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A proposed prognostic score including circulating free DNA (cfDNA) concentration in Diffuse large B-cell lymphoma (DLBCL); single center study

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INTRODUCTION

Non-Hodgkin's Lymphomas (NHLs) are common types of haematological malignancies. Due to the heterogeneity of the presentation of diffuse large B-cell lymphoma (DLBCL) patients, multiple scoring systems are used to classify the patient into different risk categories which impact the Overall survival (OS) and progression free survival (PFS). Cell free/tumour DNA (cfDNA/ctDNA) is an emerging biomarker for lymphoma that can provide genotypic information noninvasively, monitor the minimal residual disease, and monitor the response.

AIM

The aim of this study is to evaluate the possibility of using cfDNA concentration as a prognostic tool during the management of DLBCL patients without genotypic information.

METHOD

This study is a prospective interventional non-randomized open-label study that has been conducted on 36 cases of NHL (DLBCL) patients who attended the Oncology Center Mansoura University (OCMU) from 2020 to 2021 with follow-up for 2 years. Basic laboratory and radiological investigations were done for all patients for diagnosis and staging. The ctDNA extraction was performed using the QIAamp DSP Virus Spin Kit. Most of the patients were treated using the R-CHOP protocol. The study was approved by the Faculty of Medicine's Ethical Committee (Code Number: MD.20.05.332). The statistical analysis and the visualization of the data were done using the R/R-Studio (version 3.0) program

RESULTS

The analysis resulted in multiple factors affecting the survival of DLBCL patients significantly. Patient-related factors include old age (>54.5 years) (***P=0.051)*** and poor performance status (***P=0.05)***. Laboratory factors including high LDH (***P=0.0073)***, low serum albumin (***P=0.015)***, high absolute monocytic count (***P=0.05)***, BCL2 expression by IHC (***P=0.05)***, high pre-treatment cfDNA concentration (***P=0.032)***, and high post-treatment cfDNA concentration (**P=*0.032)*** were significantly associated with an inferior OS as shown in **Figure (1)**.

Based on the Multivariate analysis, we proposed a **prognostic score** formed of pre-treatment cfDNA plasma concentration (27ng/ul), LDH level ((≥378 u/l), and serum albumin (<3.8 gm/dl) as independent risk factors. This score was applied to our cohort, each factor was given one point, and the risk was classified based on the number of points; very low risk (0 points), low risk (1 point), intermediate risk (2 points), and high risk (3 points). When we applied this to our patients, the higher scores were significantly associated with a shorter OS with a (***p=0.00029)*** *as shown in* ***Figure (2).***

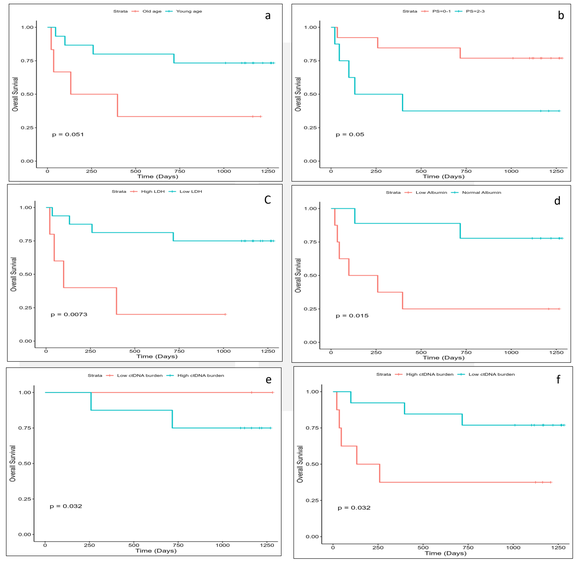


Figure 1: Factors affecting the overall survival of the patients with significant p-values using the Kaplan-Meyer test; a)Age, b)Performance status (PS) , c) LDH, d) Serum albumin level , e) Pre-treatment cfDNA concentration, f) Post-treatment cfDNA concentration

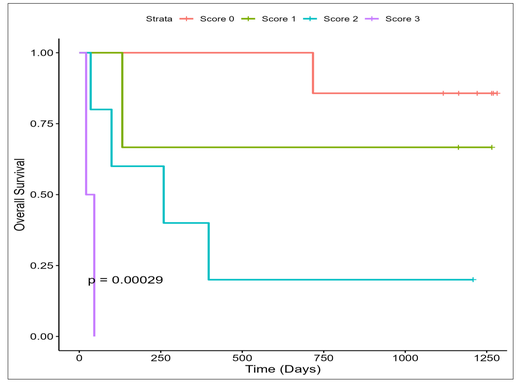


Figure 2: Kaplan-Meyer curve showing the significant difference in OS between different risk scores using the proposed prognostic score

CONCLUSIONS

In conclusion, we were able to define multiple risk factors affecting the survival of DLBCL patients and proposed a score including three independent risk factors (pre-treatment ctDNA, LDH, and serum albumin) which can be cost-effective and applicable.

The limitations of our study are the small sample size and the presence of missing data that may affect the statistical analysis. We are planning to apply this score to a larger cohort of patients and include the mutational profile for more confirmation of our findings with correlation to the clinical outcome of the patients.

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