RESEARCH ARTICLE

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The Composite Health Risk Assessment Model (CHARM) Predicted Overall Mortality and Relapse, but not Non-Relapse Mortality, in Adults Following Unrelated Single-Unit Cord Blood Transplantation

Kato S. et al.: CHARM in CBT

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Abstract

Objective: Concerns about excessive non-relapse mortality (NRM) are a major issue following allogeneic hematopoietic cell transplantation (HCT). Although the HCT-specific comorbidity index (HCT-CI) has been established as the stratification model for NRM following allogeneic HCT, the Composite Health Risk Assessment Model (CHARM) score was also developed to predict the risk of NRM and overall mortality following allogeneic HCT from adult donors, particularly in older patients, in the BMT CTN 1704 prospective study. The CHARM score has been shown to predict these outcomes better than HCT-CI alone. However, the prognostic value of the CHARM score has not been validated in patients undergoing unrelated single-unit cord blood transplantation (CBT) for adults.

Materials and Method: We retrospectively validated the impact of the CHARM score on transplant outcomes in 321 adults who underwent unrelated single-unit cord blood transplantation (CBT) at our institution.

Results: In the univariate analysis, a higher CHARM score was significantly associated with worse overall mortality (P<0.001), higher relapse (P=0.007), and NRM (P=0.048). In the multivariate analysis, overall mortality (hazard ratio [HR] 1.56, 95% confidence interval [CI] 1.06–2.29, P=0.022) and relapse (HR 1.71, 95% CI 1.09–2.69, P=0.020) were significantly higher in patients with a higher CHARM score, but NRM was not (HR 1.17, 95% CI 0.68–1.99, P=0.560). The detrimental effects of higher CHARM scores on overall mortality and relapse, compared to lower CHARM scores, were observed in subgroups of patients with high and very high risk, as defined by the refined Disease Risk Index.
Conclusion: Unlike the findings of the BMT CTN 1704 study, the CHARM score was able to predict overall mortality and relapse, but not NRM, in adults undergoing single-unit CBT.
Keywords: cord blood transplantation, Composite Health Risk Assessment Model, non-relapse mortality, HCT-specific comorbidity index, risk stratification, allogeneic hematopoietic cell transplantation

Introduction

Allogeneic hematopoietic cell transplantation (HCT) represents a possibly curative intervention for refractory hematopoietic disorders. Nonetheless, apprehensions regarding elevated non-relapse mortality (NRM) persist as a substantial problem in allogeneic HCT. Several prognostic models, such as the HCT-specific comorbidity index (HCT-CI) [1], the Pretransplantation Assessment of Mortality (PAM) score [2,3], the European Society for Blood and Marrow Transplantation risk score [4], the NRM-J index [5], and the Treatment-Related Mortality (TRM) score [6], have been developed to predict NRM following allogeneic HCT. Among these, HCT-CI has set a global standard for estimating NRM risk and guiding treatment decisions before HCT [7,8]. Recently, the Composite Health Risk Assessment Model (CHARM) was developed to improve the risk-stratification of 1-year NRM and overall mortality following allogeneic HCT in older patients, as demonstrated in the BMT CTN 1704 prospective study [9]. CHARM was found to be more effective than HCT-CI alone in this context [9].

Cord blood transplantation (CBT) serves as a recognized alternative approach for allogeneic HCT [10-13]. Delayed hematological recovery and an elevated risk of infectious complications are recognized disadvantages of CBT, resulting in an increased risk of NRM [14]. Despite this, several studies have shown that HCT-CI fails to predict NRM [15,16] or overall survival (OS) [16,17] in CBT recipients. However, HCT-CI has been validated in a large cohort of CBT recipients by our research [18]. These attempts to validate the HCT-CI in the setting of CBT have yielded mixed results. Nonetheless, the prognostic significance of the original CHARM score remains unexplored in adults receiving unrelated single-unit CBT. To address this gap, we conducted a retrospective analysis to assess whether the CHARM score influences posttransplant outcomes in adults who underwent CBT at our institution.

Methods

Study design and participants

This was a retrospective study conducted at a single center in Japan. This study conducted a retrospective review of adult patients who underwent single-unit CBT at The Institute of Medical Science, The University of Tokyo, from August 1998 to December 2023. Clinical data were acquired retrospectively from medical records. During this period, we conducted single-unit CBT as the initial allogeneic HCT for 341 adult patients at our hospital. Nineteen patients unable to be assessed for HCT-CI and one patient unable to be evaluated for alterations in body weight were eliminated from this retrospective analysis, as the CHARM score could not be computed. A total of 321 patients were ultimately included in this study. All cord blood units were sourced from the Cord Blood Bank in Japan.

The conditioning regimen and graft-versus-host disease (GVHD) prevention were established by the physicians according to patient and disease conditions [19,20,21], and the majority of patients received comparable supportive care [22] and transfusion delivery [23]. This retrospective study was performed in compliance with the Declaration of Helsinki. The Institutional Review Board of the Institute of Medical Science, University of Tokyo, sanctioned this retrospective study (2024-32-0823) and the implementation of an opt-out consent system.

Study endpoints

The primary endpoint was to examine the effect of the CHARM score on OS after CBT. The secondary endpoints aimed to assess the influence of the CHARM score on relapse, NRM, hematological recovery, and both acute and chronic GVHD following CBT.

Definitions

The CHARM score was retrospectively computed using the formula: $0.15310 \times (\text{HCT-CI}) + 0.13247 \times (\text{LOG(CRP)}) - 0.71227 \times (\text{albumin}) + 0.00119 \times (\%\ \text{weight loss})^2$, derived from medical records as per the original report [9]. Serum CRP and albumin levels were measured within three days preceding the beginning of the conditioning regimen.

Neutrophil and platelet recovery were defined as an absolute neutrophil count surpassing 0.5×10^9/L and a platelet count above 20×10^9/L without requiring platelet transfusions on the first day of three and seven consecutive days, respectively. The diagnosis and severity of acute and chronic GVHD were assessed according to published standard criteria [24,25].

OS was defined as the interval between the date of CBT and the date of death or the most recent follow-up. Relapse was characterized by morphological indications of hematological disease. NRM was characterized as mortality occurring during remission. The HCT-CI [1] and the revised Disease Risk Index (DRI) [26] were categorized based on established criteria. The number of HLA discrepancies was ascertained using low-resolution typing for HLA-A, -B, and -DR in the graft-versus-host direction.

Statistical analysis

Comparisons of baseline characteristics between the two CHARM score groups were conducted using the Mann–Whitney U test for continuous variables and the chi-squared or Fisher exact test for categorical variables. The analysis of hematopoietic recovery, GVHD, relapse, and NRM between the two CHARM score groups was conducted using the cumulative incidence method, which takes into account competing risks, and Gray's test. The Kaplan–Meier method and log-rank test were employed to analyze the difference in OS between the two CHARM score groups.

The Fine and Gray proportional hazards model was employed in the multivariate analysis to estimate hazard ratios (HR) with 95% confidence intervals (CIs) for hematopoietic recovery, GVHD, relapse, and NRM, whereas the Cox proportional hazards regression model was applied for OS. The adjusted HRs and 95% CIs for the CHARM score (lower versus higher) were calculated, accounting for all covariates, including age at CBT (<45 years vs. ≥45 years), recipient sex (male vs. female), refined DRI (low/intermediate vs. high/very high), conditioning regimen (TBI 10–12 Gy vs. TBI 2–4 Gy), cryopreserved cord blood total nucleated cell (TNC) count (<2.5 × 10^7/kg vs. ≥2.5 × 10^7/kg), and HLA disparities (0–1 vs. 2).

EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria), was used for statistical analyses [27]. Statistically significant P-values were less than 0.05 and determined using a two-sided test.

Results

Patient characteristics

Among the entire cohort, the median CHARM score was -3.31 (range, -7.45 to 3.81). To assess the impact of the CHARM score on post-transplantation outcomes, patients were categorized into 3 groups based on the similar cut-off values in the original report [9] (<2.50149 vs. 2.50149 to -2.01456 vs. ≥2.01456) (Supplementary Figure 1). Based on these data, for further univariate and multivariate analyses, patients were divided into two groups according to the original report [9] (lower group: <-2.01, and higher group: ≥-2.01). The lower CHARM score group consisted of 223 patients (69.5%), and the higher CHARM score group included 98 patients (30.5%). Patient and CBT characteristics between the two CHARM score groups are shown in Table 1. The median follow-up for survivors in the total group was 121 months, with a range of 4 to 287 months.

Patients with higher CHARM scores were older and more likely to have a high or very high risk of refined DRI compared to those with lower CHARM scores. In contrast, patients with lower CHARM scores were more likely to receive TBI-based myeloablative conditioning regimens and GVHD prophylaxis based on cyclosporine and methotrexate. Disease types varied between the two CHARM score groups. The median follow-up for survivors was 120 months (range, 4 to 273 months) in the lower CHARM score group and 103 months (range, 9 to 287 months) in the higher CHARM score group (P=0.315) (Table 1).

Neutrophil and platelet recovery

In the univariate analysis, the cumulative incidence of neutrophil recovery was comparable between the two CHARM score groups (90.7% for the lower group, 87.6% for the higher group at 30 days, P=0.162) (Supplementary Figure 2A). The cumulative incidence of platelet recovery was also similar between the two groups (83.1% for the lower group, 77.6% for the higher group at 60 days, P=0.069) (Supplementary Figure 2B). In the multivariate analysis, the CHARM score was not associated with neutrophil recovery (HR 0.88, 95% CI 0.69–1.12, P=0.320) or platelet recovery (HR 0.82, 95% CI 0.64–1.04, P=0.110) (Supplementary Table 1).

GVHD

In the univariate analysis, the cumulative incidence of grades II to IV acute GVHD (P=0.253) and grades III to IV acute GVHD (P=0.640) was similar between the two CHARM score groups (Supplementary Figure 3A, 3B). In the multivariate analysis, the CHARM score was not associated with grades II to IV acute GVHD (HR 0.75, 95% CI 0.54–1.04, P=0.091), or grade III to IV acute GVHD (HR 0.76, 95% CI 0.36–1.58, P=0.470) (Supplementary Table 2).

In the univariate analysis, the cumulative incidence of extensive chronic GVHD was also similar between the two CHARM score groups (P=0.235) (Supplementary Figure 3C). In the multivariate analysis, the CHARM score was not associated with extensive chronic GVHD (HR 0.73, 95% CI 0.42–1.28, P=0.280) (Supplementary Table 2).

OS, relapse, and NRM

In the univariate analysis, the probability of OS was significantly worse in the higher CHARM score group compared to the lower CHARM score group (65.4% for the higher group, 79.1% for the lower group at 2 years, P<0.001) (Figure 1A). In the multivariate analysis, a higher CHARM score was significantly associated with increased overall mortality (HR 1.56, 95% CI 1.06–2.29, P=0.022) (Table 2).

In the univariate analysis, the cumulative incidence of relapse was significantly worse in the higher CHARM score group compared to the lower CHARM score group (29.5% for the higher group, 18.2% for the lower group at 2 years, P=0.007) (Figure 1B). In the multivariate analysis, a higher CHARM score was significantly associated with higher relapse rates (HR 1.71, 95% CI 1.09–2.69, P=0.020) (Table 2).

In the univariate analysis, the cumulative incidence of NRM was significantly worse in the higher CHARM score group compared to the lower CHARM score group (15.5% for the higher group, 9.1% for the lower group at 2 years, P=0.048) (Figure 1C). In the multivariate analysis, the CHARM score was not associated with NRM (HR 1.17, 95% CI 0.68–1.99, P=0.560) (Table 2).

Subgroup analysis according to disease type, disease risk, or conditioning regimen

Because disease type, disease status, or conditioning regimen could affect the posttransplant outcomes in adults who underwent CBT, we also analyzed the effects of CHARM score stratification according to disease type (acute myeloid leukemia/myelodysplastic syndrome [AML/MDS] or acute lymphoblastic leukemia/ non-Hodgkin's lymphoma [ALL/NHL]), refined DRI (low/intermediate or high/very high), or conditioning regimen (TBI 12 Gy based).

In the univariate analysis, the beneficial effects of lower CHARM scores on OS compared to higher CHARM scores were observed in subgroups of patients with AML/MDS (78.6% vs. 64.8% at 2 years, P=0.002), high and very high risk by refined DRI (68.8% vs. 52.1% at 2 years, P<0.001), and TBI 12 Gy based-conditioning regimen (80.1% vs. 68.7% at 2 years, P=0.011), but not in those with ALL/NHL, or low and intermediate risk by refined DRI (Figure 2A, 3A, 4A).

In the univariate analysis, the beneficial effects of lower CHARM scores on relapse compared to higher CHARM scores were also observed in subgroups of patients with AML/MDS (17.8% vs. 28.4% at 2 years, P=0.002), high and very high risk by refined DRI (28.5% vs. 40.4% at 2 years, P=0.045), and TBI 12 Gy based conditioning regimen (18.9% vs. 27.0% at 2 years, P=0.040), but not in those with ALL/NHL, or low and intermediate risk by refined DRI (Figure 2B, 3B, 4B). The cumulative incidence of NRM was comparable between the two CHARM score groups, irrespective of disease type, disease risk, or TBI 12Gy-based conditioning regimen (Figure 2C, 3C, 4C). Restricted to patients received TBI 12 Gy-based conditioning regimen, CHARM score was not associated with incidences of acute and chronic GVHD in univariate analysis (Figure 4D,4E,4F).

Impact of serum CRP and albumin levels on relapse and NRM

We further evaluated whether serum CRP and albumin levels affected relapse and NRM. When patients were divided into two groups according to the approximate median values of serum CRP (<0.15 mg/dl vs. ≥0.15 mg/dl) and albumin (<3.9 g/dl vs. ≥3.9 mg/dl) levels, the cumulative incidence of relapse was significantly worse in the higher CRP level group compared to the lower CRP level group (26.5% vs. 16.4% at 2 years, P=0.021) (Supplementary Figure 4A), but the cumulative incidence of NRM was comparable between the two CRP level groups (Supplementary Figure 4B). In contrast, lower albumin level group was significantly associated with higher relapse (28.6% vs. 16.2% at 2 years, P=0.002) and NRM (16.1% vs. 7.2% at 2 years, P=0.044) compared to higher albumin level group (Supplementary Figure 4A, 4B). Age-adjusted HCT-CI [28] did not affect the OS, relapse and NRM in univariate analysis (Supplementary Figure 5).

Discussion

We evaluated the impact of the CHARM score on posttransplant outcomes in adults undergoing unrelated single-unit CBT. The CHARM score significantly influenced overall mortality and relapse, but not NRM, which is inconsistent with the original report [9]. Interestingly, these effects were maintained only in the subgroups of patients with AML/MDS, high and very high risk, as determined by the refined DRI, or those received TBI 12Gy based conditioning regimen. Therefore, our data indicate that the CHARM score predicts mortality through the stratification of relapse risk among both the entire cohort and several subgroup cohorts following unrelated single CBT.

Several prognostic models in allogeneic HCT aim to predict transplant outcomes through the stratification of NRM [1–6, 29]. Indeed, the original CHARM was developed to estimate 1-year NRM for older patients [9]. Each element of the CHARM, including HCT-CI, CRP, albumin, and the amount of weight loss, was derived using the HRs for NRM [9]. Among these previous prognostic models, the HCT-CI [1], the PAM score [2,3], and the NRM-J index [5] included comorbidity components, whereas the TRM score alone included serum albumin levels [6]. Previous studies have demonstrated that higher pretransplant CRP levels were associated with higher NRM [30], and worse OS [31,32] among allogeneic HCT recipients. Moreover, pretransplant hypoalbuminemia, which is a marker of nutritional status and systemic chronic inflammation, is predictive of NRM after allogeneic HCT [33,34,35]. Indeed, our current study clearly demonstrated that higher CRP levels was associated with higher relapse following CBT, whereas lower albumin levels was associated with higher relapse and NRM following CBT. Our previous study also showed that several factors related to inflammatory and nutritional status, including serum albumin and CRP, affected NRM after unrelated single CBT [36]. Indeed, our current study showed that the CHARM score was significantly associated with NRM in the univariate analysis, but this association did not hold in the multivariate analysis. The difference between our results and the original CHARM study might be partly due to the lower frequency of patients older than 60 years (13%) in our CBT cohort, which could contribute to the lack of association between the CHARM and NRM in our multivariate analysis.

Unexpectedly, our study revealed that the CHARM score predicted the relapse rate rather than NRM in unrelated single CBT for adults. Furthermore, the discriminative capacity for relapse in the CHARM score was higher in higher-risk patients compared to lower-risk patients, as defined by the refined DRI. Although the refined DRI has proven to be the most reliable and useful disease-specific predictor for relapse following allogeneic HCT [26], the CHARM score could stratify the relapse risk, particularly among higher-risk patients in our study. Some components of the CHARM may also be associated with disease aggressiveness. CRP has been shown to predict leukemic relapse following allogeneic HCT [37]. Hypoalbuminemia is also a component of the prognostication for AML in the AML-composite model (AML-CM) [38,39], which is consistent with our results showing that the discriminative capacity for OS and relapse in the CHARM score was higher in myeloid malignancies compared to lymphoid malignancies. Moreover, weight reduction and serum albumin concentrations may be affected by rigorous

treatment preceding allogeneic HCT, indicating that the CHARM score could influence disease recurrence following CBT. Therefore, the CHARM score could assist in selecting the best transplant strategy, such as determining the need for maintenance therapy in higher-risk patients undergoing unrelated single-unit CBT.

We acknowledge several limitations in this study. First, this study is retrospective, done at a single institution in Japan, and involved a rather limited cohort of exclusively Japanese patients. Therefore, the association between the CHARM score and CBT outcomes requires further investigation in cohorts from other racial groups. Second, the original CHARM study focused on patients older than 60 years. However, the frequency of patients older than 60 years in our CBT cohort was only 13%. Therefore, it is unclear whether the lower frequency of older patients contributed to the lack of association between the CHARM score and NRM in our cohort. Moreover, it remains uncertain whether our observed results are more applicable to CBT compared to adult donor HCT. Indeed, the BMT CTN 1704 prospective trial was conducted at areas in the United States [9]. Given that the higher incidence and severity of GVHD in Caucasian patients compared to Japanese patients [40], both graft source and race could affect the incidence and severity of GVHD, which could contribute to the impact of CHARM score on posttransplant outcomes.

In summary, our data demonstrated that the CHARM score could predict OS through the stratification of relapse risk rather than NRM in adults undergoing unrelated single-unit CBT, which is not consistent with the original study on the CHARM score. Further validated research is needed to clarify the impact of the CHARM score on transplant outcomes in CBT.

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Statement of Ethics

The Institutional Review Board of the Institute of Medical Science, the University of Tokyo, approved this retrospective study (2024-32-0823), and an opt-out informed consent protocol was used for use or collection of participant data for research purposes. This consent procedure was reviewed and approved by The Institutional Review Board of the Institute of Medical Science, the University of Tokyo, approval number 2024-32-0823, and the date of decision on September 2nd, 2024.

Conflict of Interest Statement

The authors declare no competing financial interests.

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Author Contributions

S. K. collected and analyzed the data, performed the statistical analysis, and wrote the manuscript. M.M.-O. collected the data. S.A., Y.O., Y.N., and S.T. participated in the treatment of the patients and acquired the clinical data. T.K. designed the research, collected and analyzed the data, performed the statistical analysis, and wrote the manuscript. All authors approved the final version.

Data Availability Statement

The data that support the findings of this study are not publicly available due to ethical and legal reasons but are available from the corresponding author upon reasonable request.

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Figure legends

Figure 1. Unadjusted probability of overall survival (OS) (A) and cumulative incidences of relapse (B) and non-relapse mortality (NRM) (C) following single-unit cord blood transplantation (CBT), stratified by the Composite Health Risk Assessment Model (CHARM) score.

Figure 1

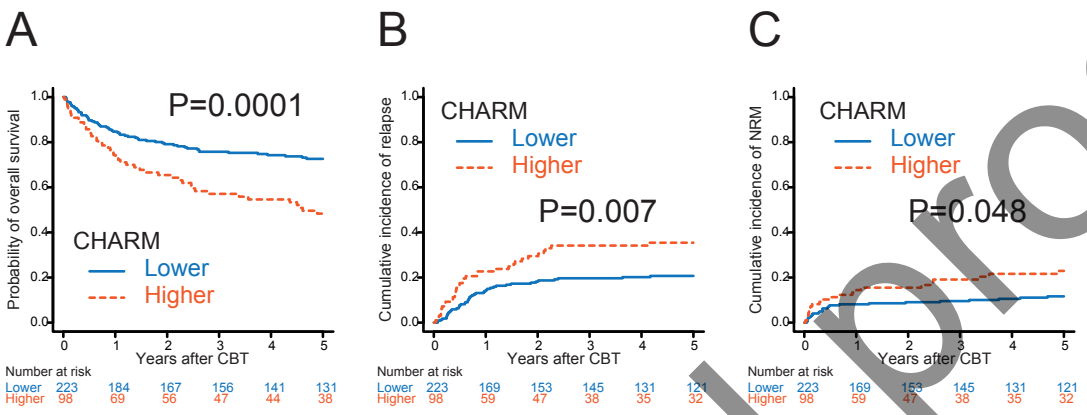

Figure 2. Unadjusted probability of OS (A) and cumulative incidences of relapse (B) and NRM (C) following single-unit CBT, stratified by CHARM score within each subgroup based on disease type (AML/MDS vs. ALL/NHL).

Figure 2

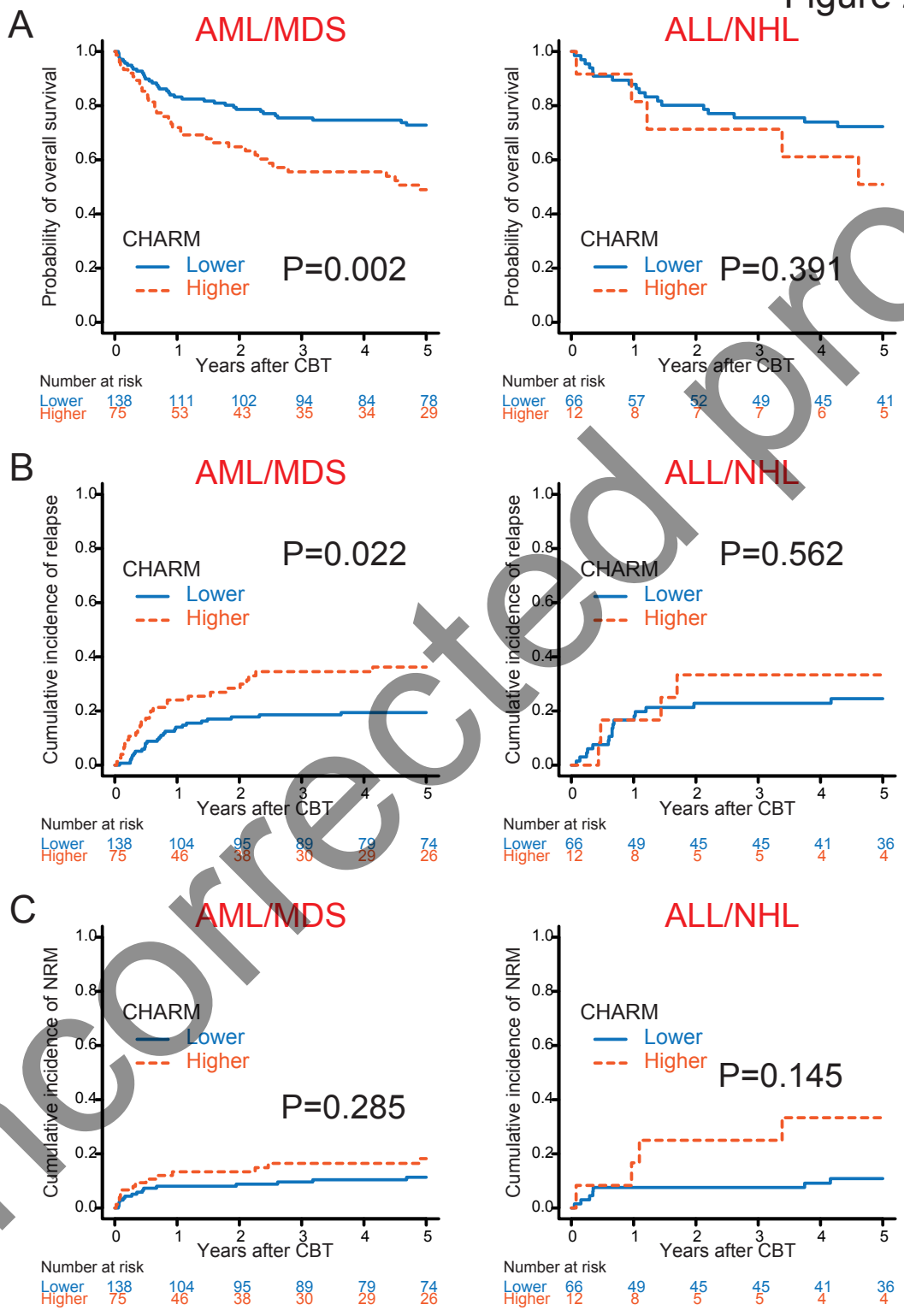

Figure 3. Unadjusted probability of OS (A) and cumulative incidences of relapse (B) and NRM (C) following single-unit CBT, stratified by CHARM score within each subgroup based on disease risk status (low/intermediate vs. high/very high) according to the refined Disease Risk Index.

Figure 3

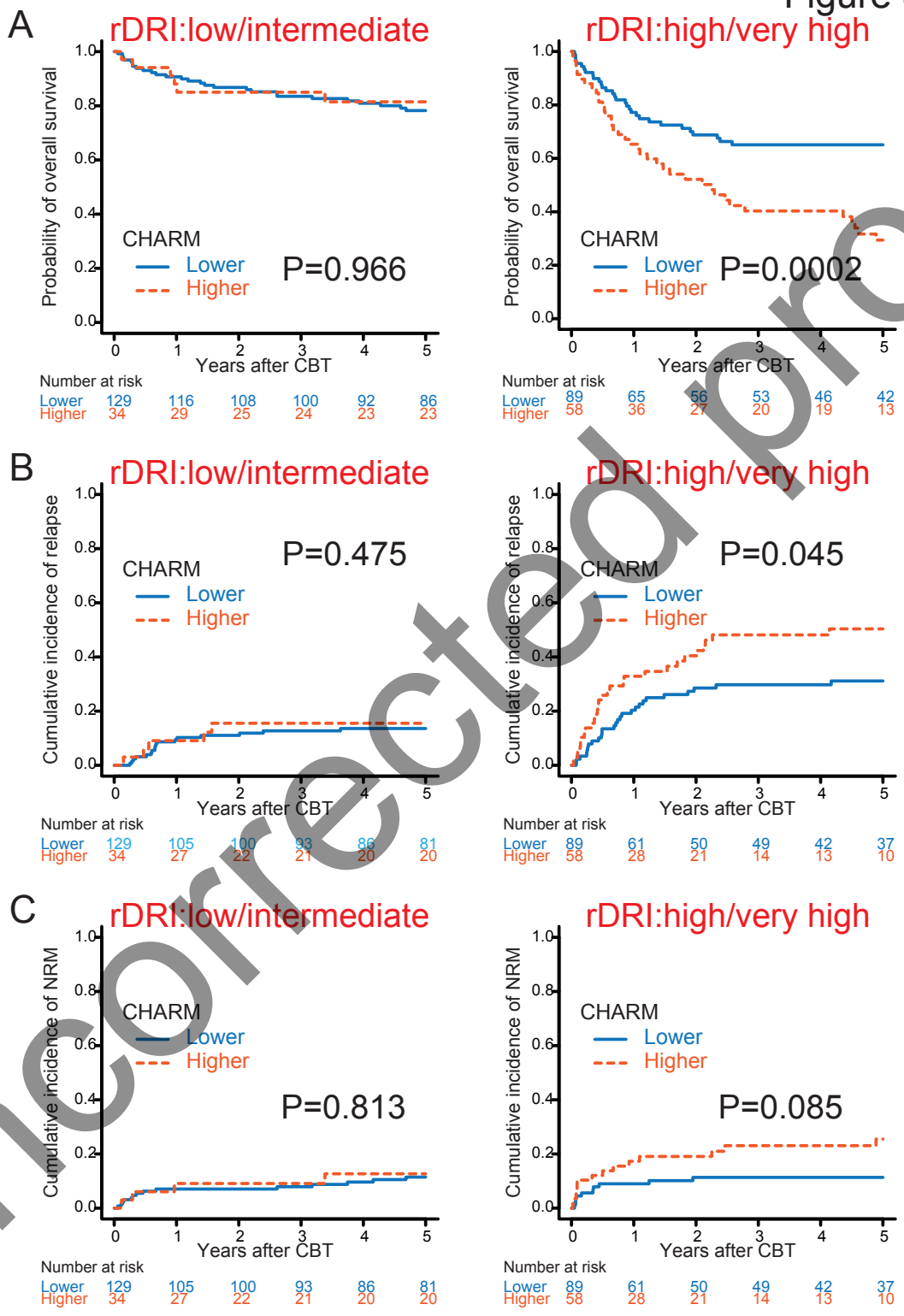

Figure 4. Unadjusted probability of overall survival (OS) (A) and cumulative incidences of relapse (B), non-relapse mortality (NRM) (C), grades II to IV acute graft-versus-host disease (GVHD) (D), grades III

to IV acute GVHD (E), and extensive chronic GVHD (F) following single-unit CBT, stratified by CHARM score among patients received TBI 12Gy-based conditioning regimen.

Figure 4

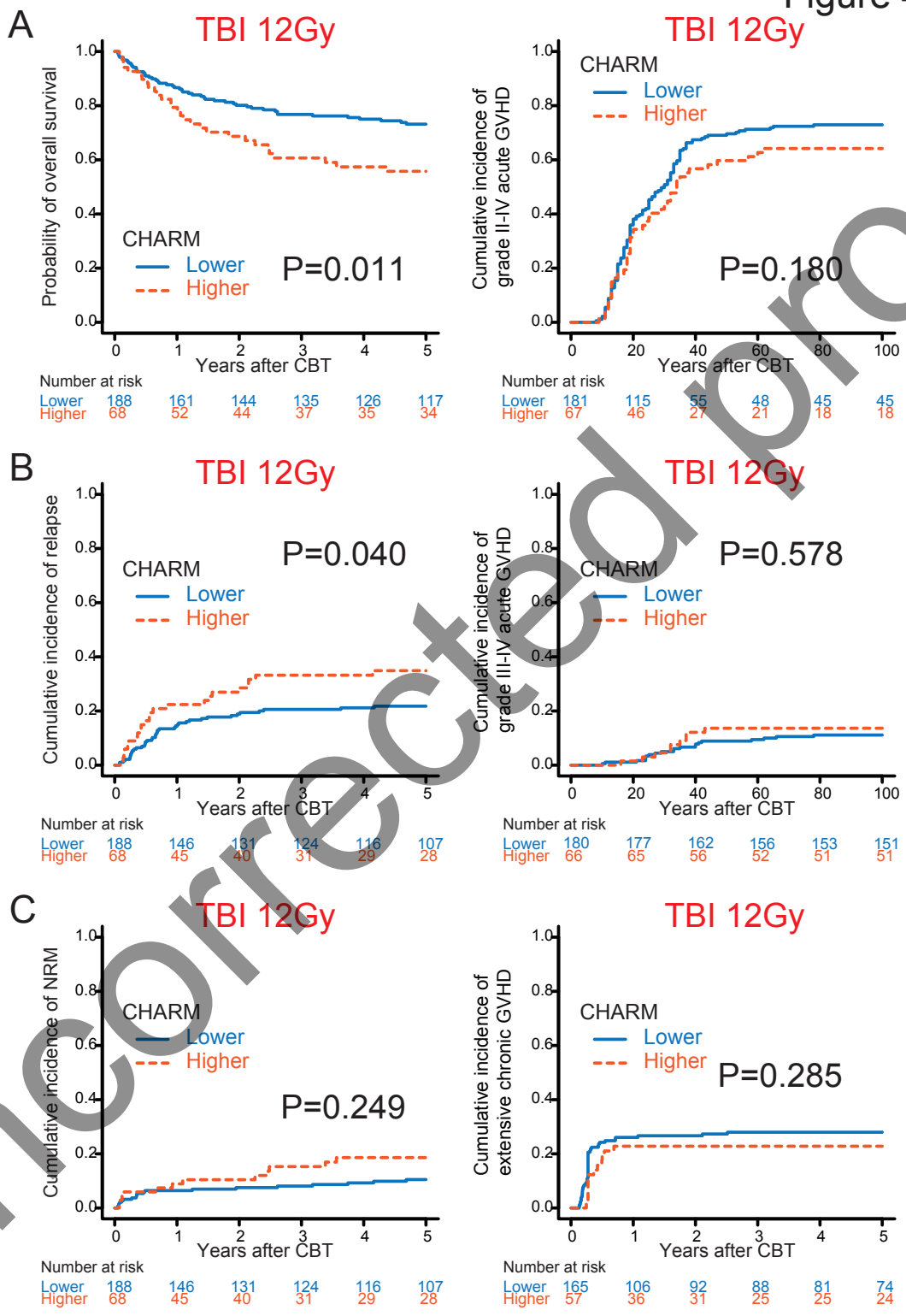

Table 1. Characteristics of patients and transplantations.

CHARM	Lower (< -2.01)	Higher (≥ -2.01)	P
Number of CBT	223 (69.5)	98 (30.5)	
Age, years, median (IQR)	43 (32.5-55.0)	48.5 (38.3-58)	**<0.001**
Sex			0.266
Male	130(58.3)	75 (56.0)	
Female	34 (29.3)	59 (44.0)	
HCT-CI			0.088
0-2	202 (90.6)	82 (83.7)	
≥ 3	21 (9.4)	16 (16.3)	
Diagnosis			**0.036**
AML	109 (48.9)	61 (62.2)	
ALL	55 (24.7)	9 (9.2)	
MDS	29 (13.0)	14 (14.3)	
CML	10 (4.5)	3 (3.1)	
MPD, PMF, CMML	5 (2.2)	4 (4.1)	
CAEBV	1(0.4)	3 (3.1)	
NHL	11 (4.9)	3 (3.1)	
Mastocytosis	1 (0.4)	0 (0.0)	
SAA	2 (0.9)	1 (1.0)	
Refined disease risk index			**<0.001**
Low/intermediate/undetermined	129 (59.2)	34 (37.0)	
High/very high	89 (40.8)	58 (63.0)	
Conditioning regimen			**<0.001**
TBI12Gy+HDAC+G+CY	113 (50.7)	56 (57.1)	
TBI12Gy+HDAC+CY	52 (23.3)	7 (7.1)	
TBI12Gy+CY	16 (7.2)	5 (5.1)	
TBI12Gy+HDAC+G+Flu	7 (3.1)	0 (0.0)	
TBI10Gy+HDAC+G+CY	10 (4.5)	0 (0.0)	
TBI 4Gy+Flu+Bu3+HDAC	24 (10.8)	20 (20.4)	
TBI 2Gy+HDAC+G+Flu	1 (0.4)	5 (5.1)	
TBI 4Gy+Flu+Mel	0 (0.0)	5 (5.1)	
GVHD prophylaxis			**<0.001**
CSP+MTX	195 (87.4)	67 (68.4)	
CSP+MMF, CSP only	28 (12.4)	31 (31.6)	
Cryopreserved TNC dose (IQR), × 10^7/kg	2.52 (2.16-3.10)	2.53 (2.15-2.98)	0.606
Cryopreserved $CD34^+$ cell dose (IQR), × 10^5/kg	1.00 (0.72-1.28)	0.95 (0.71-1.29)	0.387
Cryopreserved CFU-GM dose (IQR), × 10^3/kg	29.16 (20.67-41.51)	26.51 (20.55-38.05)	0.588
HLA disparities*			0.608
0-1	71 (31.8)	34 (34.7)	
2	152 (68.2)	64 (65.3)	
Follow-up for survivors, months, median (range)	120 (4-273)	103 (9-287)	0.315

CBT, cord blood transplantation; IQR, interquartile range; HCT-CI, hematopoietic cell transplantation specific comorbidity index; AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; MDS, myelodysplastic syndrome; CML, chronic myelogenous leukemia; CMML, chronic myelomonocytic leukemia; CAEBV, chronic active Epstein-Barr virus infection; MPN myeloproliferative neoplasm; ATL, adult T-cell leukemia; NHL, non-Hodgkin's lymphoma; MM, multiple myeloma; SAA, severe aplastic anemia; TBI, total body irradiation; MAC, myeloablative conditioning; Flu, fludarabine; Bu, busulfan;

HDCA, high-dose cytarabine; Mel, melphalan; GVHD, graft-versus-host disease; CSP, cyclosporine; MTX, methotrexate; MMF, mycophenolate mofetil; TNC, total nucleated cell; CFU-GM, colony-forming unit granulocyte-macrophage; HLA, human leukocyte antigen.

*The number of HLA disparities was defined as a low resolution for HLA-A, -B, and -DR in the graft-versus-host direction.

Table 2. Multivariate analysis of OS, relapse, and NRM.

	OS		**Relapse**		**NRM**	
	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P
CHRAM						
Lower (< -2.01)	Reference		Reference		Reference	
Higher (≥ -2.01)	1.56 (1.06-2.29)	**0.022**	1.71 (1.09-2.69)	**0.020**	1.17 (0.68-1.99)	0.560
Recipient Age						
<45 years	Reference		Reference		Reference	
≥45 years	1.80 (1.20-2.72)	**0.004**	1.10 (0.65-1.85)	0.700	2.47(1.36-4.51)	**0.003**
Recipient sex						
Male	Reference		Reference		Reference	
Female	0.68 (0.45-1.03)	0.069	1.05 (0.64-1.69)	0.840	0.54 (0.28-1.05)	0.072
Refined DRI						
Low/intermediate	Reference		Reference		Reference	
High/very high	2.50 (1.70-3.68)	**<0.001**	3.23 (1.99-5.25)	**<0.001**	1.31 (0.77-2.25)	0.310
Conditioning regimen						
TBI 10-12Gy based	Reference		Reference		Reference	
Others	0.93 (0.56-1.53)	0.776	0.62 (0.31-1.21)	0.170	1.05 (0.53-2.11)	0.870
Cord blood TNC						
< 2.5×10^7 /kg	Reference		Reference		Reference	
≥ 2.5×10^7 /kg	0.86 (0.59-1.26)	0.460	0.96 (0.61-1.51)	0.880	0.82 (0.45-1.50)	0.530
HLA mismatch						
0-1	Reference		Reference		Reference	
2-3	1.06 (0.71-1.58)	0.747	1.12 (0.68-1.85)	0.630	0.84 (0.48-1.49)	0.570

OS, overall survival; NRM, non-relapse mortality; DRI, disease risk index; TBI, total body irradiation; TNC, total nucleated cell; HLA, human leukocyte antigen; HR, hazard ratio; CI, confidence interval.

The P values in bold are statistically significant (<.05)