Treatment Choices: A Quality of Life Comparison in Acute Myeloid Leukemia and High-risk Myelodysplastic Syndrome

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Abstract

The results of the present pilot study can be used to counsel older patients with acute myeloid leukemia and high-risk myelodysplastic syndrome regarding treatment choices that will align with their goals for their quality of life. Future studies are needed with a larger and more diverse patient sample to address whether the more intensive treatment approach improves patients' quality of life.

Background: In the present exploratory, observational study, we compared the effect of intensive versus nonintensive treatment on quality of life for patients aged ≥ 60 years diagnosed with acute myeloid leukemia or high-risk myelodysplastic syndrome at 1 month after treatment. **Patients and Methods:** A total of 73 patients with acute myeloid leukemia or high-risk myelodysplastic syndrome who had been treated at the inpatient and outpatient malignant hematology at Moffitt Cancer Center, a National Cancer Institute-designated comprehensive cancer center, were included. Two paired measurements of self-reported quality of life were used, 1 before treatment and 1 at 1 month after treatment to compare intensive versus nonintensive treatment. Patients completed the Functional Assessment of Cancer Therapy—Leukemia version for the quality-of-life measurement. Repeated measures analysis of variance was used to compare the effect of treatment and time and the interaction of treatment and time. The main research variables were intensive versus nonintensive treatment as the independent variable and quality of life measured using the Functional Assessment of Cancer Therapy—Leukemia version as the dependent variable. **Results:** Physical function and leukemia symptoms improved for patients treated with intensive chemotherapy. A trend was found for improved quality of life for the intensive treatment compared with nonintensive treatment, for which the quality of life was stable at 1 month. **Conclusion:** The study participants treated with inpatient, induction chemotherapy experienced statistically significant improvement in their quality of life at 1 month. The outpatient, nonintensive study participants had stable quality of life at 1 month.

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Introduction

Patients diagnosed with acute myeloid leukemia (AML) and high-risk myelodysplastic syndrome (MDS) face the difficult decision of choosing the best treatment with the knowledge of a life-threatening illness. However, few studies are available to guide health care professionals and patients in choosing the best treatment according to quality of life (QOL). Both AML and MDS are bone marrow malignancies that occur commonly in older individuals, for whom the optimal treatment remains controversial.[1] Treatment can range from supportive care to hematopoietic stem cell transplantation. The diseases are often studied together because they have similar disease characteristics, life expectancy (for high-risk MDS), age at diagnosis, comorbidities, and treatment options.[1-3] The most common form of adult acute leukemia is AML, with approximately 18,860 cases diagnosed and 10,460 deaths in 2014.[4] The median age at diagnosis in the United States is 67 years, according to the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) data.[4] The incidence of MDS using a claims-based algorithm in conjunction with SEER data project approximately 50,000 cases annually in the Unites States, with a median age of 76 years.[5] Approximately 20,000 cases of MDS are high risk.[6] High-risk MDS is determined by calculating an

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individual score, the International Prognostic System Score, from unique patient characteristics, including the number of cytopenias, percentage of marrow blasts, and cytogenetic abnormalities present.[7] The choice of treatment is determined by patient age, performance status, comorbidities, and preference.[8] High-risk MDS and AML are treated using the same methods, have a similar prognosis, and were grouped for comparison in the present study.

Treatment

The standard AML treatment for patients aged ≥ 60 years is determined by the performance status, previous hematologic disorders, the presence of unfavorable cytogenetic or molecular abnormalities, and whether AML is related to previous chemotherapy or radiation therapy.[9] The treatment recommendations for patients with an Eastern Cooperative Oncology Group performance status of 0 to 2 include a clinical trial, intense chemotherapy with induction chemotherapy, and nonintensive chemotherapy with azacitidine or decitabine. A clinical trial, non-intensive chemotherapy, and best supportive care are recommended for patients with a performance status > 2 or significant comorbidities and for those aged > 75 years. Intense chemotherapy includes cytosine arabinoside and an anthracycline administered in the hospital, with an anticipated length of hospitalization of 4 to 6 weeks, and a cure rate of 35%.[10] Most AML and high-risk MDS patients are not able to tolerate hematopoietic stem cell transplantation, which is the standard of care for many younger patients.[11] According to the SEER data, the 5-year relative survival rate from 2007 to 2012 was 25.9% for adults.[4] In contrast, the 5-year disease-free survival rates for AML patients aged ≥ 65 years was only 5%. The survival rates for older AML patients have not changed in the past 3 decades.[12] Studies are ongoing to try to improve the overall survival and cure rates for this distinct population of patients.[13,14] In contrast, few studies have focused on the quality of their survival with different treatment approaches.[15]

The goal of treatment with high-risk MDS is to maintain the best QOL and improve survival. Cure is impossible without allogeneic stem cell transplantation. The National Comprehensive Cancer Network has recommended that age, performance status, and comorbidities determine the appropriate therapy.[8] Patients should receive supportive care, which includes QOL evaluation, psychosocial support, transfusions with blood products when needed, and infection management.[8] The treatment recommendations for high-risk MDS include low-intensity therapy with a hypomethylating agent such as azacitidine or decitabine. Hypomethylating agents are administered in the outpatient setting monthly, for as long as the patient responds or until the development of adverse side effects. Allogeneic stem cell transplantation is considered if the patient is healthy and has a human leukocyte antigen-identical donor.[8,16,17]

Most AML and high-risk MDS patients die within 5 years with or without standard treatment.[18,19] To prevent unnecessary suffering, it is important to understand how treatment influences QOL for these patients, because cure is improbable. Aggressive cancer care near the end of life has been reviewed.[20] Patients with various malignancies continued to receive intensive chemotherapy within 14 days of death in 17.1% of patients, and approximately 10% of patients remained hospitalized in the last month of life. The hematologic malignancies, such as AML and MDS, were most strongly associated with aggressive care. Additional findings included underusage of hospice services. The 1999 National Cancer Policy Board defines this as poor quality of care, when practices of known effectiveness are infrequently used.[21] Studies are needed that compare patient QOL with different treatment approaches, intense versus nonintense, and the variables that can predict patient QOL with different treatment approaches.

The purpose of the present observational study was to evaluate the effect of different treatments on QOL for older AML and high-risk MDS patients. The independent variable was the 2 approaches to treatment, intensive and nonintensive. The dependent variable was QOL. We compared the difference in QOL scores measured using the Functional Assessment of Cancer Therapy—Leukemia version for intensive chemotherapy and nonintensive therapy within 7 days of new treatment and 1 month after initiation of treatment in older patients with AML or high-risk MDS.

Patients and Methods

The scientific review committee of Moffitt Cancer Center approved the present study, followed by approval from the institutional review board of the University of South Florida. Patients were approached by the principal investigator at their scheduled appointment or during the first week of their admission to obtain informed consent and administer the questionnaires. Eligibility was confirmed using a checklist. A quiet, comfortable room was provided for the patients to complete the questionnaires. A copy of the consent form was provided to participants to keep for future reference, with contact information provided within the consent form. It was emphasized that participation was voluntary and that their care would not be altered, regardless of study participation. Demographic data were captured using a 2-page sheet completed by each patient. The Functional Assessment of Cancer Therapy—Leukemia version (FACT-Leu) and Brief Fatigue Inventory were administered within the first week of treatment. The second FACT-Leu was administered ≥ 4 weeks later. The data were stored in a locked filing cabinet in a locked office in the hematology clinic. All data were extrapolated to Excel spreadsheets coded only by the patient identification number to ensure patient confidentiality. The FACT-Leu scores were designated as FACT-Leu 1 and FACT-Leu 2 to identify the first and second measurements.

Study Design

We used an exploratory observational study design to compare the QOL between the 2 treatment approaches in patients aged ≥ 60 years with high-risk MDS and AML at 2 measurement points. The plan was to compare 3 treatment groups; however, low accrual for the supportive care group limited the evaluation to 2 groups. A randomized controlled trial was not possible because treatment decisions are based on prognostic indicators and patient preference and because of ethical concerns for randomization to specific treatment versus supportive care, given the diagnosis.

The setting was the Department of Malignant Hematology at Moffitt Cancer Center, a National Cancer Institute-designated Comprehensive Cancer Center that sees > 100 new leukemia and high-risk MDS patients annually. Recruitment occurred at the patients' appointments in the hematology clinic or during admission to the Moffitt Cancer Center for treatment evaluation of AML or high-risk MDS.