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Expression of SATB1 is a prognostic indicator for survival in diffuse large B-cell lymphoma patients

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Abstract. – OBJECTIVE: Special AT-rich Sequence-binding Protein-1 (SATB1) and Matrix Attachment Region-binding Protein were associated with high tumor stage, tumor recurrence, tumor-related death and indicating a poor prognosis. The association between SATB1 and diffuse large B-cell lymphoma (DLBCL) has been discussed controversially. Thence, this study anticipated probing the expression of SATB1 in DLBCL and the relationships with clinic pathological features and prognosis.

PATIENTS AND METHODS: 180 cases of DLBCL tissues and 180 cases of chronic Lymphadenitis tissues in Para-carcinoma of DLBCL patients were collected in Guigang City People's Hospital, Guangxi, China, from August 2010 to December 2018. Here, the expression pattern of SATB1 in patients was examined by the method of streptomycin peroxides biotin (SP) immunohistochemical and analyzed the relationship of SATB1 with clinical pathological features and patient prognosis.

RESULTS: DLBCL carcinoma tissues expression SATB1 was significantly higher than chronic lymphadenitis tissues ($p < 0.05$), and the expression of SATB1 was not correlated with age, B symptoms and the ECOG status of patients ($p > 0.05$), but correlated with tumor stage, serum level of LDH, extranodal involvement, and IPI score ($p < 0.05$). Kaplan-Meier curves and multivariate analysis showed that SATB1 is an independent factor affecting progression-free survival time and overall survival time.

CONCLUSIONS: SATB1 participates in and affects the occurrence and development of DLBCL and influences their prognosis. It has broad prospects for improving prognosis evaluation, feasibility, molecular treatment intention and allocation of the most appropriate therapy.

Key Words:
Special adenine-thymine-rich sequence-binding protein 1, Diffuse large B cell lymphoma, Clinic pathological features, Prognosis.

Introduction

Roughly 90% of human lymphomas arise from B lymphocytes at various stages of differentiation, with the remainder derived from T lymphocytes. The most common type of cancer was Non-Hodgkin Lymphoma (NHL) (the 10th of all cancers), ranking 13th as leading cause of death among all deaths due to cancers in 2012, with around 200000 deaths[1-3]. Diffuse large B-cell lymphoma (DLBCL), with FL and CLL/SLL, is responsible for 85% of NHL. DLBCL was the most common type and aggressive form of adult NHL, accounting for 30-35% of all NHL cases[1-4]. The treatment of DLBCL is relatively homogeneous and standard, mainly based on the R-CHOP regimen. However, 30-40% of patients are still failing this standard therapy. So, efforts to improve outcomes by capturing predictors of this clinical heterogeneity may guide better treatment strategies[3-7]. Factors affecting this poor prognosis in patients with DLBCL have been investigated in a previous study[8] and most of them assessed prognostic factors for survival; several prognostic factors have been reported to predict the prognosis of patients. The International Prognostic Index (IPI) is a commonly used clinical risk reference index for predicting the prognosis of DLBCL[8]. Furthermore, using immunohistochemical (IHC) methods to risk-stratify early breast cancer patients has become an increasingly routine procedure. According to biological and pathological features, Immunohistochemistry (IHC) testing analyses the expression of proteins and FISH for discovering chromosomal translocation for forecasting prognosis[9-11]. Several studies[10,11] have demonstrated that SATB1 expression by IHC is a

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prognostic factor in cancer subjects; however, to date, the prognostic value of expression of SATB1 in DLBCL remains unclear.

SATB1, a global genomics sequence organizer, is one kind of protein that binds to nuclear matrix and can regulate downstream gene expression by binding to AT-rich bases regions[12]. Recent findings have shown that SATB1 plays a major role in activation and providing help to T cells and promoting differentiation and regulating T cells. Meanwhile, most studies[12,13] have shown over-expression of SATB1 in many human solid cancer cell lines and malignancies, including lymphoma and NSCLC. Numerous studies[12,13] have demonstrated that SATB1 is implicated in tumor occurrence, development, invasion and progression, and may become a new prognostic factor and therapeutic target. Many previous reports[14-16] have demonstrated that SATB1 up-regulated as an oncogene is expressed and acts as an oncogene in many cancers, including liver cancer, esophageal cancer, gastric cancer, colon cancer, cervical cancer, esophageal cancer and other aggressive tumors. The post-transcription modification of SATB1 expression could be regulated by multiple mechanisms; gene expressions of SATB1 are post transcription regulated by micro-RNA, but the specific mechanism is not completely clear. Further studies to analyze the different epigenetic mechanisms of may target SATB1 expression are needed, including the difference between the mRNA level and protein content in tumor tissues. Unfortunately, there is little information about the expression and function of SATB1 in the tissues of DLBCL patients, and we cannot draw a clear conclusion on the impact of SATB1 on DLBCL patients. Therefore, this study using the IHC method to detect the expressions of SATB1 in 180 DLBCL tissues and 180 chronic Lymphadenitis tissues in Para-carcinoma tissues, analyzed the relationship of expression and clinicopathological features of DLBCL patients, investigating the effect of SATB1 expression in newly diagnosed DLBCL lymphoma.

Patients and Methods

Patients

One hundred ninety-eight patients were enrolled and were pathologically diagnosed as DLBCL at the People's Hospital of Guigang (Guangxi, China) from August 2010 to August 2018. Eighteen patients with DLBCL were excluded: 4 patients for insufficient information, and 4 patients because they had a history of other malignancies within 5 years, and 180 patients were analyzed. Two hematopathology's experts reviewed diagnostic specimens according to the 2008 WHO classification. Patients participating in the study did not receive radiotherapy, chemotherapy or biological therapy before diagnosing. Paraffin-embedded samples were obtained. Patients were aged 27-70 years with an average of 53.83 ± 29.70 years. Patients were fully evaluated at the beginning of the initial treatment, including computed tomography (CT) scanning of the thorax and abdomen, and/or PET-CT scanning, bone marrow biopsy. For non-commercial human samples from Clinical patient, the study was approved by Ethical clearance from the Institutional Ethics Committee of People's Hospital of Guigang in Guangxi (China) and adhered to the statutes of the Declaration of Helsinki. Patients were included after patients and/or guardians had signed a written informed consent form.

Reagents

Formalin-fixed, paraffin-embedded tissue blocks were processed by pathologists in accordance with standard procedures. We used the tumor tissue micro-array technique using the tissue arrays from patients participating in the study and undertook evaluations with antibodies. Rabbit anti-SATB1 polyclonal antibody (model: A013 12.1) was purchased from Wuhan Boster Biotechnology Co., Ltd, (Wuhan, China) with a dilution of 0.5.199/ml; ectastain ABC kit, 3,3'-Diaminobenzidine (DAB)[13,17,18].

Immunohistochemistry

Immunohistochemical (IHC) analysis was performed on formalin-fixed paraffin-embedded tissue sections (4-μm thickness) of DLBCL and chronic lymphadenitis, tissue sections were heated for 2 h at 45°C in a water bath. Antigen retrieval was performed in boiling citrate buffer for 15 min. Peroxide blocking was performed with 0.3% peroxide in absolute methanol. The slides were then incubated with Rabbit anti-SATB1 polyclonal antibody (model: A013 12.1) (diluted 1:100; Wuhan Booster Biotechnology Co., Ltd, Wuhan, China) at 4°C overnight and washed twice with phosphate-buffered saline prior to incubation with a secondary antibody (Santa Cruz Biotechnology, Santa Cruz Biotechnology, CA, USA) at room temperature for 30 min. After washing, the sections were incubated with immunoglob-

ulins conjugated with horseradish peroxidase (HRP). The reaction was then developed with 3,3'-diaminobenzidine substrates. Tissue sections were counterstained with hematoxylin or methyl green[13,18] Then, instead of SATB1 antibody, the sections treated with PBS instead of primary antibody served as the negative control in the experiment, and DLBCL sections previously diagnosed as SATB1-positive were used as the positive control[13,17,18]. The positive expression of SATB1 presented as brown yellow particles mainly localized in the nucleus. Six fields were randomly selected for each film under the microscope (400), with the percentage of positive cells subsequently calculated. I) The staining intensity scoring of positive cells was as follows: non-staining (Negative) was 0 point; pale yellow was 1 point; yellow-brown was 2 points; and dark brown was 3 points. II) Positive cells in the observed tissue ranged from 0 to 3 in percentage: 1%-10% is 0 points; 11%-25% is 1 point; 26%-50% is 2 points; >50% is 3 points. The results of multiplying the two score with more than 3 points indicated a positive SATB1 expression, while those with 0-3 points indicated decreased or absent expression and was negative SATB1 expression (Table I). Two pathologists who were blinded to the patients' clinical and pathological data reviewed all the samples[17,18].

Statistical Analysis

Data are presented in the text, Tables, and Figures as means±standard errors. Chi-square test (χ^2) was used to evaluate the relationship between SATB1 expression and clinic pathological factors. In this study, we used 5-year overall survival (OS) and 5-year DFS at the end of follow-up as the primary end-points. Using this cutoff value of SATB1 for the entire cohort, statistical analyses were performed using the non-parametric Mann-Whitney U test or Chi-square test to evaluate the association between SATB1 and clinic pathological parameters. The Kaplan-Meier method was used to calculate the OS and DFS rates, and the log-rank test was used to assess the difference between the curves. In the multivariate analysis, variables associated with DFS and OS were identified by stepwise Cox proportional hazards models. Hazard ratios (HRs) estimated from the Cox analysis are reported as relative risks with corresponding 95% confidence intervals (CIs). All statistical analyses were carried out using the Statistical Package for Social Sciences version 17.0 (SPSS Inc., Chicago, IL, USA). A two-sided $p<0.05$ was considered statistically significant.

Results

Clinicopathological Characteristics of Diffuse Large B-Cell Lymphoma Subtypes Based on SATB1 Positive Diffuse Large B-Cell Lymphoma

In this study, the relative expression levels of SATB1 in DLBCL tissues and chronic Lymphadenitis tissues in Para-carcinoma tissues were compared. The expression of SATB1 in DLBCL tissues by immunohistochemistry was observed. SATB1 was expressed positively in 126 (70%) cases of DLBCL tissues and in 19 (10.6%) out of 180 cases of chronic lymphadenitis tissues in para-carcinoma tissues. In contrast, the expression of SATB1 was significantly higher in DLBCL tissues than that in adjacent tumor tissues and chronic lymphadenitis tissues, suggesting that there are differences in the expression of SATB1 between DLBCL tissues and chronic Lymphadenitis tissues of DLBCL patients ($\chi^2 = 132.210$, $p < 0.05$, Figure 1, Table II).

Assess the Relationship Between SATB1 Expression and Clinic Pathological Features

A positive SATB1 expression was not significantly associated with age, B symptoms and

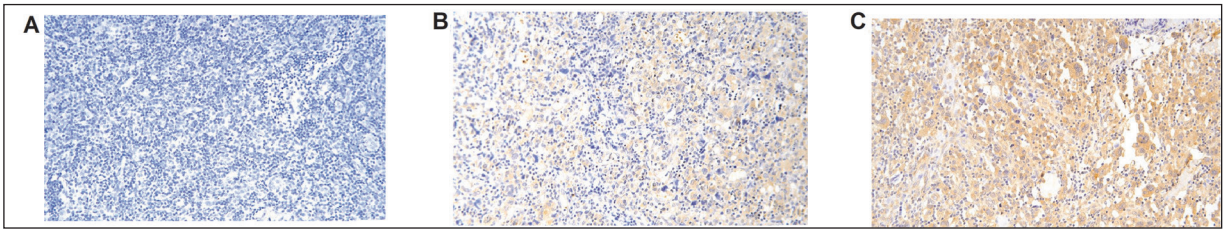

Figure 1. Representative images of SATB1 immunohistochemical staining in tissues from DLBCL, **A,** SATB1 expression by IHC. A Negative SATB1 expression, Bar = 20 μm. **B**, A Positive SATB1 expression (+), Bar = 20 μm. **C,** A Positive SATB1 expression (++), Bar = 20 μm.

Table I. SATB1 scoring system.

A	Percentage of positive cells	B	Intensity of staining
0	<10%	0	No detectable staining
1	11-25%	1	Weak staining (pale yellow)
2	26%-50%	2	Moderate staining (yellow brown)
3	>50%	3	Strong staining (dark brown)

The final score was calculated as a Multiplying of the factors A and B, more than 3 points indicated positive, 0-3 points was negative.

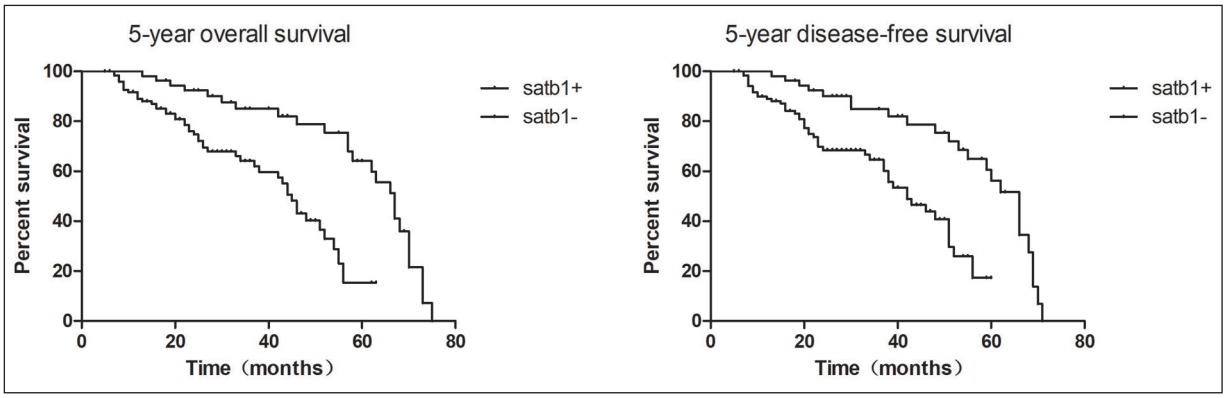

Figure 2. Kaplan-Meier estimates of (**A**) OS and (**B**) PFS between patients with strongly positive expression *vs.* those with negative expression of SATB1. OS, overall survival; PFS, progression-free survival. $p < 0.001$.

ECOG PS status in DLBCL ($p > 0.05$), but positively correlated with Tumor stage, Serum level of LDH, Extranodal involvement, and IPI score ($p < 0.05$) (Table III).

The positive expression of SATB1 linked to unfavorable OS and PFS of CRC patients, in order to determine its prognostic value of SATB1 in DLBCL, overall survival (OS) and disease-free survival (DFS) were evaluated using the Kaplan-Meier method, and multivariate analysis was performed using the Cox proportional hazard analysis. Notably, increased levels of SATB1 expression significantly correlated with a shorter PFS and OS in DLBCL patients (both $p < 0.001$; Figure 2). At multivariate analysis, SATB1 was an independent prognostic factor for both OS and PFS (OS, $p = 0.015$ and PFS, $p = 0.015$; Tables IV and V). Interpreted in light, thus, the results of the present study demonstrated that SATB1 may serve as a potential prognostic marker and therapeutic target in patients with DLBCL.

SATB1 was a negative predictor of 5-year DFS and OS ($p < 0.001$, log-rank test, Figure 2). Moreover, the correlation between SATB1 expression and clinical- pathological factors, advanced tumor stage, age, extranodal involvement, ECOG, serum level of LDH and a poor R-IPI was analyzed ($p < 0.001$). Univariate Cox proportional analysis identified older age (< 60 *vs.* > 60, $p < 0.001$), high tumor stage (stage I-II *vs.* stage III-IV, $p < 0.001$), satb1+, and IPI (0-2 *vs.* 3-5, $p < 0.001$) as the unfavorable prognostic variables for OS (Table IV. To determine the independent prognostic value of SATB1**,** a multivariate analysis, including

Table II. Expression of SATB1 in cancer tissues.

		SATB1 expression				
		No. Negative(-)	S Positive(+)	Percentage	χ^2	*p*-value
DLBCL tissues	180	54	126	70	132.210	0.000
Chronic Lymphadenitis tissues	180	161	19	10.6	2.2	

Table III. SATB1 expression and clinic pathological features of patients with DLBCL.

Clinicopathologic characteristics	SATB1 expression			Percentage	χ^2	*p*-value
	No.	Negative	Positive			
Age						
≤60	102	43	87	66.9	2.110	0.146
>60	78	11	39	78		
Tumor stage						
≤II	71	15	56	78.9	4.396	0.036
>III	109	39	70	64.2		
Extranodal involvement						
≤1	57	5	52	91.2	17.90	0.000
>1	123	49	74	60.2		
ECOG performance status						
0-1	66	19	47	71.2	0.126	0.723
>=2	114	35	79	68.7		
Serum level of LDH (IU/L)						
Normal (≤ 250)	68	14	54	79.4	4.61	0.04
Elevated (> 250)	112	40	72	64.3		
B symptoms						
Yes	62	18	44	71	0.042	0.866
No	118	36	82	69.5		
IPI score						
IPI 0-2	93	36	57	79.3	6.951	0.008
IPI 3-5	87	18	69	61.3		

age, tumor stage, IPI, extranodal, involvement, ECOG, serum level of LDH and SATB1, was performed. We also identified age ($p < 0.005$). IPI ($p < 0.005$), and our clinical outcome analysis in the present study suggested that SATB1 can serve as prognosticators factors for 5-year OS (Table III). Relating to the DFS, unaffiliated analysis showed statistical significance for older age (< 60 *vs.* > 60, $p < 0.005$), high tumor stage (stage I-II *vs.* stage III-IV, $p < 0.001$), and IPI (0-2 *vs.* 3-5, $p < 0.001$) as prognosticators of poor outcome (Table V). Furthermore, Multivariate cox regression analysis suggests that high age, high tumor stage, and SATB1 as independent prognostic factors for 5-year DFS (Table V, $p < 0.005$).

Finally, the Receiver Operating Characteristic (ROC) curves were produced by ranking all the SATB1+ and SATB1- tissue samples into one class, in order to ascertain whether SATB1 may be used as a biomarker to prognose a good pre-

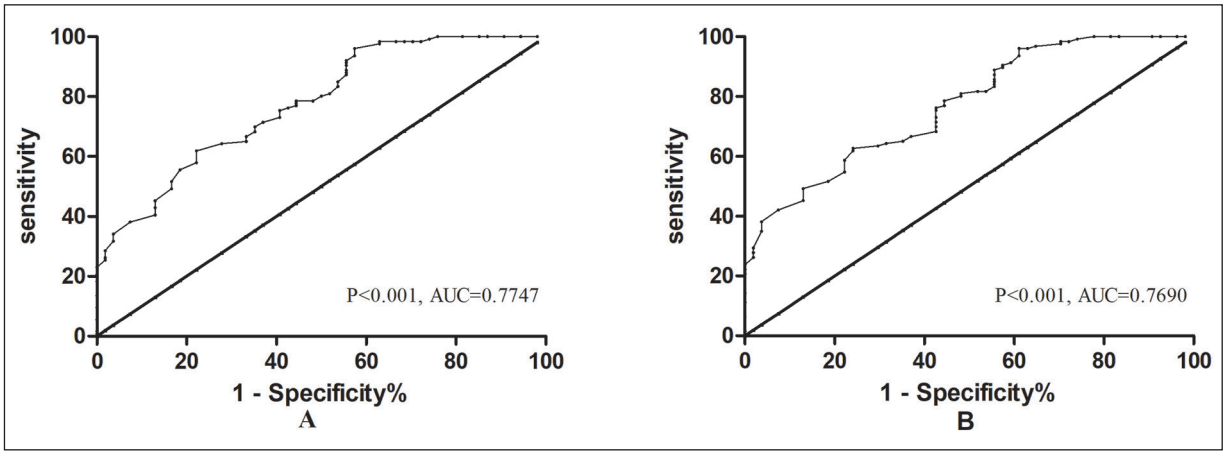

Figure 3. The time-dependent receiver operating characteristic (ROC) curve analysis was applied to evaluate the predictive accuracy of SATB1 for overall survival (OS) and disease-free survival (DFS). AUC, the area under the ROC curve.

Table IV. Univariate and multivariate analysis for the prediction of 5-year OS in DLBCL patients.

	Univariate analysis		Multivariate analysis	
Parameter	**HR (95% CI)**	***p*-value**	**HR (95% CI)**	***p*-value**
Age				
≤60				
>60	4.747 (3.273-6.886)	0.000	0.194 (0.117-0.322)	0.000
Tumor stage				
≤II				
>III	0.031 (0.008-0.127)	0.000	2.998 (1.197-7.505)	0.019
Extranodal involvement				
≤1				
>1	0.163 (0.083-0.322)	0.000	2.604 (1.203-5.634)	0.015
ECOG performance status				
0 or 1				
≥2	0.349 (0.243-0.502)	0.000	1.414 (0.957-2.090)	0.082
Serum level of LDH (IU/L)				
Normal (≤ 250)				
Elevated (> 250)	0.181 (0.111-0.295)	0.000	4.871 (2.528-9.383)	0.000
IPI score				
IPI 0-2				
IPI 3-5	0.138 (0.087-0.212)	0.000	2.753 (1.124-6.742)	0.027
SATB1				
+				
-	0.431 (0.287-0.648)		3.546 (2.132-5.900)	0.000

dictive value for DLBCL. The AUC of OS was 0.7747 ($p < 0.005$; Figure 3A) and DFS was 0.7690 ($p < 0.005$; Figure 3B), suggesting that SATB1 has excellent predictive value for PFS and OS in patients with DLBCL.

Discussion

Special adenine-thymine-rich sequence-binding protein 1 (SATB1) is a well-known oncogene gene located in the short arm of the chromosome 3 sequence for a total length of 763 amino acids[19]. SATB1 is an AT-rich DNA sequence within a high base pairing region, identified SATB1 as a nuclear matrix-associated protein because of the large proportion of the protein resides in the nuclear matrix fraction, which recruits chromatin remodeling at AT-rich sequences to regulate chromatin structure and gene expression organizes the structure of genome at the chromatin level[19,20]. It has been found that both SATB1 and MAR transcription factor have associations with sequences are enriched with S/MAR binding motifs, can promote the stable binding motifs and an origin of replication sequence through anchoring the chromosome ring, and then indeed support the critical processes participating of SATB1 in gene regulation are DNA methylation, histone modification, and chromatin remodeling[20]. Some reports observed that SATB1 is highly expressed in a variety of malignant tumours, but it is no expressed or is expressed at very low levels in normal tissues and benign tissues[13,17,18,21]. The results indicated that the expression of SATB1 was considerably higher in DLBCL tissues compared with para-carcinoma tissues (chronic Lymphadenitis tissues in para-carcinoma tissues were 10.6%). The results were consistent with the findings of previous studies. To assess the biological functions of SATB1 in human glioblastoma, the results of an *ex vivo* bench top study[22] show that SATB1 is thought to contribute to chromosomal instability and to activate the expression of proto-oncogenes is demonstrated to have tumor-promoting activity[22]. It is reported that the abnormal expression of SATB1 may be a key factor in the occurrence and development of glioma. Crocheting SATB1 gene, analysis the gene expression profile relative to DLBCL, found out that SATB1involved in controlling cell cycle, signal transduction pathways and apoptosis and then regulates the expression of oncogenes with poor prognosis. The experiments showed that SATB1 raise CDK4 expression levels, induce tumor cell proliferation through cell cycle arrest and promote apoptosis through down regulating Fas-related protein-mediated apoptosis pathway[23]. In Han' study[24], it has been found that

SATB1 in particular is highly expressed in many human breast cancer cell lines and both SATB1 protein and mRNA are over expressed in a majority of human breast cancers and it also showed that SATB1 is highly expressed in breast cancer tissue and is closely related to the prognosis of patients with breast cancer. Herein, it was found that over expression of SATB1 directly upregulates metastasis related genes, inhibits these tumor suppressor genes and promotes cell transformation, tumor growth, invasion and metastasis. In *in situ* and invasive breast cancer[21], SATB1 is highly expressed and upregulated in numerous cancers, including brain, lung, gastrointestinal, prostrate, and male germ cell tumors. Wang et al[25] observed a stage-related decrease of SATB1 expression in epidemiologic cutaneous T-cell lymphomas, suggesting that SATB1 might have potential roles in the malignant lymphoma. Therefore, more research about the mechanism of the interaction is necessary to understand the roles of SATB1 expression in B-Cell Lymphoma, especially in DLBCL.

In this study, we analyzed the expressions of SATB1 between DLBCL tissues and chronic Lymphadenitis tissues with the clinicopathological features and survival of patients with DLBCL. Furthermore, we detected the expression of SATB1 in human DLBCL tissues by immunohistochemistry and correlated the expression levels with clinicopathological features. Using IHC, we found that the expression of SATB1 protein was significantly up regulated in DLBCL tissues compared with chronic Lymphadenitis tissues. The results showed high expression of SATB1 in 126 of 180 (70%) DLBCL tissues by using immunohistochemical analysis and the over expression of SATB1 was strongly correlated to the clinical staging of patients with DLBCL ($p<0.05$). The over expression of SATB1 was strongly correlated to the clinical staging, tumor stage, serum level of LDH, extramural involvement, and IPI score of patients with DLBCL were statistically significant ($p < 0.05$). These results indicated a possible and dual role of SATB1 in DLBCL occurrence and development. However, the specific signaling mechanism involved in SATB1 in the regulation of DLBCL still requires further exploration. Diffuse large B-cell lymphoma (DLBCL), the most common subtype of adult non-Hodgkin lymphoma, is clinically heterogeneous with various immunophenotypes, different molecular and genetic abnormalities, and a wide range of clini-

Table V. Univariate and multivariate analysis for the prediction of 5-year DFS in DLBCL patients.

	Univariate analysis		Multivariate analysis	
Parameter	**HR (95% CI)**	***p*-value**	**HR (95% CI)**	***p*-value**
Age				
<=60				
>60	0.210 (0.146-0.302)	0.000	0.193 (0.119-0.314)	0.000
Tumor stage				
≤II				
>III	8.457 (4.382-16.32)	0.000	4.778 (1.736-13.15)	0.019
Extranodal involvement				
<=1				
>1	4.792 (2.747-8.359)	0.000	2.545 (1.177-5.503)	0.018
ECOG performance status				
0 or 1				
>=2	2.859 (1.991-4.107)	0.000	1.333 (0.906-1.962)	0.145
Serum level of LDH (IU/L)				
Normal (≤ 250)				
Elevated (> 250)	4.494 (2.954-6.838)	0.000	7.303 (3.525-15.128)	0.000
IPI score				
IPI 0-2				
IPI 3-5	0.116 (0.073-0.183)	0.000	3.051 (1.223-7.607)	0.017
SATB1				
+				
-	2.768 (1.866-4.105)	0.000	3.191 (1.929-5.277)	0.000

cal presentations and outcomes, which less than half of all affected patients are treated by currently available therapies. Currently, the International Prognostic Index (IPI) system has been routinely used to guide risk stratification and predict the outcome of DLBCL patients in the current clinical setting. Standard first-line treatment for DLBCL includes anthracycline-based chemotherapy, such as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) or CHOP-like regimens and its predictive capacity has been validated in the past two decades[26,27]. In our study, SATB1 expression was higher in IPI 3-5 than IPI 0-2 in DLBCL patients. Patients with T3 and T4 tumors have significantly higher SATB1 values than those with T1 and T2 stages, suggesting SATB1 plays a critical role in DLBCL cancer progression. Scholars[28] indicate aberrant expression of SATB1 in a variety of human cancers, such as liver, ovary, colorectal cancer, bladder cancer and squamous cell carcinoma of the head and neck. SATB1 might regulate the expression of many target genes that together coordinate a complex biological response to coordinate cell growth and proliferation, leading to the hypothesis that may play an important role in the expression of many genes critical to the pathogenesis of many types of human cancers[28]. Actually, in breast cancer progression and metastasis, the SATB1 protein is known as an important mediator, and it has also been implicated in numerous types of human cancers of progression and in the bone metastasis process[26-29]. Several reports revealed that expression of SATB1 is positively correlated with tumor progression and metastatic potential in cutaneous malignant melanoma and gastric cancer and may be a potential independent prognostic marker for predicting clinical outcome[30]. In the current study, in university and multivariate analysis, patients with advanced DLBCL have the over expression of SATB1 identified as an independent predictor of PFS and OS. These findings demonstrated that SATB1 expression should be routinely considered as a useful tool for guiding prognostic and therapeutic options for DLBCL patients.

Conclusions

There are several limitations that need to be considered when interpreting the results. Firstly, it should be noted that our study had a relatively small sample size. The number of patients evaluated in our study was too small to reach any definite conclusions. Then, further studies are warranted to follow-up on our findings. Secondly, the objective quantitative analysis of the RT-PCR method was not performed in the present study due to test funds. Additionally, the study was retrospectively reviewed and carried out in a single center and was controlled with historical data. Above all, our findings provide empirical evidence that further underline an important role of SATB1 in DLBCL carcinogenesis and metastasis. Therefore, SATB1 might represent an important prognostic biomarker and therapeutic target for aggressiveness and therapy responsiveness in DLBCL. However, the mechanisms through which SATB1 affects DLBCL development remain unknown, few studies have been developed on this issue and further studies are still needed.

Conflicts of Interest

The authors declare no conflicts of interest.

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