haematologica
Journal of the Ferrata Storti Foundation

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Received: August 5, 2024.
Accepted: November 28, 2024.

Citation: Wolfgang Bethge, Sarah Flossdorf, Franziska Hanke, Christoph Schmid, Mark Ringhoffer, Stefan Klein, Bernd Hertenstein, Johannes Schetelig, Matthias Stelljes, Thomas Schroeder, Igor Wolfgang Blau, Francis Ayuk, Matthias Eder, Robert Zeiser, Katharina Fleischhauer, Nicolaus Kröger, and Peter Dreger.
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Haematologica. 2024 Dec 5. doi: 10.3324/haematol.2024.286385 [Epub ahead of print]

Does size matter? Center-specific characteristics and survival after allogeneic hematopoietic cell transplantation for acute myeloid leukemia: an analysis of the German Registry for Stem Cell Transplantation and Cell Therapy

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And on behalf of the German Working Group for Hematopoietic Stem Cell Transplantation and Cellular Therapy e.V. (DAG-HSZT) and the German Registry for Hematopoietic Stem Cell Transplantation and Cell Therapy (DRST)

Collaborative Groups: German Working Group for Hematopoietic Stem Cell Transplantation and Cellular Therapy (DAG-HSZT)), German Registry for Hematopoietic Stem Cell Transplantation and Cell Therapy (DRST))

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Conflict of Interest Statement:

The authors do not declare any conflicts of interest in relation to the manuscript above.

Data sharing statement:

Original analysis data and protocols of this paper may be available to other investigators by request to the DRST (support@drst.de).

Abstract:

We investigated the effect of center-specific variables on overall survival (OS) after allogeneic hematopoietic cell transplantation (alloHCT) in acute myeloid leukemia (AML). Eligible were adult patients reported to DRST registry receiving first alloHCT for AML from a related or matched (>= 9/10 HLA-match) unrelated donor 2015-2021. Primary endpoint was OS at 12 months from alloHCT. Univariable and multivariable analyses after best subset selection was performed. Of 5328 patients, 83% received alloHCT in a high-volume center (≥40 alloHCT/year); 90% in a university hospital; 90% in a center performing alloHCT for ≥10 years; and 73% in a Joint Accreditation Committee IHCT-Europe & EBMT (JACIE) accredited center. 52% of the patients were in CR1, and ELN risk was adverse in 37% and intermediate in 42%. On multivariable analysis, center-specific factors predicting adverse 12-month OS were program duration <5-10 years (hazard ratio (HR) 1.23, 95% CI [1.02; 1.49]); center volume <40 alloHCT/year (HR 1.21, [1.02; 1.45]); and non-university hospital (HR 1.21, [0.98; 1.49]), whereas not JACIE accreditation. Spline modeling suggested a negative effect of a center volume up to 45 alloHCTs per year. Center volume, center experience, university hospital, but not JACIE accreditation have an impact on alloHCT outcomes in adult patients with AML in Germany.

Introduction

While patient-, disease- and procedure-related outcome predictors in allogeneic hematopoietic cell transplantation (alloHCT) for acute myeloid leukemia (AML) are well characterized, the impact of center-specific variables on outcomes are still a matter of debate. Standards of patient selection, conditioning regimen selection, GVHD prophylaxis and supportive care practice as well as outpatient follow-up programs and infrastructure may vary considerably between centers and health care systems(1-4). Furthermore, center size, experience, and staff expertise in addition to the frequency of alloHCT performed may influence the quality of patient care and alloHCT outcome(5-7).

Recently, German health authorities redefined the volume of alloHCT per center in Germany required to qualify for reimbursement at ≥40 alloHCT per year. This decision was largely based on a recent CIBMTR analysis by Majhail et al. reporting this threshold as outcome-relevant for alloHCT in the US(8). As health systems, infrastructure, and treatment practices may strongly differ between countries, the purpose of the present study was for the first time to investigate the effects of center-related factors, such as numbers of alloHCT procedures per year, program duration, university hospital, and Joint Accreditation Committee IHCT-Europe & EBMT (JACIE) accreditation, adjusted for common disease- and transplant-specific confounders on survival after alloHCT in Germany, using AML as a standard indication. To address these questions, we took advantage of the German Registry for Hematopoietic Stem Cell Transplantation and Cell Therapy (DRST), the German national partner of the EBMT.

Methods

Data source

The DRST is a registered association that maintains the German Registry for Hematopoietic Stem Cell Transplantation and Cell Therapy. The DRST performs data collection of hematopoietic cell transplantations (HCT) and cellular therapies in Germany in cooperation with the European Society for Blood and Marrow Transplantation (EBMT) using the EBMT database. Accreditation as a DRST center requires a signed tripartite Joint Controllership Agreement with EBMT and DRST and the submission of core data from all consecutive HCT and cellular therapy recipients to the EBMT Registry in which patients can be identified by the diagnosis of underlying disease and type of HCT resp. cellular therapy. EBMT/DRST registry data is routinely audited to determine accuracy of data collected as part of the JACIE certification. Data collection requires written informed consent using a consent form based on a standard DRST/EBMT template following the European data protection regulations and the Declaration of Helsinki.

Study design

This study was performed by request of the DAG-HSZT (German Working Group for Hematopoietic Stem Cell Transplantation and Cellular Therapy) and approved by the data access commission of DRST.

The study was performed in accordance with the Declaration of Helsinki and approved by the Ethical Committee of the University of Tuebingen (Ref. Nr. 277/2020BO2).

Eligible were adult (≥18 years) patients with AML at any disease status treated with a first allogeneic HCT using a peripheral blood or bone marrow graft from a matched or mismatched related (including haploidentical) or (9/10-10/10 HLA-compatible) unrelated donor between 2015 and 2021 and registered with the DRST.

The objective of the study was to assess the impact of center-specific factors such as number of transplant procedures/year, university hospital yes/no, JACIE accreditation yes/no, years of center experience in alloHCT in the respective year of HCT on outcome of allogeneic HCT within the German health care system.

Statistical analyses

Descriptive statistics were presented for patient-, transplant- and center-related variables separately for patients transplanted in a center with less than 40 transplants per year (low volume centers) and more than or equal to 40 transplants per year (high volume centers). Absolute and relative numbers were reported for categorical variables and mean and standard deviation for continuous variables. Allocation of the respective patients to either center with <40 and ≥40 allogeneic transplantation procedures per year was performed according to center volume in the respective year of HCT. Administrative censoring after 1 year follow-up post HCT was used for survival analysis in order to keep the dataset homogeneous. In addition, identical analyses were done without administrative censoring. OS, EFS (event defined as relapse, progression or death) and the competing risks of relapse/progression and non-relapse/progression mortality (NRM) were assessed in both univariable and multivariable analyses. In addition to center size (<40 vs. >=40), age, gender, disease status at alloHCT, graft source, donor type, conditioning, Karnofsky index, HCT-

specific Comorbidity Index (HCT-CI), European Leukemia Network AML Risk (ELN), university status, center experience and Joined Accreditation Committee of the IHCT and the EBMT (JACIE) accreditation were considered. Cox proportional hazards models (likelihood ratio test) were calculated for OS and EFS and Fine & Gray models for competing risks (univariable and multivariable respectively). The Kaplan-Meier method and the logrank-test was used for univariable OS and EFS analysis of the impact of center size and the Aalen-Johansen estimator and the Gray-test for competing risk analysis. For multivariable analysis, best subset selection with Akaike information criterion (AIC) was calculated to determine the optimal set of variables. For sensitivity analysis, center size cut-points were set at each possible value, and both univariable and multivariable analyses were calculated for all endpoints using these cut-points. Hazard ratios were observed. An additional sensitivity analysis considered center size as a continuous variable. As the relationship between center size and the observed outcomes is non-linear, it is not possible to include center size as a standard continuous variable in the multivariable model due to the assumption of linearity. Spline modelling via p-splines was used to account for this non-linear modelling (9).

Results

Patient characteristics

A total of 5328 consecutive patients treated in 52 German centers performing alloHCT and reporting to the DRST during the index period were included (Table 1). Median age was 58 years (range 18-83). 56% of patients were male. 52% of patients were documented in first CR, and 45% had a more advanced disease status at HCT. In 95% of the patients, peripheral blood stem cells were used as graft source, and bone marrow in the remainder. 1549 (20%)

patients were transplanted from an HLA-matched related (MRD), and 2595 (49%) from a matched (10/10 HLA match) unrelated donor (MUD). Each 592 (11%) patients were transplanted from a mismatched related donor (MMRD) i.e. haploidentical, and a mismatched (9/10 HLA-match) unrelated donor (MMUD), respectively. Donor source was balanced between high volume (>=40 HCT/year) and low volume (<40 HCT/year) centers apart from a slightly higher number of MRD among the low volume centers. Low volume centers had more patients with favorable performance status and HCT-CI (with HCT-CI score often missing), respectively, and used myeloablative conditioning (MAC) more frequently. High volume centers more often had >10 years center experience, were university hospitals, and were JACIE accredited.

Outcome

Kaplan-Meier-estimated OS and EFS rates at 12 months were 65.8% (95% confidence interval (95%CI) [62.7%; 69.1%]) for patients transplanted in a center with <40 HCT/year and 71.1% [69.7%; 72.5%] in a center with ≥ 40 HCT/year (p (logrank) = 0.0004) and 57.5% [54.1%; 61.0%] and 61.5% [60.0%; 63.1%] (p=0.0112), respectively (Figure 1). Cumulative incidence of the competing risks of relapse/progression and NRM estimated at 12 months were 24.2% [21.3%; 27.2%] in centers with <40 HCT/year and 22.9% [21.6%; 24.3%] in centers with ≥40 HCT/year (p (Gray-test) =0.569) and 18.4% [15.8%; 21.1%] and 15.5% [14.4%; 16.7%] (p = 0.047), respectively (Figure 2).

On univariable analysis, center-specific predictors of an adverse OS (Table 2) were center size measured in number of HCT in the year of HCT <40 vs. ≥40 (HR, 95% CI: 1.26 [1.11; 1.43], p=<0.001), University Hospital no vs. yes (1.30 [1.11; 1.53], p=0.001), center experience 5-10

years and <5 years vs. ≥10 years (1.26 [1.06; 1.50], p=0.010 and 1.22 [0.87; 1.72]), whereas JACIE accreditation had no significant effect (1.02 [0.91; 1.15], p=0.744). Patient- and disease-specific factors were also analyzed in the univariable analysis and most of them (except gender and conditioning) were statistically significant with effect sizes similar to what have reported before (Tables 2-5). Likewise, on univariable analysis of predictors for improved EFS (Table 3), the effects for center size HCT <40 vs. ≥40 (1.16 [1.04; 1.31], p=0.011), University Hospital no vs. yes (1.20 [1.04; 1.38], p=0.013), center experience 5-10 years and <5 years vs. ≥ 10 years (1.13 [0.96; 1.33], p=0.138 and 1.24 [0.93; 1.67], p=0.150), and JACIE accreditation no vs. yes (1.02 [0.92; 1.13], p=0.714) were largely similar to OS (Table 2). The same accounts for NRM, whereas significant effects of the 4 structural parameters could not be proven for the endpoint relapse/progression (**Tables 4 and 5**).

On multivariable analysis, relevant center-specific predictors for improved OS were number of HCT/year in year of HCT <40 vs. ≥40 (1.21 [1.02; 1.45], p=0.032), University Hospital no vs. yes (1.21 [0.98; 1.49], p=0.071), and center experience 5-10 years and <5 years vs. ≥10 years (1.234 [1.020; 1.494], p=0.031 and 1.063 [0.737; 1.532], 0.743), but not JACIE accreditation, which did not remain in the model after best subset selection. Patient- and disease-specific factors all remained in the model as relevant covariates, with effects similar to those in the univariable analysis. Identical analyses without administrative censoring after 1 year follow-up post HCT for survival analysis yielded essentially similar results (supplemental tables 1-4).

When the model determined for OS was calculated for the endpoints EFS and the competing events relapse/progression and NRM, the effects of center-specific factors were less strong compared to OS: center size HCT <40 vs. ≥40 (EFS: 1.12 [0.96; 1.31], p=0.164 /

Relapse/Progression: 1.05 [0.85; 1.28], p=0.668 / NRM: 1.23 [0.98; 1.56], p=0.080); University Hospital no vs. yes (1.13 [0.93; 1.36], p=0.218 / 0.96 [0.76; 1.23], p=0.764 / 1.26 [0.95; 1.66], p=0.109) and center experience 5-10 years and <5 vs. ≥10 years (1.12 [0.94; 1.34], p=0.188 and 1.10 [0.80; 1.51], p=0.564 / 1.23 [1.00; 1.53], p=0.054 and 0.92 [0.60; 1.41], p=0.701 / 0.92 [0.70; 1.21], p=0.548 and 1.23 [0.80; 1.90], p=0.338).The impact of patient- and disease-specific factors is shown in the Appendix (Tables S2-S4).

Modeling of center size effect

In order to assess whether the predefined cut-off level of 40 HCT/center/year was not just by chance significant, we performed serial analyses of multivariable Cox regression and calculated adjusted hazard ratios and 95%CIs for all cut-off points and plotted them. With this method, HRs including CIs were below 1 for all cut-off points between 30 and 70 HCTs/year, whereas all other cut-offpoints had no significant discriminative impact (Figure 3A).

To further define the ideal cut-off point of center size (which is a non-linear variable), spline modelling was performed (Figure 3B). HR and 95% CI for corresponding number of HCT/year in comparison to all other HCT numbers in multivariable analysis were plotted. For OS, 45 HCT procedures/year and for EFS, 48 HCT procedures/year were identified as the minimum center size without significantly higher hazards compared to other center sizes.

Discussion

Patient-, disease-, and procedure-specific factors influencing outcomes of allogeneic HCT have been extensively studied and reported. Factors such as age, comorbidities, disease risk,

donor and conditioning have been shown to significantly influence outcome, similar to what was observed in our cohort(9-12). In contrast, there is a paucity of studies examining the impact of transplant center characteristics, such as center experience, volume of allogeneic HCT performed, university hospital, and the existence of a certified quality management system on HCT outcome. The few analyses available are restricted to individual health care systems and are often based on relatively old data sets(7, 13-15). Most frequently, hospital procedure specific volumes and service provider level have been proposed to have an important impact(6, 14, 16). However, volume may also be just a surrogate marker for experience, structural factors, and quality measures. Recent analyses in the US and Japan have shown a significant impact of center volume and experience on HCT outcome(8, 17). The data presented here analyze for the first time the influence of center volume in the context of other center-specific factors on the outcome of allogeneic HCT in adult patients within the German health care system using a large recent (2015-2021) data set. To allow a homogeneous analysis while minimizing other confounding factors we decided to focus on AML as the major indication for adult allogeneic HCT. Apart from excluding pediatric patients and those receiving cord blood or <9/10 mismatched unrelated donor transplants, eligibility was unrestricted in terms of age, performance status, comorbidity, ELN risk, disease status, donor type, graft source, and transplant strategy in order to reflect the whole risk spectrum associated with AML allotransplants in adults. Our study discloses differences in patient selection according to the center size. Patients transplanted at high volume centers had more often a reduced Karnofsky index and were more often transplanted from an unrelated donor.

Similar to previous studies, our analysis confirmed a positive impact of center volume on survival(9, 17-19). Giebel et al found in an EBMT study on 1413 patients with AML treated with RIC alloHCT an adverse effect of an annual RIC transplant rate of 15 or less on PFS, which was largely NRM-driven. Beyond 15 transplants per year they didn't observe significant outcome effects of increasing numbers, but there were only few patients who had been transplanted in centers performing more than 50 patients per year(18). Similarly, a recent large Japanese study reported reduced survival (HR 1.31 [1.2; 1.44] associated with an annual transplant rate of 9.3 or less after alloHCT for AML, and also a second cut-off point at of 32/year disclosed a significant OS disadvantage (HR 1.11 [1.03; 1.2] for the intermediate volume group (9.1-32 allotransplants per year) compared to the centers with higher annual volumes (17). In contrast to the present study, but also to the Giebel study, the center effect was largely driven by relapse rather than NRM in the Japanese series.

Of note, with an HR of 1.12 [0.96; 1.31] on multivariable analysis the center effect was smaller for EFS than for OS in our sample, suggesting that the observed survival benefit associated with high volume centers was partly due to superior outcome *after* post-transplant failure.

A unique added value of our study is that we were able to identify for the first time a minimum ideal cut-off point for the center effect. Although on multivariable Cox modeling each individual cut-off point between 30 and 70 alloHCT per year showed a survival advantage in the centers above the cut-off point compared to those below, spline modeling suggested a significant negative effect of each center volume below 45 allotransplants per year compared to all other center sizes. Center volumes of 45 or higher do not compare

significantly worse to all other center sizes, implying that a significant OS benefit of further increasing the cut-off point does not become apparent beyond 45 allotransplants per year.

These findings are in keeping with a recent CIBMTR analysis by Majhail et al. where center transplantation volumes >40 alloHCT/year and presence of a survivorship program dedicated to HCT recipients were associated with superior OS(8). However, as already discussed by Majhail et al. one has to caution against using our threshold as singular benchmark for qualifying individual centers for allogeneic HCT. The survival difference between the two center volume categories was relatively small, and center volume is only one factor among multiple structural parameters driving alloHCT outcome. Other center-specific factors predicting favorable survival in our analysis were university hospital status and program duration >5-10 years, the latter being in line with a previous analysis of the EBMT(5). The same EBMT analysis reported an NRM-driven, modest effect of running an accredited QM system on OS(5), a finding which could not be reproduced in the present analysis and also not in the Majhail study[8]. However nearly 80% of the high-volume centers in our study were also JACIE-accredited.

Using center volume as sole benchmark for quality of patient care also potentially ignores the important aspect of center accessibility and proximity to allow close follow up for the patient. The study of Majhail already highlighted the importance of a survivorship and structured long-term follow up program. At least half of the treatment related mortality of allogeneic HCT occurs beyond day 100 after HCT(19). A number of guidelines and recommendations exist for a specific long-term follow up program after allogeneic HCT(20).

Unfortunately, we had no information on long-term follow-up program and structure within our data set.

Being a retrospective registry report, our study has several limitations. There is certainly heterogeneity in patient selection across various centers. Data quality and granularity suffers from the retrospective nature of data collection. On the other hand, particular strengths of this analysis consist in the large sample size, enabling informative risk factor analyses, and in the comprehensive coverage of the German SOC HCT activity, with almost all qualified centers contributing data. However, before being generalized, our data need to be validated in other health systems and in other alloHCT indications. In this context it will be important to explore if alloHCT experience has a disease-specific component which overrides the general allotransplant expertise, as it has been reported for less common indications(21).

Taken together, this analysis suggests that in adult patients with AML, in the German health care system the structural parameters center volume, center experience, and university hospital status have a modest effect of almost similar size on survival after alloHCT. The benefit of higher center volumes can be shown for each individual cut-off below 45 allotransplants per year. Validation of these findings in other allotransplant settings and health systems is warranted. These findings support efforts to centralize highly specialized therapeutic interventions such as alloHCT in experienced large volume, high-end care centers. However, health care planning has to simultaneously ensure easy patient access to alloHCT services also in less populated regions. This may be able by establishing decentralized network structures including regional long-term follow-up hubs and modern telemedicine approaches.

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Table 1: Patient characteristics

Variable	Group	<40 HCT/year N = 893 (16.8%)	≥40 HCT/year N = 4435 (83.2%)	Variable	Group	<40 HCT/year N = 893 (16.8%)	≥40 HCT/year N = 4435 (83.2%)	Variable	Group	<40 HCT/year N = 893 (16.8%)	≥40 HCT/year N = 4435 (83.2%)
Age (mean (sd))		54.9 (13.07)	55.57 (13.02)	Donor (N (%))	MRD	312 (34.9%)	1237 (27.9%)	HCT-CI (N (%))	0-2	570 (63.8%)	2479 (55.9%)
Gender (N (%))	male	507 (56.8%)	2460 (55.5%)		MMRD	99 (11.1%)	493 (11.1%)		3-10	233 (26.1%)	1154 (26%)
	female	386 (43.2%)	1969 (44.4%)		MMUD	95 (10.6%)	497 (11.2%)		missing	90 (10.1%)	802 (18.1%)
	unknown	-	6 (0.1%)		MUD	387 (43.3%)	2208 (49.8%)	ELN (N (%))	adverse	274 (30.7%)	1281 (28.9%)
Disease status at Tx (N (%))	CR	472 (52.9%)	2317 (52.2%)	Conditioning (N (%))	MAC	645 (72.2%)	1980 (44.6%)		BPDCN	8 (0.9%)	22 (0.5%)
	not 1. CR	400 (44.8%)	2020 (45.5%)		non-MAC	236 (26.4%)	2232 (50.3%)		favorable	129 (14.4%)	690 (15.6%)
	unknown	21 (2.4%)	98 (2.2%)		unknown	12 (1.3%)	223 (5.0%)		intermediate	269 (30.1%)	1489 (33.6%)
Graft (N (%))	PB	847 (94.8%)	4206 (94.8%)	Karnofsky Index (N (%))	90/100	630 (70.5%)	2542 (57.3%)		unknown	213 (23.9%)	953 (21.5%)
	BM	41 (4.6%)	215 (4.8%)		70/80	186 (20.8%)	1444 (32.6%)	Center Experience (N (%))	≥ 10 years	592 (66.3%)	4206 (94.8%)
	CB	1 (0.1%)	2 (0.0%)		10-60	24 (2.7%)	140 (3.2%)		5-10 years	228 (25.5%)	193 (4.4%)
	unknown	4 (0.4%)	12 (0.3%)		unknown	53 (5.9%)	309 (7.0%)		< 5 years	73 (8.2%)	36 (0.8%)
				University Hospital (N (%))	yes	458 (51.3%)	4338 (97.8%)	JACIE (N (%))	yes	369 (41.3%)	3517 (79.3%)
					no	435 (48.7%)	97 (2.2%)		no	524 (58.7%)	918 (20.7%)

Legend: HCT-CI: Hematopoietic Cell Transplantation-Comorbidity Index, ELN: European Leukemia Network Classification, CR: Complete Remission; PB: Peripheral Blood; BM: Bone Marrow; CB: Cord Blood; MRD: Matched Related Donor; MMRD: Mismatched Related Donor; MUD: Matched Unrelated Donor; MMUD: Mismatched Unrelated Donor; MAC: Myeloablative Conditioning; HCT/Tx: Hematopoietic Cell Transplantation; JACIE: Joint Accreditation Committee IHCT-Europe & EBMT

Table 2: Risk factor analysis overall survival

Variable	Reference	Exposure	univariable analysis (HR [95%-CI], p-value)	multivariable analysis (HR [95%-CI], p-value)
Center Size (HCT/year)	≥ 40	< 40	1.260 [1.108; 1.434], <0.001	1.212 [1.016; 1.445], 0.032
University Hospital	yes	no	1.303 [1.112; 1.527], 0.001	1.210 [0.984; 1.488], 0.071
Center Experience	≥ 10 years	5-10 years	1.260 [1.057; 1.503], 0.010	1.234 [1.020; 1.494], 0.031
		< 5 years	1.223 [0.870; 1.719], 0.247	1.063 [0.737; 1.532], 0.743
JACIE	yes	no	1.020 [0.907; 1.146], 0.744	
Age	continuous	-	1.028 [1.023; 1.033], <0.001	1.024 [1.019; 1.029], <0.001
Gender	m	f	0.929 [0.837; 1.031], 0.164	1.024 [0.919; 1.141], 0.667
Karnofsky Index	90/100	70/80	1.569 [1.402; 1.754], <0.001	1.368 [1.214; 1.541], <0.001
		10-60	2.388 [1.880; 3.034], <0.001	1.827 [1.428; 2.337], <0.001
		unknown	1.729 [1.435; 2.084], <0.001	1.516 [1.222; 1.881], <0.001
HCT-CI	0-2	3-10	1.407 [1.250; 1.584], <0.001	1.201 [1.061; 1.359], 0.004
		unknown	1.484 [1.295; 1.700], <0.001	1.380 [1.186; 1.606], <0.001
ELN	adverse	BPDCN	0.916 [0.474; 1.770], 0.794	1.025 [0.527; 1.992], 0.942
		favorable	0.538 [0.451; 0.642], <0.001	0.549 [0.457; 0.659], <0.001
		intermediate	0.715 [0.630; 0.811], <0.001	0.786 [0.689; 0.895], <0.001
		unknown	0.768 [0.667; 0.883], <0.001	0.710 [0.611; 0.826], <0.001
Conditioning	MAC	non-MAC	1.085 [0.977; 1.205], 0.128	0.930 [0.829; 1.043], 0.212
Disease status at Tx	1. CR	not 1. CR	2.149 [1.930; 2.392], <0.001	1.985 [1.775; 2.219], <0.001
Graft	PB	BM	1.368 [1.106; 1.694], 0.004	1.203 [0.943; 1.533], 0.136
Donor	MRD	MMRD	1.501 [1.265; 1.782], <0.001	1.305 [1.080; 1.577], 0.006
		MMUD	1.567 [1.325; 1.854], <0.001	1.405 [1.178; 1.675], <0.001
		MUD	1.053 [0.927; 1.196], 0.424	0.974 [0.852; 1.114], 0.705

Legend: HCT-CI: Hematopoietic Cell Transplantation-Comorbidity Index, ELN: European Leukemia Network Classification, CR: Complete Remission; PB: Peripheral Blood; BM: Bone Marrow; CB: Cord Blood; MRD: Matched Related Donor; MMRD: Mismatched Related Donor; MUD: Matched Unrelated Donor; MMUD: Mismatched Unrelated Donor; MAC: Myeloablative Conditioning; HCT/Tx: Hematopoietic Cell Transplantation; JACIE: Joint Accreditation Committee IHCT-Europe & EBMT; BPDCN: blastic plasmacytoid dendritic cell neoplasm

Table 3: Risk factor analysis event free survival

Variable	Reference	Exposure	univariable analysis (HR [95%-CI], p-value)	multivariable analysis (HR [95%-CI], p-value)
Center Size (HCT/year)	≥ 40	< 40	1.162 [1.035; 1.306], 0.011	1.119 [0.955; 1.310], 0.164
University Hospital	yes	no	1.200 [1.040; 1.384], 0.013	1.125 [0.933; 1.356], 0.218
Center Experience	≥ 10 years	5-10 years	1.130 [0.962; 1.329], 0.138	1.124 [0.944; 1.339], 0.188
		< 5 years	1.243 [0.925; 1.671], 0.150	1.097 [0.800; 1.506], 0.564
JACIE	yes	no	1.019 [0.920; 1.129], 0.714	
Age	continuous	-	1.012 [1.008; 1.016], <0.001	1.009 [1.005; 1.013], <0.001
Gender	m	f	0.936 [0.855; 1.026], 0.158	0.978 [0.890; 1.076], 0.650
Karnofsky Index	90/100	70/80	1.304 [1.181; 1.440], <0.001	1.205 [1.085; 1.338], 0.001
		10-60	1.840 [1.469; 2.304], <0.001	1.499 [1.189; 1.890], 0.001
		unknown	1.519 [1.282; 1.801], <0.001	1.435 [1.185; 1.738], <0.001
HCT-CI	0-2	3-10	1.168 [1.051; 1.299], 0.004	1.049 [0.939; 1.172], 0.394
		unknown	1.313 [1.163; 1.481], <0.001	1.274 [1.115; 1.455], <0.001
ELN	adverse	BPDCN	0.760 [0.407; 1.420], 0.390	0.858 [0.458; 1.609], 0.634
		favorable	0.575 [0.494; 0.670], <0.001	0.564 [0.481; 0.660], <0.001
		intermediate	0.777 [0.696; 0.867], <0.001	0.826 [0.737; 0.926], 0.001
		unknown	0.757 [0.667; 0.858], <0.001	0.700 [0.612; 0.800], <0.001
Conditioning	MAC	non-MAC	1.040 [0.948; 1.140], 0.407	0.972 [0.879; 1.075], 0.580
Disease status at Tx	1. CR	not 1. CR	1.879 [1.714; 2.061], <0.001	1.830 [1.662; 2.015], <0.001
Graft	PB	BM	1.483 [1.232; 1.785], <0.001	1.378 [1.119; 1.696], 0.003
Donor	MRD	MMRD	1.214 [1.040; 1.419], 0.014	1.056 [0.890; 1.251], 0.533
		MMUD	1.360 [1.172; 1.579], <0.001	1.260 [1.078; 1.473], 0.004
		MUD	0.989 [0.887; 1.103], 0.849	0.972 [0.867; 1.090], 0.628

Legend: HCT-CI: Hematopoietic Cell Transplantation-Comorbidity Index, ELN: European Leukemia Network Classification, CR: Complete Remission; PB: Peripheral Blood; BM: Bone Marrow; CB: Cord Blood; MRD: Matched Related Donor; MMRD: Mismatched Related Donor; MUD: Matched Unrelated Donor; MMUD: Mismatched Unrelated Donor; MAC: Myeloablative Conditioning; HCT/Tx: Hematopoietic Cell Transplantation; JACIE: Joint Accreditation Committee IHCT-Europe & EBMT; BPDCN: blastic plasmacytoid dendritic cell neoplasm

Table 4: Risk factor analysis non-relapse mortality

Variable	Reference	Exposure	univariable analysis (HR [95%-CI], p-value)	multivariable analysis (HR [95%-CI], p-value)
Center Size (HCT/year)	≥ 40	< 40	1.218 [1.022; 1.451], 0.028	1.232 [0.975; 1.556], 0.080
University Hospital	yes	no	1.311 [1.061; 1.620], 0.012	1.255 [0.951; 1.656], 0.109
Center Experience	≥ 10 years	5-10 years	0.992 [0.765; 1.287], 0.953	0.918 [0.695; 1.213], 0.548
		< 5 years	1.392 [0.905; 2.140], 0.132	1.234 [0.803; 1.896], 0.338
JACIE	yes	no	1.045 [0.894; 1.222], 0.581	
Age	continuous	-	1.038 [1.031; 1.046], <0.001	1.033 [1.025; 1.041], <0.001
Gender	m	f	0.998 [0.868; 1.148], 0.977	1.074 [0.930; 1.240], 0.328
Karnofsky Index	90/100	70/80	1.622 [1.396; 1.885], <0.001	1.375 [1.174; 1.611], <0.001
		10-60	2.661 [1.974; 3.586], <0.001	2.083 [1.536; 2.825], <0.001
		unknown	1.493 [1.136; 1.960], 0.004	1.440 [1.067; 1.943], 0.017
HCT-CI	0-2	3-10	1.607 [1.374; 1.880], <0.001	1.346 [1.143; 1.584], <0.001
		unknown	1.432 [1.187; 1.727], <0.001	1.377 [1.122; 1.690], 0.002
ELN	adverse	BPDCN	1.000 [0.426; 2.348], 1.000	1.162 [0.509; 2.653], 0.722
		favorable	0.650 [0.513; 0.824], <0.001	0.676 [0.530; 0.863], 0.002
		intermediate	0.874 [0.738; 1.037], 0.122	0.987 [0.830; 1.174], 0.886
		unknown	0.875 [0.722; 1.061], 0.174	0.870 [0.707; 1.070], 0.186
Conditioning	MAC	non-MAC	1.206 [1.047; 1.388], 0.009	0.981 [0.840; 1.146], 0.808
Disease status at Tx	1. CR	not 1. CR	1.935 [1.676; 2.234], <0.001	1.719 [1.482; 1.994], <0.001
Graft	PB	BM	1.124 [0.827; 1.527], 0.455	0.978 [0.700; 1.365], 0.894
Donor	MRD	MMRD	1.559 [1.237; 1.964], <0.001	1.461 [1.136; 1.880], 0.003
		MMUD	1.678 [1.341; 2.098], <0.001	1.481 [1.174; 1.868], 0.001
		MUD	1.108 [0.930; 1.319], 0.251	0.978 [0.814; 1.174], 0.810

Legend: HCT-CI: Hematopoietic Cell Transplantation-Comorbidity Index, ELN: European Leukemia Network Classification, CR: Complete Remission; PB: Peripheral Blood; BM: Bone Marrow; CB: Cord Blood; MRD: Matched Related Donor; MMRD: Mismatched Related Donor; MUD: Matched Unrelated Donor; MMUD: Mismatched Unrelated Donor; MAC: Myeloablative Conditioning; HCT/Tx: Hematopoietic Cell Transplantation; JACIE: Joint Accreditation Committee IHCT-Europe & EBMT; BPDCN: blastic plasmacytoid dendritic cell neoplasm

Table 5: Statistical Analysis Relapse/Progression

Variable	Reference	Exposure	univariable analysis (HR [95%-CI], p-value)	multivariable analysis (HR [95%-CI], p-value)
Center Size (HCT/year)	≥ 40	< 40	1.078 [0.927; 1.255], 0.328	1.045 [0.854; 1.280], 0.668
University Hospital	yes	no	1.055 [0.873; 1.275], 0.580	0.963 [0.755; 1.229], 0.764
Center Experience	≥ 10 years	5-10 years	1.207 [0.988; 1.474], 0.066	1.234 [0.997; 1.529], 0.054
		< 5 years	1.075 [0.732; 1.578], 0.713	0.920 [0.600; 1.410], 0.701
JACIE	yes	no	0.991 [0.869; 1.131], 0.899	
Age	continuous	-	0.994 [0.990; 0.998], 0.007	0.993 [0.988; 0.998], 0.003
Gender	m	f	0.904 [0.804; 1.016], 0.090	0.920 [0.814; 1.040], 0.182
Karnofsky Index	90/100	70/80	1.030 [0.904; 1.173], 0.660	1.012 [0.882; 1.162], 0.862
		10-60	1.099 [0.796; 1.516], 0.567	0.960 [0.690; 1.334], 0.807
		unknown	1.385 [1.122; 1.710], 0.002	1.237 [0.972; 1.573], 0.084
HCT-CI	0-2	3-10	0.867 [0.751; 0.999], 0.049	0.845 [0.728; 0.982], 0.028
		unknown	1.167 [1.001; 1.360], 0.049	1.151 [0.973; 1.363], 0.101
ELN	adverse	BPDCN	0.645 [0.260; 1.603], 0.346	0.700 [0.284; 1.729], 0.440
		favorable	0.588 [0.485; 0.715], <0.001	0.557 [0.455; 0.682], <0.001
		intermediate	0.754 [0.655; 0.867], <0.001	0.766 [0.662; 0.886], <0.001
		unknown	0.723 [0.616; 0.849], <0.001	0.662 [0.557; 0.786], <0.001
Conditioning	MAC	non-MAC	0.925 [0.822; 1.042], 0.199	0.985 [0.868; 1.117], 0.809
Disease status at Tx	1. CR	not 1. CR	1.576 [1.402; 1.772], <0.001	1.634 [1.446; 1.847], <0.001
Graft	PB	BM	1.640 [1.312; 2.051], <0.001	1.630 [1.264; 2.100], <0.001
Donor	MRD	MMRD	0.958 [0.780; 1.177], 0.681	0.804 [0.641; 1.009], 0.060
		MMUD	1.082 [0.890; 1.315], 0.430	1.065 [0.866; 1.308], 0.551
		MUD	0.921 [0.803; 1.055], 0.235	0.979 [0.848; 1.131], 0.776

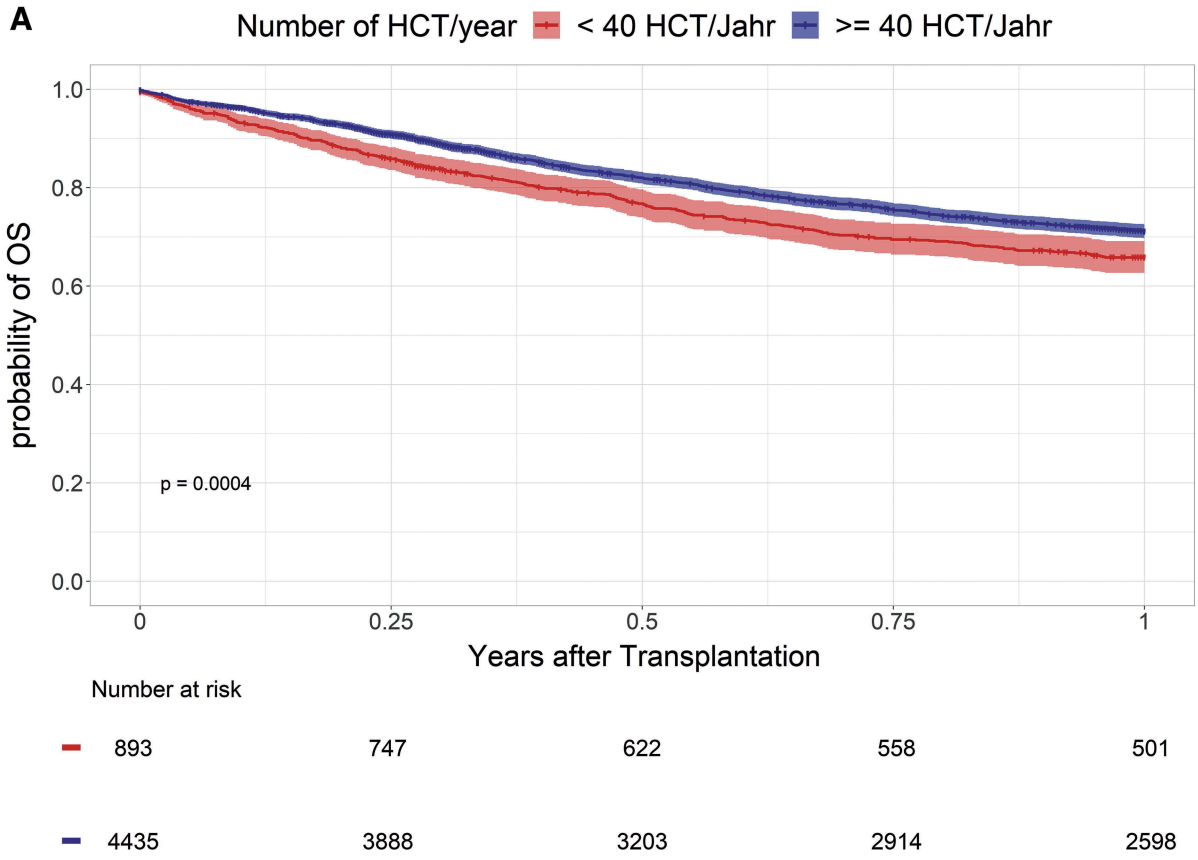
Legend: HCT-CI: Hematopoietic Cell Transplantation-Comorbidity Index, ELN: European Leukemia Network Classification, CR: Complete Remission; PB: Peripheral Blood; BM: Bone Marrow; CB: Cord Blood; MRD: Matched Related Donor; MMRD: Mismatched Related Donor; MUD: Matched Unrelated Donor; MMUD: Mismatched Unrelated Donor; MAC: Myeloablative Conditioning; HCT/Tx: Hematopoietic Cell Transplantation; JACIE: Joint Accreditation Committee IHCT-Europe & EBMT; BPDCN: blastic plasmacytoid dendritic cell neoplasm

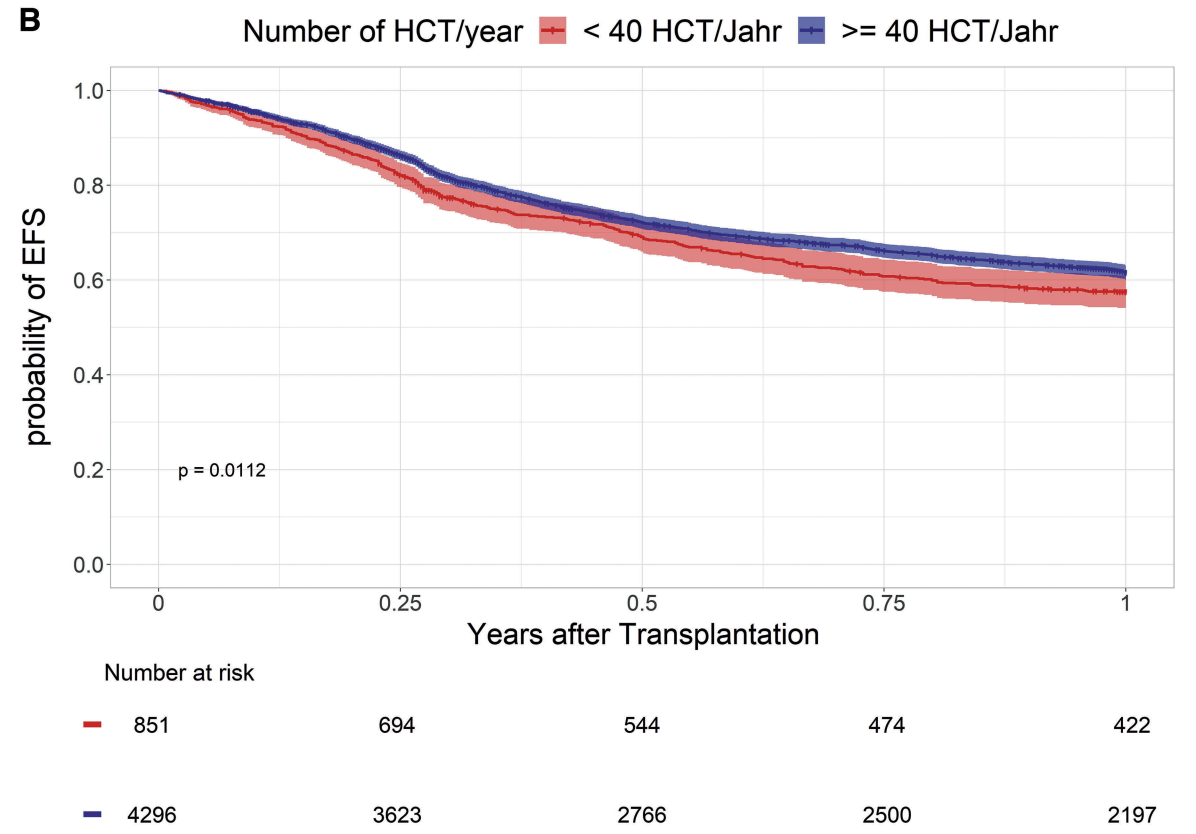
Figure Legends:

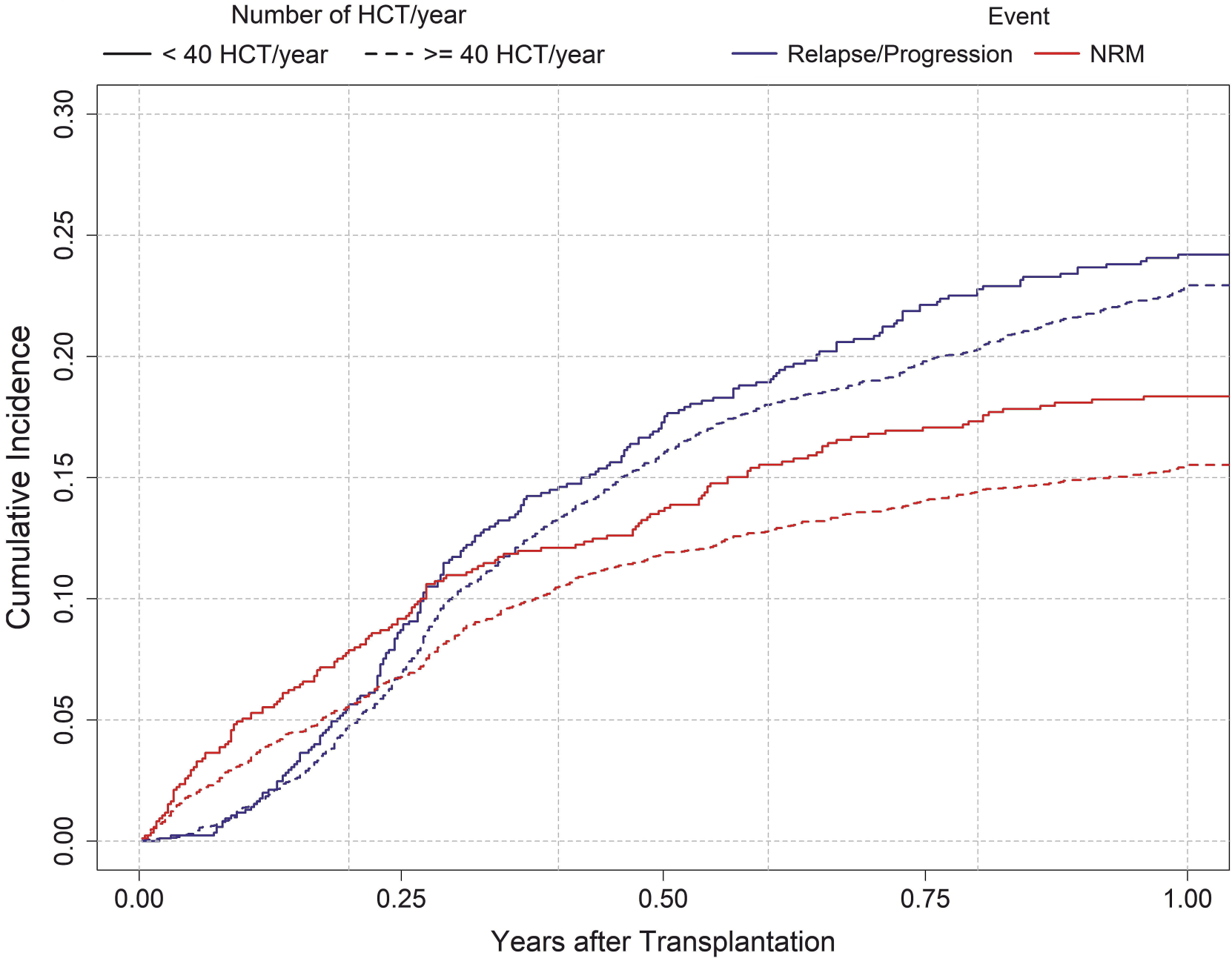
Figure 1: Kaplan-Meier Plots of Survival
A: Overall Survival
B: Event Free Survival

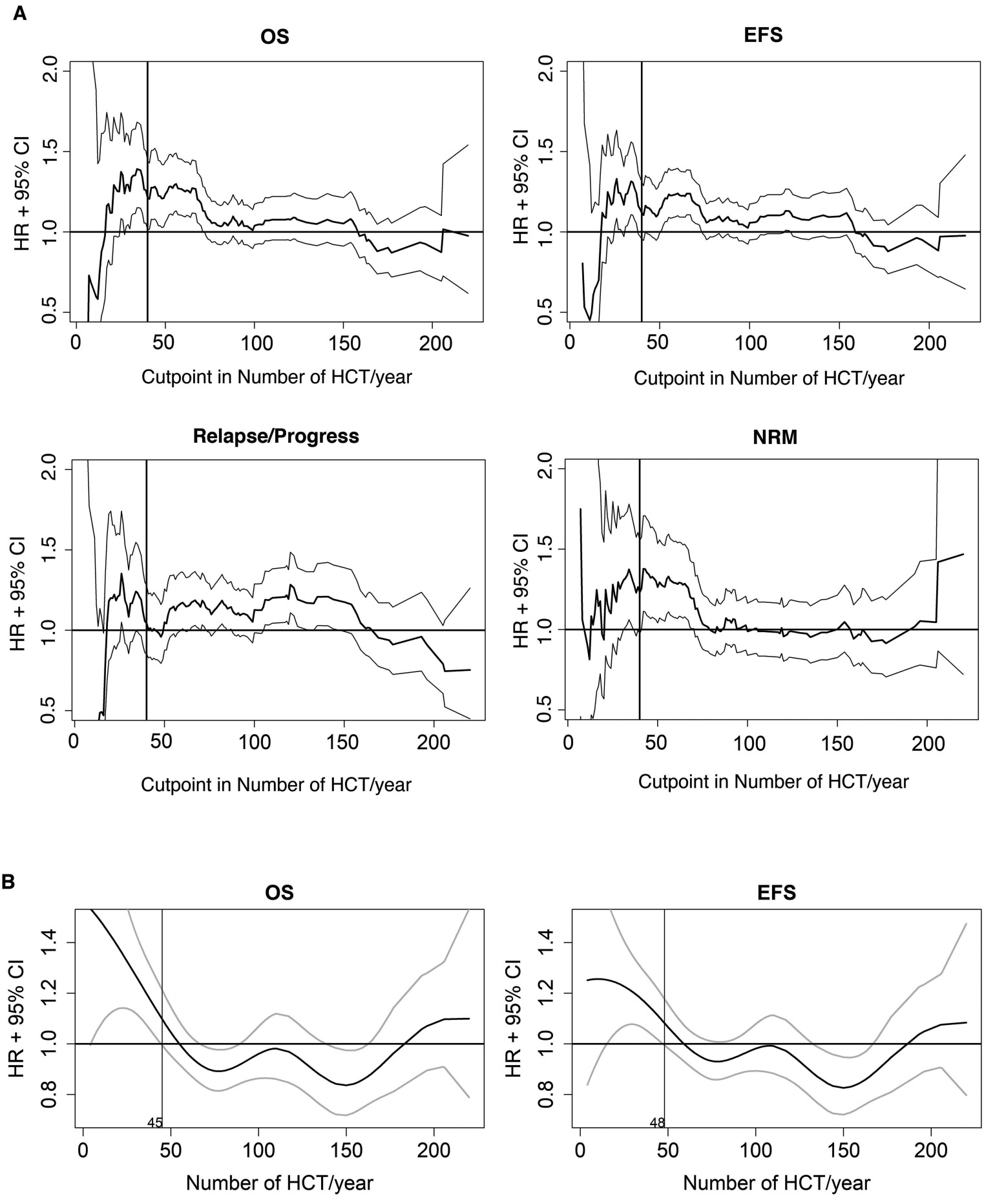
Figure 2: Cumulative Incidence Non-Relapse Mortality and Relapse

Figure 3: Multivariable analysis of HR + 95%-CI for all cutpoints.
(A) Center size as non-linear variable
(B) Evaluation by Spline Modelling. HR (95% CI) for corresponding number of HCT/year in comparison to all other HCT-numbers in multivariate analysis


A
Number of HCT/year
< 40 HCT/Jahr
>= 40 HCT/Jahr
probability of OS
1.0
0.8
0.6
0.4
0.2
0.0
p = 0.0004
0
0.25
0.5
0.75
1
Years after Transplantation
Number at risk
893
747
622
558
501
4435
3888
3203
2914
2598


B
Number of HCT/year
< 40 HCT/Jahr
>= 40 HCT/Jahr
probability of EFS
1.0
0.8
0.6
0.4
0.2
0.0
p = 0.0112
0
0.25
0.5
0.75
1
Years after Transplantation
Number at risk
851
694
544
474
422
4296
3623
2766
2500
2197


Number of HCT/year
< 40 HCT/year
>= 40 HCT/year
Event
Relapse/Progression
NRM
Cumulative Incidence
0.00
0.05
0.10
0.15
0.20
0.25
0.30
0.00
0.25
0.50
0.75
1.00
Years after Transplantation


A
OS
EFS
Relapse/Progress
NRM
HR + 95% CI
0.5
1.0
1.5
2.0
0
50
100
150
200
Cutpoint in Number of HCT/year
B
OS
EFS
HR + 95% CI
0.8
1.0
1.2
1.4
45
48
Number of HCT/year

Supplemental Tables

Does size matter? Center-specific characteristics and survival after allogeneic hematopoietic cell transplantation for acute myeloid leukemia: An analysis of the German Registry for Stem Cell Transplantation and Cell Therapy

Supplemental Table 1: Overall survival without 1 year cut off follow-up

Variable	Reference	Exposure	univariable analysis (HR [95%-CI], p-value)	multivariable analysis (HR [95%-CI], p-value)
Center Size (HCT/year)	≥ 40	< 40	1.178 [1.057; 1.312], 0.003	1.193 [1.026; 1.389], 0.022
University Hospital	yes	no	1.171 [1.023; 1.340], 0.022	1.113 [0.930; 1.331], 0.244
Center Experience	≥ 10 years	5-10 years	1.144 [0.987; 1.325], 0.075	1.087 [0.925; 1.277], 0.310
		< 5 years	1.121 [0.842; 1.493], 0.434	1.042 [0.767; 1.416], 0.793
JACIE	yes	no	1.013 [0.919; 1.117], 0.797	
Age	continuous	-	1.020 [1.016; 1.023], <0.001	1.015 [1.012; 1.019], <0.001
Gender	m	f	0.872 [0.801; 0.950], 0.002	0.939 [0.859; 1.027], 0.171
Karnofsky Index	90/100	70/80	1.461 [1.332; 1.602], <0.001	1.335 [1.210; 1.473], <0.001
		10-60	2.166 [1.757; 2.671], <0.001	1.795 [1.446; 2.227], <0.001
		unknown	1.551 [1.328; 1.812], <0.001	1.421 [1.189; 1.698], <0.001
HCT-CI	0-2	3-10	1.344 [1.218; 1.483], <0.001	1.182 [1.066; 1.310], 0.001
		unknown	1.454 [1.302; 1.624], <0.001	1.390 [1.230; 1.572], <0.001
ELN	adverse	BPDCN	0.874 [0.505; 1.513], 0.632	0.929 [0.523; 1.650], 0.801
		favorable	0.530 [0.459; 0.612], <0.001	0.535 [0.461; 0.621], <0.001
		intermediate	0.692 [0.623; 0.769], <0.001	0.757 [0.679; 0.844], <0.001
		unknown	0.766 [0.684; 0.858], <0.001	0.716 [0.634; 0.809], <0.001
Conditioning	MAC	non-MAC	1.139 [1.045; 1.241], 0.003	1.005 [0.913; 1.105], 0.926
Disease status at Tx	1. CR	not 1. CR	1.822 [1.671; 1.986], <0.001	1.702 [1.556; 1.863], <0.001
Graft	PB	BM	1.285 [1.072; 1.541], 0.007	1.167 [0.950; 1.433], 0.141
Donor	MRD	MMRD	1.257 [1.087; 1.454], 0.002	1.130 [0.962; 1.327], 0.137
		MMUD	1.374 [1.196; 1.580], <0.001	1.287 [1.113; 1.489], 0.001
		MUD	0.991 [0.895; 1.097], 0.855	0.945 [0.848; 1.052], 0.300

Legend: HCT-CI: Hematopoietic Cell Transplantation-Comorbidity Index, ELN: European Leukemia Network Classification, CR: Complete Remission; PB: Peripheral Blood; BM: Bone Marrow; CB: Cord Blood; MRD: Matched Related Donor; MMRD: Mismatched Related Donor; MUD: Matched Unrelated Donor; MMUD: Mismatched Unrelated Donor; MAC: Myeloablative Conditioning; HCT/Tx: Hematopoietic Cell Transplantation; JACIE: Joint Accreditation Committee IHCT-Europe & EBMT; BPDCN: blastic plasmacytoid dendritic cell neoplasm

Supplemental Table 2: Event free survival without 1 year cut off follow-up

Variable	Reference	Exposure	univariable analysis (HR [95%-CI], p-value)	multivariable analysis (HR [95%-CI], p-value)
Center Size (HCT/year)	≥ 40	< 40	1.116 [1.006; 1.238], 0.038	1.089 [0.943; 1.258], 0.242
University Hospital	yes	no	1.142 [1.005; 1.298], 0.042	1.121 [0.946; 1.328], 0.188
Center Experience	≥ 10 years	5-10 years	1.104 [0.959; 1.271], 0.170	1.076 [0.923; 1.255], 0.350
		< 5 years	1.018 [0.767; 1.351], 0.901	0.937 [0.695; 1.264], 0.670
JACIE	yes	no	1.000 [0.913; 1.096], 0.999	
Age	continuous	-	1.011 [1.008; 1.015], <0.001	1.009 [1.005; 1.012], <0.001
Gender	m	f	0.908 [0.838; 0.984], 0.018	0.946 [0.870; 1.028], 0.190
Karnofsky Index	90/100	70/80	1.273 [1.166; 1.390], <0.001	1.197 [1.091; 1.313], <0.001
		10-60	1.753 [1.427; 2.155], <0.001	1.486 [1.203; 1.837], <0.001
		unknown	1.425 [1.225; 1.657], <0.001	1.385 [1.169; 1.641], <0.001
HCT-CI	0-2	3-10	1.158 [1.054; 1.271], 0.002	1.048 [0.950; 1.155], 0.350
		unknown	1.307 [1.176; 1.453], <0.001	1.298 [1.156; 1.458], <0.001
ELN	adverse	BPDCN	0.795 [0.469; 1.349], 0.395	0.825 [0.475; 1.432], 0.493
		favorable	0.580 [0.508; 0.662], <0.001	0.573 [0.499; 0.657], <0.001
		intermediate	0.744 [0.674; 0.821], <0.001	0.789 [0.712; 0.874], <0.001
		unknown	0.769 [0.690; 0.858], <0.001	0.721 [0.641; 0.809], <0.001
Conditioning	MAC	non-MAC	1.071 [0.988; 1.162], 0.095	0.991 [0.906; 1.083], 0.836
Disease status at Tx	1. CR	not 1. CR	1.692 [1.562; 1.834], <0.001	1.643 [1.511; 1.787], <0.001
Graft	PB	BM	1.307 [1.099; 1.554], 0.002	1.222 [1.008; 1.483], 0.042
Donor	MRD	MMRD	1.131 [0.984; 1.300], 0.084	1.021 [0.877; 1.189], 0.789
		MMUD	1.242 [1.087; 1.420], 0.001	1.167 [1.014; 1.342], 0.031
		MUD	0.983 [0.894; 1.080], 0.720	0.966 [0.875; 1.068], 0.500

Legend: HCT-CI: Hematopoietic Cell Transplantation-Comorbidity Index, ELN: European Leukemia Network Classification, CR: Complete Remission; PB: Peripheral Blood; BM: Bone Marrow; CB: Cord Blood; MRD: Matched Related Donor; MMRD: Mismatched Related Donor; MUD: Matched Unrelated Donor; MMUD: Mismatched Unrelated Donor; MAC: Myeloablative Conditioning; HCT/Tx: Hematopoietic Cell Transplantation; JACIE: Joint Accreditation Committee IHCT-Europe & EBMT; BPDCN: blastic plasmacytoid dendritic cell neoplasm

Supplemental Table 3: Relapse/Progression without 1 year cut off follow-up

Variable	Reference	Exposure	univariable analysis (HR [95%-CI], p-value)	multivariable analysis (HR [95%-CI], p-value)
Center Size (HCT/year)	≥ 40	< 40	1.034[0.907; 1.178], 0.615	0.994 [0.830; 1.190], 0.947
University Hospital	yes	no	1.036 [0.881; 1.217], 0.671	1.000 [0.808; 1.238], 0.998
Center Experience	≥ 10 years	5-10 years	1.189 [1.004; 1.407], 0.045	1.186 [0.987; 1.425], 0.068
		< 5 years	0.921 [0.641; 1.324], 0.658	0.796 [0.538; 1.180], 0.256
JACIE	yes	no	0.978 [0.873; 1.095], 0.697	
Age	continuous	-	0.994 [0.990; 0.997], 0.001	0.993 [0.989; 0.997], 0.001
Gender	m	f	0.914 [0.827; 1.009], 0.074	0.926 [0.835; 1.027], 0.144
Karnofsky Index	90/100	70/80	0.988 [0.884; 1.104], 0.833	0.993 [0.883; 1.116], 0.904
		10-60	0.967 [0.723; 1.294], 0.823	0.891 [0.661; 1.200], 0.446
		unknown	1.338 [1.119; 1.599], 0.001	1.248 [1.024; 1.522], 0.028
HCT-CI	0-2	3-10	0.831 [0.735; 0.939], 0.003	0.820 [0.721; 0.933], 0.003
		unknown	1.178 [1.037; 1.338], 0.012	1.174 [1.022; 1.350], 0.024
ELN	adverse	BPDCN	0.656 [0.312; 1.382], 0.268	0.614 [0.271; 1.393], 0.243
		favorable	0.610 [0.518; 0.719], <0.001	0.586 [0.494; 0.696], <0.001
		intermediate	0.739 [0.654; 0.834], <0.001	0.745 [0.657; 0.846], <0.001
		unknown	0.776 [0.680; 0.886], <0.001	0.718 [0.624; 0.827], <0.001
Conditioning	MAC	non-MAC	0.945 [0.855; 1.045], 0.269	0.997 [0.895; 1.111], 0.959
Disease status at Tx	1. CR	not 1. CR	1.402 [1.270; 1.548], <0.001	1.448 [1.306; 1.606], <0.001
Graft	PB	BM	1.444 [1.176; 1.773], <0.001	1.449 [1.148; 1.829], 0.002
Donor	MRD	MMRD	0.910 [0.763; 1.087], 0.299	0.800 [0.659; 0.972], 0.025
		MMUD	0.944 [0.793; 1.123], 0.515	0.924 [0.768; 1.112], 0.403
		MUD	0.931 [0.831; 1.044], 0.222	0.987 [0.875; 1.113], 0.830

Legend: HCT-CI: Hematopoietic Cell Transplantation-Comorbidity Index, ELN: European Leukemia Network Classification, CR: Complete Remission; PB: Peripheral Blood; BM: Bone Marrow; CB: Cord Blood; MRD: Matched Related Donor; MMRD: Mismatched Related Donor; MUD: Matched Unrelated Donor; MMUD: Mismatched Unrelated Donor; MAC: Myeloablative Conditioning; HCT/Tx: Hematopoietic Cell Transplantation; JACIE: Joint Accreditation Committee IHCT-Europe & EBMT; BPDCN: blastic plasmacytoid dendritic cell neoplasm

Supplemental Table 4: Non-relapse mortality without 1 year cut off follow-up

Variable	Reference	Exposure	univariable analysis (HR [95%-CI], p-value)	multivariable analysis (HR [95%-CI], p-value)
Center Size (HCT/year)	≥ 40	< 40	1.172[1.001; 1.374],0.049	1.229 [0.995; 1.517], 0.056
University Hospital	yes	no	1.202 [0.989; 1.462], 0.065	1.179 [0.914; 1.521], 0.204
Center Experience	≥ 10 years	5-10 years	0.973 [0.773; 1.225], 0.815	0.896 [0.699; 1.148], 0.386
		< 5 years	1.109 [0.717; 1.715], 0.643	1.066 [0.692; 1.640], 0.772
JACIE	yes	no	0.992 [0.861; 1.143], 0.912	
Age	continuous	-	1.037 [1.031; 1.044], <0.001	1.031 [1.025; 1.038], <0.001
Gender	m	f	0.927 [0.818; 1.051], 0.237	0.997 [0.877; 1.134], 0.963
Karnofsky Index	90/100	70/80	1.571 [1.375; 1.795], <0.001	1.358 [1.181; 1.562], <0.001
		10-60	2.537 [1.940; 3.316], <0.001	2.056 [1.556; 2.717], <0.001
		unknown	1.306 [1.015; 1.680], 0.038	1.282 [0.971; 1.692], 0.080
HCT-CI	0-2	3-10	1.658 [1.444; 1.904], <0.001	1.399 [1.211; 1.616], <0.001
		unknown	1.392 [1.176; 1.647], <0.001	1.349 [1.124; 1.619], 0.001
ELN	adverse	BPDCN	1.152 [0.568; 2.336], 0.695	1.294 [0.649; 2.583], 0.464
		favorable	0.692 [0.563; 0.852], 0.001	0.715 [0.577; 0.885], 0.002
		intermediate	0.863 [0.740; 1.007], 0.061	0.966 [0.826; 1.130], 0.666
		unknown	0.913 [0.771; 1.080], 0.289	0.919 [0.769; 1.099], 0.357
Conditioning	MAC	non-MAC	1.262 [1.113; 1.431], <0.001	1.026 [0.893; 1.178], 0.718
Disease status at Tx	1. CR	not 1. CR	1.679 [1.480; 1.904], <0.001	1.487 [1.306; 1.694], <0.001
Graft	PB	BM	0.961 [0.715; 1.291], 0.790	0.845 [0.610; 1.169], 0.309
Donor	MRD	MMRD	1.395 [1.129; 1.723], 0.002	1.371 [1.090; 1.725], 0.007
		MMUD	1.595 [1.308; 1.945], <0.001	1.447 [1.179; 1.777], <0.001
		MUD	1.080 [0.926; 1.258], 0.326	0.954 [0.813; 1.120], 0.563

Legend: HCT-CI: Hematopoietic Cell Transplantation-Comorbidity Index, ELN: European Leukemia Network Classification, CR: Complete Remission; PB: Peripheral Blood; BM: Bone Marrow; CB: Cord Blood; MRD: Matched Related Donor; MMRD: Mismatched Related Donor; MUD: Matched Unrelated Donor; MMUD: Mismatched Unrelated Donor; MAC: Myeloablative Conditioning; HCT/Tx: Hematopoietic Cell Transplantation; JACIE: Joint Accreditation Committee IHCT-Europe & EBMT; BPDCN: blastic plasmacytoid dendritic cell neoplasm