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Feasibility of Frequent Patient-Reported Outcome Surveillance in Patients Undergoing Hematopoietic Cell Transplantation

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Abstract

Patient-reported outcomes (PROs), including symptoms and health-related quality of life (HRQOL), provide a patient-centered description of hematopoietic cell transplantation (HCT)-related toxicity. These data characterize the patient experience after HCT and may have prognostic usefulness for long-term outcomes after HCT. We conducted a study of 32 patients after HCT (10 autologous HCT recipients, 11 full-intensity conditioning allogeneic HCT recipients, and 11 reduced-intensity conditioning allogeneic HCT recipients) to determine the feasibility of weekly electronic PRO collection from HCT until day (D) + 100. We used questions from the PRO version of the Common Terminology Criteria for Adverse Events to capture symptoms, and the Patient-Reported Outcomes Measurement Information System Global Health scale to measure physical and mental HRQOL. The vast majority (94%) of patients used the electronic PRO system, with only 6% opting for paper-and-pencil only. The median weekly percentage of participants who completed the surveys was 100% in all cohorts through hospital discharge, and remained 100% for the autologous HCT and reduced-intensity allogeneic HCT cohorts through D +100. Patients were satisfied with the electronic system, giving high marks for readability, comfort, and questionnaire length. Symptom severity varied by absolute level and type of symptom across the 3 cohorts, with the full-intensity allogeneic HCT cohort exhibiting the greatest median overall symptom severity, peaking at D+7. Median physical health HRQOL scores decreased with time in the 3 cohorts, and HRQOL was generally correlated with overall symptom severity. Our results demonstrate the feasibility of frequent electronic PROs in the early

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post-HCT period. Future studies in larger populations to explore predictive models using frequent PRO data for outcomes, including long-term HRQOL and survival, are warranted.

Keywords

Symptoms; Health-related quality of life; Allogeneic transplantation; Autologous transplantation

INTRODUCTION

Hematopoietic cell transplantation (HCT) is a life-saving or life-extending treatment for incurable or advanced hematologic malignancies [1]. The efficacy and widespread application of this therapy is limited by transplantation-related toxicity and functional impacts. A clearer understanding of who is at risk for transplantation-related toxicity and how to limit this effect is needed to effectively counsel patients before HCT, to make transplantation available for others who might benefit from it, and to ameliorate long-term quality-of-life deficits associated with treatment-related toxicity.

Traditionally, transplantation-related toxicity has been measured by the metrics transplantation-related mortality (TRM) or nonrelapse mortality (NRM). Short of death, prevalent and significant morbidities include graft-versus-host disease (GVHD), infection, and conditioning-related organ dysfunction. Patient-reported outcomes (PROs), including symptoms and health-related quality of life (HRQOL), measure and describe transplantation-related toxicity from the patient's perspective [2,3]. Changes in symptoms describe the patient experience over time and may help predict the future. HRQOL can also describe beneficial patient-centered effects of transplantation, including freedom from underlying disease-related disability and long-term spiritual growth [4].

A growing body of literature documents the impact of HCT on HRQOL. Several studies have reviewed the trajectory of HRQOL over time after HCT, demonstrating early impairment in HRQOL, followed by eventual recovery in most, but not all, long-term survivors [5,6]. Periodic and infrequent HRQOL assessments by traditional measures, such as the Functional Assessment of Cancer Therapy–Bone Marrow Transplant (FACT-BMT), M.D. Anderson Symptom Inventory (MDASI), and SF-36, have been used.

Although frequent assessment of symptoms and HRQOL in the early posttransplantation period using PROs has not been explored extensively, this approach offers several potential advantages for the study of transplantation-related toxicity [7-9] and to complement performance-based and clinician-reported outcomes when evaluating the effects in HCT [10,11]. These include (1) characterizing and differentiating the patient-reported impact of discrete conditioning regimens [12,13]; (2) exploring the relationship between symptoms and early HRQOL as a possible mediator of long-term HRQOL impairment; (3) identifying early patient-reported predictors of long-term mortality, morbidity, and decreased HRQOL; and (4) informing the use of strategies, such as exercise and supportive care interventions, that might relieve symptoms and improve HRQOL.

Techniques involving frequent survey administration must be convenient, acceptable, and feasible for patients experiencing the acute effects of conditioning chemotherapy, all of whom will be hospitalized for at least some portion of this time. In addition, contemporary methods of assessing symptomatic toxicity and HRQOL in cancer patients, such as the PRO version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) and the Patient-Reported Outcomes Measurement Information System (PROMIS), might be applicable, but have yet to be well tested in patients undergoing HCT.

The purpose of the present study was to investigate the feasibility and acceptability of frequent electronic-based symptom and HRQOL assessment, using questions derived from PRO-CTCAE and PROMIS, in the early post-HCT period.

METHODS

Patients

Patients were approached for enrollment into the feasibility study if they were over 18 years of age, could read English, and were able to provide informed consent. Patients were identified in the outpatient, pre-transplantation environment through discussions with transplantation nurse coordinators, advanced practice providers, or attending physicians. The 3 planned cohorts, with a targeted enrollment of 10 patients per cohort, included patients undergoing planned autologous HCT, patients undergoing full-intensity conditioning allogeneic HCT, and patients undergoing reduced-intensity conditioning allogeneic HCT.

Once patients were identified and deemed eligible to participate in the study, those interested in enrolling were asked to sign an informed consent form approved by the University of North Carolina's Lineberger Comprehensive Cancer Center Protocol Review Committee and the University of North Carolina's Biomedical Institutional Review Board.

Survey Selection

The National Cancer Institute's (NCI) PRO-CTCAE measurement system allows patients to self-report symptomatic adverse events (AEs) [14]. The items are intended to be complementary to items in the NCI's Common Terminology Criteria for Adverse Events (CTCAE), an existing lexicon of clinician-reported adverse event items required for use in all NCI-sponsored trials [15]. The PRO-CTCAE item library comprises 124 items that assess different attributes (eg, presence, frequency, worst severity, interference with usual or daily activities) of 80 symptoms represented in the CTCAE version 4 AE lexicon. PRO-CTCAE items use a 7-day recall period, and response options for all attributes are on a 0-4 Likert scale, except for "present/not present" items, which are binary.

Only PRO-CTCAE severity items were selected for administration in this study. PRO-CTCAE severity items ask patients to rate the worst severity of a specific symptom during the specified period of recall with 1 of 5 response choices (none, mild, moderate, severe, or very severe). For the purposes of this study, 34 symptom severity questions (see the Appendix) considered relevant to patients undergoing HCT were selected from the PRO-CTCAE item library by the study team and administered weekly to patients, using a 7-day recall period, according to the schedule described below. An overall weekly symptom burden score was calculated by summing the score for each symptom question (range, 0-4) to obtain a final score ranging from 0-136. Higher scores represent a greater symptom burden. In contrast to the 34 weekly symptom questions, 21 severity items from the PRO-CTCAE were administered daily, using a 24-hour recall period, according to the schedule described below. The daily survey data are not reported here.

The PROMIS Global Health scale is a 10-question HRQOL assessment tool that elicits information on patients' perceived quality of life, general functioning and overall health, pain, and symptoms of depression or anxiety [16]. A physical health score and mental health score were derived from the PROMIS Global Health scale, each using 4 separate questions. The scores were calibrated on a T-score metric normed with a general population sample with a mean of 50 and a standard deviation of 10 [16]. Higher scores reflect better HRQOL. For the purpose of this study, the PROMIS Global Health scale was administered weekly to patients, according to the schedule described below (see the Appendix).

A separate 9-question satisfaction survey was also administered to evaluate patients' satisfaction and general ease of use of the electronic symptom-reporting system, according to the schedule described below (see the Appendix) [17].

Survey Administration

Patients were invited to take all surveys electronically, although paper-and-pencil versions of each survey were available for all patients at each time point for those who opted to use this method, based on data indicating the equivalence of these 2 modes of survey administration [18]. Electronic surveys were administered using a HIPAA-compliant survey tool provided by Qualtrics (Provo, UT). Surveys were administered on study-provided electronic tablets or on patients' personal computers or mobile phones, depending on patient preference. Surveys were accessible from a private Web site, and were accessed securely by a unique URL e-mailed daily to each patient. A research coordinator introduced each patient to the electronic survey system and was available for follow-up questions; specific training on the electronic platform beyond this was not provided or found to be necessary.

Survey Schedules

Patients in all cohorts were asked to complete the weekly PRO-CTCAE and PROMIS Global Health surveys at the time of study enrollment (baseline), on the first day of conditioning chemotherapy, and weekly from day 0 (D0, receipt of stem cell infusion) to day 100 after stem cell infusion (D+100). Autologous HCT recipients were asked to complete daily PRO-CTCAE surveys from the first day of conditioning chemotherapy until initial hospital discharge. Allogeneic HCT recipients (both full-intensity and reduced-intensity conditioning) were asked to complete daily PRO-CTCAE surveys from the first day of conditioning chemotherapy until D+100. All patients were asked to complete satisfaction surveys after completing the first PRO surveys, on the first day of conditioning chemotherapy, on D0, and on D+100.

Statistical Methods

Feasibility was defined as >60% of approached patients enrolling in the study, and >70% weekly symptom survey completion among those enrolled [17]. Secondary objectives of the study included determining the time spent completing the surveys and assessing patient satisfaction with the survey system. Descriptive statistics, correlations, and graphical analyses were used to explore symptom profiles through D+100, examine differences in individual and aggregate symptoms and HRQOL among cohorts and patients, and investigate correlations between individual symptoms and HRQOL.

Most continuous measures are presented as median and interquartile range (25th-75th percentiles) and are compared between cohorts using the Kruskal-Wallis test. Owing to the 5-level rating system for individual symptom scores, means were used to rank the symptoms from highest to lowest severity at each time point. To evaluate changes over time within cohorts for the symptom severity and Global physical health and mental health scores, the range of scores for each patient was calculated, and these ranges were then compared among cohorts, also using Kruskal-Wallis tests. Spearman correlation coefficients were used to measure correlations between symptoms and HRQOL. All analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC).

RESULTS

Patients

Of the 47 patients approached for enrollment into the study, 32 (68%) agreed to participate. The electronic PRO survey assessments were part of a larger study that also required

extensive baseline and follow-up exercise testing, and reasons that potential enrollees provided for declining included unwillingness to participate in baseline exercise testing and/ or unwillingness to return for follow-up exercise testing. Among potential patients who declined, only 1 patient specifically identified the survey requirements as a reason for declining participation. Thus, a minimum of 68% of approached patients were willing to participate in this frequent survey-based study.

Demographic data for our patients are presented in Table 1. A total of 32 patients were enrolled into 3 cohorts: 10 autologous HCT recipients, with either melphalan or BEAM conditioning; 11 full-intensity allogeneic HCT recipients, typically with full-dose busulfan and fludarabine conditioning; and 11 reduced-intensity allogeneic HCT recipients, typically with reduced-dose busulfan and fludarabine conditioning. The median age at the time of transplantation for the entire cohort was 57.8 years. Thirteen patients (41%) had a high school education or less. Seventeen patients (55%) had intermediate disease, and 9 patients (29%) had advanced disease [19]. Sixteen patients (50%) had a Hematopoietic Cell Transplantation-Specific Comorbidity Index [20] score of 3.

Feasibility

All patients were offered the opportunity to use the electronic mode of survey assessment on study-provided tablets or individual personal computers or mobile phones. Two patients (6%) opted to use paper-and-pencil only, and all others used the electronic system. Weekly electronic completion of 34 PRO-CTCAE items required a median of 4.3 minutes, and 10 PROMIS items were completed in a median of 3 minutes. Three patients (9%; 1 full-intensity allogeneic HCT recipient and 2 reduced-intensity allogeneic HCT recipients) died before D+100. The median weekly percentage of participants who took the surveys was 100% in all cohorts from the start of conditioning up to hospital discharge. The median completion rate remained 100% through D+100 in the autologous HCT and reduced-intensity allogeneic HCT cohorts, but was lower in the full-intensity allogeneic HCT cohort (80%; $P = .002$).

Satisfaction

Based on satisfaction questionnaire data, the patients indicated that the survey questions were not difficult to read (responses of at least 94% at each time point), that the questionnaire length was not too long (responses of at least 82% at each time point), and that using a computer to fill out the surveys was comfortable (responses of at least 88% at each time point). At D+100, 73% of patients indicated that the surveys helped them discuss medical issues with their healthcare provider, and 80% responded that the surveys helped remind them of symptoms that they had been experiencing. Overall, the patients were satisfied with the electronic survey questionnaires (responses of at least 94% at each time point) and would recommend the electronic survey questionnaires to others (responses of 81% at baseline, 82% at D0, and 92% at D+100). Complete satisfaction questionnaire data are presented in Table 2.

Symptoms

Table 3 lists the 5 most severe symptoms for each cohort at baseline, D0 (day of stem cell infusion, after completion of conditioning chemotherapy), D+7 (1 week after stem cell infusion, close to the expected WBC nadir and expected peak symptom severity), D+28 (approximately 1 month after stem cell infusion), and D+100 (end of the symptom reporting period). Insomnia and fatigue were common in most cohorts and time points, with other symptoms and their severity varying by cohort and time point. Mean "worst" severity scores across cohorts and time points for the 10 symptoms with the highest overall severity scores across the entire period of analysis are presented in Figure 1, ordered by severity.

Table 4 and Figure 2 present median symptom severity scores for the 34 symptoms and the PROMIS physical and mental health scores for each cohort and time point. Patients in the full-intensity allogeneic HCT cohort reported the highest overall median symptom scores, peaking at 38.0 at D+7 (from 12.0 at baseline) and decreasing to 19.0 by the end of the analysis period. In contrast, patients in the reduced-intensity allogeneic HCT cohort reported a median overall symptom score of 17.0 at D+7 (from 9.0 at baseline), decreasing to 6.5 by D+100. Patients in the autologous HCT cohort reported scores between those of the 2 allogeneic HCT cohorts. Statistically significant differences in summed symptom severity scores among the 3 cohorts were seen at D+0 (*P* .004) and D+7 (*P* = .006), and a borderline statistically significant difference was seen at D+28 (*P* = .07). Overall symptom scores varied significantly over time in the full-intensity allogeneic HCT cohort, with a median range in scores of 26, compared with 18 in the autologous HCT cohort and 10 in the reduced-intensity allogeneic HCT cohort (*P* = .009).

HRQOL

Table 4 and Figure 3 provide graphical depictions of median PROMIS Global physical health and mental health T-scores. Median physical health scores were not significantly different among cohorts at baseline (47.7 for the full-intensity allogeneic HCT cohort, 49.3 for the autologous HCT cohort, and 54.1 for the reduced-intensity allogeneic HCT cohort; *P* = .50). Physical health scores decreased at D+7 to 39.1 in the full-intensity allogeneic HCT cohort, 48.4 in the reduced-intensity allogeneic HCT cohort, and 42.7 in the autologous HCT cohort. Differences in median physical health scores among the 3 cohorts were statistically significant at D+0 (*P* = .005) and D+7 (*P* = .035). Variations in physical health scores did not differ significantly over time, with a median range in scores of 14.8 in the autologous HCT cohort, 10.3 in the full-intensity allogeneic HCT cohort, and 10.3 in the reduced-intensity allogeneic HCT cohort (*P* = .30).

Median mental health scores ranged from 50.8 to 52.1 at baseline, decreasing to a low at D +28 of 48.3 in the full-intensity allogeneic HCT cohort, 52.1 in the reduced-intensity allogeneic HCT cohort, and 47.1 in the autologous HCT cohort. Differences in median mental health scores among the 3 cohorts reached statistical significance at D+0 (*P* = .008). Mental health scores varied over time, with + a median range of 8.6 in the autologous HCT cohort, 7.7 in the full-intensity allogeneic HCT cohort, and 5.7 in the reduced-intensity allogeneic HCT cohort (*P* = .50).

Correlations

Moderate to strong negative correlations were observed between overall symptom scores and physical health scores at most time points, with strong negative correlations also observed between overall symptom scores and mental health scores at several of the same time points. Correlation coefficients are reported in Table 5.

DISCUSSION

Our results confirm the feasibility and acceptability of frequent symptom and HRQOL sampling in the early post-HCT period, and suggest several advantages and potential future applications of this approach. Among enrolled patients, many had advanced malignancies and significant comorbid illness, several were over age 60 years, and a significant minority (40%) had a high school education or less. All patients were undergoing HCT, an intensive inpatient procedure characterized by significant overall transplantation-related toxicity and periods of severe illness. Nonetheless, completion rates of weekly 44-item symptom and HRQOL surveys were very high in the overall sample. Rates were significantly lower between hospital discharge and D+100 in the full-intensity allogeneic HCT cohort compared

with the other 2 cohorts, although still high overall (80%). This difference might reflect intercurrent illness in this cohort after hospital discharge, and future studies should investigate the relationship (and potential predictive value) of incomplete surveys with morbidity. Across all cohorts, patient-reported satisfaction with the computer-based system of survey administration was quite high.

The electronic method of survey administration has several potential advantages over paper-and-pencil surveys[17,18,21]. Electronic surveys are adaptable, particularly in the context of our study design, in which computerized links were sent daily to study participants. In the future, this approach could accommodate skip logic and computerized-adaptive testing technology [22] to reduce respondent burden. Electronic PRO collection also enhances the efficiency of survey administration and data aggregation, possibly allowing this approach to be scaled to larger multisite studies with heterogeneous populations. Finally, encouraging patient comfort and familiarity with an electronic interface during the posttransplantation period allows for the opportunity to build software for additional future purposes, such as education and reminders for medications and other critical elements of self-care during this period.

Our results demonstrate the feasibility of applying symptom and HRQOL PRO measures, such as PRO-CTCAE and PROMIS, that have not been studied previously in the HCT population. PRO-CTCAE and automated symptom reporting in general have proven useful in the non-HCT cancer population [14,23-25]. The PRO-CTCAE's ability to capture key HCT-related symptoms in our study population suggests the need for further validation of this measure in HCT recipients and applications similar to those developed and tested in non-HCT patients. PROMIS has been extensively validated in cancer and noncancer populations and provides useful reference points for comparison with the general US population [26]. Additional validation within the HCT population could lead to useful potential comparisons of HRQOL in this population and populations with other cancers and chronic illnesses undergoing treatment. Other patient-reported outcome measures of symptoms and HRQOL have been used successfully in HCT recipients [5,10,11,27]. Formal comparisons of the PROMIS and PRO-CTCAE with those measures was beyond the scope of the present study, however. Although many of the same symptoms and HRQOL domains are included in all of these measures, they differ in some ways, including reference period, item phrasing, length, and scoring metric. We believe that investigators should select the measure most appropriate for their particular study design.

Although our analyses were exploratory in nature, our results demonstrate the potential usefulness of frequent patient reporting of symptoms and HRQOL during this time period. We were able to demonstrate that symptom scores changed over time, increasing and decreasing in ways consistent with expected physiological changes as the result of conditioning chemotherapy and posttransplantation effects. These changes also differed by cohort in predictable ways, consistent with the literature [7] (eg, full-intensity allogeneic HCT recipients experienced the greatest symptom burden, around the time of predicted WBC count nadir), supporting the validity of these measurements. Individual symptoms also changed over time and by cohort in unique ways, demonstrating the differential composition of the overall symptom burden for different cohorts. Our sample size did not permit a detailed analysis of which patient subsets within each cohort were most symptomatic and why; this topic could be explored in future studies using predictive modeling to examine the relationship between symptoms and long-term outcomes.

Likewise, HRQOL varied predictably over time and by cohort. Our data suggest that in particular, changes in physical HRQOL appeared to mirror changes in symptoms. Mental health HRQOL changes appeared to be less consistent in our dataset, however. Reasons for

this might be related to our small sample size, characteristics of the PROMIS mental health questions that are less well suited to an HCT recipient population, or perhaps early mental health HRQOL changes as a phenomenon distinct from physical health HRQOL. Further studies are needed to investigate this issue more specifically.

Our data confirm the findings of Cohen et al. [7], in which symptoms as measured by MDASI-BMT peaked, individually and in aggregate, at the nadir of WBC count with corresponding decrements in HRQOL. Differences in PROs by conditioning regimen were also seen in both studies. Although our findings confirm these data, additional advantages offered by our approach include the demonstrated feasibility of more frequent assessment (ie, weekly and even daily, although these data are not reported here), as well as an expanded inventory of symptom assessment questions provided by the PRO-CTCAE.

In general, our data demonstrate that symptom sampling can be used to measure the longitudinal impact of specific treatments on physiological functioning over time. Our observed correlations between symptoms and HRQOL, and the corresponding changes in symptoms with physical and mental HRQOL, reflect a potential mechanism for decreased HRQOL among HCT recipients. A larger dataset might allow the differentiation of discrete trajectories between physical and mental HRQOL, as well as the identification of which symptoms (and which specific treatment effects) are most closely related to the observed variation in each. These data also might help guide such strategies as exercise interventions, stress management, and other supportive care approaches to ameliorate symptom and HRQOL decline and potentially improve long-term outcomes.

We acknowledge several potential limitations to this study. Because this was a feasibility study, our sample size was necessarily small. All of the patients in the study were hospitalized for the duration of conditioning chemotherapy and posttransplantation engraftment, facilitating an extended learning period for the electronic survey system. At other centers, some patients are outside of the hospital for much of the peritransplantation period. However, our patients continued to use the electronic survey system after discharge in the outpatient environment. In addition, we were not able to formally compare different HRQOL scales (eg, SF-36, FACT-BMT) with PROMIS, or different symptom burden scales (MDASI) [26,27] with PRO-CTCAE, leaving the optimal method for obtaining these data in HCT recipients unclear. We did not attempt to obtain frequent PRO data for survivors beyond D+100, and did not study long-term symptom burden [28,29]. Finally, we did not use these data as part of routine clinical care; future work might formally investigate the clinical utility of these scales and evaluate whether frequent symptom or HRQOL reporting could inform day-to-day clinical decisions.

In addition to these limitations, we also were able to identify important challenges that will need to be considered as these types of studies are expanded in the future. A clear advantage of electronic PRO capture relates to the minimal to modest costs of ongoing survey administration and data aggregation. Software development costs are up front and likely feasible for research-based data collection, although they would be increased if PRO data were to be made available at the point of care to inform decision making. Finally, although our surveys were associated with high patient satisfaction and response rates, it is likely that research coordinators with experience in the PRO software system will be needed in larger studies to maintain response rates and limit missing data. This suggestion is consistent with recently published recommendations for integrating PROs into comparative effectiveness research [30].

We envision several directions for further development of this work. Studies are planned to investigate whether daily symptom data are additionally informative to weekly symptom

data. Models will be constructed to evaluate whether symptom clusters can be identified within the data collected, providing further information about the specific physiological effects of the HCT process on patients. In the future, multisite efforts should be developed to expand this approach to a larger HCT recipient population. These efforts might incorporate biomarker data and could be designed to determine whether early symptom and HRQOL data can be incorporated into predictive models for intermediate and long-term transplantation-related toxicity, such as GVHD, long-term HRQOL impairment, and TRM. Similar models relying on electronic PRO capture could be developed for other transplantation-related disease states as well, such as acute or chronic GVHD, with PROs tailored to the expected symptoms and impact of these disease states on patient functioning and experience. With these models, early interventions could then be targeted to high-risk patients to limit transplantation-related morbidity and TRM, and help improve the therapeutic index of transplantation for patients with life-threatening diseases.

Acknowledgments

Appendix

APPENDIX:

Symptoms Assessed Daily

1. Bloating of the abdomen (belly)
2. Constipation
3. Loose or watery stools (diarrhea)
4. Mouth or throat sores
5. Nausea
6. Shivering or shaking chills
7. Fatigue, tiredness, or lack of energy
8. Pain
9. Decreased appetite
10. Problems with concentration
11. Dizziness
12. Headache
13. Problems with memory
14. Anxiety
15. Sad or unhappy feelings
16. Insomnia (including difficulty falling asleep, staying asleep, or waking up early)
17. Cough
18. Shortness of breath

19. Dry skin

20. Itchy skin

21. Rash

Symptoms Assessed Weekly

1. Bloating of the abdomen (belly)

2. Constipation

3. Loose or watery stools (diarrhea)

4. Dry mouth

5. Mouth or throat sores

6. Nausea

7. Difficulty swallowing

8. Vomiting

9. Blurry vision

10. Arm or leg swelling

11. Easy bruising (black and blue marks)

12. Shivering or shaking chills

13. Fatigue, tiredness, or lack of energy

14. Pain

15. Decreased appetite

16. Joint aches (such as elbows, knees, shoulders)

17. Muscle aches

18. Problems with concentration

19. Dizziness

20. Headache

21. Problems with memory

22. Numbness or tingling in hands or feet

23. Problems with tasting food or drink

24. Anxiety

25. Sad or unhappy feelings

26. Insomnia (including difficulty falling asleep, staying asleep, or waking up early)

27. Frequent urination

28. Loss of control of urine (leakage)

29. Cough

30. Shortness of breath

31. Dry skin

32. Hair loss

33. Itchy skin

34. Rash

HRQOL Questionnaire[*]

(Global01) In general, would you say your **health** is: Excellent/Very Good/Good/Fair/Poor

(Global02) In general, would you say your **quality of life** is:

Excellent/Very Good/Good/Fair/Poor (Global03) In general, how would you rate your **physical health?**

Excellent/Very Good/Good/Fair/Poor (Global04) In general, how would you rate your **mental health**, including your mood and your ability to think?

Excellent/Very Good/Good/Fair/Poor (Global05) In general, how would you rate your satisfaction with your **social activities and relationships?**

Excellent/Very Good/Good/Fair/Poor (Global09) In general, please rate **how well you** carry out your usual social activities and roles. (This includes activities at home, at work and in your community, and responsibilities as a parent, child, spouse, employee, friend, etc).

Excellent/Very Good/Good/Fair/Poor (Global06) To what extent are you **able to** carry out your everyday physical activities such as walking, climbing stairs, carrying groceries, or moving a chair?

Completely/Mostly/Moderately/A little/Not at all (Global10) In the past 7 days: How often have you been bothered by **emotional problems** such as feeling anxious, depressed, or irritable?

Never/Rarely/Sometimes/Often/Always (Global08) In the past 7 days: How would you rate your **fatigue** on average?

None/Mild/Moderate/Severe/Very severe (Global07) In the past 7 days: How would you rate your **pain** on average?

0 = No pain

1

2

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6

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[*]The Global physical health score is generated by summing responses to Global03, Global06, Global07 (rescored), and Global08 (rescored). The Global mental health score is generated by summing responses to Global02, Global04, Global05, and Global10 (rescored).

7

8

9

10 = Worst imaginable pain

Satisfaction Survey

How easy was it to read the questions on your health?

Very difficult/Difficult/Neither difficult nor easy/Easy/Very easy How easy was it to use the computer to respond to the questions?

Very difficult/Difficult/Neither difficult nor easy/Easy/Very easy How was the length of the questionnaire that you completed today?

Very long/Long/Okay/Short/Very short How comfortable was the computer to use?

Very uncomfortable/Uncomfortable/Neither comfortable nor uncomfortable/Comfortable/Very comfortable Did taking the symptom questionnaire help you to discuss medical issues with your doctor that you might otherwise not have discussed?

No/Yes/I don't know/I haven't seen my doctor yet Did the questionnaire help remind you of symptoms you experienced such as stomach problems, headaches, or anxious feelings?

No/Yes/I don't know/I haven't seen my doctor yet In general, how satisfied were you with using the computerized questionnaire to report your symptoms?

Very dissatisfied/Dissatisfied/Neither satisfied nor dissatisfied/Satisfied/Very satisfied.

Would you recommend that other patients use the computerized symptom questionnaire?

No/Yes/I don't know What can we do to make the questionnaire or computer system better?

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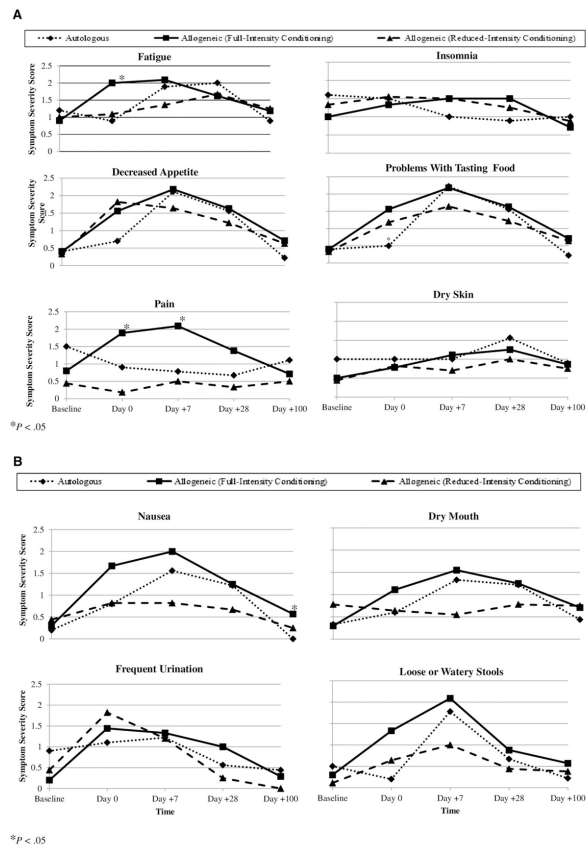
Figure 1.
Mean symptom severity. Patients reported symptoms weekly using a 34-question subset of the PRO-CTCAE. Depicted are mean severity scores for 10 individual symptoms over time by cohort (autologous, full-intensity allogeneic, and reduced-intensity allogeneic).
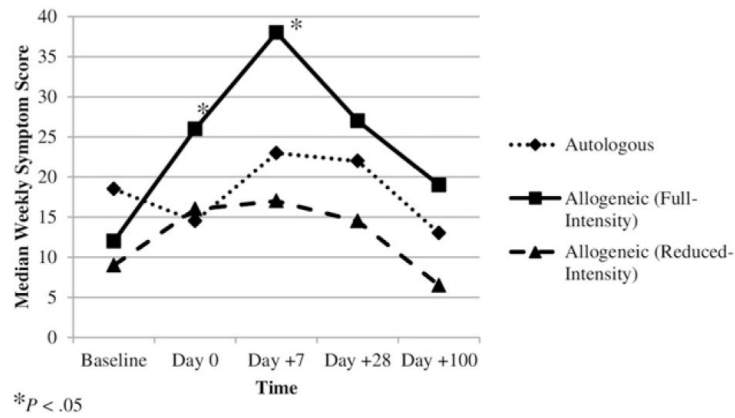
Figure 2.
Median overall symptom scores. Weekly scores for individual symptoms were summed to provide an overall weekly symptom score. Shown are median weekly symptom scores for each of the 3 cohorts. Higher scores represent worse symptom burden.
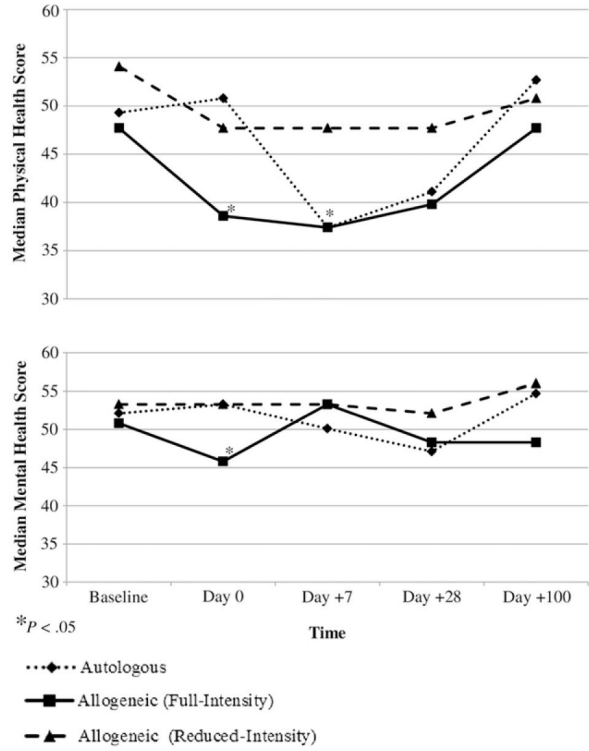
Figure 3.
Median HRQOL (physical health and mental health) scores. Weekly scores for the 10-question PROMIS Global Health measure were used to determine weekly physical health and mental health scores. Shown are median weekly physical health and mental health scores for each of the 3 cohorts. Lower scores represent worse physical health and mental health.

Table 1

Baseline Descriptive Data

	Autologous (n = 10)	Allogeneic (Full-Intensity) (n = 11)	Allogeneic (Reduced-Intensity) (n = 11)	Total (n = 32)
Age at HCT, years, median	59.8	49.7	61.2	57.8
Sex, n (%)				
Male	5 (50)	3 (27)	8 (73)	16 (50)
Female	5 (50)	8 (73)	3 (27)	16 (50)
Race, n (%)				
African American	2 (20)	2 (18)	0 (0)	4 (13)
Asian	0 (0)	1 (9)	0 (0)	1 (3)
Caucasian	8 (80)	7 (64)	11 (100)	26 (81)
Hispanic	0 (0)	1 (9)	0 (0)	1 (3)
Education, n (%)				
Less than high school	1 (10)	1 (9)	0 (0)	2 (6)
Completed high school	4 (40)	6 (55)	1 (9)	11 (34)
College degree or higher	5 (50)	4 (36)	10 (91)	19 (59)
Diagnosis, n (%)				
AML	0 (0)	7 (63)	6 (55)	13 (41)
ALL	0 (0)	2 (18)	1 (9)	3 (9)
Multiple myeloma	8 (80)	0 (0)	0 (0)	8 (25)
CML	0 (0)	1 (9)	0 (0)	1 (3)
MDS	0 (0)	1 (9)	1 (9)	2 (6)
NHL	2 (20)	0 (0)	2 (18)	4 (13)
Aplastic anemia	0 (0)	0 (0)	1 (9)	1 (3)
Cancer stage [19], n (%) *				
Early	2 (20)	1 (9)	2 (20)	5 (16)
Intermediate	8 (80)	5 (46)	4 (40)	17 (55)
Late	0 (0)	5 (46)	4 (40)	9 (29)
HCT-CI score [20], n (%)				
0	4 (40)	2 (18)	3 (27)	9 (28)
1	1 (10)	0 (0)	1 (9)	2 (6)
2	1 (10)	1 (9)	3 (27)	5 (16)
3	1 (10)	3 (27)	1 (9)	5 (16)
4	3 (30)	1 (9)	1 (9)	5 (16)
5	0 (0)	2 (18)	2 (18)	4 (13)
7	0 (0)	2 (18)	0 (0)	2 (6)
EBMT score [19],				

	Autologous (n = 10)	Allogeneic (Full-Intensity) (n = 11)	Allogeneic (Reduced-Intensity) (n = 11)	Total (n = 32)
n (%)				
0-1	0 (0)	0 (0)	0 (0)	0 (0)
2	2 (20)	2 (18)	0 (0)	4 (13)
3	4 (40)	2 (18)	2 (18)	8 (25)
4	4 (40)	4 (36)	6 (55)	14 (44)
5	0 (0)	3 (27)	1 (9)	4 (13)
6	0 (0)	0 (0)	2 (18)	2 (6)
7	0 (0)	0 (0)	0 (0)	0 (0)

[*] Aplastic anemia was not staged.

Table 2

Satisfaction Questionnaire

Question	Response	Baseline, % (n/N)[*]	D0, % (n/N)[*]	D+100, % (n/N)[*]
1.Readability of questions	Not difficult	94 (16/17)	100 (17/17)	100 (13/13)
2. Questionnaire length	Not long	100 (20/20)	82 (14/17)	93 (14/15)
3. Ease using computer	Comfortable	88 (15/17)	100 (17/17)	92 (12/13)
4. Helps in discussing medical issues with doctor	Yes	21 (4/19)	35 (6/17)	73 (11/15)
	No/don't know	42 (8/19)	47 (8/17)	27 (4/15)
	Haven't yet seen doctor	37 (7/19)	18 (3/17)	0 (0/15)
5. Reminds you of symptoms	Yes	53 (10/19)	65 (11/17)	80 (12/15)
	No/don't know	37 (7/19)	29 (5/17)	20 (3/15)
	Haven't yet seen doctor	11 (2/19)	6 (1/17)	0 (0/15)
6.Satisfied with computer questionnaire	Satisfied	94 (16/17)	100 (17/17)	100 (13/13)
7. Recommend computer questionnaire to others	Yes	81 (13/16)	82 (14/17)	92 (12/13)
	No/don't know	19 (3/16)	18 (3/17)	8 (1/13)

[*] n, number of patients who endorsed response option; N, total number of patients who responded to a question.

Table 3

Top Symptoms (Ordered by Highest Mean "Worst" Severity Ratings) by Cohort over Time

	Baseline	D0	D+7	D+28	D+100
Autologous	1. Insomnia	1. Insomnia	1. Tasting food	1. Fatigue	1. Pain
	2. Pain	2. Hair loss	2. Appetite	2. Appetite	2. Insomnia
	3. Joint aches	3. Urinary frequency	3. Fatigue	3. Dry skin	3. Fatigue
	4. Fatigue	4. Dry skin	4. Diarrhea	4. Hair loss	4. Dry skin
	5. Constipation	5. Pain	5. Nausea	5. Nausea	5. Joint aches
Allogeneic (full-intensity)	1. Insomnia	1. Fatigue	1. Tasting food	1. Hair loss	1. Fatigue
	2. Fatigue	2. Pain	2. Mouth sores	2. Tasting food	2. Anxiety
	3. Pain	3. Nausea	3. Appetite	3. Fatigue	3. Limb swelling
	4. Anxiety	4. Appetite	4. Fatigue	4. Appetite	4. Tasting food
	5. Joint aches	5. Tasting food	5. Pain	5. Insomnia	5. Dry skin
Allogeneic (reduced-intensity)	1. Insomnia	1. Insomnia	1. Appetite	1. Fatigue	1. Fatigue
	2. Fatigue	2. Appetite	2. Insomnia	2. Insomnia	2. Insomnia
	3. Dry mouth	3. Urinary frequency	3. Fatigue	3. Appetite	3. Dry skin
	4. Hair loss	4. Fatigue	4. Urinary frequency	4. Tasting food	4. Dry mouth
	5. Numbness/tingling	5. Tasting food	5. Tasting food	5. Dry skin	5. Itchy skin

Table 4

Weekly Symptom, Physical, and Mental Health Scores by Treatment over Time

	Cohort	Baseline	D0	D+7	D+28	D+100
Weekly Symptom score, median (IQR) [*]	Autologous	18.5 (8.0-33.0)	14.5 (8.0-22.0)	23.0 (18.0-36.0)	22.0 (16.0-27.0)	13.0 (4.0-18.0)
	Allogeneic (full-intensity)	12.0 (6.0-20.0)	26.0 (26.0-37.0)	38.0 (29.0-43.0)	27.0 (21.5-39.5)	19.0 (7.0-27.0)
	Allogeneic (reduced-intensity)	9.0 (4.0-22.0)	16.0 (6.0-25.0)	17.0 (12.0-29.0)	14.5 (9.0-23.0)	6.5 (4.5-20.5)
Physical Health score, median (IQR) [†]	Autologous	49.3 (42.3-57.7)	50.8 (44.9-57.7)	37.4 (37.4-44.9)	41.1 (36.2-52.5)	52.7 (45.0-61.9)
	Allogeneic (full-intensity)	47.7 (42.3-54.1)	38.6 (37.4-39.8)	37.4 (32.4-44.9)	39.8 (37.4-47.7)	47.7 (42.3-54.1)
	Allogeneic (reduced-intensity)	54.1 (47.7-57.7)	47.7 (47.7-57.7)	47.7 (44.9-54.1)	47.7 (42.3-54.1)	50.8 (42.3-54.1)
Mental Health score, median (IQR) [†]	Autologous	52.1 (50.8-59.0)	53.3 (50.8-59.0)	50.8 (45.8-59.0)	47.1 (41.2-57.5)	54.7 (47.2-61.8)
	Allogeneic (full-intensity)	50.8 (48.3-56.0)	45.8 (43.5-48.3)	53.3 (41.1-53.0)	48.3 (38.8-53.3)	48.3 (36.3-53.3)
	Allogeneic (reduced-intensity)	53.3 (48.3-59.0)	53.3 (50.8-59.0)	53.3 (53.3-59.0)	52.1 (48.3-56.0)	56.0 (50.8-59.0)

[*] Higher score is indicative of worse symptom burden.

[†] Higher score is indicative of better health.

Table 5

Correlation of Weekly Symptom Scores with Weekly Physical and Mental Health Scores (Spearman Correlations)

	Autologous	Allogeneic (Full-Intensity Conditioning)	Allogeneic (Reduced-Intensity Conditioning)
Baseline			
Symptoms versus Physical Health score	−0.57	−0.69	−0.66
Symptoms versus Mental Health score	−0.54	−0.59	−0.85
Day +0			
Symptoms versus Physical Health score	−0.48	−0.86	−0.83
Symptoms versus Mental Health score	−0.34	−0.15	−0.70
Day +7			
Symptoms versus Physical Health score	−0.50	0.70	−0.80
Symptoms versus Mental Health score	−0.20	0.45	−0.74
Day +28			
Symptoms versus Physical Health score	−0.52	−0.45	−0.45
Symptoms versus Mental Health score	−0.57	0.07	−0.52
Day +100			
Symptoms versus Physical Health score	−0.79	−0.87	−0.75
Symptoms versus Mental Health score	−0.80	−0.72	−0.63