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Longitudinal Trajectory of Frailty in Blood or Marrow Transplant Survivors: Report from the Blood or Marrow Transplant Survivor Study

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Abstract

BACKGROUND: Blood or bone marrow transplantation (BMT) survivors with frailty are at a higher risk of subsequent mortality. Longitudinal trends in the frailty state are not known and could help identify vulnerable subpopulations at risk of subsequent adverse events.

METHODS: This study included a cohort of 470 autologous and allogeneic BMT recipients who had survived ≥2 years after BMT and completed a baseline questionnaire (t1) at a median of 7.3 years after BMT and a follow-up questionnaire (t2) 13.2 years after t1. The main outcome was change in frailty state between t1 and t2. Frailty phenotype was defined as exhibiting ≥3 of the following characteristics: clinically underweight, exhaustion, low energy expenditure, slow walking speed, and muscle weakness. The following categories of change in frailty state were evaluated: worsened, improved, and stable.

RESULTS: Of the 470 participants, 36.4% were aged ≥60 years at t1, and 50.6% were men. The prevalence of frailty increased from 4.8% at t1 to 9.6% at t2. Worsening was observed in 18.8% of patients, and improvement was reported in 9.7%. Pre-BMT exposure to vincristine (odds

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AUTHOR CONTRIBUTIONS

Mukta Arora: Concept and design, integrity of data, and accuracy of data analysis; and drafting and critical revision of the article. **Yanjun Chen:** Integrity of data and data analysis and critical revision of the article. **Lindsey Hageman**, **Jessica Wu**, **Wendy Landier**, **Liton Francisco**, **Michelle Kung**, **Emily Ness**, **Alysia Bosworth**, **F. Lennie Wong**, and **Merve Pamukçuoğlu:** Administrative and technical support; acquisition, analysis, and interpretation of data; and critical revision of the article. **Daniel J. Weisdorf**, **Stephen J. Forman**, and **Saro H. Armenian:** Acquisition, analysis, and interpretation of data; and critical revision of the article. **Smita Bhatia:** Concept and design, integrity of data, and accuracy of data analysis; drafting and critical revision of the article; acquisition of funding; and supervision and administrative support.

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ratio [OR], 2.1; 95% CI, 1.3–3.39) was associated with worsening. Female sex (OR, 1.5; 95% CI, 0.93–2.4) was associated with a trend toward worsening. Pre-BMT exposure to vincristine (OR, 2.79; 95% CI, 1.44–5.43), a history of chronic graft-versus-host disease (OR, 2.58; 95% CI, 1.2–5.5), and grade 3 and 4 chronic health conditions at t1 (OR, 2.1; 95% CI, 1.08–4.33) were associated with frailty at t2.

CONCLUSIONS: In a cohort of BMT survivors who were followed longitudinally for a median of 20.6 years from BMT, the frailty status worsened for approximately20% over a 13-year timespan. BMT survivors who are at risk for worsening frailty could benefit from targeted interventions.

Keywords

cohort study; frailty; hematopoietic stem cell transplantation; longitudinal trajectory; long-term survivors

INTRODUCTION

Recent studies in young patients with cancer report a higher prevalence of frailty compared with unaffected individuals,[1–3] suggesting accelerated aging.[1,3] In our previous study, we reported that nonelderly blood or bone marrow transplantation (BMT) survivors were 8.4 times more likely to be frail compared with age-matched and sex-matched siblings. Furthermore, frail BMT survivors were at 2.7-fold higher risk of subsequent mortality compared with nonfrail survivors.[3] Although the dynamic nature of frailty has been described in community-dwelling elderly,[4,5] there is a paucity of information regarding the trajectory of frailty in BMT survivors. We addressed this gap by evaluating transitions in the frailty state over a period of 13 years in a cohort of BMT survivors enrolled in the BMT Survivor-Study (BMTSS). We hypothesized that BMT survivors have dynamic trends in frailty, and that pretransplantation, transplantation-related, and post-transplantation factors would identify subpopulations with a persistent and worsening frailty trajectory over time. This would identify patients who could benefit from interventions.

MATERIALS AND METHODS

Study Population

BMTSS is a retrospective cohort of patients who received BMT at the City of Hope, the University of Minnesota, or the University of Alabama at Birmingham between 1974 and 1998 and survived ≥2 years after transplantation. Participants completed a BMTSS questionnaire[6]; the validity of the BMTSS questionnaire to accurately report survivors' health conditions has been demonstrated.[7]

To be eligible for this report, BMT survivors had to have completed the BMTSS questionnaire between 2000 and 2004 (t1) and again between 2013 and 2017 (t2). after a median interval of 13.2 years (range, 8.5–18.8 years). Study participants were aged ≥18 years at t1. The median time was 7.3 years between BMT and t1 and 20.6 years between BMT and t2. The human subjects committees at the participating institutions approved the protocol, and informed consent was provided according to the Declaration of Helsinki.

Of the 770 t1 participants who were alive and eligible for participation at t2, 484 (63%) completed the questionnaire at t2. Frailty phenotype could not be estimated in 9 patients at t1 and 5 patients at t2, yielding 470 evaluable patients. Compared with non-participants, t2 participants were more likely to be white (86% vs 60%; $P < .0001$) and older at BMT (median age, 34 vs 28 years; $P < .0001$), were more likely to have undergone autologous BMT (43% vs 34%; $P = .02$), and were less likely to have acute leukemia or myelodysplastic syndrome (31% vs 41%; $P = .001$).

Change in Frailty State

A frailty phenotype was constructed as reported previously.[3] Briefly, frailty phenotype was defined as exhibiting ≥3 of the following characteristics: clinically underweight, exhaustion, low energy expenditure, slow walking speed, and muscle weakness. Participants who reported ≥3 of these 5 indices were classified as frail, and those who reported 1 or 2 indices were classified as prefrail. We created the following 3 categories of change in frailty state from t1 to t2: worsened (nonfrail→prefrail/frail, prefrail→frail, frail→frail), improved (frail→prefrail/nonfrail, prefrail→nonfrail), and stable (nonfrail→nonfrail, prefrail→prefrail).

Statistical Analyses

The objective of this study was to identify predictors of worsened phenotype, as well as predictors of frailty at t2, using multivariable logistic regression. The following variables were evaluated in univariate analysis: age at questionnaire (<60 vs ≥60 years), race/ethnicity (non-Hispanic whites vs other), socioeconomic status (annual household income of <$60,000 or <college-level education vs all others), smoking status (ever smoked vs never smoked), primary cancer diagnosis (acute leukemia, lymphoma, chronic myeloid leukemia, other), type of transplantation and the presence of chronic graft-versus-host disease (GvHD) (autologous BMT and allogeneic BMT without chronic GvHD vs allogeneic BMT with chronic GvHD), the use of total body irradiation (TBI) in conditioning (yes vs no), the presence of grade 3 or 4 chronic health conditions (yes vs no), the conditioning regimen used (cyclophosphamide and TBI; cyclophosphamide, etoposide, and TBI; etoposide and TBI; cyclophosphamide and etoposide; busulfan and cyclophosphamide; others), and pretransplantation therapeutic exposures (cytarabine, etoposide, vincristine, methotrexate, bleomycin, anthracyclines, alkylating agents, cisplatin, radiation). Because similar odds of frailty have been observed in survivors of allogeneic hematopoietic stem cell transplantation (HCT) without chronic GvHD and survivors of autologous HCT,[3] the 2 were combined into 1 group for the analysis (autologous BMT and allogeneic BMT without chronic GvHD vs allogeneic BMT with chronic GvHD). Variables that were significant in the univariate analysis at $P < .1$ were included in the multivariable analysis using backward selection. Results of the final adjusted model are presented. Two-sided tests with $P < .05$ were considered statistically significant. Analyses were performed using SAS software version 9.4 (SAS Institute Inc).

RESULTS

Demographic and clinical characteristics of the 470 study participants are provided in Table 1. The median time was 7.3 years between transplantation and t1 and 20.6 years between transplantation and t2. The median age at HCT was 34 years (range, 0–61 years) and was 42.9 years (range, 18.5–67.4 years) at t1 and 56.5 years (range, 31.0–80.0 years) at t2. Overall, 49.4% of participants were women, 85.3% were non-Hispanic whites, 48.5% had a college-level education or greater, 43% had an annual household income ≤$60,000, and 34.7% reported current or past smoking. In total, 57.7% of participants underwent allogeneic HCT. Among the allogeneic HCT recipients, 15.7% reported chronic GvHD. Pre-HCT receipt of vincristine was reported by 40.6% and 76.8% of participants received TBI-based conditioning.

Prevalence of Frailty and Prefrailty

Although the prevalence of prefrailty was comparable between t1 (13.8%) and t2 (16.1%; P = .4), the prevalence of frailty increased from 4.8% at t1 to 9.6% at t2 (P = .03) (Fig. 1A). Worsening was observed in 18.8% of survivors, whereas improvement was observed in 9.7% (Fig. 1B).

Predictors of Worsened Frailty Status

In multivariable analysis, survivors who had pre-BMT exposure to vincristine (reference category, no vincristine exposure) were at 2.1 times higher odds (95% CI, 1.3–3.39; P = .002) of worsening. Women exhibited a trend toward higher odds of worsening compared with men (odds ratio [OR], 1.5; 95% CI, 0.93–2.4; P = .09) (Table 2).

Predictors of Frailty at t2

Allogeneic BMT recipients with chronic GvHD (OR, 2.58; 95% CI, 1.21–5.5; P = .01; reference category, autologous BMT/allogeneic BMT without chronic GvHD), those with grade 3 and 4 chronic health conditions (OR, 2.1; 95% CI, 1.01–4.33; P = .04; reference category, grade 0–2 chronic health conditions), and those with pre-BMT exposure to vincristine (OR, 2.79; 95% CI, 1.44–5.43; P = .002; reference category, no vincristine exposure) were at higher odds of frailty at t2 (Table 2). Next, we evaluated the domains of frailty in participants with and without prior exposure to vincristine. Three domains—weakness (6.4% vs 2.2% in those with or without exposure to vincristine, respectively; P = .02), exhaustion (43.5% vs 34.7%, respectively; P = .05), and low energy expenditure (40.8% vs 30.3%, respectively; P = .02)—were more prevalent in participants who had prior exposure to vincristine.

DISCUSSION

In our study, the prevalence of frailty doubled among BMT survivors over a period of 13 years. Furthermore, almost 20% of survivors demonstrated worsening over this period. Patients who had prior exposure to vincristine were at a higher odds of worsening. Women showed a trend toward higher odds of worsening. Nonetheless, approximately 74% of patients were not frail or prefrail at t2. Placing these findings in the context of the higher

risk of subsequent mortality among frail BMT survivors indicates an urgent need for early identification and intervention[8–11] to mitigate adverse events.

Sex differences in frailty phenotype have been described previously in community-dwelling[12,13] and cancer populations.[1] The etiology remains unclear, but differential influences on muscle mass by sex hormones has been postulated.[1] We also identified an association between grade 3 and 4 chronic health conditions at t1 and the subsequent development of frailty at t2. It has been demonstrated that the presence of serious chronic health conditions adversely affects physical characteristics that may result in frailty.[1,14]

We did not observe an effect of age on frailty. In contrast, in a large, community-dwelling younger cohort (n = 493,737; aged 37–73 years), it was observed that the prevalence of frailty increased with age (from 3% to 5% in women and from 2% to 5% in men).[15] This supports the hypothesis that therapeutic exposures and post-BMT complications constitute a substantial stressor, placing younger BMT survivors at higher risk for frailty.[3]

To our knowledge, this is the first study to identify pre-BMT exposure to vincristine as a risk factor for a worsening or persistent frailty state. The prevalence of frailty was 14.5% versus 6.2% ($P = .003$) in participants who had pre-BMT exposure to vincristine versus those without vincristine exposure. Prior exposure to vincristine was more frequent in patients with acute lymphocytic leukemia and lymphoma. We also evaluated frailty characteristics in patients who were exposed to vincristine versus those who were not exposed and observed a higher prevalence of weakness, low energy expenditure, and exhaustion in those with prior exposure to vincristine. This likely represents the sequelae of vincristine-related neuropathy/muscle weakness leading to low energy expenditure in these patients, presenting yet another opportunity for intervention.

The current study identifies vulnerable populations at higher risk for subsequent frailty, providing evidence for targeted intervention even before the onset of frailty. These interventions may be in the form of physical therapy, exercise, and nutrition, preferably as individually tailored, multicomponent interventions.[16]

This study needs to be placed within context of its limitations. Our study design required patients to be alive at t1 and t2 and thus could be subject to survival bias. Therefore, the prevalence of worsening may be underestimated. This possibly could be evaluated in a prospective cohort with timed and frequent measurements of frailty status. We did not evaluate predictors of improvement in frailty status because of the smaller numbers in this group (9.7%). This study is limited by the relatively small number of events; therefore, the associations need to be interpreted with caution. Also, although we previously demonstrated[7] that there is concordance between outcomes abstracted from medical records and self-reported outcomes, these analyses relied on self-reported measures, which are subject to reporting and recall bias. There are differences between our constructs and the clinical constructs used by Fried et al.[13] Details of our construct[3] compared with the construct by Fried et al[13] are included in our prior report and are included in Table 3. Furthermore, our cohort included patients who underwent transplantation between 1974 and 1998. There have been significant changes in transplantation strategies over the past 2

decades. Thus, although it is important to study and report on survivors who were followed for an extended period, changes in practice necessitate the assessment of patients who undergo transplantation in the contemporary era as well.[3]

In a cohort of patients followed longitudinally for a median of 20.6 years after BMT, with measurement of frailty state at 2 timepoints 13.2 years apart, we observed worsening in approximately 20% of the patients. The current results identify high-risk subpopulations that could benefit from targeted interventions.[14,17]

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CONFLICTS OF INTEREST DISCLOSURES

Mukta Arora reports grants from Pharmacyclics, Kadmon, and Syndax and personal fees from Fate Therapeutics, outside the submitted work. Daniel J. Weisdorf reports grants from Incyte and personal fees from FATE Therapeutics, outside the submitted work. Stephen J. Forman reports grants and other support from Mustang Bio outside the submitted work and is a member of the board of Lixte Biotechnology. The remaining authors made no disclosures.

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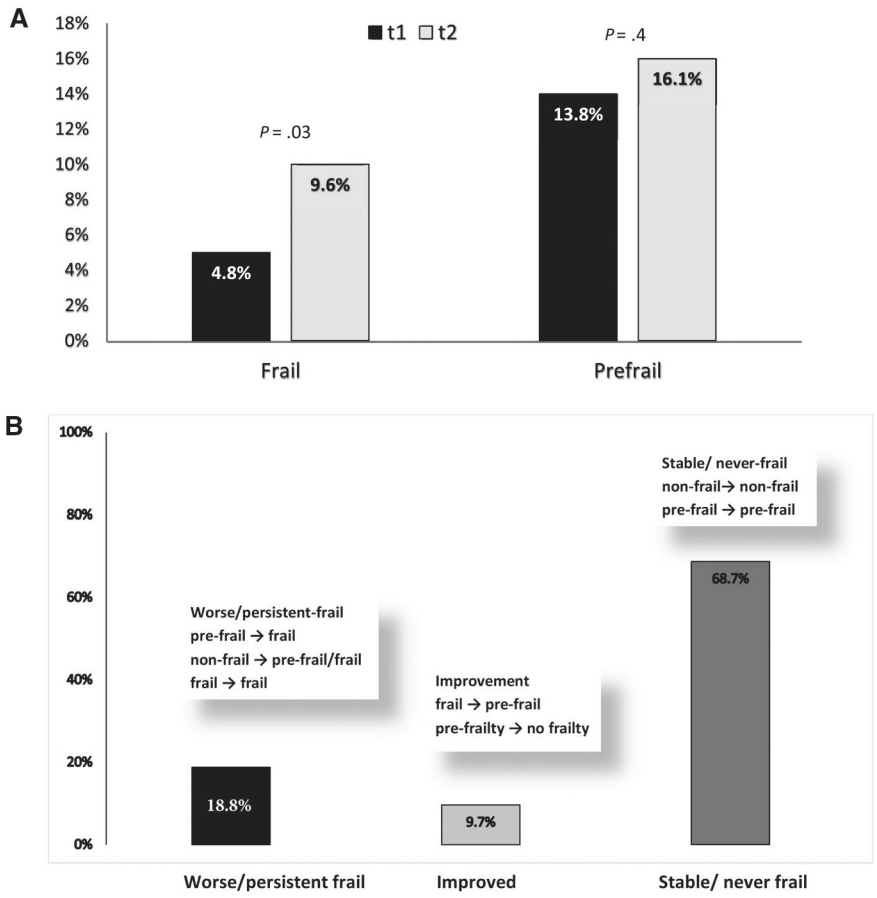

Figure 1.

(A) The prevalence of frailty and prefrailty at t1 (the time of the baseline questionnaire) and t2 (the time of the follow-up questionnaire) is illustrated along with (B) the change in frailty status over time.

TABLE 1.

Demographic and Clinical Characteristics of the 470 Study Participants

Characteristic	No. of Participants (%)
Age at questionnaire, y	
<40	46 (9.8)
40–59	253 (53.8)
≥60	171 (36.4)
Diagnosis	
Acute myeloid leukemia	109 (23.2)
Acute lymphoid leukemia	39 (8.3)
Chronic myelogenous leukemia	117 (24.9)
Non-Hodgkin lymphoma/Hodgkin lymphoma	137 (29.8)
Other diagnoses[a]	68 (14.0)
Sex	
Men	238 (50.6)
Race/ethnicity	
Non-Hispanic White	401 (85.3)
Type of transplantation	
Autologous	199 (42.6)
Allogeneic	271 (57.7)
Presence of chronic GvHD (among allogeneic BMT recipients)	
Allogeneic BMT with chronic GvHD	74 (15.7)
Education[b]	
≤High school	70 (14.9)
Some college/training	171 (36.4)
≥College	228 (48.5)
Annual household income[b]	
≤$60,000	202 (43)
Ever smoker[b]	
Yes	163 (34.7)
Conditioning regimen	
Cyclophosphamide + TBI	181 (38.5)
Cyclophosphamide + TBI + etoposide	111 (23.6)
Etoposide + TBI	50 (10.6)
Cyclophosphamide + etoposide	39 (8.3)
Busulfan + cyclophosphamide	36 (7.7)
Other	53 (11.3)
TBI	
Yes	361 (76.8)
Pre-BMT chemotherapy	
Anthracycline	280 (61.1)

Characteristic	No. of Participants (%)
Steroid	207 (45.2)
Vincristine	186 (40.6)
Alkylating agents	184 (40.2)
Cytarabine	174 (37)
Methotrexate	101 (22.1)
Etoposide	70 (15.3)
Bleomycin	63 (13.8)
Cisplatin	44 (9.6)
Pre-BMT radiation	
Yes	73 (15.9)

Abbreviations: BMT, blood or bone marrow transplantation; GvHD, graft-versus-host disease; TBI, total body irradiation.

[a]Other diagnoses included aplastic anemia (n = 23), multiple myeloma (n = 17), breast cancer (n = 11), chronic lymphocytic leukemia (n = 7), adrenoleukodystrophy (n = 3), Ewing sarcoma (n = 1), neuroblastoma (n = 10), Hurler syndrome (n = 1), severe combined immunodeficiency (n = 1), severe osteopetrosis (n = 1), Fanconi anemia (n = 1), and systemic sclerosis (n = 1).

[b]Data were missing for the variables education (n = 1), annual household income (n = 29), and ever smoker (n = 4).

TABLE 2.

Predictors of Frailty: Univariate and Multivariate Analyses

	Univariate Analysis		Multivariate Analysis	
Predictor	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
Worsened				
Age at questionnaire, y				
≥60 vs <60	1.25 (0.78–1.99)	.35		
Race/ethnicity				
Other vs non-Hispanic White	1.02 (0.45–2.29)	.97		
Socioeconomic status				
Annual income <$60,000/<college level vs annual income ≥$60,000/≥college level	1.25 (0.74–2.12)	.40		
Time between first and second questionnaire	0.95 (0.82–1.11)	.54		
Smoking status				
Ever smoked vs never smoked	0.97 (0.60–1.56)	.90		
Sex				
Men	1.00		1.00	.09
Women	1.31 (0.83–2.08)	.12	1.5 (0.93–2.4)	
Primary cancer diagnosis				
Acute leukemia	1.00			
Lymphoma	1.04 (0.59–1.81)	.90		
Chronic myeloid leukemia	0.47 (0.23–0.93)	.03		
Other	1.21 (0.6–2.42)	.60		
Conditioning regimen				
Cyclophosphamide + TBI	1.00			
Cyclophosphamide + TBI + etoposide	1.41 (0.79–2.53)	.24		
Etoposide + TBI	1.02 (0.45–2.3)	.97		
Cyclophosphamide + etoposide	1.39 (0.6–3.2)	.44		
Busulfan + cyclophosphamide	1.54 (0.66–3.59)	.32		
Others	0.59 (0.23–1.5)	.27		
TBI, yes vs no	0.94 (0.55–1.6)	.81		
Chronic GvHD at t1				

Predictor	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Allogeneic BMT with chronic GvHD vs allogeneic BMT with no chronic GvHD or autologous BMT	1.43 (0.79–2.57)	.24		
Pre-BMT therapeutic exposure, yes vs no				
Vincristine	1.95 (1.22–3.11)	< .005	2.1 (1.3–3.39)	.002
Cytarabine	1.01 (0.63–1.62)	.98		
Etoposide	1.27 (0.69–2.35)	.44		
Methotrexate	1.03 (0.59–1.79)	.92		
Bleomycin	1.35 (0.72–2.54)	.35		
Anthracyclines	1.8 (1.09–2.99)	.02		
Alkylating agents	0.96 (0.6–1.55)	.88		
Cisplatin	0.76 (0.33–1.77)	.53		
Radiation	1.58 (0.88–2.83)	.13		
Grade 3–4 conditions at t1, yes vs no	1.24 (0.68–2.25)	.48		
Frailty at t2				
Age at questionnaire, y				
≥60 vs <60	1.19 (0.63–2.22)	.60		
Race/ethnicity				
Other vs non-Hispanic White	1.02 (0.35–3.01)	.97		
Socioeconomic status				
Annual income <$60,000/<college level vs annual income ≥$60,000/≥college level	1.14 (0.56–2.31)	.72		
Time between BMT and questionnaire: t2	1.01 (0.96–1.07)	.71		
Smoking status				
Ever smoked vs never smoked	1.11 (0.58–2.13)	.75		
Sex				
Men				
Women	1.13 (0.61–2.09)	.70		
Primary cancer diagnosis				
Acute leukemia	1.00			
Lymphoma	1.0 (0.48–2.08)	0.99		
Chronic myeloid leukemia	0.44 (0.17–1.15)	.09		
Other	1.05 (0.41–2.68)	.91		

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Predictor	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Conditioning regimen				
Cyclophosphamide + TBI				
Cyclophosphamide + TBI + etoposide	1.06 (0.48–2.36)	.88		
Etoposide + TBI	0.84 (0.27–2.62)	.76		
Cyclophosphamide + etoposide	1.42 (0.49–4.11)	.52		
Busulfan + cyclophosphamide	1.93 (0.75–5.29)	.20		
Others	0.38 (0.08–1.69)	.20		
TBI, yes vs no	0.81 (0.4–1.64)	.56		
Chronic GvHD at t1				
Allogeneic BMT with no chronic GvHD or autologous BMT	1.00		1.00	.01
Allogeneic BMT with chronic GvHD	2.39 (1.19–4.81)	.01	2.58 (1.21–5.5)	
Chronic health conditions at t1				
Grade ≤2	1.00		1.00	.04
Grade 3 or 4	2.14 (1.08–4.26)	.03	2.1 (1.02–4.33)	
Pre-BMT therapeutic exposure, yes vs no				
Cytarabine	0.83 (0.43–1.6)	.58		
Etoposide	0.86 (0.35–2.13)	.75		
Methotrexate	1.04 (0.5–2.19)	.91		
Bleomycin	1.45 (0.64–3.28)	.38		
Anthracyclines	1.26 (0.65–2.41)	.50		
Alkylating agents	1.03 (0.55–1.95)	.92		
Cisplatin	0.94 (0.32–2.75)	.90		
Radiation	1.89 (0.91–3.94)	.09		
Vincristine, yes vs no	2.55 (1.35–4.82)	.004	2.79 (1.44–5.43)	.002

Abbreviations: BMT, blood or bone marrow transplantation; GvHD, graft-versus-host disease; t1, the time of the baseline questionnaire (a median of 7.3 years after BMT); t2, the time of the follow-up questionnaire (a median of 13.2 years after BMT); TBI, total body irradiation.

TABLE 3.

Frailty Phenotype

Indices	BMTSS Questionnaire	Code[a]	Fried Criteria (Fried 2001[13])	Code[a]
Low lean muscle mass	BMI calculated from self-reported weight and height (kg/m^2)	1 = <18.5 kg/m^2, 0 = ≥18.5 kg/m^2	Unintentional weight loss in prior y	1 = ≥10 lbs or loss of ≥5% of body weight
Exhaustion	BMI 18 kg/m^2: "Feeling weak in parts of your body"	0 = Not at all or a little bit; 1 = moderate, quite a bit, or extremely	CES-D scale: Two possible questions, "How often in the last week did you feel this way:" 1) "I felt that everything I did was an effort" and 2) "I could not get going"	0 = Rarely or none of the time (<1 d), 1 = some or a little of the time (1–2 d), 2 = moderate amount of the time (3–4 d), or 3 = most of the time (1 = participants answering "2" or "3")
Low energy expenditure	"On how many of the past 7 d did you exercise or do sports at least 20 min that made you sweat or breathe hard (eg, dancing, jogging, basketball etc)"	1 = <2 d; 0 = ≥2 d	Based on the short version of the Minnesota Leisure Time Activity questionnaire, asking about activities and sports; Kcals per wk expended are calculated using standardized algorithm	*Men:* 1 = <383 Kcals of physical activity per wk; *Women:* 1 = <270 Kcals of physical activity per wk
Slowness	"Over the last 2 y, how long (if at all) has your health limited you in: 1) walking uphill or climbing a few flights of stairs; 2) walking 1 block	1 = Either item limited >3 mo; 0 = other	Time to walk 15 feet	*Men:* 1 = height ≤173 cm, ≥7 s or height >173 cm, ≥6 s; *Women:* 1 = height ≤159 cm, ≥7 s or height >159 cm, ≥6 s
Weakness	Weakness or inability to move arm(s)	1 = Yes, 0 = no	Grip strength	Cutoff for grip strength (kg): *Men:* BMI ≤24 kg/m^2, ≤29-kg cutoff; BMI 24.1–26 kg/m^2, ≤30-kg cutoff; BMI 26.1–28 kg/m^2, ≤30-kg cutoff; BMI >28 kg/m^2, ≤32-kg cutoff; *Women:* BMI ≤23 kg/m^2, ≤17-kg cutoff; BMI 23.1–26 kg/m^2, ≤17.3-kg cutoff; BMI 26.1–29 kg/m^2, ≤18-kg cutoff; BMI >29 kg/m^2, ≤21-kg cutoff (*1 = grip strength ≤ cutoff*)

Abbreviations: BMT, bone marrow transplantation; BMTSS, BMT Survivor Study; BSI, Brief Symptom Inventory; CES-D, Center for Epidemiological Studies-Depression Scale.

[a]Score ≥3 = frail; score 1 or 2 = prefrail.