How to Cite:
Asadifar, A., Khazaei, R., Mokarian, P., & Kaviani, M. A. (2022). Assess the overall postoperative morbidity among patients with brain tumors by using preoperative functional magnetic resonance imaging: A systematic review and meta-analysis. *International Journal of Health Sciences*, *6*(S8), 6156–6165. https://doi.org/10.53730/ijhs.v6nS8.13746

Assess the overall postoperative morbidity among patients with brain tumors by using preoperative functional magnetic resonance imaging: A systematic review and meta-analysis

Ali Asadifar
Resident of Radiology, Kerman University of Medical Sciences, Kerman, Iran

Razieh Khazaei
Department of Radiology, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran
Corresponding author email: Farzandeiran28@gmail.com

Peyman Mokarian
Neurosurgeon, Fasa University of Medical Sciences, Fasa, Iran

Mohammad Ali Kaviani
Resident of Radiology, Kerman University of Medical Sciences, Kerman, Iran

***Abstract*---**Background and aim: the aim of present study was Assessing the Overall Postoperative morbidity among patients with brain tumors by using preoperative functional Magnetic Resonance Imaging. Method: Databases of PubMed, Scopus, Web of Science, EBSCO, ISI Web of knowledge and Embase were searched for systematic literature between 2012 to July 2022. 95% confidence interval for odds ratio with fixed effect model and Mantel–Haenszel method and were calculated. To deal with potential heterogeneity, random effects were used and I^2 showed heterogeneity. Meta-analysis was performed using Stata/MP v.17 software. Result: In the initial review, duplicate studies were eliminated and abstracts of 178 studies were reviewed, the full text of 32 studies was reviewed by two authors, finally, six studies were selected. Odds ratio of Unfavorable outcomes between functional MRI and control group was 0.46 (OR, 95% CI 0.15, 0.76; p<0.001). Odds ratio of Gross total resection between functional MRI and control group was 0.20 (OR, 95% CI -0.20, 0.59; p=0.34). Conclusion: According to the findings of the present study, the use of functional MRI before brain tumor removal is associated with a

Manuscript submitted: 9 Agst 2022, Manuscript revised: 18 Oct 2022, Accepted for publication: 27 Nov 2022

reduction in the risk of delayed or permanent neurological deficits after surgery with a two-month follow-up period.

***Keywords*---**functional magnetic resonance imaging, brain tumors, gross total resection.

Introduction

Magnetic resonance imaging (MRI) is a function of preoperative planning tools used to remove brain tumors before surgery(1). However, so far there are disagreements between the possible applications of MRI and its current use(2). Studies have shown that there is clinical and radiographic variability among neurosurgeons in the use of functional MRI(3, 4). The goal of resection of the brain tumor is to maximize it in order to avoid permanent postoperative defects(5). Studies have shown that there is a direct correlation between the survival rate of the patient and the tumor removal rate(6, 7). Imaging methods such as MRI and neuronavigation, fluorescent dyes are used for treatment planning(8). Previous studies have investigated the use of intraoperative stimulation mapping and MRI during surgery and their impact on the surgical process has been evaluated. However, their effect on neurological outcomes has not been considered and more comprehensive studies are needed in this regard(9, 10). A study has shown that the use of functional MRI during surgery can reduce the incidence of permanent neurological deficits after surgery(9). Therefore, the present study was conducted with the aim of Assessing the Overall Postoperative Morbidity Among Patients with Brain Tumors by Using Preoperative Functional Magnetic Resonance Imaging.

Method

Search strategy

Based on PRISMA guidelines(11), the present study conducts a systematic review and meta-analysis of all articles published between January 2012 and July 2022 in international databases, including PubMed, Scopus, Science Direct, Embase, and ISI Web of Knowledge. The Google Scholar search engine employed the PICO strategy to answer the research questions (Table1).

Table1. PICO strategy

PICO strategy	Description
P	Population: patients with brain tumors
I	Intervention: preoperative neuroimaging with functional MRI
C	Comparison: preoperative or intraoperative functional neuroimaging technique
O	Outcome: postoperative clinical outcome

The following keywords were used to search: ((((((("Brain Neoplasms"[Mesh]) OR ("Brain Neoplasms/complications"[Mesh] OR "Brain Neoplasms/diagnosis"[Mesh]

OR "Brain Neoplasms/diagnostic imaging"[Mesh] OR "Brain Neoplasms/surgery"[Mesh])) AND "Magnetic Resonance Imaging"[Mesh]) AND ("Magnetic Resonance Imaging/statistics and numerical data"[Mesh] OR "Magnetic Resonance Imaging/therapy"[Mesh])) AND "Preoperative Period"[Mesh])) AND ("Neuroimaging"[Mesh] OR "Functional Neuroimaging"[Mesh])) OR "Neuroimaging/surgery"[Mesh]) OR "Functional Neuroimaging/therapy"[Mesh].

Eligibility criteria
Inclusion criteria

1. Randomized controlled trials, controlled clinical trial, cohort studies, case-control and Case series
2. The article's full text was accessible.
3. studies reported postoperative clinical measure.
4. persistent during at least a 2-month follow-up period.
5. No language restrictions.
6. Human samples.

Exclusion criteria

1. in-vitro and in-vivo studies, Review studies, case reports, letters to the editor and animal studies.
2. studies reported postoperative without preoperative or intraoperative
3. imaging methods other than Functional MRI.

Selection process and Data collection process

Two reviewers blindly and independently extracted data from the included papers' full texts and abstracts for Data extraction. Kappa statistics were used to check the amount of agreement between the reviewers before the screening. The values of kappa were higher than 0.80. Studies data were reported by the first author's name, years, number of patients, Sequences Use, groups.

Risk of bias assessment

The randomized control trial studies' quality was assessed using the Cochrane Collaboration's tool (12). Low risk received a scale score of 1, while high and unclear risk received a score of 0. The scale scores have a range of 0 to 6. High quality means a higher score. Newcastle-Ottawa Scale (NOS) (13) used to assessed quality of the cohort, case-control and case series studies, This scale measures three dimensions (selection, comparability of cohorts and outcome) with a total of 9 items. In the analysis, any studies with NOS scores of 1-3, 4-6 and 7-9 were defined as low, medium and high quality, respectively.

Data analysis
Effect measures and Synthesis methods

Stata/MP. v17 software was used to analyze the data. To examine the postoperative clinical outcome used odds ratio (95% confidence interval) with fixed effect model and Mantel–Haenszel method. Hedges' g is a measure of effect size, Hedges' g with random effect model and REML method. The level of heterogeneity was assessed using the I^2 index test (I^2 50% = low levels, 50-I^2 75% = moderate, and I^2>75% = high levels).

Results

After the initial search for them in databases, 218 articles were identified. Duplicate articles were deleted (n=40) after importing all articles into the EndNote.X9 software. 178 articles were entered and examined in the second stage (abstract). At this stage, 146 unrelated articles were excluded from the study while reviewing the titles and abstract articles. The full texts of 32 articles were reviewed in the third step. six articles that met the inclusion criteria and were published between January 2012 and July 2022 eventually entered the analysis. (Figure 1).

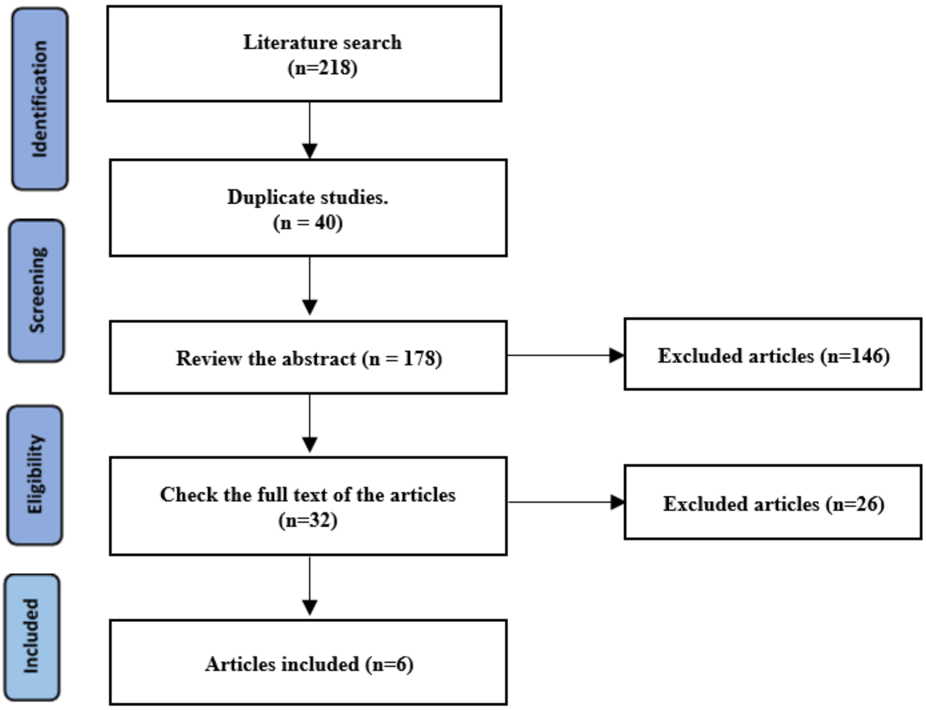

Figure 1. PRISMA flowcharts

Characteristics

A total number of patients in intervention group and control group were 326 and 433, Respectively. Data extracted from the studies are summarized in Table 2.

Risk assessment

Based on the NOS tool, two studies scored 9 out of 9, one study scored 8 out of 9, which indicates that the quality of the studies is high, and three studies scored 6 out of 9, which indicates the average quality of the studies.

Table 2. Studies selected for systematic review and meta-analysis

n	Study. Years	Number of participants				Mean of age		Sequences used	Neuronavigation?	Cortical stimulation ?	Intraop MRI
		intervention		control		intervention	control				
		male	female	male	female						
1	Kosteniuk et al., 2018 (14)	5	5	5	5	38	40	functional MRI	No	No	No
2	Vysotski et al., 2018 (15)	54	25	72	55	46	58	functional MRI	No	Yes	No
3	Panigrahi et al., 2017 (16)	4	6	17	34	44	44	functional MRI	No	Yes	No
4	Sun et al., 2015 (17)	4	26	8	22	45	43	functional MRI	No	No	No
5	Zhang et al., 2015 (18)	76	36	53	33	45	43	functional MRI	Yes	No	Yes
6	Trihn et al., 2014 (19)	85		129		NR	NR	functional MRI	Yes	Yes	No

Table3. Bias assessment (NOS tool)

Number of studies	Selection (5 score)				Comparability (2 score)	Outcome (2 score)		Total score
	representative sample	Sample size	Non respondents	Ascertainment of the exposure	Based on design and analysis	Assessment of outcome	Statistical test	
Kosteniuk et al., 2018 (14)	1	1	1	2	1	1	1	8
Vysotski et al., 2018 (15)	1	1	1	2	2	1	1	9
Panigrahi et al., 2017 (16)	1	1	1	2	2	1	1	9
Sun et al., 2015 (17)	1	1	1	1	1	0	1	6
Zhang et al., 2015 (18)	1	1	1	1	1	0	1	6
Trihn et al., 2014 (19)	1	1	1	1	1	0	1	6

Unfavorable outcomes

Odds ratio of Unfavorable outcomes between functional MRI and control group was 0.46 (OR, 95% CI 0.15, 0.76; $p<0.001$) (I^2=93.09%; P=0.00; high heterogeneity) (Figure 2). A statistically significant difference was observed between functional MRI group and control group (p=0.00). postsurgical functional deterioration was less likely when presurgical functional fMRI mapping was performed.

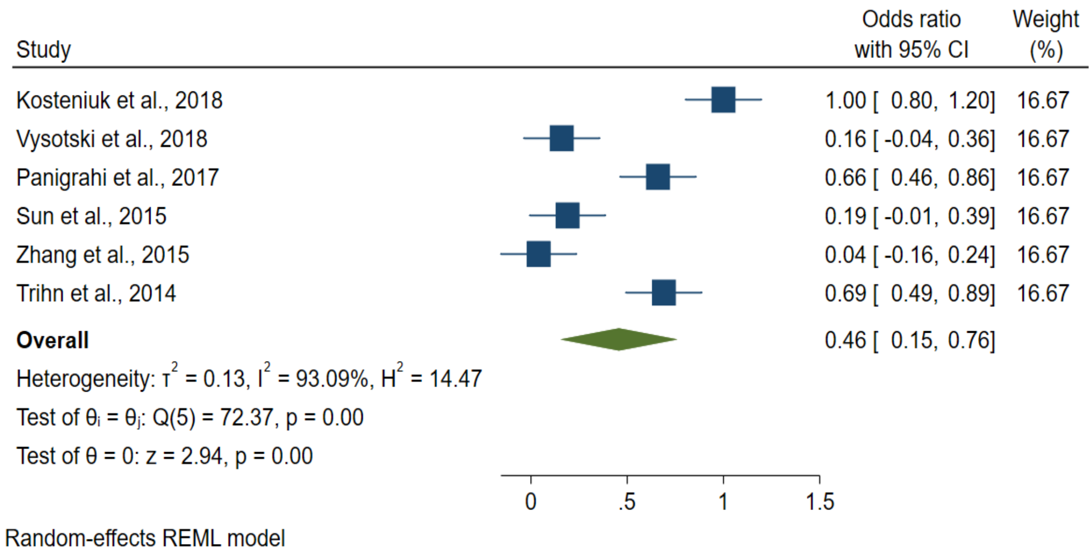

Figure 2. Forest plot sowed Unfavorable outcomes between functional MRI and control group

Gross total resection

Odds ratio of Gross total resection between functional MRI and control group was 0.20 (OR, 95% CI -0.20, 0.59; p=0.34) (I^2=82.97%; P=0.00; high heterogeneity) (Figure 3). No statistically significant difference was observed between functional MRI group and control group (p=0.34).

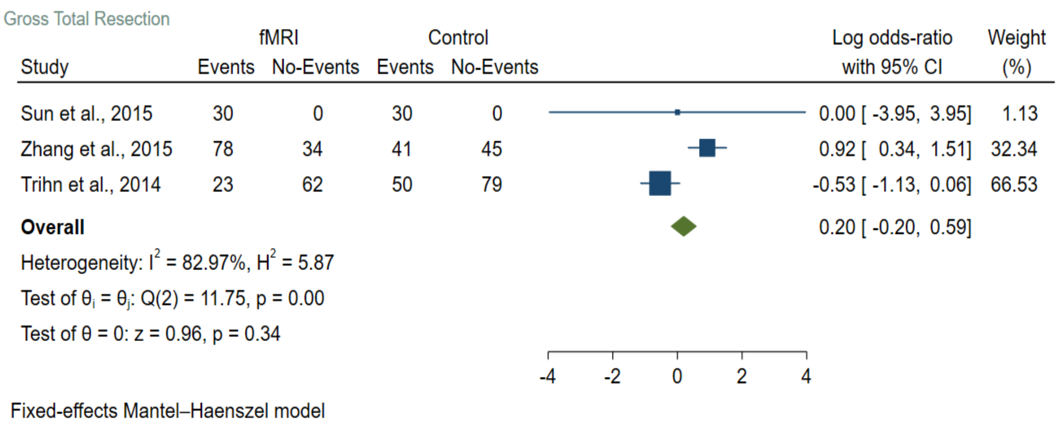

Figure 3. Forest plot sowed Gross total resection between functional MRI and control group

Karnofsky performance status scores

Hedges' g of presurgical and postsurgical Karnofsky performance status scores between functional MRI and control group was 0.14 (Hedges' g, 95% CI -0.04, 0.32; p=0.13) (I^2=43.28%; P=0.15; low heterogeneity) (Figure 4). No statistically significant difference was observed between functional MRI group and control group (p=0.13). for both groups showed a difference favoring the presurgical fMRI group.

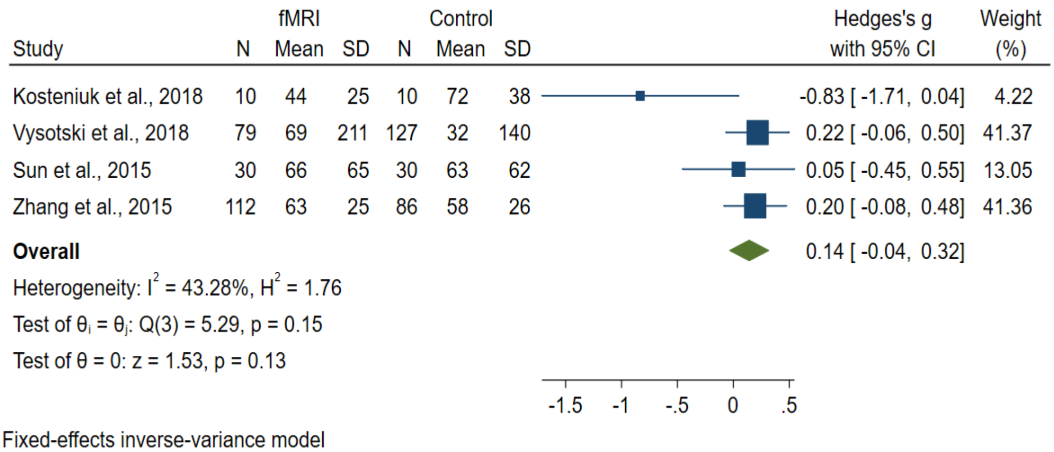

Figure 4. Forest plot sowed presurgical and postsurgical Karnofsky performance status scores between functional MRI and control group

Discussion

The aim of the present study was to assess the overall postoperative morbidity among patients with brain tumors by using preoperative functional magnetic resonance imaging, and it was tried to provide sufficient evidence in this field; The findings of the study showed that when surgeons use functional MRI before surgery and brain tumor removal, the possibility of functional deterioration after surgery decreases and Karnofsky performance status scores after surgery were higher in the group of patients who underwent functional MRI before surgery, but no statistically significant difference was observed between two groups, and both groups showed a difference favoring the presurgical fMRI group. A study showed that there is a significant positive relationship between tumor volume before surgery and neurological deficits after surgery, however, in the present study, this relationship was negative(20). Some studies have also shown that there is no significant relationship between preoperative tumor volume and postoperative neurological deficits with a follow-up period of 3 to 6 months(21-24). The use of intraoperative and preoperative MRI along with other advanced imaging techniques can help surgeons in planning treatment and better results. These results suggest more surgical effort with larger lesions (eg, fMRI and concomitant use of other advanced imaging techniques, intraoperative MRI, cortical stimulation) compared with smaller lesions, which ultimately may lead to a greater incidence of late postoperative deficits with lesions that were assumed to be more easily removed. It should be mentioned that the removal of small tumors is very challenging and these lesions can increase postoperative defects. In studies where the increase of permanent defects after surgery was more evident, it was generally the location of the frontotemporal tumor. High heterogeneity was observed between studies, this heterogeneity suggests that the findings of the present study should be interpreted with caution. The current study had limitations, firstly, the methodological heterogeneity between the studies was very high, in the studies, the definition of permanent defects after surgery was different, which can affect the results of the study, and the size of the tumors was also not the same; Other limitations were different tumor types and most of the studies were retrospective. It seems that the most important limitation is that it was not investigated whether other factors are also effective on the surgical process and its complications, and on what factors the overall effects of functional MRI depend. To reach stronger evidence, studies with similar cognitive methods and with more data are needed. However, due to the moderate quality and high heterogeneity of the studies, the results of the present study should be interpreted with caution.

Conclusion

According to the findings of the present study, the use of functional MRI before brain tumor removal is associated with a reduction in the risk of delayed or permanent neurological deficits after surgery with a two-month follow-up period. The use of advanced imaging techniques along with functional MRI can help surgeons in planning treatment before surgery so that postoperative complications are less. As a result, functional MRI before brain tumor removal can be considered a standard method in preventing postoperative complications, even in small tumors.

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