DYNAMIC ASSESSMENT OF RBC-TRANSFUSION DEPENDENCY (RBC-TD) IMPROVES THE MOLECULAR INTERNATIONAL PROGNOSTIC SCORING SYSTEM (IPSS-M) RISK STRATIFICATION OF MDS

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INTRODUCTION

- Dynamic assessment of red blood cell transfusion dependency (RBC-TD) is associated with poor prognosis independent of the Revised International Prognostic Scoring System (IPSS-R).[1]
- The molecular IPSS (IPSS-M) is a novel prognostic model for myelodysplastic syndrome (MDS) integrating somatic mutations, blood counts, bone marrow blast and cytogenetic parameters.

AIM

This study evaluates the prognostic value of dynamic assessment of RBC-TD as a predictor of overall survival (OS) in MDS along with IPSS-M in an independent cohort.

METHOD

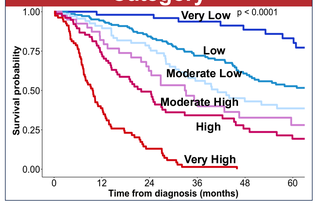
- 461 MDS or MDS/myeloproliferative neoplasm patients with somatic mutation data from the South Australian Myeloid Neoplasm (SA-MN) registry.
- IPSS-M was calculated based on diagnostic bone marrow, cytogenetic and mutation profiles and blood counts. Mean values were assigned to missing 18.1% of genetic data.[2]
- RBC-TD was defined as ≥8 RBC units within 16 weeks. Pre-transfusion blood counts were used for IPSS-M calculations in patients who were RBC-TD at diagnosis.
- Minimum one-year follow-up from diagnosis to censor April 9th, 2024. Patients were censored at time of hematopoietic stem cell transplantation.

RESULTS

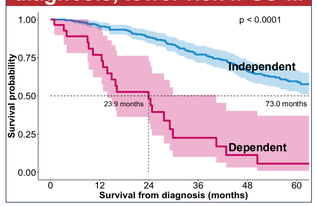
- The median age at diagnosis was 71 years
- 65.1% of patients were male
- 86.3% were MDS while 13.7% were MDS/MPN
- 67.7% died within the study period with a median overall survival of 39.6 months

RBC-TD CONFERS POOR PROGNOSIS

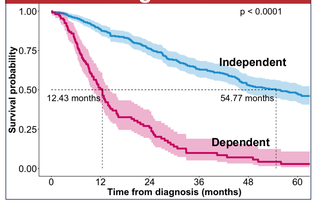
Figure 1A: OS by IPSS-M Category



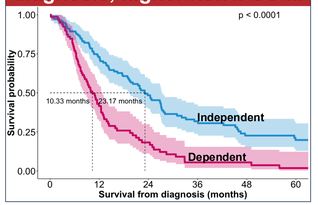
1D OS by RBC-TD status at diagnosis, lower risk IPSS-M



1B OS by RBC-TD status at diagnosis



1E OS by RBC-TD status at diagnosis, higher risk IPSS-M



1C OS by RBC-TD status at diagnosis, HMA patients

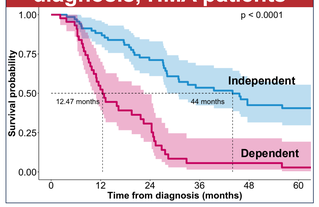


Figure 1: RBC-TD is associated with poor prognosis. **(A)** OS was progressively shorter in greater-risk IPSS-M categories with similar distribution to Bernard et al 2022[2]; **(B)** RBC-TD status at diagnosis is associated with poor prognosis (12.4 *vs.* 54.8 months; $P < 0.0001$); **(C)** this trend persisted in patients receiving hypomethylating agents (HMAs); **(4)** RBC-TD at diagnosis confers poor OS in 'lower risk' (Very Low, Low and Moderate Low IPSS-M) and **(E)** 'higher risk' (Moderate High, High, and Very High) groups.

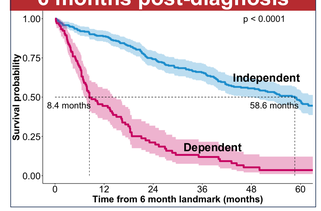
RBC-TD IS INDEPENDENT TO IPSS-M

	Variable	Hazard	P
RBC-TD	Independent		
	Dependent		<0.001
IPSS-M	Very Low		
	Low		0.004
	Moderate Low		<0.001
	Moderate High		<0.001
	High		<0.001
	Very High		<0.001
Age	Under 60		
	60-70		0.157
	70-80		0.002
	Over 80		<0.001
Sex	Female		
	Male		0.004

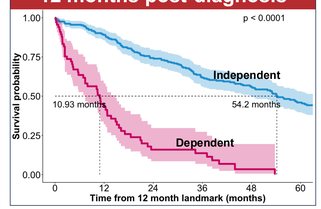
Table 1: 23.2% of patients were RBC-TD at diagnosis, with higher rates in greater risk IPSS-M categories. In multivariate Cox proportional-hazards analysis, RBC-TD was associated with poor OS independent to IPSS-M category, age at diagnosis and sex (HR 2.98, 95% CI 2.23-3.98; $P < 0.001$).

RBC-TD ASSESSED OVER TIME

Figure 2A: OS by RBC-TD 6 months post-diagnosis



2B OS by RBC-TD 12 months post-diagnosis



2C OS by RBC-TD status 24 months post-diagnosis

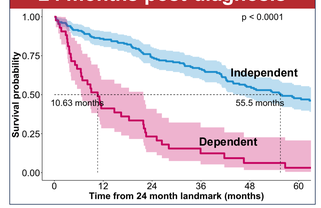


Figure 2: Dynamic assessment of RBC-TD is associated with poor survival. RBC-TD status at **(A)** 6, **(B)** 12 and **(C)** 24-months from diagnosis was associated with poor survival.

Landmark Cox proportional-hazards analysis

The hazard ratio for RBC-TD was **2.94**, **3.86** and **2.95** at 6, 12 and 24 months, respectively.

Thus, RBC-TD is a dynamic prognostic indicator that can be reassessed throughout a patient's disease course.

CONCLUSIONS

Dynamic assessment of RBC-transfusion dependency predicts poor survival independent to the IPSS-M.

RBC-TD should be considered in treatment decisions, particularly noting the poor outcomes of transfusion-dependent lower-risk IPSS-M patients.

REFERENCES

1. Hiwase et al. *Dynamic assessment of RBC-transfusion dependency improves the prognostic value of the revised-IPSS in MDS patients*. Am J Hematol. 2017 Jun;92(6):508-514
2. Bernard E et al. *Molecular International Prognostic Scoring System for Myelodysplastic Syndromes*. NEJM Evid. 2022 Jul;1(7)

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CONTACT INFORMATION

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