Acute Graft-Versus-Host Disease: Risk Scoring and Response to Treatment, Experience From Two Centers

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Background

Risk stratification system for acute graft-versus-host disease (aGVHD) are still in development. They are necessary to facilitate initiation of more appropriate and potentially effective upfront therapy.

Objective

To describe the usefulness of aGVHD risk scores (Magic and Minnesota) to predict mortality and response to treatment.

Materials and Methods

DESIGN: Retrospective cohort study.

SETTING: Two-center study at private referral hospitals. All patients who developed aGVHD after allogenic stem cell transplant (Allo-SCT) from 2017 to 2020.

MAIN OUTCOME MEASURES: Overall response (OR), complete response (CR), partial response (PR) to steroids, 6 and 12-months mortality (M) and transplant-related-mortality (TRM), according to Magic and Minnesota Scores.

Calibration of Magic score (for TRM) with test Hosmer-Lemeshow.

Results

Of 261 patients, 143 (54.8%) developed aGVHD. Median follow-up was 16 months. Median age was 55 years for patients and 35 years for donors.

Number of patients (%)	Cohort (n=261)	GVHD (n=143)
Patient age, y, median (range) **Donor age, y, median** (IQR)	43 (16-74) 32 (13-48)	55 (16-73) 35 (12-50)
Male recipient	164 (63%)	95 (66%)
Diagnosis AML MDS MDS/MPS LLA LNH MPS LH Other	84 (32%) 31 (12%) 3 (1%) 63 (24%) 28 (11%) 23 (9%) 13 (5%) 16 (6%)	44 (31%) 15 (11%) 3 (2%) 30 (21%) 20 (15%) 12 (8%) 13 (9%) 6 (4%)
HCTI 0 1 2 ≥3	103 (39,5%) 46 (17,6%) 47 (18%) 67 (24,9%)	59 (41%) 24 (17%) 28 (20%) 32 (22%)
TBI	117 (45%)	67 (46%)
Conditioning intensity RIC MAC	135 (52%) 126 (48%)	78 (54%) 65 (46%)
Response before transplantation Complete Partial Other	152 (58%) 30 (12%) 79 (30%)	75 (52%) 26 (18%) 42 (29%)
CD 34 doses (10^6/kg) **CD 3 doses (10^8/kg)**	7,56 (3,13) 2,93 (1,25)	7,54 (2,87) 2,92 (1,18)
Transplant MRD-SCT Haplo-SCT MUD-SCT	82 (31%) 85 (33%) 94 (36%)	40 (28%) 43 (30%) 60 (42%)

AML, acute myeloid leukemia; MDS, myelodysplastic syndrome; MPS, myeloproliferative syndrome; LLA, acute lymphoid leukemia; NHL, non Hodgkin lymphoma; HL, Hodgkin lymphoma. TBI, Total body irradiation; RIC, reduced-intensity conditioning; MAC, myeloablative conditioning; MRD-SCT, related hematopoietic stem cell transplant; Haplo-HSCT, haploidentical stem cell transplant; MUD-HSCT, unrelated hematopoietic stem cell transplant.

Initial aGVHD involved skin (53%), upper gastrointestinal (5%), upper or lower GI (9%), liver (1%), or multi-organ (31%). Median time to steroid therapy initiation was 52 days.

Number of patients (%)	Grade*				
	NO	1	2	3	4
Upper gastrointestinal	105 (74%)		38 (26%)		
Low gastrointestinal	97 (68%)	3 (2%)	12 (8%)	9 (6%)	22 (15,5%)
Skin	22 (16%)	50 (35%)	49 (34%)	20 (14%)	2 (1,4%)
Liver	120 (84%)	10 (7%)	5 (4%)	4 (3%)	4 (3%)

Number of patients (%)	GVHD (n=143)
Grade 3-4	40 (28%)
Number of organs 1 2 3 4	91 (64%) 28 (20%) 15 (10%) 9 (6%)
Minnesota Score Standard High	102 (71%) 41 (29%)
Magic Score I II III IV	67 (47%) 28 (20%) 22 (15%) 26 (18%)
IBMTR 0 A B C D	8 (6%) 40 (28%) 51 (36%) 19 (13%) 25 (17%)
Corticoids Response Refractory disease CR PR	24 (17%) 100 (70%) 19 (13%)

GVHD, graft versus host disease; CR, complete response; PR, partial response.

Magic Score classified 47% of patients as grade I, 29% as grade II, 15% as grade III, and 18% as grade IV. Minnesota Score classified 29% of patients as high risk (HR) and 71% as standard risk (SR).

Response to steroids:

Minnesota: OR was significantly higher for SR patients than HR patients (97% versus 52%) p=<0.0001. In logistic regression analysis, HR patients were less likely to respond to first-line therapy (odds ratio 0.03, 95% CI 0.008–0.114, p<0.0001).

Magic Score: OR was similar for grades I and II (94% and 96% respectively) but decrease in grade III (63%) and IV (27%; p=0.0001).

Number of patients (%)	Total	NR	PR	CR	p
MAGIC					<0,0001
I	61	2 (3%)	2 (3%)	57 (94%)	
II	27	0	1 (4%)	26 (96%)	
III	22	3 (14%)	5 (23%)	14 (63%)	
IV	26	19 (72%)	4 (17%)	3 (11%)	
Minnesota					<0,0001
SR	95	3 (3%)	4 (4%)	88 (93%)	
HR	41	21 (52%)	8 (19%)	12 (29%)	

CR, complete response; NR, no response; PR, partial response; SR, standard risk; HR, high risk.

Mortality

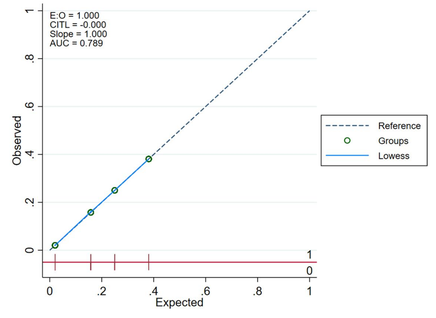
The 6 a 12-months-TRM are significantly higher in the patients with Minnesota HR (21% and 31%), Magic III (14% and 25%) and IV (26% and 38%).

The 6 a 12-months-TRM is lower in the patients with Minnesota SR, Magic I and II even when comparing with the whole cohort.

	6m-M	12m-M	6m-TRM	12m-TRM
Whole cohort	19% (CI 15-25%)	30% (CI 25-37%)	13.27% (CI 9% - 18%)	18% (CI 9-18%)
GVHD	15% (CI 10-22%)	27% (CI 19-35%)	9% (IC 5 - 16%)	15% (CI 9-23%)
MAGIC	**p=0,6**	**p=0,01**	**p=0,005**	**p=0,001**
I	10 % OR 0,5	14% OR 0,5	2% OR 0,3	2% OR 0,1
II	14 % OR 0,8	28% OR 1	8% OR 0,5	15% OR 0,7
III	14 % OR 0,8	35% OR 1,3	14% OR 1	25% OR 1,1
IV	32 % OR 1,6	45% OR 1,5	26% OR 1,5	38% OR 1,7
Minnesota	**p=0,03**	**p=0,1**	**p=0,03**	**p=0,01**
SR	11% OR0,5 (CI 6-19%)	23 % OR 0,7 (CI 15-33%)	4.5% OR 0,3 (0.1-11%)	8% OR 0,5 (CI 3-16%)
HR	25% OR1,2 (CI 13-41%)	36 % OR 1,1 (CI 21-54%)	21% OR 1,3 (CI 10-37%)	31% OR 1,5 (CI 17 - 50%)

M, Global mortality; NRM, non-relapse mortality; SR, standard risk; HR, high risk.

TRM Calibration (Magic score): the area under the ROC curve (AUC) was 0.78 (95% CI 68 - 98), and the p value for the Hosmer-Lemeshow goodness-of-fit was 0.05. This indicates good discrimination and calibration.



Conclusion

HR and III/IV GVHD are less likely to respond to steroids than standard-risk patients.

Patients with HR and III/IV GVHD have higher risks of mortality and TRM.

Patients with SR and III/IV have higher risks of mortality and TRM compared to whole cohort.

References

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