Journal of Islamabad Medical & Dental College (JIMDC); 1211(1):14-17

Original Article

Prognostic Scoring in Patients of Chronic Myeloid Leukemia: Correlation between Sokal and Hasford Scoring Systems

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Abstract:

Background: Chronic myeloid leukaemia (CML) is a clonal myeloproliferative disorder of transformed primitive hematopoietic progenitor cells. Chronic myeloid leukaemia is one of the commonest leukemias. Patients of CML are usually subjected to risk stratification according to various prognostic criteria. The Sokal scoring system is popular as a prognostic discriminator for survival in patients treated with chemotherapy. Hasford et al proposed a new CML scoring system referred to as Euro score.

Objective: Correlation of various prognostic risk groups of Hasford scoring system with comparable prognostic groups of Sokal scoring system in chronic myeloid leukemia.

Material and Methods: This descriptive study was conducted at department of pathology, Pakistan institute of medical sciences from March 2003 to October 2006. A total of 59 consecutive freshly diagnosed untreated cases of CML were subjected to Sokal and Hasford scoring systems, and the results were correlated with each other.

Results: In total of 59 cases of CML age range was from 8 to 70 years with mean ± SD of 35.39 ± 17.12 years. Six (10.1%) patients belonged to pediatric age group i.e. <15 years. Male: female ratio was 1.3:1. According to Sokal criteria about half of the patients were found in intermediate risk group; 44% were in high risk group and only 5% in low risk group. Using Hasford scoring system, 44% of patients were placed in intermediate risk, 30.5% in high risk and 15% in low risk groups.

Conclusion: Hasford score identifies more patients still in low risk group as compared to Sokal scoring system and prospective studies should be carried out to see overall survival and disease free survival of these risk groups.

Key Words: Chronic myeloid leukemia; CML; Sokal Scoring; Hasford scoring; prognostic stratification

Introduction

Chronic myeloid leukaemia is a clonal myeloproliferative disorder of transformed primitive hemopoietic progenitor cells, and is characterized by expansion of proliferating myeloid cell pool especially in the bone marrow, spleen and peripheral blood. CML is the commonest type of chronic leukemia in Pakistan, and accounts for about 15 percent of leukemias in adults. The median age of patients at presentation is 45 to 55 years. From 12-30 % of patients are 60 years of age or older.[1] In more than 90% cases of CML, Philadelphia chromosome is observed. This chromosome is produced as a result of reciprocal translocation between chromosomes 9 and 22. This translocation results in the production of a fusion gene, i.e. bcr-abl gene; the latter perturbs downstream signalling pathways in hematopoietic progenitor cells and produces the clinical phenotype of overproduction of mature myeloid cells.[2] The majority of CML patients have WBCs in excess of 100,000/µl at diagnosis. Depressed erythropoiesis proportional to the increase in myeloid cells results in anaemia in some patients. Platelet counts are elevated in 30% to 50% of cases at diagnosis.[3]

CML usually runs a biphasic or triphasic course. This process includes an initial chronic phase and a terminal blastic phase, which is preceded by an accelerated phase in 60% -80% of patients.[4] Many patients, especially if they present with delay, may have accelerated or even blast stage at the onset. Splenomegaly is documented in 30-70% of cases. The liver is enlarged in 10-40% of cases. [5]

Risk stratification of CML patients on the basis of variable prognostic factors was first proposed by Tura et al (1981) who stratified their patients into three groups, depending on presence or absence of six variables (splenomegaly, hepatomegaly, blast cells, leukocytosis, thrombocytosis and a rise in granulated precursor cells) as follows:

Low risk group; upto one risk factor present
Intermediate risk group; upto two or three risk factors
High risk group; more than three risk factors present [6]

Carvantes and Rozman (1982) emphasized on splenomegaly, erythroid precursors in blood and over 5% myeloblasts in the marrow as main prognostic factors, and stratified their patients as under: [7]

Low risk group; upto one factor present

Intermediate risk group; two factors present

High risk group; three or four risk factors present

Kantarjian et al (1990) introduced the so called simple synthetic prognostic staging system. [8] The Sokal score achieved widespread usage as a prognostic discriminator for survival in patients treated with chemotherapy (mainly busulfan and hydroxyurea).[9] This scoring system was based on a formula that takes into account the patients age, the blast cell count and the spleen size at the time of diagnosis.

The Hasford CML score also called the Euro score, uses age, spleen size (measured from the left costal margin), blast cell count, platelet count, and eosinophil count. All variables are measured at the time of diagnosis.[10]

This study was aimed to correlate various prognostic groups of Sokal and Hasford scoring systems in freshly diagnosed untreated cases of CML.

Material and Methods

This cross-sectional study was conducted at the department of pathology, Pakistan Institute of Medical Sciences from March 2003 to October 2006. A total of 59 consecutive freshly diagnosed cases of CML belonging to all age groups, both sexes and all the three clinical phases were included. Patients of CML who had received cytotoxic treatment previously were excluded from the study. A detailed account of clinical history and physical examination was entered in a performa specially pertaining to age, sex, duration of symptoms, history of fever and other constitutional features due to anaemia, bleeding, splenomegaly and hepatomegaly.

In every patient about 5ml EDTA blood sample was collected. Complete blood counts were performed on a fully automated haematology analyzer (Sysmex KX-21). Peripheral blood smears were freshly prepared and stained using Wright stain. The slides were examined under a microscope and differential count was performed. Neutrophil alkaline phosphatase (NAP) scoring was done on peripheral blood films to differentiate from leukemoid reaction. Bone marrow aspiration was done; multiple smears were made and at least two smears were stained by Wright stain. The smears were examined and at least five hundred cells were counted for myelogram.

Table 1: Stratification of cases of CML into clinical phases

Diagnosis	No. of patients	%
CML in chronic phase	55	93.2
CML in accelerated phase	03	5.1
CML in blastic phase	01	1.7

Patients were placed in chronic, accelerated and blastic phases according to the known criteria. Cytogenetic and molecular studies could not be done due to lack of these facilities at PIMS.

Sokal prognostic scoring was performed on all the cases using the following formula:

Exp.[0.0116(age -4.34)+0.0345(spleen-7.51)-0.188(% of blasts-2.1)] According to Sokal score the patients were stratified into various prognostic groups as shown below;

Low risk (good prognosis) group with score <0.8

Intermediate risk (moderate prognosis)group with score of 0.8 -1.2

High risk (poor prognosis) group with score >1.2

Hasford score was also performed on all cases using the formula:

0.6666 x age [0 when age <50 years;1,otherwise]+0.0420 x spleen size[cm below costal margin] + 0.0584 x blasts[%]+0.0413

x Eosinophils [%]+0.2039

x Basophils[0 when basophils < 3%; 1. otherwise] + 1.0956

x Platelet count[0 when platelets < 1,500 x 109/L; 1, Otherwise]x1,000.

Based on the score obtained, the patients were stratified into various groups as follows:

Low risk group <780

Intermediate risk group >780 and <1480

High risk group >1480

The results were statistically analyzed using the statistical programme SPSS version 13.

Correlation of various prognostic groups of Hasford and Sokal scoring system was also done.

Table 2: Prognostic stratification of CML cases

Prognostic groups	Sokal score	Hasford score
Low risk	03 (5.1%)	15 (25.4%)
Intermediate risk	30 (50.8%)	26 (44.1%)
High risk	26 (44.1%)	18 (30.5%)

Results

Age distribution: In a total of 59 cases of CML included in this study, the age of patients ranged from 8 to 70 years with mean ± SD of 35.39 ± 17.12 years. The median age was 35 years. Among these 34 were male and 25 female. The male to female ratio was 1.3:1. Feeling of weakness and lassitude were invariably present. History of low grade fever was given by 85% of cases. In 76% of cases, pallor was a presenting manifestation. Hepatomegaly was present in 37 (63%) of cases. Spleen was enlarged in 95% cases. The range of blasts in the bone marrow was 1-22% with mean of 3.6% $\pm$ 3.75 SD.

As shown in table 1, majority (93.2 %) of patients were in chronic phase; 6.8% were in accelerated phase, and 1.7% presented with blast crisis.

According to Hasford score 26 (44%) of patients were placed in intermediate risk group; 18 (30.5 %) were in high risk group and 15 (25.5%) patients were grouped under low risk group. Whereas according to Sokal Score, majority of the patients were in intermediate (50.8%) and poor (44.1%) prognosis groups; only 5.1% cases were observed to be in good prognosis group. (table 2)

Discussion

Typically CML if diagnosed in chronic phase can usually be controlled for some years; however, the disease invariably progresses eventually to more advanced (accelerated phase or blast transformation) which (particularly the blastic phase) are resistant to therapy and lead to death within 6–8 months.[11] The management of CML has progressively revolutionized during the last two decades. The treatment modalities switched on from busulphan and hydroxyurea to bone marrow transplantation and interferon therapy, and now molecular lesion targeted therapy using imatinib mesylate (Glevac) has incredibly improved the outlook of CML patients. Considering the importance of prognostic factors and their impact on various treatment modalities, many CML study groups have worked in this area. Many attempts have been made in the last 20 years to define clinical factors assessed at the time of diagnosis that may predict survival for individual patients with CML.[12] For example, Sokal et al identified factors that allow them to classify patients treated predominantly with busulphan into three prognostic groups and Hasford et al performed a similar analysis in patients treated predominantly with IFN-α.

In the present study we evaluated our freshly diagnosed cases of CML for Sokal and Hasford score and graded them accordingly. According to Sokal score 5.1 % of our 59 patients were placed in low risk group (score of < 0.8); 44.0% in high risk group (score >1.2 %); and 50.8% in intermediate risk group (score 0.8 to 1.2). According to Hasford score 25 % were grouped under low risk group, 44% in intermediate risk group and 30.5 % in high risk group. Thus Hasford score has placed 20% more patients in low risk group than Sokal score. The age range of these low risk patients is from 24 to 43 years. All Sokal low risk group patients were also Hasford low risk group patients, whereas the correspondence was much less for high risk patients. Thirteen of 26 patients of high Sokal were also high Hasford and the remaining 13 high Sokal cases were intermediate or even low with Hasford scoring system.

In CML survival varies from few months to years from diagnosis and an accurate prediction of duration of survival could help patients and clinicians make decisions about many treatment options. We have analyzed prognostic stratification of patients using both Hasford and Sokal scores. The main difference between these scores is that Hasford score assesses the impact of eosinophils and basophils on differential white cell count at diagnosis. Although Sokal score is still widely used, studies suggest that it is no more the best method of reliability. In a study done by Thomas et al looking at survival of these groups (grouped both by Sokal and Hasford criteria) it was found that 5 years survival was better in their low risk groups.[13] They also suggested that Sokal was less informative as their survival curve of high risk group crossed the survival of low and intermediate risk groups several times. They recommended that Hasford is a better scoring system and is highly predictive of survival particularly in patients <60 years age. In another study done by Hasford et al [9] **(**to validate Hasford scoring system) the Hasford scoring system was reinforced by finding that Sokal et al [14, 15] and Kantarjiar et al [8] do not separate the survival curves. In this study total number of their low risk group according to Hasford scoring system is 41.4% (with 5 year survival; 75%) as compared to 25.5% in our study; intermediate group represented 44.5% (with 5 year survival of 56%) vs. 44% in our study and 14.5% high risk group (with 5 year survival; 28%) vs. 30.5% in our study. Thus number of low risk group is quite low in our study and probably this is due to difference in selection criteria of patients as we have included patients in all phases and they included patients only in chronic phase. The results would have been different if we had followed the above mentioned criteria. In another study by Thomas et al[11] (analyzing the patients using both Hasford and Sokal scoring systems) the number of their high risk group according to Hasford system was still lower (7% vs. 30.5% in our study), intermediate group (39% vs. 44% in our study) and the number of patients in their low risk group was quite high (55% vs. 25.5% in our study)

The variables used in Hasford scoring system are routinely measured in clinical practice and their measurement is highly reliable. Thus one can get a reliable data needed for the calculation of this prognostic score. This scoring system has also shown a good discrimination of survival and can be considered a good tool for evaluation of risk adopted treatment. Allogeneic stem cell transplant is the only therapy that can cure CML, but age and lack of a suitable donor limit this procedure to a minority of patients.[16] Sokal and Hasford Scores however do not predict survival after allogenic stem cell transplant.[17] As for these patients pretransplant risk factors, i.e. donor type, stage of disease at time of transplantation, age of recipient, sex of donor and recipient, and interval between diagnosis and transplant are more important to predict their survival rate.[18] Similarly with use of imatinib (particularly in previously untreated patients in chronic phase), different factors predict the duration of survival and overall survival is significantly better for patients treated initially with imatinib.[19]

Conclusion

Hasford score identifies more patients still in low risk group as compared to Sokal scoring system Prospective studies to see overall survival and 5 year survival of patients in chronic phase particularly those less than 60 years who are unable to get imatinib and are on interferon therapy (after their prognostic categorization according to Hasford scoring system) will provide valuable information to oncologists/physicians both in stratifying patients into risk groups and modifying their treatment accordingly.

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