

Musculoskeletal Symptoms in Long-term Cancer Survivors

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Background

- Musculoskeletal symptoms are some of the most common problems detected in long-term cancer survivors.
- These problems persist even when overall physical function has recovered.
- Limited research exists on risk factors for these symptoms.
- Of particular interest in survivorship investigations is the relationship between muscle weakness and lack of stamina/fatigue because it is consistently the most prevalent long-term health complications reported in survivorship studies across diagnoses.

Objectives

In a Cross-sectional Design: Determine rates and risk factors for musculoskeletal symptoms in a long-term cohort of survivors of hematopoietic stem cell transplant (HSCT) after reducing the confounding effects of the natural aging process.

Hypothesis 1: A majority of survivors will indicate at least weekly moderate-severe musculoskeletal symptoms.

Hypothesis 2: Risk factors for musculoskeletal symptoms will include: female, older age, longer time since transplant, number of treatment cycles prior to HSCT, higher doses of TBI, more comorbidities, chronic graft versus host disease (GVHD), and diseases or medications known to cause musculoskeletal symptoms.

Methods

PARTICIPANTS

Inclusion criteria:

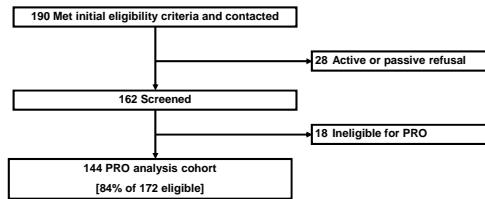
- HSCT survivors between 5-20 years post transplant
- Current age 18 to 49 when first contacted
- Transplanted for hematologic malignancy or pre-malignancy
- Residing in the Western Washington region

Exclusion criteria:

- Unable to complete assessments in English
- Received second transplant
- In active treatment for cancer during the past 2 years, except for basal or squamous cell skin cancer

PROCEDURE

- Eligible local survivors were recruited for a study on muscles, joints, and bones.
- The flow diagram below indicates participants eligible, screened and enrolled in the study.



MEASURES

- Muscle Joint and Bone (MJB) measure**
 - Muscle cramps, muscle weakness, muscle aches or stiffness (myalgias), joint aches or stiffness (arthralgias)
- Comorbidity Index (Katz PRO version of Charlson Comorbidity Index)**
- Short Form-36 Health Survey, version 2 (SF-36) component and mental component summary scales**
- Fatigue Symptom Inventory (FSI)**
- Western Ontario and MacMaster Universities Osteoarthritis Index (WOMAC)**
- Godin Leisure-Time Exercise Questionnaire (Physical activity)**

Results

Table 1. Demographic and medical characteristics

Age, M ± SD		39.6 ± 8.9
Gender, n (%)		
	Male	76 (53)
Ethnicity, n (%)		
	Hispanic	7 (4)
	Not Hispanic	137 (95)
Race, n (%)		
	Caucasian	130 (90)
	Asian American	4 (3)
	African American	1 (1)
	Other	9 (6)
Educational Attainment, n (%)		
	≤ High school degree	26 (19)
	2 year college or trade	76 (52)
	≥ 4 year college	42 (29)
Income, n (%)		
	<\$40,000	46 (32)
	\$40,000-\$79,999	32 (22)
	>\$80,000	59 (41)
	Not Reported	7 (5)
Marital Status, married n (%)		84 (58)
Diagnosis and stage, n (%)		
	Lymphoma	43 (30)
	Chronic Myeloid Leukemia	42 (29)
	Acute Non-lymphocytic Leukemia	32 (21)
	Acute Lymphocytic Leukemia	12 (8)
	Myelodysplastic Syndromes	11 (8)
	Multiple Myeloma	3 (2)
Type of transplant, n (%)		
	Myeloablative allogeneic, related	58 (41)
	Myeloablative allogeneic, unrelated	46 (31)
	Myeloablative autologous	40 (28)
Total Body Irradiation, n(%)		
	0-200 cGy	51 (35)
	800-1200 cGy	54 (38)
	1320-1575	39 (27)
cGVHD History; Yes, N (%)		60 (42)
Years post-transplant, M ± SD		11.2 (4.7)

Table 2. Patient Reported Outcomes

PRO	M, SD
Comorbidity Index	1.0 (2.0)
SF-36 Physical Component	50.0 (9.4)
SF-36 Mental Component	49.4 (10.0)
Fatigue Symptom Inventory	2.7 (1.9)
WOMAC	5.0 (14.2)
Physical Activity, Minutes/Week	180.0 (493.8)

Scores on the SF-36 indicate generally good health in this cohort with few major co-morbidities.

Figure 1. Musculoskeletal Symptoms and Severity of Long-Term Survivors

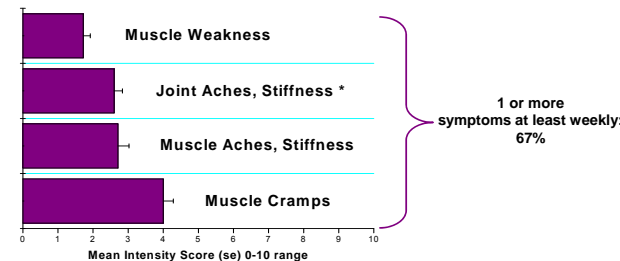


Table 3. Logistic regression final models for hypothesized risk factors for musculoskeletal symptoms

MJB Subscale	Odds Ratio	P-value
Joints		
Ongoing oral chronic GVHD medication (No is the referent)	5.81	.008
Diabetes (No is the referent)	3.99	.03
Muscle Aches		
Avascular necrosis (No is the referent)	3.88	.01
Muscle Weakness		
Ongoing oral chronic GVHD medication (No is the referent)	10.03	.001
Diabetes (No is the referent)	6.58	.005
Muscle Cramps		
Age at assessment (<40 is referent)	4.07	.002
Risk (Low is referent)		.04
Intermediate	3.81	.01
High	2.95	.05
Avascular necrosis (No is the referent)	4.08	.005
Diabetes (No is the referent)	4.15	.04

Avascular necrosis rate: 25%

Medication for diabetes rate: 11%

Limitations & Strengths

- The sample size was relatively small.
- Other limitations include:
 - We enrolled only local survivors transplanted at the Fred Hutchinson Cancer Research Center. Transplant center differences may explain some of the inconsistencies found between studies of these long-term survivors.
- Strengths include:
 - High participation rates.
 - Used standardized measures with population norms or specific to survivor symptoms.

Conclusions

- Hypothesis 1 was supported as a majority of survivors reported musculoskeletal symptoms at least weekly (67%).
- Hypothesis 2 was not fully supported and depended on the type of musculoskeletal symptom.
 - Joints and muscle weakness have the same risk factors and were different from muscle aches and cramps.
- Musculoskeletal symptoms do not resolve with time.
- However, overall physical health was consistent with general population norms.
- Musculoskeletal symptoms in these survivors require further investigation.
 - Factors related to musculoskeletal symptoms require biomarker and behavioral testing to determine mechanisms.
 - Studies indicate that exercise improves muscles in cancer survivors. Other behavioral interventions that address physical activity are needed that go beyond just assessing PRO outcomes and include an investigation of biomarkers.

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