Original Study

Marrow Hypocellularity, But Not Residual Blast Count or Receipt of Reinduction Chemotherapy, Is Prognostic on Day-14 Assessment in Acute Myeloid Leukemia Patients With Morphologic Residual Disease

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Abstract

In our single center retrospective study of day 14 bone marrow assessment in AML, we found cellularity to be a stronger predictor of response than blast percentage or receipt of re-induction chemotherapy. For patients with blast percent and cellularity.

Background: Induction chemotherapy for acute myeloid leukemia (AML) is based on the "7+3" cytarabine/anthracycline regimen. A nonhypocellular day 14 (D14) bone marrow sample with a blast count > 5% to 10% is suggestive of residual leukemia, for which a second course of induction chemotherapy has been recommended. Although the prognostic value of D14 bone marrow findings has been established, its use as a decision point is controversial because the benefit of repeat induction has been questioned. **Patients and Methods:** In the present single-center retrospective study of 113 patients with newly diagnosed AML, we evaluated the role of cellularity on the clinical outcomes of patients with residual morphologic leukemia (blasts ≥ 5%). Among 64 patients with D14 bone marrow samples, 31 had residual morphologic leukemia. **Results:** The complete remission (CR) rates were greater for the hypocellular (11 of 16) than for the nonhypocellular (4 of 15) patients ($P = .03$). The median overall survival (OS) for the hypocellular D14 patients was longer than that for the nonhypocellular patients (17 vs. 8 months; $P = .02$). No significant difference between the receipt of reinduction therapy and CR or OS was found on logistic or survival model analysis. The specificity for residual leukemia on D14 bone marrow samples was better for cellularity ≥ 20% and blasts ≥ 20% than for blasts ≥ 5%. **Conclusion:** The results of our study have shown that patients with < 20% cellularity and < 20% blasts on the D14 bone marrow assessment should continue observation until recovery rather than receive additional immediate therapy.

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Introduction

The standard induction chemotherapy for acute myeloid leukemia (AML) over the past 30 years has been based on the "7+3" regimen consisting of cytarabine and daunorubicin (DNR) or idarubicin. With this combination, complete remission (or complete response; CR) rates of 40% to 80% have typically been achieved.[1-3] Current practice, endorsed by the National Comprehensive Cancer Network recommendations, is to perform a repeat bone marrow assessment on day 14 (D14) of the initial induction cycle.[4,5] A blast count > 5% to 10% with bone marrow cellularity of 10% to 20% on D14 suggests residual leukemia, and a second round of induction chemotherapy is administered, in the absence of clinical contraindications.

The achievement of the target blast count in the bone marrow of < 5% on D14 portends a favorable outcome.[6,7] Early blast clearance confers a good prognosis, irrespective of either the specific

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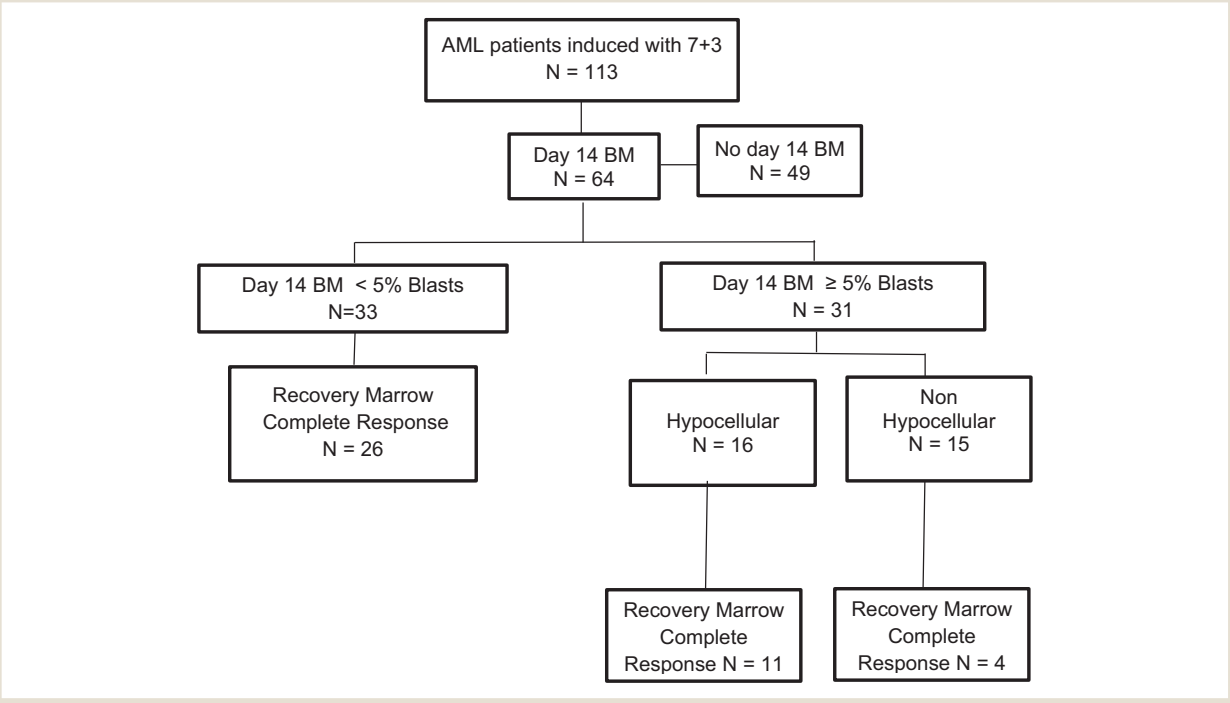
Figure 1 Flow Diagram Depicting Patient Selection Stratified by Day 14 Bone Marrow (BM) Biopsy Assessment Findings



Abbreviation: AML = acute myeloid leukemia.

day of the bone marrow assessment[8,9] or evaluation of blast clearance from the peripheral blood.[10] However, considerable disagreement exists regarding the value of immediate reinduction chemotherapy for morphologic residual leukemia found on the D14 bone marrow assessment. Several studies have suggested similar rates of CR, regardless of whether patients had received reinduction chemotherapy and suggested no benefit for additional chemotherapy for residual morphologic disease, especially in patients with 5% to 19% residual blasts.[11-13] Moreover, a recent study determined that the D14 marrow hypocellularity and not the residual blast count was the strongest predictor of CR for patients with residual blasts on the D14 bone marrow assessment among those patients who had undergone a second induction for residual leukemia.[14]

In the present single-center retrospective study, we evaluated the association between bone marrow cellularity, the initial response to chemotherapy, and receipt of reinduction treatment on CR and survival in patients with residual leukemia found on the D14 bone marrow assessment. We hypothesized that D14 cellularity and not receipt of a second induction or bone marrow blast percentage would be the strongest predictor of response and survival.

Patients and Methods

We retrospectively identified all consecutive patients aged ≥ 18 years who had undergone induction chemotherapy with DNR and cytarabine for newly diagnosed AML from January 1, 2006 to May 1, 2013 at the Rhode Island Hospital. Patients with acute promyelocytic leukemia were excluded. All patients received DNR 60 or 90 mg/m^2 on days 1 to 3 and concurrent cytarabine 100 to 200 mg/m^2/d administered as a 24-hour infusion on days 1 to 7. A subset of patients also received etoposide 100 mg/m^2 on days 1 to 3 over 2 hours, often as part of therapy in a contemporaneous clinical trial.[15] The institutional review board approved the present study.

We recorded the demographic data (age, sex, Eastern Cooperative Oncology Group performance status), AML-specific baseline characteristics (initial white blood cell count, initial bone marrow blast count, cytogenetic risk stratification, DNR dose, use of etoposide, and previous exposure to chemotherapy and/or radiation), D14 bone marrow blast count, D14 bone marrow cellularity, and outcomes of interest. The latter included achievement of CR, overall survival (OS), time to platelet recovery, time to neutrophil recovery, and number of units of packed red blood cells and platelets transfused during induction. Day 1 was defined as the first day of chemotherapy. The induction period was defined from the receipt of initial chemotherapy to day 35 after therapy or at the recovery bone marrow biopsy, whichever came first. Cytogenetic risk was categorized as favorable, intermediate, and unfavorable according to the National Comprehensive Cancer Network guidelines.[4] Too few patients had molecular data available to perform risk stratification.

D14 bone marrow assessments and the clinical decision to administer reinduction according to the D14 bone marrow assessment results were obtained per attending physician discretion. Patients were determined to have residual leukemia on the D14 bone