HemaSphere

EHA EUROPEAN HEMATOLOGY ASSOCIATION

Article
Open Access

External Validation of the Revised Pretransplant Assessment of Mortality Score in Allogeneic Hematopoietic Cell Transplantation: A Cohort Study

Nicolas Fattinger[1,2], Jan A. Roth[2,3], Helen Baldomero[1,2], Daiana Stolz[2,4], Michael Medinger[1,2,5], Dominik Heim[1,2], Michael Tamm[2,4], Jörg P. Halter[1,2], Jakob R. Passweg[1,2], Martina Kleber[1,2,5,6]

Correspondence: Martina Kleber (martina.kleber@usz.ch).

ABSTRACT

Pretransplant risk scores such as the revised Pretransplant Assessment of Mortality (rPAM) score help to predict outcome of patients receiving allogeneic hematopoietic cell transplantation (allo-HCT). Since the rPAM has not been validated externally in a heterogeneous patient population with different diseases, we aimed to validate the rPAM score in a real-world cohort of allo-HCT patients. A total of 429 patients were included receiving their first allo-HCT from 2008 to 2015. The predictive capacity of the rPAM score for 4-year overall survival (OS), nonrelapse mortality (NRM), and cumulative incidence of relapse (CIR) after allo-HCT was evaluated. Moreover, we evaluated the impact of the rPAM score for OS and used uni- and multivariable analyses to identify patient- and transplant-related predictors for OS. In rPAM score categories of <17, 17–23, 24–30, and >30, the OS probability at 4 years differed significantly with 61%, 36%, 26%, and 10%, respectively ($P < 0.0001$). In contrast to CIR, the NRM increased significantly in patients with higher rPAM scores ($P < 0.001$). Regarding the OS, the rPAM score had an area under the receiver operating characteristics curve of 0.676 (95% confidence interval [CI], 0.625-0.727) at 4 years. In the multivariable analysis, the rPAM score was associated with OS—independently of conditioning regimens (adjusted hazard ratio per 1-unit increase, 1.10; 95% CI, 1.06-1.10; $P < 0.001$). Additionally, forced expiratory volume in 1 second and the disease risk index were the components of the rPAM significantly associated with outcome. In our large real-world cohort with extended follow-up, the rPAM score was validated as an independent predictor of OS in patients with hematologic disorders undergoing allo-HCT.

INTRODUCTION

Allogeneic hematopoietic cell transplantation (allo-HCT) has become a standard treatment for numerous malignant and nonmalignant hematologic disorders.[1–3] Patient outcomes have improved over the last years, but allo-HCT is still associated with substantial transplant-related morbidity and mortality.[4–7] Therefore, evaluation of the patient- and disease-related safety profiles is essential to balance harms and benefits of allo-HCT.[8] Different scores to predict outcome after HCT have been developed. For comorbidity measurement, the Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI) is a well-established weighted comorbidity score, which reflects organ dysfunction with 17 comorbidities to predict nonrelapse mortality (NRM) and overall survival (OS) after HCT.[9,10] In contrast, the European Society for Blood and Marrow Transplantation (EMBT) pretransplantation risk score combines disease- and transplant-related risk factors by including variables such as age, disease stage, time from diagnosis, donor type, and donor–recipient sex combinations, but it does not account for comorbidities.[11]

The Pretransplant Assessment of Mortality (PAM) score was originally developed in 2006 to predict all-cause mortality after HCT and included the following 8 items: age, donor type, disease risk, conditioning regimen, serum creatinine, serum alanine aminotransferase, forced expiratory volume in 1 second (FEV1), and carbon monoxide diffusing capacity of the lung.[12] The advantage of this score is incorporating actual laboratory values to represent organ function instead of score based on dichotomized patient narratives. Due to evolving allo-HCT strategies with more frequent application of non-myeloablative conditioning regimens (MAC), the PAM score was re-evaluated and simplified 9 years later[13]: While serum creatinine, serum alanine aminotransferase, and carbon monoxide diffusing capacity were no longer identified as risk factors in allo-HCT, patient and donor cytomegalovirus (CMV) serology were associated with OS and added to the PAM score. The revised PAM (rPAM) score has been validated in a cohort of patients with acute

[1]Divisions of Hematology, University Hospital Basel, Switzerland
[2]University of Basel, Switzerland
[3]Division of Infectious Diseases and Hospital Epidemiology, University Hospital Basel, Switzerland
[4]Division of Respiratory Medicine and Pulmonary Cell Research, University Hospital Basel, Switzerland
[5]Department of Internal Medicine, University Hospital Basel, Switzerland
[6]Division of Internal Medicine, University of Zurich, Switzerland
Supplemental digital content is available for this article.

HemaSphere (2022) 6:4(e704).
http://dx.doi.org/10.1097/HS9.0000000000000704.
Received: July 9, 2021 / Accepted: February 21, 2022

myelogenous leukemia receiving allo-HCT where it was associated with all-cause mortality, cumulative incidence of relapse (CIR), and NRM.[14] However, since the rPAM score has not been validated externally in allo-HCT cohorts covering a wider spectrum of diseases, we aimed to validate the rPAM score in a real-world cohort of patients with an extended follow-up.

MATERIAL AND METHODS

Patient population and study design

We conducted a cohort study at the Division of Hematology, University Hospital Basel: From 2008 to 2015, consecutive patients receiving a first allo-HCT to treat hematological disorders were included. Patients with a missing rPAM score (15 of 429 patients) were excluded from the final analyses. The study period was chosen to allow a reasonable long-term follow-up of the patients.

We conducted the study according to the Declaration of Helsinki. Our study was approved by the Ethics Committee of Northwestern and Central Switzerland (EKNZ project number 2015-449).

Conditioning regimens and graft-versus-host disease prophylaxis

MAC included cyclophosphamide plus busulfan (n = 148), cyclophosphamide with total body irradiation (TBI) >8 Gy (n = 87), and other protocols (n = 95). Reduced conditioning regimens (RIC) consisted of fludarabine with low-dose TBI <6 Gy (n = 62), fludarabine plus busulfan (n = 26), and other protocols (n = 11). Reasons for RIC were advanced age or relevant comorbidities.[15] Graft versus host disease (GvHD) prophylaxis administered along with the MAC was cyclosporine A and methotrexate as well as anti–T-cell globulins (ATG) in case of an unrelated donor. In patients with RIC, the GvHD prophylaxis consisted of cyclosporine A, methotrexate, and ATG in case of an unrelated donor. In matched related donors ≥40 years, GvHD prophylaxis was performed according to institutional standards (if RIC was fludarabine/busulfan) or cyclosporine A and mycophenolate mofetil (if RIC was fludarabine/low-dose TBI).[15]

Pretransplantation assessment and definition

As depicted in Table 1, we analyzed patient-, disease-, and transplant related variables including all variable required to calculate the rPAM score.[12,13] Based on pretransplant patient characteristics transplant-related risk factors, comorbid conditions, and the patient performance were scored. We calculated the rPAM score via an online calculator (http://pamscore.org/[13]) dividing the study population into four risk categories: rPAM score <17, rPAM score 17–23, rPAM score 24–30, and rPAM score >30, based on the original studies of the PAM and rPAM score.[12,13] The components of the rPAM score and how it was constructed are shown in Suppl. Table S1. The disease risk index (DRI) was categorized into low, intermediate, high, and very high[16]; and the HCT-CI was scored according to Sorror et al.[10,17] Pulmonary function tests were performed routinely at baseline (ie, immediately before HCT), to include FEV1, maximal vital capacity, total lung capacity, and diffusion capacity of the lung for carbon monoxide: these results were expressed as percentages of predicted normal values.[18]

Study endpoints and statistical analysis

Our primary outcome measure was the OS at 4 years. Secondary outcomes included the NRM and CIR.

Due to the non-normal data distribution, quantitative variables were expressed as median (interquartile range [IQR]). Categorical variables were presented as proportions. The cumulative incidence function of NRM and CIR was estimated by accounting for competing risks[19]: relapse and NRM were used reciprocally for competing risks.

Probabilities of OS were estimated using Kaplan-Meier survival functions. Variables which are not part of the rPAM score such as type of conditioning regimens (RIC versus MAC), TBI (yes versus no), GvHD prophylaxis (ATG versus non–ATG-based), the Karnofsky performance status (KPS) and the rPAM score were included a priori in univariable and multivariable Cox proportional hazards models. Regarding the OS, the follow-up was specified for each patient from allo-HCT until death from any cause or the last follow-up within 4 years after allo-HCT. The proportional hazards assumption has been met in the respective models. To analyze the discrimination of the rPAM for OS, we used the area under the receiver operating characteristics curve (AUROC).

These computations relied on standard software (SPSS Statistics v25, IBM, Chicago, IL, and Stata SE v16; StataCorp LLC, College Station, TX). All P values are 2-sided and were considered significant at $P < 0.05$.

RESULTS

Patient characteristics

Of the 429 patients studied, the median age was 54 years (IQR, 43–61 years). Median follow-up of surviving patients was 62 months (IQR, 13–124 months). Main hematologic diagnoses were myeloid malignancies (59%) and lymphoid malignancies (38%) (Table 1).

Conditioning regimens were largely myeloablative (77%); 23% were reduced intensity regimens. A majority of patients (57%) received cyclosporine and methotrexate, or mycophenolate without ATG, whereas GvHD prophylaxis was ATG based in 43%.

Donor type was mostly related HLA matched donors in 39%, followed by fully HLA matched unrelated donors in 36%. The primary stem cell source was peripheral blood stem cells (91%). The rPAM could be calculated for 414 of 429 patients with a median of 15 points (IQR, 11–20). In patients receiving MAC and RIC, the median rPAM score was 15 (IQR, 11–19) and 19 (IQR, 14–22), respectively.

Patient-, disease-, and transplant-related predictors or OS, CIR, and NRM

Analysis comparing 4-year-OS, CIR, and NRM are demonstrated in Table 1. In the univariable analysis, the following factors were associated with a reduced OS: age of 65 or more years, higher disease risk, GvHD prophylaxis, KPS <80%, higher HCT-CI and rPAM scores. In patients with different rPAM score categories of <17, 17–23, 24–30, and >30, the OS at 4-year decreased in each rPAM score category from 61% versus 36% versus 26% to 10% ($P < 0.0001$), respectively (Table 1, Figure 1). Correspondingly, the 4-year NRM ($P < 0.001$, Figure 2) and the 4-year CIR ($P = 0.178$) increased with an increasing rPAM score (Table 1). Of note, the rPAM score as a continuous variable was not only significant for OS, NRM, but also for CIR (subdistribution hazard ratio of 1.03 [95% confidence interval {CI}, 1.001–1.051; $P = 0.043$]).

In the final, multivariable analysis, non–ATG-based GVHD prophylaxis (adjusted hazard ratio [HR] 1.76; 95% CI, 1.28-2.240; $P < 0.001$), an impaired performance status of <80% (adjusted HR 1.67; 95% CI, 1.05-2.65; $P = 0.031$), and the rPAM score (adjusted HR per 1-unit increase 1.10; 95% CI, 1.06-1.10; $P < 0.001$) were associated with OS within 4 years (Table 2).

To evaluate each component of the rPAM score on OS, we analyzed the rPAM score in a multivariable analysis (Table 3). Results showed that higher DRI and worsening FEV1 levels (displayed as a continuous linear variable and HR representing

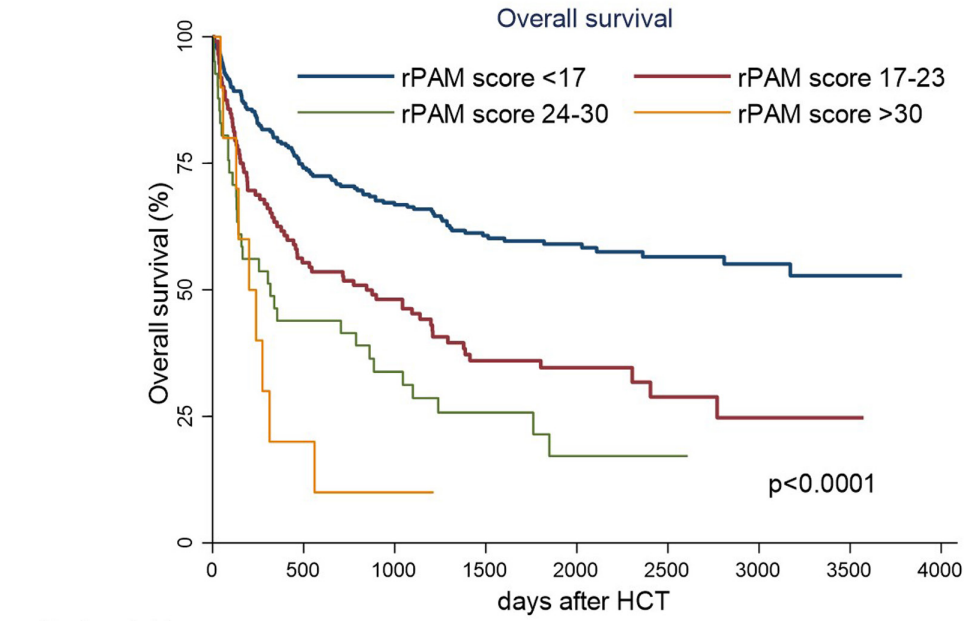
Table 1.

Patient Characteristics and 4-y Outcomes After Allogeneic Hematopoietic Cell Transplantation

Variables	Frequency, n (%)	OS, % (95% CI)	CIR, % (95% CI)	NRM, % (95% CI)
All patients	429 (100)	50 (45-55)	36 (32-41)	20 (16-24)
Age (y)				
<65	377 (88)	52 (47-57)	38 (33-43)	18 (15-22)
≥65	52 (12)	35 (22-49)	35 (22-48)	33 (21-46)
P value		0.041	0.791	0.018
Diagnosis				
Myeloid malignancy	253 (59)	47 (41-53)	40 (34-46)	19 (14-24)
Lymphoid malignancy	164 (38)	53 (45-61)	36 (30-4)	21 (15-28)
Bone marrow failure	12 (3)	67 (34-86)	n.a.	33 (10-59)
P value		0.446	<0.0001	0.365
DRI				
Low risk	61 (14)	74 (61-83)	16 (8-27)	17 (9-27)
Intermediate risk	304 (71)	50 (44-55)	39 (34-45)	20 (16-25)
High risk	54 (13)	30 (18-43)	46 (33-59)	24 (14-36)
Very high risk	10 (2)	30 (7-58)	50 (18-75)	20 (3-47)
P value		<0.0001	0.005	0.743
Conditioning regime				
MAC	330 (77)	53 (47-58)	35 (30-40)	19 (15-24)
RIC	99 (23)	41 (31-50)	45 (35-54)	22 (15-31)
P value		0.112	0.067	0.622
TBI				
No	247 (58)	50 (44-57)	38 (32-44)	19 (14-24)
Yes	182 (42)	50 (42-57)	36 (29-43)	22 (16-28)
P value		0.836	0.796	0.348
CMV status patient/donor				
Pos/pos	135 (31)	46 (37-54)	42 (33-50)	19 (13-26)
Pos/neg	109 (25)	49 (39-58)	34 (25-43)	22 (15-30)
Neg/pos	41 (10)	53 (36-67)	32 (18-46)	28 (15-42)
Neg/neg	144 (34)	55 (46-62)	38 (30-46)	17 (12-24)
P value		0.382	0.456	0.587
Donor type				
Related matched	168 (39)	55 (47-62)	44 (36-51)	11 (7-17)
Related mismatched	14 (3)	43 (14-70)	43 (18-6)	14 (2-37)
Unrelated matched	152 (36)	43 (35-51)	35 (27-42)	27 (21-35)
Unrelated mismatched	95 (22)	54 (44-64)	29 (20-39)	24 (16-33)
P value		0.265	0.112	0.006
GvHD prophylaxis				
Non–ATG-based	246 (57)	46 (39-52)	39 (33-45)	22 (17-27)
ATG-based	183 (43)	56 (48-64)	35 (28-42)	18 (13-24)
P value		0.013	0.276	0.310
KPS (%)				
<80	31 (7)	32 (17-49)	48 (30-64)	23 (10-38)
≥80	398 (93)	51 (46-56)	36 (32-41)	20 (16-24)
P value		0.001	0.068	0.658
HCT-CI				
0	155 (36)	61 (53-68)	31 (24-38)	19 (14-26)
1–2	133 (31)	49 (40-58)	43 (35-52)	14 (9-20)
>2	141 (33)	39 (30-47)	39 (31-48)	27 (20-34)
P value		<0.001	0.042	0.032
rPAM score				
<17	251 (59)	61 (55-67)	35 (30-42)	13 (9-18)
17-23	112 (26)	36 (27-45)	41 (31-50)	27 (19-35)
24–30	41 (10)	26 (13-40)	47 (31-62)	35 (21-49)
>30	10 (2)	10 (1-36)	50 (18-75)	40 (12-67)
Missing	15 (3)			
P value		<0.0001	0.187	<0.001

CI = confidence interval; CIR = cumulative incidence of relapse; CMV = cytomegalovirus; DRI = disease risk index; EBMT = European Group for Blood Marrow Transplantation Risk Score; GvHD = graft-vs-host-disease; HCT-CI = Hematopoietic Cell Transplant Co-Morbidity Index; KPS = Karnofsky Performance Status; MAC = myeloablative conditioning; n.a. = not applicable; NRM = nonrelapse mortality, P values were calculated by using univariate Cox regression models (OS) and competing risk regression models (CIR and NRM); OS = overall survival; rPAM = revised Pretransplant Assessment of Mortality Score; RIC = reduced-intensity conditioning; TBI = total body irradiation.

changes in hazard with each decrease in FEV1 by 10%) were the most relevant risk factors for impaired OS. In contrast, age, donor type, and donor/recipient CMV status failed to reach significance in our cohort. Regarding the discrimination of the rPAM for OS within 4 years, an AUROC of 0.676 (95% CI, 0.625-0.727) was observed.



Number at risk

rPAM score <17	251	185	162	114	81	55	29	10	0
rPAM score 17-23	112	62	52	27	16	10	4	1	0
rPAM score 24-30	41	18	13	6	3	1	0	0	0
rPAM score >30	10	2	1	0	0	0	0	0	0

Figure 1. Overall survival (OS) stratified by rPAM score categories after allo-HCT. OS according different rPAM score categories of <17 (blue line), 17–23 (brown line), 24–30 (green line) and >30 (yellow line). HCT = hematopoietic cell transplantation; rPAM = revised Pretransplant Assessment of Mortality.

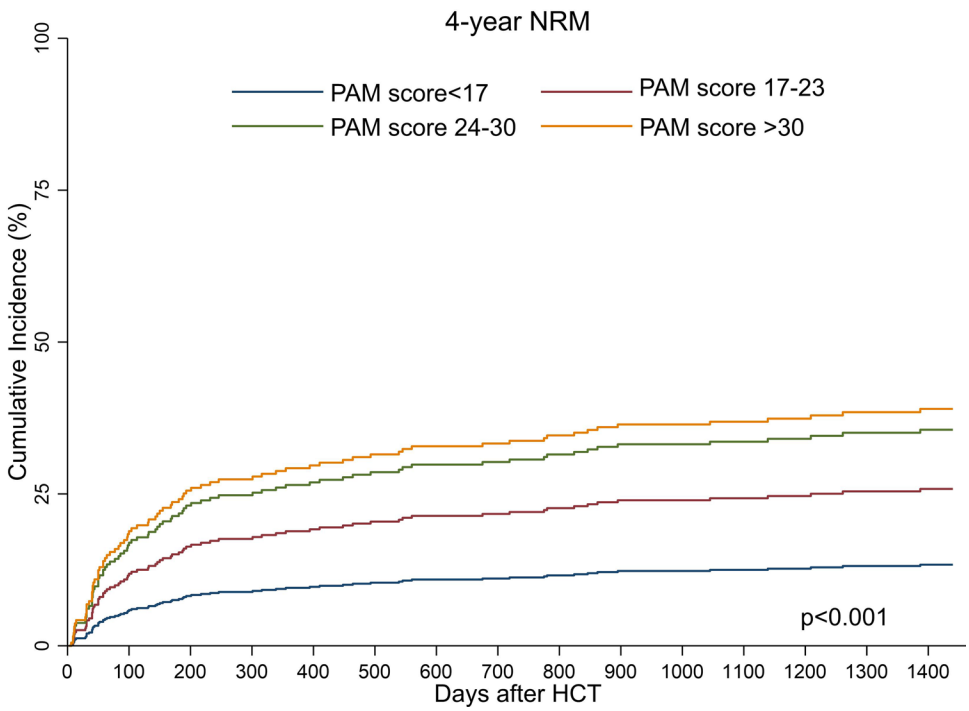


Figure 2. Four-year non-relapse mortality (NRM) according different rPAM score categories after allo-HCT. Four-year NRM according different rPAM score categories of <17 (blue line), 17–23 (brown line), 24–30 (green line) and >30 (yellow line). HCT = hematopoietic cell transplantation; rPAM = revised Pretransplant Assessment of Mortality.

DISCUSSION

We have validated the rPAM score in a large, real-world allo-HCT cohort. Regarding our primary outcome, we could demonstrate that the rPAM score is an independent predictor of OS in patients undergoing allo-HCT for various hematological disorders. Furthermore, we observed that NRM (but also CIR with the rPAM as a continuous variable) increased substantially with higher rPAM scores.

Table 2.

Uni- and Multivariable Analysis for Overall Survival With the rPAM Score

	Univariable Analysis			Multivariable Analysis		
Variable	**HR**	**95% CI**	***P* Value**	**HR**	**95% CI**	***P* Value**
Conditioning regimens						
Myeloablative	Ref.			Ref.		
Reduced-intensity	1.26	0.94–1.69	0.13	0.92	0.66–1.27	0.6
TBI						
Yes	Ref.			Ref.		
No	1.01	0.77–1.31	0.96	1.24	0.90–1.69	0.2
GvHD prophylaxis						
ATG-based	Ref.			Ref.		
Non–ATG-based	1.38	1.05–1.82	0.02	1.76	1.28–2.40	<0.001
KPS (%)						
≥80	Ref.			Ref.		
<80	1.96	1.25–3.07	0.004	1.67	1.05–2.65	0.031
rPAM score[a]	1.08	1.06–1.10	<0.001	1.10	1.06–1.10	<0.001

Number of subjects included in the univariable and multivariable model n = 414.

[a]rPAM used as a continuous variable (HR per 1-unit increase).

ATG = anti-thymocyte globulin; CMV = cytomegalovirus; CI = confidence interval; GvHD = graft-vs-host-disease; HR = hazard ratio; KPS = Karnofsky Performance Status; OS = overall survival; RIC = reduced-intensity conditioning; rPAM = revised Pretransplant Assessment of Mortality Score; TBI = total body irradiation.

Allo-HCT offers a curative option for many patients with hematological disorders.[20] Despite optimized transplant practice (including supportive care), allo-HCT continues to be associated with considerable transplant-related morbidity and mortality, which differ between patient subgroups. The potential risk for treatment-related complications highlights the importance of balancing the goal of disease control/-cure with treatment-related morbidity and mortality. To address these challenges, several prognostic models and scores were developed.[14,20,21] Due to the variability of analyzed outcomes, some prognostic scores include disease-related factors to predict relapse (eg, DRI), whereas other integrate patient-related risk factors (eg, HCT-CI) reflecting comorbid conditions predicting transplant-related mortality.[16,21] A more universal approach pursues the EBMT score, which incorporates transplant- and disease-related risk factors[22] and the rPAM score with the integrated patient-, disease-, and donor-specific features.[13] The PAM score was originally developed to predict OS, but an external validation of the rPAM score for outcomes such as NRM or CIR has not been performed in detail.[14,21] The results of our study support the use of the rPAM score in clinical practice for pretransplant risk stratification in allo-HCT.

Table 3.

Multivariable Analysis of the rPAM Score (n = 414) Variables for OS

Variable	**n (%)**	**HR**	**95% CI**	***P* Value**
Age (y)				
<65	363 (88)	Ref		
≥65	51 (12)	1.40	0.95-2.04	0.088
Donor type				0.200
Related matched	165 (40)	Ref.		
Related mismatched	14 (3)	1.41	0.64-3.08	0.397
Unrelated matched	148 (36)	1.32	0.96-1.80	0.086
Unrelated mismatched	87 (21)	1.43	0.97-2.07	0.059
Disease risk index				0.001
Low risk	48 (12)	Ref.		
Intermediate risk	302 (73)	2.14	1.23-3.71	0.007
High risk	54 (13)	3.41	1.83-6.36	<0.001
Very high risk	10 (2)	3.33	1.32-8.42	0.011
FEV1[a]	414 (100)	1.13	1.05-1.22	0.001
CMV status				0.127
Neg/neg	140 (34)	Ref.		
Neg/pos	40 (10)	1.26	0.88-1.79	0.212
Pos/neg	104 (25)	1.41	1.01-1.96	0.046
Pos/pos	130 (31)	0.89	0.52-1.50	0.765

[a]FEV1 displayed as a continuous linear variable and HR representing changes in hazard with each.

CI = confidence interval; CMV = cytomegalovirus; FEV1 = forced expiratory volume in 1 s; HR = hazard ratio; OS = overall survival; rPAM = revised Pretransplant Assessment of Mortality Score.

The available scores differ substantially in their discriminating capacity[20]: for instance, the reported AUROCs for OS within 2 years in allo-HCT were 0.58 (EBMT score), 0.62 (rDRI), 0.55 (HCT-CI), and 0.64 (rPAM score).[21] In our cohort, the respective AUC of the rPAM score for OS within 4 years was 0.68. Our results are in line with the discrimination capacity reported by Shouval et al[21] in patients with primarily acute myeloid leukemia (2-year AUROC of the rPAM: 0.64) and by Middeke et al[14] in a homogenous cohort of acute myeloid leukemia patients (4-year AUROC of the rPAM: 0.703).

In our investigation, the rPAM score was a predictor of OS—independent of the conditioning regimen. Previous analyses showed that the rPAM score has more predictive strengths in patients receiving MAC regimens compared to RIC. This could be due to the fact that patients treated with RIC have more often comorbid conditions which are not covered by the rPAM score.[13,14] Compared to the current literature, our results support the use of rPAM score independently of treatment intensity.

The prediction capacity of each prognostic model is driven by its components, which implies regular validation of each parameter.[20] Previous analyses could demonstrate that the DRI is probably the strongest predictor for allo-HCT outcomes[16,21] and therefore the predictive power of the rPAM may be primarily based on the incorporation of the DRI.[23] In our multivariable analyses, each component of the rPAM score for OS was analyzed and we could confirm that the higher discrimination of the rPAM score is primarily caused by the incorporation of the DRI and more interestingly by the pretransplant lung function defined by FEV1. The latter demonstrating that comorbid patients-related risk factors such as pulmonary function is an essential diagnostic test to derive an important prognostic conclusion about the validity of the rPAM score.[20,24] The rPAM score was originally derived to predict OS. Several validation studies[14,21] have also provided encouraging data for the value of rPAM in predicting CIR. Only the DRI was significantly associated with CIR, while age, CMV status, and donor type did not

reach statistical significance, that probably reduce the predictive value of the rPAM with respect to CIR.

In our multivariable analysis, we observed that other prognostic factors (not covered by the EBMT, HCT-CI, or rPAM score) such as non–ATG-based GvHD prophylaxis and an impaired KPS were independent predictors of OS—besides the rPAM score.

Our study has certain limitations including the design as a retrospective single-center study and the heterogeneous study population, the latter also reflecting the strength of a real-world cohort. Additionally, the use of the rPAM score requires pretransplant pulmonary function testing.

However, we were able to validate the rPAM score in a large allo-HCT cohort of patients with heterogeneous hematological diseases treated with different conditioning regimens. Until now, the rPAM score is not commonly incorporated in the pretransplant risk score measurement. The results of our study may stimulate the clinicians to use the rPAM score in combination to other well-established pretransplant scores such as the EMBT and HCT-CI score, to receive additional information on the potential risk for impaired outcome after allo-HCT. Since novel therapeutic approaches become available in hematology, the balance between benefit of allo-HCT and risks becomes increasingly important.

In conclusion, in our real-world cohort with extended follow-up, the rPAM score was an independent predictor of the OS, in particular of the NRM, in patients undergoing allo-HCT for different hematologic disorders.

AUTHOR CONTRIBUTIONS

NF, JRP and MK designed research, performed research, analyzed data and wrote the manuscript. JAR analyzed data and wrote the manuscript. HB contributed to data extraction and reviewed the manuscript. DS, MM, DH, MT, JPH analyzed data and reviewed the manuscript.

DISCLOSURES

The authors have no conflicts of interest to disclose.

REFERENCES

1. Copelan EA. Hematopoietic stem-cell transplantation. *N Engl J Med*. 2006;354:1813–1826.
2. Gratwohl A, Baldomero H, Aljurf M, et al. Hematopoietic stem cell transplantation: a global perspective. *JAMA*. 2010;303:1617–1624.
3. Ljungman P, Bregni M, Brune M, et al. Allogeneic and autologous transplantation for haematological diseases, solid tumours and immune disorders: current practice in Europe 2009. *Bone Marrow Transplant*. 2010;45:219–234.
4. Cooper JP, Storer BE, Granot N, et al. Allogeneic hematopoietic cell transplantation with non-myeloablative conditioning for patients with hematologic malignancies: improved outcomes over two decades. *Haematologica*. 2021;106:1599–1607.
5. Gooley TA, Chien JW, Pergam SA, et al. Reduced mortality after allogeneic hematopoietic-cell transplantation. *N Engl J Med*. 2010;363:2091–2101.
6. Hahn T, McCarthy PL Jr, Hassebroek A, et al. Significant improvement in survival after allogeneic hematopoietic cell transplantation during a period of significantly increased use, older recipient age, and use of unrelated donors. *J Clin Oncol*. 2013;31:2437–2449.
7. Fuchs E, Hardak E, Rak OL, et al. Long-term pulmonary function tests and complications following allogeneic stem cell transplantation. *Bone Marrow Transplant*. 2021;56:2299–2301.
8. Sorror ML, Maris MB, Storer B, et al. Comparing morbidity and mortality of HLA-matched unrelated donor hematopoietic cell transplantation after nonmyeloablative and myeloablative conditioning: influence of pretransplantation comorbidities. *Blood*. 2004;104:961–968.
9. Guilfoyle R, Demers A, Bredeson C, et al. Performance status, but not the hematopoietic cell transplantation comorbidity index (HCT-CI), predicts mortality at a Canadian transplant center. *Bone Marrow Transplant*. 2009;43:133–139.
10. Sorror ML, Maris MB, Storb R, et al. Hematopoietic cell transplantation (HCT)-specific comorbidity index: a new tool for risk assessment before allogeneic HCT. *Blood*. 2005;106:2912–2919.
11. Gratwohl A, Stern M, Brand R, et al. Risk score for outcome after allogeneic hematopoietic stem cell transplantation: a retrospective analysis. *Cancer*. 2009;115:4715–4726.
12. Parimon T, Au DH, Martin PJ, et al. A risk score for mortality after allogeneic hematopoietic cell transplantation. *Ann Intern Med*. 2006;144:407–414.
13. Au BK, Gooley TA, Armand P, et al. Reevaluation of the pretransplant assessment of mortality score after allogeneic hematopoietic transplantation. *Biol Blood Marrow Transplant*. 2015;21:848–854.
14. Middeke JM, Kollinger F, Baldauf H, et al. Validation of the revised pretransplant assessment of mortality score in patients with acute myelogenous leukemia undergoing allogeneic hematopoietic stem cell transplantation. *Biol Blood Marrow Transplant*. 2018;24:1947–1951.
15. Binkert L, Medinger M, Halter JP, et al. Lower dose anti-thymocyte globulin for GvHD prophylaxis results in improved survival after allogeneic stem cell transplantation. *Bone Marrow Transplant*. 2015;50:1331–1336.
16. Armand P, Gibson CJ, Cutler C, et al. A disease risk index for patients undergoing allogeneic stem cell transplantation. *Blood*. 2012;120:905–913.
17. Sorror ML. How I assess comorbidities before hematopoietic cell transplantation. *Blood*. 2013;121:2854–2863.
18. Quanjer PH, Tammeling GJ, Cotes JE, et al. Lung volumes and forced ventilatory flows. *Eur Respir J*. 1993;6(suppl 16):5–40.
19. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. *J Am Stat Assoc*. 1999;94:496–509.
20. Potdar R, Varadi G, Fein J, et al. Prognostic scoring systems in allogeneic hematopoietic stem cell transplantation: where do we stand? *Biol Blood Marrow Transplant*. 2017;23:1839–1846.
21. Shouval R, Fein JA, Shouval A, et al. External validation and comparison of multiple prognostic scores in allogeneic hematopoietic stem cell transplantation. *Blood Adv*. 2019;3:1881–1890.
22. Gratwohl A. The EBMT risk score. *Bone Marrow Transplant*. 2012;47:749–756.
23. Armand P, Kim HT, Logan BR, et al. Validation and refinement of the Disease Risk Index for allogeneic stem cell transplantation. *Blood*. 2014;123:3664–3671.
24. Xhaard A, Porcher R, Chien JW, et al. Impact of comorbidity indexes on non-relapse mortality. *Leukemia*. 2008;22:2062–2069.