Revista Brasileira de Hematologia e Hemoterapia
Brazilian Journal of Hematology and Hemotherapy
www.rbhh.org

Original article

Acute myeloid leukemia: survival analysis of patients at a university hospital of Paraná

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ARTICLE INFO

Article history:
Received 20 December 2013
Accepted 16 June 2014
Available online 21 November 2014

Keywords:
Acute myeloid leukemia
Survival analysis
Prognosis
Adult
Cytogenetics

ABSTRACT

Objective: The aim of this study was to analyze the prognostic factors correlated with survival of patients with acute myeloid leukemia at the Hospital de Clínicas, Universidade Federal do Paraná between 2003 and 2009, as well as to investigate the clinical and epidemiological profile.

Methods: The overall survival and disease-free survival were statistically evaluated using the Kaplan–Meier method, the log-rank test and multivariate evaluation by Cox regression analysis.

Results: The study population was predominantly younger than 60 years old (81,6%), had intermediate cytogenetic risk (40.8%), in first complete remission after induction chemotherapy (46.9%), with a white blood count at diagnosis of less than 30×10^9/L (57.1%) and *de novo* acute myeloid leukemia (62.2%). Survival curves showed that better prognosis was related to age below 60 years (median:12,4 months; *p*-value = 0,2227; Odds Ratio = 0,6676), good prognostic cytogenetic markers (median: 97.7 months; *p*-value = 0.0037; Odds Ratio = 0.4239) and white blood cell count at diagnosis of less than 30×10^9/L (median survival: 23.6 months; *p*-value = 0.0001; Odds Ratio = 0.3651). Regarding the French-American-British subgroups, the median overall survival was 23.5 months for M0, M1 and M2, 97.7 months for M3 and 7.4 months for M4, M5, M6, and M7 (*p*-value = 0.0288).

Conclusion: Prognostic factors strongly influenced patient survival, as well as guided treatment. Moreover, these factors were consistent with the available literature adjusted for the population in question.

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http://dx.doi.org/10.1016/j.bjhh.2014.11.008

Introduction

Neoplastic diseases were historically associated with economically developed countries. For approximately four decades, however, this situation has changed and a lot of the onus is observed in developing countries. Infectious diseases are not the main cause of death anymore and cancer has acquired a greater dimension, becoming a global public health problem.[1]

Hematological malignancies represent 7% of new cancer cases each year.[2] According to The Brazilian National Cancer Institute, it has been estimated that there were 4570 new cases in men and 3940 in women in 2012. Acute myeloid leukemia (AML) is the most common acute leukemia in adults and accounts for approximately 80% of the cases in this group, with an annual incidence of 2.7 cases per 100,000 population.[3]

AML is a relatively rare disease with high heterogeneity in the affected population in terms of morphology, immunophenotype, cytogenetics and molecular abnormalities. It is a clonal proliferation of myeloid precursors, the result of genetic and epigenetic alterations that disrupt self-renewal, proliferation and differentiation of cells, with accumulation of leukemic blasts or immature cells in the bone marrow.[4] The clinical outcome is extremely variable, with survival from a few days to a definitive cure of some clinical and biological aspects, which is useful in predicting outcomes.[4–6]

Several clinical features can predict complete remission and the event-free survival (EFS) of these patients. The most important prognostic factors regarding adverse clinical presentations, include age, cytogenetic abnormalities, secondary leukemia, white blood cell (WBC) count and complete remission after the first induction.[5,7]

The cases can be morphologically subclassified according to the French-American-British (FAB) system. This form of organization does not provide additional prognostic information, but it is important to systematize acute promyelocytic leukemia, a biological and clinical variant of AML, classified as AML M3 in the FAB system, currently called acute promyelocytic leukemia with t(15,17)(q24.1,q21.1), and PML-RARA, in the World Health Organization (WHO) classification system.[8–10]

Brazil has peculiarities regarding its territorial dimensions, with important regional differences in the occurrence of the disease and distribution of associated risk factors and so local information is extremely important for analytical exploration of this malignancy.

Prospects for patients have improved over the last 30 years, but despite significant progress, the treatment outcome is variable and frequently suboptimal. More than half of young and adult patients, and about 90% of the deaths of over 60-year-old patients in this population are disease related.[5,6,11,12]

This study shows the indispensability of registries with standardized, up-to-date and representative information, due the considerable variations between populations in relation to survival and epidemiological characteristics which can predict treatment outcome.

The aim of this study was to analyze the influence of prognostic factors described in the literature correlated with survival of patients with acute myeloid leukemia treated between 2003 and 2009 at the Hematology and Oncology Service of the Hospital de Clínicas, Universidade Federal do Paraná (HC-UFPR), Brazil, as well as to trace the clinical and epidemiological profile of the patients.

Methods

This retrospective analytical study was conducted at HC-UFPR after being approved by the Ethics Committee of the hospital.

The study population was selected using records from the Computer Information Service and the Hospital Cancer Registry of HC-UFPR using the following inclusion criteria: the International Classification of Diseases (ICD) of AML, older than 15 years old and diagnosis between January 2003 and December 2009. The initial patient set consisted of patients, predominantly treated with combined induction chemotherapy using cytarabine and daunorubicin (the so-called "7 + 3" regimen) for non-M3 leukemias, and all-trans retinoic acid (ATRA) alone or combined with an anthracycline for the M3 subtype.

Patients who were not treated exclusively in the Hematology and Oncology Service, HC-UFPR were excluded as were those who had biphenotypic leukemia, Fanconi anemia either associated with myelodysplastic syndrome or in isolation, those who were diagnosed before 2003 and those whose medical records were not available. The flowchart for selection of the study population is detailed in Figure 1.

Data collection was based on the review of medical records available from the Medical Archive Service (SAME), based on the results of cytogenetic and immunophenotyping examinations provided by the respective laboratories, as well as records from the Hospital Epidemiology Service of HC-UFPR. Information of interest was input on an Excel spreadsheet to facilitate further analysis of the variables and to compile the results.

Data for clinical and epidemiological characterization of the study population, such as gender, age at diagnosis, race, family history of cancer, cytogenetics, the presence of the t(15;17), complete remission rate after the first induction, WBC count at diagnosis and type of evolution (primary or secondary) were arranged in a table of absolute and relative frequencies, with calculations performed using the Microsoft Excel program.

Regarding the analysis of overall survival (OS) and EFS of the patients, survival curves were constructed by the Kaplan–Meier method, using the statistical program PRISM (version 5.0). The definitions used for the calculation of survival followed the revised recommendations of the International Working Group for therapeutic studies in acute myeloid leukemia.[13] The OS was defined as the time interval between the date of diagnosis and date of death or date of last follow-up visit. The EFS was taken as the period between the date of diagnosis and the date of relapse, induction failure or date of death from any cause.

The curves of OS and EFS were also correlated with certain prognostic factors as reported in the literature, such as age at diagnosis, FAB classification, cytogenetics, WBC count at diagnosis and evolution (primary and secondary).[11,12,14] A comparison of different curves was performed using the log-rank test and differences with p-value < 0.05 being considered statistically significant. The comparative analysis of the