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The Effect of Unrelated Donor Marrow Transplantation on Health-Related Quality of Life: A Report of the Unrelated Donor Marrow Transplantation Trial (T-Cell Depletion Trial)

Elizabeth M. Altmaier,[1] Marian Ewell,[2] Richard McQuellon,[3] Nancy Geller,[4] Shelly L. Carter,[2] Jean Henslee-Downey,[5] Stella Davies,[6] Esperanza Papadopoulos,[7] Saul Yanovich,[8] Roger Gingrich[9]

[1]The University of Iowa, Iowa City, Iowa; [2]The EMMES Corporation, Rockville, Maryland; [3]Wake Forest University-Baptist Medical Center/Comprehensive Cancer Center, Winston-Salem, North Carolina; [4]National Heart, Lung and Blood Institute, Bethesda, Maryland; [5]University of South Carolina, Division of Transplantation Medicine, Columbia, South Carolina; [6]University of Minnesota, Minneapolis, Minnesota; [7]Memorial Sloan-Kettering Cancer Center, New York, New York; [8]Medical College of Virginia, Richmond, Virginia; [9]University of Iowa Hospitals and Clinics, Iowa City, Iowa

Correspondence and reprint requests: Elizabeth M. Altmaier, PhD, 360 Lindquist Center, University of Iowa, Iowa City, IA 52242 (e-mail: elizabeth-altmaier@uiowa.edu).

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ABSTRACT

The primary objective of this study was to compare health-related quality of life (HRQL) in adult patients undergoing either ex vivo T cell–depleted bone marrow transplantation or conventional marrow transplantation. Data on patients' HRQL were gathered as part of a multicenter randomized trial comparing the effect of ex vivo T-cell depletion versus methotrexate and cyclosporine immunosuppression on disease-free survival. HRQL assessments were conducted at baseline, day +100, 6 months, 1 year, and 3 years. There were no treatment arm differences 1 year after transplantation on the Functional Assessment of Cancer Therapy, Bone Marrow Transplantation, the Medical Outcomes Study Short-Form 36, and the Centers for Epidemiological Studies of Depression. The lack of treatment differences was robust across types of data analyses that took baseline functioning into account and that recognized the sensitivity of outcome measures to assumptions concerning missing data. The trajectory of recovery revealed an initial decrease in function and then a recovery to pretreatment levels that were similar for both treatment arms. Furthermore, the patients in both treatment groups returned to a functional level that approximated general US population norms. Even though the incidence of acute graft-versus-host disease was slightly higher in the conventional treatment arm, T-cell depletion did not differentially affect HRQL at 1 year after transplantation.

KEY WORDS

Quality of life • Bone marrow transplantation • T-cell depletion

INTRODUCTION

Unrelated donor marrow transplantation offers a possible cure for patients with malignant diseases, but it has high treatment-related morbidity and mortality. Acute and chronic graft-versus-host disease (GVHD) are among the complications that may adversely affect the transplantation patient's health-related quality of life (HRQL). A treatment such as T-cell depletion (TCD) that reduces acute GVHD could improve HRQL through its effect on patient physical well-being. Among the potential advantages of TCD is the reduced need for prolonged posttransplantation immunosuppressant medication [1]. Others have reported reduced peritransplantation complications such as hepatic veno-occlusive disease and pulmonary dysfunction [2-4] and a potentially greater likelihood of disease-free survival and cure [5].

The comparison of HRQL outcomes for varying methods of bone marrow transplantation (BMT) is essential to evaluate their relative costs and benefits

and to provide information to patients regarding the effects of transplantation on all health-related aspects of their lives: not just survival. Although some patients exhibit few post-BMT complications, other patients experience a range of physical, psychological, and social difficulties. Reported post-BMT concerns include occupational disability, sexual dysfunction, cognitive impairment, emotional distress, chronic physical symptoms, and perceptions of poor health [6,7].

In 1995, the National Heart, Lung and Blood Institute funded a multicenter randomized trial that examined ex vivo TCD BMT versus conventional BMT. The primary findings of this trial [7] were that TCD did not differentially affect disease-free survival, chronic GVHD, infections, relapse, or transplantation-related mortality measured at 3 years after transplantation; there was a reduction in acute GVHD among patients who underwent TCD transplantations. Specifically, the time to the first occurrence of grade II to IV acute GVHD was significantly delayed among recipients of TCD, and grades III and IV acute GVHD were reduced by TCD. The incidence of acute GVHD among TCD patients at 100 days was 15% (HLA matched marrow) to 25% (1 antigen mismatched marrow); among non-TCD patients, it was 34% to 45%.

This study assessed the effect of these treatments on HRQL. The primary analyses focused on treatment differences in HRQL 1 year after transplantation, because that time point is most typically associated with "returning to normal" in studies of BMT patients and is also the time when acute GVHD might be expected to affect function. Secondary analyses for the complete study sample were conducted to determine the longitudinal trajectory of HRQL scores across all assessment points. Additionally, patient function was placed in a national, normative context for cancer patients and for a general population to consider the degree to which these patients have returned to normal functioning.

In this study, HRQL was defined multidimensionally [8-11]. Life quality was assessed across 4 domains: physical health, personal and occupational functioning, interpersonal functioning, and psychological distress and well-being. Additionally, life quality was assessed by using both disease-specific and generic measures. The use of generic measures allows the experience of patients in this study to be compared with data provided by patients with chronic illnesses as well as a healthy age-matched group.

METHODS

Clinical Trial

Between March 1995 and October 2000, 15 transplantation centers enrolled 410 patients to evaluate the effects of 2 different methods of TCD of donor bone marrow compared with conventional methotrexate/cyclosporine to prevent GVHD on 3-year disease-free survival. Of the 410 patients, 404 were considered to be evaluable for acute GVHD; 5 patients died before transplantation, and 1 underwent transplantation 2 years after enrollment (no acute GVHD information was available). The conditioning regimen varied by type of GVHD prophylaxis. For elutriation centers, conditioning was cyclophosphamide (CY) 120 mg/kg over 2 days and total body irradiation (TBI) 1320 to 1375 cGy over 4 days for recipients of conventional transplants and an identical CY/TBI regimen plus antithymocyte globulin (ATGAM; Pharmacia, Kalamazoo, MI) 90 mg/kg over 3 days for recipients of TCD transplants. For T10B9 centers, conditioning was CY 120 mg/kg over 2 days and TBI 1350 cGy over 5 days for recipients of methotrexate/cyclosporine and CY 100 mg/kg over 2 days, cytosine arabinoside g/m^2 over 3 days, and TBI 1410 cGy over 4 days for recipients of TCD grafts. Supportive care included antibiotics, transfusions, and pharmacologic drug management standardized according to the multicenter trial protocol. A complete description of all clinical procedures has been published [7].

Assessing HRQL

All consenting patients aged 18 years or older at the time of randomization onto the main trial were eligible for the adult HRQL component of the trial (which was reviewed and approved by institutional review boards). Baseline assessment interviews took place within 4 days before conditioning, typically once the patient had arrived at the transplantation center. Posttransplantation interviews were scheduled at 100 days, 6 months, 1 year, and 3 years. All interviews were conducted by telephone, and patients received a package of response materials before each interview. The telephone interviews generally lasted 45 to 60 minutes, with the possibility of 2 sessions if the patient was too ill or tired to complete the interview in 1 session. Interviews were conducted in English, but interpretation was possible for patients with language difficulties; 4 patients needed translators for a total of 5 interviews.

Instruments

HRQL instruments were chosen according to empirical evidence of reliability, validity, and sensitivity to differences over time, and published the availability of normative data for comparison. Additionally, all HRQL instruments were pilot-tested to verify their acceptability, efficiency, clarity, and face validity with BMT patients.

The disease-specific HRQL measure was the Functional Assessment of Cancer Therapy (FACT) [12]. The