Predictive Value of the Immunodeficiency Scoring Index for COVID-19 Related Outcomes in Hematopoietic Cell Transplant Recipients

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Introduction

- Coronavirus disease 2019 (COVID-19) related mortality in allogeneic hematopoietic cell transplant (allo-HCT) recipients was reported as high as 21%. HCT recipients also had a rate of 14% of severe COVID-19.
- A scoring algorithm to predict severity and mortality related to COVID-19 in HCT recipients would identify patients that may require support and antiviral therapy to prevent complications.
- The Immunodeficiency Scoring Index (ISI) was developed as a prognostic tool in allo-HCT recipients with respiratory syncytial virus to predict severe infections and mortality. It has been validated in multiple cohorts for other viruses.
- The purpose of this study was to correlate the ISI in allo-HCT recipients with COVID-19 and associated complications such as hospitalization, supplemental oxygen use, and mortality.

Methods

- We performed a cohort study of HCT recipients of all ages with COVID-19 between March 2020 and October 2021.
- We included patients who were diagnosed by PCR-based assays. We excluded patients for whom an ISI score could not be calculated.
- Components of the ISI are shown in Table 1.
- Based on the ISI, patients are stratified into low (0-2), moderate (3-6), and high (7-12) risk groups. For the purpose of our analysis, low and moderate-high were analyzed as binary variables.
- Outcomes of interest included hospital and ICU admission due to COVID-19, supplemental oxygen use, and 60-day mortality.
- A univariate analysis using Fischer exact testing and Wilcoxon rank sum were used as appropriate.

Table 1: Immunodeficiency Scoring Index

ANC <500/μL	3
ALC <200/μL	3
Age ≥40 years	2
Myeloablative conditioning regimen	1
GvHD (acute or chronic)	1
Corticosteroid use	1
Recent or pre-engraftment allo-HCT	1

Abbreviations: ALC (absolute lymphocyte count); allo-HCT (allogeneic hematopoietic cell transplantation); ANC (absolute neutrophil count); GvHD (graft versus host disease)

Table 2: Patients' Characteristics

Variable		HCT recipients with COVID-19 N=118
	Median age in years (range)	60 (6-85)
Gender (%)	Male	66 (56)
	Female	52 (44)
Ethnicity (%)	African American	14 (12)
	Asian	6 (5)
	Caucasian	67 (57)
	Hispanic	29 (25)
	Middle Eastern	2 (2)
Non-Cancer Comorbidities (%)	Hypertension	63 (53)
	Diabetes mellitus type 1 or 2	44 (37)
	Hyperlipidemia	49 (42)
	COPD	4 (3)
	BMI > 30	44 (37)
Indication for Transplant (%)	Acute Lymphocytic Leukemia	9 (8)
	Acute Myeloid Leukemia/Myelodysplastic Syndrome	37 (31)
	Aplastic Anemia	2 (2)
	Chronic Lymphocytic Leukemia	4 (3)
	Chronic Myeloid Leukemia/Myeloproliferative Disorder	6 (5)
	Hodgkin's Lymphoma	4 (3)
	Non-Hodgkin's Lymphoma	19 (16)
	Myeloma	35 (30)
	Solid Tumor	1 (<1)
	Other	1 (<1)
Type of Transplant (%)	Matched Related Donor	30 (25)
	Matched Unrelated Donor	25 (21)
	Haploidentical	7 (6)
	Mismatched Unrelated Donor	2 (2)
	Cord Blood	2 (2)
	Autologous	52 (44)

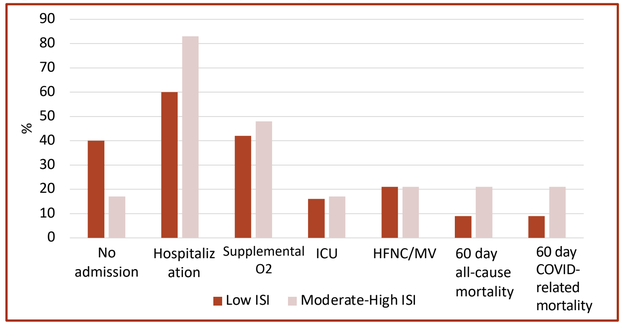
Abbreviations: COPD (chronic obstructive pulmonary disease); BMI (body mass index)

Table 3: Characteristics of COVID-19

Median Time from Transplant in Days (range)	615 (2-5692)	
Median Number of Patients Presenting with Pneumonia (%)	97 (82)	
Vaccination Status at Time of Infection (%)	Partially Vaccinated	1 (<1)
	Primary Series (2 doses)	2 (2)
	Primary Series + Booster	7 (6)
	Unvaccinated	108 (92)
ISI analysis	Median ISI (range)	3 (0-11)
	Low ISI (%)	43 (36)
	Moderate-High ISI (%)	75 (64%)
	ISI ≥ 4 (%)	39 (33)
Treatment for COVID-19 (%)	Remdesivir	63 (53)
	Steroids for COVID-19	45 (38)
	Anakinra	4 (3)
	Convalescent Plasma	40 (34)
	Tocilizumab	12 (10)
	Hydroxychloroquine and Azithromycin	3 (3)
	COVID-19 Specific Monoclonal Antibodies	6 (5)

Abbreviations: ISI (immunodeficiency scoring index); COVID-19 (coronavirus disease 2019)

Figure 1: COVID-19 Outcomes by ISI Group

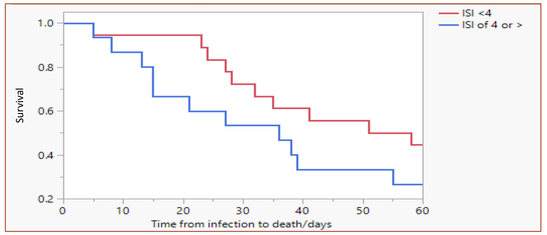


Abbreviations: HFNC (high flow nasal cannula); ICU)(intensive care unit); MV (mechanical ventilation); O2 (oxygen)

Results

- A cohort of 118 patients were analyzed.
- The median age was 60 years (range 6-85). Most of the patients were male (56%), had undergone HCT for acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS) (31%), and had undergone an allogeneic HCT (56%) (Table 2).
- The median time from transplant to COVID-19 was 615 days (range 2-5692). 82% presented with pneumonia, 92% were unvaccinated (Table 3).
- The median ISI was 3 (range 0-11). 36% had a low ISI and 64% a moderate-high ISI (Table 3).
- Patients with moderate-high ISI had an increased risk of COVID-19 related outcomes (Figure 1). However, on univariate analysis, an ISI of moderate to high (score ≥3) was associated with COVID-19 related hospitalization [p=0.0147].
- On univariate analysis, an ISI of ≥4 was associated with 60-day all-cause (p=0.045) and COVID-19-related (p-0.019) mortality.
- A Kaplan-Meier Curve comparing time to death in patients with an ISI ≥4 is shown in Figure 2 (Log-Rank 0.0295).

Figure 2: Kaplan-Meier Curve Comparing Time to Death in Patients with an ISI Score of 4 or Greater (Log-Rank 0.0295)



Discussion

- Our study demonstrates that the ISI may be used to predict COVID-19 related complications, such as hospital admission and mortality.
- Our study is in line with other studies that validated the use of ISI for COVID-19 to predict complications in HCT recipients.
- Further studies are needed to determine if the ISI can identify patients that would benefit the most from early antiviral therapy.

References

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