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Geriatric assessment in older patients with acute myeloid leukemia: A retrospective study of associated treatment and outcomes

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ABSTRACT

We explored whether geriatric assessment variables predicted mortality in addition to known prognostic factors in 101 patients aged ≥65 with newly diagnosed AML. Baseline comorbidity score (HR = 1.92; 95%CI 1.18–3.11), difficulty with strenuous activity (HR = 2.18; 95%CI 1.19–4.00), and pain (HR = 2.17; 95%CI 1.19–3.97) were independent prognostic factors for greater risk of death in a multivariable model that included cytogenetic risk group. They remained independent predictors in the subset of patients with baseline ECOG PS 0-1. Our results support the use of geriatric assessment to better predict prognosis in older patients with AML, even among those with excellent functional status.

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1. Introduction

Acute myeloid leukemia (AML) is a disease of older adults whose incidence will increase dramatically in coming decades due to population aging [1]. AML patients over age 65 have much worse prognosis than younger patients, with a five-year disease-specific survival of only 5% [2]. These poor outcomes are due to a combination of age-related changes in disease biology and clinical factors such as decreased physiologic reserve, functional impairment and frailty [3–5]. Previous work has identified age, performance status, comorbidity, and cytogenetic risk group as important prognostic factors in older patients with AML [6]. However, few studies have explored the relationship between geriatric assessment and AML outcomes.

Comprehensive geriatric assessment (CGA) is a systematic method of identifying multiple predictors of morbidity and mortality in older adults that may impact cancer treatment and is recommended for older cancer patients by NCCN guidelines [7]. This recommendation was in part based on a multicenter study demonstrating that a self-administered geriatric assessment identified important prognostic factors in cancer patients [8]. A geriatric evaluation includes assessment of multiple domains including comorbidity and physical, cognitive and social function. The feasibility of performing a modified CGA in older patients with AML has been demonstrated, but it is not yet known how this information predicts outcomes [9].

Careful assessment of the potential benefits and risks of therapy is particularly vital in AML, as intensive chemotherapy with cytarabine and an anthracycline is the only treatment that gives hope of long-term survival. Response to induction is poor among older adults and toxicity is substantially higher than in younger individuals, but selected patients can achieve remission and cure [10–12]. Patients who are not candidates for induction may benefit from non-intensive treatments such as hypomethylating agents, and some are best served by purely palliative approaches [13,14]. However, it can be difficult to predict which older patients will benefit from chemotherapy using routine clinical and biological factors alone. Growing evidence suggests that measures of comorbidity

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Table 1
Demographic and clinico-pathologic characteristics.

Characteristic	*N* (%)
Age at diagnosis (years)	
65–70	41 (40.6%)
71–75	24 (23.8%)
75–80	20 (19.8%)
>80	16 (15.8%)
Male	63 (62.4%)
White	99 (98.0%)
BMI (kg/m^2), mean ± SD	27.9 ± 4.9
Physician-rated ECOG PS	
0	25 (24.8%)
1	55 (54.5%)
2	17 (16.8%)
3	4 (4.0%)
HCT-comorbidity index	
≤1	64 (63.4%)
>1	37 (36.6%)
Number of medications, mean ± SD	5 ± 3
History of tobacco use	59 (59.6%)
Family history of hematologic malignancy	15 (14.9%)
Origin of disease	
De novo	55 (54.5%)
Secondary to MDS	34 (33.7%)
Treatment-related	12 (11.9%)
Cytogenetic risk group	
Favorable	2 (2.0%)
Intermediate	47 (46.5%)
Adverse	32 (31.7%)
Unknown	20 (19.8%)
Percent blasts in bone marrow, mean ± SD	40.7 ± 24.2
Initial treatment received	
Induction chemotherapy	35 (35.0%)
Decitabine or Azacitidine	34 (34.0%)
Other[a]	7 (7.0%)
Palliative only	24 (24.0%)
Consolidation chemotherapy	20 (19.8%)
Stem cell therapy	18 (17.8%)
Initial treatment on clinical trial	23 (23.0%)
Patients achieving complete response by initial treatment	
Induction chemotherapy	25 (71.4%)
Decitabine or Azacitidine	2 (5.9%)
Other[a]	0 (0.0%)
Palliative only	0 (0.0%)
Relapse	12 (11.9%)

[a] Other includes oral 6-mercaptopurine, Iressa clinical trial (CT), FLT3 inhibitor with mTOR inhibitor CT, CT with Revlimid and Velcade, histone deacetylase inhibitor CT, Cloretazine CT, and all-trans retinoic acid.

and functional status may also be valuable prognostic factors in elderly patients with AML [15–18]. We utilized prospectively collected quality of life data to evaluate the utility of geriatric factors as predictors of survival in older patients with AML across varying treatment intensities.

2. Methods

2.1. Data collection

We performed a retrospective cohort study of consecutive patients ≥65 years of age that presented to Dana-Farber Cancer Institute (DFCI) between 2006 and 2011 for evaluation of a new diagnosis of AML. At the DFCI, all new patients with hematologic malignancies are asked to participate in a research protocol that involves a baseline questionnaire and prospective collection of clinical data into the Cancer Research Information System (CRIS) database. CRIS includes information collected by trained abstractors on patient demographics, initial treatment assignment, disease characteristics, pathology tests, hospitalizations, treatments and date and cause of death. We used CRIS to identify all patients ≥65 years of age who presented between January 2006 and December 2011 with a new diagnosis of AML. We excluded patients who filled out their survey after beginning chemotherapy for AML.

The survey includes items from the European Organization for Research and Treatment of Cancer (EORTC) quality of life questionnaire (QLQ) for the evaluation of health-related quality of life of cancer patients (QLQ-C30) (Table 2). Responses to questions about function and symptoms are rated on a scale of 1 (not at all) to 4 (very much). Chart review was performed by a trained medical student (AS) and verified by a geriatric oncologist (JD). We validated all clinical data provided by CRIS. We gathered additional information on baseline diagnosis and pathology, laboratory tests, oncologist assigned Eastern Cooperative Oncology Group (ECOG) performance status (PS) and cytogenetic data. We recorded the course of treatment, number and length of hospitalizations, and survival. We considered inclusion of standard anthracycline and cytarabine regimens in initial treatment as induction. All patients provided written informed consent for their data to be included in the CRIS database. This study was approved by the DFCI Institutional Review Board.

2.2. Definition of predictors and outcomes

To determine if geriatric assessment variables predict mortality in our population, we selected questions from the QLQ-C30 that correspond to geriatric domains, including physical function, social function, cognition, psychological state, nutritional status, and pain (Table 2). We divided survey responses into two categories: 1–2 ("not at all" or "a little") versus 3–4 ("quite a bit" or "very much"). We assessed comorbidities by means of the Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI), a tool designed to quantify the effect of comorbid conditions on mortality in patients with hematologic disease [19]. We defined a low albumin as <3.5 mg/dL. We used median age at diagnosis as our age variable. We defined cytogenetic risk as favorable, intermediate, or adverse [20]. We defined overall survival (OS) as the time from the date of diagnosis of AML at DFCI to the date of death or the date of last follow-up. Disease-specific survival considered only deaths attributed to AML. Complete remission (CR) was defined according to the International Working Group [21]. There was no distinction made between those achieving CR after one or two cycles of induction chemotherapy [22]. We categorized initial treatment assignment into the following groups: induction chemotherapy, hypomethylating agents, and palliative/other therapies.

2.3. Statistical methods

We used Kaplan–Meier (KM) survival curves to describe the survival of the cohort, and to determine the univariate association between variables of interest and mortality. The log-rank test was employed to test the difference in KM curves between groups. Only variables that predicted mortality on univariate analyses ($P < 0.05$) were included in the multivariate analysis. We used multivariate Cox proportional hazard models to determine which factors were independently associated with mortality. We used Chi-squared tests to identify variables associated with reception of induction chemotherapy. We included these factors in a multivariate binary logistic regression model to determine independent predictors of receiving induction. A *P*-value <0.05 was considered significant. Statistical analyses were performed using SPSS 20.0 software (SPSS Inc., Chicago, IL).

3. Results

Between 2006 and 2011, 368 patients 65 and older presented to the DFCI with a diagnosis of AML. Of these, 163 (44.3%) did not complete the new patient survey prior to hospitalization for AML, 62 (16.8%) received previous chemotherapy for AML, and 42 were missing information on key variables, leaving 101 patients for the analysis. Baseline characteristics of the cohort are listed in Table 1. Overall, the cohort was white (98%), had a performance status ≤1 (79.3%), and had ≤1 comorbidity (72.4%).

About one-third (35.0%) of the patients underwent induction, 20 (19.8%) underwent consolidation chemotherapy, and 18 (17.8%) patients received stem cell therapy (SCT), most of which was non-myeloablative from a matched unrelated donor. 41.0% of patients received chemotherapy other than standard induction, and about a quarter (24%) of the cohort received only palliative or supportive care. 23% of patients received initial treatment in a clinical trial.

Self-reported geriatric assessment variables are displayed in Table 2. Answers to questions ranged from 1 (not at all) to 4 (very much) and asked patients to consider their condition in the past week. One-third of patients reported substantial ("quite a bit" or "very much") difficulty doing strenuous activities or limitations in their work or daily activities, and only 3 patients reported requiring more help with activities of daily living (ADLs) including eating, dressing, washing, and toileting. Cognitive complaints were relatively uncommon, although nearly half (47.5%) of patients reported feeling more depressed in the past week. 15.8% of patients reported substantial pain during the past week.

The median overall survival of the group was 7.8 months. The one-year OS was 37.4% and the one-year disease-specific survival was 39.0%. Survival based on demographic, tumor, treatment,