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Biomarkers for prediction of prognosis in cancer patients- A myth or reality ?

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Abstract

Acute lymphocytic leukemia (ALL) is a common cancer in pediatrics whose multiple factors are not well understood. Prediction of prognosis is crucial for decisions concerning treatment options and disease-free survivability. There is no good model available to predict prognosis at the time of diagnosis of cancer patients, hence we tried integrate our clinic-pathological and genomics data to select Biomarkers of the disease. For doing this we not only carried out SNP studies along with demographic recording and chromosome aberration studies, we tried a novel strategy to interpret this heterogenous data by applying a mathematical model using Chi-square Automatic Interaction Detection (CHAID) and Discriminant Function Analysis (DFA) to predict cancer prognosis and to identify the best biomarker among the various parameters investigated. One thirty five ALL patients with mean age of 4.2 years formed our study group for analyzing the data from our investigations on Chromosomal abnormalities, DNA damage, SNPs of various genes such as Glutathione S-transferases (GST M1 and GST T1), Methylene tetrahydrofolate reductase (MTHFR exon 4 and 7), Dihydropyrimidine dehydrogenase (DPD) IVS14+1G>A, and FLT3/ITD (folin-like tyrosine kinase internal/ tandem duplication).

The two mathematical models CHAID regression and DFA helped us to predict not only survivability in ALL but we could use a multitude of diagnostic features to predict prognosis. CHAID regression model revealed that the MTHFR mutated types were strongly associated with survivability of ALL cases (P value =0.003,*Chi*-square = 14.197 at 2 degrees of freedom), whereas DFA allowed us to derive a discriminant score for diagnosis. The discriminant score predicted the survival category of patients as the value from 0.064 to 3.458 indicated resistance to treatment, while a value from -0.45 to 0.063 indicated a disease-free survival. The CHAID and DFA models reported herein for the first time determined prognosis at the time of diagnosis, utilizing multiple diagnostic factors of ALL patients. CHAID revealed that among these variables MTHFR SNPs were strongly associated with ALL and can be useful as biomarkers for establishing a more accurate prognosis.