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Quality of life and physical function in adults treated with intensive chemotherapy for acute myeloid leukemia improve over time independent of age☆

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ABSTRACT

Objectives: Intensive chemotherapy (IC) is the primary treatment of acute myeloid leukemia (AML) but is associated with significant toxicity, particularly in older adults. We characterized the impact of AML and its treatment on quality of life (QOL) and physical function in younger (age 18–59) and older (age 60+) patients with AML over 1 year from diagnosis.

Materials and methods: AML patients undergoing IC without stem-cell transplant at two tertiary care centers were enrolled in a prospective, longitudinal study. Assessments were done pre-IC and at 7 time points over the next year. QOL, fatigue, and physical performance (grip strength, 2-minute walk test (2MWT), timed chair stands) were measured in all patients whereas daily function was measured only in older patients. Data were analyzed using mixed effects regression models.

Results: 237 patients were recruited (140 younger and 97 older, 56% male). One-year survival was 79% and 60% among younger and older patients, respectively. For patients in remission, global QOL and fatigue improved significantly over time ($p < 0.001$ for both); trends were similar between older and younger patients. Grip strength did not change over time ($p = 0.58$) whereas both the 2MWT ($p < 0.001$) and timed chair stands ($p < 0.001$) improved significantly. Daily function improved significantly over time ($p = 0.003$).

Conclusions: Survivors of AML in remission after IC achieve significant improvements in QOL, fatigue, and physical function over time with similar trajectories for older and

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younger patients. These data suggest that appropriately selected older patients do well following IC.

1. Introduction

Acute myeloid leukemia (AML) is an aggressive hematological malignancy primarily occurring in older adults, with a median age of onset of 68 years, and a 3-year survival below 20% in adults over age 60.[1] There are three main initial treatment options: intensive chemotherapy (IC), supportive care, and investigational agents, with IC being preferred for most otherwise fit patients in terms of disease control and improved survival.[2] IC consists of one or two cycles of induction followed by several cycles of consolidation chemotherapy. Although IC is associated with improved survival, it is also associated with significant toxicity and long periods of hospitalization, which may negatively affect quality of life (QOL) and physical function.

Older adults with AML have a poorer prognosis than younger adults and higher treatment-related morbidity and mortality.[3] Moreover, aging is associated with significant declines in physiologic function and reparative ability across a wide range of organ systems.[4,5] This leaves older adults particularly vulnerable to treatment toxicity and prolonged hospitalization, which may reduce QOL and worsen physical function. This perception of major declines in QOL and physical function may contribute to the significantly lower rates of IC in older versus younger adults with AML.[6,7]

To date, relatively few studies have analyzed QOL and physical function in patients undergoing this treatment. One prospective study (n = 27) found that induction treatment was associated with physical and psychological distress, as well as decreased QOL.[8] Another study involving 61 patients aged 16–70 undergoing IC concluded that subjective benefits reported by patients outweighed the adverse effects,[9] although data were not analyzed by age group. We are aware of only one study that prospectively compared QOL and physical function in older and younger adults undergoing IC.[10] We previously reported a preliminary analysis of the first 103 patients included in the present study who were assessed over the first three cycles of chemotherapy. We found small improvements in global QOL and physical function, with no change in fatigue, over these three cycles. In general, younger and older adults had similar trajectories of QOL over time, although physical function improved more in younger adults.[10]

Understanding QOL and physical function in survivors of AML is important for several reasons. First, there have been slow but steady improvements in longer-term survival, particularly among younger patients, over the past few decades.[6,11,12] As survival continues to improve, longer-term survivorship issues become more pertinent. Second, the prognosis of older adults lags significantly behind younger adults, and clinicians continue to debate the merits of offering IC to newly diagnosed older adults with AML. This is particularly important with the availability of non-intensive therapies such as hypomethylating agents. Understanding the level of QOL and physical function in older adults who achieve remission with IC is important, since these two areas are paramount in the minds of older adults with cancer.[13]

Our objectives were: (1) to investigate the impact of the treatment of AML with IC on QOL, fatigue, and physical function over 12 months from diagnosis; (2) to compare changes in these outcomes between older (aged ≥60 years) and younger (18–59 years) patients; and (3) to examine the impact on daily activities in older adults.

2. Methods

2.1. Patient Population

This prospective longitudinal cohort study was conducted at two university-affiliated tertiary care cancer centers in Toronto, Canada: the Princess Margaret Cancer Centre and the Odette Cancer Centre. The study was reviewed and approved by respective institutional research ethics boards. Patients were recruited from May 2008 to March 2012. Consecutive adult patients age 18 years or older who were newly diagnosed with AML, and who opted to undergo IC were eligible. Patients were recruited before or within three days of starting cycle 1 of IC, which consisted of daunorubicin 60 mg/m^2/day for three days plus cytosine arabinoside (Ara-C) 200 mg/m^2/day (100 mg/m^2/day for patients aged ≥60) as a continuous infusion for seven days. Patients achieving a complete remission (CR) then received two cycles of consolidation therapy as described previously.[10] Patients who did not achieve CR with one cycle of IC could receive a second induction, consisting of mitoxantrone, etoposide, and Ara-C.[14]

Patients who consented were seen at eight time points over 12 months: pre-IC, after each of the first three cycles of chemotherapy, which were roughly at 4–6 weeks, 9–12 weeks, and 13–16 weeks, and then at six months, eight months, ten months, and 12 months after diagnosis.

Demographic information, disease characteristics, performance status (PS) using the Eastern Cooperative Oncology Group (ECOG) scale, and co-morbidities were obtained from the patient's hospital record. Cytogenetic risk group was categorized using the Medical Research Council system.[1] At each visit, patients completed a series of self-administered questionnaires and three physical function tests. We recorded when patients were present for the visit but too unwell or unwilling to complete physical function tests. Patients were censored from the study if they went on to bone marrow transplantation (BMT), at the time of disease relapse, or if they did not achieve CR after one or two cycles of IC with no further plans for IC.

2.2. Patient-reported Outcomes

Patient-reported outcomes completed at each visit included the European Organisation for the Research and Treatment of Cancer (EORTC) 30-item questionnaire (QLQ-C30)[15] and the Functional Assessment of Cancer Therapy fatigue subscale (FACT-Fatigue).[16] The EORTC QLQ-C30 is a validated generic QOL scale for cancer patients that has been widely translated

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