Original Study

Racial Differences in the Overall Survival of Hairy Cell Leukemia in the United States: A Population-Based Analysis of the Surveillance, Epidemiology, and End Results Database

Smith Giri,[1] Rajesh Shrestha,[2] Ranjan Pathak,[3] Vijaya Raj Bhatt[4]

Abstract

This was a retrospective population-based study of adult patients with hairy cell leukemia diagnosed between 1978 and 2011 in the United States. The 10-year overall survival was significantly lower for African American compared with white and Asian/Pacific Islander individuals (54% vs. 72% vs. 75%; *P* < .001). In a multivariate analysis, African American race remained an independent predictor for a worse overall survival (hazard ratio, 1.77; 95% confidence interval, 1.30-2.40; *P* < .001) after adjusting for age, sex, year of diagnosis, and marital status. Only half of African American but more than two-thirds of hairy cell leukemia patients from other racial groups were alive at 10 years.

Background: Several studies have reported excellent long-term overall survival (OS) of patients with hairy cell leukemia (HCL) without racial disparity. Studies in other cancers have demonstrated worse mortality among African American (AA) individuals. **Patients and Methods:** We used the Surveillance, Epidemiology, and End Results 18 database to identify HCL patients diagnosed between 1978 and 2011. Kaplan–Meier curves were plotted to estimate OS. Univariate analysis using the life table method and multivariate Cox regression model were used to determine the independent effect of race on OS. **Results:** The study population included 78% men and had a median age of 56 years. Race included 93% white, 3.5% Asian/Pacific Islander, and 3.5% AA. The 10-year OS was significantly less for AA as compared with white and Asian/Pacific Islander individuals (54% vs. 72% vs. 75%; $P < .001$). A Kaplan–Meier survival curve showed a significantly worse OS for AA versus other races ($P < .001$). In a multivariate analysis, AA race remained an independent predictor for a worse OS (hazard ratio 1.77; 95% confidence interval, 1.30-2.40; $P < .001$) after adjusting for age, sex, year of diagnosis, and marital status. **Conclusion:** In this population-based study, only half of AA patients but more than two-thirds of HCL patients from other racial groups were alive at 10 years. Such drastic racial differences in OS of HCL patients at the population level mandates further evaluation of the contributory biological, socioeconomic, health system, and other factors. Understanding and overcoming such racial disparities might close the racial differences in OS of this potentially curable disease.

Clinical Lymphoma, Myeloma & Leukemia, Vol. 15, No. 8, 484-8
Keywords: African American, Caucasian, Indolent B-cell lymphoproliferative disorder, Marital status, Racial disparity

Introduction

Hairy cell leukemia (HCL) is an indolent B-cell malignancy, which comprises of 1% of all lymphoproliferative disorders and 2% of all leukemias.[1-3] In the United States, 600 to 800 new cases are diagnosed annually.[4] It is more common in Caucasian men in their fifth decade of life[5] and among Ashkenazi Jewish men and less common among African and Asian descendants, particularly Japanese individuals.[4] Recent advances in the therapeutic

Smith Giri and Rajesh Shrestha contributed equally to this work.

[1]Department of Medicine, University of Tennessee Health Science Center, Memphis, TN
[2]Department of Medicine, Memorial Hospital of Rhode Island, Brown University, Providence, RI
[3]Department of Medicine, Reading Health System, Reading, PA
[4]Division of Hematology and Oncology, Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE

Submitted: Feb 8, 2015; Revised: Mar 18, 2015; Accepted: Mar 18, 2015; Epub: Mar 24, 2015

Address for correspondence: Vijaya Raj Bhatt, MBBS, University of Nebraska Medical Center, Department of Internal Medicine, Division of Hematology-Oncology, 987680 Nebraska Medical Center, Omaha, NE 68198-7680
Fax: 402-559-6520; e-mail contact: vijaya.bhatt@unmc.edu

2152-2650/$ - see frontmatter
http://dx.doi.org/10.1016/j.clml.2015.03.001

armamentarium have significantly improved the life expectancy of HCL patients, which is close to that of the general population.[6] In 1994, the Italian Cooperative Group for HCL study (n = 177) demonstrated a complete remission of 17%, partial remission of 62%, and minor remission of 16% with the use of interferon and splenectomy among patients younger than 66 years of age. The actuarial 5-year survival rate was 96% for the entire cohort.[7] The advent of purine analogues such as cladribine and pentostatin, which are the current preferred front-line chemotherapy options in symptomatic patients, has further increased the response rate and overall survival (OS).[8,9] A phase III randomized trial (n = 313) demonstrated significantly higher response rates ($P < .0001$) and longer relapse-free survival ($P < .0001$) with pentostatin than with interferon.[10] A long-term follow-up of this study demonstrated a 10-year OS of 81% with pentostatin.[11] The Scripps Research Institute study (n = 209) revealed an overall response rate of 100% and a complete response rate of 95% with the use of continuous intravenous infusion of cladribine. This resulted in an OS of 97% at 108 months.[12] Although not directly compared head to head, pentostatin and cladribine seem to have comparable efficacy.[13,14] None of these studies report any racial differences in outcomes. Racial differences, however, have been demonstrated in several other malignancies. For example, a joint study from M.D. Anderson Cancer Center and Duke University Cancer Center demonstrated African American race as an independent predictor of shorter OS independent of other relevant prognostic factors such as cytogenetic and immunoglobin mutation status in chronic lymphocytic leukemia.[15] A recent study has indicated worse outcomes in African American patients with HCL.[16] This study used the Surveillance, Epidemiology, and End Results (SEER)-17 database, had data until 2008, and focused on trends in OS over time. Hence, the study does not provide the OS data for different racial groups and does not compare the OS of Asian/Pacific Islander and American Indian/Alaska Native with Caucasian individuals. Our study used data from the SEER-18 database until the calendar year 2011 and applied strict exclusion criteria. For example, we excluded patients with > 1 primary malignancy, which can influence survival and confound the results. We also present actual OS data and hazard ratio for OS for different racial groups including ethnic minorities. Thus, we provide much more elaborate data and focus on the racial disparities in outcomes of HCL.

Patients and Methods

We used the SEER 18 database to extract data on HCL patients diagnosed and treated between 1973 and 2011. SEER is a program of the National Cancer Institute that provides cancer data from population-based cancer registries and covers data from 28% of the total US population. The database covers data from 25% of white population, 26% of African American, 38% of Hispanic, 50% of Asian, 44% of American Indian and Alaska Native, and 67% of Hawaiian/Pacific Islander populations.[17] Eligible patients were identified using International Classification of Diseases (ICD)-O-3 code 9940/3. After exclusion of patients with > 1 primary malignancy (n = 1157), lack of histological confirmation (n = 126), and missing data on race (n = 111), age (n = 1), or marital status (n = 298), 3125 patients were selected. Further, we excluded 92 additional patients diagnosed between 1973 to 1977, because the specific ICD-O-3 code for HCL was developed in 1978. Hence, a total of 3033 patients were selected for final analysis.

Statistical Analysis

Descriptive statistics including medians along with their range and frequencies were computed for various demographic and clinical characteristics of the study population. Median OS, 1-year, 2-year, 5-year, and 10-year OS were computed using the actuarial (life table) method. The difference between 1-year, 2-year, 5-year, and 10-year OS were compared using a Z test of the difference between 2 population proportions. Kaplan–Meier survival curves were plotted to estimate OS based on race, and the differences in the curves were compared using the log rank test. Multivariate analysis was performed using the Cox proportional hazard regression model to estimate the independent effect of race on survival after controlling for age, sex, year of diagnosis, and marital status. Presence of colinearity in the multivariate model was assessed using a variance inflation factor in which a value of > 3 was considered significant evidence of multicollinearity. All *P* values were 2-sided and the level of significance was chosen at .05. An institutional review board waiver was obtained from the University of Nebraska Medical Center institutional review board.

Results

A total of 3033 patients were selected for final analysis using the mentioned study criteria. Our study population included 77.6% men (n = 2354) and had a median age at diagnosis of 56 years (range, 20-102; Table 1). Ethnicity included 2816 white patients (93%), 107 Asian/Pacific Islanders (3.5%), and 105 African American individuals (3.4%). Marital status included 2159 married patients (71.2%), 441 singles (14.5%), and 433 other (14.3%). The median year at diagnosis was 2002 (range, 1978-2011). This included 835 patients (27.5%) diagnosed earlier than 1995, 459 (15.1%) diagnosed between 1995 and 2000, 774 (25.5%) diagnosed between 2000 and 2005, and 965 (31.8%) diagnosed in 2006 and later.

The median OS was 291 months for white individuals and not reached for other races, compared with 133 months for African American individuals (Table 2). Although the 1-year OS was similar between the white and African American groups ($P = .10$), the 2-year, 5-year, and 10-year OS were significantly less for African American individuals compared with white individuals ($P < .01$ in all cases). The 1-year, 2-year, 5-year, and 10-year OS were similar for Asian/Pacific Islander and Native American/Alaska Native individuals compared with white individuals. Figure 1 shows the Kaplan–Meier survival curves for white, African American, and other races with HCL. The difference between the curves was statistically significant as suggested by the log rank test with a $P < .01$.

A summary of multivariate analysis using the Cox proportional hazard regression model is shown in Table 3. The independent variables in the model included race, age (stratified into groups), sex, marital status, and year of diagnosis (stratified into groups). There was no evidence of multicollinearity between the independent variables with the computed variance inflation factors < 2 in all cases. African American ethnicity remained an independent predictor of a worse OS (hazard ratio, 1.77; 95% confidence interval, 1.30-2.40; $P < .001$) after adjusting for other covariates as mentioned earlier. Other predictors of a worse OS included older age ($P < .01$),