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### Authors

Rosenthal, Emily A  
Ho, Pei-Shu  
Joe, Galen O  
et al.

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## Motor ability, function, and health-related quality of life as correlates of symptom burden in patients with sclerotic chronic graft-versus-host disease receiving imatinib mesylate

Emily A. Rosenthal<sup>1</sup>, Pei-Shu Ho<sup>1</sup>, Galen O. Joe<sup>1</sup>, Sandra A. Mitchell<sup>2</sup>, Susan Booher<sup>3</sup>, Steven Z. Pavletic<sup>4</sup>, Kristin Baird<sup>4,5</sup>, Edward W. Cowen<sup>6</sup>, Leora E. Comis<sup>1</sup>

<sup>1</sup>Rehabilitation Medicine Department, Clinical Center, National Institutes of Health, MSC 1604, 10 Center Drive, Bethesda, MD 20892, USA

<sup>2</sup>Outcomes Research Branch, Division of Cancer Control and Population Sciences, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA

<sup>3</sup>Autoimmunity and Mucosal Immunology Branch, Division of Allergy, Immunology and Transplantation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Rockville, MD, USA

<sup>4</sup>Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA

<sup>5</sup>Office of Tissues and Advanced Therapies, Center for Biologics Evaluation and Research, Food and Drug Administration, Silver Spring, MD, USA

<sup>6</sup>Dermatology Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, USA

### Abstract

**Purpose**—To explore improvement in motor ability, function, health-related quality of life (HRQOL), and symptom severity in patients with sclerotic chronic graft-versus-host disease (ScGVHD) in response to treatment as well as the relationship among changes on such measures.

**Methods**—This study was a secondary analysis of data from 13 individuals with severe ScGVHD enrolled in a clinical trial evaluating the efficacy of imatinib mesylate ([clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT00702689) identifier: NCT00702689). Self-reported, clinician-reported, and performance-based indicators of motor ability, function, HRQOL, and symptom severity were assessed at baseline and 6 months following the administration of imatinib mesylate.

**Results**—Participants did not show statistically significant improvement on any measures over time. Approximately one-third of patients displayed clinically significant improvement on

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Leora E. Comis, [comisl@cc.nih.gov](mailto:comisl@cc.nih.gov).

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**Compliance with ethical standards** The protocol was approved by the National Cancer Institute Institutional Review Board.

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measures of motor ability (palmar pinch strength, dominant hand, 30.8%), functioning (Manual Ability Measure—36, 41.7%), HRQOL (Short Form 36 [SF-36] Mental Component Summary, 33.3%), and symptom severity (Lee Symptom Scale, 38.5%). Improvement in cGVHD symptom burden was correlated with improvement in function (Assessment of Motor and Process Skills [AMPS] and Disabilities of the Arm, Shoulder, and Hand [DASH] scores) and HRQOL (SF-36 Physical Component Summary scores).

**Conclusions**—Findings suggest the potential utility of administering patient-reported and performance-based functional measures, such as the DASH and the AMPS, to patients with cGVHD. By understanding the functional consequences of ScGVHD, interdisciplinary teams of health care providers, including rehabilitation professionals, can work to improve long-term outcomes.

### Keywords

Chronic graft-versus-host disease; Sclerosis; Functional impairment; Symptom burden; Health-related quality of life; Allogeneic hematopoietic stem cell transplantation

## Introduction

Worldwide, approximately 30,000 allogeneic hematopoietic stem cell transplants are performed each year to combat various hematologic diseases, around 87% of which are malignant [1]. Chronic graft-versus-host disease (cGVHD) is a common complication, affecting around half of allogeneic hematopoietic stem cell transplant survivors [2–4]. The disease occurs when the donor's immune cells iatrogenically respond to the recipient's tissues after identifying them as foreign. Chronic GVHD can manifest in one or more organs, including the skin, mouth, eyes, gastrointestinal tract, liver, lungs, joints/ fascia, and genitals [5]. The disease is associated with an inability to maintain employment [6], functional impairment [3], poor health-related quality of life (HRQOL) [6, 7], high symptom distress [4], and heightened risk of non-relapse mortality [2].

The sclerotic form of chronic graft-versus-host disease (ScGVHD) is a manifestation of skin cGVHD characterized by deep and superficial sclerosis [5] that appears in 15–23% of patients with cGVHD [8–10]. Compared to individuals with non-sclerotic cGVHD, patients having ScGVHD are likely to experience physical limitations [11], poor HRQOL [12], and a prolonged course of immunosuppressive therapy [10].

In order to improve the diagnosis, assessment, and treatment of cGVHD, there have been efforts to standardize outcome measurement in observational and drug efficacy trials. The 2014 National Institutes of Health (NIH) Consensus Development Project established recommendations for the diagnosis and severity scoring of cGVHD [5], as well as for the provision of ancillary and supportive care to patients with the disease [13]. In addition, these recommendations advocate for the use of a standard set of patient- and clinician-reported measures of HRQOL and disease severity to assess therapeutic response in this patient population [14]. Self-reported measures of symptom burden, cGVHD symptom severity, and HRQOL are associated with clinician-reported cGVHD severity [12, 15] and performance-based measures of motor ability [16]. However, none of the aforementioned indicators of

clinical response evaluates activities of daily living (ADL) performance and/or disability. Adding self-reported and/or performance-based measures of functional impairment may allow clinicians to more fully characterize the impact of cGVHD on daily life and more effectively target treatment and rehabilitative efforts.

The inclusion of functional measures may be especially valuable in the context of cGVHD drug efficacy trials. Patients often fail to respond to the first line of systemic immunosuppressive therapy commonly used to alleviate cGVHD manifestations [10]. Given the ineffectiveness of traditional salvage therapy for many patients with ScGVHD in particular [9], imatinib mesylate has been investigated for its potential anti-fibrotic benefit. In preclinical models, imatinib mesylate inhibited platelet-derived growth factor and transforming growth factor  $\beta$ , both of which are implicated in the pathogenesis of fibrosis and systemic sclerosis [17]. Therefore, researchers have explored clinical response to the drug among patients with ScGVHD, though such researchers have typically not studied how treatment may influence the performance of ADLs [18–20].

In 2015, Baird and colleagues published a study investigating the degree to which imatinib mesylate improved range of motion (ROM) among patients with severe ScGVHD [19]. The authors found that 84% of patients (sample  $n = 13$ ) displayed some improvement in ROM over a 6-month period. This was categorized as a partial response for 38.5% of patients and as stable disease for the remaining 45.5% of patients. The present study extends upon the findings of Baird et al. in a secondary analysis of the motor, functional, and HRQOL outcomes.

The objectives of this study were twofold. First, we explored whether administering imatinib mesylate to patients with ScGVHD was associated with improvements in motor ability, function, HRQOL, and cGVHD symptom severity. Given that most patients displayed improved ROM in response to imatinib mesylate [19], we predicted that patients would also experience statistical and clinical improvement in these areas. Second, we investigated whether changes in cGVHD symptom severity were associated with changes in motor ability, function, and HRQOL. We hypothesized that improvement in clinician-rated symptom severity and patient-reported cGVHD symptom burden would be related to motor, functional, and HRQOL gains.

## Methods

This study was a secondary analysis of data from a single-arm prospective clinical trial investigating the efficacy of imatinib mesylate for patients with treatment-refractory ScGVHD ([clinicaltrials.gov](https://clinicaltrials.gov) identifier: [NCT00702689](https://clinicaltrials.gov/ct2/show/study/NCT00702689)) [19]. The protocol was approved by the National Cancer Institute Institutional Review Board. Participants were primarily recruited from the NIH Natural History Study of cGVHD ([clinicaltrials.gov](https://clinicaltrials.gov) identifier: [NCT00092235](https://clinicaltrials.gov/ct2/show/study/NCT00092235)). Individuals who met the 2005 NIH Consensus Group Criteria for ScGVHD [21] who agreed to participate in the study were enrolled at the NIH between December 2008 and February 2011. Data were collected at baseline, 3 months, and 6 months following the initiation of treatment. Six months was the primary endpoint of interest.

Eligibility criteria included biopsy-confirmed ScGVHD resulting in ROM deficits ≥ 25% in one or more joints [22], lack of cGVHD response to systemic corticosteroids or reliance on such medication to maintain stable disease, Karnofsky Performance Status Scale score < 60%, and age < 4 years. Exclusion criteria included pregnancy; concurrent receipt of other investigational agents; and residual/recurrent or relapsed metastatic disease. Baird and colleagues have reported detailed information on inclusion and exclusion criteria as well as dose escalation for this study [19].

## Measures

Indicators of motor ability included the Jebsen-Taylor Hand Function Test (JTHFT), Grooved Pegboard Test (GPT), pinch strength, grip strength, and 2 Minute Walk Test (2MWT). The Disabilities of the Arm, Shoulder, and Hand (DASH); Human Activity Profile (HAP); Assessment of Motor and Process Skills version 7 (AMPS); and Manual Ability Measure (MAM-36) evaluated functional impairment. The Short-Form 36 version 2 (SF-36) measured HRQOL. Chronic GVHD symptom severity was assessed using the Lee Symptom Scale and Provider Global Rating (PGR).

A physiatrist assessed grip strength and 2MWT performance. A trained occupational therapist administered the AMPS, JTHFT, GPT, and pinch strength. A transplant oncologist with expertise in cGVHD completed the PGR. The same providers administered assessments at all time points and for all patients.

**Motor ability**—The JTHFT is a performance-based assessment of manual ability [23]. Scores reflect the time patients require to perform seven functional tasks with each hand. The GPT is a performance-based measure of motor speed and manual dexterity [24]. Participants are timed as they unilaterally insert grooved pegs into a 5 × 5 peg board. The 2MWT is a performance-based measure of physical ability that records the distance patients walk over the course of 2 min [25]. Grip strength was measured three times in the dominant hand using a dynamometer. Performance was then averaged across trials [26]. Key, Palmar, and Tip-to-Tip pinch strength were assessed in both hands using a pinch gauge [26].

**Functional impairment**—The DASH is a 30-item self-reported measure of upper extremity function, symptoms, and disability [27]. Scores range from 0 to 100, with higher scores indicating greater disability. The HAP is a 94-item self-reported measure of energy expenditure and physical fitness that produces a Maximum Activity Score (MAS) and an Adjusted Activity Score (AAS), which can range from 0 to 94 [28]. This measure has been validated for use in patients with cGVHD [29]. The AMPS is a performance-based assessment of the quality of one's ADL performance [30]. After observing patients complete two ADL tasks, a trained occupational therapist rates performance on a 36-item scale, producing ADL motor skill and ADL process skill scores in logit units. The MAM-36 is a self-reported measure assessing the ease with which individuals can perform common daily activities that require the use of one or both hands [31]. Scores on this 36-item scale range from 0 to 100, with higher scores indicating greater manual ability.

**Health-related quality of life**—The SF-36 is a validated 36-item self-reported measure of general HRQOL [32]. This instrument assesses eight domains of physical and mental health: physical functioning, physical role functioning, bodily pain, perceptions of general health, vitality, social functioning, emotional role functioning, and mental health. Subscales are used to create Physical Component Summary (PCS) and Mental Component Summary (MCS) scores expressed as T-scores based on population norms, with a population mean of 50 and standard deviation of 10.

**cGVHD symptom severity**—The Lee Symptom Scale is a 30-item self-reported assessment of cGVHD-specific symptom burden [33]. This measure captures the extent the respondent is bothered by skin, eye/mouth, muscle/joint, nutrition, lung, energy, and psychological cGVHD symptoms. Responses are summed and linearly transformed to create summary scores that range from 0 to 100. Higher scores indicate greater cGVHD symptom burden. The validity and reliability of this measure have been established in patients with cGVHD [33]. For PGR scores, physicians rate the severity of patients' signs and symptoms of cGVHD on an 11-point Likert scale. Possible scores range from 0 to 10. Higher scores reflect more severe cGVHD symptoms [34].

### Statistical analysis

Descriptive statistics were calculated for the analytic sample's demographic, cGVHD, motor, functional, and HRQOL characteristics. Wilcoxon signed-rank tests assessed change between baseline and 6 months. Spearman's rank correlations evaluated the relationship between change in symptom severity (Lee Symptom Scale and PGR) and change in motor, functional, and HRQOL outcomes over this 6-month period. To reduce the likelihood of type I error, p values less than 0.01 were considered statistically significant. All statistical analyses were performed using R version 3.4.0 (R Foundation for Statistical Computing, Vienna, Austria).

The guidelines set forth by the 2014 cGVHD Response Criteria Working Group were used to identify minimal clinically important differences (MCID) for all measures [14]. Established MCID values were used for the AMPS [30], DASH [35], and PGR [14]. Half the standard deviation of baseline scores was used as the MCID for all other measures. MCID values obtained using this metric were similar to those reported in larger samples of patients with cGVHD or related conditions (See Supplemental Table 1) [29, 31, 36–39]. Consistent with previous work and the recommendations of the 2014 Response Criteria Working Group, half of the population standard deviation (5 points) was used as the MCID for SF-36 PCS and MCS scores [6, 7, 14]. The standard deviation of baseline Lee Symptom Scores was small in this study ( $0.5\ SD = 2.37$ ) compared with that in previous literature that used this same criterion to define MCID values (MCID between 6 and 7) [33, 37, 38]. Therefore, a more conservative score of 6.5 was used as the MCID on this measure. At baseline, despite differing patterns of responses on individual items, four patients (30.8% of the sample) reported Lee Symptom Scale Scores of 25, which contributed to the measure's unexpectedly small standard deviation in this study.

## Results

### Patient characteristics

Twenty patients enrolled in the study. Six individuals were not available for primary endpoint analysis due to toxicity (1), relapse (1), or withdrawn consent (4). One additional patient experienced cGVHD progression between baseline and 3 months and was therefore taken off the study prior to assessment at 6 months. Demographic and disease characteristics presented in Table 1 reflect the analytic sample ( $n = 13$ ). At enrollment, the median age of participants was 52.5 years (range, 6.8–60.9). A majority of patients were male (76.9%) and all identified as non-Hispanic white. Most patients were married (53.8%), lived in Midwestern or Northeastern states (84.6%), and one-third were working (30.8%).

Patients entered the study a median of 52.6 months post-transplant (range, 12.7–121.0 months) and 39.1 months following cGVHD diagnosis (range, 4.8–112.9 months). A majority of patients received myeloablative conditioning regimens (53.8%), grafts from HLA-matched donors (6/6 or 10/10; 92.3%), and peripheral blood stem cell transplants (84.6%). At baseline, all patients had severe NIH cGVHD global scores, severe NIH cGVHD skin organ scores, and a median of five affected organs (range, 2–7).

### Change over time

Table 2 reports median scores on all outcomes at baseline and 6 months and statistical change over time. Table 3 summarizes clinical changes in motor ability, function, HRQOL, and symptom severity between baseline and 6 months. Patients did not display statistically significant change over time (see Table 2) nor did the majority of patients experience clinically significant improvement on any outcome of interest (see Table 3). MCID values used to categorize clinically significant change for all measures are also reported in Table 3.

Clinically significant improvement on motor outcomes was most common for palmar pinch strength with the dominant hand (30.8%). Just over 30% of patients displayed clinically significant decline on the GPT with the dominant hand (30.8%). On most measures of motor ability, less than 10.0% of patients experienced clinically significant deterioration over time (JTHFT, 2MWT, grip strength, and pinch strength).

On functional outcomes, just under half of patients reported clinically significant improvement on the MAM-36 (41.7%) and one-quarter improved on the HAP AAS (25%), HAP MAS (25%), and DASH (25%). A similar proportion of patients had clinically important worsening on the DASH (25%), AMPS ADL Motor Skill (23.1%), and AMPS ADL Process Skill (23.1%).

Approximately one-third of patients displayed clinically significant improvement in HRQOL as measured by the SF-36 MCS (33.3%) and a quarter of patients reported clinically significant improvement on the SF-36 PCS (25.0%).

Between baseline and 6 months, over one-third of patients had clinically significant improvement on the Lee Symptom Scale (38.5%) and 15.4% experienced clinically



significant improvements in PGR scores. However, the same proportion of patients (15.4%) displayed clinically significant worsening of PGR scores over this period.

Patients that Baird and colleagues classified as partial responders to imatinib mesylate ( $n = 5$ ) [19] did not show a consistent pattern of clinically significant improvement or decline on any motor, functional, or HRQOL outcomes (See Supplemental Table 2).

### Correlations among change scores on relevant measures

The relationship between change in cGVHD symptom severity and changes in motor ability, function, and HRQOL are reported in Table 4. Change in PGR scores was not significantly correlated with the change on any performance-based or patient-reported outcomes.

Reduced symptom burden (Lee Symptom Scores) was strongly correlated with improved physical HRQOL (SF-36 PCS,  $r = -0.72$ ,  $p = 0.008$ ) and improved functioning as indicated by both AMPS ADL motor skill scores ( $r = -0.84$ ,  $p < 0.001$ ) and DASH scores ( $r = 0.71$ ,  $p = 0.010$ ). Change in symptom burden was not correlated with change on any indicators of motor ability.

### Discussion

Symptom severity and HRQOL are important potential indicators of therapeutic response in patients with cGVHD [14]. Although ScGVHD causes significant impairment [11] and may respond poorly to treatment [9], functional performance is not routinely used as an outcome in clinical trials. Therefore, this study examined motor ability, function, and HRQOL in patients with ScGVHD following treatment with imatinib mesylate. A second aim of the present study was to investigate whether change in motor and functional abilities correlated with the change on established measures of cGVHD symptom severity. There was no statistically significant improvement on any outcome over time, although around a third of patients experienced clinically important improvement on measures of function, HRQOL, and symptom severity. In addition, reduced symptom burden correlated with improvement on two indicators of functioning.

In contrast to ROM results reported previously [19], motor ability, functional impairment, HRQOL, and cGVHD symptom severity remained relatively stable over time. Arai et al. and Inamoto et al. similarly failed to observe changes in patient-reported functional capacity and HRQOL, respectively, despite significant response to cGVHD treatment [18, 37]. Inamoto and colleagues found that such null findings were specific to patients who had been diagnosed with cGVHD more than 3 months prior to study enrollment [37]. A similar lack of responsiveness may have occurred in our analysis, given that most patients had long-standing treatment-refractory skin fibrosis.

Curtis et al. found that lower clinician-rated cGVHD severity was related to higher patient-reported HRQOL [15]. We did not identify such a relationship in this sample, which could be due to insufficient sensitivity of PGR scores or a lack of statistical power. Notably, change in clinician-reported symptom severity was not associated with change in symptom burden, corroborating findings from a previous cross-sectional study [15]. PGR scores capture clinician impressions of cGVHD symptom severity, whereas Lee Symptom Scores



may reflect patients' perceptions of the impact of such symptoms on daily life. These results support the continued use of both scales in patients with cGVHD given that they appear to assess relevant but distinct constructs.

Contrary to expectations, improvement in cGVHD symptom burden was not related to improvement in motor ability. Most of our indicators of motor capacity reflect manual ability (JTHFT, GPT, grip strength, and pinch strength), though the wrist was a target joint for only a third of patients (30.8%, see Supplemental Table 3). If the wrist and hand were not affected, burdened, or limited by ScGVHD, reduced symptoms and symptom burden could occur without parallel improvement on our measures of motor ability. The lack of an association between change in 2MWT distance and symptom burden could be due to the 2MWT's insufficient sensitivity to clinical response among patients with cGVHD [16, 38]. As of 2014, the cGVHD Response Criteria Working Group no longer recommends using the 2MWT as an indicator of therapeutic response [14].

In this study, improved physical HRQOL (SF-36 PCS), enhanced ability to perform ADLs (AMPS ADL motor skill), and reduced upper extremity impairment (DASH) were associated with decreased symptom burden. Lee et al. similarly demonstrated a longitudinal association between reduced symptom burden and improved HRQOL in patients with cGVHD [33]. Among patients undergoing allogeneic hematopoietic stem cell transplantation, symptom distress is a predictor of reduced physical and mental health [40], poor HRQOL [41], and diminished likelihood of survival [42].

The relationship between symptom burden and functional impairment in patients with cGVHD has had limited study. Currently, the 2014 NIH Consensus Development Project recommends administering the HAP as an ancillary measure of therapeutic response in patients with cGVHD. This measure was originally intended to assess energy expenditure and physical fitness [28], though scores are often interpreted as reflecting physical functioning more generally [29, 38]. The HAP provides valuable information regarding the level of activity participation, but does not provide insight into the cause of limitations therein (e.g., ROM restrictions in the upper versus lower extremity, pain, fatigue, dyspnea, and weakness) to inform specific supportive care interventions for cGVHD patients.

In contrast, as patient-reported and performance-based accounts of disability and ADL limitations, respectively, the DASH and AMPS provide more detailed information about both the cause and extent of limitations in activity engagement. Neither of these measures evidenced ceiling or floor effects at any time point (see Figs. 1 and 2), and both have displayed reliability and validity in diverse clinical populations [30, 43]. Given their longitudinal association with symptom burden, the DASH and the AMPS may be useful indicators of functioning in patients with cGVHD and should be studied as potential ancillary measures of clinical response in future trials. Due to the importance of and distinction between self-reported and performance-based assessments of functioning [44], administering multiple measures may be necessary to inform care decisions.

More generally, such measures may allow clinicians to better understand the functional restrictions experienced by patients with cGVHD, thereby promoting individualized clinical

care and rehabilitative efforts. Following effective assessments of patient limitations, occupational therapists, physical therapists, and physiatrists can work to address unmet rehabilitative needs among cancer patients [45]. Through the provision of orthotics, adaptive equipment, targeted exercises, ADL training, and patient education, rehabilitation professionals can work to aid patients with cGVHD. Future research should continue to explore the utility and feasibility of patient-reported and performance-based functional measures in patients with cGVHD and rehabilitation professionals' ability to use patient scores to inform decisions regarding care.

The present study should be interpreted in the context of several limitations. Given the small size of our sample, it is unclear if null effects were due to a true lack of a relationship or due to insufficient statistical power. Although reducing our alpha level to 0.01 reduced the likelihood of type I error, it simultaneously lowered our power and increased the likelihood of type II error. Therefore, it is possible that significant relationships will emerge in future studies that examine larger samples of patients with ScGVHD. Data were collected as part of a clinical trial of patients with severe ScGVHD, so findings may not generalize to individuals with non-sclerotic or non-severe cGVHD. Finally, all results are correlational, so we cannot determine the directionality of relationships between constructs.

This study has several strengths. A wide range of assessments were administered to explore a comprehensive set of motor, functional, and HRQOL outcomes among patients with ScGVHD. The same clinicians collected data longitudinally to ensure consistent scoring. Further, to our knowledge, this is the first study to explore the use of the DASH, AMPS, MAM-36, and JTHFT in patients with cGVHD. Future studies should replicate and extend upon findings in larger and more diverse samples.

In conclusion, these results support the continued use of the Lee Symptom Scale and the SF-36 to measure therapeutic response in patients with cGVHD. The association between reduced symptom burden and improved ADL ability (AMPS ADL motor skill) and disability (DASH) indicates the potential importance of including these constructs when evaluating this patient population. The use of the DASH, AMPS, and other functional measures will enable rehabilitation professionals to provide targeted, evidence-based, and individualized care to patients with cGVHD in clinical practice.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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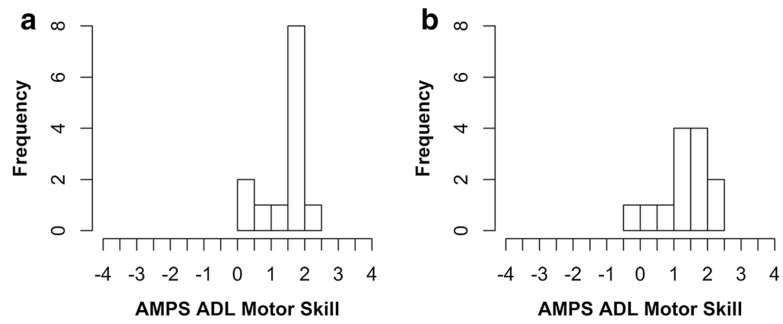
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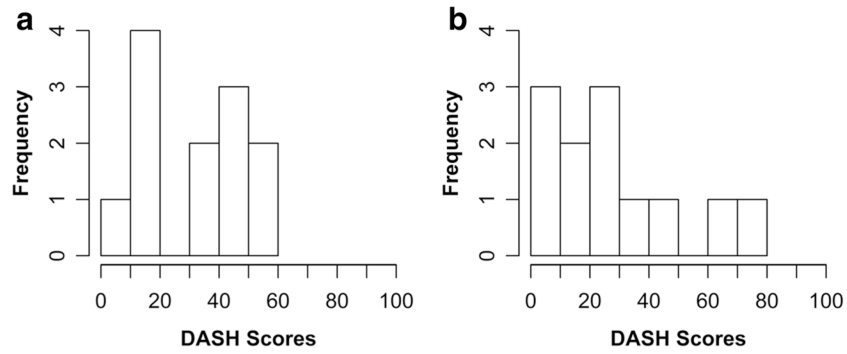
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**Fig. 1.** Histograms of AMPS ADL motor skill at baseline (a) and 6 months (b),  $n = 13$ . AMPS ADL motor skill scores are in logit units. At baseline, scores ranged from  $-0.02$  to  $2.35$ . At 6 months, scores ranged from  $0.18$  to  $2.44$ . There is no evidence of ceiling or floor effects at either time point (created using RStudio)





**Fig. 2.** Histograms of DASH scores at baseline (a) and 6 months (b),  $n = 12$ . Possible scores range from 0 to 100, with higher scores indicating greater disability. At baseline, scores ranged from 6.7 to 55. At 6 months, scores ranged from 7.8 to 71.0. There is no evidence of ceiling or floor effects for DASH scores at either time point (created using RStudio)

**Table 1**

## Patient demographic and clinical characteristics

Characteristics ( <i>n</i> = 13)	Value
Age <sup>a</sup> , median years (range)	52.5 (6.8–60.9)
<18	1 (7.7)
18–29	2 (15.4)
30–39	1 (7.7)
40–49	2 (15.4)
50	7 (53.8)
Gender, <i>n</i> (%)	
Male	10 (76.9)
Female	3 (23.1)
Race and ethnicity, <i>n</i> (%)	
White non-Hispanic	13 (100.0)
Region of residency, <i>n</i> (%)	
Midwestern United States	6 (46.2)
Northeastern United States	5 (38.5)
Southern United States	1 (7.7)
Western United States	1 (7.7)
Employment status, <i>n</i> (%) <sup>b</sup>	
Working	4 (30.8)
Not working	6 (46.2)
Student	3 (23.1)
Marital status, <i>n</i> (%)	
Married	7 (53.8)
Not married <sup>c</sup>	4 (30.8)
18 years old	2 (15.4)
Months from transplant, median (range)	52.6 (12.7–121.0)
Months from cGVHD diagnosis, median (range)	39.1 (4.8–112.9)
Number of affected organs, median (range)	5 (2–7)
Source of transplant, <i>n</i> (%)	
Peripheral blood stem cells	11 (84.6)
Bone marrow	2 (15.4)
HLA match, <i>n</i> (%)	
Match <sup>d</sup>	12 (92.3)
Mismatch	1 (7.7)
Conditioning regimen, <i>n</i> (%)	
Myeloablative	7 (53.8)
Reduced intensity	1 (7.7)
Non-myeloablative	5 (38.5)
Diagnosis, <i>n</i> (%)	

Characteristics ( <i>n</i> = 13)	Value
Leukemia <sup>e</sup>	5 (30.8)
Lymphoma	3 (23.1)
Multiple myeloma	2 (15.4)
Myelodysplastic syndromes	2 (15.4)
Polycythemia vera myelofibrosis	1 (7.7)
History of acute GVHD, <i>n</i> (%)	
Yes	9 (69.2)
No	4 (30.8)

Demographic and disease characteristics for the analytic sample at study enrollment

<sup>a</sup>Age at the time of consent

<sup>b</sup>“Working” includes individuals who work full or part time. “Not work-ing” includes individuals who are retired, unemployed, or serve as homemakers

<sup>c</sup>Includes individuals who are divorced

<sup>d</sup>Match defined as having a 6/6 or 10/10 HLA match with donor

<sup>e</sup>Includes both chronic and acute leukemia

**Table 2**

Median motor ability, function, HRQOL, and symptom severity at baseline and 6 months and statistical change over time

Measures	N <sup>a</sup>	Median		Wilcoxon signed-rank test	
		Baseline	6 months	6 months	p value
<b>Motor</b>					
JTHFT	13	45.2	49.4		0.685
GPT	13	101.5	106.6		0.735
Grip strength (lbs) Pinch strength (lbs)	12	50.8	54.8		0.230
Tip-to-tip	13	10.0	9.0		0.679
Palmar	13	14.0	16.0		0.401
Key	13	15.0	17.0		0.331
2MWT (ft)	11	610.2	607.0		0.413
<b>Functional</b>					
<b>AMPS</b>					
ADL motor skill	13	1.7	1.5		0.340
ADL process skill	13	1.9	1.7		0.505
DASH	12	34.2	22.9		0.733
<b>HAP</b>					
AAS	12	69.0	69.5		0.247
MAS	12	78.0	79.5		0.552
MAM-36	12	66.0	69.0		0.223
<b>Quality of life</b>					
<b>SF-36</b>					
PCS	12	35.3	38.6		0.910
MCS	12	51.3	52.2		0.677
<b>Symptom severity</b>					
Provider Global Rating	13	6.0	6.0		0.551
Lee Symptom Scale	13	25.0	22.5		0.102

JTHFT, GPT, and pinch strength scores refer to performance with the dominant hand. Higher scores on the DASH, JTHFT, and GPT indicate poorer performance. Higher scores on the PGR and Lee Symptom Scale indicate greater symptom severity. On all other measures, higher scores indicate improved performance

<sup>a</sup>Number of patients with data on each measure at both baseline and 6 months. Data for these individuals were used to calculate median scores at each time point. DASH, HAP, MAM-36, and SF-36 scores were missing from one patient due to young age (< 18 years old). For the 2MWT and grip strength, missing data were not collected

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Clinically important change on assessments of motor ability, function, HRQOL, and symptom severity between baseline and 6 months

**Table 3**

Measures	MCIDs			
	N <sup>a</sup>	Value	Improve, n (%)	Decline, n (%)
Motor				
JTHFT	13	15.32 <sup>b</sup>	1 (7.1)	1 (7.1)
GPT	13	13.82 <sup>b</sup>	2 (15.4)	4 (30.8)
Grip strength (lbs)	12	13.95 <sup>b</sup>	1 (8.3)	1 (8.3)
Pinch strength (lbs)				
Tip-to-tip	13	2.60 <sup>b</sup>	1 (7.7)	0 (0.0)
Palmar	13	2.84 <sup>b</sup>	4 (30.8)	1 (7.7)
Key	13	2.50 <sup>b</sup>	3 (23.1)	1 (7.7)
2MWT (ft)	11	50.35 <sup>b</sup>	1 (9.1)	1 (9.1)
Functional				
AMPS				
ADL Motor skill	13	0.3 logits <sup>c</sup>	2 (15.4)	3 (23.1)
ADL Process skill	13	0.3 logits <sup>c</sup>	3 (23.1)	3 (23.1)
DASH	12	15 <sup>c</sup>	3 (25.0)	3 (25.0)
HAP				
AAS	12	8.81 <sup>b</sup>	3 (25.0)	1 (8.3)
MAS	12	5.03 <sup>b</sup>	3 (25.0)	1 (8.3)
MAM-36	12	7.60 <sup>b</sup>	5 (41.7)	2 (16.7)
Quality of life				
SF-36				
PCS	12	5 <sup>c</sup>	3 (25.0)	2 (16.7)
MCS	12	5 <sup>c</sup>	4 (33.3)	2 (16.7)

Measures	MCIDs			
	N <sup>a</sup>	Value	Improve, n (%)	Decline, n (%)
Symptom severity				
Provider Global Rating	13	2 <sup>c</sup>	2 (15.4)	2 (15.4)
Lee Symptom Scale	13	6.50 <sup>c</sup>	5 (38.5)	2 (15.4)

JTHFT, GPT, and pinch strength scores refer to performance with the dominant hand. Higher scores on the DASH, JTHFT, and GPT indicate poorer performance. Higher scores on the PGR and Lee Symptom Scale indicate greater symptom severity. On all other measures, higher scores indicate improved performance

<sup>a</sup>Number of patients with data on each measure at both baseline and 6 months. DASH, HAP, MAM-36, and SF-36 scores were missing from one patient due to young age (< 18 years old). For the 2MWT and grip strength, missing data were not collected

<sup>b</sup>Half the standard deviation of baseline scores for individuals who also had scores at 6 months

<sup>c</sup>Established MCID value



Relationship between changes in symptom burden, symptom severity, and measures of motor ability, function, and HRQOL

**Table 4**

Measures	Provider Global Rating		Lee Symptom Scale	
	Correlation coefficient ( $\rho$ )	<i>p</i> value	Correlation coefficient ( $\rho$ )	<i>p</i> value
<b>Motor</b>				
JTHFT	0.082	0.789	0.194	0.526
GPT	-0.085	0.782	0.432	0.140
Grip strength (lbs)	-0.422	0.171	-0.438	0.154
<b>Pinch strength (lbs)</b>				
Tip to tip	-0.282	0.351	-0.214	0.482
Palmar	-0.332	0.268	0.438	0.134
Key	0.033	0.915	-0.612	0.026
2MWT (ft)	-0.100	0.757	-0.357	0.255
<b>Functional</b>				
<b>AMPS</b>				
ADL Motor skill	0.409	0.166	-0.845	< 0.001
ADL Process skill	-0.196	0.520	-0.057	0.853
DASH	-0.116	0.719	0.707	0.010
<b>HAP</b>				
AAS	-0.020	0.951	-0.248	0.437
MAS	-0.068	0.834	0.020	0.952
MAM-36	-0.226	0.480	-0.103	0.751
<b>Quality of life</b>				
<b>SF-36</b>				
PCS	0.306	0.334	-0.724	0.008
MCS	-0.342	0.276	-0.223	0.487
<b>Symptom severity</b>				
Lee Symptom Scale	-0.226	0.458		

JTHFT, GPT, and pinch strength scores refer to performance with the dominant hand. Higher scores on the DASH, JTHFT, and GPT indicate poorer performance. Higher scores on the PGR and Lee Symptom Scale indicate greater symptom severity. Higher scores on all other measures indicate better performance. Italicized values indicate significant Spearman's rank correlations between change scores (*p* 0.01)