Systematic Review and Meta-Analysis

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Rehabilitation therapy for patients with glioma

A PRISMA-compliant systematic review and meta-analysis

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Abstract

Background: Glioma is the most common type of brain tumor because of the destructiveness of the disease itself and the side effects of treatment, patients often leave symptoms of neurological defects. At present, rehabilitation treatment is not popular in glioma patients. There is a lack of definite evidence to prove the benefits of rehabilitation therapy for glioma patients. The purpose of this meta-analysis is to determine whether rehabilitation therapy can significantly improve the prognosis of neurological function and improve the quality of life of patients with glioma.

Methods: The articles about rehabilitation treatment of glioma in Cochrane, PubMed, and Embase, Web of Science, and Medline database from January 1990 to May 2020 were searched. Before rehabilitation as the control group, after rehabilitation as the experimental group. The Functional Independence Measure (FIM) was used as the outcome index, including total FIM, motor FIM, and cognitive FIM. Use STATA12.0 for meta-analysis.

Results: A total of 8 articles were included in the study, with a total of 375 glioma patients. Meta-analysis of total FIM (SMD = 0.96, 95%CI = 0.66–1.26, $P < .001$), motor FIM (SMD = 0.75, 95%CI = 0.54–0.96, $P < .001$) and cognitive FIM (SMD = 0.35, 95%CI = 0.19–0.50, $P < .001$) indicated that the neurological function of rehabilitation was significantly improved in total, motor and consciousness.

Conclusion: The published studies show that rehabilitation therapy can improve the functional prognosis and quality of life of glioma patients. More attention should be paid to the therapeutic value of rehabilitation for glioma patients in the future.

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Abbreviations: FIM = functional independence measure, GBM = Glioblastoma multiforme, HGG = high-grade gliomas, LGG = low-grade gliomas, ROBINS-I = risk of bias in non-randomized studies of interventions, WHO = World Health Organization.

Keywords: functional recovery, glioma, meta-analysis, rehabilitation

1. Introduction

Glioma is a tumor originating from brain glial cells, which is the most common in primary brain tumors.[1] The World Health Organization (WHO) classifies gliomas as I-IV grade, of which low-grade gliomas (LGG) are I-II grade and high-grade gliomas (HGG) are III-IV grade.[2] The disease has a certain risk of recurrence, especially in the high-level group. Including in situ recurrence, distant recurrence and spinal cord dissemination, and other special ways, of which in situ recurrence is the most common.[3] The main clinical manifestations include increased intracranial pressure, epilepsy, neuromotor function, and cognitive impairment. The treatment is mainly surgical treatment, postoperative combined with radiotherapy and chemotherapy, and other comprehensive treatment. The disease requires the cooperation of neurosurgery, radiology, pathology, and rehabilitation medicine to adopt individual comprehensive treatment to achieve the best treatment benefit and improve the quality of life of patients.[4] Tumor self-destruction and surgical treatment or postoperative radiotherapy and chemotherapy lead to obvious symptoms of neurological impairment in many patients.

Functional Independence Measure (FIM) was a functional assessment standard developed in the 1980s, which reflected the ability of daily life of the disabled more objectively and comprehensively, including self-care, sphincter control, mobility, locomotion, communication, and social cognition. There are 18 items in the above 6 categories. 1–7 points for each item, out of a total of 126 points. Motor FIM contains a total of 13 items in the first 4 categories, while cognitive FIM refers to a total of 5 items in the last 2 categories.[5] FIM increases the content of cognitive and social aspects, and the evaluation of each item is more detailed, so it is more sensitive and accurate than the Barthel index in

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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describing disability level and functional independence, closer to the overall goal of rehabilitation, and has better judgment consistency and reliability.[6]

Vincenzo Formica's previous meta-analysis of a Mono-Institutional Experience and 11 retrospective studies showed that neurological symptoms of patients with brain tumors increased by 36% after rehabilitation, but the study included not only gliomas but also meningiomas. At the same time, this study has been going on for almost 10 years.[7] Currently, rehabilitation for glioma patients is recommended,[8] but there is a lack of high-quality evidence to support this recommendation. there is a lack of definite evidence to prove that rehabilitation can improve the symptoms of neurological deficit and improve the quality of life in patients with glioma.[9] The purpose of rehabilitation is to effectively improve the motor, consciousness, and psychology of glioma patients. However, it is a pity that the rehabilitation treatment for gliomas is not yet universal, especially for patients with high-grade gliomas.[10] Therefore, it is necessary to conduct a new meta-analysis of the improvement of neurological function after the rehabilitation treatment of gliomas. We conducted a meta-analysis of the Total FIM, motor FIM, cognitive FIM included in the literature, hoping to comprehensively evaluate the effect of rehabilitation treatment on glioma patients from all aspects. And then to clarify the role of rehabilitation in glioma.

2. Materials and methods

2.1. Literature search strategy

A range of electronic databases was searched: PubMed, Embase, Web of Science, Cochrane, and Medline (from January, 1990 to May 2020). The following keywords and MeSH terms were used: Glioma, Gliomas, Glial Cell Tumors, Glial Cell Tumor, Tumor, Glial Cell, Tumors, Glial Cell, Mixed Glioma, Glioma, Mixed, Gliomas, Mixed, Mixed Gliomas, Malignant Glioma, Glioma, Malignant, Gliomas, Malignant, Malignant Gliomas Rehabilitation, Habilitation, functional outcome, etc. We also performed a manual search to find other potential articles.

2.2. Selection criteria

1. The language of the article was English and the full text was available.
2. Only patients with gliomas were studied.
3. The study must provide data for the evaluation of complete function before and after rehabilitation treatment. The evaluation scale selected in this study is FIM, including Total FIM, Motor FIM, and Cognitive FIM.

2.3. Quality assessment

In this study, the data of the patients themselves before and after inclusion in the literature were extracted as control trials, which belonged to Non-randomized studies of the effects of interventions (NRSI). Risk of bias in non-randomized studies of interventions (ROBINS-I), a biased assessment tool, was selected to evaluate the quality of the literature. ROBINS-I was published in the British medical journal in October 2016.[11] it was used to evaluate the effect of the intervention in a variety of non-random research types, a total of 7 areas were evaluated, and finally, Low risk of bias, Moderate risk of bias, Critical risk of bias, No information was obtained.

2.4. Data extraction

Two researchers read the full text of the literature together and then extracted the data from the relevant literature independently. If there are differences, we can reach an agreement through discussion or consult third-party experts to solve them. The contents extracted from each study included the name of the first author, year of publication, sample size, sex, age, WHO grade, type of FIM, FIM score at admission, and discharge. For some missing data in the article, we contacted the author and tried our best to obtain the original data. If the original author did not reply, Then the formula was calculated from other data provided in the literature.[12–14]

2.5. Ethical review

This study was a systematic review and meta-analysis, so ethical approval was abandoned and it was not necessary.

2.6. Statistics

FIM results of the treated cases (i.e., after rehabilitation) with those of the control group (i.e., before rehabilitation) as continuous variables, were expressed by mean and standard deviation, and then meta-analysis was carried out by Stata software. Observe whether the shapes of the funnel were symmetrical to judge the publication bias and further Egger test to evaluate the publication bias of the included literature ($P \leq .05$ indicating that the publication bias is obvious). Q test and I^2 test were used to evaluate the heterogeneity. $I^2 \leq 50\%$ indicated that there was no obvious heterogeneity, then a fixed effect model was used; if $I^2 > 50\%$, the random effect model was used to analyze the heterogeneity, and subgroup analysis was used to analyze the possible sources of heterogeneity. Sensitivity analysis determined whether the results were robust by observing the changes in the overall effect value after the deletion of a single study. The FIM score was described by the combined SMD, 95%CI. Using the Z test, the difference was statistically significant ($P < .05$).

3. Results

Literature retrieval results: 1405 related literature were initially retrieved, and 4 more literature were added through other channels, and the remaining 1222 were left after excluding 187 repetitive literature. After reading the abstract, 891 articles were excluded, including reviews, magazine letters, case reports, and so on.118 articles that could not obtain the full text, 113 were Irrelevant studies, 17 articles with incomplete outcome data, and 14 articles without accurate information of glioma were excluded. Finally, 8 articles were included in the meta-analysis, the specific content of which is shown in Figure 1.

A total of 375 glioma patients were recorded in 8 literature,[15–22] including 201 males and 174 females. According to ROBINS-I, 5 articles were Moderate risk of bias, the other 3 were low risk of bias. In Julia's study, there were 2 groups of patients, including initial diagnosis of glioblastoma (iGBM) and recurrent glioblastoma (rGBM), so we included two groups of data.[22] Fu's study provided two sets of data for LGG and HGG respectively.[18] (Table 1)

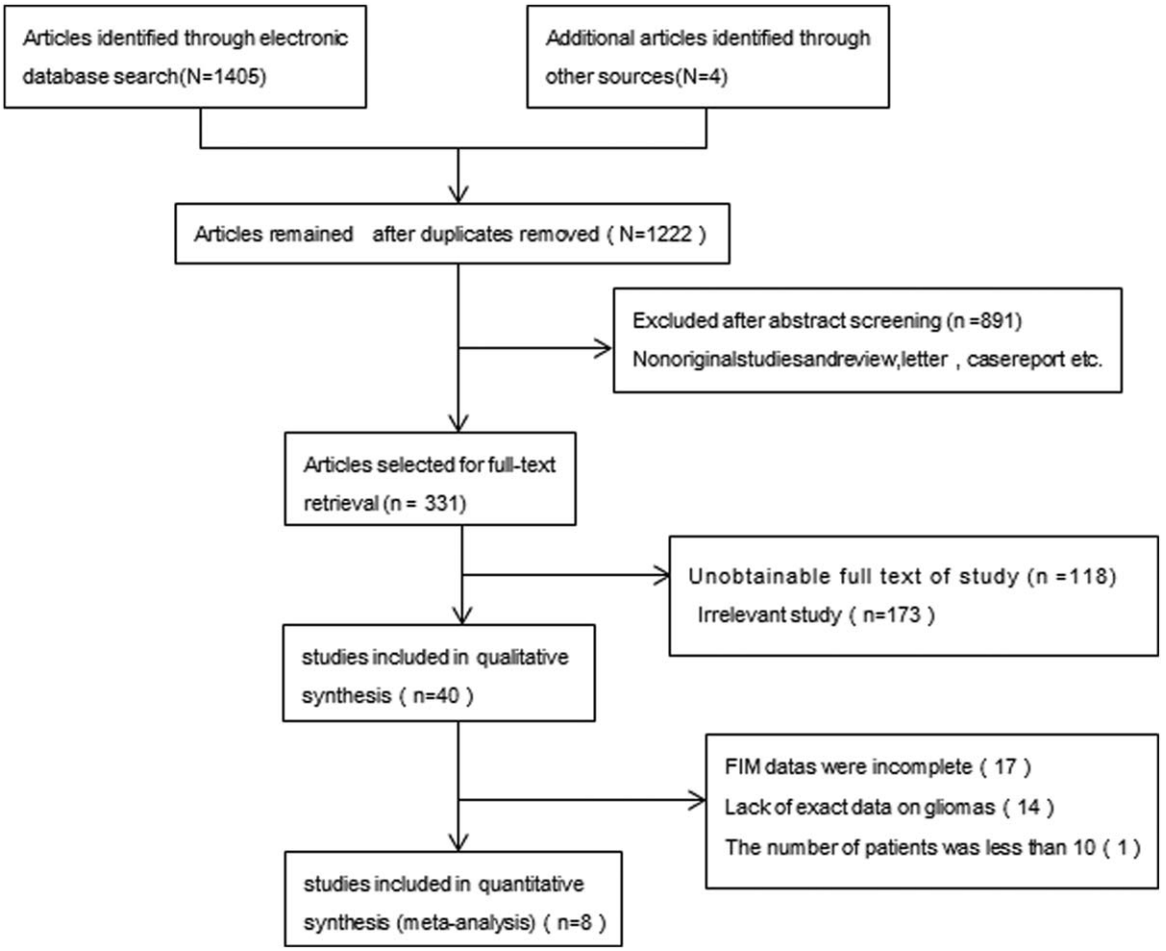

Figure 1. The flow chart shows the study selection procedure. Eight studies were included in this meta-analysis.

Table 1

Characteristics of Studies Included in Meta-analyses.

Study	Year	Glioma grade	Male/ Female	Age (year, mean)	Functional index	Admission number	Admission score mean ± SD	Discharge number	Discharge score mean ± SD
Christina	2001	WHO (I-IV)	18/16	51.2	FIM	34	FIM motor = 41.2 ± 13.5 FIM cogn = 21.1 ± 7.4	34	FIM motor = 55.7 ± 19.7 FIM cogn = 23.7 ± 6.2
Greenberg	2006	WHO (I-IV)	20/20	54.1	FIM	40	FIM total = 68.2 ± 24.2 FIM motor = 46.7 ± 30.9 FIM cogn = 13.0 ± 6.7	40	FIM total = 80.7 ± 33.6 FIM motor = 59.3 ± 36.6 FIM cogn = 13.3 ± 8.7
Vivien Tang	2008	WHO IV	8/10	61.4	FIM	18	FIM total = 85.3 ± 20.9 FIM motor = 52.7 ± 22.5 FIM cogn = 31.3 ± 4.8	18	FIM total = 92.0 ± 19.3 FIM motor = 66.3 ± 26.5 FIM cogn = 30.6 ± 7.2
Jack B.Fu	2010	WHO (I-II)	10/11	31.0	FIM	16 20	FIM total = 73.6 ± 17.3 FIM cogn = 25.1 ± 6.7	16 20	FIM total = 86.6 ± 21.1 FIM cogn = 26.7 ± 6.3
		WHO (III-IV)	12/9	31.7	FIM	15 18	FIM total = 64.9 ± 11.1 FIM cogn = 20.4 ± 8.6	15 18	FIM total = 86.6 ± 14.1 FIM cogn = 25.0 ± 7.0
Bartolo	2011	WHO IV	21/22	62.0	FIM	43	FIM total = 43.3 ± 16.5 FIM cogn = 20.9 ± 9.5	43	FIM total = 72.5 ± 24.2 FIM cogn = 26.6 ± 7.1
Fary Khan	2014	WHO (I-IV)	22/31	53.1	FIM	53	FIM motor = 68.0 ± 10.7 FIM cogn = 25.5 ± 4.2	41	FIM motor = 77.5 ± 14.2 FIM cogn = 30.5 ± 4.2
Pamela S	2014	WHO IV	58/37	62.5	FIM	95	FIM total = 54.2 ± 17.1 FIM cogn = 18.9 ± 6.8	95	FIM motor = 73.9 ± 20.0 FIM cogn = 17.7 ± 7.0
Julia M	2020	WHO IV (iGBM)	17/8	61.6	FIM	25	FIM total = 55.4 ± 14.5 FIM motor = 33.7 ± 11.5 FIM cogn = 19.5 ± 5.7	25	FIM total = 74.4 ± 23.4 FIM motor = 48.6 ± 18.6 FIM cogn = 22.6 ± 10.2
		WHO IV (rGBM)	15/10	60.8	FIM	25	FIM total = 54.8 ± 14.5 FIM motor = 33.9 ± 11.5 FIM cogn = 18.6 ± 5.7	25	FIM total = 78.5 ± 23.4 FIM motor = 52.2 ± 18.6 FIM cogn = 22.6 ± 10.2

FIM = functional independence measure, iGBM = initial glioblastoma, rGBM = recurrent glioblastoma.

3.1. Meta-analysis results

The effect of rehabilitation on total FIM of glioma patients, 6 of the 8 articles included recorded 8 sets of complete data. Julia and Fu's studies contain two sets of data each. The heterogeneity among the studies was obvious (heterogeneity test: $P = .016$, $I^2 = 59.4\%$), so the random effect model was used. The results showed that rehabilitation treatment had statistical significance in improving total FIM score SMD = 0.96, 95%CI = 0.66–1.26 ($P < .005$). The heterogeneity was large, but there were less than 10 articles, so there was no Meta-regression analysis. According to the subgroup analysis of glioma WHO grade, we found that the high-grade glioma (HGG) subgroup $I^2 = 45.9\%$ and the non-high-grade glioma (NHGG) including low-grade glioma group and mixed glioma group was heterogeneity $I^2 = 0.0\%$, indicating that the WHO grade of the tumor may be the source of heterogeneity. There were 5 articles providing 6 groups of data in motor FIM, 7 articles providing 9 groups of data in cognitive FIM. The study of Fu recorded the data of high-grade

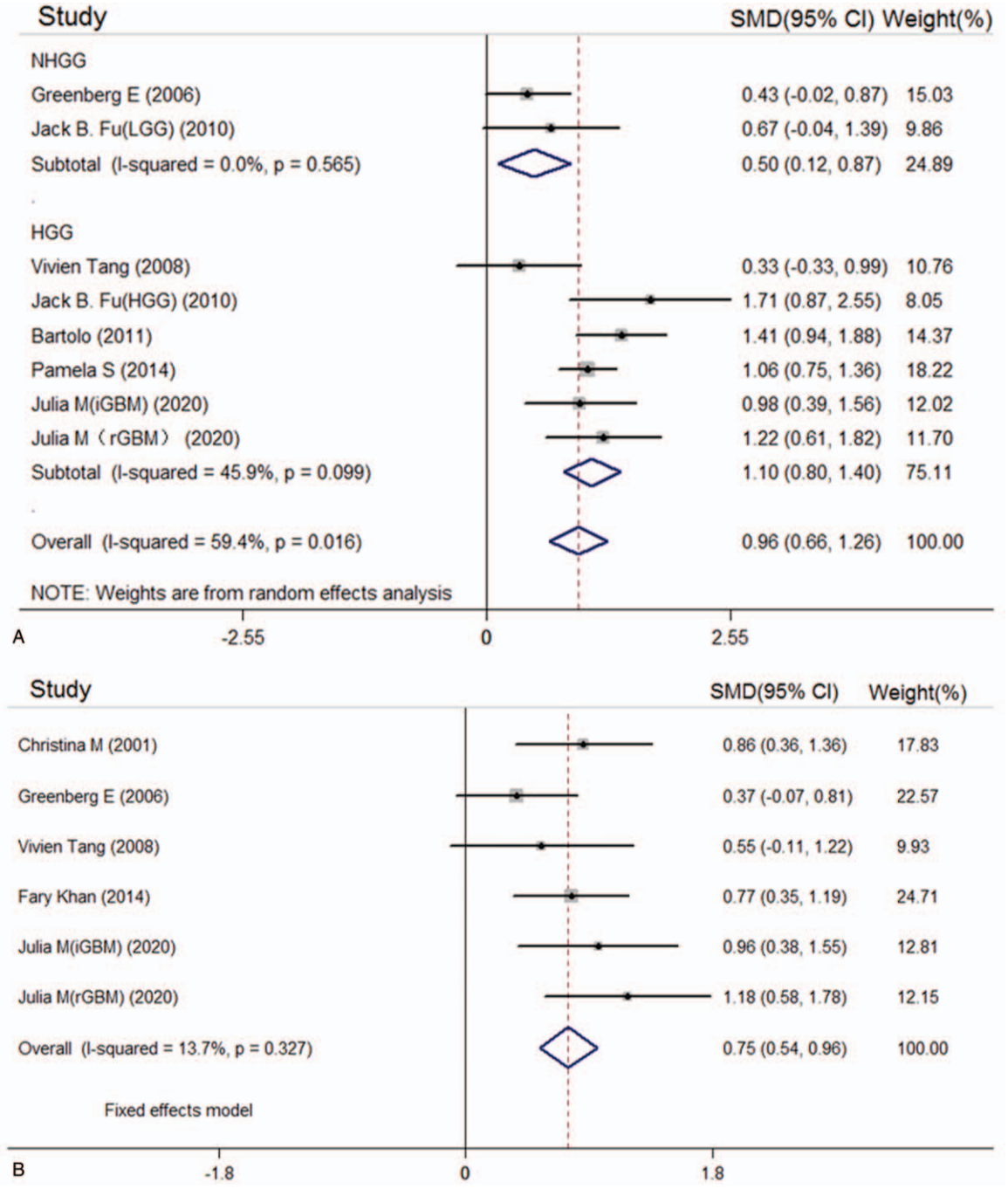

Figure 2. A. Forest plots for total FIM (HGG = high-grade gliomas; NHGG = non high-grade gliomas). B. Forest plots for motor FIM. C. Forest plots for cognitive FIM.

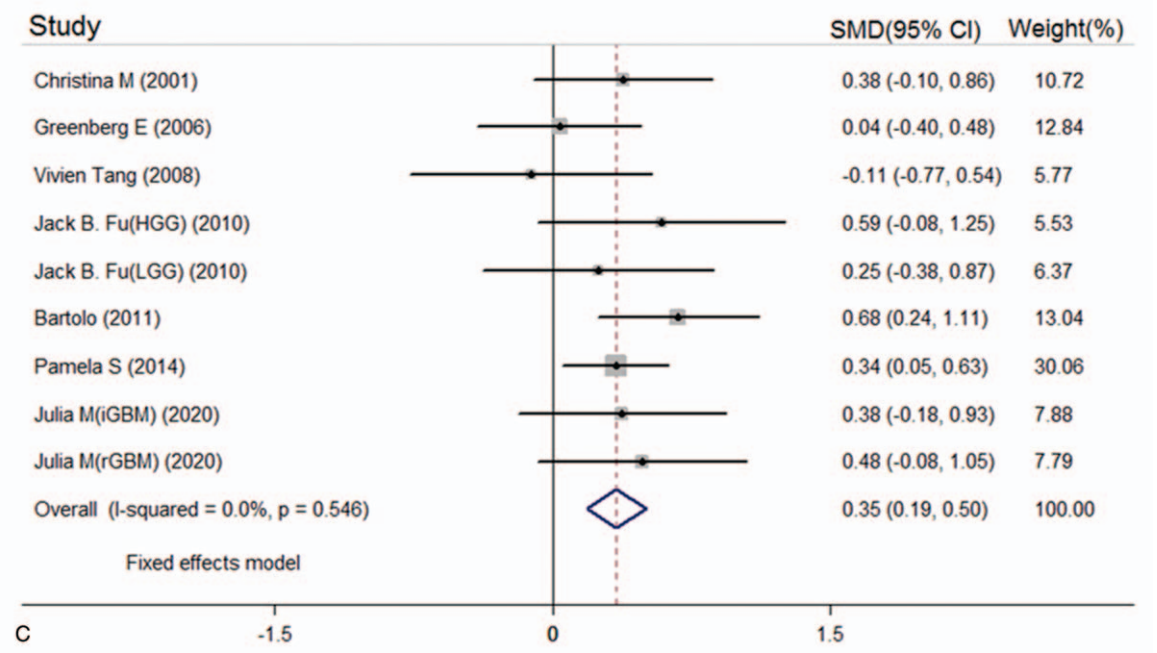

Figure 2. (Continued).

and low-grade glioma patients, while Julia recorded the data of primary GBM and recurrent GBM. The heterogeneity of motor and cognitive subscale of FIM were $I^2 = 13.7\%$, $P = .327$ and $I^2 = 0\%$, $P = .546$, respectively. Under the fixed-effect model, the Meta-analysis showed that the scores of motor FIM and cognitive FIM of rehabilitation treatment were SMD = 0.75, 95%CI = 0.54, 0.96 and SMD = 0.35 95%CI = 0.19, 0.50 respectively ($P < .05$). (Fig. 2A–C)

The shapes of the funnel were symmetrical (Fig. 3A–C). The results of the Egger test were shown in Table 2, indicating that there was no obvious publication bias in the three groups.

In the sensitivity analysis of 3 groups, no study was found to affect the total merger effect. (Fig. 4A–C)

4. Discussion

Gliomas are the most common brain tumor, accounting for 81% of brain malignant tumors, with an annual incidence of about 5.26 million. Glioma is a serious disease that endangers human health and affects the quality of life.[23] Gliomas originate from neuroectoderm, including astrocytoma, oligodendroglioma, ependymoma, mixed glioma, and so on. The treatment is combined with radiotherapy and chemotherapy after surgical resection. With the application of functional magnetic resonance imaging and neuronavigation, the development of fluorescent chromogenic technology and bioengineering technology, the improvement of radiotherapy and chemotherapy, and the rapid progress of new therapies such as gene therapy and immunotherapy, the treatment of glioma has also made great progress. However, due to the strong invasiveness of the tumor itself, high recurrence rate, and poor prognosis, the average survival time is only 14 to 16 months.[24]

Due to the destruction of the disease itself and the side effects of treatment, most patients with gliomas have varying degrees of functional and psychosocial disorders, daily activities and social participation are limited, and the quality of life is reduced. Proper rehabilitation can improve the function of most patients. The purpose of rehabilitation for cancer patients is to enable them to improve their motor ability based on adapting to their physical state and strive to achieve self-care and let them live independently.[25] At present, a large number of studies have confirmed that rehabilitation is of significance for the functional improvement of patients with brain tumors.[15,17–19,26–29] However, there are some differences in the research results. Fary Khan found that during the follow-up of the effect of rehabilitation treatment in patients with primary brain tumors, the gain of 'sphincter', and "cognitive" subscales was statistically significant, other subscales had no difference including motor.[21] Pamela found that although rehabilitation treatment could not significantly improve the survival time of patients, it could improve the prognosis of most GBM patients, mainly in the field of the motor, but the improvement of disturbance of cognition and sphincter control was not significant.[20] Tang found that patients with Glioblastoma multiforme (GBM) and intracranial metastases tended to show longer survival if their FIM scores increased significantly after rehabilitation.[17] It can be seen that rehabilitation therapy has different views on the improvement of disturbance of cognition and survival time of glioma. Studies on cognition, have shown that rehabilitation therapy was less efficient for glioma patients than stroke patients, because stroke patients had more damage to this area, so they would get better gain in this area.[19] Cognitive impairment was not conducive to the rehabilitation of patients, the mental state of admission was poor, the rehabilitation effect was also poor, there was a significant positive correlation.[30,31] Besides, there were individual differences in the degree of patients' response to rehabilitation intervention. For the selection of people with rehabilitation

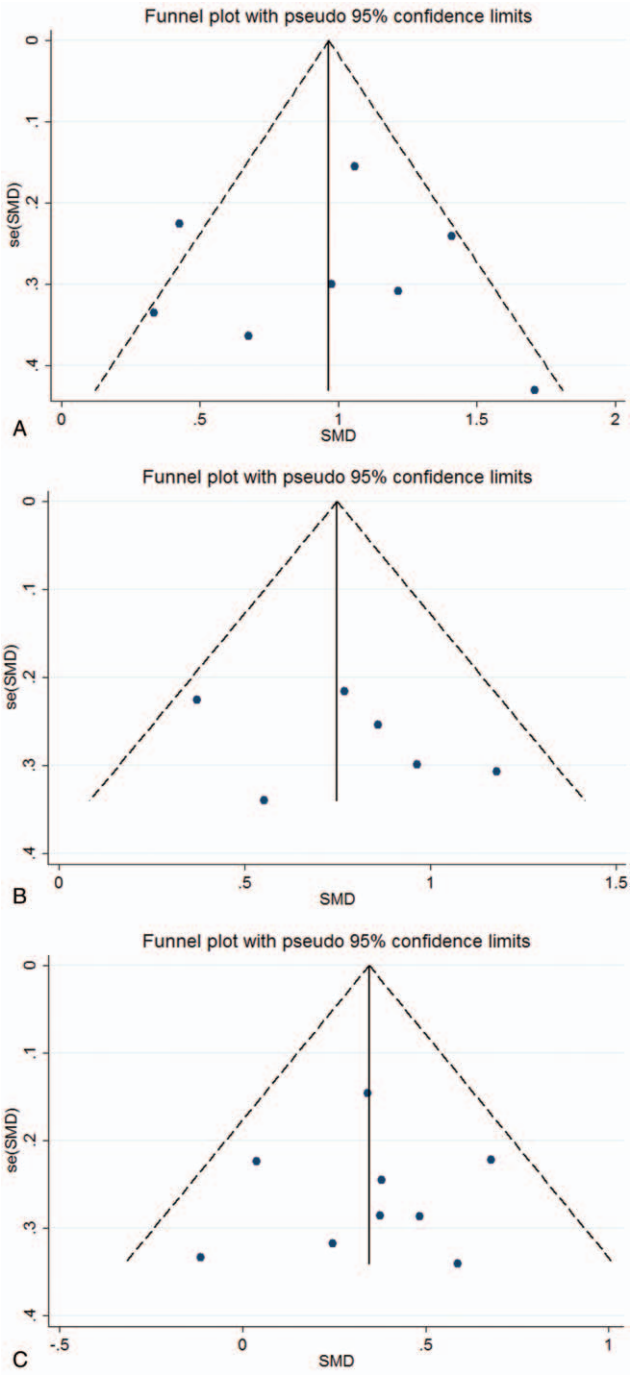

Figure 3. A. The shape of the funnel in total FIM group. B. The shape of the funnel in the motor FIM group. C. The shape of the funnel in the cognitive FIM group.

Table 2

Egger test for publication bias.

Type of test	Total FIM	Motor FIM	Cognitive FIM
Egger test (P)	$P = .985$	$P = .418$	$P = .855$

effect, researchers had also conducted some studies, the degree of fatigue was an independent risk factor affecting the prognosis,[32] and disturbance of cognition was an independent risk factor affecting the survival of patients.[33] The evidence suggested that exercise behavior was an independent predictor of survival in patients with high-grade gliomas,[34] but there was still a lack of conclusive evidence that improved mobility could improve patient survival. Some hypotheses could help explain why improving patients' exercise ability to improve patient survival. For example, the motor could reduce the risk of complications such as deep venous thrombosis and pulmonary infection; there was evidence that exercise could improve the tumor microenvironment by regulating cytokines.[34]

In this study, the results show that rehabilitation treatment could significantly improve the quality of life of glioma patients, including the improvement of motor and cognition. Besides, this study used the method of the subgroup to analyze the source of heterogeneity in the total FIM group and concluded that WHO classification was the source of heterogeneity. It is generally believed that high-grade gliomas are seriously invasive and rehabilitation therapy may not be effective in improving neurological function, but some studies have pointed out that the destruction of brain tissue is not an important factor affecting the effect of rehabilitation.[35] Fu's study on the rehabilitation effect of different grades of gliomas found that in the high and low-grade gliomas, the functional improvement after rehabilitation treatment was statistically significant, and rehabilitation treatment could make high-grade glioma patients get higher neurological function gain, but their hospital stay was significantly longer than that of low-grade glioma patients.[18] Piil pointed out that rehabilitation was beneficial to improve patients' neurological prognosis, memory, and stress relief, and suggested that clinical guidelines for rehabilitation be developed for patients with high-grade gliomas.[9] Our result analysis also showed that even in the high-grade glioma group, the FIM score was significantly improved after rehabilitation.

There are some limitations in this study; first of all, because ROBINS-I was published recently and the operation is complex, there is no convenient software for evaluation, so it is difficult for beginners to make a completely correct evaluation for inclusion in the literature. Second, we chose a traditional method function independence measurement, which may not be comprehensive enough to evaluate the functional prognosis of patients. In some studies,[21,26] the exercise rating scale (MAS), Stroke posture rating scale (PASS) and Berg balance scale (BBS), depression, anxiety stress scale, perceived impact problem profile and cancer rehabilitation evaluation system, Massachusetts General Hospital Functional Ambulation Classification, Standing Balance score, Sitting Balance score, Hauser Index and so on were added to evaluate the functional recovery more accurately and comprehensively.[19] Our study has not yet determined whether rehabilitation can prolong the survival of glioma patients.

5. Conclusion

The published studies show that rehabilitation therapy can improve the functional prognosis and quality of life of glioma patients. More attention should be paid to the therapeutic value of rehabilitation for glioma patients in the future.

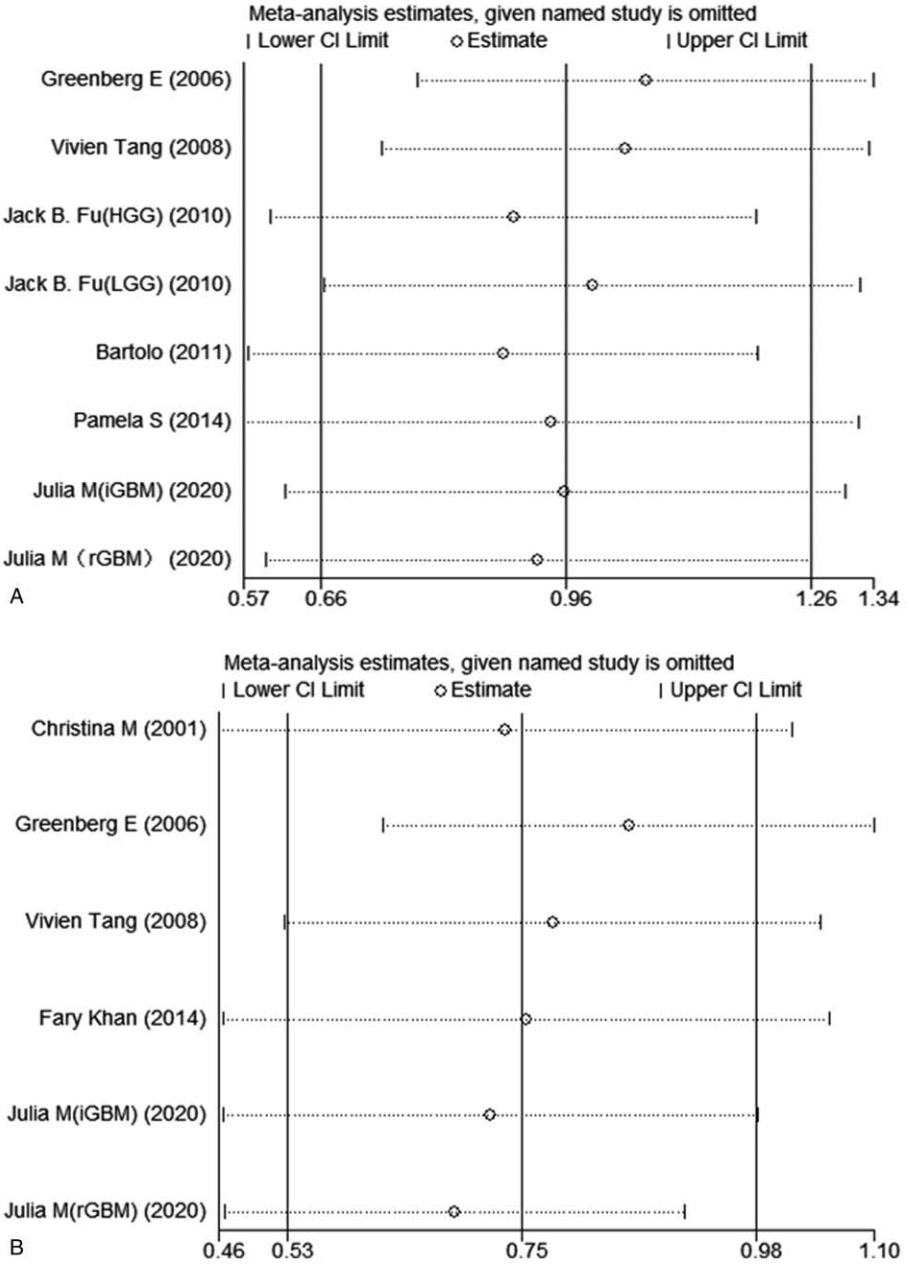

Figure 4. A. The influence of a single study on the overall effect of total FIM. B. The influence of a single study on the overall effect of motor FIM. C. The influence of a single study on the overall effect of cognitive FIM.

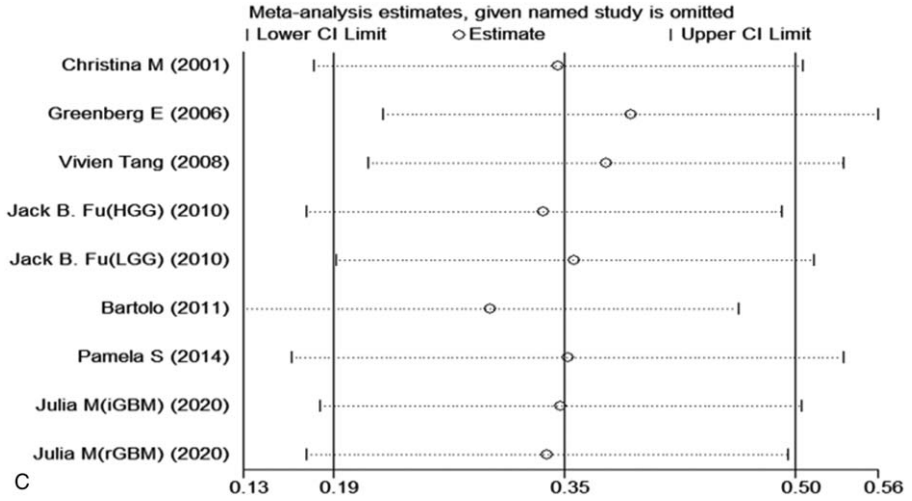

Figure 4. (Continued).

Author contributions

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Funding acquisition: Ninghui Zhao
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Supervision: Ninghui Zhao
Writing – original draft: Kai Zhao
Writing – review & editing: Kai Zhao, Ninghui Zhao

References

[1] Ostrom QT, Gittleman H, Truitt G, et al. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2011-2015. Neuro Oncol 2018;20:v1–86.
[2] Louis DN, Perry A, Reifenberger G, et al. The 2016 World Health Organization classification of tumors of the central nervous system: a summary. Acta Neuropathol 2016;131:803–20.
[3] Brandes AA, Tosoni A, Franceschi E, et al. Recurrence pattern after temozolomide concomitant with and adjuvant to radiotherapy in newly diagnosed patients with glioblastoma: correlation With MGMT promoter methylation status. J Clin Oncol 2009;27:1275–9.
[4] Nabors LB, Portnow J, Ammirati M, et al. NCCN guidelines insights: central nervous system cancers, Version 1.2017. J Natl Compr Canc Netw 2017;15:1331–45.
[5] Keith RA, Granger CV, Hamilton BB, et al. The functional independence measure: a new tool for rehabilitation. Adv Clin Rehabil 1987;1:6–18.
[6] Hamilton BB, Laughlin JA, Fiedler RC, et al. Interrater reliability of the 7-level functional independence measure (FIM). Scand J Rehabil Med 1994;26:115–9.
[7] Formica V, Del Monte G, Giacchetti I, et al. Rehabilitation in neuro-oncology: a meta-analysis of published data and a mono-institutional experience. Integr Cancer Ther 2010;10:119–26.
[8] Pace A, Dirven L, Koekkoek JAF, et al. European Association for Neuro-Oncology (EANO) guidelines for palliative care in adults with glioma. Lancet Oncol 2017;18:e330–40.
[9] Piil K, Juhler M, Jakobsen J, et al. Controlled rehabilitative and supportive care intervention trials in patients with high-grade gliomas and their caregivers: a systematic review. Bmj Support Palliat 2016;6:27–34.
[10] Catt S, Chalmers A, Fallowfield L. Psychosocial and supportive-care needs in high-grade glioma. Lancet Oncol 2008;9:884–91.
[11] Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ (Clinical research ed) 2016;355:i4919.
[12] Luo D, Wan X, Liu J, et al. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. Stat Methods Med Res 2018;27:1785–805.
[13] Wan X, Wang W, Liu J, et al. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. Bmc Med Res Methodol 2014;14:135.
[14] Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. Bmc Med Res Methodol 2005;5:13.
[15] Marciniak CM, Sliwa JA, Heinemann AW, et al. Functional outcomes of persons with brain tumors after inpatient rehabilitation. Arch Phys Med Rehab 2001;82:457–63.
[16] Greenberg E, Treger I, Ring H. Rehabilitation outcomes in patients with brain tumors and acute stroke: comparative study of inpatient rehabilitation. Am J Phys Med Rehab 2006;85:568–73.
[17] Tang V, Rathbone M, Park Dorsay J, et al. Rehabilitation in primary and metastatic brain tumours: impact of functional outcomes on survival. J Neurol 2008;255:820–7.
[18] Fu JB, Parsons HA, Shin KY, et al. Comparison of functional outcomes in low- and high-grade astrocytoma rehabilitation inpatients. Am J Phys Med Rehabil 2010;89:205–12.
[19] Bartolo M, Zucchella C, Pace A, et al. Early rehabilitation after surgery improves functional outcome in inpatients with brain tumours. J Neuro-Oncol 2012;107:537–44.
[20] Roberts Pamela S, Nuño M, Sherman D, et al. The impact of inpatient rehabilitation on function and survival of newly diagnosed patients with glioblastoma. Pm&R 2014;6:514–21.
[21] Khan F, Amatya B, Drummond K, et al. Effectiveness of integrated multidisciplinary rehabilitation in primary brain cancer survivors in an Australian community cohort: a controlled clinical trial. J Rehabil Med 2014;46:754–60.
[22] Reilly Julia M, Gundersen Alexandra I, Silver Julie K, et al. A comparison of functional outcomes between patients admitted to inpatient rehabilitation after initial diagnosis versus recurrence of glioblastoma multiforme. PM R 2020;10:975–83.
[23] Ostrom QT, Bauchet L, Davis FG, et al. The epidemiology of glioma in adults: a "state of the science" review. Neuro-Oncol 2014;16:896–913.
[24] Silginer M, Weller M, Stupp R, et al. Biological activity of tumor-treating fields in preclinical glioma models. Cell Death Dis 2017;8:e2753.
[25] National Council for Hospice and Specialist Palliative Care ServicesVoluntary euthanasia: the council's view. Nurs Ethics 1998;5:371–4.
[26] Geler-Kulcu D, Gulsen G, Buyukbaba E, et al. Functional recovery of patients with brain tumor or acute stroke after rehabilitation: a comparative study. J Clin Neurosci 2009;16:74–8.
[27] Huang ME, Cifu DX, Keyser-Marcus L. Functional outcome after brain tumor and acute stroke: a comparative analysis. Arch Phys Med Rehab 1998;79:1386–90.

[28] O'Dell MW, Barr K, Spanier D, et al. Functional outcome of inpatient rehabilitation in persons with brain tumors. Arch Phys Med Rehab 1998;79:1530–4.
[29] Bell KR, O'Dell MW, Barr K, et al. Rehabilitation of the patient with brain tumor. Arch Phys Med Rehabil 1998;79:S37–46.
[30] Barker-Collo S, Feigin V. The impact of neuropsychological deficits on functional stroke outcomes. Neuropsychol Rev 2006; 16:53–64.
[31] Toglia J, Fitzgerald KA, O'Dell MW, et al. The mini-mental state examination and montreal cognitive assessment in persons with mild subacute stroke: relationship to functional outcome. Arch Phys Med Rehab 2011;92:792–8.
[32] Peters KB, Coan AD, West MJ, et al. Prognostic importance of quality of life and fatigue in patients with recurrent high-grade glioma. Neuro Oncol 2011;13(suppl 3):iii121–6.
[33] Meyers CA, Hess KR, Yung WK, et al. Cognitive function as a predictor of survival in patients with recurrent malignant glioma. J Clin Oncol 2000;18:646–50.
[34] Ruden E, Reardon DA, Coan AD, et al. Exercise behavior, functional capacity, and survival in adults with malignant recurrent glioma. J Clin Oncol 2011;29:2918–23.
[35] Huang ME, Wartella J, Kreutzer J, et al. Functional outcomes and quality of life in patients with brain tumours: a review of the literature. Brain Injury 2001;15:843–56.