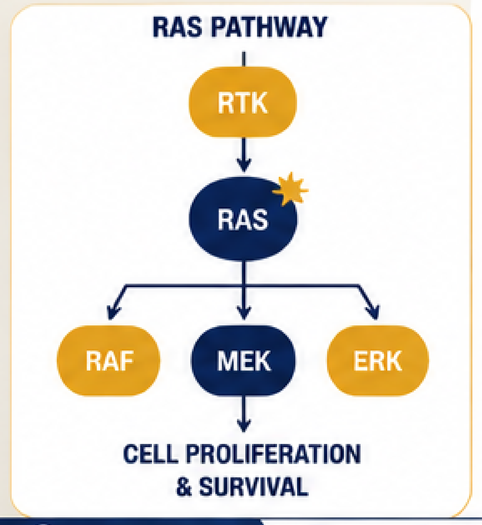

Prognostic Impact of RAS Pathway Mutations in Myelodysplastic Syndromes:

A Systematic Review and Meta-Analysis

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KEYWORDS: Myelodysplastic Syndrome, RAS, Mutations, Prognosis, Meta-Analysis

BACKGROUND

AS pathway mutations, including NRAS, KRAS, and PTPN11, are frequently identified in myelodysplastic syndromes (MDS), but their prognostic significance remains uncertain. This study aimed to systematically evaluate the association between these mutations and survival outcomes in MDS.

METHODS

A comprehensive search of PubMed, Embase, Scopus, Web of Science, and GEO was performed from database inception to January 10, 2025. Studies including adult patients with MDS that evaluated the impact of RAS pathway mutations on survival outcomes were eligible. Hazard ratios (HRs) for overall survival (OS), leukemia-free survival (LFS), and leukemia transformation reported, individ when HRs were not directly reported, individual patient data were reconstructed from Kaplan-Meier curves. Pooled estimates were calculated using a random-effects model with restricted maximum likelihood.

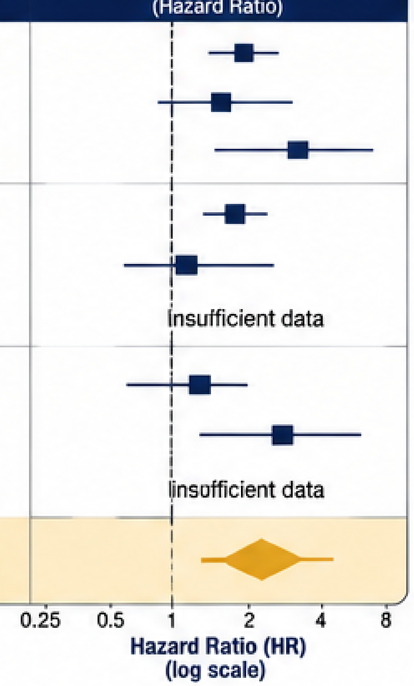
RESULTS: STUDY SNAPSHOT

16 retrospective cohort studies included

9,021 patients included

7,969 patients underwent mutation testing

Mutation	Outcome	Hazard Ratio (95% CI)	I^2 (%)	I^2 (%)
NRAS	Overall survival (OS)	**1.73**	1.46 – 2.04	5.3
	Leukemia transformation	**1.64**	1.17 – 2.30	0
	Leukemia-free survival (LFS)	**2.48**	1.47 – 4.18	71.5
KRAS	Overall survival (OS)	**1.66**	1.32 – 2.08	8.7
	Leukemia transformation	**1.41**	0.90 – 2.20	12.1
	Leukemia-free survival (LFS)	–	–	–
PTPN11	Overall survival (OS)	**1.36**	1.01 – 1.85	0
	Leukemia transformation	**2.11**	1.41 – 3.16	0
	Luukemia-free survival (LFS)	–	–	–
All RAS mutations	**Overall survival (OS)**	**2.23**	**1.51 – 3.29**	**37.5**



KEY FINDINGS

NRAS mutations
associated with worse OS, higher risk of leukemia transformation, and inferior LFS.

KRAS mutations
associated with reduced OS but not significantly with leukemia transformation.

PTPN11 mutations
associated with poorer OS and increased leukemia transformation risk.

Overall, RAS mutations
associated with significantly worse OS.

CONCLUSIONS

RAS pathway mutations are associated with adverse survival outcomes in MDS, **particularly for NRAS and PTPN11. These findings support the incorporation of RAS mutational status into prognostic models.**
Further prospective studies are needed to validate these results and guide therapeutic strategies.