

Original article

Revista Brasileira de Hematologia e Hemoterapia Brazilian Journal of Hematology and Hemotherapy

www.rbhh.org



A model for the functional assessment of elderly with myeloid neoplasms



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ARTICLE INFO

Article history: Received 1 November 2014 Accepted 26 December 2014 Available online 17 February 2015

Keywords:

Performance tests Karnofsky performance status Aged Leukemia, myeloid Myelodysplastic-myeloproliferative diseases

ABSTRACT

Objective: Myeloid neoplasms are heterogeneous diseases that are more incident in the elderly. The goals of this study were to aggregate a geriatric approach to the patient assessment, to show the impact of gender, age, hemoglobin concentration and comorbidities on the functionality of elderly with myeloid neoplasms and to better understand how the instruments of functional assessment work according to the aggressiveness of the disease. *Methods*: Elderly patients (≥ 60 years old) with myeloid neoplasms were assessed using the Karnofsky scale, Eastern Cooperative Oncologic Group scale, and basic and instrumental activities of daily living scales. The hematopoietic cell transplantation-comorbidity index assessed the comorbidities. A mixed logistical regression model was fitted to estimate the impact of gender, age, hemoglobin concentration and the hematopoietic cell transplantation-comorbidity index on patients' functionality.

Results: Eighty-two patients with a mean age of 72.8 years (range: 60–92 years) were evaluated. Eighty percent had good Karnofsky and Eastern Cooperative Oncologic Group scales and 39% were independent according to the daily living activity scales. All of the patients with poor Karnofsky and Eastern Cooperative Oncologic Group scales were classified as dependent by the daily living activity scales. The mixed logistic regression models showed that age, gender, hemoglobin concentration and the comorbidity index impacted on the daily living activity scales. Karnofsky and Eastern Cooperative Oncologic Group scales were affected by hemoglobin and the comorbidity index. The model hypothesized the hemoglobin concentration at which there was a higher risk of poor Karnofsky and Eastern Cooperative Oncologic Group scales. This hemoglobin concentration depended on comorbidities and on the aggressiveness of the myeloid neoplasm.

Conclusion: The geriatric approach improved the sensitivity and specificity of the patients' assessment. Hemoglobin concentration associated to the risk of poor Karnofsky and Eastern Cooperative Oncologic Group scales depended on the comorbidity score and on the disease aggressiveness. The Karnofsky and Eastern Cooperative Oncologic Group scales had higher sensitivity in patients with more aggressive diseases.

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Introduction

Myeloid neoplasms (MN) are a group of heterogeneous diseases that include myeloproliferative neoplasms (MPN), myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML). All these diagnosis are more incident and prevalent in elderly individuals.

This group of diseases includes from indolent entities such as polycythemia vera and essential thrombocythemia, to aggressive diseases, such as AML and MDS with excess of blasts. Chronic myeloid leukemia and myelofibrosis have some risk to evolve aggressively.¹

The management of older individuals with MN takes into account characteristics related to the patient and to the disease.^{2–6} The chronological age, the performance status (PS) and the comorbidity score are patient-related variables that are considered during treatment decision making of elderly individuals.^{7–9}

The PS assessment is carried out using the Karnofsky Performance Scale¹⁰ (KPS) or by the Eastern Cooperative Oncologic Group¹¹ (ECOG) scale. However, over the last thirty years, several studies have demonstrated the low sensitivity of these instruments to evaluate function in older individuals with cancer.^{12–14} Thus, it has been recommended to aggregate geriatric tools to the PS assessment.

The major clinical challenge in the management of all myeloid neoplasms is the treatment of AML in older patients. Depending on the clinical and functional reserve of the patient, the therapeutic approach may be excessively toxic.² Thus, it is very helpful to distinguish the impact of the aging process separated from the impact of the disease.¹⁵

The objectives of this study were to assess the functionality of elderly patients with MN aggregating the basic activity¹⁶ (ADL) and instrumental activity¹⁷ (IADL) of daily living scales to the KPS and ECOG and to evaluate the impact of gender, age, hemoglobin (Hb) concentration and comorbidity score on the functionality of these patients. A third objective was to design a model to show how functional assessment instruments work in respect to the aggressiveness of the disease.

Methods

Elderly patients (\geq 60 years old) with MN followed at the Hematologic Outpatient Clinic of the Universidade Federal de São Paulo, (UNIFESP) were included in this study.

Diagnoses were based on the World Health Organization (WHO) Classification of tumors of hematopoietic and lymphoid tissues¹⁸ using the analysis of peripheral blood and bone marrow smears, the histology of bone marrow biopsy, and immunophenotypic, cytogenetic and molecular studies.

The patient's functional evaluation was performed by a hematologist just before the clinical consultation and included PS assessed employing the KPS and ECOG scales and functional status with the ADL and IADL scales. Comorbidities were evaluated according to the hematopoietic cell transplantation-comorbidity index (HCT-CI) developed by Sorror in 2005.¹⁹ The Hb concentration was measured by an automated technique employing a multichannel hematology analyzer (CELL-DYN Ruby, Abbott Diagnostic Division) using a blood sample taken before the consultation.

Patients with transfusion positive status received red blood cells prior to the determination of the Hb concentration in the month preceding the functional assessment. The decision to transfuse was based on the drop in Hb and its related symptoms. Demographic and clinical data were obtained from medical records.

The study was approved by Research Ethics Committee of UNIFESP (#0262/10) and the procedures undertaken were in accordance with the Declaration of Helsinki of 1975, revised in 2008.²⁰ All patients signed informed consent forms.

Statistical analysis

Analyses of means of age and Hb concentration were performed using Student's t test or ANOVA with Tukey's test. The frequencies of categorical variables were evaluated with Fisher's exact test.

Two mixed logistic regression models were fitted to assess the impact of gender, age, HCT-CI and Hb concentration on PS, dichotomized as good (KPS \geq 80% and ECOG < 2) or poor, and on functional status, as independent or dependent (need help in at least one daily task).

Generally, mixed models consider the information hierarchically structured at the unit and cluster levels. These cluster levels result from a grouping process outlined by characteristics shared by the units. Moreover, in mixed models the assumption of independence is violated, because there is a correlation between the units that belong to the same cluster. Random effects are included on considering this fact.

Mixed models incorporate these random effects and estimate them for each group. Therefore, the groups are represented by random effects and the variability across the groups is described by the intercept or the slope variability. The mixed model belongs to generalized linear mixed models (MLGM), which is an extension of generalized linear models (GLM).^{21,22}

Statistical analysis was performed using R statistics (v2.15) and the Statistical Package for the Social Sciences (SPSS – v18).

Results

Eighty-two patients, 40 men and 42 women, with a mean age of 72.8 years old (range: 60–92 years), were evaluated. Table 1 shows the descriptive statistics of the demographic data, functionality scores and comorbidity indices.

Of the fifteen patients with polycythemia vera (PV) and six with essential thrombocythemia (ET), 73% and 50% were JAKV617F positive, respectively. Ninety percent of these patients were taking hydroxycarbamide to control the disease.

All the nine patients who had chronic myeloid leukemia (CML) were in the chronic phase; seven were taking imatinib mesylate and four were in molecular remission.

Nine out of 25 patients with myelofibrosis (MF) were in the sclerotic phase, two in blastic transformation and the remaining 14 were in the cellular phase. Eleven patients were JAKV617F positive and 80% were taking hydroxycarbamide. Download English Version:

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