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A Prognostic Score for Patients with Acute Leukemia or Myelodysplastic Syndromes Undergoing Allogeneic Stem Cell Transplantation

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ABSTRACT

Allogeneic hematopoietic stem cell transplantation (SCT) has the potential to cure patients with acute leukemia or myelodysplastic syndromes (MDS), but a number of prognostic factors can influence the outcome of transplantation. At present, no transplantation-specific risk score exists for this patient population. We propose a simple scoring system for patients with acute myelogenous leukemia (AML), acute lymphoblastic leukemia (ALL), or MDS, based on a retrospective analysis of 445 patients undergoing SCT at our institution (divided into training and validation subsets). The score depends on 5 variables: age, disease, stage at transplantation, cytogenetics, and pretransplantation ferritin. It divides patients into 3 groups of comparable size, with 5-year overall survival (OS) of 56% (low risk), 22% (intermediate risk), and 5% (high risk). This prognostic score could be useful in making treatment decisions for individual patients, in stratifying patients entering clinical trials, and in adjusting transplantation outcomes across centers under the new federal reporting rules.

KEY WORDS

Allogeneic stem cell transplantation • Acute myeloid leukemia • Acute lymphoblastic leukemia • Myelodysplastic syndrome • Cytogenetics • Iron overload

INTRODUCTION

Allogeneic hematopoietic stem cell transplantation (SCT) can be curative for patients with acute myelogenous leukemia (AML) [1], acute lymphoblastic leukemia (ALL) [2], or myelodysplastic syndromes (MDS) [3]. However, there is considerable heterogeneity in transplantation outcomes within this group of patients, with many patient-related, disease-related, and transplant-related factors influencing prognosis. A prognostic score that is specifically applicable to this patient population would be useful in several ways: first, it would help with prognostication at the time of transplantation consideration, which could have an impact on treatment decisions; second, it would allow stratification of patients entering clinical trials of transplantation. Successful prognostic scores developed for other diseases, such as the International Prognostic Index for patients with aggressive non-Hodgkin lymphoma (NHL) [4] or the International Prognostic Scoring System (IPSS) for patients with MDS [5], have been tremendously useful to clinicians and researchers alike for prognostication and clinical trial stratification. Unfortunately, there are at present few prognostic scores designed specifically for patients undergoing SCT. Three general risk scores have been proposed that are applicable to all patients undergoing transplantation [6-8]; however, by design, those scores rely minimally if at all on disease-specific factors (such as cytogenetics). The European Group for Blood and Marrow Transplantation (EBMT) developed a risk score for patients with chronic myelogenous leukemia (CML) [9]. No such score currently exists specifically for patients with acute leukemia or MDS undergoing SCT, despite the fact that they account for a substan-

tial fraction of transplantation patients (52% of all allogeneic transplants reported from the International Bone Marrow Transplant Registry to the Center for International Blood and Marrow Transplant Research (CIBMTR) [10]). Although the IPSS has prognostic values for patients with MDS undergoing transplantation [11,12], this score was derived on a cohort of patients who were not transplanted, and thus may not be an optimal prognostication tool in the context of SCT.

There is yet another benefit to transplant-specific prognostic scores. In December 2005, the U.S. Stem Cell Therapeutic and Research Act of 2005 created the C.W. Bill Young Cell Transplantation Program. As part of this program, U.S. centers will be required to report outcomes data for all allogeneic transplantation, and this data will be publicly available. It will therefore be critical to have well-defined risk stratification tools to allow calibration of outcomes across centers that may transplant patients with different risk profiles.

In this study, we propose and validate a simple prognostic score for patients with AML, ALL, or MDS undergoing SCT, based on the outcomes of 445 patients transplanted at our institution.

METHODS

Patients

We studied 660 consecutive adult patients with AML, ALL, or MDS who underwent allogeneic stem cell transplantation at the Dana-Farber/Brigham and Women's Hospital transplant program between January 1997 and December 2005. Patients with therapy-related AML or AML arising out of MDS were included. Patients with CMML were excluded. The following pretransplantation variables were collected: age, sex, disease type and stage, prior leukemogenic therapy, cytogenetics, donor HLA match, stem cell source, conditioning regimen, graft-versus-host disease (GVHD) prophylaxis regimen, cytomegalovirus (CMV) serostatus of donor and recipient, sex of donor, and pretransplantation serum ferritin [13]. Ferritin was included because we have recently demonstrated that it has an important prognostic impact for patients with MDS or acute leukemia receiving myeloablative conditioning [13]. For patients receiving reduced intensity conditioning (RIC), ferritin was not included as a prognostic factor in the multivariable models. Patients with missing data were excluded; this left 445 patients, who form the basis of this study. Institutional review board (IRB) approval was obtained from the Office for the Protection of Research Subjects (OPRS) at Dana-Farber/Harvard Cancer Center, in accordance with the principles of the Declaration of Helsinki.

Cytogenetics

Cytogenetics were determined by standard metaphase karyotype analysis or fluorescence in situ hybridization (FISH; without requiring central review). For ALL, t(9;22) and t(4;11) are considered adverse, and all others intermediate. We used the MRC classification scheme for AML [14], and the cytogenetic classification scheme of the IPSS for MDS [5]. For risk group assignment purposes, we used the cytogenetics at diagnosis for patients in remission, and the pretransplantation cytogenetics for patients with active disease.

Transplantation

Patients were transplanted under several treatment and investigational protocols over the 9-year period covered by this study. Myeloablative conditioning regimens consisted mostly of cyclophosphamide (3600 mg/m^2 or 120 mg/kg) plus either total body irradiation (TBI) (1400 cGy in 7 fractions) or busulfan (16 mg/kg by mouth or 12.8 mg/kg i.v.). Reduced intensity regimens consisted mostly of fludarabine (120 mg/m^2) with busulfan (3.2 mg/kg). Patients received either bone marrow or peripheral blood stem cells, from matched or mismatched, related or unrelated donors. Thirteen patients received umbilical cord blood (UCB) transplants. GVHD prophylaxis regimens consisted mostly of a combination of calcineurin inhibitor and methotrexate (MTX), tacrolimus plus sirolimus, with or without low-dose methotrexate, or T cell depletion (TCD).

Statistics

Patient baseline characteristics were reported descriptively. Overall survival (OS) and disease-free survival (DFS) were calculated using the Kaplan-Meier method. OS was defined as the time from stem cell infusion to death from any cause. Patients who were alive or lost to follow-up were censored at the time last seen alive. DFS was defined as the time from stem cell infusion to relapse or death from any cause, whichever occurred first. Patients who were alive without relapse were censored at the time last seen alive and relapse-free. The log-rank test was used for comparisons of Kaplan-Meier curves. Cumulative incidence curves for nonrelapse death and relapse with or without death were constructed reflecting time to relapse and time to nonrelapse death as competing risks. The difference between cumulative incidence curves in the presence of a competing risk was tested using the Gray method [15]. Time to relapse and time to nonrelapse death were measured from the date of stem cell infusion.

The entire cohort was split randomly 2:1 into a training set (n = 297) and a validation set (n = 148). Potential prognostic factors for survival were examined in the proportional hazards model, as were rele-

vant interaction terms. The proportional hazards assumption was tested for all important variables both graphically and analytically [16]. Regression assumptions were tested using Martingale and deviance residual analysis. Transformation for continuous variables to categoric variables was done by visual analysis of residual plots. A parsimonious model was built using a stepwise variable selection method, with an entry criterion of $P \leq .1$ and a retention criterion of $P < .05$. To create the risk score, each variable was assigned an integral number of points based roughly on its associated hazard ratio (HR) from the Cox model, as described in the text. We calculated the *c*-statistic for the validation cohort [17], defined as the proportion of informative patient pairs whose outcomes are correctly ordered by the risk score. All calculations were done using SAS 9.1 (SAS Institute Inc, Cary, NC), R (version 2.3.1), Splus (version 3.4), and Matlab 6.5 (Mathworks, Natick, MA).

RESULTS

Patient Characteristics

We retrospectively reviewed the posttransplantation outcomes of 445 adult patients with AML, ALL, or MDS transplanted at our institution between 1997 and 2005. Median follow-up for survivors was 25 months (range: 6-102). Table 1 lists the baseline characteristics of those patients. The median age in this cohort was 45 years (range: 18-71). Forty-three percent of patients had AML, 18% had ALL, and 39% had MDS (including 18% with secondary AML). Twelve percent of patients had therapy-related disease. Forty-eight percent of patients were transplanted in first complete remission (CR1) or with untreated MDS, whereas 33% had active disease at the time of transplantation. Sixty-nine percent had myeloablative conditioning (mostly cyclophosphamide + TBI), whereas 31% had nonmyeloablative conditioning (mostly low-dose busulfan + fludarabine); 41% of patients received a graft from an HLA-matched sibling; 61% received peripheral blood stem cells (PBSC), whereas 36% received bone marrow and 3% received cord blood.

Cytogenetics was available for all 445 patients. AML and MDS cytogenetics were classified according to the MRC [14] and IPSS [5] grouping schemes, respectively. For ALL, we considered t(9;22) and t(4;11) to be adverse, and all others to be intermediate. When classified in this way, 47% of the patients had intermediate cytogenetics, 23% had favorable cytogenetics, and 30% had adverse cytogenetics.

Outcomes and Prognostic Factors

For the entire cohort, the 5-year OS was 32%, and the 5-year DFS was 31%; the 5-year cumulative inci-

Table 1. *Baseline Characteristics of the Patients*

Variable	Total, No. (%)*
Number of patients analyzed	445 (100%)
Median age in years (range)	45 (18-71)
Disease	
ALL	80 (18)
AML	191 (43)
MDS	174 (39)
RA/RARS/RCMD	79 (18)
RAEB	17 (4)
AML from MDS	78 (18)
Therapy-related disease	54 (12)
Stage	
Untreated MDS	86 (19)
Untreated AML/ALL	10 (2)
CR1	131 (29)
CR ≥ 2	74 (17)
Induction failure	75 (17)
Active relapse	69 (16)
Cytogenetics†	
Favorable	102 (23)
Intermediate	210 (47)
AML/MDS adverse	101 (23)
ALL adverse	32 (7)
Graft source	
Peripheral blood	271 (61)
Bone marrow	161 (36)
Cord blood	13 (3)
Donor HLA match	
MRD	184 (41)
MUD	193 (43)
Mismatched related	9 (2)
Mismatched unrelated	59 (13)
Conditioning	
Myeloablative	309 (69)
Cy/TBI	297 (67)
Bu/Cy	9 (2)
Other	3 (0)
Reduced intensity	136 (31)
Bu/flu	127 (29)
Other	9 (2)
GVHD prophylaxis	
CnI ± steroids ± MMF	50 (11)
CnI + MTX ± steroids	172 (39)
CnI + Siro ± MTX	165 (37)
TCD	58 (13)
Sex‡	
Female -> Male	98 (22)
Male -> Female	112 (25)
Male -> Male	137 (31)
Female -> Female	95 (21)
CMV seropositivity	
Recipient	182 (41)
Donor	164 (37)

ALL indicates acute lymphoblastic leukemia; AML, acute myelogenous leukemia; MDS, myelodysplastic syndrome; RA, refractory anemia; RARS, refractory anemia with ringed sideroblasts; RCMD, refractory cytopenia with multilineage dysplasia; RAEB, refractory anemia with excess blasts; CR, complete remission; MRD, matched related donor; MUD, matched unrelated donor; Cy, cyclophosphamide; TBI, total body irradiation; Bu, Busulfan; flu, fludarabine; GVHD, graft-versus-host disease; CnI, calcineurin inhibitor (cyclosporine or tacrolimus); MMF, mycophenolate mofetil; MTX, methotrexate; Siro, Sirolimus; TCD, T cell depletion; CMV, cytomegalovirus.

*Percentages may not add to 100 because of rounding.

†See Methods section for details.

‡Donor sex information was missing for 3 patients.

dence of relapse (CIR) was 42%, and the 5-year cumulative incidence of nonrelapse mortality (NRM) was 27%. We divided the patients 2:1 by random assignment into a training set and a validation set. All subsequent analyses to establish the risk score were performed on the group of patients in the training set (n = 297). Within this group, we performed proportional hazards univariate and multivariate analyses to determine the prognostic factors for OS. All the variables from Table 1 were included in the model. We also included pretransplantation serum ferritin for patients receiving myeloablative conditioning (as this is the patient subgroup for which ferritin has a significant prognostic impact [13]) in the model, as well as year of transplantation. The results are shown in Table 2. The variables that had a significant impact on OS in multivariate analysis were: age, disease, stage at transplantation, cytogenetics, pretransplantation ferritin (for patients undergoing myeloablative transplantation), and year of transplantation. We also built a parsimonious model using stepwise variable selection; in this analysis, the same 5 variables were selected (data not shown). Donor HLA match, conditioning regimen intensity, graft source, GVHD prophylaxis regimen, sex mismatch, CMV serostatus, and therapy-related disease were not significant in this model. We also examined the effect of pretransplantation Eastern Cooperative Oncology Group (ECOG) performance status on outcome. This data was available for 32% of the patients in this study, with a median value of 0 (range: 0-3). Perfor-

Table 2. *Univariate and Multivariate Analyses for Overall Survival*

	Univariate Analysis		Multivariate Analysis	
Variable	**HR**	***P***	**HR**	***P***
Age ≥40	1.4	.036	2.0	.0007
Disease				
AML	1.0	ref	1.0	ref
ALL	1.0	1.0	1.0	.9
Low-risk MDS*	0.8	.4	1.0	1.0
High-risk MDS*	2.4	.040	3.1	.023
AML arising from MDS	1.6	.034	1.6	.071
Therapy-related disease	1.4	.2	1.2	.7
Cytogenetics				
Favorable	0.8	.2	0.6	.037
Intermediate	1.0	ref	1.0	ref
Adverse ALL	1.1	.8	1.3	.4
Adverse AML/MDS	1.8	.002	1.6	.051
Stage				
CR1/Unt MDS	1.0	ref	1.0	ref
CR >1	1.0	.9	1.5	.2
Untreated AML/ALL	1.9	.2	2.1	.2
Induction failure	2.2	<.0001	2.2	.0007
Relapse	2.0	.003	2.6	.0001
Ferritin >2500†	1.4	.067	1.5	.043
Graft source				
Bone marrow	1.0	ref	1.0	ref
Peripheral blood‡	1.0	.8	1.2	.4
Donor match				
MRD	1.0	ref	1.0	ref
Non-MRD	1.0	.9	1.1	.8
Conditioning regimen				
Ablative	1.0	ref	1.0	ref
Reduced intensity	1.1	.5	1.0	.9
GVHD prophylaxis				
CnI ± MTX ± MMF	1.0	ref	1.0	ref
CnI + Siro ± MTX	0.7	.055	0.8	.4
TCD	0.7	.2	0.9	.6
Gender mismatch	1.2	.3	1.1	.7
Donor CMV seropositive	1.2	.2	1.1	.5
Recipient seropositive	1.0	.9	1.0	.9
Year of transplantation				
1997-2000	1.0	ref	1.0	ref
2001-2005	0.7	.081	0.6	.034

HR indicates hazard ratio; ref, reference group; Unt MDS, untreated MDS; other abbreviations are described in Table 1.
*Low-risk MDS was defined as RA, RARS, and RCMD; high-risk as RAEB-1 and RAEB-2.
†For patients receiving myeloablative conditioning (see text).
‡Including umbilical cord blood recipients.

mance status had no significant effect on posttransplantation outcome (HR for mortality 1.3, $P = .2$).

Results were similar if we grouped cytogenetics according to our recently proposed grouping scheme [18]. The model fit was slightly stronger (Akaike's information criterion (AIC) 1685 versus 1735, with a lower score indicating a better model fit), but the conclusions were unaltered. We also reclassified ALL cytogenetics according to the results of the MRC UKALLXII/ECOG 2993 study [19]; this had no substantial effect on the model fit (AIC 1735).

Derivation of the Prognostic Score

For each of the significant variables in the multivariate analyses above, we created categoric variables using proportional hazards model or visual analysis of Martingale/deviance residuals against each continuous predictor. The results (not shown) allowed us to categorize age into 2 groups (<40 versus ≥40); disease type into 2 groups (low-risk MDS, AML, or ALL, versus high-risk MDS or MDS transformed to AML); stage into 3 groups (AML/ALL in CR1 or untreated MDS, versus CR > 1 or induction failure, versus active relapse or untreated leukemia); cytogenetics into 3 groups (favorable versus intermediate versus adverse); and pretransplantation ferritin into 2 groups (myeloablative conditioning and ferritin ≥2500 ng/dL, versus RIC or ferritin <2500 ng/dL). The resulting multivariat model using those categoric variables is shown in Table 3. The results were essentially identical when using an ALL cytogenetics classification based on the MRC/ECOG ALL study [19] (not shown).

We then created a risk score by assigning each variable a number of points. We strove for a simple risk score that could be calculated easily during a clinical encounter. Therefore, we chose integer values for the points, and assigned them based on the HR in the proportional hazards model from Table 3. To variables with HR between 1.5 and 2.0, we assigned a score of 1; and to those with HR above 2.0, we assigned a score of 2. The scoring system thus obtained is described in Table 4. Each variable is assigned a score; the sum of the individual components is the overall prognostic score. This defines 3 risk categories, low (score ≤2), intermediate (score = 3), and high (score ≥4). The OS of the 297 patients in the training set, stratified according to their prognostic score, is plotted in Figure 1A.

Table 3. *Final Multivariable Model for Overall Survival*

Variable	HR	P
Age		
<40	1.0	ref
≥40	1.8	.001
Disease		
Low-risk MDS/AML/ALL	1.0	ref
High-risk MDS/transformed MDS	2.0	.0005
Cytogenetics		
Favorable	1.0	ref
Intermediate	1.7	.014
Adverse	3.2	<.0001
Stage		
CR1 or untreated MDS	1.0	ref
CR >1 or Induction failure	1.8	.001
AML/ALL untreated or active relapse	2.4	<.0001
Ferritin		
RIC OR ferritin <2500	1.0	ref
Ablative AND ferritin ≥2500	1.7	.007

RIC indicates reduced-intensity conditioning; other abbreviations are as described in Tables 1 and 2.

Table 4. *Calculation of the Prognostic Score*

Variable	Score
Age	
<40	0
≥40	1
Disease	
Low-risk MDS,* AML, or ALL	0
High-risk MDS* or transformed MDS	1
Cytogenetics†	
Favorable	0
Intermediate	1
Adverse	2
Stage	
CR1 or untreated MDS	0
CR >1 or induction failure	1
AML/ALL untreated or active relapse	2
Ferritin	
RIC OR ferritin <2500 ng/dL	0
Ablative AND ferritin ≥2500 ng/dL	1
Final score‡	**Risk group**
≤2	Low
3	Intermediate
≥4	High

*Low-risk MDS is defined as RA, RARS, or RCMD; high-risk MDS is defined as RAEB.

†For ALL, t(9;22) and t(4;11) are considered adverse, and all others intermediate. AML cytogenetics are grouped according to the MRC classification scheme, and MDS cytogenetics according to the IPSS scheme.

‡This is calculated as the sum of the individual components.

Abbreviations are as described in Tables 1 to 3.

Validation of the Risk Score

We calculated the risk score for the 148 patients in the validation set, whose outcomes were not used for the derivation of the score. Their OS is shown in Figure 1B. The prognostic score remained a highly statistically significant in this group (log-rank $P < .0001$). We also calculated the *c*-statistic in the validation cohort. This statistic indicates how often informative pairs of patients are correctly ordered by the risk score with regard to their survival. A score of 1.0 indicates perfect agreement with the data. For the validation group, using time of death as a continuous variable, the *c*-statistic was 0.66 (for comparison, in

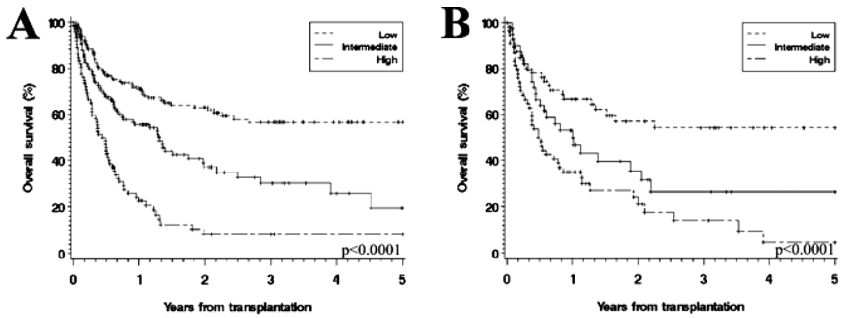

Figure 1. OS of patients stratified by risk score. A, Training set; B, validation set.

the validation set of Sorror et al.'s comorbidity score study the corresponding *c*-statistic was 0.62[6]). If we considered the binary outcome of survival to 2 years (as in the Pretransplantation Assessment of Mortality [PAM] score of Parimon and colleagues [8]), the *c*-statistic was 0.79 (for comparison, it was 0.72-0.76 in the PAM study [8]).

Outcomes by Risk Group

We calculated the prognostic score for all 445 patients (including both those in the training and those in the validation set). As shown in Table 5, the patients are thus divided into 3 groups of comparable size (each comprising between 28% and 41% of patients). Figure 2 shows the outcomes of all patients stratified by their risk score. OS is shown in Figure 2A, and DFS in Figure 2B. The 5-year values for OS, DFS, cumulative CIR, and NRM for each risk group are given in Table 5.

DISCUSSION

We have created a new prognostic score for patients with acute leukemia or MDS undergoing allogeneic stem cell transplantation (SCT). This score depends on only 5 patient and disease characteristics: age, disease, stage at transplantation, cytogenetics, and pretransplantation serum ferritin (for patients undergoing myeloablative transplantation). By combining these 5 variables, our scoring system stratifies patients into 3 groups of roughly comparable size at very different risk of death after transplantation (with 5-year OS ranging from 56% in the low-risk group to 5% in the high-risk group), through an effect on both relapse and NRM. This scoring system was based on retrospective transplantation results at a single institution. Nonetheless, it retained its high prognostic significance when applied to a validation set of randomly selected patients who were not included in the derivation of the score (see Figure 1B). The *c*-statistic, which quantifies the agreement of the prognostic score with the outcome of interest (here, OS) was at least as high as that of other prognostic scores [6,8], which were not designed specifically for patients with acute leukemia or MDS. In its current form, this scoring system does not include pretransplantation comorbidity score, which was not available in our cohort but could be incorporated in future versions. It must also be noted that many of the patients included in this study were part of the cohorts used in our previous work on the prognostic impact of cytogenetics and ferritin levels [13,18]. However, the intent of the present study is not to validate our prior results, but to integrate them into a more versatile scoring system.

All of the variables included in this score have been previously shown to have a prognostic impact after transplantation. Age is often considered an adverse prognostic factor through an increase in NRM [20,21] (although at least 2 retrospective multicenter studies failed to document a significant effect on OS [22,23]). The possibility of a superior outcome for low-risk MDS compared to high-risk MDS has been previously suggested [24,25]. More advanced disease stage is always associated with worse outcome (as demonstrated, eg, by the data of the CIBMTR). Pretransplantation serum ferritin has also been shown to carry prognostic significance for patients undergoing

Table 5. *Summary of Outcomes in the Entire Cohort By Risk Group*

Risk Group	% of pts	5-y OS	5-y DFS	5-y CIR	5-y NRM
Low	41%	56% (48-64)	51% (43-59)	25% (18-32)	24% (17-30)
Intermediate	31%	22% (10-33)	22% (12-32)	53% (42-65)	25% (17-32)
High	28%	5% (0-12)	6% (0-12)	58% (48-67)	36% (26-47)

Numbers in parentheses are 95% confidence intervals.

OS indicates overall survival; DFS, disease-free survival; CIR, cumulative incidence of relapse; NRM, non-relapse mortality. Risk groups are defined in Table 4.

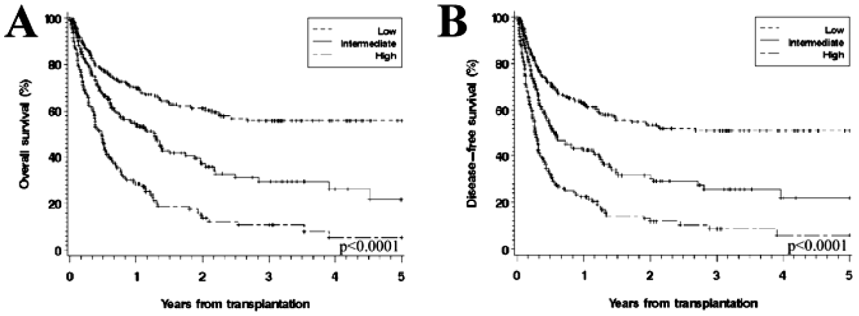

Figure 2. Outcomes for the entire cohort (training and validation sets combined) stratified by risk score. A, OS; B, DFS.

ablative transplantation, through an effect on NRM [13,26]. Finally, the prognostic importance of cytogenetics has been confirmed in several studies [27-31], including our own, where we demonstrated that cytogenetics influenced the risk of relapse, and proposed a transplantation-specific cytogenetics grouping scheme [18]. Although our grouping scheme allowed a better model fit to the data, it was derived on a cohort that included most of the patients in the current study. Because we have not yet validated our grouping scheme in a multi-institution study, we did not use it for the present risk score. In the future, the recognition of prognostic subtypes based on molecular analyses within the normal karyotype category will undoubtedly alter the scheme [32] and subdivide this category, which still includes the majority of patients.

This scoring system could be used in several ways. First, it should allow clinicians to easily estimate the prognosis of patients with MDS or acute leukemia who are candidates for SCT. This could be helpful in discussing the value of transplantation and in choosing a treatment course. It also identifies a subgroup of patients (high-risk) with a dismal prognosis (5-year OS of 5%), for whom the value of transplantation may be questionable, and who may especially benefit from enrollment into clinical trials. Second, this scoring system could be used to stratify patients entering clinical trials of transplantation. At present, there is no consensus as to how to perform such stratification, and some variables that are commonly used, such as donor HLA match, may not be nearly as prognostically important today as less commonly used variables (such as cytogenetics). Similar prognostic scores, such as the IPI for aggressive lymphoma and the IPSS for MDS, are widely used in clinical trial design. Finally, our prognostic score could be used under the new federal reporting requirements for transplant centers to adjust for differences in patient mix and allow a fairer comparison of outcomes across centers.

Prospective validation of this scoring system through a multicenter collaboration would confirm its utility and possibly fine-tune the score assignments. Further in the future, it is possible that improvements in the care of specific patient subgroups (eg, chelation of iron-overloaded patients, or the use of tyrosine kinase inhibitors after transplantation for Ph+ ALL) would require reevaluation of the scoring scheme. This reevaluation could be accomplished through a periodic reexamination of multicenter transplantation data, such as those that will be reported to the Stem Cell Therapeutic Outcome Database, which the CIBMTR will administer. This process could even be semiautomated such that clinicians worldwide would have ready access to up-to-date, international prognostic scoring systems for patients with a variety of diseases undergoing SCT.

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