Dynamic Assessment of Quality of Life After Autologous Bone Marrow Transplantation


To determine the quality of life in adult patients after autologous bone marrow transplantation (BMT), we administered a questionnaire to a cohort of patients seen at a single referral-based center. The sample included adults 18 years and older during the 1 year following an autologous BMT. Both disease-free patients and those who relapsed with 1-year of follow-up data available were included. Of 59 eligible patients, 58 (98%) responded to the questionnaire. Patients completed a telephone questionnaire administered by a nurse specialist in the field of BMT approximately every 90 days. At the time of initial contact on day +90, the mean quality of life was 7.8 (range, 1 to 10) on a scale of 1 to 10, with 10 being the best. By the end of the first year of follow-up, the mean quality of life was 8.9 (range, 3 to 10).

Seventy-eight percent of the patients were employed. Twenty-one percent lost weight during the first year, with the majority reporting voluntary weight loss. Fourteen percent reported difficulties with sexual activity. Only 5% reported difficulty with sleeping or with frequent colds. One patient felt that her appearance was worse, and none of the patients reported a poor appetite. Eighty-eight percent of surviving adult patients reported an above-average to excellent quality of life 1 year following autologous BMT. This outcome is encouraging and suggests that this procedure is not associated with long-term morbidity in the surviving adult patient.

© 1992 by The American Society of Hematology.

SIGNIFICANT GAINS have been achieved in various areas of cancer therapy. Diseases that were uniformly fatal years ago can now be frequently eradicated and the patient returned to a disease-free state. The initial emphasis of cancer therapy was on the specific therapeutic agents, doses, and spectrum of activity necessary to cure a patient. However, as results improved and patients survive disease-free, it is important to move beyond just morbidity and mortality evaluations. Concerns about patients' feelings, psychological and physical fitness, functional status, and overall quality of life must be addressed. These studies have been hampered in the past by concerns that "quality" of life is subjective and, therefore, scientifically difficult to measure quantitatively. Recently, several investigators have proposed specific instruments for measurement of quality of life. These have usually included measurements of functional, psychological, and physical well-being, treatment side effects, and financial concerns. These studies have provided valuable information with respect to specific therapies.

Bone marrow transplantation (BMT) has evolved over the past 20 years as a curative option for various diseases. As patients are cured and returned to a fully functional status, it is imperative that issues related to their quality of life be addressed to help guide selection of therapy, not only in terms of the procedure as a whole, but also specific components such as drug toxicity or radiation damage. We, and several other investigators, have reported on quality-of-life studies in patients receiving allogeneic BMT. These studies suggest that the majority of patients will return to an acceptable quality of life from the viewpoint of the patient. However, the expectation is that autologous patients' quality of life should be equal to if not higher than those receiving allogeneic BMT, as long-term treatment-related side effects are fewer. Little has been reported on the results of autologous BMTs. We have developed a unique, dynamic questionnaire for our patients undergoing autologous BMT to address the physiological, psychological, and functional well-being and treatment-related side effects in autologous BMT. This questionnaire was administered every 90 days through a telephone inter-view. Continuous data acquisition allows for a better overall picture of the changes in the patient's life and the healing process (or lack thereof).

MATERIALS AND METHODS

All patients undergoing autologous BMT for lymphomas and nonlymphoblastic leukemia at Stanford University Medical Center over the age of 18 were eligible to participate. All protocols were reviewed and approved by the Human Subjects Review Committee. No financial incentives were offered for participation. The questionnaire (Fig 1) was administered to the patient over the telephone by a nurse specialist with experience in the field of BMT.

Patients. Between January 1988 and March 1990, a total of 102 patients received autologous BMT. Patients in this report had a minimum follow-up of 1 year. Fifty-nine patients were alive 1 year after BMT and had completed questionnaires. Ninety-eight percent (58/59) of eligible patients participated. The patient characteristics are shown in Table 1. The median age at transplantation was 36 years (range, 19 to 53). There were 24 patients with Hodgkin's disease, 23 with non-Hodgkin's lymphoma, and 11 with acute nonlymphoblastic leukemia (ANLL). Thirty-two men and 26 women participated. Educational status for our group was: less than high school, 1; high school degree, 23; college, 26; and beyond college, 8 patients. Thirty-five patients were married and 23 single or separated/divorced.

From the Bone Marrow Transplantation Program, Division of Hematology and Oncology, Departments of Medicine and Health Research and Policy, Stanford University Medical Center, Stanford, CA; and the School of Public Health, University of California, Berkeley, CA.

Submitted November 1, 1991; accepted April 9, 1992.

Supported by US Public Health Service Grant No. CA IPOI 49605 from the National Cancer Institute, DHSS.

Address reprint requests to Nelson J. Chao, MD, Bone Marrow Transplantation Program, H-1353, Stanford University Medical Center, 300 Pasteur Dr, Stanford, CA 94305.

The publication costs of this article were defrayed in part by page charge payment. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. section 1734 solely to indicate this fact.

© 1992 by The American Society of Hematology.

0006-4971/92/8003-0023$3.00/0
The preparative regimen for patients with Hodgkin’s or non-Hodgkin’s lymphoma consisted of 1,200 cGy fractionated total body irradiation (FTBI), etoposide (60 mg/kg), and cyclophosphamide (100 mg/kg) for patients less than 50 years of age who had not received prior radiotherapy that would preclude the use of FTBI (ie, mantle radiation). All other patients with the exception of three received carmustine (15 mg/kg), etoposide (60 mg/kg), and cyclophosphamide (100 mg/kg). Two patients received lomustine instead of carmustine and one of the patients received nitrogen mustard instead of cyclophosphamide. Ten patients with ANLL were prepared for BMT with busulfan (16 mg/kg) and etoposide instead of carmustine and one of the patients received nitrogen cyclophosphamide (100 mg/kg). Two patients received lomustine body irradiation patients have relapsed from their disease and are included in this analysis. Twenty-one patients had two or more chemotherapy regimens before autologous BMT.

**Measurement.** The most difficult task in quality-of-life research is to select measures that truly reflect a person’s quality of life. In a review of more than 30 different measurement scales, 10 were selected as distinct dimensions. These were physical concerns, functional ability, family well-being, emotional well-being, spirituality, treatment satisfaction, future orientation, sexuality, social function, and occupational function. These investigators concluded that a measurement vehicle should contain at least three of these 10 dimensions to be able to assess a patient’s quality of life. The design of our questionnaire arose from our perceived needs to evaluate specific areas that may be unique to BMT patients. We used a combined approach that included disease specific symptoms, specific measures of quality of life, and a global measure. Disease-specific symptoms after BMT include weight change, susceptibility to viral infections such as colds, changes in sleep patterns and appetite, and medication use. Following Schipper, we included three specific measures of quality of life—appearance, sexual activity, and return to work. Finally, a self-reported summary measure was used and a Karnofsky performance status was given. The single-item rating of quality of life was done on a linear analogue scale with 10 being their “best ever,” 1 being the “low point” of their life, and 5.5 being “average.” No other qualifiers were used. This questionnaire was repeated every 90 days. Adjustment difficulties were also elicited at the time of initial contact (day +90) as shown in the questionnaire.

**Table 1. Patient Characteristics Quality of Life**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Day 90</th>
<th>Day 365</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td><strong>Mean</strong></td>
<td><strong>SD</strong></td>
</tr>
<tr>
<td><strong>Diagnosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hodgkin’s disease</td>
<td>24</td>
<td>7.8</td>
</tr>
<tr>
<td>Non-Hodgkin’s</td>
<td>21</td>
<td>8.1</td>
</tr>
<tr>
<td>ANLL</td>
<td>11</td>
<td>7.0</td>
</tr>
<tr>
<td><strong>Preparative regimen</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiochemotherapy</td>
<td>18</td>
<td>8.3</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>38</td>
<td>7.5</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>30</td>
<td>7.5</td>
</tr>
<tr>
<td>Female</td>
<td>26</td>
<td>8.0</td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>33</td>
<td>8.0</td>
</tr>
<tr>
<td>Not married</td>
<td>23</td>
<td>7.4</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school</td>
<td>22</td>
<td>7.3</td>
</tr>
<tr>
<td>College</td>
<td>26</td>
<td>8.2</td>
</tr>
<tr>
<td>&gt; College</td>
<td>8</td>
<td>7.8</td>
</tr>
</tbody>
</table>

The mean age is 36 years (range, 19 to 53).

Abbreviation: QOL, quality of life.
are missing for two patients. Therefore, only 56 of 58 cases were included in the analysis involving the 90-day ratings.

For each patient characteristic with two categories (preparative regimen, sex, marital status), the $t$ test was used to test for differences in the means of quality-of-life ratings. For each of the patient characteristics with three categories (diagnosis and education), one-way analysis of variance was used to test for associations. Correlation between the continuous variables “age” and “quality-of-life rating” was tested using simple regression analysis.

Statistical analysis was also performed to test for association between 90-day quality-of-life ratings and each patient response at that time. The categorical variables are listed in Table 2. Again, the $t$ test was used for variables with two categories (preparative regimen, sex life satisfaction and medication). Patients who responded with “sex life not active” were not included in the test. The F test was used to test for associations between quality-of-life ratings and each three-category variable.

RESULTS

The questionnaire was administered quarterly after autologous BMT. The data presented below are the results obtained on day +90 and +365. The values from day +180 and +270 were between those found on day +90 and +365 and represented a continuum in all patients. Initially, patients with ANLL had the lowest quality of life ratings (mean, 7.0), while those with non-Hodgkin's lymphoma had the highest ratings (mean, 8.0). The ratings are higher for those whose preparative regimen was radiochemotherapy than those with chemotherapy (mean, 8.3 vs 7.5). Married individuals and women reported higher quality-of-life assessments than those who were unmarried or male. Finally, college graduates reported higher ratings than those completing high school. None of these variables reached statistical significance on day +90 (or +365). By 1 year after BMT, most ratings had increased by one unit and differences between groups had disappeared (Table 1).

Questionnaire Results

Physical Concerns

Weight. At 90 days, 44.6% of the patients maintained a stable weight; 26.7% lost weight; the remainder gained weight. By the end of the year after BMT, the number who maintained a stable weight increased to 53%.

Appetite. At 90 days, 66% of patients described their appetites as good and the remainder complained of variable or poor appetite. By the 1-year mark, 88% stated that their appetite was good. Seven (12%) complained that their appetite was variable. No patient complained of poor appetite.

Sleep patterns. At 90 days, 68% of the patients did not have difficulty with sleep. By 1 year after BMT, 72% had good sleep patterns compared with 5% (n = 3) of patients with difficulty sleeping. Thirteen patients (22%) described their sleep pattern as variable.

Colds. At 90 days, 66% of patients stated that they did not experience frequent colds. This did not change by 1 year after BMT. Sixteen patients had occasional colds, and three patients (5%) had frequent colds, both at 90 day and 1 year.

Medication. At 90 days, 54% of the patients were not on any medication. This did not change by 1 year (55%). Patients were on at least one medication—most frequently birth control pills or thyroid hormone replacement.

Occupational Functioning

Employment. At 90 days, approximately 1 month after leaving the hospital, 50% of patients were employed. Of those who were employed, 12 were employed full-time and 16 part-time. By the end of 1 year following BMT, 40 patients had returned to their prior line of work and five had found new jobs, for a total of 77.5% of the patients being employed—37 patients employed full-time and 8 part-time.

Sexual Functioning

Sexual activity. At 90 days, 64% described their sexual activity to be as satisfying as pretransplant. This percentage did not change by 1 year post-BMT. It was not applicable in 13 patients who were not sexually active before BMT. These not sexually active patients were not included in the correlation analysis between sex and quality of life.

Body Image

Appearance. At 90 days, 68% of the patients felt that their appearance had improved following BMT. The majority noted that the regrowth of hair was of major importance.
By 1 year after BMT, 98% described their appearance to be back to normal. Only one patient described her perceived appearance as poor. This patient consistently rated her quality of life as poor, primarily based on her appearance, although objectively to the physicians, there was nothing disfiguring attributable to BMT.

Quality of Life

We found improvements in self-rated (or global) quality of life. The mean score for global quality of life was 7.8 at 90 days and had increased to 8.9 at 365 days. To observe whether there may be inconsistency in each patient’s quality of life ratings from day 90 to day 365, the absolute value of the difference between each of the pair of ratings was undertaken (n = 56). The mean difference between ratings is 1.32 (SD = 1.22). The maximum difference is 5.

More than 75% of the patients had a difference of 2 or less, and 50% had a difference of 1 or less. To observe whether there is any overall difference between the two ratings, the variable “365-day rating minus 90-day rating” was assessed. The mean difference is 1.07 (SD = 1.45). The two extreme differences were −4 and 5. Of the patients, 75% had a difference of 2 or less, and 50% had a difference of 1 or less. This difference is significantly different from zero (P = .0001). On average, ratings increased by 1.07 from 90 days to 365 days posttransplant. Figure 2 includes the results from three time points: day 90, 180, and 365. Each patient’s Karnofsky performance status was also recorded. The median Karnofsky score on day +90 was 80% (range, 50% to 100%) compared with 100% (range, 60% to 100%) at the end of 1 year.

Statistical Results

We assessed the mean quality-of-life ratings for each of the specific indications of quality of life at 90 days after BMT (Table 2). Of the specific concerns, there were significant differences between individuals rating their appetite as poor or variable with those rating them as good (P = .0003), and those rating their sleep as good compared with poor or variable (P = .008). Global quality-of-life ratings did not differentiate individuals’ history of weight, colds, or use of mediation. Individuals who worked full-time rated their quality of life significantly higher than those who were not working or working part-time (P = .0004). Body image was also significantly related to quality-of-life ratings (P = .0003), but sexual satisfaction was not. By the end of 1 year of follow-up, most ratings had increased by one unit and differences between groups had disappeared.

Adjustment Difficulties

The majority of the patients identified the most difficult aspect of autologous BMT, as well as the most difficult adjustment on returning home. During the month after BMT, the patients’ difficulties were, as expected, related primarily to the toxic side effects of the preparatory regimen resulting in nausea, vomiting, and mucositis. The overall length of stay and “fear of the unknown outcome” also ranged high among patients’ concerns. Other problem areas are listed in Table 3. Following discharge, the patients’ most difficult adjustment was fatigue. Other toxicities, such as neuropathies with balance problems, were also noted frequently by this patient group (Table 3). However, follow-up interviews indicate that these peripheral neuropathies continue to improve over time.

DISCUSSION

Effective therapies for malignant diseases have been developed over the past 30 years. Several types of cancers are curable in the true sense of the word, similar to certain infectious diseases. As these patients are truly free of disease and return to “normal” life, we must evaluate treatment outcome beyond basic morbidity and mortality data. A “good life” is truly a universal quest. When modern medicine can cure a particular disease, then the important concern becomes the quality of life. For example, is a
QUALITY OF LIFE AFTER AUTOLOGOUS BMT

with emphasis on empathy, humanity, and, ultimately, disease, radiation, weakness.

Curative therapy with a high mortality or persistent morbidity worth it? Does the time gained have sufficient quality for the survivor? More importantly, what is the patient’s perception of what is important for their global quality of life is simply life itself, the good and the bad. From this perspective, a “healthy comparison” is less meaningful.

Questions relating specifically to toxic sequelae from BMT are also addressed in this unique group of patients. Moreover, various toxicities reported by the patients are likely related to radiation and/or chemotherapy administered in the past, before BMT. Therefore, more heavily pretreated patients, such as those with Hodgkin’s disease or ANLL, are likely to be affected even more by BMT. For example, all patients who complained of peripheral neuropathy had prior therapy with vincristine.

While multiple measurement scales may be preferred over a single scale, these tend to be cumbersome to administer, are time-consuming, and are usually considered intrusive in our patient population. We designed a questionnaire that addresses areas that we as investigators felt might contribute to our patients global quality of life after BMT. Our questionnaire was well accepted, as evidenced by the 98% response rate. The continued response rate was excellent, with all of the initial patients continuing to participate in this study. The reliability measure was sufficiently high to suggest the measure is stable, but not so high to suggest lack of sensitivity.

Most of our patients consistently rated their quality of life above average (midpoint or higher on the linear analogue scale). Although one may question the validity of the linear analogue scale, the perception of the patients’ own quality of life evaluated repeatedly over time suggests strongly that, in the individual patients’ own perception, his or her quality of life was above average. We recognize that our instrument does not assess emotional well-being and we plan to include this parameter in our future studies. Finally, using the Karnofsky scale provides an objective metric for comparing healthy, nontreated patients with those receiving BMT.

The issue of quality of life is important to patients who are considering autologous BMT. Our results suggest that quality of life by 1 year in the majority of the patients (88%) returns to a reasonable and acceptable degree. Continued accumulation of such data allows us to define the primary difficulties from our patients’ point of view and to address these needs before, during, and after BMT.

ACKNOWLEDGMENT

The authors thank the Stanford housestaff and fellows, and the nursing staff of Stanford University Bone Marrow Transplantation Program for their outstanding patient care. The authors also acknowledge the expert secretarial assistance of Sara Clark.

Table 3. Most Difficult Aspects

<table>
<thead>
<tr>
<th></th>
<th>During Admission for BMT (n)</th>
<th>Following Discharge From Hospital (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>11</td>
<td>None</td>
</tr>
<tr>
<td>Isolation</td>
<td>7</td>
<td>Fatigue</td>
</tr>
<tr>
<td>Mouth sores</td>
<td>6</td>
<td>Neuropathy</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>6</td>
<td>Platelet transfusions</td>
</tr>
<tr>
<td>Length of stay</td>
<td>5</td>
<td>Lack of balance</td>
</tr>
<tr>
<td>Fear of unknown</td>
<td>4</td>
<td>Headaches</td>
</tr>
<tr>
<td>Family problems</td>
<td>2</td>
<td>Other†††</td>
</tr>
<tr>
<td>&quot;Coping&quot;</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Lack of control</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Central venous line</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

*One each: diarrhea, waiting in clinic, eating, hospital discharge, intensive care unit, numbness, pain, marrow infusion, veno-occlusive disease, radiation, weakness.
†††One each: mouth sore, cough, lack of perspiration, hot flashes, poor memory, red blood cell transfusions, shingles, dry skin, vaginal dryness, joint pains.

BMT is now regarded as a curative modality for many malignant disorders that were previously fatal. Initial enthusiasm for such cures has continued. However, as patients are cured of their disease, long-term issues need to be addressed. These issues include the possibility of second malignancies, aseptic necrosis, permanent sterility, early cataracts, pulmonary fibrosis, etc. Issues pertaining to the quality of life of such patients are only now beginning to be addressed in BMT patients. We have developed and implemented a “continuous” assessment of issues that bear directly on a patient’s quality of life (or lack thereof) through various points in time. Such an analysis provides a more meaningful picture of issues that are short-lived and affected by acute toxicity to longer-term disabilities. As illustrated in Fig 2, some parameters improve rapidly, such as appetite and appearance. Other parameters measured suggest a more gradual improvement, such as sleep and stable weight. Sexual difficulties did not seem to change with time, with the same number of patients continuing to report some sexual dissatisfaction. There was a slight increase over time in the number of individuals on some form of chronic medication. The reason for this was most commonly use of birth control pills for hormonal cycling. As shown in the last bars of Fig 2, the overall quality of life gradually continues to improve over time.

Measurement of quality of life has been debated over the past decade as to whether self-reported (subjective), global, and disease-specific assessments are more valid than more objective assessments using standardized instruments and multidimensional assessments. It is our view that quality-of-life measures are subjective, reflecting the individual’s assessment of his/her life at one time relative to his/her previous state and prior experiences. After all, it is the patients’ own evaluation of his or her quality of life that is important. The patient’s perception of his own quality of life may be specially poignant after BMT. Many of the patients are happy or satisfied simply with the fact that they are alive following such intensive therapy. It may be that a patients’ perception of what is important for their global quality of life is simply life itself, the good and the bad. From this perspective, a “healthy comparison” is less meaningful.

The authors thank the Stanford housestaff and fellows, and the nursing staff of Stanford University Bone Marrow Transplantation Program for their outstanding patient care. The authors also acknowledge the expert secretarial assistance of Sara Clark.

From www.bloodjournal.org by guest on April 13, 2017. For personal use only.
REFERENCES

Dynamic assessment of quality of life after autologous bone marrow transplantation

NJ Chao, DK Tierney, JR Bloom, GD Long, TA Barr, BA Stallbaum, RM Wong, RS Negrin, SJ Horning and KG Blume