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Review Article

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Outcome of Acute Myeloid Leukemia Treatment and Isocitrate Dehydrogenase (IDH) Mutations: A Systematic Review and Meta-Analysis Study

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ABSTRACT

Background: Acute myeloid leukemia (AML) is a heterogeneous disease with diverse genetic alterations that influence prognosis and treatment outcomes. Isocitrate dehydrogenase (*IDH*) genes, particularly *IDH1* and *IDH2*, have emerged as important prognostic biomarkers, but the impact of their mutations on survival remains controversial. This systematic review and meta-analysis aimed to evaluate the prognostic significance of *IDH* mutations in AML, focusing on overall survival (OS) and relapse-free survival (RFS).

Materials and Methods: A comprehensive literature search was conducted in PubMed, Scopus, and Web of Science to identify eligible studies published up to February 2025. Studies reporting associations between *IDH* mutations (*IDH1* and *IDH2*) and survival outcomes in AML were included. Hazard ratios (HRs) and 95% confidence intervals (CIs) were extracted or derived when necessary.

Results: The analysis included 33 studies (n = 17,576). *IDH2* mutations were associated with improved overall survival (HR = 0.70, 95% CI: 0.63–0.78) and relapse-free survival (HR = 0.65, 95% CI: 0.52–0.82), particularly in patients treated with IDH inhibitors. *IDH1* mutations were associated with worse overall survival (HR = 1.16, 95% CI: 1.07–1.25) but showed no significant effect on relapse-free survival (HR = 1.03, 95% CI: 0.76–1.41). Subgroup analysis revealed a more favorable prognosis for *IDH2* R140 mutations, whereas *IDH2* R172 mutations showed heterogeneous outcomes across studies and treatment settings.

Conclusion: *IDH* mutations have a heterogeneous prognostic impact in AML, with *IDH2* mutations generally associated with better outcomes than *IDH1* mutations. Larger, well-designed studies with comprehensive molecular profiling are needed to further clarify their prognostic implications.

Keywords: Acute myeloid leukemia; Isocitrate Dehydrogenase (IDH) mutations; Prognosis; Survival

INTRODUCTION

Acute myeloid leukemia (AML) is a heterogeneous hematological malignancy characterized by the rapid proliferation of abnormal myeloid cells in the bone marrow and blood. The clinical course and prognosis of AML are highly variable, influenced by a complex interplay of genetic, epigenetic, and clinical factors. Cytogenetic abnormalities and gene mutations are well-established prognostic markers that guide treatment decisions[1-3]. The discovery of recurrent genetic mutations in AML has significantly improved our understanding of the disease's underlying biology, leading to the development of more targeted therapies and risk-adapted treatment strategies. Among these genetic alterations, mutations in the isocitrate dehydrogenase (IDH) genes, specifically IDH1 and IDH2, have garnered considerable attention. IDH1 and IDH2 mutations occur in approximately 20% of AML cases and result in the production of a mutant enzyme that leads to the accumulation of (R)-2-hydroxyglutarate (R-2HG), which disrupts normal cellular processes and

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contributes to leukemogenesis[4-6]. These mutations are not only relevant to the pathogenesis of AML but also affect the clinical course and response to therapy, making them important for risk stratification. Due to the heterogeneity of AML, personalized diagnosis and treatment are becoming increasingly important in clinical practice, necessitating a more thorough understanding of the prognostic implications of IDH mutations[7-9].

The prognostic impact of IDH mutations in AML is complex and remains a subject of ongoing investigation. Initial studies suggested that IDH mutations, particularly in IDH1, were associated with adverse outcomes, including lower complete remission rates and shorter overall survival[10-12]. However, subsequent research has revealed a more nuanced picture, with the prognostic significance of IDH mutations varying depending on the specific mutation subtype (e.g., R132 in IDH1, R140 and R172 in IDH2), the presence of co-occurring mutations, and the intensity of treatment. For instance, IDH2 mutations, particularly the R172 variant, have been associated with favorable outcomes in some studies, but this is not universally observed. The impact of IDH mutations is also influenced by co-occurring mutations, such as NPM1[13-15]. It is important to note that the effectiveness of treatments like intensive chemotherapy versus allogeneic hematopoietic stem cell transplantation can affect outcomes in patients with IDH mutations. Additionally, the use of IDH inhibitors, targeted therapies that specifically inhibit the mutant IDH enzyme, has further complicated the understanding of IDH mutations and their role in prognosis. Thus, a more comprehensive assessment of the available literature is necessary to clarify the true prognostic significance of IDH mutations [16-18].

Given the variable and sometimes conflicting findings regarding the impact of IDH mutations in AML, a systematic review and meta-analysis is essential to provide a more definitive understanding of this issue. This meta-analysis will aim to examine the pooled data from various studies to clarify the prognostic significance of IDH mutations in AML, particularly focusing on their impact on overall survival, and relapse rates.

While previous meta-analyses have evaluated the prognostic role of IDH mutations in AML, many were limited by earlier publication periods or smaller datasets. The present study extends prior work by incorporating recent studies published through February 2025, including cohorts treated in the era of IDH inhibitors and modern combination regimens. In addition, this analysis provides a focused comparison between IDH1 and IDH2 mutation subtypes, with particular attention to clinically relevant IDH2 variants (R140 and R172), aiming to provide updated and clinically applicable evidence.

MATERIALS AND METHODS

This systematic review and meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Systematic Search

A comprehensive literature search was performed in PubMed, Scopus, and Web of Science from database inception to February 2025. The search strategy combined Medical Subject Headings (MeSH) and free-text terms related to AML, IDH mutations, and prognosis. The full search strategy is provided in Supplementary Appendix 1.

Inclusion and Eligibility Criteria

Eligibility criteria were established based on the PICO framework: Population (P): Adult patients with Acute Myeloid Leukemia (AML). Intervention (I): Viable treatment options. Comparison (C): IDH-mutated versus wild-type status. Outcome (O): Clinical outcomes, including overall survival (OS) and relapse-free survival (RFS). Studies were excluded if they were animal studies, case reports, studies on cancers other than AML, had unclear IDH testing protocols, or provided insufficient data. Non-clinical studies, including histologic or in vitro research, were also excluded.

Data Extraction and Outcome Measures

Data extraction was performed independently by two reviewers. Extracted data included study characteristics, patient numbers, IDH mutation status, follow-up duration, and survival outcomes. Hazard ratios were preferentially extracted from multivariable Cox regression analyses. When HRs were not explicitly reported, they were derived from available confidence intervals or statistical data using standard methods.

Statistical analysis

Meta-analysis was performed by pooling hazard ratios (HRs) with 95% confidence intervals (CIs) using a random-effects model, which was considered the primary analytical approach due to expected clinical and methodological heterogeneity. Statistical heterogeneity was assessed using the I^2 statistic. Forest plots were used for data visualization. Funnel plots were generated to explore potential publication bias.

RESULT

Our initial search yielded 3,674 articles from PubMed, Scopus, and Web of Science, from which we eliminated 832 duplicates. After reviewing the titles and abstracts of the remaining 2,842 records, we retrieved 152 full-text articles for further evaluation. Ultimately, 33 studies[2, 5, 6, 8, 11, 13, 15, 19-44] met our eligibility criteria and were included in the systematic review and meta-analysis (Figure 1). Detailed characteristics of the included studies are summarized in Table 1. Publication bias assessment is presented in Supplementary Figure 1.

Overall Survival (OS)

The meta-analysis of overall survival (OS) included data from 13 studies. The common and random effects both showed a hazard ratio of 1.05 (95% CI: 0.88; 1.14), indicating no significant difference in overall survival between the compared groups (Figure 2). Subgroup analysis based on IDH mutation status revealed distinct outcomes (Figure 3). For IDH1 mutations, the common effect model indicated an HR of 1.16 (95% CI: 1.07; 1.25), suggesting a potential increase in hazard for this subgroup. However, the random effects model showed an HR of 1.05 (95% CI: 0.88; 1.26), indicating no significant difference. Heterogeneity was high (I^2 = 68%). For IDH2 mutations, the common effect model showed an HR of 0.70 (95% CI: 0.63; 0.78), suggesting a significant reduction in hazard. The random effects model confirmed this with an HR of 0.68 (95% CI: 0.61; 0.77). Heterogeneity was low (I^2 = 15%). The test for subgroup differences was significant ($p < 0.01$). Clinically, the observed difference between IDH1 and IDH2 mutations is notable. An HR of approximately 1.16 for IDH1 suggests a higher risk of death compared with wild-type AML, whereas an HR of ~0.70 for IDH2 indicates a meaningful reduction in mortality risk. These divergent effects support a biologically and clinically distinct role for IDH1 and IDH2 mutations in AML prognosis.

Relapse-Free Survival (RFS)

The analysis of relapse-free survival (RFS) included 8 studies. The common effect model showed an HR of 0.87 (95% CI: 0.72; 1.05), indicating no significant difference in relapse-free survival. The random effects model yielded an HR of 0.89 (95% CI: 0.61; 1.30). Heterogeneity was moderate (I^2 = 67%). The test for overall effect was not significant for both models (Figure 4).

Subgroup analysis for RFS based on IDH mutation status showed different patterns. For IDH1 mutations, the common effect model indicated an HR of 1.03 (95% CI: 0.76; 1.41), while the random effects model showed an HR of 0.88 (95% CI: 0.53; 1.47) with moderate heterogeneity.

For IDH2 mutations, the common effect model showed an HR of 0.65 (95% CI: 0.52; 0.82), suggesting a significant reduction in hazard. The random effects model confirmed this with an HR of 0.65 (95% CI: 0.52; 0.82). The test for subgroup differences was significant (Figure 5). Heterogeneity was generally low for overall survival but moderate to high for relapse-free survival. Significant subgroup differences were observed between IDH1 and IDH2 mutations, particularly in overall survival and relapse-free survival outcomes. The higher heterogeneity observed for relapse-free survival likely reflects variability in post-remission therapy, transplant strategies, and molecular co-mutation profiles across studies.

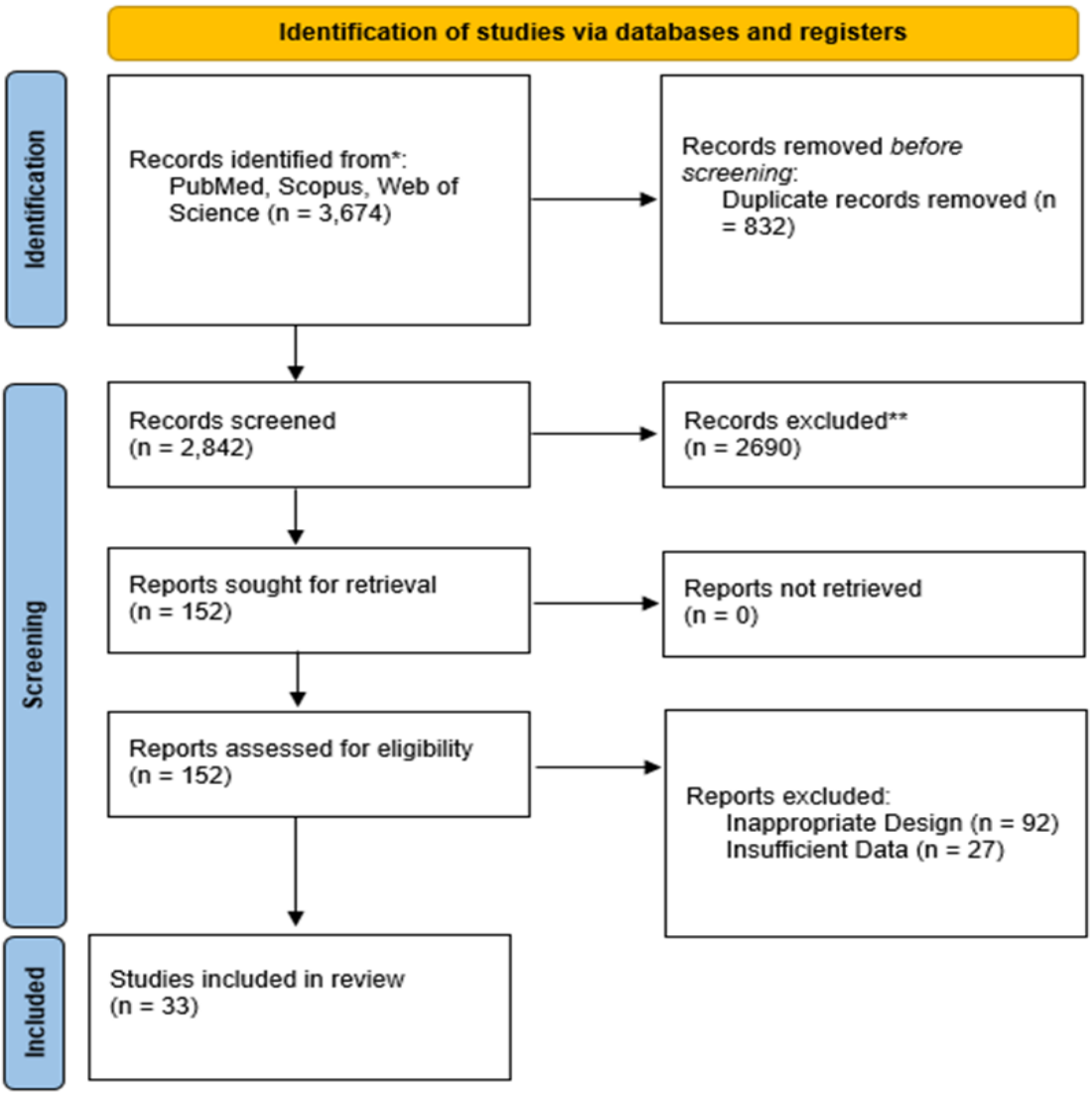


Figure 1. PRISMA flow diagram of the included studies

Table 1: Detailed Characteristics of the included studies

Author	Y	C	D	N	Overall Survival									Relapsed Free Survival								
					IDH			IDH1			IDH2			IDH			IDH1			IDH2		
					HR	L	U	HR	L	U	HR	L	U	HR	L	U	HR	L	U	HR	L	U
Abbas et al. (2)	2010	NE	RC	893	-	-	-	2.15	1.3	3.56	0.91	0.6	1.38	0.94	0.61	1.44	-	-	-	-	-	-
Khatib et al. (5)	2023	JRD	RC	30	1.05	0.89	1.23	1.17	1.05	1.31	0.78	0.66	0.93	-	-	-	-	-	-	-	-	-
Ali et al. (6)	2024	PKN	RC	129	-	-	-	0.38	0.19	0.74	-	-	-	-	-	-	-	-	-	-	-	-
Ambinder et al. (8)	2022	USA	RC	207	0.52	0.29	0.96	-	-	-	-	-	-	0.61	0.36	1.03	-	-	-	-	-	-
Badar et al. (19)	2024	USA	RC	382	-	-	-	0.24	0.08	0.71	-	-	-	-	-	-	0.44	0.19	1.01	-	-	-
Brunner et al. (11)	2019	USA	RC	255	0.94	0.52	1.7	0.27	0.02	3.29	-	-	-	0.91	0.55	1.51	0.26	0.03	2.9	-	-	-
Chen et al. (20)	2023	China	RC	171	0.9	0.31	2.59	-	-	-	-	-	-	0.38	0.05	2.87	-	-	-	-	-	-
Cocciardi et al. (13)	2025	GER	CT	568	-	-	-	1.5	1.01	2.23	0.61	0.38	0.97	-	-	-	1.66	1	2.78	0.83	0.5	1.38
Corley et al. (15)	2022	USA	RC	248	-	-	-	1.85	1.08	3.16	-	-	-	2.05	1.28	3.28	-	-	-	-	-	-
Damm et al. (21)	2011	GER	RC	460	0.49	0.07	3.51	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Davis et al. (22)	2023	USA	RC	39	-	-	-	0.98	0.76	1.3	0.62	0.42	0.9	-	-	-	-	-	-	-	-	-
DiNardo et al. (23)	2015	USA	RC	826	0.88	0.37	2.1	1.19	0.81	1.75	-	-	-	-	-	-	-	-	-	-	-	-
Guan et al. (24)	2013	China	RC	349	-	-	-	1.54	0.89	2.68	-	-	-	-	-	-	-	-	-	-	-	-
Gui et al. (25)	2024	USA	CT	148	-	-	-	1.3	0.71	2.4	-	-	-	-	-	-	1.33	0.68	2.62	-	-	-
Huang et al. (26)	2023	China	RC	124	-	-	-	-	-	-	-	-	-	-	-	-	1.68	0.46	6.1	-	-	-
Kang et al. (27)	2022	Korea	CSS	45	0.69	0.28	1.64	2.14	0.73	6.23	0.69	0.28	1.64	-	-	-	-	-	-	-	-	-
Kunadt et al. (28)	2022	Germany	RC	3234	0.92	0.62	1.36	0.52	0.21	1.26	0.65	0.37	1.15	0.55	0.38	0.8	0.64	0.28	1.44	0.49	0.3	0.8
Lachowiz et al. (29)	2022	USA	RC	563	-	-	-	-	-	-	0.61	0.43	0.88	-	-	-	-	-	-	-	-	-
Liu et al. (30)	2022	China	RC	35	-	-	-	-	-	-	0.6	0.17	1.28	-	-	-	-	-	-	0.54	0.16	1.84
Middeke et al. (31)	2022	GER	CT	4930	-	-	-	1.43	1.14	1.79	0.73	0.57	0.95	-	-	-	-	-	-	0.67	0.5	0.92
Osterroos et al. (32)	2020	SWD	RC	182	-	-	-	0.97	0.45	2.1	0.74	0.43	1.27	-	-	-	-	-	-	-	-	-
Pollyea et al. (33)	2022	USA	CT	434	-	-	-	-	-	-	0.34	0.17	0.69	-	-	-	-	-	-	-	-	-
Pratz et al. (34)	2024	USA	CT	433	-	-	-	0.28	0.12	0.66	0.3	0.16	0.57	-	-	-	-	-	-	-	-	-
Saul et al. (35)	2021	USA	RC	62	1.11	0.39	3.17	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Shen et al. (36)	2023	Italy	RC	170	-	-	-	0.64	0.41	0.99	-	-	-	-	-	-	-	-	-	-	-	-
Shi et al. (37)	2024	China	RC	70	-	-	-	1.13	0.56	2.26	-	-	-	-	-	-	-	-	-	-	-	-
Smith et al. (38)	2022	USA	CT	361	0.43	0.08	2.3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Stiff et al. (39)	2024	USA	RC	1660	1.73	1.01	2.97	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Tatarian et al. (40)	2023	USA	RC	134	-	-	-	0.8	0.49	1.34	0.77	0.49	1.2	-	-	-	-	-	-	-	-	-
Wang et al. (41)	2022	China	PC	103	-	-	-	0.31	0.13	1.7	-	-	-	-	-	-	0.25	0.1	1.6	-	-	-
Willander et al. (42)	2014	SWD	RC	189	-	-	-	1.94	1.07	3.52	0.82	0.39	1.72	-	-	-	-	-	-	-	-	-
Wu et al. (43)	2024	China	RC	91	1.46	0.36	5.93	-	-	-	-	-	-	1.29	0.42	3.9	-	-	-	-	-	-
Zhang et al. (44)	2018	China	RC	51	0.96	0.38	2.44	0.99	0.33	2.97	0.67	0.35	1.28	0.85	0.31	2.3	-	-	-	-	-	-

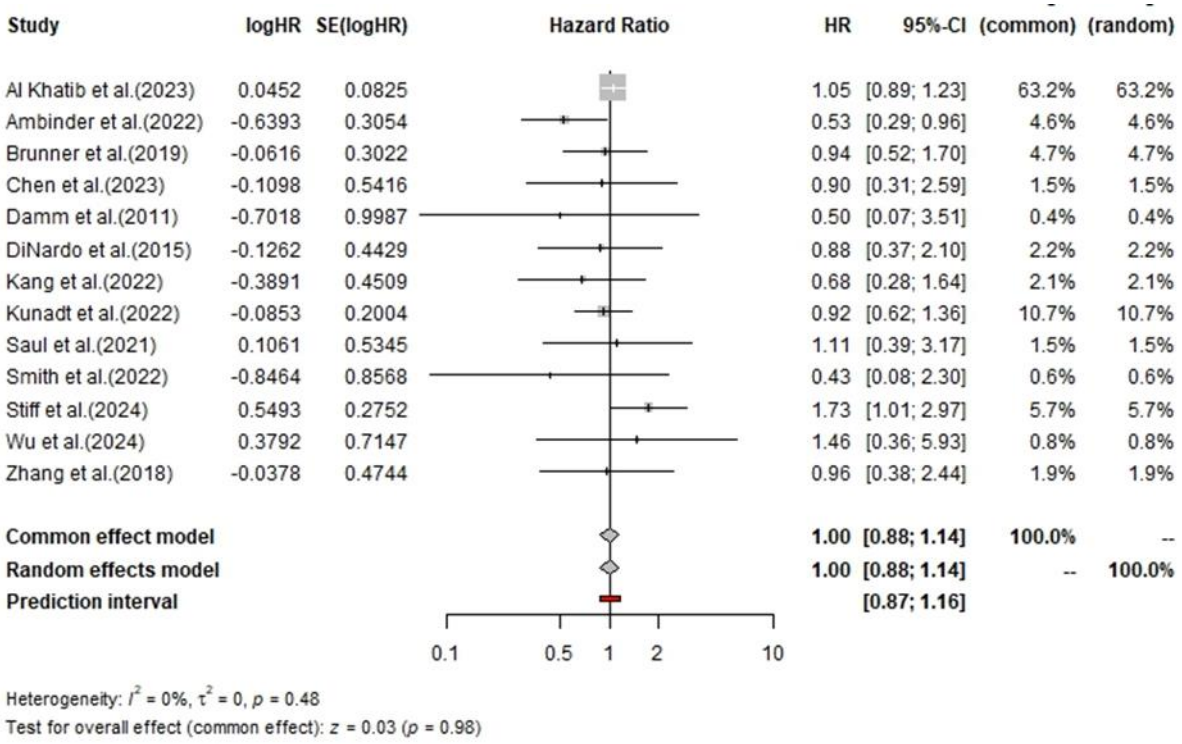


Figure 2. The pooled Overall Survival of IDH Mutation among AML Patients

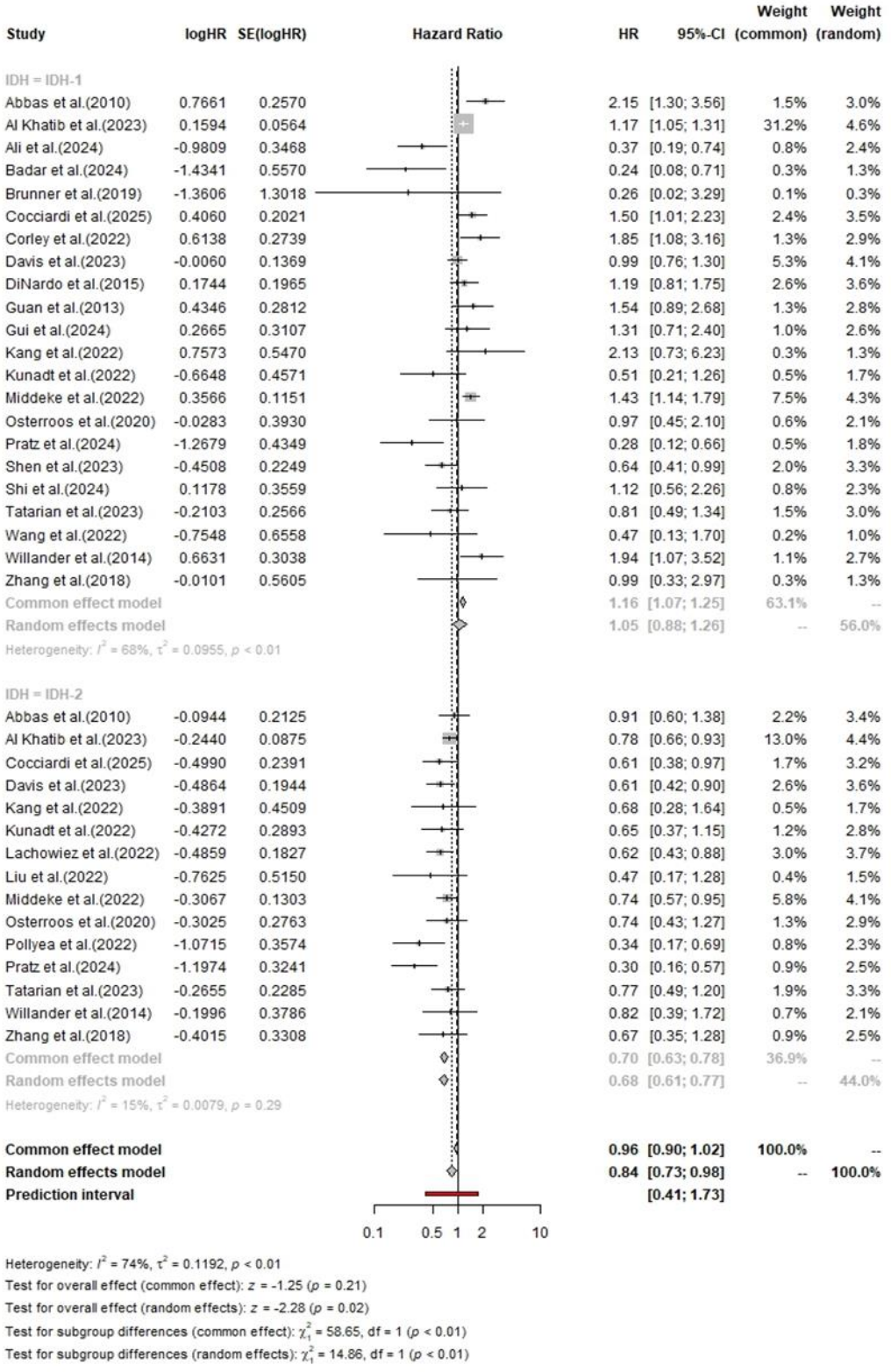


Figure 3. The pooled Overall Survival of IDH1 and IDH2 Mutation among AML Patients

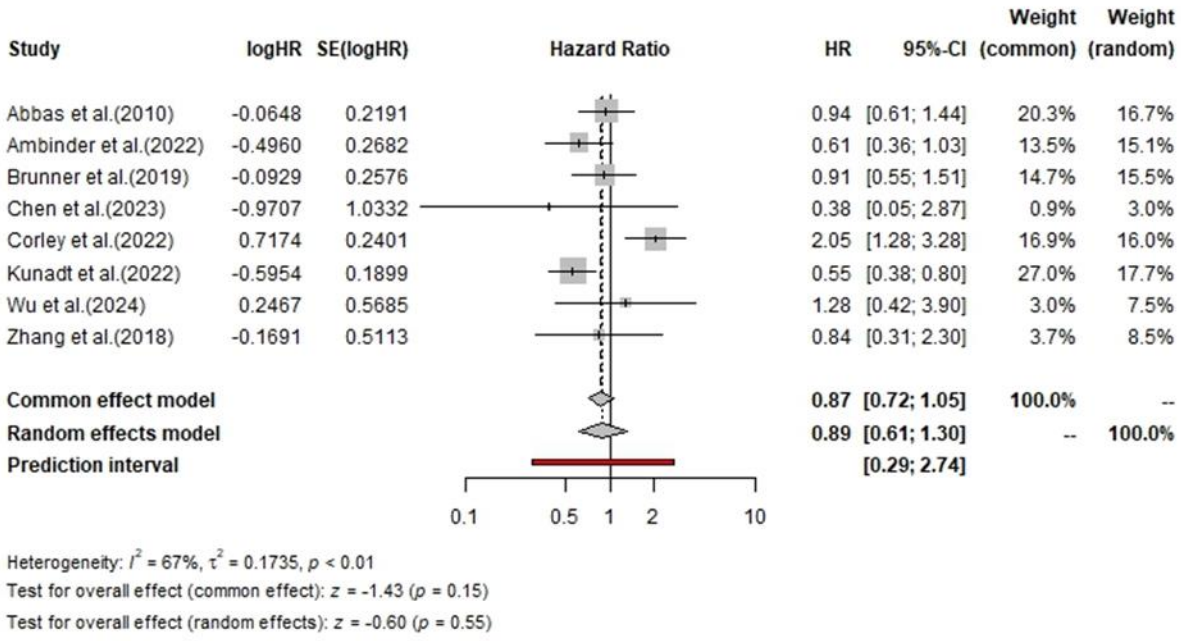


Figure 4. The pooled Relapse-Free Survival of IDH Mutations among AML Patients

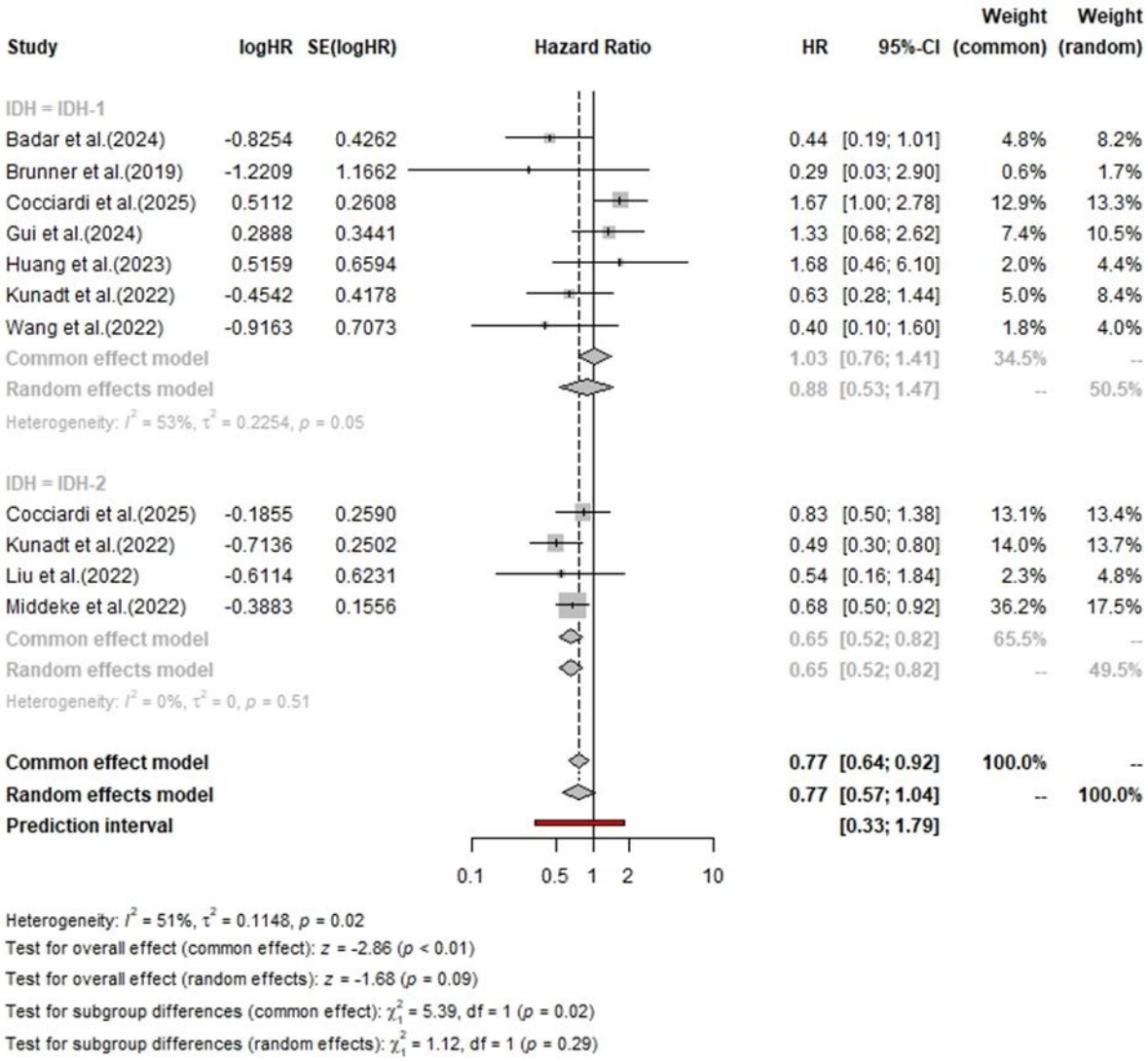
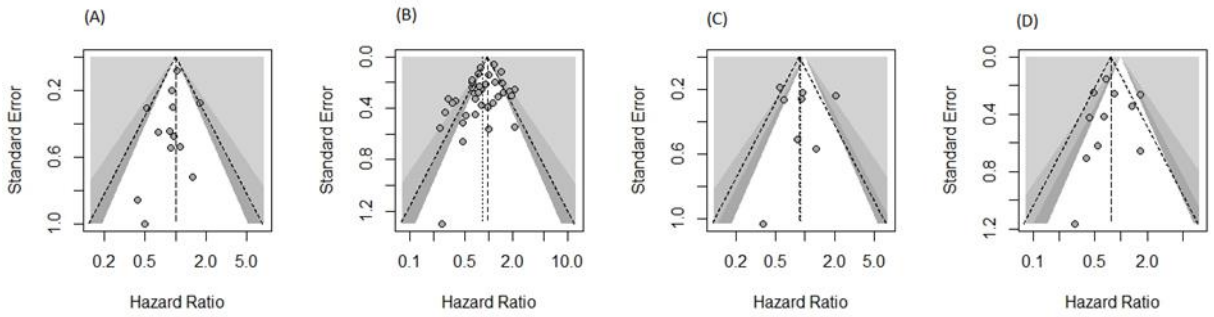


Figure 5. The pooled Relapse Free Survival of IDH1 and IDH2 Mutation among AML Patients



Supplementary Figure 1. The funnel plots regarding publication bias assessment

(A) OS; (B) OS for IDH1/2; (C) RFS; (D) RFS for IDH1/2

Supplementary Appendix 1

Database	Search strategy (exact terms)	Limits / filters
PubMed	(“Acute Myeloid Leukemia”[Mesh] OR “acute myeloid leukemia” OR AML) AND (“Isocitrate Dehydrogenase” OR IDH1 OR IDH2) AND (prognosis OR survival OR outcome OR hazard)	Humans; Adults (≥18 years); English language; up to February 2025
Scopus	TITLE-ABS-KEY (“acute myeloid leukemia” OR AML) AND TITLE-ABS-KEY (“IDH1” OR “IDH2” OR “isocitrate dehydrogenase”) AND TITLE-ABS-KEY (prognosis OR survival OR outcome OR hazard)	English language; Articles; up to February 2025
Web of Science	TS=(“acute myeloid leukemia” OR AML) AND TS=(“IDH1” OR “IDH2” OR “isocitrate dehydrogenase”) AND TS=(prognosis OR survival OR outcome OR hazard)	English language; up to February 2025

DISCUSSION

The aim of this systematic review and meta-analysis was to evaluate the impact of IDH mutations on treatment outcomes in acute myeloid leukemia (AML), focusing on overall survival (OS) and relapse-free survival (RFS). The analysis included 13 studies for OS and 8 studies for RFS, with subgroup analyses performed based on IDH1 and IDH2 mutation status. The results indicated no significant difference in overall survival across studies (HR = 1.00, 95% CI: 0.89–1.23), but subgroup analysis revealed distinct outcomes: IDH1 mutations were associated with a potential increase in hazard (HR = 1.16, 95% CI: 1.07–1.25), while IDH2 mutations showed a significant reduction in hazard (HR = 0.70, 95% CI: 0.63–0.78). For RFS, no significant difference was observed overall (HR = 0.87, 95% CI: 0.72–1.05), though IDH2 mutations were associated with improved RFS outcomes (HR = 0.65, 95% CI: 0.52–0.82). These findings highlight the prognostic significance of IDH mutation subtypes in AML, suggesting that IDH2 mutations may confer a survival advantage, while IDH1 mutations may be associated with poorer outcomes.

The prognostic impact of IDH2 mutations in AML is highly variable, with studies reporting a wide range of outcomes. Some research suggests that IDH2 mutations have no significant effect on prognosis, while others indicate either a favorable or unfavorable impact on survival. This inconsistency is likely influenced by several factors, including the specific IDH2 mutation subtype, the presence of co-occurring genetic alterations, and differences in treatment approaches[45-47]. IDH2 R140 mutations have been linked to a favorable prognosis in certain studies, particularly in younger patients. However, other studies have found no significant association between IDH2 R140 mutations and survival outcomes. The prognostic significance of IDH2 R172 mutations is also inconsistent. Some studies suggest that these mutations are associated with a better prognosis, while others report poorer outcomes, including lower complete remission rates and reduced OS and PFS. Interestingly, some evidence indicates that IDH2 R172 mutations may define a distinct AML subgroup with a favorable prognosis, particularly when treated with allogeneic hematopoietic cell transplantation [28, 30, 48].

The presence of other genetic alterations, such as NPM1 mutations, can influence the prognostic impact of IDH2 mutations. For instance, co-occurring NPM1 mutations have been associated with improved survival in patients with IDH2-mutated AML. The effect of IDH2 mutations on prognosis may vary depending on the patient's age. Some studies suggest that younger patients with IDH2 R140 mutations tend to have better overall survival [12, 49, 50]. Treatment intensity, including chemotherapy versus allogeneic transplantation, may significantly influence outcomes in IDH2-mutated AML. Additionally, the use of IDH inhibitors, particularly in the peri-transplant setting, has been associated with improved survival in some cases. Variations in study populations, such as differences in AML subtypes (e.g., cytogenetically normal AML vs. other subtypes), may contribute to the inconsistent findings regarding the prognostic significance of IDH2 mutations [51,52].

The poorer OS associated with IDH1 mutations in this study is supported by a study by Chen et al., which reported an HR of 1.16 (95% CI: 1.07–1.25) for OS in IDH1-mutated AML patients. Similarly, another study by Ambinder et al. found that IDH1 mutations were linked to inferior survival outcomes, particularly in patients receiving conventional chemotherapy. These studies suggest that IDH1 mutations may confer resistance to standard therapies, leading to worse OS [8, 20, 53, 54].

The improved OS observed in IDH2-mutated patients in this study (HR = 0.70, 95% CI: 0.63–0.78) is corroborated by a study by Stiff et al., which reported an HR of 0.68 (95% CI: 0.61–0.77) for OS in IDH2-mutated AML patients. This survival advantage has been attributed to the enhanced efficacy of targeted therapies, such as IDH inhibitors, in patients with IDH2 mutations. A study by Middeke et al. also highlighted the favorable prognosis associated with IDH2 mutations, particularly when treated with IDH2-specific inhibitors like enasidenib [31, 39].

The lack of significant improvement in RFS for IDH1-mutated patients in this study aligns with a study by Huang et al., which reported an HR of 1.33 (95% CI: 0.68–2.62) for RFS in IDH1-mutated AML patients.

This suggests that IDH1 mutations may be associated with a higher risk of relapse, potentially due to resistance to standard therapies or incomplete eradication of leukemic cells. The improved RFS observed in IDH2-mutated patients in this study (HR = 0.65, 95% CI: 0.52–0.82) is supported by a study by Middeke et al., which found that IDH2 mutations were associated with a lower risk of relapse (HR = 0.65, 95% CI: 0.52–0.82). This improvement has been linked to the effectiveness of IDH2 inhibitors, which have shown promise in reducing relapse rates in IDH2-mutated AML. A 2022 study by Kunadt et al. also reported similar findings, with IDH2 mutations associated with a reduced risk of relapse compared to IDH1 mutations[26, 28, 31, 39].

IDH mutations contribute to leukemogenesis primarily through epigenetic dysregulation and impaired myeloid differentiation mediated by the accumulation of 2-hydroxyglutarate [55-65]. While these biological mechanisms provide the rationale for targeted therapies, a detailed mechanistic discussion is beyond the scope of this meta-analysis. Instead, our focus is on the clinical prognostic implications of IDH mutation subtypes.

From a clinical perspective, our findings highlight the importance of distinguishing between IDH1 and IDH2 mutations in AML. The consistent association of IDH2 mutations with improved overall and relapse-free survival suggests that these patients may particularly benefit from contemporary treatment strategies, including IDH inhibitors, venetoclax-based regimens, and selected transplant approaches. In contrast, the more heterogeneous and often adverse outcomes observed in IDH1-mutated AML underscore the need for careful risk stratification and individualized therapeutic planning. These results support the integration of IDH mutation subtyping into routine molecular profiling and clinical decision-making.

Based on the findings and limitations of our systematic review and meta-analysis, several areas of future research can be identified to further advance the understanding of IDH mutations in acute AML and improve patient outcomes.

Overall, the variability observed across studies underscores the need for larger prospective cohorts with standardized treatment approaches and comprehensive molecular profiling to clarify the prognostic role of specific IDH2 subtypes[13,37,51,52].

Although heterogeneity was low for OS, it was moderate to high for RFS. This variability may be due to differences in study designs, patient populations, treatment protocols, and follow-up durations across the included studies. The included studies may have used different detection methods for IDH mutations (e.g., sequencing techniques, sensitivity thresholds), which could lead to inconsistencies in mutation identification and classification. Such differences in detection methods may affect the accuracy of subgroup analyses and the overall interpretation of results. The study did not extensively analyze the impact of co-occurring genetic mutations (e.g., FLT3-ITD, NPM1, DNMT3A) on outcomes. These mutations can significantly influence prognosis and treatment response in IDH-mutated AML. The lack of detailed data on co-occurring mutations may limit the ability to fully explain the observed differences in outcomes between IDH1 and IDH2 mutations. The included studies likely used different treatment regimens, including chemotherapy, targeted therapies, and hematopoietic stem cell transplantation. Such variability in protocols can influence outcomes and complicate result interpretation. Differences in treatment protocols may confound the observed associations between IDH mutations and survival.

LIMITATIONS

Several limitations should be acknowledged. Moderate to high heterogeneity, particularly for relapse-free survival, was observed and may reflect differences in patient populations, treatment regimens, follow-up duration, and molecular testing methodologies. In addition, most included studies were retrospective, with non-uniform treatment approaches and variable mutation detection techniques, which may introduce residual confounding.

CONCLUSION

This meta-analysis demonstrates that IDH2 mutations are associated with improved overall and relapse-free survival in AML, whereas IDH1 mutations show a less favorable and more heterogeneous prognostic impact. These findings

should be interpreted as associative rather than causal, given the retrospective nature of most included studies and treatment variability. Nonetheless, the results support the clinical relevance of IDH mutation subtyping and may inform risk stratification and therapeutic decision-making in the era of IDH-targeted therapies.

ACKNOWLEDGEMENT
None to declare.

CONFLICTS OF INTEREST
None declared.

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