Title
Functional Status as Measured by Geriatric Assessment Predicts Inferior Survival in Older Allogeneic Hematopoietic Cell Transplantation Recipients.

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Functional status as measured by geriatric assessment predicts inferior survival in older allogeneic hematopoietic cell transplant recipients

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Abstract

Allogeneic hematopoietic cell transplantation (alloHCT) has been increasingly offered to older adults with hematologic malignancies. However, optimal methods to determine fitness for alloHCT have yet to be defined. We evaluated the ability of a comprehensive geriatric assessment (CGA) to predict post-alloHCT outcomes in a single-center prospective cohort study of patients aged 50 and older. Outcomes included overall survival (OS), progression-free survival (PFS), and non-relapse mortality (NRM). A total of 148 patients were included, with median age 62 years (range 50–76). In multivariate regression analysis, several CGA measures of functional status were predictive of post-alloHCT outcomes, after adjusting for traditional prognostic factors. Any deficit in Instrumental Activities of Daily Living (IADL) was associated with inferior OS (hazard ratio [HR] 1.81, 95% confidence interval [CI] 1.07–3.08, p=0.03) and PFS (HR 1.85, 95% CI 1.15–2.99, p=0.01). Medical Outcomes Study Physical Health scale (MOS-PH) score <85 was associated with inferior OS (HR 1.96, 95% CI 1.13–3.40, p=0.02), PFS (HR 1.75, 95% CI 1.07–2.88, p=0.03), and increased NRM (subdistribution HR 2.57, 95% CI 1.12–5.92, p=0.03). MOS-PH was also associated with the number of non-hematologic grade >3 adverse events within the first 100 days after alloHCT (rate ratio 1.61, 95% CI 1.04–2.49, p=0.03). These findings support previous

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work suggesting that IADL is an important prognostic tool prior to alloHCT. MOS-PH is newly identified as an additional metric to identify older patients at higher risk of poor post-alloHCT outcomes, including toxicity and NRM.

Keywords

allogeneic transplantation; geriatric assessment; functional status

Introduction

Allogeneic hematopoietic cell transplantation (alloHCT) offers the potential for cure for many hematologic malignancies but is associated with high risk of morbidity and mortality, and thus has been historically reserved for younger patients. Nevertheless, older adults disproportionately suffer from hematologic malignancies that have indications for alloHCT, such as acute myeloid leukemia and myelodysplastic syndrome, which have median ages at diagnosis of 68 and 77 years, respectively.(1) With improved supportive care and the development of reduced intensity conditioning regimens, the number of alloHCT for older adults has been increasing in recent years. (2–4) Evidence from retrospective and prospective studies supports a benefit of alloHCT with reduced intensity conditioning in well selected older adults with hematologic malignancies.(5–8)

Determining eligibility of an older patient being considered for alloHCT is often not straightforward. Traditionally, age, performance status, and comorbidities are among the clinical variables that enter into this decision. However, these do not provide a complete assessment, and physicians often rely on subjective, non-quantitative impressions of eligibility. There remains a need for a more nuanced risk assessment approach to identify those who are at highest risk of poor transplant outcomes, or conversely those who may be lower risk in spite of high chronologic age.

Comprehensive geriatric assessment (CGA) has been proposed as a way to perform a more comprehensive risk assessment of the older alloHCT candidate. CGA is a standardized battery of assessments designed to measure geriatric domains including functional status, cognition, mental health, nutritional status, polypharmacy, and social support. Limited prior studies of CGA in the alloHCT setting have revealed a high prevalence of impairments in geriatric domains, even in patients clinically deemed fit enough for alloHCT,(9–11) and only two prospective studies to our knowledge have evaluated the impact of these impairments on transplant outcomes. One study of 203 alloHCT patients aged >50 years showed that a number of pre-transplant geriatric metrics were associated with inferior overall survival (OS), including functional status as measured by limitations in instrumental activities of daily living (IADL), slow gait speed, and poor mental health.(12) A second study of 108 patients aged >60 years found that a different measure of gait speed (Timed-up-and-go; TUG) was associated with OS, but IADL was not.(13)

In this prospective cohort study, our objective was to investigate the value of pre-alloHCT CGA, including IADL and other functional status measures, in predicting post-alloHCT OS, progression-free survival (PFS), and non-relapse mortality (NRM) in older adults aged >50

years. Age 50 years was selected as the eligibility threshold because a high prevalence of baseline geriatric impairments has been identified by CGA in similar study populations.(9, 10) We also investigated the ability of CGA measures to predict secondary endpoints including hospital length of stay (LOS), number of non-hematologic grade >3 adverse events, and readmissions within the first 100 days after alloHCT. We utilized the cancer-specific Hurria CGA developed and validated by the Cancer and Aging Research Group, with some minor modifications.(14–16)

Materials and Methods

Participants

We conducted a prospective cohort study at the University of California San Francisco. Patients planning to undergo alloHCT were screened for enrollment by the study staff. Inclusion criteria were: age >50 years, able to read and write in English (due to the availability of CGA validated only in English), able to provide informed consent and complete the protocol requirements. The decision to pursue alloHCT was made by the treating physician and the patient prior to screening, and results of the CGA were not made available to the treating physician (with the exception of severe cognitive impairment, which triggered additional clinical evaluation). The research protocol was approved by the University of California San Francisco Institutional Review Board.

Study design and data collection

Eligible subjects completed a CGA within three months prior to alloHCT. The CGA consisted of a subject questionnaire which takes approximately 30 minutes to complete.(17) A provider portion was completed by trained study staff and included the following four items: TUG,(18) Blessed Orientation-Memory-Concentration (BOMC),(19) body mass index, and weight loss in the past 6 months (assessed both by self-report and review of medical records).

Subjects also completed the Functional Assessment of Cancer Therapy-Bone Marrow Transplant (FACT-BMT) quality of life instrument(20) and reported sociodemographic information including race/ethnicity, marital status, and education.

The following data were recorded by the subject's physician as part of routine clinical care and extracted from the medical record by study staff: diagnosis, remission status, donor type, preparative regimen, disease risk by American Society for Blood and Marrow Transplantation (ASBMT) classification, and Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI) score.(21) Hospital LOS for alloHCT, number of non-hematologic grade >3 adverse events within 100 days after alloHCT, and readmissions within 100 days after alloHCT were also extracted from the medical record. Graft-versus-host disease (GVHD), when it occurred within the first 100 days, was not recorded as an adverse event unless it met grade >3 criteria for the specific GVHD manifestation.

Statistical analysis

Descriptive statistics were used to summarize subjects' baseline characteristics. The Kaplan-Meier method was used to summarize OS and PFS, and univariate and multivariate Cox proportional hazards models were used to evaluate the association with baseline CGA variables. Cumulative incidence functions and the Fine-Gray models for competing risks were used to summarize and analyze NRM, where progressive disease was considered a competing event. Log-linear models, logistic regressions, and linear regressions were used to analyze number of non-hematologic grade >3 adverse events within 100 days of alloHCT, readmissions within 100 days, and alloHCT hospital LOS, respectively. Multivariate regression models were further adjusted for prespecified prognostic factors (age, provider-rated Karnofsky Performance Status [KPS], HCT-CI, remission status, conditioning intensity) as well as a small set of other clinical variables found to be statistically significant or borderline significant in univariate analyses (sex and marital status for OS and PFS models). Statistical analyses were performed using R statistical software.

Results

Study population

Between October 2011 to September 2017, 228 patients aged 50 or older underwent alloHCT at University of California San Francisco. Of these, 148 were consented to participate in the study. Median age was 62 years (range 50–76 years). Median time between baseline CGA and alloHCT was 13 days (interquartile range 8–21 days). Baseline patient demographic, disease, and transplant characteristics are described in Table 1.

Pre-transplant CGA measures

Baseline findings on the CGA and FACT-BMT are summarized in Table 2. At baseline, 39% of participants had at least one deficit in IADL. On the MOS-PH scale, 88% had at least one deficit in physical abilities, and 57% had scores below 85, a cut-off representing the normative population median for adults aged 55–64 years.(22) Twenty-eight percent of patients rated their own KPS as <80, and 21% had fallen in the last 6 months. Significant depression and/or anxiety were reported by 44% of patients.

Age and patient-rated KPS were weakly associated (r=0.24, p<0.001). There were only very weak associations between age and the following functional status measures: IADL (Spearman r=−0.12, p=0.17), MOS-PH (r=0.13, p=0.12), provider-rated KPS (r=0.06, p=0.49). IADL was weakly associated with provider-rated KPS (r=−0.26, p<0.001) and strongly associated with patient-rated KPS (r=−0.64, p<0.001). Provider- and patient-rated KPS were weakly associated (r=0.39, p<0.001).

Post-transplant outcomes

Median follow-up time on study was 20.3 months (range 0.9–80 months). During the follow-up period, 29 patients (20%) died without experiencing disease progression, 54 (36%) experienced disease progression (42 died after progression), and 65 (44%) were alive and did not experience disease progression at the end of follow-up. The risk of NRM in the first 3 months after alloHCT was 5.4% (95% confidence interval [CI] 1.7–9.1%) and at 1

year was 14.9% (95% CI 9.1–20.6%). Median PFS was 22.9 months (95% CI 9.5–60.0 months), and median OS was 46.5 months (95% CI 27.5 months-not reached).

Univariate Analysis of Pre-transplant Measures and Post-AlloHCT Outcomes

The univariate associations between pre-transplant characteristics and post-alloHCT outcomes with p 0.05 are reported in Table 3. Multiple CGA functional status measures were strongly predictive of inferior OS. Having any IADL deficit was associated with a median OS of 16.5 months compared to 48.9 months in those without IADL deficits (hazard ratio [HR] 1.70, 95% CI 1.06–2.71, p=0.03; Figure 1a). MOS-PH score <85 was associated with a median OS of 23.2 months, while median OS was not reached in those with MOS-PH score 85 (HR 1.84, 95% CI 1.12–3.04, p=0.02; Figure 1b). Other functional status measures associated with inferior OS included lower patient-rated KPS and worse FACT functional wellbeing subscale score. Worse cognitive function as measured by BOMC score was associated with inferior OS (HR 1.07 per 1-point increase in score, 95% CI 1.00–1.15, p=0.05).

Multiple functional status measures were also predictive of inferior PFS. Having any IADL deficit was associated with a median PFS of 8.0 months compared to 42.7 months in those without IADL deficits (HR 1.72, 95% CI 1.11–2.65, p=0.02; Figure 2a). MOS-PH score <85 was associated with a median PFS of 10.0 months compared to 48.9 months in those with scores >85 (HR 1.64, 95% CI 1.04–2.59, p=0.03; Figure 2b). Other functional status measures associated with inferior PFS include gait speed as measured by the TUG test and FACT functional wellbeing subscale. Worse cognitive function as measured by BOMC was associated with inferior PFS (HR 1.08 per 1-point increase in score, 95% CI 1.01–1.15, p=0.03).

The only statistically significant predictor of NRM was remission status, defined as not being in first complete or partial remission at time of transplant (subdistribution hazard ratio [SHR] of 2.15, 95% CI 1.02–4.51, p=0.04). MOS-PH also had a strong association with NRM (SHR 2.15, 95% CI 0.96–4.78, p=0.06), though it did not reach statistical significance.

The strongest predictor of the number of non-hematologic grade >3 adverse events was MOS-PH score <85 (rate ratio [RR] 1.66, 95% CI 1.11–2.49, p=0.02). MOS-PH score <85 also predicted an increase in alloHCT hospital LOS by 6.1 days (95% CI 1.5–10.7 days, p=0.01). Each decile decrease in patient-rated KPS also predicted an increase in LOS by 1.9 days (95% CI 0.4–3.5 days, p=0.01), while provider-rated KPS was not significantly predictive. Age was also inversely associated with LOS, with each decade increase in age associated with 4.7 fewer days (95% CI 1.1–8.4 days, p=0.01). This is likely due to use of reduced intensity conditioning in older adults; age was no longer statistically significantly associated with LOS when adjusted for transplant intensity.

Other CGA measures were not significantly predictive of any post-alloHCT outcomes in univariate analyses. There were no statistically significant predictors of readmission within 100 days after alloHCT. Of note, traditional clinical risk factors such as age (Figures 1c and 2c), HCT-CI score, and provider-rated KPS were also not significantly predictive of outcomes including OS, PFS, or NRM.

Multivariate Analysis of Pre-transplant Measures and Post-AlloHCT Outcomes

Individual CGA measures found to be statistically significant at p 0.05 in univariate analyses were each adjusted for five pre-specified clinical prognostic factors: age, HCT-CI score, remission status, provider-rated KPS, and conditioning intensity. For OS and PFS, sex and marital status were also included in the models because they were statistically significant or borderline significant in univariate analyses.

Results of the multivariate analyses are displayed in Table 4. After adjusting for traditional prognostic factors as above, any deficit in IADL remained significantly associated with both OS and PFS, with HR of 1.81 (95% CI 1.07–3.08, p=0.03) and 1.85 (95% CI 1.15–2.99, p=0.01), respectively. FACT-BMT functional wellbeing subscale also remained prognostic for both OS (HR 1.06, 95% CI 1.01–1.10, per 1-point decrease in score, p=0.02) and PFS (HR 1.06, 95% CI 1.02–1.10, p=0.008).

MOS-PH <85 was also significantly associated with both inferior OS and PFS in the adjusted analysis, with HR of 1.96 (95% CI 1.13–3.40, p=0.02) and 1.75 (95% CI 1.07–2.88, p=0.03), respectively. Additionally, MOS-PH <85 was associated with a greater number of non-hematologic grade >3 adverse events in the first 100 days after alloHCT (RR 1.61, 95% CI 1.04–2.49, p=0.03). Given the consistent effect of MOS-PH on these outcomes, we performed an exploratory analysis evaluating the effect of MOS-PH on NRM when adjusted for traditional clinical risk factors. Although MOS-PH was only of borderline significance in univariate analysis of NRM (SHR 2.15, 95% CI 0.96–4.78, p=0.06), the association became stronger in multivariate analysis (SHR 2.57, 95% CI 1.12–5.92, p=0.03).

Discussion

In this single-center prospective cohort study, we found that patient-reported functional status pre-alloHCT was significantly associated with post-alloHCT outcomes in patients aged >50 years. Functional status measures identified as prognostic included IADL, MOS-PH, and the FACT-BMT functional wellbeing subscale. In this study, these parameters were better predictors of outcome than age or HCT-CI score. Our findings support prior studies establishing functional status as a useful predictor in alloHCT and add to the growing literature of utilizing CGA for risk stratification in malignant hematology.

Similar to previous studies, CGA identified a high number of baseline geriatric impairments in patients clinically deemed fit for alloHCT.(9–11) To our knowledge, only two previous studies have utilized a CGA prospectively to predict post-alloHCT outcomes in older alloHCT patients.(12, 13) Muffly *et al* originally reported the ability of any IADL deficit to predict post-alloHCT OS, a finding that was not replicated by Deschler *et al.* Our study validates the utility of IADL in this setting. One potential explanation for the discrepancy in results is a difference in "physiologic age" of the different cohorts. Deschler *et al* described their cohort as a group of "independent, otherwise nearly uncompromised older individuals" who may have low physiologic age despite their higher age cut-off of >60 years. For comparison, 31% of the Deschler cohort had any IADL impairment compared to 40% in the Muffly cohort and 39% in our cohort, despite our use of the younger age cut-off of >50 years. This highlights the importance of looking beyond chronologic age and evaluating

physiologic age when assessing risk for alloHCT. CGAs may be most useful for individuals with higher physiologic age, regardless of their chronologic age. The use of CGAs should not be limited to the typical "geriatric" age cut-offs of 60 or 65 years. The potentially broader applicability of CGA in the alloHCT population is further supported by studies examining patient-reported physical functioning, a key component of the CGA, in patients of all ages. In two studies of alloHCT patients of all ages (median ages 54 and 55), patient-reported physical function was found to be predictive of OS after adjusting for traditional clinical, demographic, and transplant factors.(23, 24)

While our study validates the utility of IADL as a specific metric in the alloHCT setting, it also validates the utility of measuring the functional status construct itself, as MOS-PH and FACT-BMT functional wellbeing subscale were additional functional status metrics that were associated with outcomes in this study. MOS-PH in particular was not only predictive of OS and PFS, but also non-hematologic grade >3 adverse events, and in an exploratory analysis, NRM. The ability of MOS-PH to predict both measures of toxicity and survival suggests it may be a particularly useful risk assessment tool for transplant evaluations. The Short Form-36 Physical Component Summary scale, a related broader instrument which contains the MOS-PH, has been evaluated in both patients of all ages (23, 24) and adults aged >50,(12) with mixed results. Since MOS-PH by itself has not been assessed in prior alloHCT studies, our findings will need to be validated.

While the functional status construct is clearly important, the optimal functional status metric for use in the alloHCT population has yet to be determined. The ideal instrument would be highly sensitive and specific, predictive of clinically relevant outcomes, and straightforward to implement in clinical practice. In addition to comparing among patient-reported metrics such as IADL or MOS-PH, physical performance measures such as TUG or gait speed may also provide valuable information that complements patient-reported measures. Physical performance measures are more objective, but some tests may be more time- and space-consuming to administer, and often only measure one aspect of function (e.g. gait speed measures only physical walk speed, while IADL also includes cognitive aspects of function such as managing medications or finances). Although in our study TUG was not predictive of outcomes, other studies have found the following physical performance measures to be predictive of survival or mortality in multivariate analysis: 15-feet walk speed in older alloHCT patients,(12) Short Physical Performance Battery in older acute myeloid leukemia patients,(25) and 4-meter gait speed in older patients with hematologic malignancies.(26)

Our study found no statistically significant association between both age and HCT-CI score and post-alloHCT outcomes. With respect to age, this may be a function of examining a well selected older patient population, already deemed clinically fit for alloHCT. However, it is striking that within this population aged 50–76 years, functional status measures were better predictors of outcomes than chronologic age. With respect to HCT-CI score, it may be that our sample size was insufficient to see a difference between low (0-2) vs high (3+) scores. Alternatively, this may be due to heavy weighting of HCT-CI on pulmonary disease which relies on pulmonary function testing. Evidence suggests that the method used to calculate diffusion capacity may significantly affect HCT-CI score.(27) If individual centers'

pulmonary function labs use different calculation methods, single-center studies may not yield comparable HCT-CI scores.

It is not entirely clear why functional status measures are associated with PFS. It is possible that patients who are more heavily pretreated for higher risk disease may have worse functional status at the time of alloHCT, and high disease risk would lead to inferior PFS. Alternatively, patients who have worse functional status at baseline may not be treated as aggressively before alloHCT and may have inadequate disease control at transplant. We have attempted to control for this by including remission status in our multivariate model. Finally, one can hypothesize an underlying common mechanism that adversely impacts both functional status and relapse risk. For example, increased inflammation or changes in cytokine milieu may increase host frailty and also influence cancer biology, possibly through tumor micro-environment changes or immune modulation. This is clearly speculative and will need to be investigated in larger studies, potentially with biomarkers of inflammation.

Our study has several limitations. First, a sample size of 148 subjects may not provide adequate power to evaluate the predictive value of certain pre-transplant factors, such as age and HCT-CI, or additional relevant CGA measures that were of borderline statistical significance in this study. Second, this single-center study only included patients who were deemed fit for transplant by their physician. Thus, our results may not be generalizable to patient populations at other institutions where the clinical selection process may be different. It is possible that this may explain differences in results with other published single-institution studies. Third, we included subjects aged >50 years which is younger than many studies of "older" patients with more traditional age cut-offs of 60 or 65 years. However, the alloHCT patient population that would benefit most from use of the CGA has not yet been defined, and the largest study to date used the same age cut-off of 50 years.(12) The prevalence of multiple geriatric impairments in our population without an association of these impairments with age, as well as the prognostic value of such impairments, support the use of CGA in this age group.

In conclusion, functional status as prospectively measured by CGA prior to alloHCT was predictive of post-alloHCT outcomes. While this study validates prior work identifying IADL as a useful metric of functional status, it also identifies MOS-PH as an additional metric which is associated with measures of survival as well as post-alloHCT toxicity and NRM. MOS-PH is oriented toward the subject's self-reported ability to perform physical tasks, ranging from bathing and dressing to vigorous activities such as running. Interestingly, a recent study showed that a physical therapy-based assessment of physical function also predicted treatment-related mortality and OS after alloHCT.(28) Routine implementation of a CGA in pre-transplant evaluations, or at least a formal, validated functional status evaluation beyond KPS, may improve our ability to more appropriately assess physiologic age and risk stratify patients. If the implementation of a full CGA is felt to be too time-consuming, distilling the CGA down to the most predictive component of functional status may improve broader adoption. In particular, IADL and MOS-PH are both brief patient self-reported measures that do not require provider time to administer.

Moving forward, efforts are underway to develop a core set of prognostic measures for older adults undergoing alloHCT in the Blood and Marrow Transplant Clinical Trials Network protocol 1704 "CHARM" study. More importantly, research should move beyond risk prediction to investigate interventions for risk modification, particularly since functional status is a potentially modifiable risk factor. These findings, if validated, may provide the basis for designing physical therapy-based "pre-habilitation" or rehabilitation interventions in the peri-transplant period to optimize outcomes for physiologically older adults undergoing alloHCT.

Acknowledgements

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Highlights

- Functional status predicts post-allogeneic transplant survival in older patients

- Physical function predicts both post-allogeneic transplant survival and toxicity

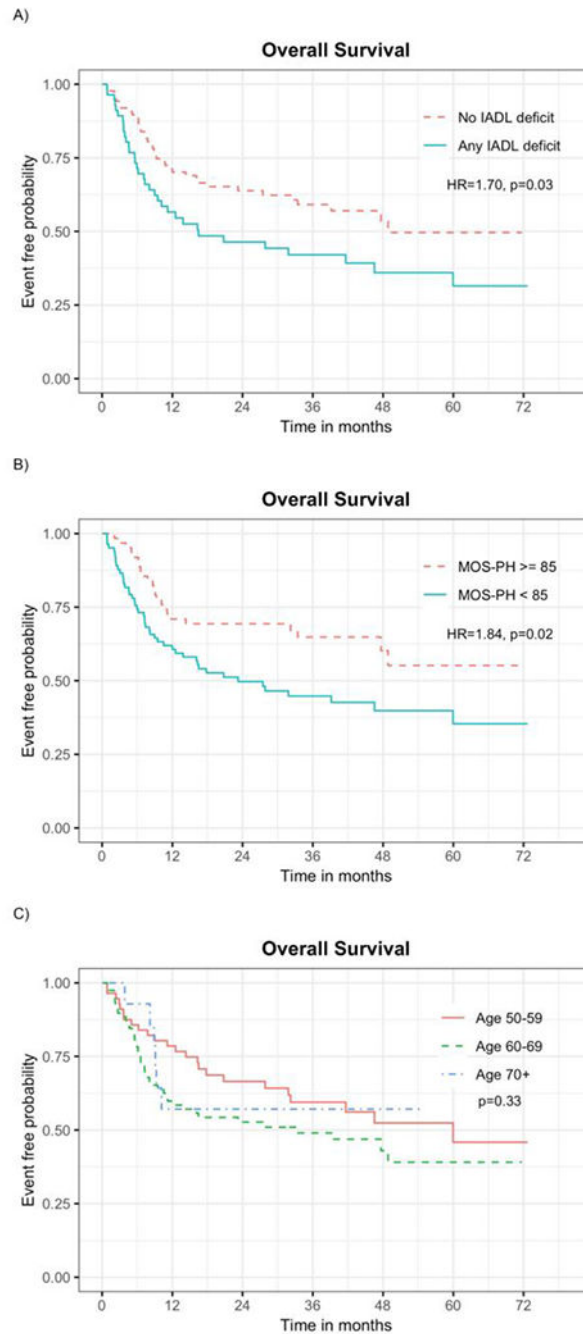- These associations were independent of age and comorbidities

Figure 1.
Kaplan-Meier curves for overall survival by A) Instrumental Activities of Daily Living (IADL), B) Medical Outcomes Study Physical Health score (MOS-PH), and C) age group. IADL deficits and MOS-PH score <85 were associated with inferior overall survival.
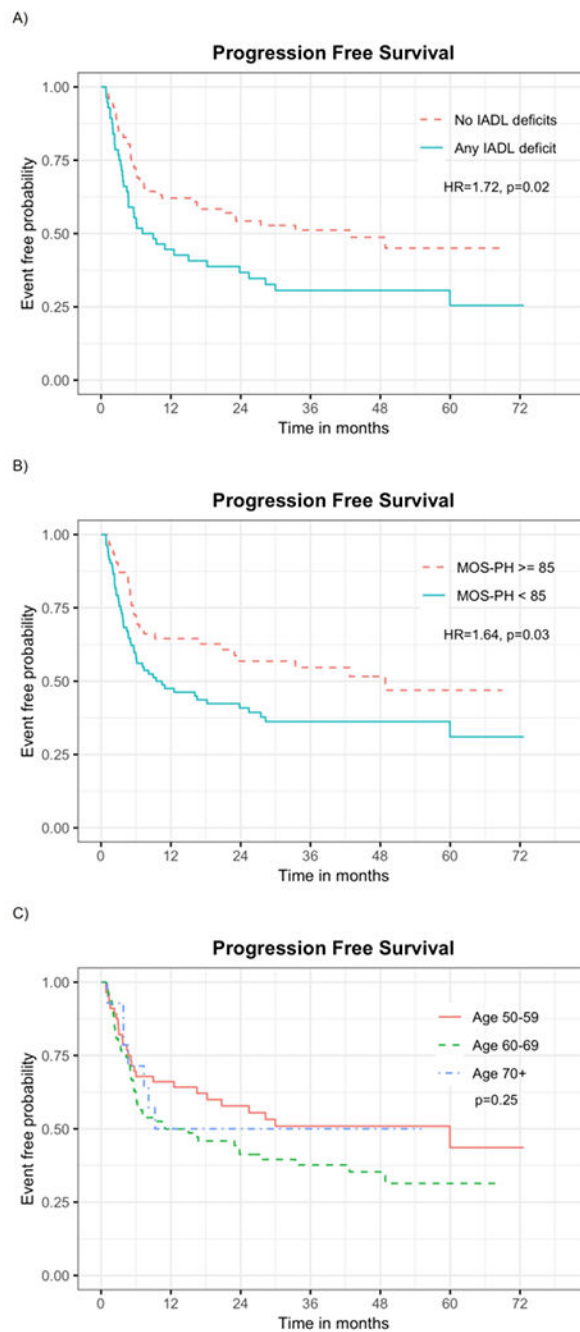
Figure 2.
Kaplan-Meier curves for progression-free survival by A) Instrumental Activities of Daily Living (IADL), B) Medical Outcomes Study Physical Health score (MOS-PH), and C) age group. IADL deficits and MOS-PH score <85 were associated with inferior progression-free survival.

Table 1.

Baseline patient demographic, disease, and transplant characteristics

	N = 148
Age, median (range)	62 (50-76)
Age categories, n (%)	
50-59	56 (38 %)
60-69	78 (53 %)
70+	14 (9 %)
Female, n (%)	58 (39 %)
Married, n (%)	115 (78 %)
Race, white, n (%)	113 (76 %)
Education, n (%)	
Through high school	25 (17 %)
Through college	72 (49 %)
Post-college	51 (35 %)
Diagnoses	
Acute myeloid leukemia	63 (43 %)
Myelodysplastic syndrome	38 (26 %)
Myeloproliferative neoplasms	18 (12 %)
Acute lymphoblastic leukemia	14 (9 %)
Other	15 (10 %)
Remission status, CR1/PR1, n (%)	78 (53 %)
ASBMT disease risk	
Low	78 (52 %)
Intermediate	26 (18 %)
High	38 (26 %)
Other/unknown	6 (4 %)
KPS, provider-rated, median (range)	90 (30-100)
HCT-CI score	
0	19 (13%)
1-2	81 (55 %)
3+	48 (32 %)
Stem cell source, n (%)	
Peripheral blood	136 (92 %)
Bone marrow	7 (5 %)
Umbilical cord	5 (3 %)

	N = 148
Donor type, n (%)	
Matched sibling	46 (31 %)
10/10 MUD	64 (43 %)
9/10 MUD	25 (17 %)
Other	13 (9 %)
Reduced intensity conditioning, n (%)	101 (68 %)

CR/PR = complete/partial remission. KPS = Karnofsky performance status. HCT-CI = Hematopoietic Cell Transplantation-Comorbidity Index. ASBMT = American Society of Blood and Marrow Transplantation. MUD = matched unrelated donor.

Table 2.

Baseline cancer-specific comprehensive geriatric assessment measures

Domain	Measure	Sample median (observed range)	Impairment threshold (possible range)	Sample % impaired
Functional status	MOS Physical Health subscale (22, 29)	80 (0-100)	<85 (0-100)	57 %
	Instrumental Activities of Daily Living (OARS subscale) (30)	0 (0-10)	1 (0-14)	39 %
	KPS, patient-rated (31, 32)	90 (30-100)	<80 (0-100)	28 %
	Timed-up-and-go (18)	9 (4-50)	>13.5 sec	8 %
	Number of falls in last 6 months (33)	0 (0-7)	1 fall	21 %
Cognition	Blessed Orientation-Memory-Concentration Test (19)	2 (0-14)	11 (0-28)	1 %
Mental health	Mental Health Inventory (34, 35)	80 (40-100)	76 (0-100)	44 %
Nutrition	Body mass index (36)	26 (17-45)	<18.5	1 %
	% unintentional weight loss in 6 months (37)	−1% (−32 - 47%)	--	--
Polypharmacy	Number of medications (OARS Physical Health section) (30)	5 (0-24)	--	--
Social support	MOS Social Support survey (38)	98 (0-100)	-- (0-100)	--
Quality of life	FACT-physical wellbeing	5 (0-26)	-- (0-28)	--
	FACT-social wellbeing	26 (8-28)	-- (0-28)	--
	FACT-emotional wellbeing	7 (0-20)	-- (0-24)	--
	FACT-functional wellbeing	19 (0-28)	-- (0-28)	--
	FACT-BMT	29 (15-40)	-- (0-40)	--

Impairment thresholds not provided for measures that do not have established cut-ol

BMT=bone marrow transplant, FACT= Functional Assessment of Cancer Therapy, KPS=Karnofsky performance status, MOS=Medical Outcomes Study, OARS=Older Americans Resources & Services.

Table 3.

Univariate Analysis of Associations Between Pre-AlloHCT Measures and Post-AlloHCT Outcomes with p 0.05

Post-transplant Outcome	Pre-transplant Measure	Effect size (95% CI)	p-value
Overall survival	Sex *(female)*	HR 1.63 (1.02-2.61)	0.04
	Marital status *(not married)*	HR 1.77 (1.05-2.97)	0.03
	Patient-rated KPS *(per decile decrease)*	HR 1.15 (1.00-1.32)	0.05
	IADL (any deficit)	HR 1.70 (1.06-2.7)	0.03
	MOS Physical Health *(score <85)*	HR 1.84 (1.12-3.04)	0.02
	Blessed Orientation-Memory-Concentration test *(per 1-point increase/worsening)*	HR 1.07 (1-1.15)	0.05
	FACT functional wellbeing *(per 1-point decrease/worsening)*	HR 1.06 (1.02-1.10)	0.006
Progression-free survival	Marital status *(not married)*	HR 1.92 (1.18-3.11)	0.008
	IADL *(any deficit)*	HR 1.72 (1.11-2.65)	0.02
	MOS Physical Health *(score <85)*	HR 1.64 (1.04-2.59)	0.03
	Blessed Orientation-Memory-Concentration test *(per 1-point increase/worsening)*	HR 1.08 (1.01-1.15)	0.03
	FACT functional wellbeing *(per 1-point decrease/worsening)*	HR 1.06 (1.02-1.10)	0.006
	Timed-up-and-go *(per second increase)*	HR 1.05 (1.01-1.09)	0.01
Non-relapse mortality	Remission status *(not in CR1/PR1)*	SHR 2.15 (1.02-4.51)	0.04
Number of grade 3 adverse events within 100 days	MOS Physical Health *(score <85)*	RR 1.66 (1.11-2.49)	0.02
	FACT functional wellbeing *(per 1-point decrease/worsening)*	RR 1.04 (1.01-1.08)	0.02
Hospital Length of Stay	Age *(per decade increase)*	DD –4.7 days (–8.4–-1.1)	0.01
	Patient-rated KPS *(per decile decrease)*	DD 1.9 days (0.4-3.5)	0.01
	MOS Physical Health *(score <85)*	DD 6.1 days (1.5-10.7)	0.01

CI=confidence interval, CR1/PR1=first complete or partial remission, DD=difference in duration, FACT=Functional Assessment of Cancer Therapy, HR=hazard ratio, IADL=Instrumental activities of daily living, KPS=Karnofsky Performance Status, MOS=Medical Outcomes Study, RR=rate ratio, SHR=subdistribution hazard ratio.

Table 4.

Multivariate Analysis of Associations Between Pre-AlloHCT CGA Measures and Post-AlloHCT Outcomes

Post-transplant Outcome	Pre-transplant Measure	Effect size (95% CI)	p-value
Overall survival [*]	IADL *(any deficit)*	HR 1.81 (1.07-3.08)	0.03
	MOS Physical Health *(score <85)*	HR 1.96 (1.13-3.40)	0.02
	FACT functional wellbeing *(per 1-point decrease/ worsening)*	HR 1.06 (1.01-1.10)	0.02
Progression-free survival [*]	IADL *(any deficit)*	HR 1.85 (1.15-2.99)	0.01
	MOS Physical Health *(score <85)*	HR 1.75 (1.07-2.88)	0.03
	FACT functional wellbeing *(per 1-point decrease/ worsening)*	HR 1.06 (1.02-1.10)	0.008
	Blessed Orientation-Memory-Concentration test *(per 1-point increase/worsening)*	HR 1.083 (1.01-1.17)	0.03
Non-relapse mortality [†]	MOS Physical Health *(score <85)*	SHR 2.57 (1.12-5.92)	0.03
Number of grade 3 adverse events within 100 days [†]	MOS Physical Health *(score <85)*	RR 1.61 (1.04-2.49)	0.03

CI=confidence interval, FACT=Functional Assessment of Cancer Therapy, HR=hazard ratio, IADL=Instrumental activities of daily living, MOS=Medical Outcomes Study, RR=rate ratio, SHR=subdistribution hazard ratio.

[*] Multivariate models adjusted forage, HCT-CI, remission status, provider-rated KPS, transplant intensity, sex, marital status.

[†] Multivariate models adjusted for age, HCT-CI, remission status, provider-rated KPS, transplant intensity.