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The Survival Implications of Extramedullary Disease in Acute Myeloid Leukemia: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 October 2023 and was last updated on 10 October 2023.

INTRODUCTION

Review question / Objective The prognosis of AML patients with extramedullary disease (EMD) can be compared to AML patients without EMD in terms of overall survival (OS), disease-free survival (DFS), relapse-free survival (RFS), event-free survival (EFS). The selected studies can include randomized controlled trials, retrospective studies, prospective cohort studies, and other relevant study designs.

Condition being studied Acute myeloid leukemia (AML) is a malignant hematological tumor characterized by the unrestricted proliferation of immature progenitor cells and the infiltration of the bone marrow (BM). In some cases, malignant leukemias can result in the formation of extramedullary masses, known as extramedullary disease (EMD), when the cells infiltrate tissues outside the BM. The incidence of EMD at the time of initial diagnosis varies, and it can occur in various locations. However, the exact cause remains unknown. The implications of EMD involvement in AML have not been fully established, and understanding its prognostic impact could contribute to refining the treatment approaches for AML patients.

METHODS

Participant or population We conducted a study involving consecutive adult patients who were 15 years of age or older and had newly diagnosed AML. Additionally, we included isolated myeloid sarcoma (MS) in our study since it is considered a type of AML according to the World Health Organization classification of myeloid neoplasms and acute leukemia.

Intervention AML patients with extramedullary disease.

Comparator AML patients without extramedullary disease.

Study designs to be included Randomized controlled trials, retrospective studies, prospective cohort studies, and other relevant study designs.

Eligibility criteria Inclusion Criteria:Articles that compare the overall survival (OS), disease-free survival (DFS), relapse-free survival (RFS), and event-free survival (EFS) between AML patients with extramedullary disease (EMD) and AML patients without EMD.Studies that include survival data.Exclusion Criteria:Duplicate articles, conference abstracts, reviews, letters, comments, and case reports.Studies involving children with AML or patients with non-AML diseases.Articles that are not relevant to the topic.

Information sources PubMed, Web of Science, Embase, and Cochrane Library.

Main outcome(s) Hazard ratio (HR) for overall survival (OS) in AML patients with EMD compared with AML patients without EMD. HR for disease-free survival (DFS), relapse-free survival (RFS), and event-free survival (EFS), when available, in AML patients with EMD compared with AML patients without EMD. HR for OS in AML patients with EMD and without EMD after hematopoietic stem cell transplantation (HSCT)
Secondary results:
Odds Ratio (OR) for laboratory and clinical features in AML with and without EMD.

Quality assessment / Risk of bias analysis The Cochrane Risk of Bias tool was utilized to evaluate the risk of bias in randomized controlled trials (RCTs), while the Newcastle-Ottawa Scale was employed to assess the risk of bias in cohort studies. Two assessors independently evaluated the studies, and any discrepancies were resolved through consensus or with the involvement of a third party.

Strategy of data synthesis To compare the overall survival (OS) of AML patients with and without EMD, assuming that the hazard ratio (HR) remains constant over time, a meta-analysis can be conducted using either a fixed-effects or random-effects model to calculate pooled HRs and their corresponding 95% confidence intervals (CIs). If feasible, a comparison of OS between AML patients with and without EMD in the context of hematopoietic stem cell transplantation (HSCT) can also be performed. If there are available data on disease-free survival (DFS), relapse-free survival (RFS), or event-free survival (EFS), the same methods can be used to perform a combined analysis. The data was analyzed using Stata 17.0 and Revman 5.4 software.

Subgroup analysis Subgroup analysis was used to evaluate the impact of different diagnostic methods, specific molecular and genetic features, as well as variations in the definition criteria for extramedullary disease (EMD), on the outcomes of AML patients with EMD.

Sensitivity analysis Sensitivity analysis was conducted to assess the stability of the results by systematically excluding one study at a time. If the exclusion of a particular study does not significantly impact the final results, it suggests that the findings are robust and stable.

Country(ies) involved China.

Keywords Acute myelogenous leukemia, Chloroma, Myeloid sarcoma, Granulocytic sarcoma, Extramedullary disease, Extramedullary involvement, Leukemia cutis, Meta-analysis.

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