Geriatric assessment to predict survival in older allogeneic hematopoietic cell transplantation recipients

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ABSTRACT

Allogeneic hematopoietic cell transplantation is increasingly utilized in older adults. This study prospectively evaluated the prognostic utility of geriatric assessment domains prior to allogeneic transplantation in recipients aged 50 years and over. Geriatric assessment was performed prior to transplant, and included validated measures across domains of function and disability, comorbidity, frailty, mental health, nutritional status, and systemic inflammation. A total of 203 patients completed geriatric assessment and underwent transplant. Median age was 58 years (range 50-73). After adjusting for established prognostic factors, limitations in instrumental activities of daily living (HR 2.38, 95%CI: 1.59-3.56; P<0.001), slow walk speed (HR 1.80, 95%CI: 1.14-2.83; P=0.01), high comorbidity by hematopoietic cell transplantation-specific comorbidity index (HR 1.56, 95%CI: 1.07-2.28; P=0.02), low mental health by short-form-36 mental component summary (HR 1.67, 95%CI: 1.13-2.48; P=0.01), and elevated serum C-reactive protein (HR 2.51, 95%CI: 1.54-4.09; P<0.001) were significantly associated with inferior overall survival. These associations were more pronounced in the cohort 60 years and over. Geriatric assessment measures confer independent prognostic utility in older allogeneic transplant recipients. Implementation of geriatric assessment prior to allogeneic transplantation may aid appropriate selection of older adults.

Introduction

The proportion and absolute number of older adults undergoing allogeneic hematopoietic cell transplantation (HCT) is rapidly rising such that almost 40% of transplant recipients are now aged 50 years and over.[1] A growing number of reports now demonstrate the utility of HCT in older adults with long-term outcomes that compare favorably to non-transplant series and transplant survival rates that approach those seen in younger adults.[2-4] Most authors have thus concluded that older age should no longer remain a barrier to transplant. However, despite these promising advances, only a small fraction of older adults with high-risk hematologic malignancies actually undergo HCT, presumably, in part, due to ongoing concerns regarding tolerability and transplant success in this population.[5,6]

A major barrier to patient selection for aggressive therapy remains the lack of health status information reported in treatment studies of older patients with hematologic malignancies.[7] Better characterization of health-related prognostic factors may aid pre-transplant risk stratification, thereby facilitating early referral of appropriate candidates. Apart from age, traditional tools used for HCT prognostication have included disease status, donor type, graft source, and physician-rated Karnofsky performance status (KPS).[8] A major advancement in transplant prognostication was achieved when Sorror and colleagues developed the hematopoietic cell transplantation-specific comorbidity index (HCT-CI), a comorbidity scoring system that predicts for transplant-related toxicity and overall survival (OS).[9-11] The HCT-CI is now routinely incorporated into pre-transplant assessment. However, as a single domain, comorbidity cannot sufficiently describe all areas of health relevant to older adults. For example, simple functional impairments (e.g. difficulty walking) may have an equivalent or greater impact on long-term survival.[12]

A more comprehensive assessment of health across domains relevant to older adults may be obtained through a geriatric assessment (GA). Originally developed by geriatricians as a multidisciplinary evaluation of older patients, geriatric assessment is increasingly fundamental to the field of solid tumor oncology, where GA variables independently predict for chemotherapy toxicity and mortality and may facilitate guided interventions in older cancer patients.[13-15] Despite recommendations regarding the use of GA from the International Society of Geriatric Oncology[16] and practice guidelines outlined by the National Comprehensive Cancer Network, this powerful tool has not been described for transplant patients. This probably stems from the fact that HCT recipients have historically been younger than the typical geriatric population, but may also be due to the widely held belief that only fit older adults undergo transplant. We recently reported a high prevalence of health-related vulnerabilities uncovered by prospective GA among older HCT recipients.[17] We now report on the prognostic significance of pre-transplant GA in a large series of older HCT recipients.

Methods

Patient population and treatment regimen

Patients aged 50 years and over and scheduled to undergo allogeneic HCT at The University of Chicago were eligible for inclusion, as

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previously described.[17] We selected a threshold age of 50 years because the optimal age for GA in this population has not been studied and this was the age at which reduction in transplant regimen intensity may be justified.[18] A trained research assistant or nurse carried out the GA within one month prior to initiation of transplant conditioning. Occasionally, GA occurred 1-2 days after conditioning began. The treating physician determined suitability to undergo HCT and appropriate HCT treatment plan independent of GA results. After completing a prospective institutional review board approved protocol,[17] GA continued on a clinical basis. All patients provided written informed consent.

Geriatric assessment variables

The GA consisted of six distinct domains of health: functional status, frailty, comorbidity, mental health, nutritional status, and degree of inflammation. Functional status was assessed by physician-rated Eastern Cooperative Oncology Group performance status (PS) (range 0-5),[19] Katz's Activities of Daily Living (ADL) (range 0-12; higher score indicates less need for assistance),[20] modified Lawton's Instrumental Activities of Daily Living (IADL) (range 0-14; higher score indicates less need for assistance),[21] and Physical Component Summary of the Medical Outcomes Short Form-36 health-related quality of life questionnaire (SF36-PCS) (range 0-100; higher score indicates better self-reported physical health).[22] Frailty was documented by the Fried Frailty Index (FI) (range 0-5; 1-2 indicates pre-frail, 3-5 indicates frail),[23] which incorporates two performance-based measures (grip strength and walk speed over 15 feet) and three self-report measures (exhaustion, weight loss, and physically frail). Comorbidity was classified using the HCT-CI (range 0-≥3; 1-2 indicates intermediate comorbidity, ≥3 indicates high comorbidity)[10] and the Cumulative Illness Rating Scale-Geriatrics (CIRS-G) (range 0-56; higher score indicates more comorbidity).[24] Mental health was derived from the Mental Component Summary of the Medical Outcomes Short Form-36 health-related quality of life questionnaire (SF36-MCS) (range 0-100; higher score indicates better mental health).[22] Serum albumin (<3.5 mg/dL threshold), and self-reported weight loss (element of Frailty Index) represented nutrition. Inflammation, a biological marker of aging,[25] was measured by serum C-reactive protein (CRP) (≥10 mg/L threshold based on published effects on transplant outcome).[26,27] Of note, the modified IADL omits "the ability to do laundry" item for the original survey.[28]

Statistical analysis

Descriptive statistics summarized patients', disease, and transplant characteristics, as well as geriatric assessment results. Definitions of disease risk followed the American Society for Blood and Marrow Transplantation Request for Information (RFI) disease classification (*www.asbmt.org*). GA impairments were determined using published instrument cut-off points when available. SF36-PCS and SF36-MCS were scored using QualityMetric Software (Lincoln, RI, USA); 1 standard deviation below population norm (i.e. score <40) was considered impaired. CIRS-G scores above the median were considered impaired. Instruments missing any individual question or component were not scored, and instead were rendered as missing data. Time-to-event variables were defined as time elapsed from date of stem cell infusion to date of death from any cause (OS), date of death unrelated to underlying disease progression (non-relapse mortality (NRM)), or date of disease relapse. Survival curves were generated using the Kaplan-Meier method, and groups were compared using the log rank test. Cumulative incidence estimates of probabilities of NRM and relapse were used to accommodate these competing risks, and groups were compared using Gray's test. Univariate Cox proportional hazards regression models were used to evaluate associations between OS and standard pre-transplant parameters as well as GA variables. Each GA variable associated with OS (P<0.1) was then evaluated in a multivariate model adjusting for age, HCT-CI score, conditioning intensity, and disease risk (standard HCT prognostic factors); adjusted hazard ratios (HR), 95% confidence intervals (95%CI), and P-values are reported. PS and hematopoietic cell donor were not included in multivariate models, as neither variable was significantly associated with survival in univariate analysis. Cytomegalovirus (CMV) serostatus was also excluded from multivariate models due to missing CMV data in a number of patients and the finding that inclusion of CMV did not alter results. Statistical analyses were performed using Stata, version 12.1 (StataCorp, College Station, TX, USA) and R.[29]

Table 1. Patients' demographic and clinical characteristics.

Demographic/Characteristic	N.	%
Total evaluable	203	100
Age, years		
50-59	124	61
60-69	75	37
≥70	4	2
Sex		
Male	130	64
Female	73	36
Primary disease		
AML	87	43
MDS	30	15
NHL	38	19
ALL	12	6
CML	11	5
CLL	10	5
Other	15	7
Disease risk at HCT		
Standard	112	55
High	91	45
Hematopoietic cell donor		
Matched related	92	45
Matched unrelated, 8/8	81	40
Mismatched unrelated, 7/8	2	1
Cord*	28	14
Conditioning regimen intensity		
Ablative	49	24
RIC	154	76
CMV serostatus		
CMV^+	123	60
CMV^-	40	20
CMV missing	40	20

*AML: acute myeloid leukemia; MDS: myelodysplastic syndrome; NHL: non-Hodgkin lymphoma; ALL: acute lymphoblastic leukemia; CML: chronic myeloid leukemia; CLL: chronic lymphocytic leukemia; RIC: reduced-intensity conditioning; HCT: hematopoietic cell transplantation; CMV+: cytomegalovirus seropositive in donor and/or recipient; CMV-: cytomegalovirus seronegative in donor and recipient. *Singe cord blood unit augmented by haploidentical $CD34^+$ selected related donor.*

Results

Patients' disease, and transplant characteristics

Between April 2005 and March 2012, 203 of 271 adults aged 50 years or over who underwent allogeneic HCT at the University of Chicago completed the GA (Table 1). GA was completed in a median time of 20 minutes (range 15-27 min); additional details regarding feasibility have been previously reported.[17] Median age was 58 years

Table 2. Limitations by geriatric assessment in patients 50 years or over undergoing HCT.

	Total Population			50-59 Years			60-73 Years		
		Impaired*			Impaired*			Impaired*	
GA Domain/Measure	Evaluable	No	%	Evaluable	No.	%	Evaluable	No	%
Functional status									
PS	203	58	29	124	37	30	79	21	27
ADL	162	12	7	98	6	6	64	6	9
IADL	162	64	40	98	33	34	64	31	48
SF36-PCS	195	82	42	120	52	43	75	30	40
Frailty									
Pre-Frail	154	87	56	95	52	55	59	35	59
Frail	154	38	25	95	26	27	59	12	20
Select frailty components**									
Grip strength	186	44	24	116	25	22	70	19	27
Physical	195	52	27	119	33	28	76	19	25
Exhaustion	193	64	33	118	37	31	75	27	36
Walk speed	153	50	33	97	28	29	56	32	39
Comorbidity									
HCT-CI, intermediate	202	75	37	124	47	38	78	28	36
HCT-CI, high	202	94	47	124	54	44	78	40	51
CIRS-G	202	112	55	124	60	48	79	52	66
Mental health									
SF36-MCS	197	110	56	122	64	52	75	46	61
Nutritional status									
Albumin, mg/dL	202	30	15	124	15	12	78	15	19
Weight loss	198	114	58	121	76	63	77	38	49
Inflammatory biomarker									
CRP, mg/L	138	49	36	83	31	37	55	18	33

*PS: performance status; ADL: activities of daily living; IADL: instrumental activities of daily living; SF36-PCS: Medical Outcomes Short Form Physical Component Summary; HCT-CI: hematopoietic cell transplantation-specific comorbidity index; CIRS-G: cumulative illness rating scale- geriatrics; SF36-MCS: Medical Outcomes Short Form Mental Component Summary; CRP, C-reactive protein. *Impairments defined as: PS ≥1; ADL <12; IADL <14; SF36-PCS <40; pre-frail, FI 1-2; frail, FI ≥3; FI 1-2; Intermediate HCT-CI 1-2; High HCT-CI ≥3; CIRS-G ≥7; SF36-MCS <40; Albumin <3.5; CRP ≥10. **Frailty components were assigned as impaired on a dichotomous scale based on published guidelines.*

(interquartile range 54-63 years, mean 59 years, range 50-73 years). Forty-five percent were high disease risk and 14% underwent cord blood transplantation (single cord unit augmented by haploidentical $CD34^+$ selected related donor).[30] The majority (76%) received reduced-intensity conditioning regimens, most commonly fludarabine, melphalan, and alemtuzumab.[31] The remainder (24%) underwent myeloablative transplants with either a TBI-based regimen (12 Gy) or fludarabine and busulfan.[32]

Geriatric assessment findings

Table 2 lists the proportion of impairments detected by GA. Limitations across GA measures did not differ when stratified by age group (50-59 years *vs.* ≥60 years) with the exception of comorbidity by CIRS-G, which revealed significantly increased comorbidity in the older cohort (66% *vs.* 48%; *P*=0.02).

Outcomes

The median duration of follow up for surviving patients was 36 months (range 3-121 months). During this time, 113 patients died, 67 without relapse (NRM), and 46 after disease relapse. Median OS was 15.6 months and the probabilities of OS, NRM, and relapse at two years were 45% (95%CI: 38-52), 33% (95%CI: 26-39), and 35% (95%CI: 28-42), respectively.

Univariate analysis of 2-year NRM, relapse, and OS

Unadjusted effects of routine clinical parameters and GA measures on transplant outcomes are reported in Table 3. The following variables were significantly associated with inferior OS: age ≥ 60 years (*P*=0.0007), ablative conditioning regimen (P=0.048), CMV^+ donor and/or recipient (*P*=0.03), higher HCT-CI (*P*=0.03) IADL limitations (*P*<0.0001), slow walk speed (*P*=0.01), lower mental health (*P*=0.01), low albumin (*P*=0.008), and high CRP (*P*=0.0003). Age 60 years or over (*P*=0.0005), IADL limitations (*P*=0.0003), higher HCT-CI (*P*=0.03), and high CRP (*P*=0.029) significantly increased risk of NRM, whereas only high disease risk (*P*=0.02) and slow walk speed (*P*=0.03) were associated with disease relapse.

Adjusted model

After adjusting for routine clinical parameters of age, HCT-CI, disease risk, and regimen intensity, IADL limitations (*P*<0.0001), slow walk speed (*P*=0.01), low SF36-MCS (*P*=0.01), and high CRP (*P*<0.001) remained significantly associated with worse OS (Table 4).

Simplified risk score

We devised a simple stratification tool for survival by adding the most prognostic GA measure, IADL, to the HCT-CI (Figure 1A). This was motivated by prior work demonstrating an additive effect of functional status and comorbidity for transplant prognostication.[9,33] High HCT-CI and any IADL limitation were given 1 point and thus patients could have a total of 0, 1 or 2 points. Compared to no points, 1 point conferred significantly inferior 2-year

Table 3. Univariate analysis of baseline characteristics and GA measures on transplant outcomes.

Variable	2-year OS (%)	P	2-year NRM (%)	P	2-year Relapse (%)	P
Age						
50-59	54.5	0.0007	24.1	0.0005	40.3	0.05
≥60	30.0		46.3		26.6	
Disease risk at HCT						
Standard	45.5	0 .11	34.4	0.71	28.0	0.02
High	43.0		31.8		43.6	
Hematopoietic cell donor						
Related/Unrelated	44.3	0.69	30.6	0.14	37.3	0.13
Cord*	50.4		46.6		21.6	
Conditioning regimen intensity						
Ablative	35.4	0.048	33.1	0.79	37.7	0.51
RIC	48.1		31.6		34.2	
CMV serostatus						
CMV+	40.2	0.03	38.7	0.14	33.5	0.94
CMV-	58.4		26.0		33.8	
PS						
0	45.9	0.31	33.9	0.84	29.9	0.05
1-2	42.4		30.2		46.9	
ADL						
No limitation	44.5	0.69	33.4	0.57	33.3	0.44
Any limitation	41.7		41.7		34.1	
IADL						
No limitation	56.0	<.0001	23.5	0.0003	34.7	0.82
Any limitation	26.3		50.1		33.1	
SF36-PCS						
Normal	50.3	0.11	27.8	0.23	34.3	0.58
Low	38.7		37.2		38.1	
FI						
Not frail	51.4	0.53	41.2	0.86	34.8	0.56
Pre-frail	44.4		31.6		31.7	
Frail	44.6		29.3		41.9	
Grip strength from FI						
Not frail	49.3	0.16	31.4	0.81	32.6	0.36
Frail	40.0		30.3		42.7	
Physical from FI						
Not frail	44.4	0.34	35.0	0.17	33.8	0.66
Frail	50.1		27.7		36.0	
Exhaustion from FI						
Not frail	48.5	0.06	29.3	0.06	35.6	0.90
Frail	38.4		40.3		34.6	
Walk speed from FI						
Not frail	50.0	0.009	33.1	0.37	27.7	0.03
Frail	38.0		32.7		44.8	
Comorbidity, HCT-CI						
None	66.1	0.03	24.8	0.03	25.6	0.46
Intermediate	49.2		22.3		42.2	
High	34.2		43.5		33.0	
Comorbidity, CIRS-G						
Low	49.7	0.11	29.1	0.26	35.0	0.97
High	40.9		35.7		35.0	
SF36-MCS						
Normal	53.2	0.01	29.9	0.33	31.7	0.59
Low	38.5		34.3		39.2	
Albumin						
Normal	47.9	0.008	31.3	0.20	32.8	0.11
Low	29.2		37.6		48.2	
Weight loss from FI						
Absent	46.5	0.65	35.4	0.76	32.0	0.27
Present	44.1		31.4		37.0	
CRP						
Not high	50.9	0.0003	31.9	0.029	30.1	0.28
High	32.0		43.1		35.0	

*GA: geriatric assessment; OS: overall survival; NRM: non-relapse mortality; HCT: hematopoietic cell transplantation; MRD: HLA matched related donor; MUD: HLA matched unrelated donor; RIC: reduced intensity conditioning; CMV+, cytomegalovirus seropositive in donor and/or recipient; CMV-: cytomegalovirus seronegative in donor and recipient; PS: performance status; ADL: activities of daily living; IADL: instrumental activities of daily living; SF36-PCS: Medical Outcomes Short Form Physical Component Summary; FI: Frailty index; HCT-CI: hematopoietic cell transplantation comorbidity index; CIRS-G: cumulative illness rating scale- geriatrics; SF36-MCS: Medical Outcomes Short Form Mental Component Summary; CRP: C-reactive protein *Single cord blood unit augmented by haploidentical CD34+ selected related donor.*

survival (44% *vs.* 62%; HR 1.74, 95%CI: 1.1-2.86; *P*=0.026), and 2 points resulted in only a 13% 2-year survival rate (HR 3.66, 95%CI: 2.1-6.4; *P*<0.001). The IADL/HCT-CI risk score was independent of disease risk, as high disease risk was found in 43.6%, 53.2%, and 43.3% of patients' scores of 0, 1, and 2, respectively (*P*=0.47).

Age and geriatric assessment

We further stratified the adjusted survival analyses by the two age cohorts of 50-59 years *versus* 60 years or over (Table 4). HRs for all GA measures were quantitatively higher in the older age cohort, suggesting a greater predictive effect of GA in older transplant recipients. The prognostic effect of the IADL/HCT-CI risk score was similarly amplified in the older cohort (Figure 1B and C). For example, 2-year OS for those patients aged 60 years or over with an IADL/HCT-CI score of 1 was 29% (compared to 53% for 50-59 year olds with a score of 1), and for those aged 60 years or over with a score of 2 was 0%.

Discussion

In this study, the first to report on the use of prospective geriatric assessment specifically in a large group of older allogeneic HCT recipients, we demonstrate that Geriatric Assessment prior to HCT offers substantial prognostic value. After controlling for several established predictors of transplant outcome, health impairments across geriatric domains of functional status, comorbidity, mental health, and systemic inflammation all retained a significant association with decreased survival following transplantation. Our findings extend the utility of GA previously established in solid tumor oncology[13,15,16] and build upon a nascent literature in the hematologic malignancies.[7,34]

As growing numbers of older adults are considered for HCT, an intensive and expensive therapeutic modality, more accurate assessment of 'biological age' rather than simply chronological age has gained importance. Implementation of GA tools into the routine pre-transplant workup for older adults may move us a step closer to achieving this distinction. For example, although physician assessment of performance status is useful for transplant prognostication in those with impaired PS,[4,35] our data and those of others demonstrate most older adults undergoing HCT have a well-preserved PS (ECOG 0-1 or KPS ≥ 80); a mild reduction in PS (ECOG 0 *vs.* 1) has a relatively small impact on transplant outcomes and may be quite subjective.[2,36] In contrast, validated tools of function evaluating instrumental activities of daily living (patient reported complex skills required to maintain independence in the community) and measurement of 15-foot walk speed not only revealed functional vulnerabilities; they were each prognostic for survival following transplant. Furthermore, mental health assessed by SF-36 MCS also provided interesting clinical insights (56% scored more than 1 SD below population norm for mental function) and prognostic value.

Assessment of comorbidities is integral to geriatric assessment, and has become central to assessing candidates for transplantation. Our findings confirm the prognostic utility of comorbidity by the HCT-CI specifically in older adults.[2] However, our data also show that GA domains have added prognostic value, independent of HCT-CI, and may be necessary to fully characterize health status of older transplant patients. We built on the prognostic value of comorbidity by combining the HCT-CI to our best functional status measure, IADL limitations, to create a simple 3-point risk score (1 point for high HCT-CI and 1 point for IADL limitation) that may be readily tested and applied in future studies where a complete GA may not be feasible. Patients with any IADL limitation and high comorbidity suffered dismal outcomes, especially in those aged 60 years or over. In sharp contrast, those aged 60 years or over with a low or intermediate comorbidity

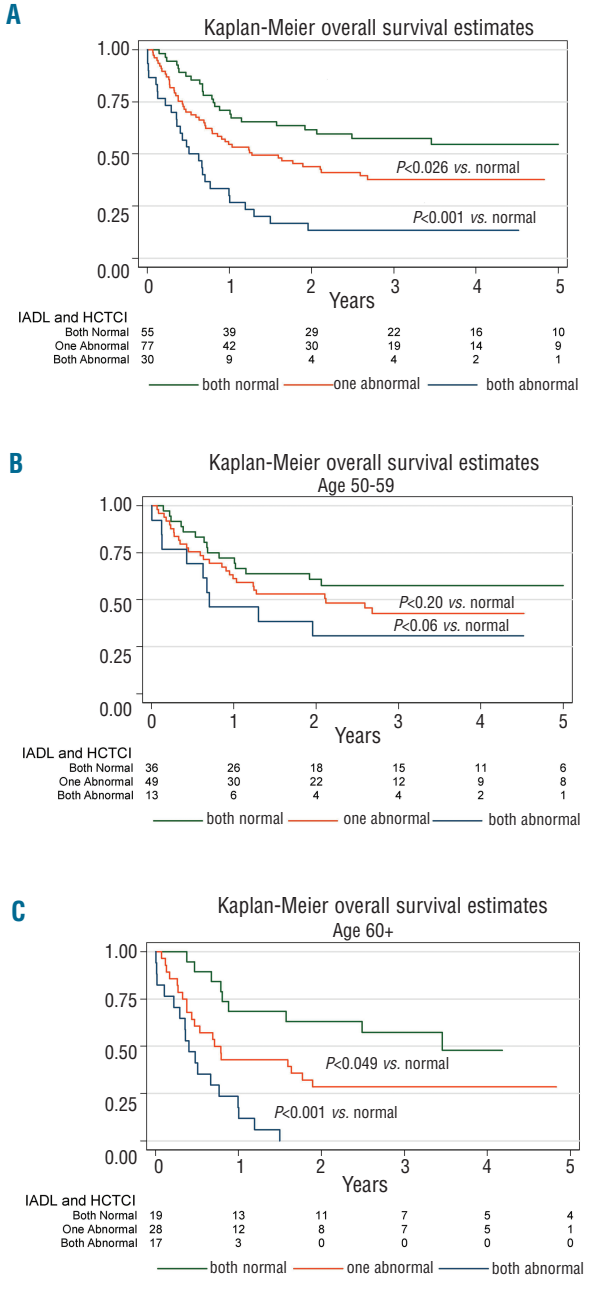

Figure 1. Overall survival by IADL and HCT-CI risk score for total cohort (A), age 50-59 years (B), and age 60-73 years (C). Abnormal IADL required at least one limitation and abnormal HCT-CI required a score of 3 or more.

Table 4. Multivariate analyses* of geriatric assessment on overall survival following allogeneic HCT, stratified by age group.

Variable	Total population			50-59 years			60-73 years		
	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
Main model variables									
Age >60	1.83	1.26-2.65	0.001	–	–	–	–	–	–
HCT-CI ≥3	1.56	1.07-2.28	0.02	1.50	0.88-2.53	0.13	1.72	0.99-2.98	0.05
Active disease at HCT	1.31	0.90-1.90	0.16	1.54	0.92-2.58	0.10	1.27	0.71-2.27	0.42
Myeloablative regimen	1.54	1.02-2.31	0.04	2.14	1.24-3.69	0.01	1.07	0.54-2.10	0.85
GA variables									
IADL impairment	2.38	1.59-3.56	<0.001	1.86	1.07-3.24	0.03	3.25	1.75-6.05	<0.001
Slow walk speed	1.80	1.14-2.83	0.01	1.16	0.60-2.28	0.66	3.27	1.68-6.39	0.001
Reduced mental health	1.67	1.13-2.48	0.01	1.55	0.92-2.62	0.10	1.87	1.01-3.49	0.04
Low albumin	1.52	0.94-2.46	0.09	1.23	0.57-2.63	0.60	2.62	1.26-5.47	0.01
High CRP	2.51	1.54-4.09	<0.001	1.89	0.94-3.79	0.07	3.13	1.52-6.46	0.002

*HR: hazard ratio; 95% CI: 95% confidence interval; GA: geriatric assessment; HCT-CI: hematopoietic cell transplantation comorbidity index; HCT: hematopoietic cell transplantation; IADL: instrumental activities of daily living; SF36-MCS: Medical Outcomes Short Form Mental Component Summary; CRP: c-reactive protein. *Each GA variable significant at P <0.10 in OS univariate analysis was modeled separately, adjusting for main model variables.*

score and no IADL limitations did quite well with 63% 2-year survival, and could be targeted for early transplant referral.

These novel results raise intriguing questions about how best to apply GA in transplant patients. First, we recommend larger confirmatory studies focusing on the GA tools most prognostic in our study such as IADL, walk speed, and self-report mental health targeting adult HCT recipients 60 years and over. Our inclusion of an inflammatory biomarker associated with aging and functional decline,[37] (i.e. CRP) in a GA is not standard. The mechanisms behind inflammation in patients prior to transplant may relate to infection, disease, hepatic dysfunction and/or dysregulated inflammation. Given the prognostic relevance, CRP warrants study not only as a simple readily available prognostic marker, but also as a target for anti-inflammatory therapeutic strategies. Widespread adoption of GA will require paring the GA down to the essential components to create GA-derived scoring systems that mirror larger geriatric oncology studies.[14,38] A validated tool should help guide physicians make appropriate transplant referrals for older adults, improve patient counseling, and provide a means to more accurately describe the health status of older adults in future transplant studies. Pending larger confirmatory studies, the IADL/HCT-CI risk score could be tested as this only requires the IADL questionnaire as the HCT-CI is routine prior to transplant.

The value of detailed health assessment by GA lies not only in predicting survival, but additionally and perhaps more importantly, in creating a transplant supportive care package targeted to GA-defined limitations. For example, unlike comorbidity, which may be difficult to modify in the peri-transplant period, impairments in both functional status and mental health may be amenable to aggressive physical therapy or strengthening psychological support, respectively. Moreover, a GA often reveals patient assets that can be leveraged to mitigate limitations. For example, strong social support can be actively engaged to facilitate functional recovery in those with functional impairment or ensure medication adherence in patients requiring medication management assistance.

There are several limitations to this study. Our decision to include patients starting from 50 years of age led to a younger cohort than that found in the typical GA study. Our findings indicate that the prognostic impact of GA impairments is pronounced in HCT recipients aged 60 years or over relative to those aged 50-59 years. In contrast to recent reports on HCT outcomes in older age,[2-4] we found older age to be adversely prognostic. This may relate to our study population, which included varying diseases, disease risk, and conditioning regimen intensities. As the largest study of GA in transplant recipients, the large number of variables prevents all clinical and GA variables to be modeled together or generation of a validation set in this study cohort. This will require a large cooperative group study. Also we could not determine whether pre-transplant limitations were derived from prior treatments (e.g. induction chemotherapy) and/or were present at diagnosis as we lacked GA data at diagnosis or serially collected. For example, the surprising association of slow walk speed to disease relapse, rather than NRM, would be clarified by confirmation in a uniform population (e.g. acute myeloid leukemia in remission) and/or walk speed measured at diagnosis. Finally, our GA did not include all domains that may be of importance, such as cognition and caregiver support. Our institution has now implemented a GA validated by Hurria and colleagues[39] that includes these potentially relevant domains.

In conclusion, this study demonstrates the potential prognostic value of geriatric assessment applied to older HCT recipients. If validated, a comprehensive health status assessment including at least some GA measures may aid transplant prognostication and patient selection, and will ultimately provide the basis for future interventions targeted at reducing transplant morbidity and mortality while maintaining the global health of older HCT recipients.

Authorship and Disclosures

Information on authorship, contributions, and financial & other disclosures was provided by the authors and is available with the online version of this article at www.haematologica.org.

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