H: Mantel-Haenszel method to estimate pooled odds ratio, CI: Confidence Interval. Each blue quadrilateral and adjacent black line represent the study weight and Confidence interval respectively. The black diamond shape box represents the overall effect size.

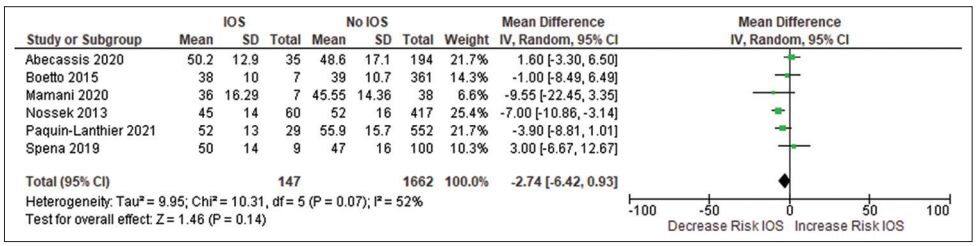

Figure 2l: Forest plot of pooled odds ratio of age of patient. IOS: Intraoperative Seizure(s), M-H: Mantel-Haenszel method to estimate pooled odds ratio, CI: Confidence Interval. Each green quadrilateral and adjacent black line represent the study weight and Confidence interval respectively. The black diamond shape box represents the overall effect size.

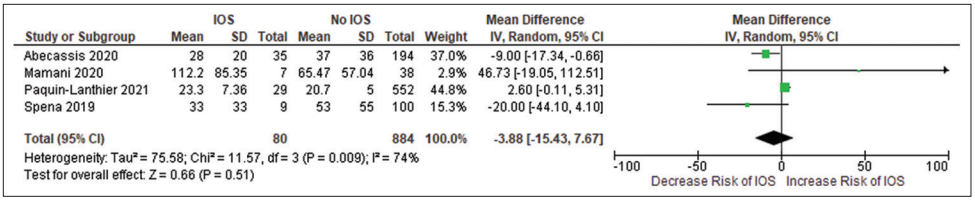

Figure 2m: Forest plot of pooled odds ratio of volume of tumor. IOS: Intraoperative Seizure(s), M-H: Mantel-Haenszel method to estimate pooled odds ratio, CI: Confidence Interval. Each green quadrilateral and adjacent black line represent the study weight and Confidence interval respectively. The black diamond shape box represents the overall effect size.

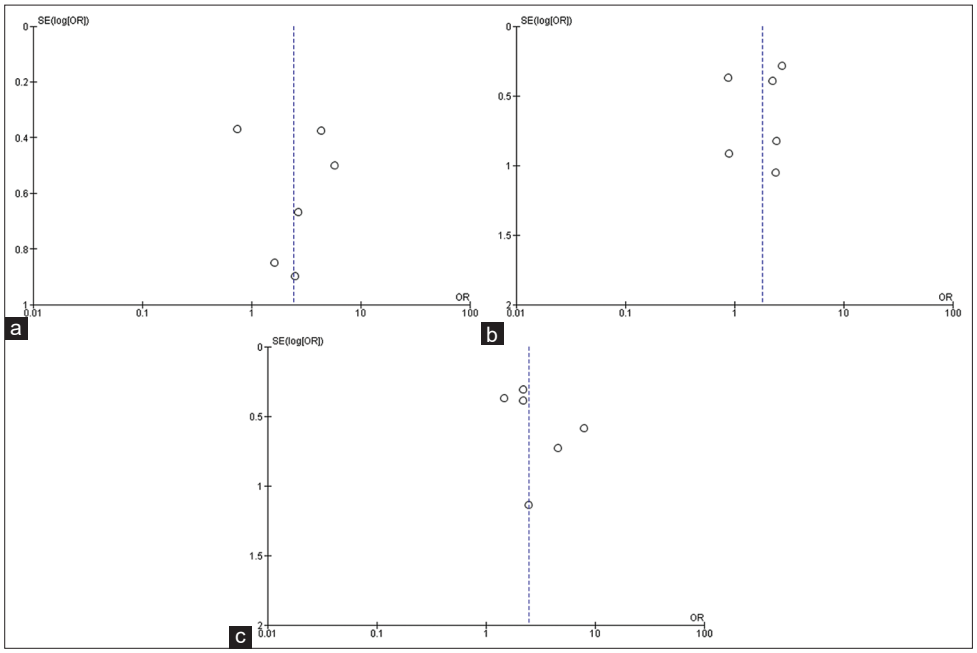

Figure 3: (a) Funnel plot for frontal lobe tumors across studies. (b) Funnel plot for history of seizure across studies. (c) Funnel plot for use of antiepileptic drug across studies. SE: standard error, OR: Odds ratio.

has been on the method of anesthesia and surgery technique. Some studies have delved into tumor location and grading, as well as patient's age at the time of procedure.[22] The difference in the incidence of IOS in monolingual and bilingual patients has been explored and needs to be subjected to analysis.[27]

To date, there has been no consensus regarding factors that predict IOS.[30] To the best of our knowledge, this meta-analysis is the first to comprehensively examine the potential association of proposed factors with the risk of IOS during AC.

Current literature points toward the importance of lesions in developing IOS, and it is generally accepted that certain brain areas are more predisposed to developing IOS than others, where a frontal lesion is commonly associated with an elevated risk of IOS.[10,12,16,24,30,40] This is supported by the results of our work, as consistent with published literature, we were able to demonstrate a significant association of IOS with frontal lobe lesions.

Tumors have distinct intrinsic epileptogenicity, LGG being the most epileptogenic tumors.[8,39] Theoretically, patients with low-grade tumors are at higher risk of developing IOS. Nevertheless, authors who have specifically analyzed the grade of tumor have reported contradictory findings. Hervey-Jumper *et al*.[12] and Boetto *et al*.[4] reported no association, but Gonen *et al*., Nossek *et al*., and Pace *et al*. found an association.[10,24,25] However, our study found no association.

Patients with a history of seizures preoperatively are at a higher risk of presenting seizures intraoperatively.[36] Hervey-Jumper and Nossek found a strong association between a history of seizures preoperatively and the risk of IOS.[32,38] In contrast, Wang *et al*. and Eseonu *et al*. in their works, report no association.[9,40] We assessed the role of preexisting seizure, either as a long-term history of seizures or as the presenting complaint, and our results showed that patients who experienced preoperatively seizure regardless of subtype and frequency of seizure were more likely to have IOS. However,

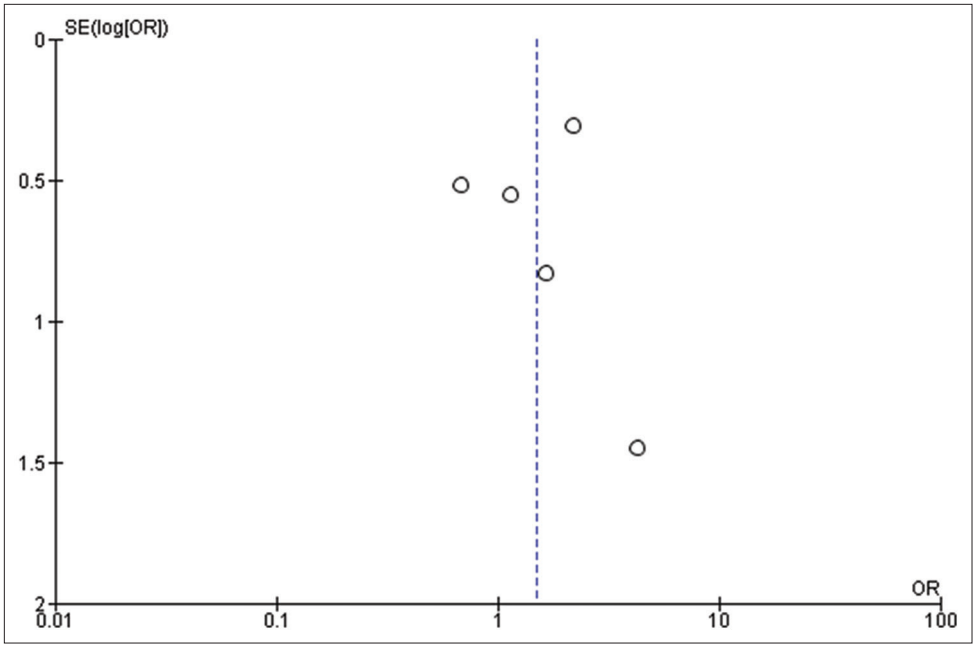

Figure 3d: Funnel plot for low-grade gliomas across studies. SE: standard error, OR: Odds ratio.

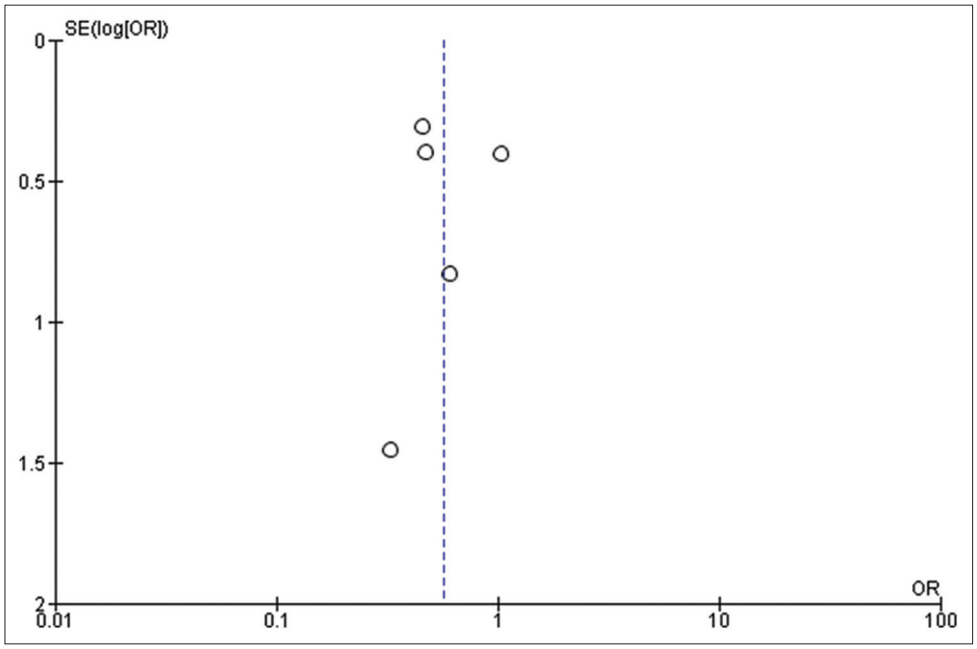

Figure 3e: Funnel plot for high-grade gliomas across studies. SE: standard error, OR: Odds ratio.

the frequency of prior seizures in relation to IOS was not assessed. The conversion of AC to craniotomy under GA has been reported as a rare, yet serious outcome of IOS,[23] and this remains consistent with our analysis as 0.77% procedures (14 out of 1815) were reverted to GA.

We looked at individuals on AED and we found a strong association between patients on AED and IOS. Although we did not evaluate the number and type of AED the patient was taking and its association with IOS. Age and sex differences in IOS have been debatable in the literature. Although, there is a slight predilection of IOS toward younger age and female gender.[24,27] However, our study found no significant gender disparity in the incidence of IOS in AC procedures.

The mean preoperative tumor volume in Eseonu *et al*.[9] was 30.7 cm^3, which was associated with IOS in univariate

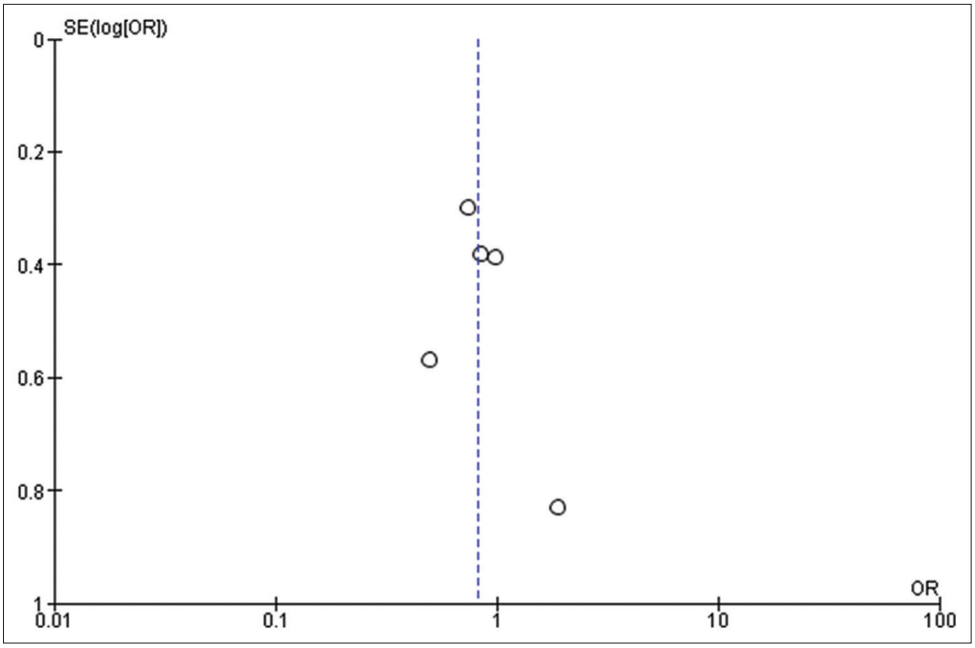

Figure 3f: Funnel plot for left hemisphere gliomas across studies. SE: standard error, OR: Odds ratio.

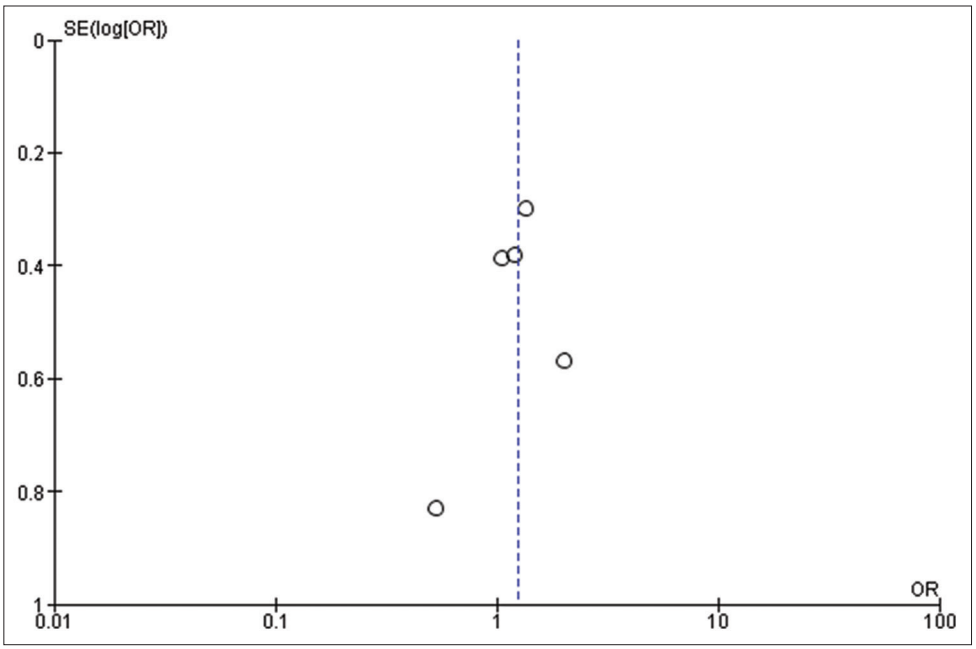

Figure 3g: Funnel plot for right hemisphere gliomas across studies. SE: standard error, OR: Odds ratio.

analysis. However, a multivariate logistic regression could not reveal a significant association. In contrast, the mean preoperative tumor volume in Mamani *et al*.[18] was 112.2 cm^3, and he reported a significantly higher tumor volume in the IOS group. Nonetheless, our study found no significant association between the volume of tumor and IOS.

Studies have suggested a disparity in the incidence of IOS in AC procedures using different forms of anesthesia.[38] Current knowledge on the techniques of anesthesia during AC has shown promising results in comparison to GA.[38] There has been much difference in the incidence of IOS reported in different studies, also depicting variability

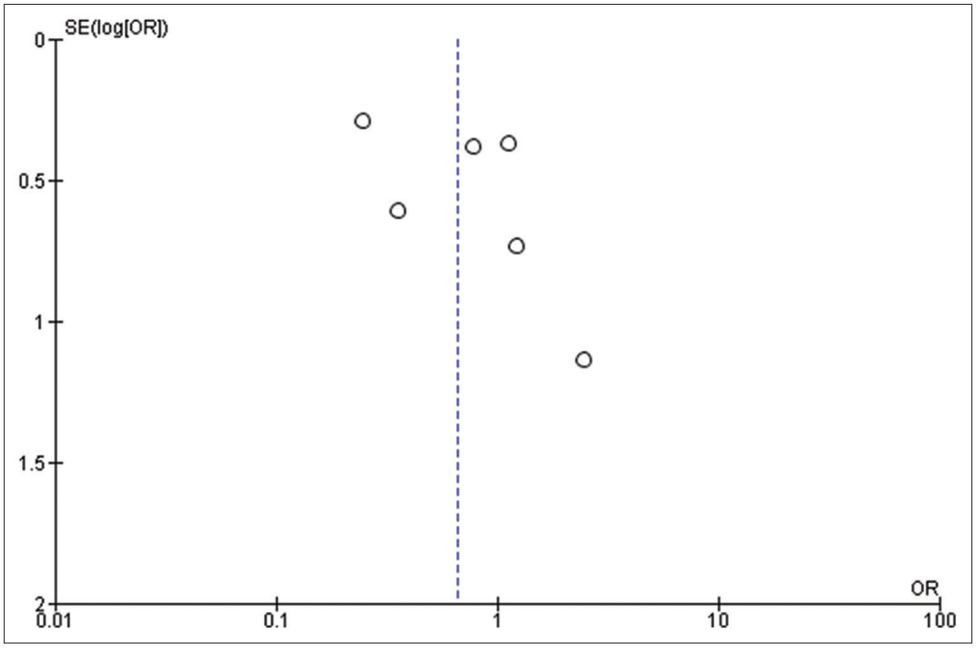

Figure 3h: Funnel plot for male gender across studies. SE: standard error, OR: Odds ratio.

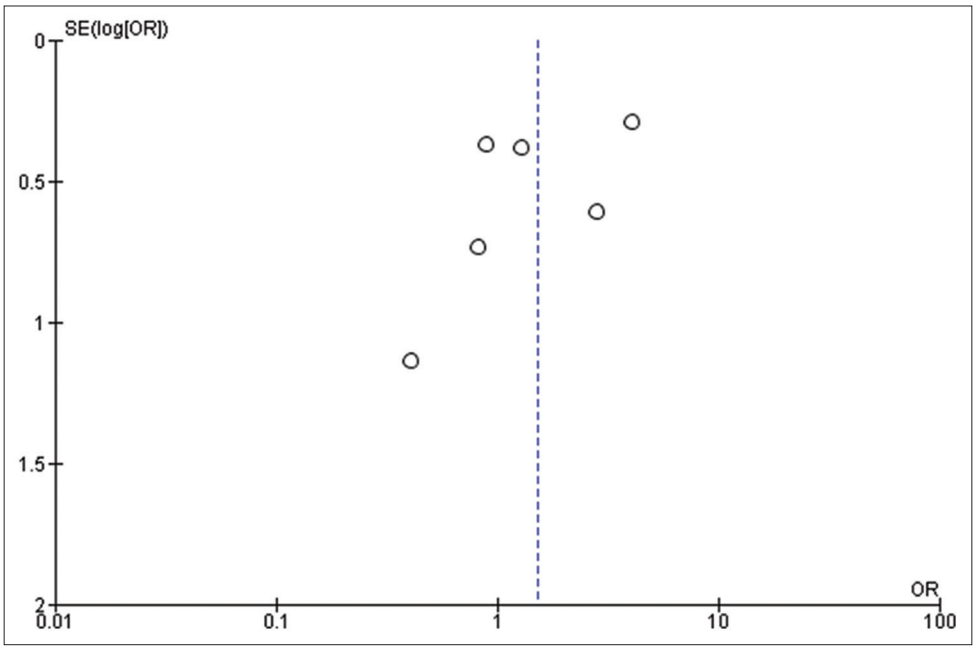

Figure 3i: Funnel plot for female gender across studies. SE: standard error, OR: Odds ratio.

with modifiable risk factors such as the preferred drug of anesthesia.[11,27,34] The method of cortical and subcortical stimulation is another factor of interest and warrants more analysis for its significance.[36] Preoperative drug regimens have also been studied in previous publications and require a more expansive sample size to investigate significance.

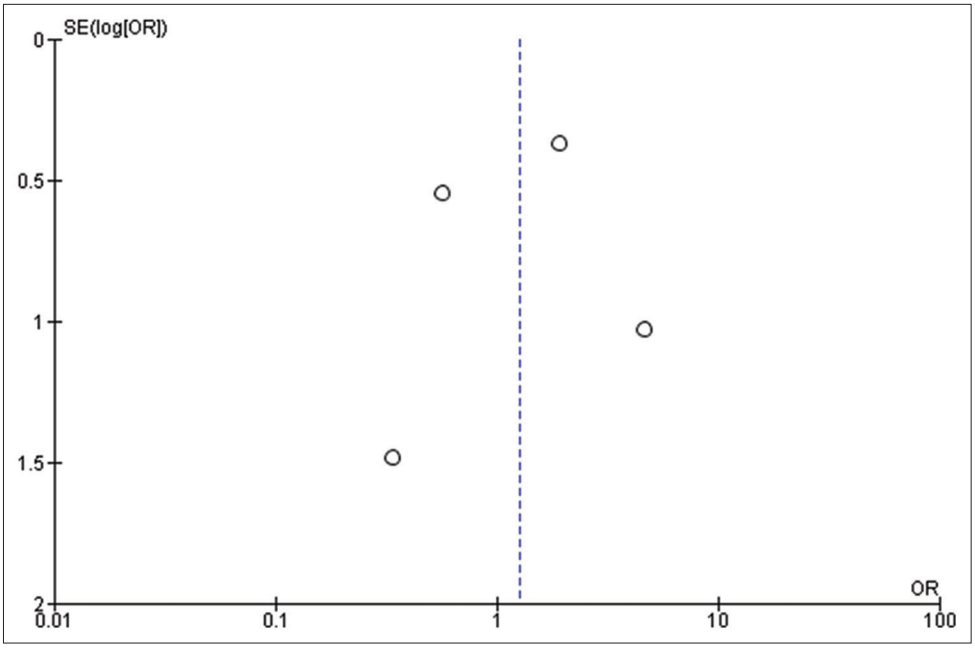

Figure 3j: Funnel plot for female parietal lobe tumor across studies. SE: standard error, OR: Odds ratio.

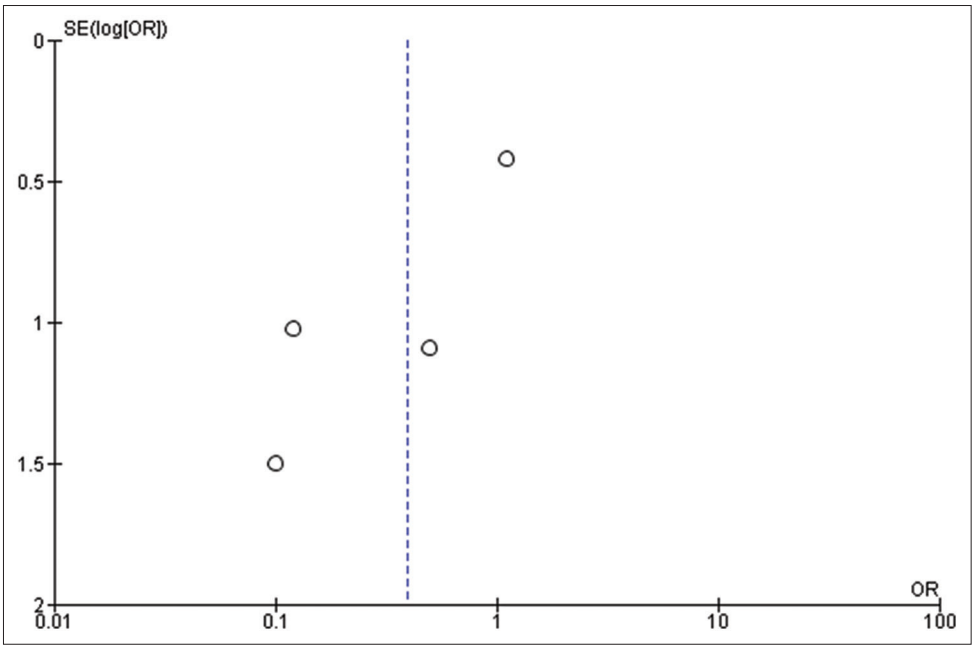

Figure 3k: Funnel plot for female temporal lobe tumor across studies. SE: standard error, OR: Odds ratio.

Only one study in our analysis studied operative time as a potential risk factor for IOSs[27] and another study looked at increased operative time as a consequence of IOSs;[2] however, both studies were not able to find any significant associations (P = 0.38 and P = 0.56, respectively.).

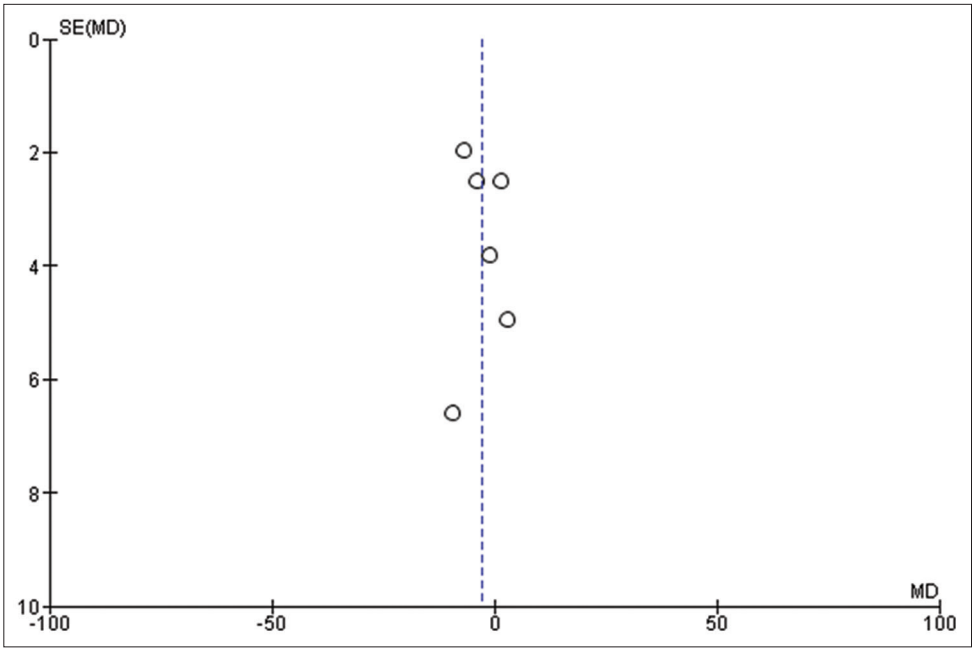

Figure 3l: Funnel plot for age of patient across studies. SE: standard error, OR: Odds ratio.

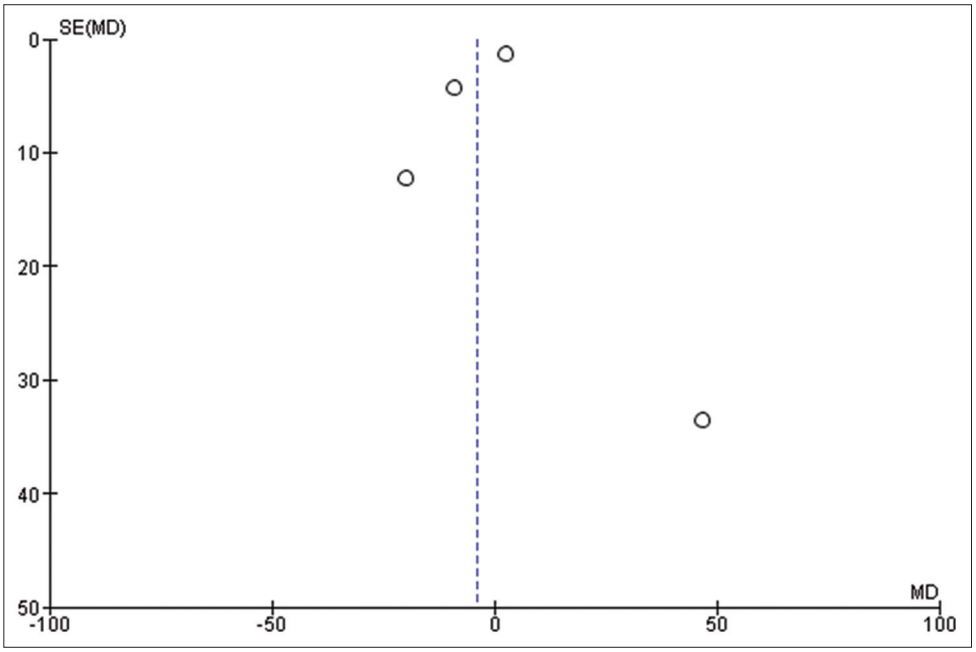

Figure 3m: Funnel plot for volume of tumor across studies. SE: standard error, OR: Odds ratio.

Limitations

The findings of our meta-analysis are limited by the retrospective nature of included studies and their heterogeneity. Further, analyses such as meta-regression to explore the potential confounders could not be performed appropriately, as we were hindered by the scarcity of relevant studies. In addition, small sample sizes in a few included studies may carry intrinsic publication bias and make the file-drawer issue worse.

We only searched for articles in the English language; therefore, not all the research that met our inclusion criteria may have been found. Studies that implemented intraoperative magnetic resonance imaging guidance for the procedure were also disregarded. The grounds for elimination

were due to the facilities' low generalizability to the hospital, which does not have a complicated infrastructure.

Some of the potential risk factors of IOS, such as preoperative Karnofsky Performance Scale scoring, specific anesthesia regimens for conscious sedation, length of surgery, intensity of current and duration of stimulation during mapping, isocitrate dehydrogenase mutation gliomas, O (6)-methylguanine-DNA methyltransferase methylation, and intraoperative use of electrocorticography (ECoG), could not be included in our meta-analysis because of the limited data available.

Moreover, it must be noted that there may have been variations in the studies' identification of IOSs and other risk variables. Hence, the pooling of these studies was rational, credible, and justifiable despite their discrepancies.

Future direction

Going forward, preliminary steps will comprise small prospective studies to ascertain predictors of IOS. Subsequently, to fully account for the confounders and bias present in retrospective research, a sizable prospective and cohort study and RCT are required. Our meta-analysis results emphasize the need for additional robust data from large prospective cohorts and RCT studies and help fill up the current gaps in the literature available.

CONCLUSION

This study highlights the importance of preoperative recognition of individuals who are more susceptible to IOSs to avoid this devastating AC complication. Patients with lesions of the frontal lobe, a prior seizure history, and patients on AEDs are at higher risk of experiencing IOSs. These factors must be considered during the patient's preparation for AC. However, it is sometimes difficult to predict IOS precisely, so the presence of a multidisciplinary team, consisting of neurosurgeons, neuroanesthesiologists, Electroencephalography, and ECoG specialists, should be present, prepared to timely detect and intervene to avoid an intractable seizure and consequently a failed AC.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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SUPPLEMENTARY FILE

Search Strings

PubMed

((("Risk factors"[All Fields] OR ("predictor"[All Fields] OR "predictors"[All Fields])) AND ("intraop"[All Fields] OR "intraoperative"[All Fields] OR "intraoperatively"[All Fields]) AND ("seizural"[All Fields] OR "seizures"[All Fields] OR "seizured"[All Fields] OR "seizures"[MeSH Terms] OR "seizures"[All Fields] OR "seizure"[All Fields] OR "seizuring"[All Fields])) OR ("epilepsie"[All Fields] OR "epilepsy"[MeSH Terms] OR "epilepsy"[All Fields] OR "epilepsies"[All Fields] OR "epilepsys"[All Fields])) AND "Awake Craniotomy"[All Fields]

CINAHL

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