BAX AND BCL-2 POLYMORPHISMS MODULATING AGGRESSIVENESS AND PROGNOSIS IN DIFFUSE LARGE B-CELL LYMPHOMA

A.B.C. Brito1, C. Oliveira2, M.T. Delamain2, C.A. De Souza2, J. Vassallo1, C.S.P. Lima2
1Department of Internal Medicine, Laboratory of Cancer Genetics, Campinas, BRAZIL
2Department of Internal Medicine, University of Campinas, Campinas, BRAZIL

Aim: Apoptosis, with participation of the pro-apoptotic BAX and the anti-apoptotic BCL-2 proteins, plays a key role in outcome of patients with diffuse large B cell lymphoma (DLBCL). The ability to induce apoptosis is variable in humans, since several proteins enrolled in the process are encoded by polymorphic genes. The G wild allele of the BAX G(-248)A and the variant A allele of the BCL2 C(-717)A single nucleotide polymorphisms (SNPs) are related to lower transcriptional activity and higher BCL-2 protein expression, respectively, compared with the A variant and C wild alleles. Since the roles of these SNPs in clinical aspects and prognosis of DLBCL are still unknown, investigation of these were the aims of the present study.

Methods: Our analysis included 154 consecutive DLBCL patients at diagnosis seen at the University Hospital from December 2007 to March 2014. Genomic DNA from peripheral blood was analyzed by polymerase chain reaction followed by enzymatic digestion for discrimination of distinct genotypes of each SNP. Multivariate analysis using the logistic regression model served to assess the associations between genotypes and clinical aspects. Overall survival (OS) was calculated using the Kaplan-Meier estimate probabilities, and differences between survival curves were analysed by the log-rank test.

Results: The frequencies of BAX GG and BAX GG plus BCL-2 AA genotypes were higher in patients with stage IV tumors compared to those with tumors of I + II + III stages (95% vs. 77%, P = 0.01; 94% vs. 54%, P = 0.02), respectively. The median time of observation of patients was 22 months (range: 1-75). On univariate analysis, the presence of B symptoms (68% vs. 87%, P = 0.02), bone marrow involvement (53% vs. 79%, P = 0.009), high LDH levels (64% vs. 81%, P = 0.03), high risk disease (52% vs. 76%, P = 0.002), and stage IV (61% vs. 81% P = 0.01) were predictive of worse outcome at 24 months of follow up. Moreover, at the same time, patients with BCL2 CA + AA genotypes had worse outcome than others (68% vs. 88%, P = 0.04).

Conclusions: Our data indicate, for the first time, that inherited abnormalities in intrinsic apoptosis pathway, related to the BAX G(-238)A and BCL2 C(-717)A SNPs, influence aggressiveness and outcome of DLBCL patients.

Disclosure: All authors have declared no conflicts of interest.