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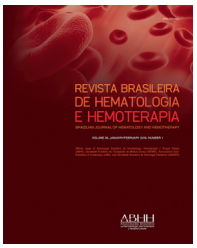

Original article

Age-adjusted international prognostic index is a predictor of survival in gastric diffuse B-cell non-Hodgkin lymphoma patients

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ABSTRACT

Background: The clinical course of gastric lymphoma is heterogeneous and clinical symptoms and some factors have been related to prognosis.
Objective: The present study aims to identify prognostic factors in gastric diffuse B-cell non-Hodgkin lymphoma diagnosed and treated in different countries.
Methods: A consecutive series of gastric diffuse B-cell non-Hodgkin lymphoma patients diagnosed and treated in Brazil, Portugal and Italy, between February 2008 and December 2014 was evaluated.
Results: Of 104 patients, 57 were female and the median age was 69 years (range: 28–88). The distribution of the age-adjusted international prognostic index was 12/95 (13%) high risk, 20/95 (21%) high-intermediate risk and 63/95 (66%) low/low-intermediate risk. Symptoms included abdominal pain (63/74), weight loss (57/73), dysphagia (37/72) and nausea/vomiting (37/72). Bulky disease was found in 24% of the cases, anemia in 33 of 76 patients and bleeding in 22 of 72 patients. The median follow-up time was 25 months (range: 1–77 months), with 1- and 5-year survival rates of 79% and 76%, respectively. The multivariate Cox Regression identified the age-adjusted international prognostic index as a predictor of death (hazard risk: 3.62; 95% confidence interval: 2.21–5.93; p-value <0.0001).
Conclusions: This series identified the age-adjusted international prognostic index as predictive of mortality in patients treated with conventional immunochemotherapy.

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Introduction

Gastric lymphoma is the most common extra nodal diffuse B-cell non-Hodgkin lymphoma (DLBCL) and accounts for 30% of cases of lymphoma in the stomach.[1] According to the current WHO lymphoma classification criteria, gastric DLBCLs are classified with or without features of MALT.[2] Recent studies revealed that *Helicobacter pylori*-related gastric DLBCL is a distinct less aggressive entity with greater chemosensitivity, thereby highlighting the heterogeneity of these lymphomas. The clinical presentation and course are also variable with clinical symptoms, laboratorial abnormalities and *H. pylori*, hepatitis B, and C infections, in addition to classical international prognostic index (IPI) factors having been related to prognosis.[3] Different clinical behaviors may reflect distinct unidentified pathogenic mechanisms.[4] A better characterization of prognostic factors is required in order to discover new potential disease mechanisms, improve outcomes and individualize treatment approaches. The present study aims to identify prognostic factors in patients with gastric DLBCL diagnosed and treated in different countries by analyzing demographic and clinical characteristics, response to treatment and outcome.

Patients

A retrospective study of 104 consecutive patients with DLBCL diagnosed and treated in hematology centers in Brazil, Italy and Portugal between February 2008 and December 2014 was performed. The inclusion criteria were age >18 years old, lymphoma primarily located in the stomach, with or without the involvement of other intra-abdominal structures and with a confirmed DLBCL histology. All cases were diagnosed according to World Health Organization (WHO) classification criteria.[2] Patients with transformation from another type of lymphoma to DLBCL were excluded. Patients were considered *H. pylori* positive when their histology results were positive.

Data were retrieved from patient's charts with all patients having signed a consent form submitted to the local ethics committee in the diagnosis period. All patients were subjected to a detailed physical evaluation including an investigation of B symptoms (pain, nausea, dysphagia, bleeding, obstruction), routine blood exams (hemoglobin, total and differential leukocyte counts, platelet count and peripheral smear for abnormal/blast cells), biochemical exams [liver function tests, serum lactate dehydrogenase (LDH), β_2 microglobulin, albumin, urea, creatinine and uric acid] and serologic investigations for hepatitis B and C and HIV. Upper gastrointestinal endoscopic examinations were performed in 95% of the patients. Imaging studies included chest radiographs and/or computed tomography scans and abdominal and pelvic computed tomography scans or ultrasonography. Bulky disease was defined as lesions with a diameter >10 cm. All patients underwent bone marrow aspiration and biopsy as part of the staging procedure. The international prognostic index (IPI), age-adjusted IPI (aaIPI)[5] and Ann Arbor stage[6,7] were calculated for each patient.

All patients were treated by systemic chemotherapy mostly consisting of six cycles of the rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP) regimen with the intention to cure.[8] Patients with residual disease received local radiotherapy. Imaging studies and endoscopic examinations were used to evaluate response.

The influence of the following parameters were evaluated in the response to treatment and survival: LDH, β_2 microglobulin, albumin, presence of bulky disease, B symptoms (fever, weight loss, pain, nausea, vomiting), aaIPI, type of treatment (surgery plus chemotherapy, chemotherapy alone), anemia, dysphagia, bleeding, obstruction and presence of *H. Pylori* at diagnosis. Anemia was defined as hemoglobin <12.0 g/dL and elevated LDH levels as >240 U/L.

All patients underwent imaging and follow-up endoscopic examinations (with a biopsy of suspicious lesions) to document treatment response. At the end of chemotherapy, response was classified as complete remission (CR), partial response (PR), stable disease (SD) or progressive disease (PD) according to the International Working Group criteria.[6] Patients who failed initial therapy with R-CHOP (PR, SD and PD) received high-dose chemotherapy together with autologous stem cell transplant. Patients with *H. pylori* at diagnosis also received antibiotic therapy.

Statistical analysis

Survival was estimated using the Kaplan–Meier method and compared using the log-rank test. The prognostic value of the different variables for clinical outcome was estimated by univariate and multivariate analyses, applying the Cox proportional hazards regression model. Two-sided p-value <0.05 was considered significant. The Statistical Package for the Social Sciences (SPSS version 15.0) software (Chicago, IL, USA) was used for data analysis.

Results

Clinical and histological features

The clinic pathologic characteristics of the 47 male (45%) and 57 female (55%) patients with gastric DLBCL with a median age of 69 years (range: 28–88 years) are listed in Table 1. The main presenting symptom was abdominal pain (85% of the cases) and the two most common serum alterations were elevations in β_2 microglobulin and LDH in 71% and 41% of the cases, respectively. Hypoalbuminemia was found in 26/83 (31%) patients. Bleeding and obstruction were uncommon at presentation and anemia was only present in 43% (33/76) of cases. Among the 45 patients who were tested for *H. pylori*, 13 were positive. Localized disease (Ann Arbor stages I or II) was present in 46% of the cases, and most patients (67%) were in the low/low intermediate risk group according to the aaIPI; 48% had good performance status [Eastern Cooperative Oncology Group (ECOG) score 0].

Treatment, outcome and prognostic factors

Only 10% of the patients required surgery due to obstruction, perforation or upper gastrointestinal bleeding. In contrast,