Frailty as a Predictor of Neurosurgical Outcomes in Brain Tumor Patients: A Systematic Review and Meta-Analysis

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Abstract

Purpose The object of this study is to describe the existing evidence and completed the first systematic review meta-analysis between frailty and neurosurgical outcomes in brain tumor patients. The primary outcome is mortality and postoperative complications, the second outcomes including readmission rate, discharge disposition, length of stay (LOS) and hospitalization costs.

Methods Seven English databases and four Chinese databases were searched to identify the neurosurgical outcomes and frailty among patients with brain tumor. With no restrictions on the publication period. According to the JBI manual for evidence synthesis and the PRISMA guidelines, two independent reviewers applied the Newcastle-Ottawa Scale (NOS) for cohort studies, the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Cross-Sectional Studies to evaluate the methodological quality of each study.

Results 13 papers included in the systematic review and prevalence of frailty ranged from 1.48% to 57%. Frailty is significantly associated with increased the risk of mortality ($OR, 1.63$; $CI, 1.33-1.98$; $P=0.001$), postoperative complications ($OR, 1.48$; $CI, 1.40-1.55$; $P=0.001$; $I^2=33\%$), non-routine discharge position than home ($OR, 1.72$; $CI, 1.41-2.11$; $P=0.001$), prolonged LOS in brain tumor patients ($OR=1.25$; $CI=1.09-1.43$; $P=0.001$) and higher hospitalization costs in brain tumor patients. But Frailty was not independently associated with readmission ($OR, 0.99$; $CI, 0.96-1.03$; $P=0.74$).

Conclusion Frailty is an independent predictor of mortality, postoperative complications, non-routine discharge position rate, LOS and hospitalization costs in brain tumor patients. Besides frailty has a significant potential role in risk stratification, preoperative shared decision-making and perioperative management.

Introduction

Histologically, brain tumor can be categorized into primary and metastatic tumors [1]. It is reported that the incidence of malignant brain tumors is 7.1/100,000 and 13.8/100,00 for benign tumors [2]. Brain tumor could happen at any age and the most common reported in adults with median age of 59 [3]. In addition, malignant brain tumor is the most common solid tumor of children with more than 4600 cases estimated in 2016 [2]. Moreover, brain tumor is the second highest level of symptom burden diseases in the world which is just after lung cancer although only account for 1.4% of all cancers [4–5]. It has been long recognized as producing a high rate of mortality and disability usually have a poor prognosis for survival with diverse physical, cognitive and behavioral impairments [5]. The 5-year survival rate through the full age spectrum is just 34% on averages, and only 6.1% among the group of greater than 75 years old. Especially patients with glioblastoma are approximately 5%, and the median survival of newly diagnosed glioblastoma ranges from less than 1 to 3 years, with an average of 12 ~ 14 months [6–7].

As the population ages and increasing need for surgery, the role of risk stratification tools becomes critical to surgical planning. It has been shown the age is an important predictor of health status and cancer outcomes, but it is not the only factor to consider in perioperative planning [8]. Frailty describes a state of increased vulnerability and decreased physiological reserve that can be defined multidimensional components, including physical, psychological, and social factors [9]. The new concept of patient frailty in surgery, particularly complex surgical interventions including cranial neurosurgery makes frailty a concern in neurosurgical outcomes [8, 10]. Patients with frailty are at a higher risk of poor health outcomes and frailty has been explored as a predictor of adverse events, such as perioperative complications, readmissions, falls, disability and mortality in many neurosurgical literature [11–12]. But so far, the precise relationship between frailty and brain tumor has not been previously established with certainty, preventing evidence-based advancements in neurosurgical management.

The object of this study is to describe the existing evidence and completed the first systematic review meta-analysis between frailty and neurosurgical outcomes in brain tumor patients. The primary outcome is mortality and postoperative complications, the second outcomes including readmission, discharge disposition, length of stay (LOS) and hospitalization costs.

Methods

This systematic review was designed based on guidelines from the Joanna Briggs Institute (JBI) [13], and was reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines [14] (Online Resource 1). The review is registered with the PROSPERO International Prospective Register of Systematic Reviews (registration number CRD42021248424) on 12 April, 2021 and will end on December, 2021. We will continue to update any amendments on PROSPERO.

Eligibility criteria

Study designs:

Studies that provided observational data on cross-sectional or prospective associations between frailty and neurosurgical outcomes among patients with brain tumor were included. Besides, duplicate studies, abstracts, conference proceedings, comments, letters, correspondences, editorials, unavailability of full articles were excluded. Published in languages other than English and Chinese studies were excluded. Corresponding authors were contact if additional information is needed.

Types of participants

Patients confirm diagnosis of brain tumor at any age based on international criteria and guideline definitions, including intracranial metastatic from systematic cancers, brain neoplasms, cerebral tumor, glioma, meningioma, hypophysoma and pituitary tumor.

Interest of context

Frailty was assessed using validated assessment instruments, such as the Johns Hopkins Adjusted Clinical Groups (JHACG) frailty-defining diagnoses indicator, Frail Index (FI), the modified Frailty Index (mFI), 5-factor Modified Frailty Index (mFI-5), the Hopkins Frailty Score (HFS), et al.

Types of outcome measures

Studies that reported any neurosurgery outcomes were included. Such as mortality, postoperative complications, readmission, discharge disposition, length of stay (LOS) and hospitalization costs.

Data Sources and Search Strategy

Seven electronic databases included Web of Science, EMBASE, CINAHL, Scopus, MEDLINE, PubMed, the Cochrane Library and four Chinese databases included China National Knowledge Infrastructure, China Science and Technology Journal Database, Wanfang Database, and Chinese Biomedicine Literature Database were analyzed. The search was limited in English and Chinese, with no restrictions on the publication period. After conducting the preliminary search of various databases to analyze the keywords and determine the index terms. The tailored search strategy was used on various databases to ensure that all available studies were obtained. Subsequently, the search was modified according to different databases and was limited by the language of publication. The search strategy was as follows: (frail OR frailty) AND ("brain neoplasms" OR "brain tumor" OR "cerebral tumor" OR glioma OR meningioma OR hypophysoma OR "pituitary tumor"). Online Resource 2 describes the search strategy of MEDLINE and Web of Science. Titles, abstracts, and full texts were screened and examined for eligibility independently by two investigators. Reference lists of relevant articles were reviewed for additional studies.

Study selection

Following the database search, all identified studies were collected, and duplicates were removed. Firstly, two independent reviewers screened the titles and abstracts, and then downloaded and read the full article according to the inclusion and exclusion criteria to assess eligibility. The documents screened and selected in each step were managed through the Note Express V.3.3.0 software.

Data extraction

The extracted data included specific details about the first author, published year, country, design, number of patients, type of patients, age, gender, frailty assessment, study period, prevalence of frailty, covariates and neurosurgical outcomes. The data was recorded in Microsoft Excel for analysis.

Data analysis

A random-effects or fixed-effects meta-analysis was used to combine odds ratio (*OR*) or hazard ratio (*RR*) for categorical data and weighted mean differences for continuous data of neurosurgical outcomes. And 95% confidence intervals (*CI*) calculated for analysis. Heterogeneity was statistically evaluated using Cochran's Q statistic and I^2 , and I^2 values of 25%, 50%, and 75% were considered as low, moderate, and high heterogeneity, respectively. $P < 0.05$ was considered statistically significant. The finding was described in narrative form including figures and tables if statistical pooling is not possible. All analysis was performed on Review Manager version 5.3. (The Cochrane Collaboration)

Assessment of methodological quality

Risk of bias was assessed using the Newcastle-Ottawa Scale (NOS) [15] (Online Resource 3) for cohort studies, the Joanna Briggs Institute (JBI) Critical Appraisal Checklist [16] (Online Resource 4) for Cross-Sectional Studies to evaluate the methodological quality of each study. The NOS uses 2 tools for case control and cohort studies and encompasses 3 quality parameters: selection, comparability, and exposure/outcome assessment. It assigns a maximum of 4 points for selection, 2 points for comparability, and 3 points for exposure or outcome (for a total of up to 9 points). The NOS scores of 7 or higher were considered high-quality studies, and scores of 5 to 6 denoted moderate quality [15]. The Joanna Briggs Institute (JBI) Critical Appraisal Checklist included 11 items and each need to answer Yes, No, Unclear or Not/Applicable [16]. Two researchers appraised the articles independently, and any disagreement was discussed until a consensus was reached.

Assessment of reporting bias

The reporting bias was explored using a funnel plot if the included studies are more than 10. Risk of bias was assessed as visual inspection of a funnel plot constructed by plotting effect size versus SE.

Quality of evidence

Quality assessment was conducted using the Grading of Recommendations Assessment, Development and Evaluation system [17]. Papers were ranked four categories-high, moderate, low, and very low.

Results

Literature search process

Papers identified through databases searching were 473, and hand searching were 2. After removed duplicated papers were 274. Then excluded 225 papers by title and abstract, 36 papers by full-text screened. Finally, 13 papers included in the systematic review underwent assessed for eligibility. The selection process was summarized in a PRISMA flow diagram (Fig.1).

Study characteristics

This review included thirteen studies which designed eleven retrospective studies [18-21, 23-24, 26-30], one prospective study [22] and one retrospective cross-sectional study [25] with sample sizes ranging from 76 to 115317 (Table 2). Publication location come from the United States [18-20, 22-30] and Columbia [21] between 2013 and 2021. Frailty was assessed using mFI [18,21,25,29-30], JHACG [19-20,27-28], HFS [22], mFI-5[23-24,26]. Prevalence of frailty ranged from 1.48% to 57%.

Risk of Bias

12 studies [18-24,26-30] assessed using the NOS [15], the overall studies were high-quality with 9 scores of 7 studies [20,23-29], 8 scores of 3 studies [18,22,30] and 7 scores of 2 studies [19,21] (Tables 2). According to the JBI critical appraisal checklist, the methodological quality one study [25] was strong with the score of 8 (Tables 3).

Frailty as a predictor of neurosurgical outcomes

Frailty is significantly associated with the risk of mortality in brain tumor patients

Seven studies included 30-day mortality subgroup reported frailty is significantly associated with increased risk of mortality in brain tumor patients (*OR*,1.63; *CI*,1.33-1.98; *P*0.001). No significant difference in 60-day mortality and 90-day mortality subgroup between the two cohorts. However, the total outcome reported the same outcome of 30-day mortality (total *OR*,1.56; *CI*,1.30-1.86; *P*0.001) (Fig.2).

Frailty is significantly associated with the risk of postoperative complications in brain tumor patients

Frailty is significantly associated with increased risk of postoperative complications in brain tumor patients as eleven studies reported (Fig.3). The cross meta-analysis of the fixed-effects (*OR*,1.48; *CI*,1.40-1.55; *P*0.001; *I*²=33%) and random-effects (*OR*,1.48; *CI*,1.37-1.60; *P*0.001; *I*²=33%) reported that there is little difference between the two models, the research results are reliable.

Frailty is significantly associated with the risk of non-routine discharge position in brain tumor patients

Eight studies reported discharge disposition as an outcome and the data shows frailty is significantly associated with increased the risk of non-routine discharge position than home in brain tumor patients (*OR*,1.72; *CI*,1.41-2.11; *P*0.001) (Fig.4). As a result, frail patients had a higher rate of nonroutine hospital discharges compared to non-frail patients, which encompasses transfers to skilled nursing home facilities, short-term hospitals, and home health care.

Frailty is significantly associated with the risk of readmission in brain tumor patients

Readmissions were classified 30-day, 90-day, 180-day subgroup. Frail patients had lower 90-day readmission rates compared with non-frail patients (*OR*,0.94; *CI*,0.89-0.99; *P*0.05). However, no difference was seen at the 30-day (*OR*,1.04; *CI*,0.99-1.10; *P*=0.12) or 180-day (*OR*,1.04; *CI*,0.91-1.18; *P*=0.56) between the two cohorts. Frailty was not independently associated with readmission (*OR*,0.99; *CI*,0.96-1.03; *P*=0.74) (Fig.5).

Frailty is significantly associated with longer LOS in brain tumor patients

Four studies reported frailty prolonged LOS in brain tumor patients ($OR=1.25$; $CI=1.09-1.43$; $P=0.001$) (Fig.6). Frailty is significantly increased the LOS in the studies by Asemota [19] (9.27 days [CI , 7.79–10.75] vs 4.46 days [CI , 4.39–4.53], $P < 0.001$), Bonney [20] (incident rate ratio, 1.92; CI , 1.87–1.98; $P < 0.0001$), Cloney [21] (6 days vs 4 days), Shahrestani1[27] (13.79 ± 19.10 days vs 4.37 ± 5.22 days, $p < 0.001$). Shahrestani2[28] (16.1 ± 13.9 days vs 9.0 ± 8.1 days, $P < 0.0001$). Theriault [29] found for every unit increase in the mFI, the expected LOS increased by 1.678 days on average, holding other variables constant ($P = 0.046$).

Frailty is significantly associated with higher hospitalization costs in brain tumor patients

Frailty is significantly associated with higher hospitalization costs in brain tumor patients reported by Asemota [19] (\$109,614.33 [CI \$92,756.09–\$126,472.50] vs \$56,370.35 [CI \$55,595.72–\$57,144.98], $P < 0.001$), Shahrestani1[27] (\$191,129.27 $\pm$ \$244,619.10 vs \$89,269.91 $\pm$ \$82,787.67, $P < 0.001$), Shahrestani2[28] (\$39,114.69 $\pm$ \$38,249.02 vs \$27,924.03 $\pm$ \$23,886.26, $P < 0.0001$). In addition, with each 1-point increase in mFI-5 score, total charges increased by \$5846 (CI \$3971–\$7721, $P < 0.001$) [23].

Assessment of reporting bias

The effect size estimates for mortality (Fig.7) and complications (Fig.8) all fell within the pseudo 95% confidence limits of the funnel plot. There are no large reported bias effects.

Discussion

This is the first systematic review and meta-analysis to report frailty as a predictor of neurosurgical outcomes in brain tumor patients. Neurosurgical outcomes not only include short-term but also include long-term outcomes. Frailty was found to be an independent risk factor for brain tumor patients of all ages, with increased adverse outcomes including mortality, non-routine discharge position rate, LOS and hospitalization costs, especially postoperative complications. This conclusion may be particularly important not only for elderly, but also for young patients diagnosed with brain tumors. Because physicians are used to thinking that age is an important predictor of complications, but in fact, frailty may be the strongest predictor. However, our review found there is no significant difference between frail and non-frail patients in readmission rate, particularly 30-day and 180-day readmission.

Prevalence of frailty ranged from 19.3–55.3% using mFI, 41.3–57% using mFI-5, 1.48–50.3% using JHACG, and 25.4% using HFS. Different assessment tools may differ slightly. One study demonstrated that the mFI is > 3 times the rate of frailty compared to the JHACG method [30]. Although more than 12 of methods for frailty definition in the past 5 years, regardless, there remains limited instrument tools that specifically target the frailty of neurosurgical patients. Furthermore, the ideal instrument of frailty defined is more likely uses history and physical examination characteristics which is more objective, according to a correlation between examination-based and diagnosis-based instruments [31]. Therefore, this area warrants further exploration in the future.

The adverse outcomes associated with frailty were linked each other. For example, frailty patients have higher incidence of postoperative complications, which led to longer LOS, then increased total hospitalization costs. Additionally, postoperative medical and surgical complications also result in higher mortality. On the contrary, shorter LOS was associated with decreased fewer hospital-acquired infections, then led to lower complication rates, at the same time, decreased the hospitalization costs and then improved patient's satisfaction [32–33]. These association explained frailty could also serve as a useful risk adjustment tool which were related to hospital quality and reimbursement.

Given preoperative neurological deficits, neurosurgical oncology patients may be more heavily dependent on preoperative functional status than in other surgical populations [34]. As an independent risk factor for worse outcomes following brain tumor surgery, frailty has tremendous potential for risk stratification and outcome prediction. These allow frailty as a part of surgical risk-benefit assessment to underscore the utility of preoperative careening. Frailty should be stringently evaluated with multidisciplinary program prior to surgery, and it may aid clinical decision making [35–36]. Patients will also be considered to be unsuitable between surgery or other forms of management [37]. In addition, a frailty assessment could also lead to increase intraoperative and postoperative interdisciplinary treatment program and care pathway that targeting specific elements of frailty such as nutrition, mobilization, and hydration [38]. Especially benign brain tumor makes the majority of surgeries exclusively elective or at least nonurgent because of the slow or nongrowing nature of these tumors. This may give us opportunity to tailor preoperative interventions or pre-habilitation to optimize surgical readiness [39], which aimed at decreasing frailty and improve postoperative outcomes.

Limitations

There were limitations of this study. Because of the limitation article, our study failed to include all neurosurgical outcomes, such as some studies reported frail patients were more likely to undergo reoperations [19, 29]. Further, owing to the majority studies were retrospective design which included our systematic review, thus our analysis outcome may affect by the original study data contained in the database. Fortunately, our review included 13 studies and 257,822 brain tumor patients, the data came from large case volume across multiple healthcare settings and countries, which compensate the limitation and improve the accuracy of outcomes.

Conclusions

Frailty is an independent predictor of mortality, postoperative complications, non-routine discharge position rate, LOS and hospitalization costs in brain tumor patients. And frailty has a significant potential role in risk stratification, preoperative shared decision-making and perioperative management. Further study

could be designed as prospective to explore the association between frailty and neurosurgical outcomes as well as quality-of-life.

Declarations

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Competing interests

The authors declare that they have no competing interests.

Availability of data and material

All data generated or analysed during this study are included in this published article

Code availability

Author's contributions

Design of this systematic review protocol: JZ and LC; literature search, data extraction and appraisal, data synthesis and interpretation, manuscript drafting: JZ, FW and QX; data selection, data appraisal, data synthesis, manuscript critical revision, and arbitrate in cases of disagreement: JZ, FW, PY and CJ. All the authors have read, provided feedback, and approved the final manuscript.

Ethics approval

Not applicable

This review only uses secondary data, ethical approval is not required. No other ethical issues are foreseen.

Consent to participate

Not applicable

Consent for publication

Not applicable

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None

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Tables

Table 1

Characteristics of included studies

Study (year)	Country	Design	No. of patients	Type of patients	Median age (range) years	Gender (% women)	Frailty assessment	Study period	Preva of fra
Adams [18] 2013	America	Retrospective study	6727	Inpatients who underwent operations	54.7	49.7%	mFI	The NSQIP participant use files for the period 2005 through 2010	49.7%
Asemota [19] 2019	America	Retrospective study	115317	Pituitary tumors or disorders who had undergone transsphenoidal pituitary surgery	57.14 ± 16.96 (frail) VS 51.91 ± 15.88 (non-frail)	50.9%	JHACG	The 2000~2014 National (Nationwide) Inpatient Sample	1.48%
Bonney [20] 2021	America	Retrospective study	87835	Patients undergoing craniotomy for brain tumors	≥ 65 57% (frail) VS 45.1% (non-frail)	53.0%	JHACG	The Nationwide Readmissions Database from 2010~2014	8.2%
Cloney [21] 2016	Columbia	Retrospective study	243	Geriatric patients who underwent resection of glioblastoma, including reoperation for recurrent disease.	73.1±5.5	None	mFI	Columbia University Medical Center New York Presbyterian Hospital from 2000 to 2012	19.3%
Harland [22] 2020	America	Prospective study	260	patients ≥ 18 years old scheduled for elective resection of tumor	56.1 (frail) VS 50.6 (non-frail)	53% (frail) VS 41% (non-frail)	HFS	The University of Colorado over a 3-year period (October 2014 to August 2017).	25.4%
Huq [23] 2021	America	Retrospective cohort study	1692	Brain tumor patients who underwent primary surgery	55.5	52%	mFI-5	At a single institution between January 1, 2017 and December 31, 2018.	57%
Khalafallah [24] 2020	America	Retrospective cohort study	1692	Adult patients who were operated on for brain tumors	55.49 ± 15.22	52.3%	mFI-5	At a single institution between January 1, 2017, and December 31, 2018	None
Pitts [25] 2019	America	Retrospective cross-sectional study	410	Patients presenting to an academic hospital following a surgical procedure for a head and neck cancer diagnosis	61.9 ± 10.5	26%	mFI	Between January 2014 and December 2017	42.2%
Sastry [26] 2020	America	Retrospective cohort study	20,333	Adult patients undergoing elective cranial surgery for tumor	54.85 ± 12.11	55.76%	mFI-5	2012-2018 NSQIP Participant Use File	41.3%

Shahrestani1[27] 2020	America	Retrospective cohort study	746	Patients undergoing microscopic or endoscopic resection of a Pituitary adenomas	63.7(frail) VS 63.5(non-frail)	41.6%VS 38.3%	JHACG	The 2016 and 2017 National Readmission Database	None
Shahrestani2[28] 2020	America	Retrospective cohort study	13342	Geriatric patients receiving cranial neurosurgery for a primary CNS neoplasm	73.7 ± 6.2	45.2%	JHACG	Between 2010 and 2017 by using the Nationwide Readmission Database	50.3%
Theriault [29] 2020	America	Single-center retrospective cohort study	76	Patients who underwent intracranial meningioma resection	55.8±15.3	72.6%	mFI	At Westchester Medical Center in Valhalla between August 2012 and May 2018	55.3%
Youngerman [30] 2018	America	Retrospective cohort study	9149	Patients who underwent neurosurgical procedures for intracranial neoplasms	< 45: 22.6% 45–54:20.8% 55–64:26.5% ≥ 65:30.1%	52.9%	mFI	2008-2012 NSQIP Participant Use File	48.5%

mFI=Modified Frailty Index; mFI-5=5-factor Modified Frailty Index; JHACG=The Johns Hopkins Adjusted Clinical Groups; HFS=The Hop-kins Frailty Score; NSQIP=National Surgical Quality Improvement Program; ASA=American Society of Anesthesiologists; LOS=Lengths of Hospital Stay; KPS=Karnofsky Performance Status; BMI=Body Mass Index; CCI=Charlson Comorbidity Index; mFI=Modified Frailty Index; mFI-5=5-factor Modified Frailty Index; JHACG=The Johns Hopkins Adjusted Clinical Groups; HFS=The Hop-kins Frailty Score; NSQIP=National Surgical Quality Improvement Program; ASA=American Society of Anesthesiologists; LOS=Lengths of Hospital Stay; KPS=Karnofsky Performance Status; BMI=Body Mass Index; CCI=Charlson Comorbidity Index

Table 2

Quality assessment of studies using the Newcastle-Ottawa Scale

Study	Year	Selection				Comparability	Outcome			To SC
		Representative of the exposed cohort	Selection of the non- exposed cohort	Ascertainment of exposure to implants	Demonstrate that outcome of interest was not present at start of study	Comparability of cohorts on the basis of design or analysis (variables)	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow- up of cohorts	
Adams[18]	2013	1	1	1	1	1	1	0	1	8
Asemota[19]	2019	1	1	1	0	2	1	0	1	7
Bonney [20]	2021	1	1	1	1	2	1	1	1	9
Cloney[21]	2016	1	1	1	1	1	1	0	1	7
Harland[22]	2020	1	1	1	1	2	1	0	1	8
Huq[23]	2021	1	1	1	1	2	1	1	1	9
Khalafallah[24]	2020	1	1	1	1	2	1	1	1	9
Sastry[26]	2020	1	1	1	1	2	1	1	1	9
Shahrestani1[27]	2020	1	1	1	1	2	1	1	1	9
Shahrestani2[28]	2020	1	1	1	1	2	1	1	1	9
Theriault[29]	2020	1	1	1	1	2	1	1	1	9
Youngerman[30]	2018	1	1	1	1	2	1	0	1	8

Table 3

Quality assessment of studies using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist

study	year	Were the criteria for inclusion in the sample clearly defined?	Were the study subjects and the setting described in detail?	Was the exposure measured in a valid and reliable way?	Were objective, standard criteria used for measurement of the condition?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the outcomes measured in a valid and reliable way?	Was appropriate statistical analysis used?	Total score
Pitts[25]	2019	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8

Figures

PRISMA 2009 Flow Diagram

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

Figure 1

PRISMA flow diagram of literature search and study selection

Figure 2

Forest plots presenting frailty is the risk of mortality in brain tumor patients

Figure 3

Forest plots presenting frailty is the risk of complications in brain tumor patients

Figure 4

Forest plots presenting frailty is the risk of non-routine discharge disposition in brain tumor patients

Figure 5

Forest plots presenting frailty is the risk of readmission in brain tumor patients

Figure 6

Forest plots presenting frailty is the risk of LOS in brain tumor patients

Figure 7

Funnel plots assessing for report bias of frailty on mortality in brain tumor patients

Figure 8

Funnel plots assessing for report bias of frailty on complications in brain tumor patients

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [OnlineResource1PRISMA2020checklist.pdf](#)
- [OnlineResource2SearchStrategy.pdf](#)
- [OnlineResource3NewcastleOttawaScaleNOS.pdf](#)
- [OnlineResource4JBICriticalAppraisalChecklist.pdf](#)