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High expression of SRY-box transcription factor 30 associates with well differentiation, absent lymph node metastasis and predicts longer survival in nonsmall-cell lung cancer patients

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Abstract

The present study aimed to investigate SRY-box transcription factor 30 (SOX30) expression in nonsmall-cell lung cancer (NSCLC) tumor tissues and adjacent noncancerous tissues, and further explore the correlation of tumor SOX30 expression with clinical characteristics and survival profiles in patients with NSCLC.

Totally, 365 patients with NSCLC who underwent resection were screened, and SOX30 expression was detected in their tumor tissues and adjacent noncancerous tissues via immunohistochemistry (IHC) assay, which was assessed by a semiquantitative method considering the multiplying staining intensity score and staining density score. According to the tumor SOX30 expression, patients were categorized as tumor SOX30 low (IHC score $\leq$3) and high (IHC score 4–12) patients, the latter were further divided into tumor SOX30 high+ (IHC score 4–6), high++ (IHC score 7–9), and high+++ (IHC score 10–12) patients.

SOX30 was downregulated in NSCLC tumor tissues compared with adjacent noncancerous tissues. Meanwhile, tumor SOX30 high expression associated with well differentiation, absent lymph node metastasis, decreased TNM stage, but did not associated with age, gender, history of smoke and drink, hypertension, hyperlipidemia, diabetes, tumor size, or carcinoembryonic antigen level. Both accumulating disease-free survival and overall survival were the longest in tumor SOX30 high+++ patients, followed by tumor SOX30 high++ patients, and tumor SOX30 high+ patients, and the shortest in tumor SOX30 low patients. Besides, tumor SOX30 high expression was an independent predictor for longer disease-free survival and overall survival.

Tumor SOX30 exhibits the potential to be a novel biomarker for survival prediction of patients with NSCLC.

Abbreviations: DFS = disease-free survival, IHC = immunohistochemistry, NSCLC = nonsmall-cell lung cancer, OS = overall survival, SOX30 = SRY-box transcription factor 30, TNM = Tumor-Node-Metastasis.

Keywords: clinical characteristics, immunohistochemistry, nonsmall-cell lung cancer, SRY-box transcription factor 30, survival

1. Introduction

Nonsmall-cell lung cancer (NSCLC) accounts for approximately 83% of total lung cancer cases, and one recent global cancer statistics report indicates that NSCLC is one of the main causes of cancer-related mortality with only a 5-year survival rate of 23%.[1,2] The treatment for NSCLC, including surgery, chemotherapy, radiotherapy, and target treatment, has underwent a great improvement and achieved prolonged survival in a proportion of patients with NSCLC; however, the treatment efficacy is still impaired by drug resistance and the survival data remains unsatisfied owing to the tumor locoregional recurrence and distant metastasis.[3,4] Hence, it is important to pay attention to the cancer surveillance in the long-term follow-up care, and meanwhile, to further investigate into the underlying mechanisms of NSCLC as well as novel biomarkers, which helps to improve the prognosis in NSCLC management.

SRY-box transcription factor 30 (SOX30), as a member of SOX family, is characterized as a sex-determining factor existing throughout the mammals, and it is involved in the spermatogonial differentiation and has regulatory effects on spermatogenesis function.[5,6] Recently, SOX30 is shown to function as a tumor

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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suppressor through attenuating oncogenic pathway in various cancers, such as lung cancer, hepatocellular carcinoma, and ovarian cancer.[7–11] For example, in vitro experiments of lung cancer show that SOX30 promotes cancer cell apoptosis but inhibits cancer cell metastasis via diminishing Wnt-signaling and attenuating β-catenin transcriptional activity.[12] In another study of NSCLC, SOX30 induces expression of desmosomal genes via directly binding to the desmosomal genes promotor region, which inactivates Wnt signaling and ERK signaling and further inhibits cell proliferation, migration, and invasion.[13] According to the aforementioned studies, we hypothesized that SOX30 might be of clinical significance in NSCLC management. However, the related research is still limited. Therefore, we conducted this study to detect the SOX30 expression in the tumor tissues as well as the noncancerous tissues of patients with NSCLC, and further investigate the correlation of tumor SOX30 expression with clinical characteristics and survival profiles in patients with NSCLC.

2. Methods

2.1. Patients

In this retrospective study, a total of 365 eligible patients with NSCLC who underwent resection were screened from our hospital between January 2015 and December 2019. The main inclusion criteria were: histologically confirmed as primary NSCLC; age ranging from 18 to 80 years old; TNM stage I-IIIA; tumor tissues and adjacent noncancerous tissues excised from surgery were well preserved; the records of tumor features before resection were complete; and follow-up data were eligible for calculating disease-free survival (DFS) and overall survival (OS). The main exclusion criteria were: relapse or secondary NSCLC; history of malignancies; poorly controlled hepatorenal disorders; and severe abnormities in hematologic indexes. This study was approved by the Ethics Committee of our hospital. All patients or their family members proved the written informed consents.

2.2. Immunohistochemistry assay

After acquiring agreement from the Pathology Department of our hospital, the expressions of SOX30 in the formalin-fixed and paraffin-embedded tumor tissues and formalin-fixed and paraffin-embedded adjacent noncancerous tissues were detected by immunohistochemistry (IHC) assay. anti-SOX30 antibody (1:100; Abcam, Cambridge, MA) and goat anti-rabbit IgG H&L (HRP) (1:5000; Abcam) were used in IHC assay. All procedures were carried out according to application manuals of the antibodies. The total IHC score was assessed by multiplying staining intensity score and staining density score as previously described.[14] Briefly, the staining intensity was scored as: 0 (no staining), 1 (weak staining), 2 (moderate staining), and 3 (strong staining). The staining density was scored as: 0 (no positively stained cells), 1 (1–25% of positively stained cells), 2 (26–50% of positively stained cells), 3 (51–75% of positively stained cells), and 4 (76–100% of positively stained cells). The total IHC score was ranging from 0 to 12. SOX30 high expression was defined as total IHC score >3, and SOX30 low expression was defined as the total IHC score ≤ 3. The SOX30 high expression were further divided into SOX30 high+ (IHC score 4–6), SOX30 high++ (IHC score 7–9), and SOX30 high+++ (IHC score 10–12).[14]

2.3. Data collection and follow-up

The demographics and major preoperative tumor features were extracted from database of our hospital, and the survival data were obtained from survival data of our hospital. The last follow-up date was December 31, 2019, and the median follow-up duration was 30.0 months. DFS was defined as the duration from surgery to disease relapse, disease progression, or death, and OS was defined as the duration from surgery to death.

2.4. Statistical analysis

All statistical analyses were performed using SPSS version 22.0 (IBM, Chicago, IL), and all figures were plotted using GraphPad Prism version 7.00 (GraphPad Software, La Jolla, CA). Comparison of SOX30 expression between tumor tissues and noncancerous tissues was determined by paired-samples *t* test, McNemar test, or McNemar–Bowker test. Comparison of clinical characteristics between SOX30 high expression group and SOX30 low expression group was determined by Chi-squired test, Fisher exact test, or Wilcoxon rank sum test. DFS and OS were displayed using Kaplan–Meier curves. Comparison of DFS and OS between 2 groups or among 4 groups was determined by Log-rank test. Factors predicting DFS and OS were analyzed by univariate Cox proportional hazard regression model, and factors with $P < .05$ in the univariate Cox regression were included in the forward stepwise multivariate Cox regression analysis. P value $<.05$ was considered as significant.

3. Results

3.1. Clinical characteristics of patients with NSCLC

The average age of patients with NSCLC (N = 365) was 61.6 ± 10.0 years (Table 1). The number of males and females were 298 (81.6%) and 67 (18.4%), respectively. Regarding tumor features, the number of patients with well, moderate, and poor differentiation were 67 (18.3%), 213 (58.4%), and 85 (23.3%), respectively. The mean tumor size was 5.3 ± 2.1 cm, and there were 213 (58.4%) patients with ≤ 5 cm tumor and 152 (41.6%) patients with >5 cm tumor. Besides, there were 121 (33.2%) patients with lymph node (LYN) metastasis. The number of patients with TNM stage I, II, III were 115 (31.5%), 133 (36.4%), and 117 (32.1%), respectively. More detailed information of clinical characteristics of patients with NSCLC is exhibited in Table 1.

3.2. SOX30 expression in NSCLC tumor tissues and noncancerous tissues

The expression of SOX30 in the tumor tissues and adjacent noncancerous tissues was detected by IHC assay, and all tissues were classified as SOX30 high expression (total IHC score >3) and SOX30 low expression (total IHC score ≤ 3). The SOX30 high expression were further divided into SOX30 high+ (total IHC score 4–6), SOX30 high++ (total IHC score 7–9), and SOX30 high+++ (total IHC score 10–12). Representative IHC images of SOX30 low expression in tumor tissue and SOX30 high expression in noncancerous tissue are shown in Figure 1A. The average SOX30 IHC score was decreased in NSCLC tumor tissue (2.9 ± 2.5) compared with noncancerous tissue (4.7 ± 3.1) ($P < .001$), suggesting that SOX30 was downregulated in NSCLC tumor tissues compared with noncancerous tissues (Fig. 1B).

Table 1

Features of patients with NSCLC.

Items	NSCLC patients (N = 365)
Demographic features	
Age, yrs, mean ± SD	61.6 ± 10.0
Gender (male/female), n	298/67
History of smoke, n (%)	202 (55.3)
History of drink, n (%)	145 (39.7)
Commonly chronic complications	
Hypertension, n (%)	132 (36.2)
Hyperlipidemia, n (%)	116 (31.8)
Diabetes, n (%)	58 (15.9)
Tumor features	
Differentiation	
Well	67 (18.4)
Moderate	213 (58.4)
Poor	85 (23.3)
Tumor size, cm, mean ± SD	5.3 ± 2.1
≤5	213 (58.4)
>5	152 (41.6)
LYN metastasis, n (%)	
Absent	244 (66.8)
Present	121 (33.2)
TNM stage, n (%)	
I	115 (31.5)
II	133 (36.4)
III	117 (32.1)
CEA, ng/mL, median (IQR)	5.9 (2.7–26.9)
Normal*	170 (46.6)
Abnormal*	195 (53.4)

CEA = carcinoembryonic antigen, IQR = interquartile range, LYN = lymph node, NSCLC = nonsmall-cell lung cancer, SD = standard deviation.

* CEA abnormal level > 5.0 ng/mL, CEA normal level ≤ 5.0 ng/mL.

There were 278 (76.2%) patients with tumor SOX30 low expression and 87 (23.8%) patients with tumor SOX30 high expression; meanwhile, there were 205 (56.2%) patients with noncancerous SOX30 low expression and 160 (43.8%) patients with noncancerous SOX30 high expression; further comparison analysis indicated that SOX30 was downregulated in NSCLC tumor tissues compared with noncancerous tissues ($P < .001$) (Fig. 1C). In addition, there were 278 (76.2%), 54 (14.8%), 22 (6.0%), and 11 (3.0%) patients with tumor SOX30 low, high+, high++, and high+++ expression, respectively; while there were 205 (56.2%), 77 (21.1%), 56 (15.3%), and 27 (7.4%) patients with noncancerous SOX30 low, high+, high++, and high+++ expression, respectively; further comparison analysis also indicated that SOX30 was downregulated in NSCLC tumor tissues compared with noncancerous tissues ($P < .001$) (Fig. 1D).

3.3. Correlation of tumor SOX30 with clinical characteristics in patients with NSCLC

There was no correlation of tumor SOX30 with age ($P = .529$), gender ($P = .336$), history of smoke ($P = .596$), history of drink ($P = .888$), hypertension ($P = .529$), hyperlipidemia ($P = .535$), or diabetes ($P = .465$) in patients with NSCLC (Table 2). As for the correlation of tumor SOX30 with tumor features, it was associated with well differentiation ($P = .020$) (Fig. 2A), absent LYN metastasis ($P = .047$) (Fig. 2C) and decreased TNM stage ($P = .003$) (Fig. 2D); however, there was no correlation of tumor SOX30 with tumor size ($P = .192$) (Fig. 2B) or carcinoembryonic antigen (CEA) level ($P = .270$) (Fig. 2E).

3.4. Correlation of tumor SOX30 with DFS in patients with NSCLC

Accumulating DFS was increased in tumor SOX30 high expression patients compared with tumor SOX30 low expression patients ($P = .002$) (Fig. 3A). Furthermore, accumulating DFS was the longest in tumor SOX30 high+++ expression patients, followed by tumor SOX30 high++ patients and tumor SOX30 high+ expression patients, and the shortest in tumor SOX30 low expression patients ($P = .014$) (Fig. 3B).

3.5. Factors affecting DFS in patients with NSCLC

Univariate Cox regression revealed that tumor SOX30 high expression (hazard ratio [HR] = 0.612, $P = .003$) was positive-

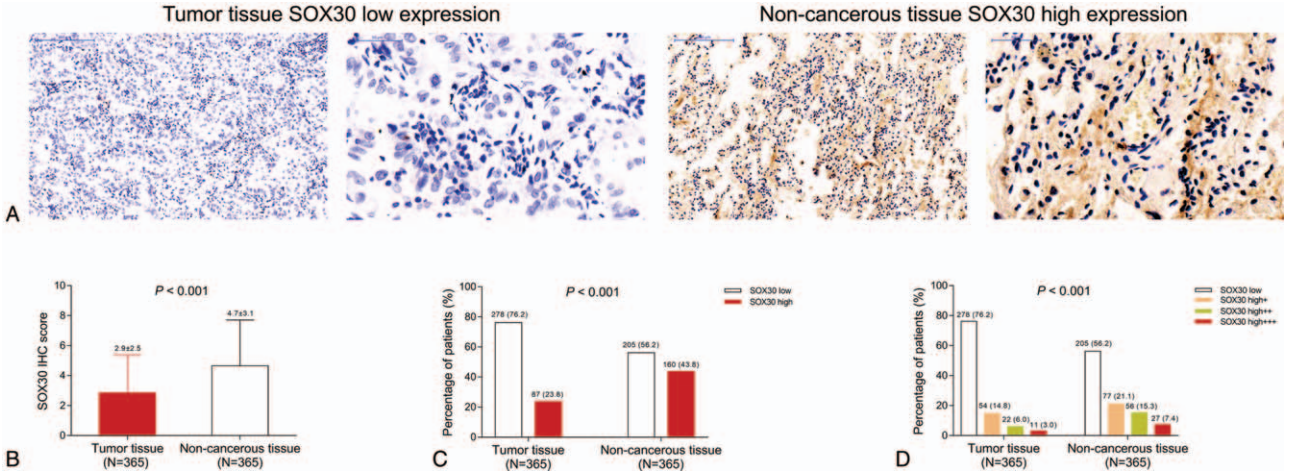

Figure 1. SRY-box transcription factor 30 (SOX30) expression in nonsmall-cell lung cancer (NSCLC). Representative immunohistochemistry (IHC) images of SOX30 low expression in NSCLC tumor tissue and SOX30 high expression in noncancerous tissue (A). Comparison of SOX30 IHC score between tumor tissues and noncancerous tissues (B). Comparison of the percentage of SOX30 high/low expressions between tumor tissues and noncancerous tissues (C). Comparison of the percentage of SOX30 low/SOX30 high+/SOX30 high++/SOX30 high+++ expressions between tumor tissues and noncancerous tissues (D).

Table 2

Correlation of SOX30 expression with demographic features and commonly chronic complications.

Items	SOX30 low (n = 278)	SOX30 high (n = 87)	*P* value
Age, yr, n (%)			.529
≤65	164 (59.0)	48 (55.2)	
>65	114 (41.0)	39 (44.8)	
Gender, n (%)			.336
Female	48 (17.3)	19 (21.8)	
Male	230 (82.7)	68 (78.2)	
History of smoke, n (%)			.596
No	122 (43.9)	41 (47.1)	
Yes	156 (56.1)	46 (52.9)	
History of drink, n (%)			.888
No	167 (60.1)	53 (60.9)	
Yes	111 (39.9)	34 (39.1)	
Hypertension, n (%)			.529
No	175 (62.9)	58 (66.7)	
Yes	103 (37.1)	29 (33.3)	
Hyperlipidemia, n (%)			.535
No	192 (69.1)	57 (65.5)	
Yes	86 (30.9)	30 (34.5)	
Diabetes, n (%)			.465
No	236 (84.9)	71 (81.6)	
Yes	42 (15.1)	16 (18.4)	

Comparison was determined by Chi-squared test.
SOX30 = sex-determining region Y-box 30.

ly associated with DFS, while poor differentiation (HR = 1.461, $P = .012$), larger tumor size (>5 cm) (HR = 1.371, $P = .016$), LYN metastasis (HR = 2.257, $P < .001$), advanced TNM stage (HR = 2.105, $P < .001$), and abnormal CEA (HR = 1.509, $P = .002$) were negatively associated with DFS (Table 3). Forward stepwise multivariate Cox regression further indicated that tumor SOX30 high expression (HR = 0.702, $P = .035$) was an independent predictive factor for increased DFS, while LYN metastasis (HR = 1.876, $P < .001$), advanced TNM stage (HR = 1.471, $P = .014$), and abnormal CEA (HR = 1.523, $P = .002$) were independent predictive factors for decreased DFS.

3.6. Correlation of tumor SOX30 with OS in patients with NSCLC

Accumulating OS was increased in tumor SOX30 high expression patients compared with tumor SOX30 low expression patients ($P = .001$) (Fig. 4A). Furthermore, accumulating OS was longest in tumor SOX30 high+++ expression patients, followed by tumor SOX30 high++ expression patients and tumor SOX30 high+ expression patients, and the shortest in tumor SOX30 low expression patients ($P = .007$) (Fig. 4B).

3.7. Factor affecting OS in patients with NSCLC

Univariate Cox regression revealed that tumor SOX30 (HR = 0.531, $P = .002$), poor differentiation (HR = 1.586, $P = .005$), larger tumor size (>5 cm) (HR = 1.457, $P = .013$), LYN metastasis (HR = 2.871, $P < .001$), advanced TNM stage (HR = 1.883, $P < .001$), and abnormal CEA (HR = 1.647, $P = .001$) were negatively associated with OS (Table 4). Forward stepwise multivariate Cox regression revealed that tumor SOX30 high expression (HR = 0.625, $P = .022$) was an independent predictive factor for increased OS, but poor differentiation (HR = 1.446, $P = .026$), LYN metastasis (HR = 2.859, $P < .001$), and abnormal CEA (HR = 1.599, $P = .003$) were independent predictive factors for decreased OS.

4. Discussion

In the present study, we found that SOX30 was downregulated in NSCLC tumor tissues compared with noncancerous tissues. SOX30 was associated with well differentiation, absent LYN metastasis and decreased TNM stage in patients with NSCLC. SOX30 high expression was an independent predictive factor for longer DFS and OS in patients with NSCLC.

Emerging evidence has been published that SOX protein family mediates DNA binding via high-mobility group domain and

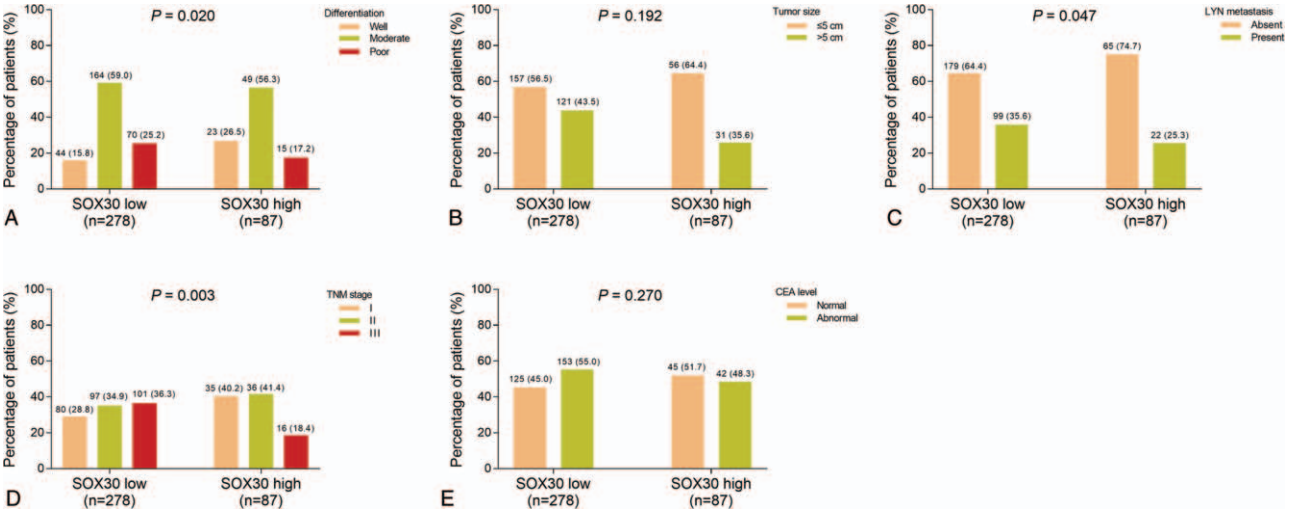

Figure 2. Comparison of tumor features between tumor SRY-box transcription factor 30 (SOX30) high patients and tumor SOX30 low patients. Comparison of tumor differentiation (A), tumor size (B), lymph node (LYN) metastasis (C), TNM stage (D), and carcinoembryonic antigen (CEA) level (E) between tumor SOX30 high patients and tumor SOX30 low patients.

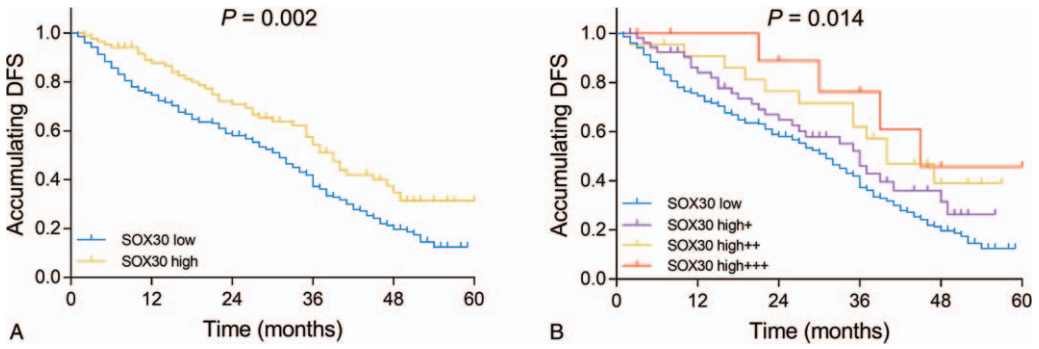

Figure 3. Comparison of disease-free survival (DFS) among nonsmall-cell lung cancer (NSCLC) patients with different tumor SRY-box transcription factor 30 (SOX30) expressions. Comparison of accumulating DFS between tumor SOX30 low patients and tumor SOX30 high patients (A). Comparison of accumulating DFS among tumor SOX30 low patients, tumor SOX30 high+ patients, tumor SOX30 high++ patients, and tumor SOX30 high+++ patients (B).

exerts various functions in cell development and differentiation.[15] SOX30 is located on the chromosome 5, and is of physiologic and biologic function during the tumorigenesis, tumor metastasis has also been disclosed in several cancers.[9–12,16] For example, one study exhibits that, in bladder cancer, SOX30 expression is markedly decreased in tumor tissues compared to the adjacent noncancerous tissues, and in vitro experiments disclose that SOX30 overexpression attenuates cell proliferation, invasion, and migration, but promotes apoptosis.[16] As for the implication of SOX30 in lung cancer, one study indicates that SOX30 suppresses cancer cell migration and invasion, and at transcriptional level, SOX30 represses the activity of β-catenin promotor via C-terminus, which inactivates the Wnt-signaling pathway.[12] Another study reveals that SOX30 upregulates the expression of 3 known tumor suppressor, including desmoplakin, junction plakoglobin and desmocollin 3, via directly binding to their promotor region, which inactivates Wnt/β-catenin signaling pathway, and further inhibits cell proliferation, migration, and invasion in lung adenocarcinoma.[13] According to these previous studies, we hypothesized that SOX30 might have clinical significance in NSCLC. To test this hypothesis, we performed the present study and found that SOX30 was downregulated with the previous studies that SOX30 was downregulated in various cancer tissues (bladder cancer, lung cancer, and NSCLC) compared with adjacent noncancerous tissues.[12,13,16] We further explored the association of tumor SOX30 with clinical characteristics in patients with NSCLC, and observed that high expression of tumor SOX30 was associated with well differentiation, absent LYN metastasis, and decreased TNM stage in patient with NSCLC. The possible reasons might include that based on the prior study, the antitumor effect of SOX30 is exerted via directly activating p53

Table 3

Cox proportional hazard regression model analyses of factors affecting DFS.

	Cox proportional hazard regression model			
			95% CI	
Items	***P* value**	**HR**	**Lower**	**Higher**
Univariate Cox regression				
SOX30 high	.003	0.612	0.442	0.847
Age (>65 yr)	.081	0.792	0.609	1.029
Male	.232	0.820	0.592	1.135
History of smoke	.918	1.014	0.783	1.312
History of drink	.517	1.090	0.840	1.416
Hypertension	.382	0.886	0.677	1.161
Hyperlipidemia	.320	1.150	0.873	1.514
Diabetes	.233	0.801	0.557	1.153
Differentiation (poor vs moderate/well)	.012	1.461	1.089	1.961
Tumor size (>5 cm)	.016	1.371	1.060	1.773
LYN metastasis	<.001	2.257	1.738	2.932
TNM stage (III vs II/I)	<.001	2.105	1.619	2.736
CEA abnormal*	.002	1.509	1.159	1.963
Forward stepwise multivariate Cox regression				
SOX30 high	.035	0.702	0.504	0.976
LYN metastasis	<.001	1.876	1.382	2.546
TNM stage (III vs II/I)	.014	1.471	1.080	2.004
CEA abnormal*	.002	1.523	1.168	1.984

Only factors with $P < .05$ in the univariate Cox regression were included in the forward stepwise multivariate Cox regression analysis.

CEA = carcinoembryonic antigen, CI = confidence interval, DFS = disease-free survival, HR = hazard ratio, LYN = lymph node, SOX30 = sex-determining region Y-box 30.

* CEA abnormal level > 5.0 ng/mL, CEA normal level ≤ 5.0 ng/mL.

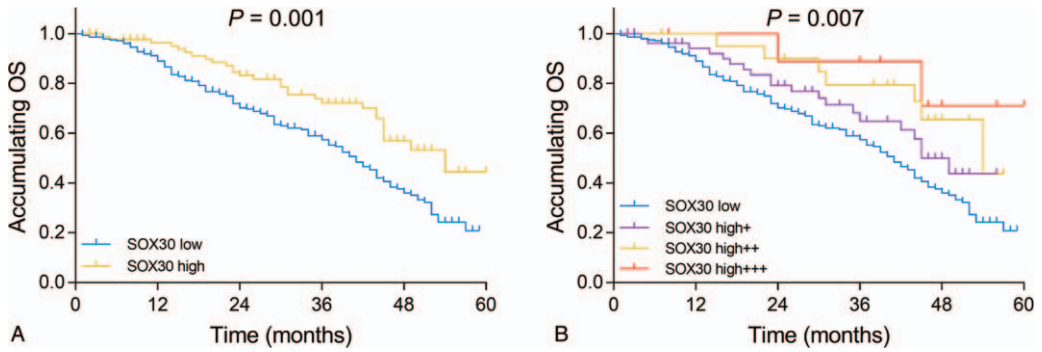

Figure 4. Comparison of overall survival (OS) among nonsmall-cell lung cancer (NSCLC) patients with different tumor SRY-box transcription factor 30 (SOX30) expressions. Comparison of accumulating OS between tumor SOX30 low patients and tumor SOX30 high patients (A). Comparison of accumulating OS among tumor SOX30 low patients, tumor SOX30 high+ patients, tumor SOX30 high++ patients, and tumor SOX30 high+++ patients (B).

transcription, and the restoration of p53 is suggested to restrain tumor progression against the Ras oncogenic signaling pathway.[10,17] Therefore, tumor SOX30 is associated with favorable tumor features in patients with NSCLC. In addition, as previously stated, SOX30 prevents the characteristics of epithelial-mesenchymal transition (EMT) via regulating the markers of EMT, such as E-cadherin and fibronectin, and EMT is reported to cause organ fibrosis and lead to initiation and progression of cancers via through diverse mechanisms.[10,18,19] The activation of EMT permits NSCLC cells to be of migratory, invasive and stem-like properties; therefore, patients with tumor SOX30 low expression has decreased rate of LYN metastasis and advanced TNM stage. However, the detailed underlying molecular mechanism of the regulatory role of SOX30 in NSCLC needed further exploration.

Existing evidence demonstrate that SOX30 is positively correlated with favorable prognosis in patients with various cancers.[10,15,16] For example, in bladder cancer, low SOX30 expression is correlated with decreased survival rate.[16] In another study, high SOX30 expression exhibits value in predicting desirable OS and serves as an independent prognostic factor in advanced-stage patients with ovarian cancer.[10] Consistently, in the present study, we also found that accumulating DFS was the longest in tumor SOX30 high+++ expression patients, followed by tumor SOX30 high++ expression patients and tumor SOX30 high+ expression patients, and the shortest in tumor SOX30 low expression patients. More notably, tumor SOX30 high expression was an independent predictive factor for increased DFS and OS in patients with NSCLC. The possible reasons might include that according to

Table 4

Cox proportional hazard regression model analyses of factors affecting OS.

	Cox proportional hazard regression model			
			95% CI	
Items	***P* value**	**HR**	**Lower**	**Higher**
Univariate Cox regression				
SOX30 high	.002	0.531	0.356	0.791
Age (>65 yrs)	.243	0.836	0.618	1.130
Male	.683	0.922	0.626	1.360
History of smoke	.703	0.944	0.702	1.270
History of drink	.278	1.179	0.875	1.589
Hypertension	.358	0.864	0.632	1.180
Hyperlipidemia	.207	1.224	0.894	1.674
Diabetes	.192	0.757	0.499	1.150
Differentiation (poor vs moderate/well)	.005	1.586	1.149	2.190
Tumor size (>5 cm)	.013	1.457	1.083	1.960
LYN metastasis	<.001	2.871	2.129	3.872
TNM stage (III vs II/I)	<.001	1.883	1.390	2.551
CEA abnormal*	.001	1.647	1.212	2.239
Forward stepwise multivariate Cox regression				
SOX30 high	.022	0.625	0.418	0.934
Differentiation (poor vs moderate/well)	.026	1.446	1.044	2.002
LYN metastasis	<.001	2.859	2.117	3.860
CEA abnormal*	.003	1.599	1.172	2.182

Only factors with $P < .05$ in the univariate Cox regression were included in the forward stepwise multivariate Cox regression analysis.

CEA = carcinoembryonic antigen, CI = confidence interval, HR = hazard ratio, LYN = lymph node, OS = overall survival, SOX30 = sex-determining region Y-box 30.

* CEA abnormal level > 5.0 ng/mL, CEA normal level ≤ 5.0 ng/mL.

aforementioned results, tumor SOX30 was associated with well differentiation, absent LYN metastasis and decreased TNM stage in patients with NSCLC, and well differentiation, absent LYN metastasis were independent predictive factors for increased survival; therefore, SOX30 could predict favorable prognosis in patients with NSCLC. Based on the previous studies, SOX30 could suppress the EMT progression, and EMT was reported to possess the NSCLC cell with various cellular characteristics, including invasiveness, drug resistance, stemness, and the ability to form metastases, which led to increased chemoresistance during the cancer treatment as well as cancer recurrence, further resulting to unfavorable prognosis.[20,21] Hence, SOX30 conferred favorable prognosis in patients with NSCLC.

However, our study still existed some limitations including: as our study was a retrospective study, there might be some selective bias and substantial compounding factors. (2) Since the underlying molecular mechanism of SOX30 at transcriptional level of NSCLC cell was not included in our study, further cellular experiments were needed. The follow-up period was relative short; therefore, the long-term prognostic significance of SOX30 needed further investigation.

In conclusion, tumor SOX30 is associated with well differentiation, absent LYN metastasis, decreased TNM stage, and independently predicts longer DFS and OS in patients with NSCLC, which suggests its potential role as a prognostic biomarker in NSCLC management.

Author contributions

Conception and design: C Liu and X Li; Administrative support: Q Feng; Provision of study materials or patients: Y Liu, J Tian and S Zhang; Collection and assembly of data: X Zhai and Q Feng; Data analysis and interpretation: C Liu, Y Liu, J Tian, S Zhang and X Li; Manuscript writing: All authors. Final approval of manuscript: All authors.

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