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Translation, Cross-Cultural Adaptation, and Validation of the Lee Chronic Graft-versus-Host Disease Symptom Scale in a Brazilian Population

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A B S T R A C T

The Lee Chronic Graft-versus-Host Disease (GVHD) Symptom Scale is a patient-reported instrument developed and validated in English to measure the symptoms and functional impact of cGVHD. This tool has not yet been validated in a Latin American population, however. The Brazil-Seattle Chronic GVHD Consortium conducted a multicenter study at 5 Brazilian institutions to validate the Lee cGVHD Symptom Scale in adults with cGVHD. Study objectives included the translation and validation of the instrument in Brazilian Portuguese and evaluation of the correlation with other quality of life (QoL) tools, including the Medical Outcomes Study Short Form 36 (SF-36) and Functional Assessment of Chronic Illness Therapy with Bone Marrow Transplant subscale (FACT-BMT). Translation and validation were done according to the American Association of Orthopedic Surgeons Outcome Committee guidelines. Spearman's correlation coefficient was used to measure construct validity. Reliability was assessed using Cronbach's α and intraclass correlation coefficients. Between April 2011 and August 2012, 47 patients with cGVHD based on the 2005 National Institutes of Health criteria (29 males [62%], 18 females [38%]; median age, 48 years; range, 23 to 69 years) were enrolled in this study. The reliability of the Lee cGVHD Symptom Scale was adequate (Cronbach's $\alpha = 0.62$ to 0.83). The correlations between similar domains of the Lee cGVHD Symptom Scale, SF-36, and FACT-BMT were moderate to high. Our data indicate that the Brazilian Portuguese version of the Lee cGVHD Symptom Scale is valid and reliable and can be used in clinical trials of cGVHD in Brazil.

INTRODUCTION

Chronic graft-versus-host disease (cGVHD) is a common late complication of allogeneic hematopoietic stem cell transplantation (HSCT), and is associated with increased morbidity and mortality among HSCT survivors [1]. The incidence of cGVHD varies from 30% to 70% of allogeneic HSCTs depending on various factors, including recipient and donor ages, previous acute graft-versus-host disease, donor type, patient/recipient sex match, stem cell source, graft manipulation, post-transplantation use of cyclophosphamide, use of post-transplantation donor lymphocyte infusion, and the clinical diagnostic criteria used [1,2]. Clinical manifestations of cGVHD often affect multiple systems, including mucocutaneous, ocular, gastrointestinal, hepatic,

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and musculoskeletal, and cGVHD is associated with immunologic impairment [1]. cGVHD is also associated with a graft-versus-tumor effect, resulting in a higher disease-free survival rate compared with that in patients with no previous history of cGVHD [1].

Although the pathophysiology of cGVHD is better understood and new treatments are emerging, the management of severe cGVHD remains a challenge. Quality of life (QoL) studies in survivors of allogeneic HSCT suggest that cGVHD is associated with a decrease in functional status resulting not only from disease-related impairments, but also from adverse effects of treatment [3,4]. Patients with cGVHD are known to have lower physical, sexual, and social functioning, and show impaired physical and psychosocial recovery at 1 year after transplantation and beyond compared with patients without cGVHD [3]. In addition, patients with active cGVHD are at increased risk for developing a life-threatening clinical condition and somatic distress compared with patients with no or inactive cGVHD even 10 years after HSCT [4]. Indeed, many physical dimensions and emotional functions may be impaired by cGVHD over the lifespan. Data on QoL associated with clinical manifestations provide an indicator of health for use in clinical trials as well as for counseling patients and guiding treatment [4,5]. Moreover, higher functional levels are related to good health and longevity and should be considered when assessing disease processes [4].

Numerous QoL instruments have been developed for assessing distinct populations and their specific needs. The Lee Chronic GVHD Symptom Scale was developed and validated in English by Lee et al. [6] as a patient-reported instrument to measure symptoms and specific functional losses in cGVHD. The scale provides a simple, sensitive assessment of cGVHD manifestations. It includes 30 questions with 7 subscales containing 2 to 7 symptom items representing domains of skin, eye, mouth, respiratory system, gastrointestinal system, energy, and psychological status [6], with responses collected on a Likert scale. Completion takes less than 5 minutes.

The Lee Chronic GVHD Symptom Scale remains a broadly used patient-reported measure, recommended by the 2005 and 2014 National Institutes of Health (NIH) Chronic GVHD Consensus Response Criteria Working Group [7,8]. Several reports have validated the scale as a sensitive tool for evaluating cutaneous, fascia, joint, and ocular manifestations of cGVHD [9-11].

The Brazil-Seattle Chronic GVHD Consortium was established to facilitate collaborative studies, initially in cGVHD [12-14]. This consortium was recently adopted by the Brazilian Bone Marrow Transplantation Society as one of the first working groups focused on cGVHD and other late effects of HSCT, the Grupo de Estudos da Doença do Enxerto e Outras Complicações do TMO (GEDECO). The present multicenter study was conducted by the GEDECO at 5 Brazilian institutions. The purpose of the study was to translate, adapt, and validate the Lee Chronic GVHD Symptom Scale in a Brazilian cohort of adult patients with cGVHD, including its correlation with other QoL tools, including the Medical Outcomes Study Short Form 36 (SF-36) and the Functional Assessment of Chronic Illness Therapy with Bone Marrow Transplant subscale (FACT-BMT). Validation of the Lee Chronic GVHD Symptom Scale in different cultures and languages will support its relevance as a QoL instrument in cGVHD studies, and is necessary for its use in Brazil.

PATIENTS AND METHODS

This was a cross-sectional multicenter GEDECO study conducted at 5 participating centers between April 2011 and August 2012. Criteria for study inclusion were adult patients (aged ≥18 years) with active cGVHD diagnosed according to the 2005 NIH consensus criteria. Exclusion criteria included an inability to complete the questionnaires and less than 6 months of life expectancy owing to comorbidity or relapse of primary disease. The study was approved by the Institutional Review Boards of the participating centers, and all participants provided written informed consent.

Study Procedure

This study was initially registered in the national ethical information system for research studies (SISNEP no. 0507.0.146.000-10) and later in the Plataforma Brasil Registry (no. 01782412.1.1001.0071). Appropriate patients were identified by individual physicians at the time of clinical visits. Potentially eligible patients were approached for the study and invited to participate. Study participants were asked to complete the Portuguese Lee Chronic GVHD Symptom Scale (Appendix), along with the validated Portuguese versions of the SF-36 and FACT-BMT [15,16]. All study surveys were completed at a single patient visit. All study participants at each center met with the study coordinator before and after completing the surveys. Participants were instructed to ask for clarification if they had any questions while finishing the surveys. All cGVHD assessment forms completed by the patient and the physician were obtained at study entry. Electronic data from each center were assembled in a centralized data base by the coordinating center, the Universidade de Campinas (UNICAMP).

Translation and Application

The translation into Portuguese and validation of the Lee Chronic GVHD Symptom Scale were done in accordance with American Association of Orthopedic Surgeons Outcome Committee guidelines, as reported previously [17]. The Translation Committee was composed of 2 psychiatrists, 1 hematologist, 1 oral surgeon, 1 biostatistician, and 1 linguistic professional. Two questions regarding discrepancies on the back translation version 1 and version 2 were raised by the Translation Committee and were addressed by e-mail communication with Stephanie Lee, MD, MPH, the creator of the Lee Chronic GVHD Symptom Scale. The suggested correct terms were then considered for the final Portuguese version of the scale (Appendix).

The Lee Chronic GVHD Symptom Scale uses 5-point Likert scales to evaluate symptoms that reflect multiorgan manifestations of cGVHD. It is composed of 30 questions in 7 domains: skin, eyes, mouth, nutrition, lung, energy, and psychological functioning [6]. The "bother" scale is graduated from "not at all" to "slightly," "moderately," "quite a bit," and "extremely," with corresponding scores of 0 to 4. The SF-36 is a broadly used multidimensional QoL instrument with 36 questions distributed in 8 domains: physical functioning, social functioning, role limitations related to physical problems, role limitations related to emotional problems, mental health, vitality, pain, and general health state [18-20]. Two summary scores, physical and mental, may be calculated from the SF-36. The FACT-BMT is a specific HSCT scale composed of 47 questions distributed in 6 domains: physical well-being, family/social well-being, relationship with the doctor, emotional well-being, functional well-being, and additional worries. The FACT-BMT responses are captured on a Likert scale and scored according to domain as the sum of scores for responses [20].

Patients and physicians also were asked to grade cGVHD severity at the study evaluation. For the patient self-evaluation, severity was assessed by a single multiple-choice question in which the patient classified his or her disease: "Overall, do you think your chronic GVHD is mild, moderate, or severe?" Physicians were asked to score the patients' cGVHD severity as none, mild, moderate, or severe (scale A) and also on a numerical scale ranging from 0 (as mild as cGVHD symptoms can be) to 10 (as severe as cGVHD symptoms can be) (scale B). Global severity was based on the single-item clinician assessment of mild, moderate, or severe disease.

Statistical Analysis

Descriptive analyses were performed for demographic and disease data. Construct validity was assessed comparing the Lee Chronic GVHD Symptom Scale with the already validated Portuguese versions of the SF-36 and FACT-BMT. Spearman's correlation coefficient was used to assess the correlations among domains of the FACT-BMT, SF-36, and Lee scales and between clinical and demographic data and the QoL instruments. The associations between the QoL instruments and patients' self-evaluation and physicians' severity scores of cGVHD were tested. Reliability was assessed using Cronbach's α coefficients and intraclass correlation coefficients measuring internal consistency. The statistical analyses were performed using SPSS version 15.0 (SPSS Chicago, IL).