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Patterns and predictors of functional decline after alloHCT in older adults

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Abstract

Background: As allogeneic hematopoietic cell transplantation (alloHCT) is increasingly offered to older adults, geriatric assessments (GA) have been identified as a useful tool for predicting outcomes, particularly functional status. However, very few studies have examined the longitudinal change in GA measures in the post-alloHCT period.

Objectives: The objectives of this study are to 1) describe the longitudinal change in GA and QOL measures after alloHCT and to 2) identify predictors of greater functional decline post-transplant.

Study Design: In this single-center prospective cohort study, patients aged 50 years or older planning to undergo alloHCT completed a cancer-specific GA and the Functional Assessment of Cancer Therapy-Bone Marrow Transplant (FACT-BMT) survey at baseline prior to alloHCT and then at 3, 6, and 12 months after transplant. Changes in GA and QOL measures at each post-transplant time point (3, 6, or 12 months) compared to baseline were analyzed using paired t-tests. Exploration of potential predictors of greater post-transplant functional decline, as measured by instrumental activities of daily living (IADL) and Medical Outcomes Study Physical Health

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scale (MOS-PH), were examined using linear regressions and chi-squared two-sample test of proportions.

Results: Mean functional status generally exhibited a pattern of decline at 3 to 6 months post-alloHCT, with recovery to near baseline by 12 months. Mean mental health and emotional QOL were lowest at baseline and improved at all time points post-transplant. Differences in baseline clinical characteristics were not associated with any differences in functional trajectories. Differences in baseline GA measures (patient-rated KPS, IADL, MOS-PH, Timed-Up-and-Go, Blessed Orientation-Memory-Concentration test, Mental Health Inventory 5) also did not predict greater functional decline at 3 months. Patients whose IADL was improved or maintained at 3 months generally maintained their functional status at 6 and 12 months. Similarly, most patients who had IADL decline at 3 months still had functional decline at 6 months, though a portion did have functional recovery by 12 months. Compared to those with improved/maintained IADL at 3 months, those with declined IADL at 3 months were significantly more likely to have persistent functional decline at 6 months ($p<0.0001$) and 12 months ($p=0.02$).

Conclusions: In older alloHCT patients, mean functional status declines short-term after alloHCT with possibility of recovery by 6 to 12 months, while mean mental and emotional health improve post-alloHCT. Functional decline at 3 months post-alloHCT is associated with persistent functional decline at 12 months.

Keywords

geriatric assessment; allogeneic transplant; older adults; functional status

Introduction

With advances in non-myeloablative transplant techniques and supportive care, allogeneic hematopoietic cell transplantation (alloHCT) is increasingly offered to older adults with hematologic malignancies in the US, with adults aged 65 and older now accounting for 26% of allogeneic transplant recipients as of 2019.[1,2] While studies suggest well-selected older adults can benefit from alloHCT with good outcomes,[3,4] the morbidity and mortality of alloHCT remain higher for older adults than for their younger counterparts.[5] Geriatric assessments (GA) have been identified as a useful tool for predicting post-alloHCT outcomes. In particular, pre-transplant functional status has been shown to be predictive of transplant outcomes including non-relapse mortality (NRM), overall survival (OS), or progression-free survival (PFS) in older adults.[6–10] Additionally, cognitive impairment was identified as a predictor of higher NRM in a multicenter study.[11] The incorporation of a GA into the standard pre-transplant evaluation may improve our ability to risk-stratify and counsel patients, as well as to allow for planning of better supportive care and risk mitigation for high-risk patients who can benefit from alloHCT but may require additional support.[12]

While the body of literature on the utility of a GA pre-transplant is growing, there is a paucity of data on serial GA measurements after alloHCT and whether they can be used to identify patients at risk for impaired outcomes. To date, very few studies have examined the longitudinal change in GA measures in the post-transplant period.[8,13,14] In addition to standard survival outcomes, change in functional status is an understudied area

in older adults who undergo alloHCT. Functional decline is of particular importance to older adults since it impacts their ability to live independently and may limit future treatment options should maintenance be required or should relapse occur. Improved knowledge of GA trajectories after alloHCT will not only improve patient counseling regarding post-transplant expectations but may also facilitate earlier identification of high-risk patients who would benefit from additional supportive care.

In this study, we describe the multidimensional patient experience after alloHCT by reporting the longitudinal change in GA and QOL measures in adults aged 50 and older at 3, 6, and 12 months after alloHCT. In addition, we sought to identify predictors of greater functional decline post-alloHCT.

Materials and Methods

Patient population

In this prospective cohort study at the University of California San Francisco, patients planning to undergo alloHCT were screened for enrollment if they met the following inclusion criteria: age ≥50 years, able to read and write in English, able to provide informed consent and complete the protocol requirements. The results of the GA were not made available to the treating physician except when severe cognitive impairment was detected, which triggered additional evaluation. The age threshold of 50 years was chosen based on prior literature in similar populations showing a high prevalence of GA impairments.[15,16] The research protocol was approved by the University of California San Francisco Institutional Review Board.

Study design and data collection

Patients completed a cancer-specific GA[17] and the Functional Assessment of Cancer Therapy-Bone Marrow Transplant (FACT-BMT) survey[18] at baseline within 3 months prior to alloHCT and then at 3, 6, and 12 months after transplant. Patients also reported sociodemographic information including race/ethnicity, marital status, and education. The following data were extracted from the medical record by study staff: diagnosis, remission status, donor type, preparative regimen, graft-versus-host disease (GVHD) prophylaxis, disease risk by American Society for Blood and Marrow Transplantation (ASBMT) classification,[19] and Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI) score.[20] At each study time point (3, 6, 12 months), the incidence of GVHD since the last study assessment was collected.

Assessments

The cancer-specific GA used in this study includes minor modifications from the original[17,21] and has been described in prior transplant studies at our center.[9,22,23] It is comprised of a standardized battery of validated assessments of multiple geriatric domains including functional status, cognition, mental health, nutrition, polypharmacy, and social support (Table 1). We focused in particular on the functional status measures of instrumental activities of daily living (IADL)[24] and the Medical Outcomes Study Physical Health scale (MOS-PH)[25,26] because these were most strongly associated with poor transplant outcomes

in our prior research.[9] The FACT-BMT[18] is a validated QOL assessment comprised of subscales evaluating physical well-being, social well-being, emotional well-being, functional well-being, and a bone marrow transplant specific subscale (Table 1).

Statistical analysis

Mean GA and QOL measures at each time point (baseline, 3, 6, or 12 months) were depicted graphically. Changes from baseline at each post-transplant time point (3, 6, or 12 months) were analyzed using paired t-tests. To explore associations between baseline clinical variables and post-transplant functional trajectory, we plotted the IADL and MOS-PH mean trajectories by subgroup determined by baseline clinical variables, including age, sex, HCT-CI, provider-rated KPS, transplant intensity, diagnosis, and ASBMT disease risk. Analysis of variance was used to compare different subgroups at each study time point.

To evaluate the association between any baseline clinical or GA measures with greater functional change at 3 months, we performed univariate linear regressions for IADL and MOS-PH change from baseline to 3 months, where the covariates include selected clinical characteristics (age, sex, HCT-CI, provider-rated KPS, transplant intensity, diagnosis, ASBMT disease risk) and baseline GA measures (IADL, MOS-PH, TUG, patient-rated KPS, BOMC, MHI5). We also performed univariate linear regressions to evaluate associations between functional change from baseline to 3 months with having any acute GVHD during the first 3 months. Similarly, we evaluated associations between functional change from baseline to 6 and 12 months with having any chronic GVHD during the first 6 and 12 months, respectively.

We visualized the distributions of IADL and MOS-PH “improvers/maintainers” and “decliners” at each post-transplant time point. Decliners were defined as those who had declined by at least one point for IADL and two points for MOS-PH; these thresholds were chosen based on prior data suggesting these as the minimal important differences in these scales.[23,27,28] Improvers were those who improved by the minimal important difference, and maintainers were those who did not change by the minimal important difference. These two groups were combined for analysis due to a small number of improvers, which may be due to a ceiling effect for the functional status metrics. The two-sample test of proportions was used to compare the probability of functional decline at 6 and 12 months for those who are either improvers/maintainers or decliners at 3 months.

Lastly, we performed a landmark analysis from day +100 to look at whether functional decline at 3 months post-alloHCT is associated with worse OS or NRM. The Kaplan-Meier method was used to summarize OS, and univariate Cox proportional hazards models were used to evaluate the association with IADL and MOS-PH decline. 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. Any patients who were lost to follow-up or died prior to the landmark time were excluded from the analysis.

For all analyses, p-values were two-sided and not adjusted for multiple comparisons. Statistical analyses were performed using R version 3.4.4 (R Foundation for Statistical Computing, Vienna, Austria) and Stata 15 (StataCorp, College Station, Texas, USA).

Results

Patient population

Between October 2011 and September 2017, 148 patients enrolled in our study. Median age was 62 years (range 50–76 years). Baseline patient demographic, disease, and transplant characteristics are described in Table 2. A significant proportion of this study cohort had impairments identified by GA at baseline, and the impact of such impairments on transplant outcomes has been previously reported.[9] The median overall survival was 46.5 months with median duration of follow-up of 20.3 months (range 0.9–80 months). At 3, 6, and 12 months, the percentage of surviving patients experiencing any grade of GVHD since the previous study assessment were 43.5%, 59.5%, and 78.5%, respectively.

GA and QOL trajectories in the first year after alloHCT

The trajectories of GA measures and mean change from baseline at 3, 6, and 12 months are presented in Figure 1. Mean scores for functional status measures (IADL, MOS-PH, patient-rated Karnofsky Performance Status [KPS]) declined significantly at 3 months, started to recover at 6 months (though still significantly different from baseline), and recovered to near baseline levels by 12 months. The mean number of falls trended higher at 3 months, increased significantly at 6 months, and then decreased at 12 months and was not significantly different at that time point compared to baseline. On average, cognition as measured by Blessed Orientation Memory Concentration test (BOMC) trended toward greater impairment at 3 months and recovered at 6 and 12 months, though at no point was significantly different from baseline. On average, mental health as measured by Mental Health Inventory-5 (MHI-5) was stable in the first 6 months after transplant but trended toward improvement from baseline at 12 months post-transplant, although the difference was not statistically significant. Mean body mass index (BMI) decreased significantly after transplant and remained lower than baseline throughout the 12 months post-transplant. Patients reported the most social support at 3 months but less support at 6 and 12 months, consistent with our program’s requirement of having full-time caregiver support during the first 3 months after transplant, although these differences did not reach statistical significance.

The trajectories of FACT-BMT QOL measures over time and changes from baseline at 3, 6, and 12 months are presented in Figure 2. Mean physical well-being and functional well-being followed a pattern similar to the GA functional status measures, with significant decline at 3–6 months but recovery to baseline levels at 12 months. Mean social well-being declined significantly at all time points post-transplant. In contrast, emotional health was on average lowest at baseline and improved significantly at all points post-transplant.

Evaluating associations between baseline clinical predictors and functional status post-alloHCT

Baseline clinical variables (age, sex, HCT-CI, transplant intensity, diagnosis, ASBMT disease risk) were not significantly associated with different IADL and MOS-PH scores at 3, 6, and 12 months post-transplant (Figure 3, sex and ASBMT disease risk not shown). For example, patients aged 50–59, 60–69, and 70+ years had similar IADL and MOS-PH scores at each time point. Patients with better provider-rated KPS generally had better IADL and MOS-PH scores across all time points, which is expected as KPS, IADL, and MOS-PH are all functional measures.

We did not find any significant associations between change in IADL and MOS-PH scores at 3 months and selected baseline characteristics (age, sex, HCT-CI, provider-rated KPS, patient-rated KPS, transplant intensity, diagnosis, ASBMT disease risk) or baseline GA measures (IADL, MOS-PH, Timed-Up-and-Go, BOMC, MHI-5). The occurrence of any acute GVHD during the first 3 months was not significantly associated with change in IADL or MOS-PH scores at 3 months, and the occurrence of any chronic GVHD by 6 and 12 months was not significantly associated with change in IADL or MOS-PH scores at 6 and 12 months, respectively.

Evaluating patterns of maintaining or declining functional status

Figure 4a shows the IADL status at 6 and 12 months, grouped by IADL status at 3 months, ie whether patients were improvers/maintainers at 3 months, decliners at 3 months, or had missing IADL data at 3 months post-alloHCT. Most patients who had improved or maintained IADL at 3 months also maintained their IADL at 6 months (41/55=75%) and 12 months (30/55=55%). Similarly, most who had IADL decline at 3 months still had IADL decline at 6 months (40/69=58%); at 12 months, one quarter still had persistent IADL decline (18/69=26%), one third had functional recovery (21/69=30%), another third were deceased (23/69=33%), and 10% were alive with missing data. Compared to those who were IADL improvers/maintainers at 3 months, those who were IADL decliners at 3 months were significantly more likely to have persistent functional decline at 6 months ($p<0.0001$) and 12 months ($p=0.02$).

Similar results for MOS-PH are shown in Figure 4b. Most patients who improved or maintain their MOS-PH score at 3 months maintained MOS-PH at 6 months (27/37=73%) and 12 months (17/37=46%). Most with MOS-PH decline at 3 months still had functional decline at 6 months (55/87=63%); at 12 months, over a third still had persistent functional decline (32/87=37%), another third was deceased (27/87=31%), a minority had functional recovery (17/87=20%), and 13% were alive with missing data. Compared to those who were MOS-PH improvers/maintainers at 3 months, those who were MOS-PH decliners at 3 months were more likely to have persistent functional decline at 6 months ($p<0.0001$) and 12 months ($p=0.05$).

Landmark analysis for functional decline at 3 months and OS and NRM

In our landmark survival analysis from day +100, median OS was 39 months for 3-month IADL decliners (95% confidence interval [CI] 20.8-not reached) and was not reached

for IADL maintainer/improvers (95% CI 47.7-not reached), a difference which was not statistically significant (unadjusted hazard ratio [HR] 1.40; 95% CI 0.82–2.37; p=0.21). Landmark results for MOS-PH were similar: median OS was 55 months for 3-month MOS-PH decliners (95% CI 31.9-not reached) and not reached for MOS-PH maintainer/improvers (95% CI 41.7-not reached), with unadjusted HR 1.44 (95% CI 0.79–2.64; p=0.23). There were also no differences in landmark analysis for NRM; the unadjusted sub-distribution HR for IADL 3-month decliners vs improver/maintainers was 1.44 (95% CI 0.57–3.63, p=0.44) and 1.22 (95% CI 0.44–3.40, p=0.7) for MOS-PH 3-month decliners vs improver/maintainers.

Discussion

While GA and specifically functional status are increasingly recognized as useful tools for improving pre-transplant risk assessment of older adults undergoing alloHCT, there are extremely limited data on how GA measures change over time post-transplant and how these changes impact outcomes. To our knowledge, only Deschler et al.[8] have described the trajectory of GA and QOL measures in adults aged 60 and older for the first 6 months after alloHCT. Our study adds to the literature by describing in detail the trajectory of a more comprehensive multidimensional GA and QOL assessment in patients aged 50 and older in the first year after alloHCT, providing a valuable roadmap of what patients can expect to experience after alloHCT. In addition, we explored potential predictors of greater functional decline at 1 year after transplant using serial GA data and found that functional decline at 3 months was predictive of persistent functional decline at 1 year, suggesting a way to identify a high-risk subgroup who may benefit from enhanced supportive care or other interventions. To our knowledge no study has evaluated predictors of functional decline after alloHCT.

By tracking the trajectory of GA and QOL changes in the first year after alloHCT, we found that mean values for GA-measured functional status, function-related FACT QOL measures (functional/physical well-being), and the FACT BMT subscale decline most at 3 months, start to recover at 6 months, and recover to near baseline at 12 months after alloHCT. These findings are consistent with those of Deschler et al.[8] who showed that activities of daily living (ADL), KPS, and global QOL were lowest at day +30 with steady improvement at day +100 and +180. Cognition by Mini Mental Status Exam was significantly worse at day +30 but recovered subsequently; this general pattern of early decline with quick recovery is reflected in the BOMC trajectory in our study, though mean values at each post-alloHCT timepoint were not statistically different from baseline. In the prior study, nutritional status (as measured by Mini Nutritional Assessment) declined significantly at day +30 and +100 but recovered at day +180, while we found that mean BMI was lower at all post-alloHCT timepoints. Our study also examined social support and mental health, which were not evaluated by Deschler et al. On average, GA social support peaked at 3 months while FACT social well-being decreased over time, likely reflecting the different natures of the two assessments. Interestingly, mean mental health and FACT emotional well-being subscale scores actually improved after transplant, suggesting that allocating more resources into optimizing functional health may be a greater need.

Baseline clinical characteristics or GA metrics were not predictive of post-alloHCT functional decline. These findings are similar to a recent study by Ombres et al.[13] which examined the association between baseline frailty (defined as abnormalities in exhaustion, physical activity, weight loss, grip strength, and gait speed) and frailty or death at 3 or 6 months after alloHCT. They found that neither baseline frailty, baseline abnormal GA, or any individual component of the baseline GA was significantly associated with the composite outcome of frailty or death at 3 months and 6 months. Our findings are in contrast to our sister study in autologous stem cell transplant patients,[23] which found comorbidities and disease status to be predictive of functional decline. Altogether, this suggests patients' functional outcomes after alloHCT may be less determined by their baseline characteristics and more related to events in the early post-alloHCT period, and a post-transplant evaluation may be needed to identify those at high risk for functional decline who may benefit from interventions.

We found that functional status at 3 months can be highly informative for predicting further functional trajectory. Patients whose function declines at 3 months are at higher risk of persistent functional decline at 6 and 12 months. While functional decline at 3 months was not statistically significantly associated with OS in landmark analysis, our study was not powered to evaluate this outcome. The hazard ratio of 1.4 for inferior OS in 3-month functional decliners is potentially clinically meaningful if a similar effect size with a narrower confidence interval could be corroborated in a larger study. Post-transplant functional status has been found to be predictive of survival outcomes in other studies. Deschler et al.[8] found subjective functional status to be predictive as a time varying covariate for both OS and PFS. Mishra et al.[29] measured subjective and objective functional status in adults aged 18 or older pre- and post-alloHCT at day +30, +90, and +180 and found objective functional status (6 minute walk test) at day +30 to be predictive of OS and NRM. Lin et al.[14] retrospectively evaluated the incidence of new functional impairment in alloHCT recipients who survived for at least 2 years and found that, as a time-dependent covariate in multivariate analysis, new functional impairment after the 2-year landmark was associated with inferior OS and increased NRM. These findings in sum show that short-term post-alloHCT functional status can be informative for longer term outcomes. Our findings suggest that allocating post-alloHCT resources to assessing early post-alloHCT functional status at 3 months and targeting those with functional decline at 3 months for additional support or interventions such as physical and occupational therapy evaluation may be beneficial and should be further investigated.

We acknowledge several limitations to our study. First, a sample size of 148 patients may have insufficient power to evaluate the predictive value of certain GA and QOL measures. This is a single institution study, and our transplant eligibility criteria may be different from other institutions and thus may influence generalizability. Our study population was limited to English speakers which may also limit generalizability. Our age cut-off of 50 years may be considered by some to be too young for the use of "geriatric" assessments. However, the high prevalence of both baseline and post-alloHCT GA impairments as well as the prognostic value of such impairments shown in prior and present studies support the utility of GA in this population. Another limitation is that patients who progressed within one year remained on study, so disease and treatment effects may impact subsequent functional

outcomes. In addition, our data set had missing post-alloHCT assessments, and it is possible that the missing data may be informative. For example, our institution is a transplant referral center for a wide area of community oncology practices; patients who progressed after transplant may have been more likely to have returned to their community oncologist for salvage therapy, resulting in missing data. Lastly, as expected with alloHCT studies, 50 of 148 patients died by 12 months. Trajectory descriptions necessarily reflect the trajectories of survivors only, but in our maintainer/decliner data, we have incorporated information on subjects who are missing but alive and those who are deceased.

In summary, we found that mean functional status decreases most at 3 months post-alloHCT and subsequently recovers near baseline at one year. The patient subset with functional decline at 3 months is at higher risk for persistent functional decline at one year, and early functional decline post-alloHCT has been shown in other studies to also predict survival. Future studies should examine whether targeting interventions for those with greater functional decline at 3 months could help improve outcomes at 1 year and beyond.

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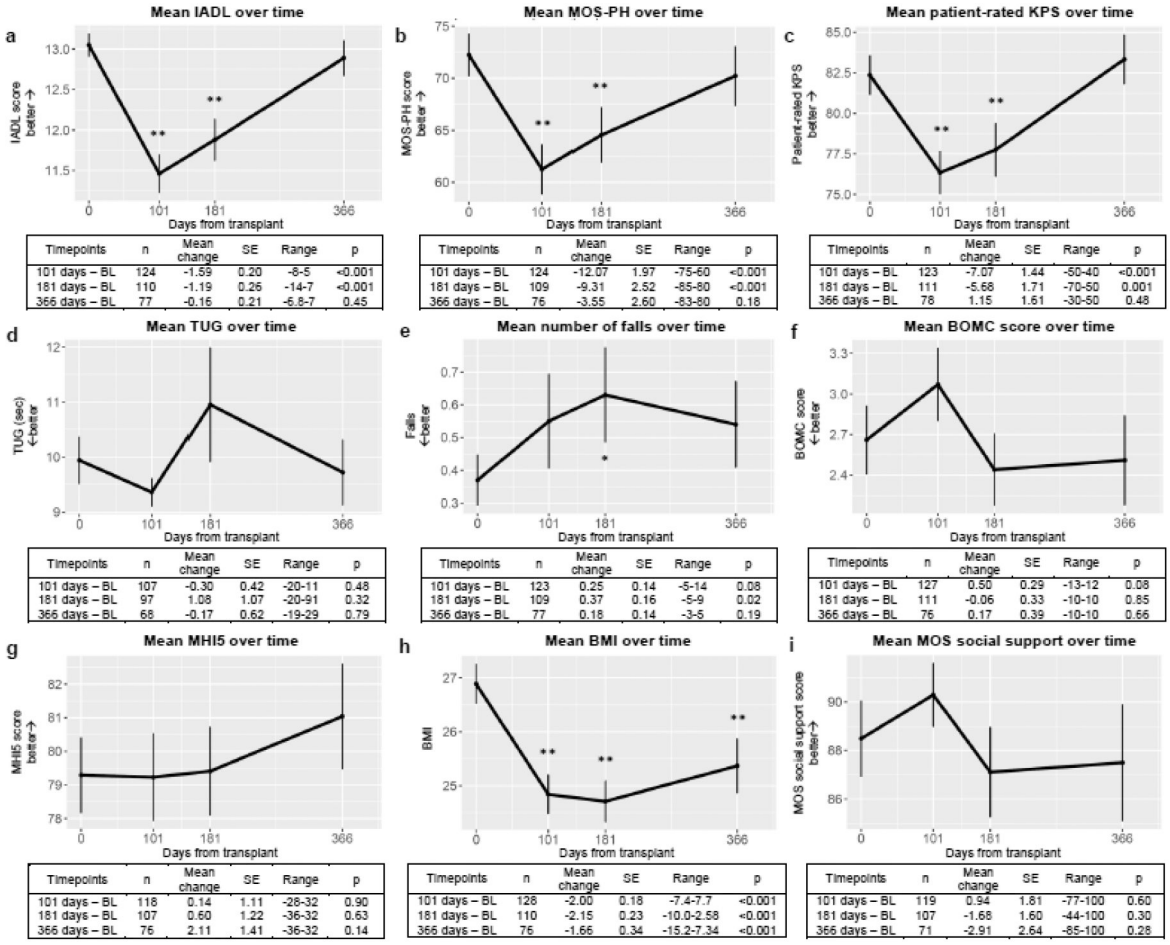
Highlights

- Mean functional status declines at 3 months after allogeneic transplant
- No baseline clinical characteristic predicted functional decline
- Functional decline at 3 months is associated with persistent decline at 6–12 months



Timepoints	n	Mean change	SE	Range	p
101 days – BL	124	-1.59	0.20	-8-5	<0.001
181 days – BL	110	-1.19	0.26	-14-7	<0.001
366 days – BL	77	-0.16	0.21	-6.8-7	0.45

Timepoints	n	Mean change	SE	Range	p
101 days – BL	124	-12.07	1.97	-75-60	<0.001
181 days – BL	109	-9.31	2.52	-85-80	<0.001
366 days – BL	76	-3.55	2.60	-83-80	0.18

Timepoints	n	Mean change	SE	Range	p
101 days – BL	123	-7.07	1.44	-50-40	<0.001
181 days – BL	111	-5.68	1.71	-70-50	0.001
366 days – BL	78	1.15	1.61	-30-50	0.48

Timepoints	n	Mean change	SE	Range	p
101 days – BL	107	-0.30	0.42	-20-11	0.48
181 days – BL	97	1.08	1.07	-20-91	0.32
366 days – BL	68	-0.17	0.62	-19-29	0.79

Timepoints	n	Mean change	SE	Range	p
101 days – BL	123	0.25	0.14	-5-14	0.08
181 days – BL	109	0.37	0.16	-5-9	0.02
366 days – BL	77	0.18	0.14	-3-5	0.19

Timepoints	n	Mean change	SE	Range	p
101 days – BL	127	0.50	0.29	-13-12	0.08
181 days – BL	111	-0.06	0.33	-10-10	0.85
366 days – BL	76	0.17	0.39	-10-10	0.66

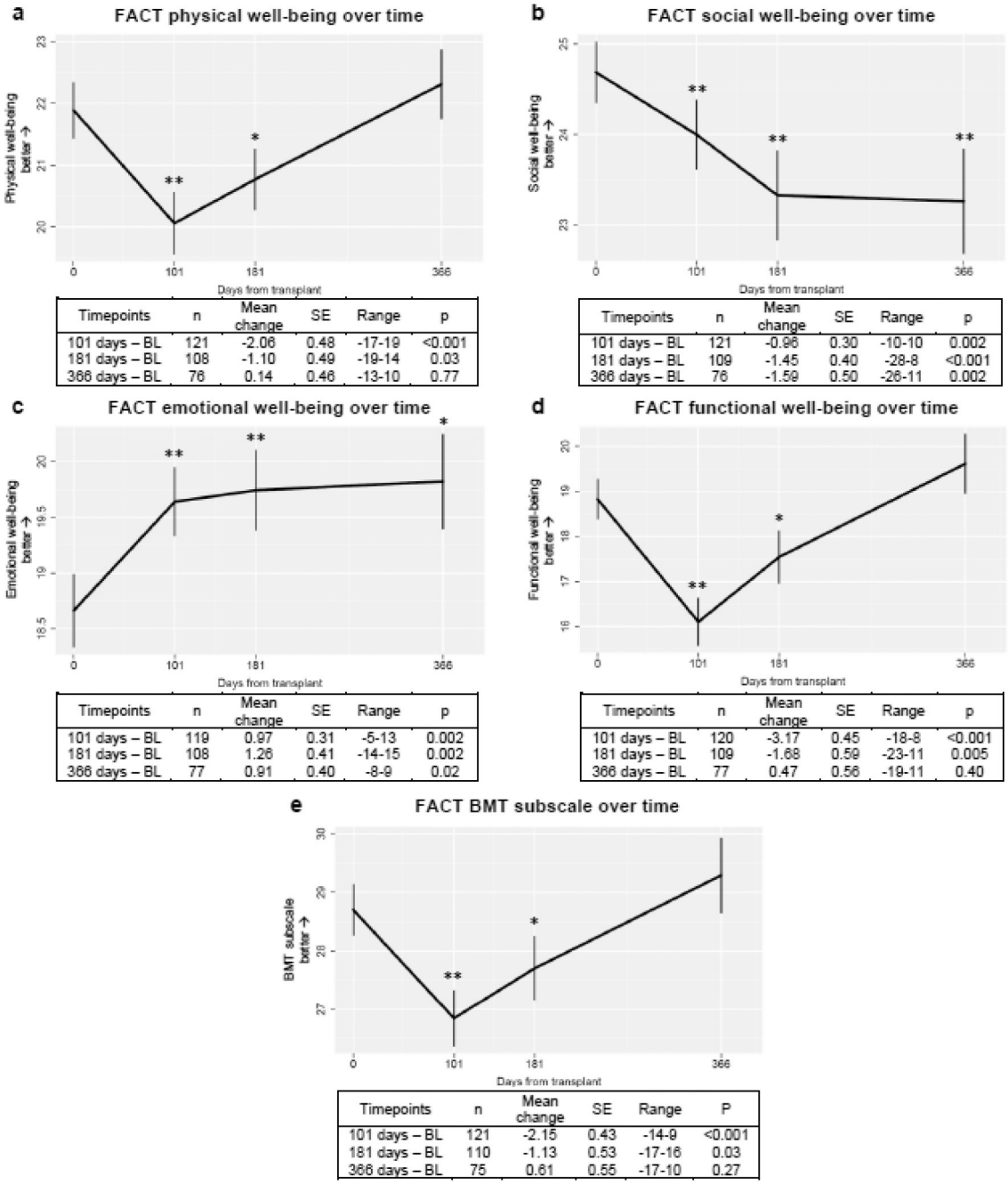
Timepoints	n	Mean change	SE	Range	p
101 days – BL	118	0.14	1.11	-26-32	0.90
181 days – BL	107	0.60	1.22	-36-32	0.63
366 days – BL	76	2.11	1.41	-36-32	0.14

Timepoints	n	Mean change	SE	Range	p
101 days – BL	126	-2.00	0.18	-7.4-7.7	<0.001
181 days – BL	110	-2.15	0.23	-10.0-2.58	<0.001
366 days – BL	76	-1.66	0.34	-15.2-7.34	<0.001

Timepoints	n	Mean change	SE	Range	p
101 days – BL	119	0.94	1.81	-77-100	0.60
181 days – BL	107	-1.68	1.60	-44-100	0.30
366 days – BL	71	-2.91	2.64	-85-100	0.28

Figure 1.

Trajectories of mean geriatric assessment measures over time after transplant: (a) instrumental activities of daily living (IADL) score, (b) Medical Outcomes Study-Physical Health (MOS-PH) score, (c) patient-rated Karnofsky Performance Status (KPS), (d) Timed-Up-and-Go (seconds), (e) number of falls in last 6 months, (f) Blessed Orientation-Memory-Concentration test, (g) Mental Health Inventory-5 score, (h) body mass index, (i) Medical Outcomes Study Social Support. Vertical lines indicate the standard error of the measures at a given time point. P-values correspond to comparisons between mean score at a given timepoint with the mean score at baseline; * = p-value <0.05, ** = p-value <0.005. BL=baseline, SE=standard error, p=p-value.



Timepoints	n	Mean change	SE	Range	p
101 days – BL	121	-2.06	0.48	-17-19	<0.001
181 days – BL	108	-1.10	0.49	-19-14	0.03
366 days – BL	76	0.14	0.46	-13-10	0.77

Timepoints	n	Mean change	SE	Range	p
101 days – BL	121	-0.96	0.30	-10-10	0.002
181 days – BL	109	-1.45	0.40	-28-8	<0.001
366 days – BL	76	-1.59	0.50	-26-11	0.002

Timepoints	n	Mean change	SE	Range	p
101 days – BL	119	0.97	0.31	-5-13	0.002
181 days – BL	108	1.26	0.41	-14-15	0.002
366 days – BL	77	0.91	0.40	-8-9	0.02

Timepoints	n	Mean change	SE	Range	p
101 days – BL	120	-3.17	0.45	-18-8	<0.001
181 days – BL	109	-1.68	0.59	-23-11	0.005
366 days – BL	77	0.47	0.56	-19-11	0.40

Timepoints	n	Mean change	SE	Range	P
101 days – BL	121	-2.15	0.43	-14-9	<0.001
181 days – BL	110	-1.13	0.53	-17-16	0.03
366 days – BL	75	0.61	0.55	-17-10	0.27

Figure 2.

Trajectories of mean Functional Assessment of Cancer Therapy (FACT) quality of life measures over time after transplant: (a) physical well-being, (b) social well-being, (c) emotional well-being, (d) functional well-being, (e) bone marrow transplant (BMT) subscale. Vertical lines indicate the standard error of the measures at a given time point. P-values correspond to comparisons between mean score at a given timepoint with the mean score at baseline; * = p-value <0.05, ** = p-value <0.005. BL=baseline, SE=standard error, p=p-value.

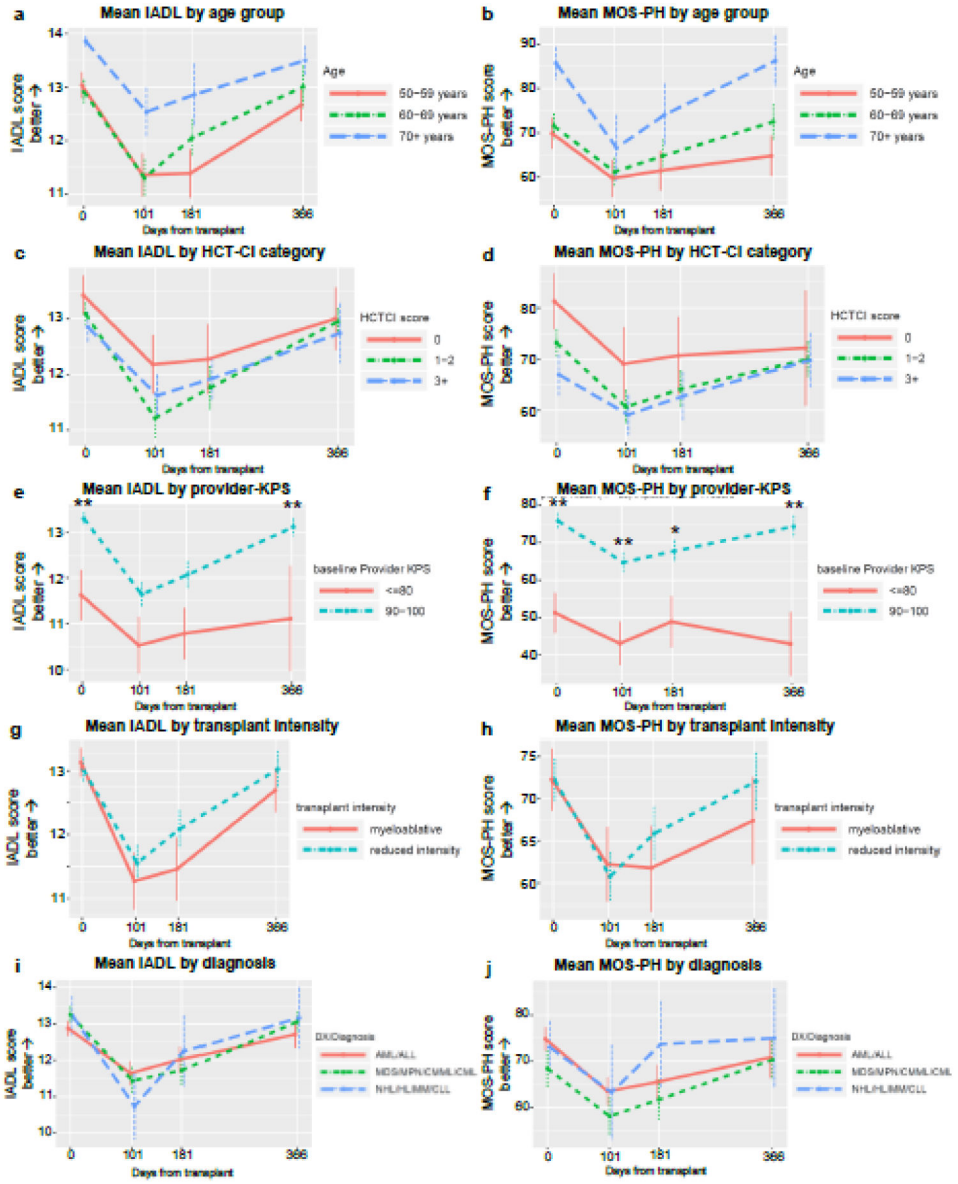


Figure 3.

Trajectories of mean instrumental activities of daily living (IADL) and Medical Outcomes Study Physical Health (MOS-PH) scores by baseline characteristics, respectively: (a-b) age, (c-d) Hematopoietic cell transplantation comorbidity index (HCT-CI), (e-f) provider-rated Karnofsky Performance Status (KPS), (g-h) transplant intensity, (i-j) diagnosis. Vertical lines indicate the standard error of the measures at a given time point. P-values correspond to comparisons between mean scores between subgroups at each timepoint; * = p-value <0.05, ** = p-value <0.005. AML=acute myeloid leukemia, ALL=acute lymphoblastic leukemia, MDS=myelodysplastic syndrome, MPN=myeloproliferative neoplasm, CMML=chronic myelomonocytic leukemia, CML=chronic myeloid leukemia, NHL=non-Hodgkin lymphoma, HL=Hodgkin lymphoma, MM=multiple myeloma, CLL=chronic lymphocytic leukemia.

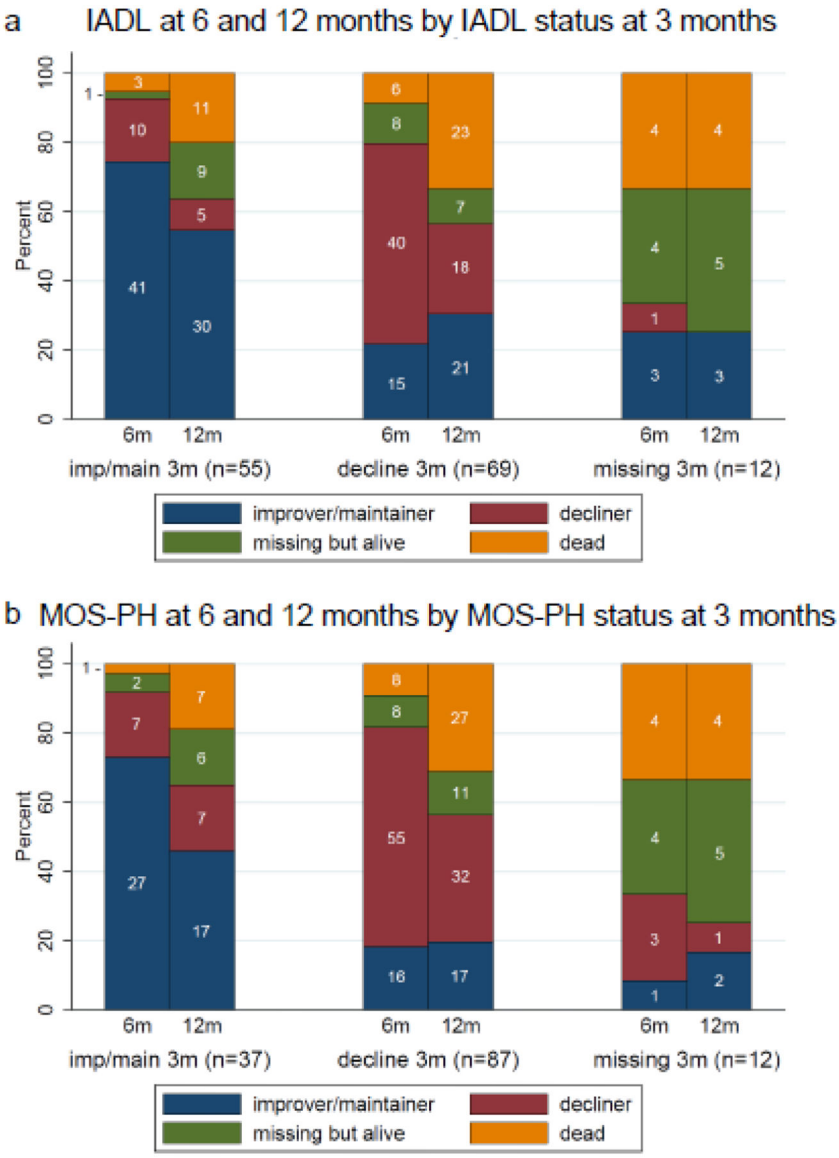


Figure 4.

Impact of 3-month post-transplant functional change on longer term functional status. (a) Instrumental activities of daily living (IADL) change from baseline at 6 and 12 months according to whether patients demonstrated improved/maintained IADL scores (imp/main 3m), declined IADL scores (decline 3m), or were missing but alive (missing 3m) at 3 months post-transplant. (b) Medical Outcomes Study Physical Health (MOS-PH) change from baseline at 6 and 12 months according to whether patients demonstrated improved/maintained MOS-PH scores (imp/main 3m), declined MOS-PH scores (decline 3m), or were missing but alive (missing 3m) at 3 months post-transplant.

Table 1.

Cancer-specific geriatric assessment and quality of life measures

Domain	Measure	Possible score range	Score interpretation
Cancer-specific Geriatric Assessment			
Functional status	MOS Physical Health subscale[25,26]	0–100	Higher is better function
	Instrumental Activities of Daily Living (OARS subscale)[24]	0–14	Higher is better function
	KPS, patient-rated[30,31]	0–100	Higher is better function
	Timed-up-and-go[32]	--	Lower is better function
	Number of falls in last 6 months[33]	--	Lower is better function
Cognition	Blessed Orientation-Memory-Concentration Test[34]	0–28	Lower is better cognition
Mental health	Mental Health Inventory[35,36]	0–100	Higher is better mental health
Nutrition	Body mass index[37]	--	--
	% unintentional weight loss in 6 months[38]	--	--
Polypharmacy	Number of medications (OARS Physical Health section)[24]	--	--
Social support	MOS Social Support survey[39]	0–100	Higher is better support
FACT-BMT [18]			
Quality of Life	Physical well-being	0–28	Higher is better QOL
	Social well-being	0–28	Higher is better QOL
	Emotional well-being	0–24	Higher is better QOL
	Functional well-being	0–28	Higher is better QOL
	Bone marrow transplant subscale	0–40	Higher is better QOL

MOS = Medical Outcomes Study. OARS = Older Americans Resources & Services. KPS = Karnofsky performance status. FACT-BMT = Functional Assessment of Cancer Therapy-Bone Marrow Transplant. QOL = quality of life.

Table 2.

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 %)
Marital status, n (%)	
Married	115 (78 %)
Divorced/Separated	22 (15%)
Single	6 (4%)
Widowed	5 (3%)
Race, n (%)	
White	113 (76%)
Black	5 (3%)
Asian	5 (3%)
Other	3 (2%)
Unknown/did not respond	22 (15%)
Ethnicity, n (%)	
Non-Hispanic	125 (84%)
Hispanic	8 (5%)
Unknown/did not respond	15 (10%)
Education, n (%)	
Less than high school	5 (3%)
High school graduate	20 (14%)
Some college/Junior college	44 (30%)
College graduate	28 (19%)
Post-college/Advanced degree	51 (34%)
Diagnoses, n (%)	
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, n (%)	
Low	78 (52 %)
Intermediate	26 (18 %)
High	38 (26 %)
Other/unknown	6 (4 %)

	N = 148
KPS, provider-rated, n (%)	
100	59 (40%)
90	66 (45%)
≤80	22 (15%)
Unknown	1 (1%)
HCT-CI score, n (%)	
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 %)
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 %)
Preparative regimen, n (%)	
Fludarabine/Busulfan/ATG	75 (51%)
Fludarabine/Busulfan	27 (18%)
Fludarabine/Melphalan +/− ATG	17 (11%)
Fludarabine/Cyclophosphamide/TBI +/− ATG	11 (7%)
TBI-based	9 (6%)
Clofarabine/Melphalan	5 (3%)
Other	4 (3%)
GVHD prophylaxis, n (%)	
Tacrolimus/MTX	94 (64%)
Tacrolimus/MTX/MMF	37 (25%)
Other calcineurin-based regimen	11 (7%)
PTCy/Tacrolimus/MMF	6 (4%)

CR/PR = complete/partial remission. ASBMT = American Society of Blood and Marrow Transplantation. KPS = Karnofsky performance status. HCT-CI = Hematopoietic Cell Transplantation-Comorbidity Index. MUD = matched unrelated donor. ATG = anti-thymocyte globulin. TBI = total body irradiation. GVHD = graft-versus-host disease. MTX = methotrexate. MMF = mycophenolate mofetil. PTCy = post-transplant cyclophosphamide.