

Validation of Refined Disease Risk Index and analysis of host and transplant factors in two Brazilian institutions for allogeneic HSCT

Leonardo J. Arcuri¹, Andreza Ribeiro², Simone Maradei¹, Vinicuis Mattos², Andre Oliveira¹, Cinthya Silva², Simone Lermontov¹, Nelson Hamerschlak², Renato Castro¹

¹Centro de Transplante de Medula Óssea, Instituto Nacional de Cancer, Rio de Janeiro, Brazil

²Hospital Israelita Albert Einstein, São Paulo, Brazil

Introduction: Allogeneic hematopoietic stem cell transplantation (HSCT) is a potentially curative therapy for many hematologic malignancies. Risk assessment before transplant is crucial for balancing morbidity and mortality associated with this procedure. Currently some algorithms are used in clinical practice for this assessment. The Disease Risk Index, which was refined in 2014, was developed as a tool for comparing different populations. In Brazil about 1000 allogeneic transplants were performed in 2014. We report the results of a retrospective study in two highly heterogeneous institutions in Brazil, designed to evaluate DRI as a tool to predict transplant outcome.

Results: 277 patients were included. Median follow-up was 34 months. Median age was 36 (range 1-75). The cohort included a broad representation of diseases: 101 AML patients; 77 ALL patients; 35 lymphoproliferative disorders and 24 myelodysplastic syndromes. Other patients' characteristics are reported in Table 1. Mortality at 100 days was 25%. Kaplan-Meier estimate of overall survival at 1 year and 2 years was 54% and 42%. Overall survival curves according to DRI score are reported in Figure 1. Multivariate analyses (Table 2) identified age, unrelated and haploidentical donors, and DRI high/very high risk as risk factors. Age > 50 years, conditioning intensity and stem cell source were not related to death in multivariate analysis, although cord blood was associated to worse outcome in univariate analysis. Interaction test was negative for DRI and age, and DRI and donor type.

Conclusion: DRI predicted outcome in our population, which also included alternative donors (as haploidentical and cord blood) and children, and allowed us to make inferences about other risk factors. Our data suggests that age alone does not negatively influence outcomes, confirming previous reports. Unexpectedly, unrelated donors were associated to poorer outcome. This could be explained by differences in patient referral and delay until transplant.

Table 1. Patients' Characteristics

	HIAE	INCA	P value
Total	111	166	
Gender			0.861
Male	65 (59.6%)	102 (61.4%)	
Female	44 (40.4%)	64 (38.6%)	
Age (years)			< 0.001
<18	19 (17.4%)	53 (31.9%)	
18-50	46 (42.2%)	88 (53%)	
>50	44 (40.4%)	25 (15.1%)	
Disease Risk Index			0.192
Low	9 (8.3%)	9 (5.4%)	
Intermediate	66 (60.6%)	99 (59.6%)	
High	30 (27.5%)	41 (24.7%)	
Very High	4 (3.7%)	17 (10.2%)	
Stem Cell Source			0.571
Bone Marrow	65 (59.6%)	104 (62.7%)	
Peripheral Blood	29 (26.6%)	46 (27.7%)	
Cord Blood	15 (13.8%)	16 (9.6%)	
Donor			< 0.001
Sibling	33 (30.3%)	112 (67.5%)	
Unrelated	58 (53.2%)	52 (31.3%)	
Haploidentical	18 (16.5%)	2 (1.2%)	
Conditioning			< 0.001
Reduced Intensity	43 (39.4%)	16 (9.6%)	
Myeloablative	66 (60.6%)	150 (90.4%)	

HIAE, Hospital Israelita Albert Einstein.
INCA, Instituto Nacional de Cancer

Patients & methods: This is a retrospective study. All patients with hematologic malignancies who underwent first allogeneic HSCT at HSCT Unit of the Hospital Israelita Albert Einstein and at Instituto Nacional do Cancer between Jan'2010 to Dec'2014 were included. DRI was defined retrospectively. Survival estimates were calculated using Kaplan-Meier survival curves. Risk factor for death were estimated by Cox model, stratified for center.

References:

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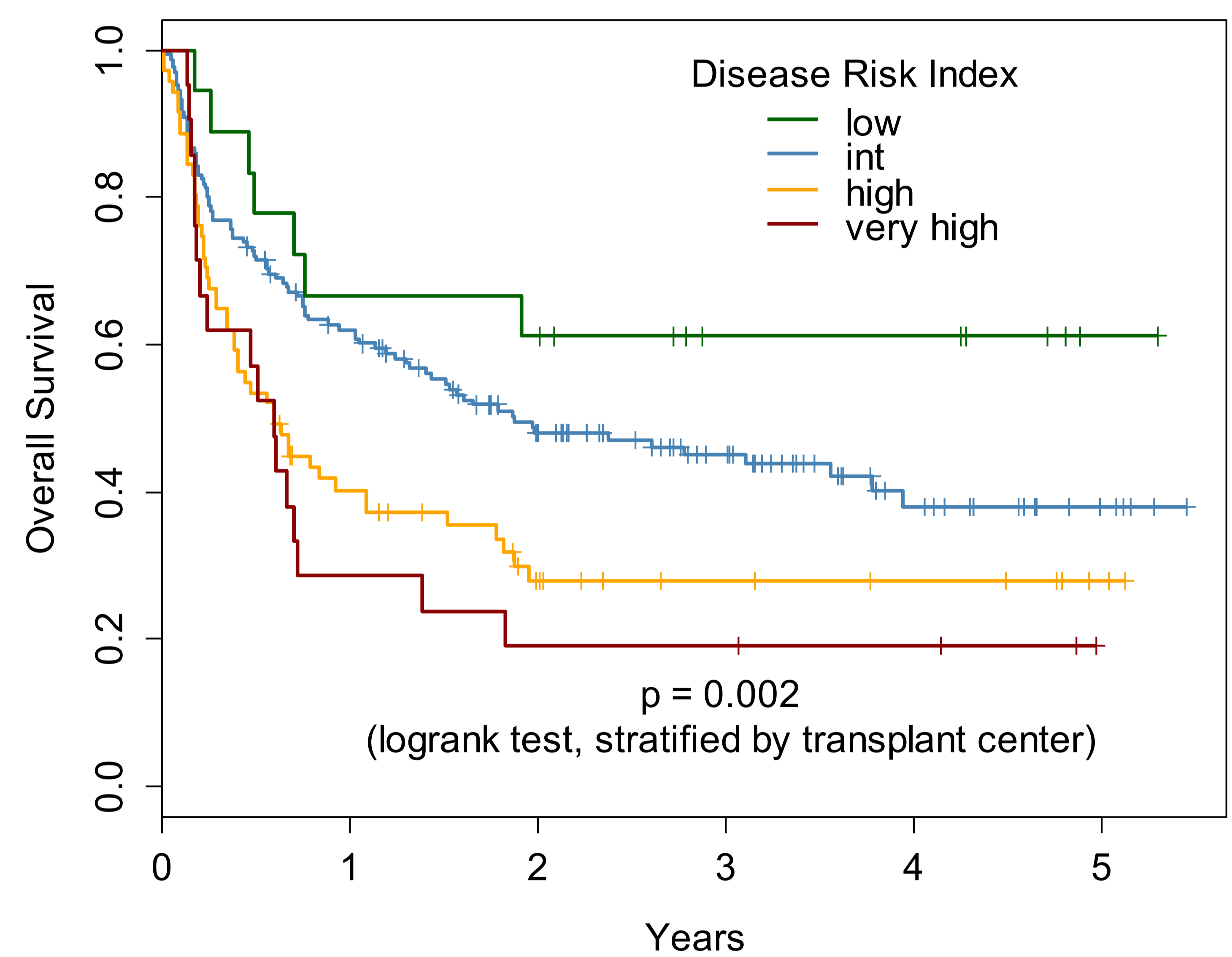


Table 2. Uni and multivariate analysis for overall survival

	Univariate		Multivariate	
	HR	P-value	HR	P-value
Age				
<18	0.86 (0.58 – 1.27)	0.44	0.54 (0.35 – 0.84)	0.006
18 – 50	Ref		Ref	0.17
>50	1.28 (0.88 – 1.87)	0.20	1.31 (0.89 – 1.92)	
Gender				
Male			Ref	
Female	0.85 (0.62 – 1.17)	0.32	0.79 (0.56 – 1.10)	0.17
Disease Risk Index				
Low	0.59 (0.27 – 1.28)	0.18	0.62 (0.28 – 1.35)	0.23
Int	Ref		Ref	
High/Very High	1.71 (1.24 – 2.36)	0.001	1.80 (1.27 – 2.54)	< 0.001
Stem Cell Source				
BM	Ref		Ref	
PB	1.35 (0.96 – 1.92)	0.09	1.16 (0.81 – 1.67)	0.42
UCB	2.00 (1.25 – 3.19)	0.004	1.32 (0.77 – 2.27)	0.31
Donor Type				
Sibling	Ref		Ref	
Unrelated	1.94 (1.38 – 2.74)	< 0.001	1.96 (1.32 – 2.90)	< 0.001
Haploidentical	2.05 (1.04 – 4.04)	0.04	2.54 (1.27 – 5.08)	0.008

Stratified by transplant center