

A Simplified 3-Marker Panel for MDS Prognostic Outperforms IPSS-R

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Abstract

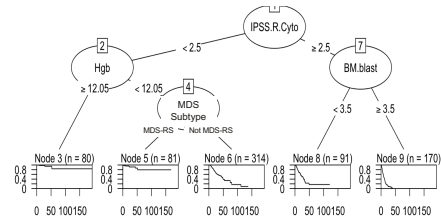
Myelodysplastic syndromes (MDS) are a group of hematopoietic stem-cell disorders with heterogeneous survival rates. The most popular prognostic scoring system for MDS patients is the Revised International Prognostic Scoring System (IPSS-R)¹. IPSS-R panel comprises of 5 patient characteristics: hemoglobin (Hgb), bone marrow blast (BM Blast), absolute neutrophil count (ANC), cytogenetics, and platelets (Plt); all in the form of categorical variables, and classifies patients into 5 different survival groups. This prognostic scoring system still lacks the ability to differentiate patients with high accuracy, thereby better prognostic models is warranted.

Material and Method

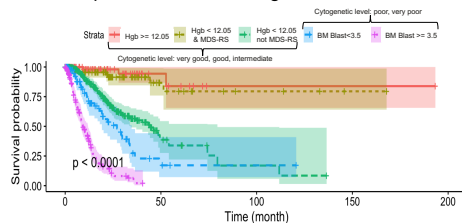
The primary study outcome was overall survival, the time between first diagnosis and death or last follow-up, and probability of death for 982 MDS patients treated at MDACC between 2009 and 2019. Among them, 45% of patients were MDS-EB, 28% MDS-MLD, 12% MDS-RS, 6% MDS-SLD, 6% MDS-U, 2% 5q-, and the rest MDS-MLD-RS. The median time to follow-up was 12 months with a 36% incidence of death. Patients were randomly split into 75% training and 25% testing cohorts. On training set, we used different methods to perform feature selections such as Cox Lasso, tree regression, univariate, and multivariate analyses and the common covariates across these 4 approaches are considered as key features.

Results: R-Part Model

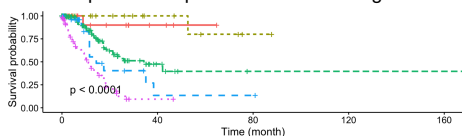
R-part model developed on training set with the number of trees corresponding to the minimum relative error



- Survival probability of different groups derived from r-part model on training set



- The r-part model performance on testing cohort



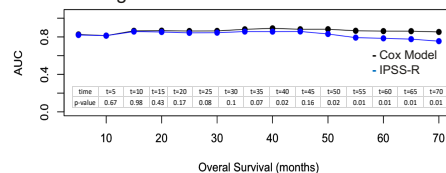
Results: Cox Regression Model

Cox Regression Hazard Model developed on training set based on Hgb, cytogenetic level & MDS subtype

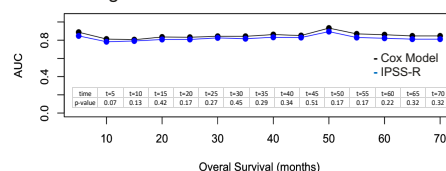
	Hazard Ratio (95% Confidence Interval)		P-value
Hgb	0.752	(0.7, 0.81)	< 2e-16
IPSS.R.Cyto	1.681	(1.55, 1.83)	< 2e-16
MDS-EB	1.132	(0.53, 2.42)	0.75
MDS-MLD	0.522	(0.24, 1.14)	0.102
MDS-MLD-RS	0.604	(0.07, 4.96)	0.639
MDS-RS	0.233	(0.1, 0.57)	0.001
MDS-SLD	0.678	(0.29, 1.56)	0.362
MDS-U	0.522	(0.21, 1.3)	0.163

Time AUC performance comparison between Cox model & IPSS-R

Training set

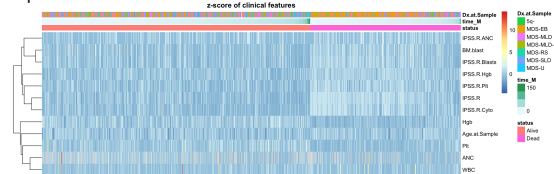


Testing set



Results: Clinical Features

Heatmap showing clinical features variation versus last follow-up time & incidence of death



Conclusions

- We have compared different algorithms to interrogate key factors on MDS prognostic through IPSS-R and ended up with 3 essential covariates
- Our proposed Cox regression hazard model was trained on training set from the common features: Hgb, Cytogenetic level, and disease subtype
- Not only does the new model utilize fewer variables, it also showed AUC performances of 0.85, 0.86, and 0.93 in the testing cohort at 70, 60, and 50 months, respectively which corresponds to an average of 4% AUC improvement compared to IPSS-R score.
- We anticipate that this improvement be the result of including disease subtypes and considering Hgb as a continuous variable rather than factorial

Reference

1. Greenberg, Peter L., et al. "Revised international prognostic scoring system for myelodysplastic syndromes." *Blood, The Journal of the American Society of Hematology* 120.12 (2012): 2454-2465. Journal Article, Name of Journal