International Journal of Nursing and Health Care Research

OPEN ACCESS

Li H, et al. Int J Nurs Health Care Res 6: 1417

www.doi.org/10.29011/2688-9501.101417

www.gavinpublishers.com

GAVIN PUBLISHERS

Review Article

Prognostic Significance of MicroRNAs in Medulloblastoma: A Systematic Review and Meta-Analysis

Haima Li[1#], Jian Wen[2#], Dongdong Li[3], Ruen Liu[1,4*]

[1]People's Clinical Medical College Affiliated Nanchang University, Department of Neurosurgery, Jiangxi Provincial People's Hospital, Nanchang, 330006, People's Republic of China.

[2]Department of Orthopedics, Jiangxi Provincial People's Hospital, Nanchang, 330006, People's Republic of China

[3]Department of Pulmonary and Critical Care Medicine, Jiangxi Provincial People's Hospital, Nanchang, 330006, People's Republic of China

[4]Department of Neurosurgery, Peking University People's Hospital, 11th Xizhimen South St., Beijing 100044, People's Republic of China

[*]**Corresponding author:** Ruen Liu, Department of Neurosurgery, Jiangxi Provincial People's Hospital, Nanchang, 330006, People's Republic of China

Citation: Li H, Wen J, Li D, Liu R (2023) Prognostic Significance of MicroRNAs in Medulloblastoma: A Systematic Review and Meta-Analysis. Int J Nurs Health Care Res 6:1417. DOI: 10.29011/2688-9501.101417

Received Date: 14 April, 2023; **Accepted Date:** 22 April, 2023; **Published Date:** 26 April, 2023

Abstract

Objective: Medulloblastoma (MB) is the most common malignant brain tumor in children with high mortality. Therefore, it is essential to identify a reliable and comprehensive prognostic biomarker. Thus, we intend to investigate the relationship between microRNAs (miRNAs) and the prognosis of patients with MB. **Design:** Systematic review with meta-analysis. **Methods:** 4 databases were searched, including PubMed, Web of Science, Embase, and Cochrane Library. All the English publications until 1 November 2022 will be searched without any restriction of countries or article type. The retrieved articles are carefully screened according to the selection criteria. In meta-analysis studies, hazard ratio (HR) and 95% confidence interval (CI) of patient survival outcomes were used to explore the relationship between overall survival (OS) and the expression of miRNAs. **Results:** The expressions of 10 miRNAs in 855 MB patients from 6 studies were studied to explore the association between the predictive role of miRNAs and survival outcomes. The estimated overall pooled effect of HR was 0.57 (95% CI: 0.33-0.99), suggesting that miRNA marker expression reduced the risk of death in patients with MB. Subgroup analyses showed that tumor miRNA level prognostic efficacy for better OS was stronger in MB patients of the four molecular subsets (HR：0.37; 95% CI：0.19-0.73； P=0.670) than those with Group3 and Group4 molecular subsets only (HR：0.79; 95% CI：0.29-2.16； P=0.024). **Conclusions:** Our analysis indicates that high miRNAs expression in MB patients may associate with the better OS. Thereby, the expression of miRNAs in MB patients may act as a potential biomarker for prognosis.

Keywords: Medulloblastoma; miRNAs; Biomarkers; Prognosis; Survival; Systematic review; Meta-analysis

Introduction

Medulloblastoma (MB) is one of the most malignant neuroepithelial tumors of the central nervous system in children [1]. According to current consensus, MB has four core molecular subsets: WNT, SHH, Group 3and Group 4 [2], which differ not only distinct in their underlying genetic changes but also differ in clinical characteristics like age, gender-related incidence, the incidence of metastasis, and overall survival rates [3,4]. Standard treatment for MB includes surgery, adjuvant chemotherapy, and craniospinal irradiation; aggressive interventions lead to prolonged sequelae and poor quality of life [5]. Approximately 75% of pediatric MB patient's recurrence within a few years [6]. Therefore, the treatment of MB remains a challenge in pediatric oncology. Baliga S et al. [7] Studies indicate that the 10-year OS for standard and intermediate/high-risk patients was 86.9% and 68.9%, respectively. Despite progress in the treatments, approximately 30% of MB children will die from current treatment strategies [8], so reducing mortality and morbidity is urgent.

MicroRNAs (miRNAs) are small non-coding RNA molecules that regulate gene expression at the post-transcriptional level [9]. MiRNAs bind to complementary sequences in the 3′ untranslated areas of numerous target genes, usually leading to their silencing [10]. Each miRNA is thought to target hundreds of genes. It has been revealed as a critical regulator during normal tissues and cancers [11,12]. More evidence indicates that miRNA expression disorder plays a vital role in pathogenesis, cancer progression and response to treatment [13]. Consequently, they have been extensively studied as diagnostic and prognostic cancer biomarkers in recent years [14,15]. These efforts aim to find new molecular markers and targeted therapies to achieve early diagnosis and better treatment. MiRNAs are associated with prognosis in patients with MB, but the conclusions have been inconsistent. A previous systematic review explored the relationship between miRNA and prediction in MB patients. However, only two studies were included, thus lacking relevant data. The survival outcome of tumor patients was not quantitatively analyzed, and miRNA was not found to have guiding significance for the prognosis of pediatric MB patients. This systematic review and meta-analysis aim to clarify the relationship between miRNA and the prognosis of patients with MB through a systematic and comprehensive qualitative and quantitative analysis of existing original studies.

Materials and Methods

Guidelines and Registration

The Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) criteria were used to perform the study [16]. This study is based on the PROSPERO that was registered under the ID CRD42021289410.

Section and Topic	Item #	Checklist item	Location where item is reported
Title			
Title	1	Identify the report as a systematic review.	1
Abstract			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2-3
Introduction			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	4
Methods			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5
Information sources	6	Specify all databases, registers, websites, organizations, reference lists and other sources searched or consulted to identify studies. Specify thedate when each source was last searched or consulted.	5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	5-6

Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each recordand each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	6-7
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	6-7
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in eachstudy were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	7
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	7
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	7
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	7
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics andcomparing against the planned groups for each synthesis (item #5)).	8
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or dataconversions.	8
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	8
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe themodel(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	8
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	8
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	8
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	8
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	8

Section andTopic	**Item #**	**Checklist item**	**Location where itemis reported**
Results			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included inthe review, ideally using a flow diagram.	8
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	8
Study characteristics	17	Cite each included study and present its characteristics.	8-10

Risk of bias in studies	18	Present assessments of risk of bias for each included study.	8
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision(e.g. confidence/credible interval), ideally using structured tables or plots.	8
Results of syntheses	20a	For each synthesis, briefly summarize the characteristics and risk of bias among contributing studies.	9-10
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g.confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	9-10
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	9-10
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	9-10
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	11
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	11
Discussion			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	12-14
	23b	Discuss any limitations of the evidence included in the review.	12-14
	23c	Discuss any limitations of the review processes used.	12-14
	23d	Discuss implications of the results for practice, policy, and future research.	12-14
Other Information			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	5
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	5
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	5
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	15
Competing interests	26	Declare any competing interests of review authors.	15
Availability of data, code andother materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	--

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, et al. (2022) The PRISMA 2022 statement: an updated guideline for reporting systematic reviews. BMJ 372: n71.

Search Strategy

We will search for the articles in 4 electronic databases including PubMed, Web of Science, Embase and Cochrane Library. Searches were conducted using medical subjective headings (MeSH) and free words. All the English publications until 1 November 2022 will be searched without any restriction of countries or article type. The reference lists of retrieved articles were also checked for relevant literatures. The searches typically included 3 key terms "Medulloblastoma," "MicroRNAs," and "Prognosis." We searched PubMed using the following strategy: ((("Medulloblastoma"[Mesh]) OR ((((((((((((((((((((Medulloblastoma) OR (Medulloblastomas)) OR (Melanocytic Medulloblastoma)) OR (Medulloblastoma, Melanocytic)) OR (Medulloblastomas, Melanocytic)) OR (Melanocytic Medulloblastomas)) OR (Medulloblastoma, Childhood)) OR (Childhood Medulloblastoma)) OR (Childhood Medulloblastomas)) OR (Medulloblastomas, Childhood)) OR (Medullomyoblastoma)) OR (Medullomyoblastomas)) OR (Arachnoidal Cerebellar Sarcoma, Circumscribed)) OR (Sarcoma, Cerebellar, Circumscribed Arachnoidal)) OR (Medulloblastoma, Desmoplastic)) OR (Desmoplastic Medulloblastoma)) OR (Desmoplastic Medulloblastomas)) OR (Medulloblastomas, Desmoplastic)) OR (Medulloblastoma, Adult)) OR (Adult Medulloblastoma)) OR (Adult Medulloblastomas)) OR (Medulloblastomas, Adult))) AND (("MicroRNAs"[Mesh]) OR ((((((((((((((((MicroRNA) OR (miRNAs)) OR (Micro RNA)) OR (RNA, Micro)) OR (miRNA)) OR (Primary MicroRNA)) OR (MicroRNA, Primary)) OR (Primary miRNA)) OR (miRNA, Primary)) OR (pri-miRNA)) OR (pri miRNA)) OR (RNA, Small Temporal)) OR (Temporal RNA, Small)) OR (stRNA)) OR (Small Temporal RNA)) OR (pre-miRNA)) OR (pre miRNA)))) AND (("Prognosis"[Mesh]) OR (((((Prognoses) OR (Prognostic Factors)) OR (Factor, Prognostic)) OR (Factors, Prognostic)) OR (Prognostic Factor))).

Inclusion Criteria

- Full-text articles in English; including patients with histopathologically diagnosed MB.
- Measured the expression of miRNAs in tumor tissue, serum, or plasma, as well as the survival prognosis of patients.
- Reported the survival curves for overall survival (OS) or disease-free survival (DFS) or cause-specific survival (CSS) or recurrence-free survival (RFS) with or without the hazard ratio (HR) and its 95% confidence intervals (CIs).

Exclusion Criteria

- Lack of patient survival data.
- Studies that included non-human data.
- Reviews, preclinical studies, and duplicate reports were excluded.

Data Extraction and Quality Assessment

Two authors independently performed database search, data extraction, and quality evaluation. The discussion will resolve any disagreement until consensus is reached or consulting a third author. Including miRNAs studied, first author's names, publication year, study location, platform, source of a clinical sample, sample size, study design, metastasis or not, result, survival data (HR and 95%CI), and Newcastle-Ottawa Scale (NOS). If HRs and 95% CIs were not provided directly in the included articles, we estimated them from Kaplan-Meier survival curves with methods described by Tierney et al. using Engauge Digitizer version 4.1 [17]. Two reviewers systematically evaluated the quality of included studies according to NOS. The higher the score, the better the quality of the essay. A joint review solved disagreement.

Statistical Analysis

Meta-analyses were performed to summarize the association between miRNA expression and OS in MB patients. HR and the corresponding standard errors were estimated from 95% CIs or p-values and were logarithmically transformed to obtain a normal distribution. The Cochrane's Q test and I^2 test were performed to evaluate the heterogeneity [18]; an $I^2 > 50\%$ indicates significant heterogeneity. A random-effect model was applied if substantial heterogeneity was detected; otherwise, a fixed-effect model was applied. Egger's test and funnel plot symmetry were used to assess the risk of publication bias. Sensitivity analyses were performed to evaluate the stability of the results by omitting each of the included studies one at a time [19]. The STATA software (Version 16.0; Stata Corporation, TX, USA) was used for the statistical analyses.

Results

Study Selection

As shown in (Figure 1), the initial search resulted in 152 articles from PubMed (n = 38) and the Web of Science (n = 27), Embase (n = 87). After excluding, studies unrelated to our systematic review and meta-analysis according to the exclusion criteria, 22 articles were considered to be screened. The full text of the 22 articles was reviewed, and 8 of them did not measure miRNAs expression, non-human sample studies (n = 2), and the full text of the studies could not be obtained (n = 2). Full-text studies of qualitative synthesis according to inclusion criteria (n = 10), 4 of which lacked relevant data. Finally, 10 studies were included for systematic analysis, of which 6 papers could be further meta-analyzed.

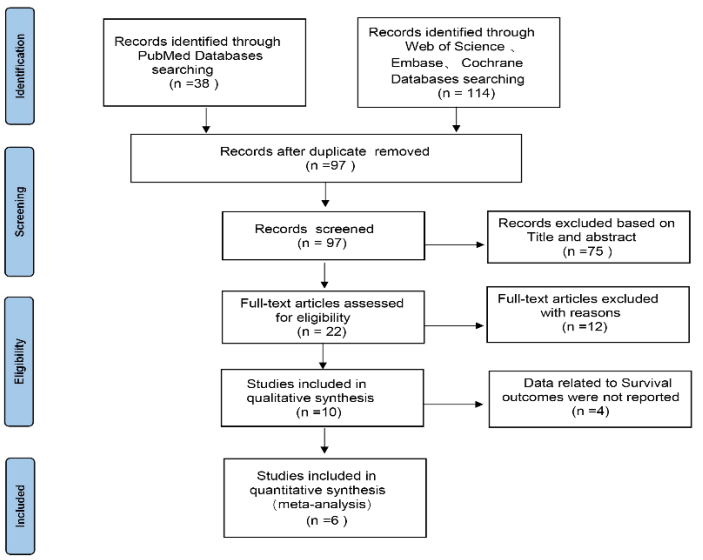

Figure 1: Flow diagram of the study selection for the present meta-analysis.

Study Characteristics

The characteristics of the included studies are shown in (Table 1). Overall, the meta-analysis included 855 MB patients from 6 studies in China, Switzerland, Brazil, and India. All articles are published in English. Since the 2 studies included 2 independent miRNAs, respectively, and 1 study included 3 independent miRNAs, the relationship between miRNA expression in tumors and OS prognosis during follow-up was assessed in the article, so these were included independently. Finally, 10 miRNAs from 6 studies were included in the meta-analysis. The samples included ranged from 32 to 470. 6 miRNAs in the 4 studies included 4 molecular subsets in MB patients. In comparison, 4 miRNAs in the other 2 studies included Group 3 and Group 4 patients in the molecular subsets of MB. No cutoff value was mentioned in the 2 studies, and the median miRNA expression value was used as a cutoff value in the remaining 4 studies. 5 studies only used QRT-PCR for miRNA quantification, and 2 studies used both QRT-PCR and microarray analysis, and the outcome of OS was reported during follow-up. The NOS ranged from 6 to 8 in the included studies.

MicroRNAs	First author	Year	Country	platform	Sample	Number	Study design	Metastasis	Result	HR(H/L)	95%CI	NOS
miR-182	Kuader R et al.-set 1	2013	India	qRT-PCR Microarray	Tissue	37	R	NA	OS	3.527	1.045-11.9	6
miR-592	Kuader R et al.-set 2	2013	India	qRT-PCR Microarray	Tissue	37	R	NA	OS	0.39	0.03-5.32	6
miR-9	Fiaschetti G et al.	2014	Switzerland	qRT-PCR	Tissue	34	R	NA	OS	0.5	0.04-5.96	6
miR-495	Wang et al.	2015	China	qRT-PCR	Tissue	62	R	M0 51	OS	0.26	0.08-0.85	8
miR-100	Pezuk JA et al. -set 1	2016	Brazil	qRT-PCR	Tissue	32	R	NA	OS	1.16	0.14-9.94	7
miR-126	Pezuk JA et al.-set 2	2016	Brazil	qRT-PCR	Tissue	32	R	NA	OS	1.26	0.11-14.87	7
miR-219	Pezuk JA et al.-set 3	2016	Brazil	qRT-PCR	Tissue	32	R	NA	OS	0.86	0.03-22.43	7
miR-204	Bharambe SH et al.-set 1	2019	India	qRT-PCR	Tissue	144	R	M0 78	OS	0.53	0.17-1.67	7
miR-204	Bharambe SH et al.-set 2	2019	India	qRT-PCR	Tissue	470	R	M0 220	OS	0.46	0.28-0.74	7
miR-137	Ji et al.	2021	China	qRT-PCR	Tissue	76	R	M0 45	OS	0.25	0.08-0.73	8
NOS: Newcastle-Ottawa scale; OS: Overall Survival; HR: Hazard Ratio; M0:Metastasis; M+:NOT Metastasis; NA: Not Available												

Table 1: The main features of the studies included in the systematic review and meta-analysis.

Comprehensive Meta-Analysis

In 855 MB patients from 6 included studies, the prognostic significance of 10 miRNAs was investigated (Figure 2). 7 miRNAs were upregulated, while 3 miRNAs were downregulated. The overall pooled effect estimates of HR for (upregulated and down-regulated) miRNA expressions were 0.57, with a 95 percent CI of 0.33 -0.99, meaning that miRNAs expression reduced the risk of death in MB patients when using a fixed-effect model.

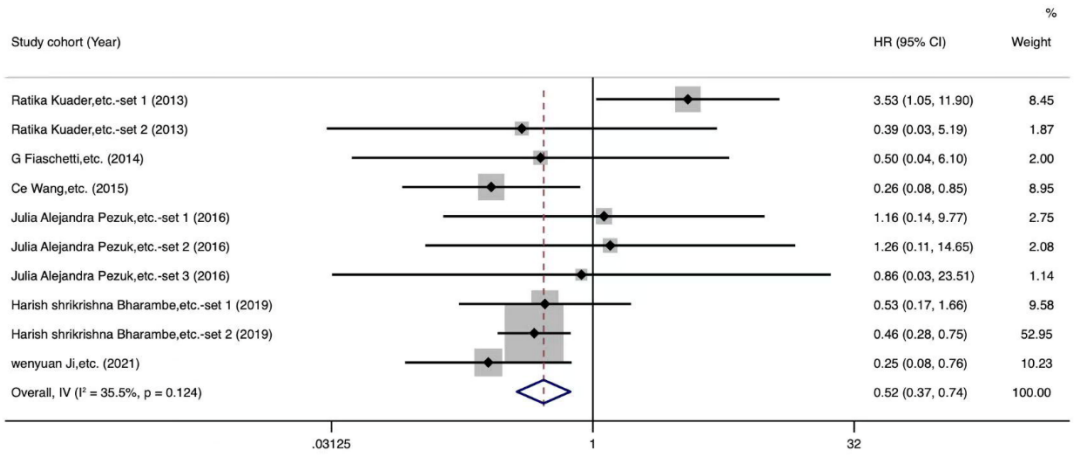

Figure 2: Forest plots for the meta-analysis of the prognostic efficacy of tumor miRNAs for OS in patients with MB.

Subgroups Analysis

Subgroup analyses showed that prognostic efficacy of tumor miRNA level for better OS was stronger in MB patients of the four molecular subsets (HR：0.37; 95% CI：0.19-0.73；P=0.670) than those with Group3 and Group4 molecular subsets only (HR：0.79; 95% CI：0.29-2.16；P=0.024). The prognostic efficacy of tumor miRNA level was consistent in Asians (HR: 0.53; 95% CI: 0.26-1.08; p = 0.0026) and non - Asians patients with MB (HR: 0.92; 95% CI: 0.26-3.22; p = 0.953). The detailed results are shown in (Figure 3).

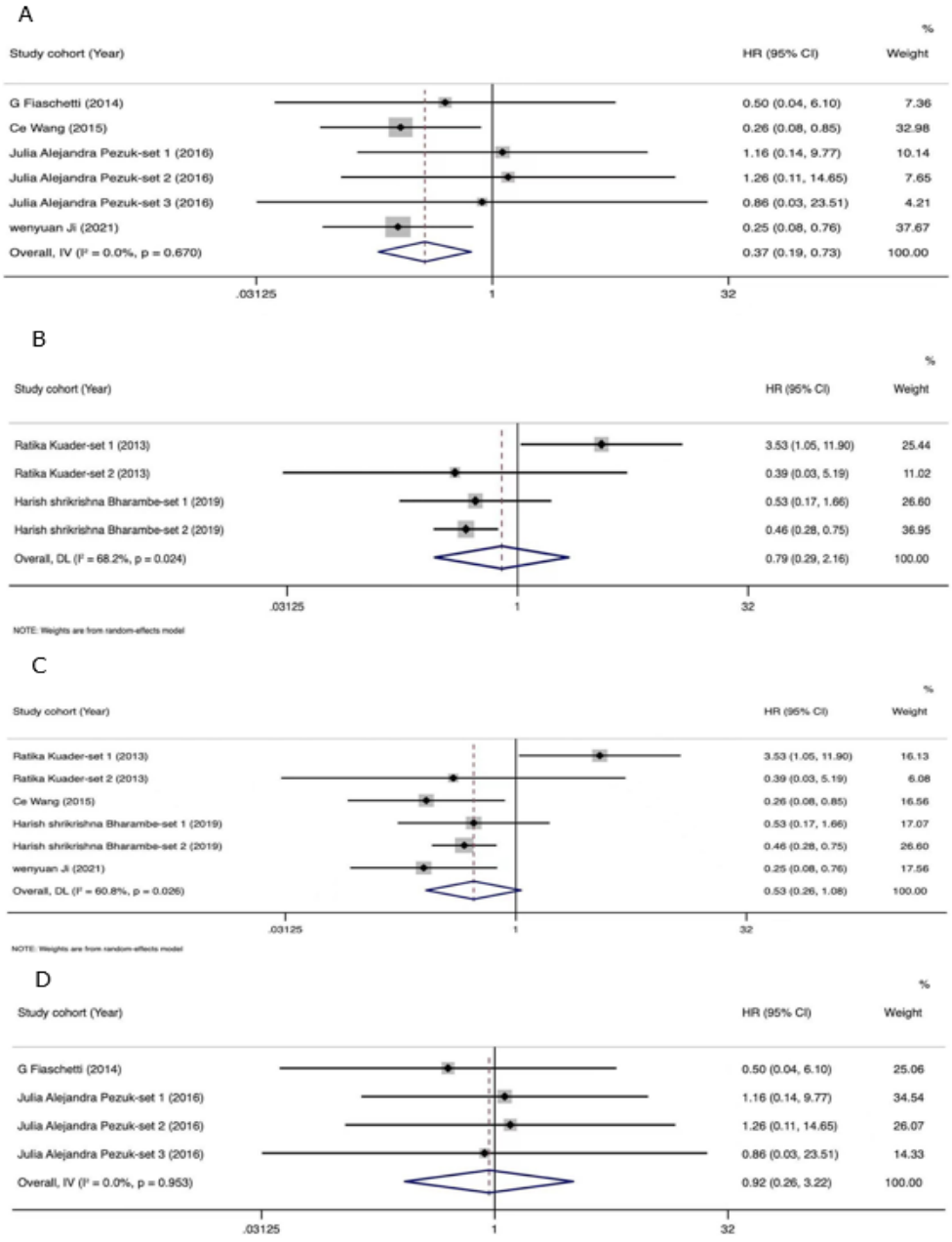

Figure 3: Subgroup analyses for the meta-analysis of the prognostic efficacy of miRNAs for OS in patients with MB according to the molecular subset and patient origin. (A) Subgroup analyses in MB patients of the four molecular subsets. (B) Subgroup analyses in MB patients with Group3 and Group4 molecular subsets. (C) Subgroup analyses in Asians patients. (D) Subgroup analyses in non - Asians patients.

Publication Bias

In the pooled analysis, funnel plot symmetry was used to assess the risk of publication bias. The funnel plot of the overall study is shown in Figure 4. The funnel plot symmetry was confirmed by visual examination, suggesting that the potential risk of publication bias was negligible. The result of Egger's test for this meta-analysis also demonstrated no significant publication bias. Results show that no significant publication bias was found in the analysis.

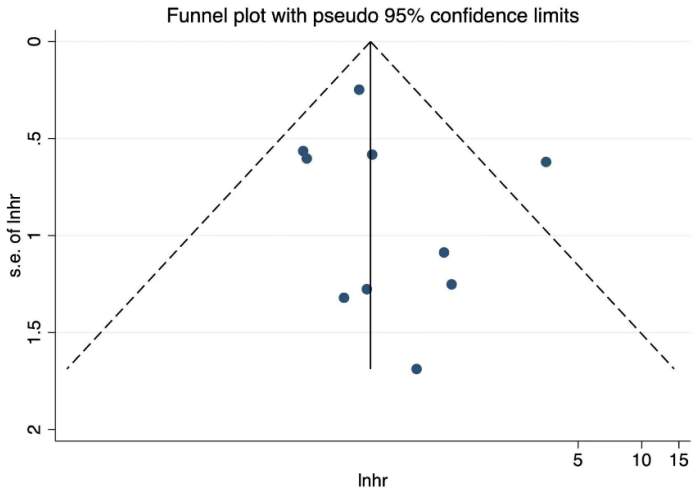

Figure 4: Funnel plot in the meta-analysis of the association between microRNAs expression and OS in patients with MB.

Sensitivity Analysis

Sensitivity analysis was performed by removing individual studies in turn. Our results were unchanged, indicating that our combined HRs and 95%CIs were stable in this meta-analysis. The result is shown in (Figure 5).

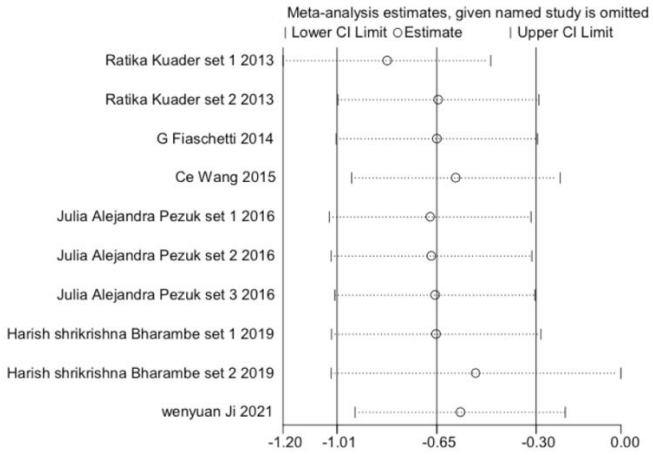

Figure 5: Forest plot in the meta-analysis random-effects estimates (exponential form) sensitivity analysis by omitting one study by turns.

Discussion

The prognostic efficacy of miRNAs in various tumors has been studied, including breast cancer, gastric cancer, glioma, lung cancer and other cancers [20-23]. MiRNA, as a short non-coding RNA, regulates gene expression at the post-transcriptional level, especially playing a crucial role in the occurrence and development of human cancer [24]. Abnormal regulation of miRNA results in changes in downstream oncogenes, related cancer suppressors, and signaling pathway molecules [25]. Some patients with MB experience local or metastatic relapses after standard therapy, a condition associated with very poor prognosis [26]. Though the prognostic relationship between miRNA-182 [27], 204 [28], 100 [29], 137 [30] and other miRNAs and MB patients has been studied, the results are inconsistent. Previous systematic reviews and meta-analyses have also explored the potential prognostic role of miRNAs in many other cancers. Still, no quantitative meta-analysis has been studied to investigate the prophetic role of miRNA in MB patients [31-33]. Our meta-analysis is novel and examines miRNAs' prognostic meaning as biomarkers in MB patients using a continuous version pooled meta-analysis. The primary purpose is to study the relationship between miRNAs and the prognosis of MB patients and provide further theoretical evidence for clinical application.

Our meta-analysis investigated 855 MB patients with 10 miRNAs from 6 studies. The HR combined effect of related miRNAs expression (up-regulation and down-regulation) was estimated to be 0.57 with a 95% CI 0.33-0.99. These results suggested that the overall pooled effect of miRNA expression related to the prognosis of MB update could reduce the risk of death in MB patients. In addition, Subgroup analyses showed that prognostic efficacy of tumor miRNA level for better OS was stronger in MB patients of the four molecular subsets (HR : 0.37; 95% CI : 0.19-0.73 ; P=0.670) than those with Group 3 and Group 4 molecular subsets only (HR : 0.79; 95% CI : 0.29-2.16 ; P=0.024). The results are consistent with previous studies [34-36]. they have observed how miRNA expression differs depending on molecular subsets and metastasis factors. Both univariate and multivariate analyses were used to explore the survival rate of MB patients. The results indicate that dysregulation miRNA expression was associated with poor prognosis in MB with the Group3 and Group4 molecular subsets or in patients with metastases, suggesting that molecular subsets and metastasis may be independent prognostic factors of MB patients. We also found the prognostic efficacy of tumor miRNA level was consistent in Asians (HR: 0.53; 95% CI: 0.26-1.08; p = 0.0026) and non - Asians patients with MB (HR: 0.92; 95% CI: 0.26-3.22; p = 0.953). Results show that no significant publication bias was found in the analysis. Sensitivity analysis shows that our conclusions are robust and reliable. The included studies were assessed as good quality using quality evaluation methods. Shaw p et al. [37] the study suggests that increased overall pooled effect of miRNA expression is associated with poor overall survival in nasopharyngeal carcinoma (NPC) patients. in our study. However, some miRNAs expression was up-regulated in MB patients, and some were down-regulated. But in conclusion, the overall pooled effect of miRNAs expression in MB may predict better survival. Based on the limited original data available, the role of miRNAs

as prognostic biomarkers should be fully confirmed in more prospective studies with large cohorts studies.

Some limitations of our study should be considered in the analysis of results. First, the study included a limited sample size of 855 MB patients with 10 miRNAs. Secondly, some HRs and 95%CIs data could not be obtained directly. We calculated them by using Kaplan Meier survival curve, which may induce minor errors in the analysis. Finally, Since the cut-off values for grouping patients with higher or lower miRNA may differ among the studies, this variable may have also led to heterogeneity.

In conclusion, a systematic and comprehensive qualitative and quantitative analysis of existing studies shows that increased miRNA expression in MB patients is associated with improved overall survival. It indicates that miRNA may provide some guidance for molecular targeted therapy of MB in the future, and this study has practical clinical significance.

Conclusion

This meta-analysis elaborated the influence of dysregulated miRNA expression on the survival of MB patients. Our analysis indicates that high miRNAs expression in MB patients may associate with the better OS. Thereby, the expression of miRNAs in MB patients may act as a potential biomarker for prognosis.

Author Contributions

Haima LI conceived the study. Jian WEN and Dongdong LI performed the literature search. Haima LI and Jian WEN extracted the required data. Hai ma LI performed the statistical analyses. Hai ma LI wrote a draft. Ruen LIU reviewed the paper. All authors contributed to the article and approved the submitted version.

Competing Interests

The authors declare no conflict of interest.

Ethics Approval

Neither ethics approval nor participant consent was required as this study was based solely on the summary results of previously published articles.

Date Availability Statement

No additional data are available.

Patient and Public Involvement

No patient involved.

References

1. Ostrom QT, Cioffi G, Gittleman H, Patil N, Waite K, et al. (2019) CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2012-2016. Neuro Oncol 21: v1-v100.
2. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, et al. (2016) The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol 131: 803-820.
3. Northcott PA, Korshunov A, Pfister SM, Taylor MD (2012) The clinical implications of medulloblastoma subgroups. Nat Rev Neurol 8: 340-351.
4. Taylor MD, Northcott PA, Korshunov A, Remke M, Cho YJ, Clifford SC, et al. (2012) Molecular subgroups of medulloblastoma: the current consensus. Acta Neuropathol 123: 465-472.
5. Strejczek A, Woszczyk D, Urbaniak H, Różańska M, Robak M, et al. (2021) Epigenetic-Based Therapy-A Prospective Chance for Medulloblastoma Patients' Recovery. Int J Mol Sci 22: 4925.
6. Voskamp MJ, Li S, van Daalen KR, Crnko S, Ten Broeke T, et al. (2021) Immunotherapy in Medulloblastoma: Current State of Research, Challenges, and Future Perspectives. Cancers (Basel) 13: 5387.
7. S Baliga, S Gallotto, B Bajaj, J Lewy, E Weyman, et al. (2021) Decade Long Disease, Secondary Malignancy, and Brainstem Injury Outcomes in Pediatric and Young Adult Medulloblastoma Patients Treated with Proton Radiotherapy. Neuro Oncol 24: 1010-1019.
8. Fiaschetti G, Abela L, Nonoguchi N, Dubuc AM, Remke M, et al. (2014) Epigenetic silencing of miRNA-9 is associated with HES1 oncogenic activity and poor prognosis of medulloblastoma. Br J Cancer 110: 636-647.
9. Visser H, Thomas AD (2021) MicroRNAs and the DNA damage response: How is cell fate determined?. DNA Repair (Amst) 108: 103245.
10. Peng Y, Croce CM, (2016) The role of MicroRNAs in human cancer. Signal Transduct Target Ther 1: 15004.
11. Wu N, Zhang C, Bai C, Han YP, Li Q, (2014) MiR-4782-3p inhibited non-small cell lung cancer growth via USP14. Cell Physiol Biochem 33: 457-467.
12. Pan W, Wang H, Jianwei R, Ye Z, (2014) MicroRNA-27a promotes proliferation, migration and invasion by targeting MAP2K4 in human osteosarcoma cells. Cell Physiol Biochem 33: 402-412.
13. Fernandez LA, Northcott PA, Taylor MD, Kenney AM, (2009) Normal and oncogenic roles for microRNAs in the developing brain. Cell Cycle 8: 4049-4054.
14. Wang X, Holgado BL, Ramaswamy V, Mack S, Zayne K, et al. (2018) miR miR on the wall, who's the most malignant medulloblastoma miR of them all?. Neuro Oncol 20: 313-323.
15. Wang Y, Zhang Q, B Guo, J Feng, D Zhao, (2020) miR-1231 Is Downregulated in Prostate Cancer with Prognostic and Functional Implications. Oncol Res Treat 43: 78-86.
16. Li J, Lu X, Zou X, Jiang Y, Yao J, et al. (2018) COX-2 rs5275 and rs689466 polymorphism and risk of lung cancer: A PRISMA-compliant meta-analysis. Medicine (Baltimore) 97: e11859.
17. Wang Y, Zeng T, (2013) Response to: Practical methods for incorporating summary time-to-event data into meta-analysis. Trials 14: 391.
18. Higgins JP, Thompson SG, (2002) Quantifying heterogeneity in a meta-analysis. Stat Med 21: 1539-1558.

19. Patsopoulos NA, Evangelou E, Ioannidis JP, (2008) Sensitivity of between-study heterogeneity in meta-analysis: proposed metrics and empirical evaluation. Int J Epidemiol 37: 1148-1157.

20. Hücker SM, Fehlmann T, Werno C, Weidele K, Lüke F, et al. (2021) Single-cell microRNA sequencing method comparison and application to cell lines and circulating lung tumor cells. Nat Commun 12: 4316.

21. Gao S, Lu X, Ma J, Zhou Q, Tang R, et al. (2021) Comprehensive Analysis of lncRNA and miRNA Regulatory Network Reveals Potential Prognostic Non-coding RNA Involved in Breast Cancer Progression. Front Genet 12: 621809.

22. Zhao X, Xiao Z, Li B, Li H, Yang B, et al. (2021) miRNA-21 may serve as a promising noninvasive marker of glioma with a high diagnostic performance: a pooled analysis of 997 patients. Ther Adv Med Oncol 13: 1758835920987650.

23. Li F, Liu J, Li S, (2013) MicorRNA 106b approximately 25 cluster and gastric cancer. Surg Oncol 22: e7-10.

24. Friedman RC, Farh KK, Burge CB, Bartel DP, (2009) Most mammalian mRNAs are conserved targets of microRNAs. Genome Res 19: 92-105.

25. Zhang L, Li J, Wang Q, Meng G, Lv X, et al. (2017) The relationship between microRNAs and the STAT3-related signaling pathway in cancer. Tumour Biol 39: 1010428317719869.

26. Kumar V, Kumar V, McGuire T, Coulter DW, Sharp JG, et al. (2017) Challenges and Recent Advances in Medulloblastoma Therapy. Trends Pharmacol Sci 38: 1061-1084.

27. Kunder R, Jalali R, Sridhar E, Moiyadi A, Goel N, et al. (2013) Real-time PCR assay based on the differential expression of microRNAs and protein-coding genes for molecular classification of formalin-fixed paraffin embedded medulloblastomas. Neuro Oncol 15: 1644-1651.

28. Bharambe HS, Paul R, Panwalkar P, Jalali R, Sridhar E, et al. (2019) Downregulation of miR-204 expression defines a highly aggressive subset of Group 3/Group 4 medulloblastomas. Acta Neuropathol Commun 7: 52.

29. Pezuk JA, Brassesco MS, de Oliveira RS, Machado HR, Neder L, et al. (2017) PLK1-associated microRNAs are correlated with pediatric medulloblastoma prognosis. Childs Nerv Syst 33: 609-615.

30. Ji W, Zhe X, Li L, Cheng Y, Zhao X, et al. (2021) Prognostic Value of miR-137 in Children with Medulloblastoma and its Regulatory Effect on Tumor Progression. Neuromolecular Med 24: 215-223.

31. Gruszka R, Zakrzewski K, Liberski PP, Zakrzewska M, (2020) microRNA interaction with MAPK and AKT pathways in paediatric brain tumours - preliminary results and review of the literature. Folia Neuropathol 58: 123-132.

32. Kaid C, Assoni A, Marçola M, Semedo-Kuriki P, Bortolin RH, et al. (2020) Proteome and miRNome profiling of microvesicles derived from medulloblastoma cell lines with stem-like properties reveals biomarkers of poor prognosis. Brain Res 1730: 146646.

33. Shalaby T, Fiaschetti G, Baumgartner M, Grotzer MA, (2014) Significance and therapeutic value of miRNAs in embryonal neural tumors. Molecules 19: 5821-5862.

34. Gershanov S, Toledano H, Michowiz S, Barinfeld O, Pinhasov A, et al. (2018) MicroRNA-mRNA expression profiles associated with medulloblastoma subgroup 4. Cancer Manag Res 10: 339-352.

35. Ramaswamy V, Remke M, Bouffet E, Bailey S, Clifford SC, et al. (2016) Risk stratification of childhood medulloblastoma in the molecular era: the current consensus. Acta Neuropathol 131: 821-831.

36. Kanchan RK, Perumal N, Atri P, Chirravuri Venkata R. Thapa I, et al. (2020) MiR-1253 exerts tumor-suppressive effects in medulloblastoma via inhibition of CDK6 and CD276 (B7-H3). Brain Pathol 30: 732-745.

37. Shaw P, Senthilnathan R, Krishnan S, Suresh D, Shetty S. et al. (2021) A Clinical Update on the Prognostic Effect of microRNA Biomarkers for Survival Outcome in Nasopharyngeal Carcinoma: A Systematic Review and Meta-Analysis. Cancers (Basel) 13: 4369.