A Single Center Survey of Health-Related Quality of Life among Acute Myeloid Leukemia Survivors in First Complete Remission

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Abstract

Background: Acute myeloid leukemia (AML) is one of the most common types of leukemia in adults, but there is limited information on survivors' quality of life (QOL) after remission.

Objective: We piloted a survey exploring patient-reported outcomes for people with AML in first complete remission (CR1) to determine whether patients felt the survey is relevant to their well-being and to summarize patient characteristics.

Design/Measurements: Cross-sectional survey of a convenience sample of AML patients in CR1 assessing QOL and functioning (European Organization for Research and Treatment of Cancer [EORTC] QLQ-C30 v 3.0), well-being (QOL-cancer survivor [QOL-CS]), fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue [FACIT-Fatigue]), and anxiety and depression (hospital anxiety and depression scale [HADS]). The survey contained five open-ended questions.

Results: Eighteen patients completed the survey. Most felt it was completely or mostly relevant (88.8%) in describing their QOL. Participants scored well on the EORTC QLQ-C30, fatigue being the most common symptom (83%). The FACIT-Fatigue mean score was 28.7 and median score was 33.5 (normal ≥ 30). Two scored in the abnormal range for anxiety and one for depression on the HADS. On the QOL-CS, participants scored more than 6 out of 10 in most domains, except the subscales of distress and fear.

Conclusions: The survey content and length were appropriate. Patients reported ongoing fatigue, fears of future test results, getting a second cancer, and recurrence of cancer. Survivors experience ongoing symptoms, highlighting the importance of providers performing ongoing symptom and needs assessments.

Keywords: acute myeloid leukemia; cancer survivorship; complete remission

Background

ACUTE MYELOID LEUKEMIA (AML) is one of the most common types of leukemia in adults.¹ AML survivors may experience more uncertainty, depression, fear of cancer recurrence (FCR), anxiety, as well as request more assistance for physical, emotional, social, and spiritual well-being than other leukemia subtype survivors.^{2,3} In recent years, there is growing interest in integrating palliative medicine more upstream for patients with serious illnesses, and survivorship care can be a natural extension of this specialty.

Reviews assessing the impact of AML and its treatments on quality of life (QOL) described studies with wide variations in instruments used for outcome assessment.^{4,5} To better understand the QOL among AML survivors, we piloted a survey for patients in first complete remission (CR1)—the survey package consists of validated instruments, five open-ended questions, and participant feedback questions. The primary objective was to determine whether patients felt the survey package was relevant to their well-being and whether the length was appropriate. The exploratory objectives were to summarize patient QOL outcome using previously validated

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instruments measuring symptom burden, depression, anxiety, and well-being to inform future prospective studies.

Participants were given a self-administered questionnaire and compensated with a \$25 gift card.

Methods

The study received Institutional Review Board approval for a cross-sectional survey of AML patients at the Sidney Kimmel Comprehensive Cancer Center. Recruitment was between March and July 2013 in the outpatient clinics.

Adults between the ages of 18 and 65 years diagnosed with AML and in CR1 were eligible. After verbal consent, par-

Survey instrument

The questionnaire consisted of seven sections:

- (1) The European Organization for Research and Treatment of Cancer (EORTC) core 30-item questionnaire (QLQ-C30 v.3.0) covering five functioning domains (physical, role, emotional, cognitive, social, and global) and symptoms.⁶

TABLE 1. PARTICIPANT DEMOGRAPHICS AND CHARACTERISTICS

	<i>All patients N = 18</i>	<i>Patients in CR <2 years N = 9</i>	<i>Patients in CR 2+ years N = 9</i>
Age—median (range)	59.5 (38–70)	61 (38–69)	53 (43–70)
Gender—no. (%)			
Male	7 (39)	4 (44)	3 (33)
Female	11 (61)	5 (56)	6 (67)
Time in CR—no. (%)			
0–6 months	4 (22)	4 (22)	0 (0)
7 months to 2 years	5 (28)	5 (56)	0 (0)
>2 years	9 (50)	0 (0)	9 (100)
Not Hispanic or Latino—no. (%)	18 (100)	9 (100)	9 (100)
Race—no. (%)			
White	17 (94)	9 (100)	8 (89)
Other	1 (6)	0 (0)	1 (11)
Stem cell transplant—no. (%)	11 (65)	7 (78)	4 (44)
Employment status			
Employed—no. (%)	6 (33.3)	3 (33.3)	3 (33.3)
Self-employed—no. (%)	3 (16.7)	1 (11.1)	2 (22.2)
Homemaker—no. (%)	4 (22.2)	2 (22.2)	2 (22.2)
Retired—no. (%)	5 (27.8)	3 (33.3)	2 (22.2)
Unable to work (%)	2 (11.1)	2 (22.2)	0
Income—no. (%)			
<\$30K	2 (11.1)	1 (11.1)	1 (11.1)
\$30–60K	2 (11.1)	1 (11.1)	1 (11.1)
\$60–90K	9 (33.3)	4 (44.4)	2 (22.2)
\$90K+	8 (44.4)	3 (33.3)	5 (55.6)
Health insurance			
Medicare—no. (%)	5 (27.8)	3 (33.3)	2 (22.2)
Medical assistance program—no. (%)	2 (11.1)	1 (11.1)	1 (11.1)
Private insurance—no. (%)	15 (83.3)	7 (77.8)	8 (88.9)
Self-pay—no. (%)	4 (22.2)	2 (22.2)	2 (22.2)
Blood transfusions—no. (%)			
1+ times/week	1 (5.5)	1 (11.1)	0 (0)
Once a month	1 (5.6)	1 (11.1)	0 (0)
Do not require	16 (88.9)	7 (77.8)	9 (100)
Self-reported medical conditions—no. (%)			
Cancer (not AML)	3 (16.7)	2 (22.2)	1 (11.1)
Depression	6 (33.3)	4 (44.4)	2 (22.2)
Diabetes	1 (5.6)	0 (0)	1 (11.1)
Ulcers	1 (5.6)	1 (11.1)	0 (0)
Emphysema (COPD)	1 (5.6)	1 (11.1)	0 (0)
Anxiety	2 (11.1)	1 (11.1)	1 (11.1)
Thyroid problems	3 (16.7)	1 (11.1)	2 (22.2)
High blood pressure	5 (27.8)	2 (22.2)	3 (33.3)
Asthma	2 (11.1)	2 (22.2)	0 (0)
GVHD	6 (33.3)	4 (44.4)	2 (22.2)
Pneumonia	6 (33.3)	3 (33.3)	3 (33.3)
Arthritis	5 (27.8)	1 (11.1)	4 (44.4)

GVHD, graft-versus-host disease.

- (2) The 40-item QOL-CS scale assessing physical, psychological, spiritual well-being, and social concerns of cancer survivors. The QOL-CS psychological subscale contains two subcomponents assessing patients' perceived amount of distress and fear.⁷
- (3) The 13-item Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) scale version 4.^{8,9}
- (4) The 14-item hospital anxiety and depression scale (HADS).¹⁰
- (5) Five qualitative questions.
- (6) Sociodemographic information, medical history, and exercise history using the Godin Leisure-Time Exercise Questionnaire.¹¹
- (7) Participant feedback questions: three questions regarding the primary objective of the survey: "How relevant did you find the questions in this questionnaire in understanding your quality of life," "What do you think about the length of this questionnaire," and "Any additional suggestions or comments?"

Statistical methods

Participant characteristics were summarized using descriptive statistics. Validated measures were scored according to scoring guidelines. For each scale, a summary score was calculated. For some scales, scores were calculated within specific domains (i.e., distress and fear subcomponents). Patient QOL scores were summarized by duration of CR (short-term CR was defined as less than two years and long-term CR was defined as two years or more).

The five open-ended responses were analyzed using the grounded theory approach. Responses were independently reviewed by the first author and coauthor (A.M.), using a line-by-line process to generate preliminary coding categories.¹² Responses were independently reviewed and coded. The responses were compared and consensus was reached and themes generated.

Results

Twenty patients were approached, and 18 completed the survey. Participants' mean and median age were 57.2 and 59.5 years, respectively. Nine patients were in CR for less than two years, and nine were in CR for two years or more. Eleven patients (61%) underwent stem cell transplant and six reported chronic graft-versus-host disease (GVHD) (Table 1).

Eight participants felt the survey was completely relevant (44.4%) and eight felt mostly relevant (44.4%) in understanding their QOL. Fourteen felt the length of the survey was optimal (77.8%), three (16.7%) felt it was somewhat too long, and one participant felt it was too short. Participant comments are provided in Table 2.

In the EORTC QLQ-C30 questionnaire, participants scored the best in physical function (mean [standard deviation (SD)] = 86.3 [12.6]) and worst in cognitive function (mean [SD] = 77.8 [20.6]). Listed symptoms reported ranged from 11% (constipation) to 83% (fatigue). (Table 3).

The mean score (SD) on the FACIT-Fatigue (worst 0, best 52, normal ≥ 30) was 28.7 (12.6) and median score (range) was 33.5 (2–43) (Table 3).

TABLE 2. PARTICIPANT SURVEY COMMENTS AND FEEDBACK

Participant feedback question 3: "Any additional suggestions or comments?"

Great survey...It was therapeutic to answer the questions. Add questions about support system.

Very thorough survey. Well constructed.

Good length—need to have enough depth to the survey.

If patients can receive and do the survey at home so they don't have to spend so much time at clinic. Doing the survey on internet.

No, but thanks for looking into this—it make me feel better knowing others are going through the same things I am going through after fighting cancer.

More physical symptoms detailed.

I wasn't sure how to interpret the words "distressed" and "fearful." To me, distressed means that you can't think things through and it is too difficult to make a rational decision. I was never unable to come up with a reasonable solution. Fearful... Although I am fearful that the Leukemia will come back, I don't live my life in Fear. Does that make sense?

Qualitative questions: Context? During what time frame? In relation to what?

On the HADS anxiety score, two participants scored in the borderline range and two in the abnormal range. On the HADS score, one participant scored in the abnormal range (Table 3).

The mean scores for all participants in the QOL-CS questionnaire (worst 0, best 10) were more than six in all four well-being domains, with the exceptions of the psychological subscales of distress and fear (Table 3).

In the fear subscale, participants in both CR groups reported similarly when asked (1) To what extent are you fearful of future diagnostic tests (CR <2 years mean 5.2, CR ≥ 2 years mean 5.6); (2) To what extent are you fearful of a second cancer (CR <2 years mean 4.7; CR ≥ 2 years mean 5.6); (3) To what extent are you fearful of recurrence of your cancer (CR <2 years mean 6; CR ≥ 2 years mean 5.8).

In the Godin exercise questionnaire, 13 participants (76.5%) reported not engaging in strenuous activity any day of the week. When asked, "During a typical 7-Day period, in your leisure time, how often do you engage in any regular activity long enough to work up a sweat (heart beats rapidly)?" three, five, and nine participants reported working up a sweat often, sometimes, and rarely or never working up a sweat, respectively.

All 18 participants completed five open-ended questions. Themes and sample responses are given in Table 4.

Conclusions

In this pilot study of AML survivors in CR1, most participants felt the content and length of the survey were appropriate. Most scored well on physical, emotional, role, cognitive, and social function scores. Although it is difficult to generalize the findings of this study because of the small sample size, our results are similar to prior studies assessing QOL of patients in CR1.^{13,14} Our study incorporated

TABLE 3. PATIENT-REPORTED OUTCOMES FOR PARTICIPANTS IN SHORT-TERM AND LONG-TERM COMPLETE REMISSION

	All patients median (range), mean (SD), or no. (%) N=18	Patients in CR <2 years median (range), mean (SD), or no. (%) N=9	Patients in CR 2+ years median (range), mean (SD), or no. (%) N=9
EORTC QLQ-C30 V3.0 median (range) and mean (SD) 0 = worst, 100 = best			
Physical function	86.7 (46.7–100), 86.3 (12.6)	86.7 (46.7–100), 83 (15.7)	93.3 (80–100), 89.6 (8.2)
Role function	100 (50–100), 85.2 (19.7)	83.3 (50–100), 83.3 (18.6)	100 (50–100), 87.0 (21.7)
Emotional function	79.2 (33.3–100), 78.2 (16.7)	75 (66.7–100), 78.7 (11.9)	83.3 (33.3–100), 77.8 (21.2)
Cognitive function	83.3 (33.3–100), 77.8 (20.6)	83.3 (33.3–100), 77.8 (20.4)	83.3 (33.3–100), 77.8 (22)
Social function	100 (16.7–100), 81.5 (26.1)	100 (16.7–100), 77.8 (30)	100 (33.3–100), 85.2 (22.7)
Global health/QoL	83.3 (33.3–100), 78.2 (19.8)	75 (50–100), 77.8 (17.2)	83.3 (33–100), 78.7 (23.2)
EORTC QLQ-C30 any symptom–no. (%)			
Any fatigue	15 (83.3)	8 (89.8)	7 (77.8)
Any nausea/vomiting	4 (22.2)	2 (22.2)	2 (22.2)
Any pain	7 (38.9)	2 (22.2)	5 (55.6)
Any dyspnea	5 (27.8)	3 (33.3)	2 (22.2)
Any insomnia	7 (38.9)	4 (44.4)	3 (33.3)
Any appetite loss	4 (22.2)	3 (33.3)	1 (11.1)
Any constipation	2 (11.1)	2 (22.2)	0 (0)
Any diarrhea	7 (38.9)	5 (55.6)	2 (22.2)
Any financial difficulty	8 (44.4)	3 (33.3)	1 (11.1)
FACIT-Fatigue median (range) and mean (SD) 0 = worst, 52 = best	33.5 (2–43), 28.7 (12.6)	31 (2–43), 26.2 (14.2)	36 (10–42) 31.1 (11)
QOL-CS median (range) and mean (SD) 0 = worst, 10 = best			
Physical well-being	8.7 (3.4–9.8), 8.2 (1.7)	8.5 (5.1–9.8), 8.2 (1.3)	9.2 (3.4–9.6), 8.2 (2.2)
Psychological well-being	7.9 (4–10), 7.4 (2)	7.3 (4–9.7), 7 (1.9)	8.8 (4.4–10), 7.8 (2.1)
Distress	4.7 (1–9), 4.7 (2.1)	4.2 (2.4–9), 4.8 (2.1)	5.6 (1–6.8), 4.5 (2.2)
Fear	4.5 (0–10), 4.8 (3.4)	4.3 (0–10), 4.7 (3.6)	4.7 (0–10), 4.8 (3.4)
Social concerns	7.1 (2–9.9), 6.7 (1.8)	6.2 (4.1–9.9), 6.6 (1.7)	7.5 (2–8.6), 6.8 (2)
Spiritual well-being	7.4 (4.1–10), 7 (1.9)	5.9 (4.1–10), 6.5 (2.1)	8.1 (5–10), 7.6 (1.5)
HADS-anxiety no. (%)			
Normal	14 (78)	6 (67)	8 (89)
Borderline	2 (11)	2 (22)	0 (0)
Abnormal	1 (5)	1 (11)	1 (11)
HADS no. (%)			
Normal	17 (94)	8 (89)	9 (100)
Borderline	0 (0)	0 (0)	0 (0)
Abnormal	1 (6)	1 (11)	0 (0)

EORTC, European Organization for Research and Treatment of Cancer; FACIT–Fatigue, Functional Assessment of Chronic Illness Therapy–Fatigue; HADS, hospital anxiety and depression scale; QOL-CS, quality of life–cancer survivor; SD, standard deviation.

TABLE 4. THEMES AND SAMPLE RESPONSES TO THE FIVE OPEN-ENDED QUESTIONS

<i>Themes</i>	<i>Sample quotes</i>
What were your expectations after being in complete remission?	
Life to return to normal	To jump back into life physically and mentally the way I was prior to cancer. To have a normal life as before my illness.
Did not expect ongoing symptoms	Before the bone marrow transplant, I expected to have it and be exactly how I was before I had leukemia. After almost one year out, I realized that I will never be exactly the same. I will have a new normal.
Greater appreciation for life	That I would be happier with life and put more value on time.
Yearly tests	Tests yearly
Fight negative thinking	To be 100% cured. Fight any bad thinking. That I would be happier with life and put more value on time.
Describe how AML has affected you physically?	
Feeling fatigued	My strength is gone. My legs feel weak when I walk upstairs. Body looks different. Not as much energy. I am tired a lot.
Ongoing physical symptoms	Dry eyes, peripheral neuropathy in hands and feet. Tired a lot. Hair never came back the way they use to.
General health awareness	Made me more aware of diet and exercise. More aware of health.
No significant effect	It hasn't affected me that much. I did feel the initial month or two back at work was tough [...] but it improved quite rapidly.
Describe how AML has affected you emotionally?	
Ongoing anxiety	Struggle with anxiety and depression because of experience. Can't do my job like I use to. I get very emotional when I hear of others with cancer—I am afraid of getting sick again.
Increase awareness of mortality	Puts you in touch with your mortality. Want to do more now. I know everybody's time is finite.
Enhanced outlook on life	Emotionally I have a greater appreciation of each day and each moment. And I try to use time as if it is precious
Uncertain about the future	Not sure what's going to happen
Greater appreciation for life	Emotionally I have a greater appreciation of each day and each moment. And I try to use time as if it is precious.
Concerns for family	More desire to take care of my wife in case I am not around for her.
Describe how AML has affected you socially?	
Isolation	Have not delved into another relationship. Afraid of being rejected because of cancer diagnosis. [Want others] seeing me as a strong a courageous person and not a damaged person.
Increased sense of connection	I have met a lot more people I am open to talk about my cancer and help others.
Increased compassion for others	I have gone out of my way to be more kind and compassionate to others. I plan to try to help other people as much as I can.
No change from prior	It doesn't really affect me socially.
Describe how AML has affected you spiritually?	
Strengthening spiritual lives	I have become more spiritual and have relied on prayer often. I have never been a big prayer like some people do.
Trusting in a higher power	Although, while I was in the hospital and in Baltimore for 5 months, I prayed hard.
Challenging one's faith	Recognizing that God is faithful and trusting Him that He knows what He is doing. It definitely makes you question everything you've believed. The recovery has been longer than I expected and difficult. I have still held onto my faith, but it has been challenged.
Gratefulness	Grateful to be alive
Less worry about smaller things	I tend not to let smaller things bother me as much.

additional validated scales with cancer survivor-specific questions, symptoms of interest, and open-ended questions.

Fatigue continues to be one of the most common symptoms that persists despite being in disease remission. Although the etiology is multifactorial,^{15–18} we wanted to better understand survivors' activity levels and exercise patterns because these can have health implications.^{19,20} Our study suggests that both short-term and long-term CR patients are not as likely to engage in any regular activity long enough to work up a sweat. Whether this holds true in a larger sample

and whether activity level correlates with fatigue is an area for further exploration.

Our results raise the question of whether there is a population of cancer survivors who are coping less well. A theme observed in both the quantitative and qualitative responses is an ongoing fear of future diagnostic test results, developing a second cancer and the recurrence of cancer. In the cancer survivorship literature, FCR is one of the most frequently cited area of unmet need.^{21,22} FCR has been associated with psychological factors such as distress, anxiety, and depression.^{23,24}

Black and White examined the relationship between FCR and post-traumatic stress symptomatology (PTSS) in hematological cancer survivors. They found that FCR correlated positively with PTSS and 17% of the sample met DSM-IV criteria for post-traumatic stress disorder.²⁵ Further qualitative evaluations may better elucidate when FCR shifts from normal fear to interfering with everyday life.

It will also be informative to interview survivors who experienced serious illness in a positive life-transforming way as was hinted by some of the themes from the open-ended questions. Qualitative studies in other populations reported a phenomenon wherein participants reported subjective changes in response to life-threatening illnesses, leading to personal growth.^{26,27} One hypothesis is that the ability to experience illness in a transformative manner is protective against clinically significant distress. Finally, it is vital to note that even long-term survivors can continue to report ongoing symptoms and the importance of ongoing symptom and needs assessments.

There are several limitations to this study. The primary objective was to determine whether participants think the survey was relevant to their overall well-being and whether the length was appropriate before its use in prospective studies and was not designed to assess the activity of individual subgroups. The cross-sectional survey of a convenience sample also limits firm conclusions. The sample was small and demographically homogeneous. More than half of the participants have undergone a stem cell transplant. Since GVHD can have a profound impact on survivors' QOL, better characterization of those who developed chronic GVHD would have provided a fuller description of the burden of GVHD, including its impact on fatigue. Future studies should plan for separate chemotherapy-only and post-transplant groups as these are distinct populations in terms of disease risk, treatment course, and complications. Despite these limitations, this study is an initial step toward using this survey for better understanding of AML survivors' health and well-being.

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Author Disclosure Statement

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