

## Original Article

# Preoperative serum bilirubin levels associated with stage and prognosis in patients with stages I-III of non-small cell lung cancer in Jiangxi province, China

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**Abstract:** Bilirubin is an important indicator of liver function. However, its roles in lung cancer remain unknown. The current retrospective study investigated whether preoperative serum bilirubin may be a prognostic biomarker in patients with non-small cell lung cancer (NSCLC). Clinical data of 393 patients with NSCLC was reviewed and evaluated via statistical analysis. Kaplan-Meier curves and Cox's proportional hazards models were used to perform survival analysis. Results showed that preoperative serum totals and direct bilirubin (TBIL, DBIL) levels were inversely associated with progression of stages I-III NSCLC. Moreover, overall survival (OS) rates of NSCLC patients in the low-TBIL group and low-DBIL group were poor. Preoperative serum DBIL was identified as an independent prognostic factor for OS. Thus, preoperative serum TBIL and DBIL levels with NSCLC (I to III) were inversely associated with progression. Preoperative serum TBIL and DBIL levels may be independent prognostic factors for patients with NSCLC stages I-III in Jiangxi Province, China.

**Keywords:** Non-small cell lung cancer, bilirubin, stage, prognosis

## Introduction

Lung cancer is the most common malignant tumor and one of the leading causes of cancer-related deaths worldwide [1]. In the United States in 2017, there were approximately 222,500 new cases of lung cancer and 155,870 related deaths [2]. Non-small cell lung cancer (NSCLC) accounts for approximately 85% of lung cancer cases in the U.S. [3]. Although advancements in treatment have been achieved in recent years, 5-year survival rates of all stages of NSCLC remain less than 15% and <7% of patients survive 10 years [4, 5]. Thus, accurate prediction of prognosis in NSCLC patients is of great significance to guarantee more appropriate treatment strategies and enhance effective communication between doctors and patients.

The traditional tumor-node-metastasis (TNM) staging system, based on evaluation of pathologic samples of patients with existing cancer, has been identified as a useful prognostic fac-

tor. It has been used to guide decisions concerning systemic therapy for NSCLC [6]. However, the current TNM staging system cannot accurately predict the prognosis of patients. Due to different nutritional statuses and treatments, survival prediction of patients at the same stage of NSCLC may vary greatly [7, 8]. Furthermore, established markers used for postoperative evaluations are costly and time-consuming. Hence, it is necessary to find an accurate, effective, and economical pre-treatment biomarker for prognostic prediction of NSCLC.

Bilirubin is the major end product of heme metabolism, showing antioxidative properties [9]. There are 2 forms of bilirubin in the peripheral blood, conjugated and unconjugated. Both are measured by total bilirubin testing (TBIL). Conjugated bilirubin is measured separately as direct bilirubin (DBIL). Unconjugated bilirubin is referred to as indirect bilirubin (IBIL). Total bilirubin is the sum of DBIL and IBIL [10]. In recent years, experimental and clinical studies have

increasingly indicated that cancerogenesis may be related to oxidative stress [11, 12]. A potent antioxidant, it has been speculated that bilirubin may inhibit cancer progression [13, 14]. The research of Wei et al. [15] confirmed that pre-operative serum bilirubin, including TBIL, DBIL, and IBIL, is associated with stages in gastric cancer. Furthermore, Sun et al. [16] identified serum TBIL to be an independent predictor of prognosis in gastric cancer patients.

However, little is known about the association between serum bilirubin levels, cancer stage, and survival outcomes in NSCLC. Moreover, most studies have reported that serum bilirubin levels were positively correlated with survival in various cancers, including nasopharyngeal carcinoma [17], breast cancer [18], and gastric cancer [16]. However, some studies have concluded that high bilirubin levels led to poor prognosis in patients with stage IV colorectal cancer [19]. Therefore, the prognostic value of bilirubin in cancer remains controversial. The purpose of the current study was to investigate the relationship between preoperative serum bilirubin levels with cancer stage and prognosis of NSCLC stages I-III in Jiangxi province, China.

### Materials and methods

The Ethics Committee and Institutional Review Board of First Affiliated Hospital of Nanchang University approved the current retrospective study.

#### *Study population*

The current retrospective study included 472 patients diagnosed with NSCLC (stage I-III), between March 2013 and July 2018. They were treated in the Department of Respiratory Medicine, First Affiliated Hospital of Nanchang University. Inclusion criteria: Aged >18 years; Pathological diagnosis of NSCLC (I-III); Without any treatments prior to serum collection; Complete clinical data and pathological results available. Exclusion criteria: Hepatobiliary diseases and pancreatic diseases; Severe cardiovascular, kidney, blood, or autoimmune diseases; Elevated parameters in liver function tests (alanine aminotransferase >50 U/L; aspartate aminotransferase >40 U/L); TBIL <3  $\mu\text{mol/L}$  for either gender; TBIL >40  $\mu\text{mol/L}$  and >30  $\mu\text{mol/L}$  in men and women, respectively. Ultimately, 393 eligible patients were enrolled.

Histopathological diagnosis of NSCLC was determined in accordance with TNM criteria of the Eighth (2017) Edition of the Union for International Cancer Control (UICC)/American Joint Committee on Cancer (AJCC).

#### *Clinical parameters and laboratory results*

Clinical, pathological, and laboratory data of the patients were collected from electronic medical records, including age, gender, smoking history, stage, histological type, liver function tests, renal function tests, and tumor markers.

Liver function tests included a group of routine blood tests. Fasted blood sampling was required, aiming to reflect the basic condition of liver function. This assisted in the diagnosis of hepatobiliary diseases. Renal function tests are a good method of judging renal function. They may be used to determine whether examination indexes are normal or are directly related to the function of renal. Liver and renal function tests were analyzed with an automatic biochemical analyzer 7600 (Hitachi High-tech, Tokyo, Japan), including alanine aminotransferase (ALT), aspartate aminotransferase (AST), TBIL, DBIL, total protein (TP), albumin (ALB), gamma-glutamyl transpeptidase (GGT), alkaline phosphatase (ALP), creatinine (CRE), urea nitrogen (UN), and uric acid (UA). Normal levels of TBIL and DBIL are indicated by 3.42-20.5  $\mu\text{mol/L}$  and 0-6.48  $\mu\text{mol/L}$ , respectively.

Tumor markers were examined using a Roche E601 analyzer (Roche, Basel, Switzerland), including carcinoembryonic antigen (CEA), carbohydrate antigen 12-5 (CA12-5), carbohydrate antigen 15-3 (CA15-3), carbohydrate antigen 19-9 (CA19-9), neuro-specific enolase (NSE), and ferritin (FER).

For NSCLC patients whose data was obtained after diagnosis, blood samples were collected from 5-8 a.m. prior to initial treatment. If multiple values were obtained for the same parameter, only the first measured value was recorded.

#### *Follow-ups*

NSCLC patients were discharged after treatment with follow-ups every 3 to 6 months for the first 2 years. Follow-ups continued every 6 months for the next 3 to 5 years until death, up

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**Table 1.** Clinical characteristics of all patients

Characteristics	Patients	%
No.	393	
Age (y)		
≤60	150	38.2
>60	243	61.8
Gender		
Male	265	67.4
Female	128	32.6
Smoking history		
Y	255	64.9
N	138	35.1
Stage		
I	242	61.6
II	73	18.6
III	78	19.8
Tumor stage		
T1	278	70.7
T2	77	19.6
T3	25	6.4
T4	13	3.3
Node stage		
N0	274	69.7
N1	51	13.0
N2	58	14.8
N3	10	2.5
Lymph node metastases		
Negative	274	69.7
Positive	119	30.3
Histological type		
Squamous cell carcinoma	121	30.8
Adenocarcinoma	253	64.4
Large cell carcinoma	19	4.8

through December 31, 2018. Regular visits were requested in accordance with the 2017 Eighth UICC/AJCC Lung Cancer Standards. The median follow-up period was 27 months (range: 2-65 months). Overall survival (OS) was defined as the interval from the date of the operation to death or the last follow-up. Acquisition of OS rates was mainly through hospital records or phone interviews, determining current situations of the patients.

### Statistical analysis

IBM software SPSS version 23.0 (SPSS, Chicago, IL, USA) and GraphPad Prism version 7.00 (GraphPad Software, La Jolla, CA, USA) were used to perform statistical calculations.

Kolmogorov-Smirnov testing was applied, evaluating whether each continuous variable conformed to normal distribution. Continuous variables with normality are presented as mean  $\pm$  standard deviation and were estimated by one-way ANOVA. Non-normally distributed continuous variables are shown as medians (first-third interquartile range [IQR]) and were evaluated by Kruskal-Wallis *H* tests. Categorical variables were assessed by Chi-square tests and are presented as percentages. Association levels between continuous variables were evaluated by Spearman's correlation analysis. Receiver operative characteristic (ROC) curves were utilized to calculate optimal cut-off values and area under the ROC curve (AUC) for TBIL and DBIL. Survival analysis was performed using Kaplan-Meier curves and Cox's proportional hazards model, confirming independent prognostic factors for NSCLC. All *P*-values (2-sided) were  $<0.05$ , indicating statistical significance.

## Results

### Clinical characteristics of all patients

Clinical characteristics of all patients are summarized in **Table 1**. A total of 393 NSCLC patients were enrolled in this study, including 265 (67.4%) males and 128 (32.6%) females. According to the TNM criteria of the UICC/AJCC-8, 242 cases (61.6%), 73 cases (18.6%), and 78 cases (19.8%) of NSCLC patients were in stages I, II, and III, respectively.

### Association between preoperative serum bilirubin levels and NSCLC stage

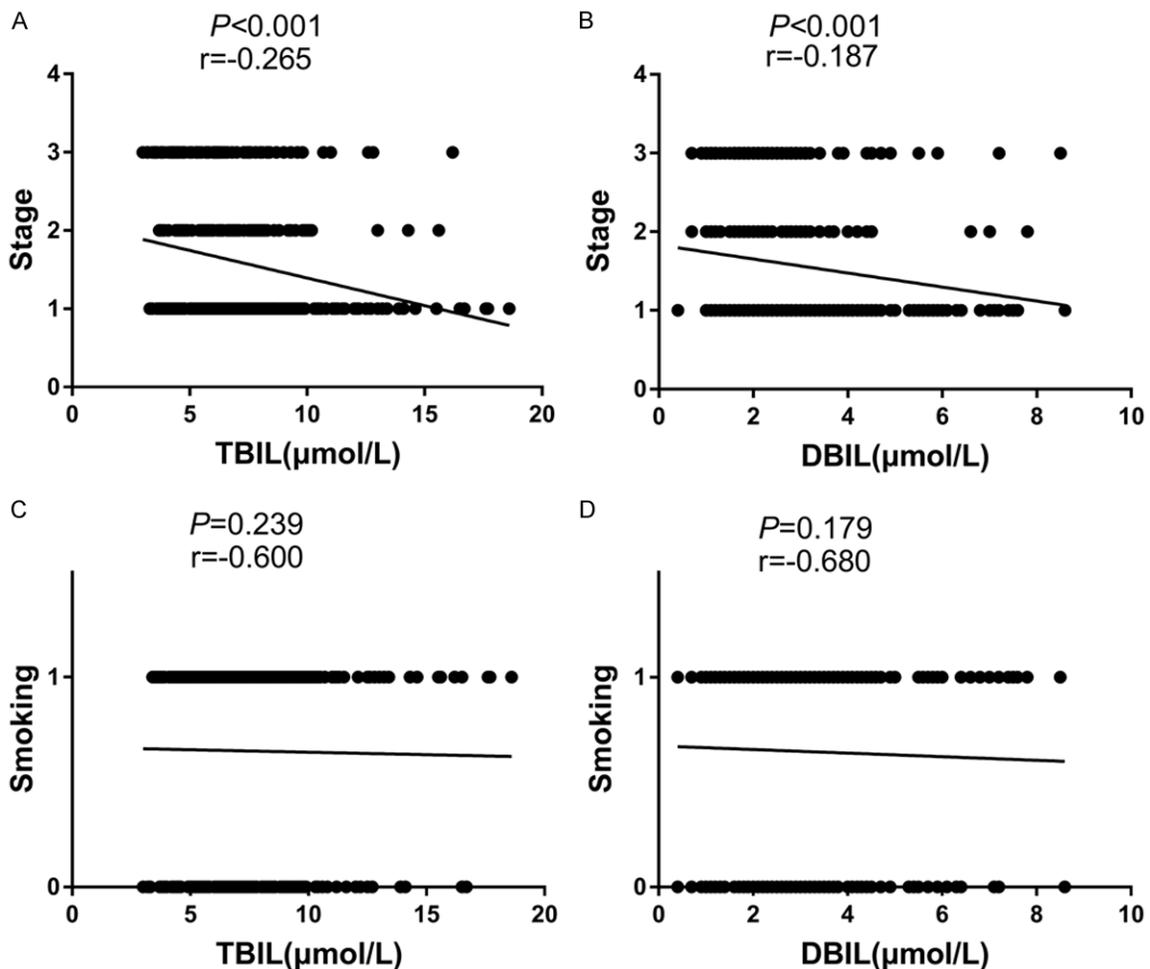
As shown in **Table 2**, a total of seventeen laboratory data items were investigated according to NSCLC stage. Significant association levels were observed between cancer stage and TBIL ( $P<0.001$ ), DBIL ( $P<0.001$ ), ALP ( $P=0.002$ ), CEA ( $P<0.001$ ), NSE ( $P<0.001$ ), and FER ( $P=0.015$ ). Moreover, Spearman's correlation analysis revealed that preoperative levels of serum bilirubin, both TBIL and DBIL, showed significant negative correlation ( $P<0.001$  for both) with progression stages NSCLC I~III (**Figure 1A, 1B**). Spearman's correlation analysis, however, showed that preoperative serum bilirubin levels, both TBIL and DBIL, were not correlated with smoking status ( $P>0.05$  for both) (**Figure 1C, 1D**).

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**Table 2.** Association between laboratory data and NSCLC stage

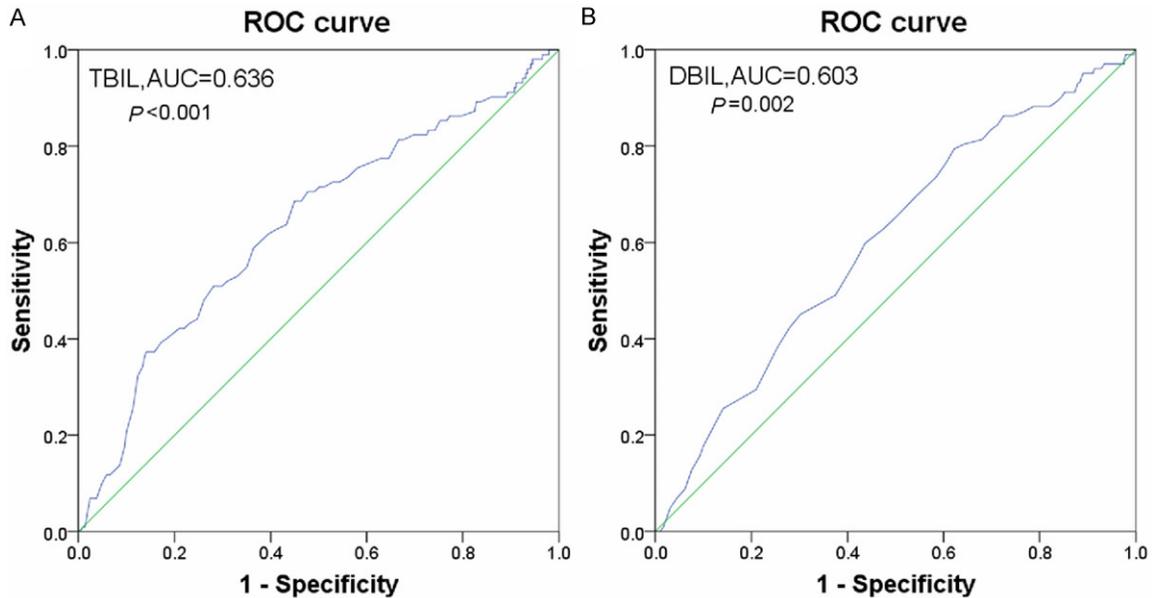
Characteristic	Total patients	Stage			P value
		I	II	III	
ALT (U/L)	16 (11-24)	15 (11-24)	16 (11-22)	18 (12-26)	0.492
AST (U/L)	22 (18-28)	22 (18-28)	22 (18-28)	23 (18-29)	0.796
TBIL ( $\mu\text{mol/L}$ )	6.8 (5.3-8.8)	7.6 (5.8-9.2)	6.6 (5.1-8.2)	5.8 (4.3-7.5)	<0.001
DBIL ( $\mu\text{mol/L}$ )	2.4 (1.8-3.4)	2.6 (1.9-3.7)	2.1 (1.8-2.9)	2.1 (1.6-2.9)	<0.001
TP (g/L)	68.0 (63.3-72.5)	67.6 (63.2-72.6)	68.7 (62.8-72.3)	68.7 (64.4-72.5)	0.648
ALB (g/L)	39.9 (35.8-43.4)	39.4 (35.3-43.1)	41.2 (36.6-44.0)	40.8 (36.5-43.8)	0.166
GGT (U/L)	22 (16-38)	23 (16-38)	19 (14-34)	23 (17-40)	0.086
ALP (U/L)	100 (81-126)	99 (80-121)	92 (77-121)	109 (92-145)	0.002
CRE ( $\mu\text{mol/L}$ )	69.1 (57.7-80.2)	69.6 (57.9-81.2)	66.7 (55.0-78.1)	69.0 (57.9-78.3)	0.581
UN (mmol/L)	5.1 (4.2-6.3)	5.2 (4.2-6.4)	5.4 (4.0-6.3)	4.8 (4.0-6.1)	0.315
UA ( $\mu\text{mol/L}$ )	295 $\pm$ 88	293 $\pm$ 88	299 $\pm$ 86	296 $\pm$ 88	0.864
CEA (ng/mL)	6.33 (3.09-19.27)	5.18 (2.87-10.93)	10.30 (4.11-33.20)	8.43 (3.44-32.76)	<0.001
CA12-5 (U/mL)	29.46 (17.44-79.99)	29.83 (17.75-79.49)	26.51 (14.80-70.76)	30.57 (16.95-105.35)	0.490
CA15-3 (U/mL)	14.20 (8.42-23.74)	13.53 (8.18-23.66)	14.32 (8.36-24.03)	16.45 (8.90-23.64)	0.402
CA19-9 (U/mL)	14.73 (9.35-28.45)	13.96 (7.82-26.29)	16.54 (9.66-31.67)	15.78 (10.45-32.09)	0.055
NSE (ng/mL)	20.76 (14.98-28.16)	18.89 (13.81-24.93)	23.94 (17.02-31.32)	24.03 (18.65-35.40)	<0.001
FER ( $\mu\text{g/L}$ )	276.50 (170.90-388.95)	295.30 (182.55-424.33)	261.70 (170.90-349.50)	219.25 (148.30-337.10)	0.015

ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin; DBIL, direct bilirubin; TP, total protein; ALB, albumin; GGT, gamma-glutamyl transpeptidase; ALP, alkalinephosphatase; CRE, creatinine; UN, urea nitrogen; UA, uric acid; CEA, carcinoembryonic antigen; CA12-5, carbohydrate antigen 12-5; CA15-3, carbohydrate antigen 15-3; CA19-9, carbohydrate antigen 19-9; NSE, neuro-specific enolase; FER, ferritin. Data were analyzed with Kruskal-Wallis *H* test and one-way analysis of variance. *P*<0.05 indicates significance.



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**Figure 1.** Correlation analysis between preoperative serum bilirubin levels clinical parameters. (A) TBIL and NSCLC stage; (B) DBIL and NSCLC stage; (C) TBIL and smoking status; (D) DBIL and smoking status.



**Figure 2.** Receiver operating characteristic (ROC) curves analysis of preoperative (A) TBIL; and (B) DBIL for predicting overall survival in patients with NSCLC.

### *Optimal cut-off values for preoperative serum TBIL and DBIL levels*

ROC curve analysis was used to determine optimal cut-off values of laboratory indicators associated with NSCLC stage, including TBIL, DBIL, ALP, CEA, NSE, and FER. For OS, the optimal cut-off value of TBIL was 7.0  $\mu\text{mol/L}$  (AUC: 0.636, 95% CI: 0.572-0.701,  $P<0.001$ ; **Figure 2A**). The optimal cut-off value of DBIL was 3.0  $\mu\text{mol/L}$  (AUC: 0.603, 95% CI: 0.540-0.666,  $P=0.002$ ; **Figure 2B**). Furthermore, the patients were apportioned to groups with high or low TBIL ( $>7.0 \mu\text{mol/L}$  or  $\leq 7.0 \mu\text{mol/L}$ , respectively) and high or low DBIL ( $>3.0 \mu\text{mol/L}$  or  $\leq 3.0 \mu\text{mol/L}$ , respectively).

### *Association between different levels of TBIL, DBIL, and clinical characteristics*

**Table 3** shows the correlation between different levels of TBIL, DBIL, and clinical characteristics. There were significant between-group differences between high-TBIL and low-TBIL groups with respect to stage ( $P<0.001$ ) and node stage ( $P<0.001$ ). Moreover, there were statistically differences in age ( $P=0.008$ ), stage ( $P=0.001$ ), and node stage ( $P<0.001$ ) between high-DBIL and low-DBIL groups.

### *Association between preoperative serum TBIL and DBIL levels and prognosis*

Survival analysis using Kaplan-Meier curves showed that OS in the low TBIL group was lower than that in the high TBIL group ( $P<0.001$ , log-rank test; **Figure 3A**). OS rates of the low DBIL group were worse than those of the high DBIL group ( $P<0.001$ , log-rank test; **Figure 3B**).

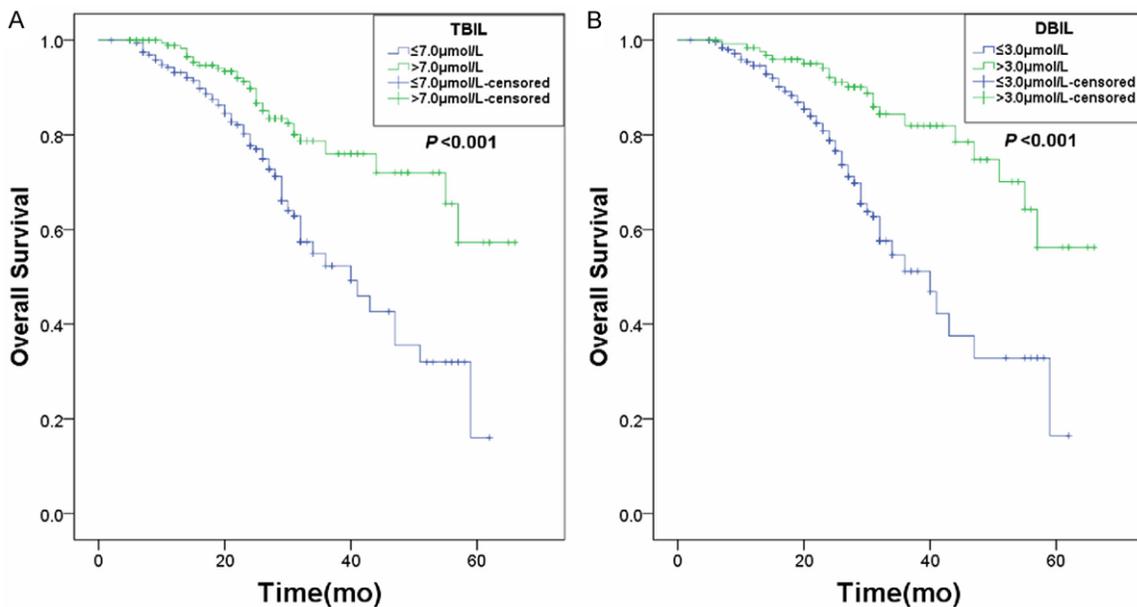
Aiming to authenticate independent prognostic factors, laboratory indicators related to NSCLC stage, including TBIL, DBIL, ALP, CEA, NSE, and FER, along with various clinicopathological variables, were incorporated to calculate OS using Cox's proportional hazards model (**Table 4**). According to univariate analysis, smoking history ( $P=0.019$ ), stage ( $P<0.001$ ), tumor stage ( $P=0.010$ ), node stage ( $P<0.001$ ), TBIL ( $P<0.001$ ), DBIL ( $P<0.001$ ), and NSE ( $P<0.001$ ) showed significant association with OS. Multivariate analysis showed the nodular period (HR: 3.275, 95% CI: 2.142-5.007,  $P<0.001$ ), TBIL (HR: 0.720, 95% CI: 0.450-1.150,  $P=0.015$ ), and DBIL (HR: 0.456, 95% CI: 0.274-0.756,  $P=0.002$ ) to be independent prognostic factors for OS.

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**Table 3.** Association between different levels of TBIL, DBIL, and clinical characteristics

Characteristics	TBIL≤7.0	TBIL>7.0	P value	DBIL≤3.0	DBIL>3.0	P value
	(μmol/L)	(μmol/L)		(μmol/L)	(μmol/L)	
	n=201	n=192		n=262	n=131	
Age			0.130			0.008
≤60	84	66		112	38	
>60	117	126		150	93	
Gender			0.908			0.879
Male	135	130		176	89	
Female	66	62		86	42	
Smoking history			0.238			0.179
Y	136	119		176	79	
N	65	73		86	52	
Stage			<0.001			0.001
I	104	138		144	98	
II	43	30		57	16	
III	54	24		61	17	
Tumor stage			0.224			0.091
T1-2	178	177		232	123	
T3-4	23	15		30	8	
Node stage			<0.001			<0.001
N0	122	152		166	108	
N1-3	79	40		96	23	
Histological type			0.624			0.422
Squamous cell carcinoma	58	63		75	46	
Adenocarcinoma	134	119		174	79	
Large cell carcinoma	9	10		13	6	

TBIL, total bilirubin; DBIL, direct bilirubin. Data are presented with Chi-square tests.  $P < 0.05$  indicates significance.



**Figure 3.** Kaplan-Meier curves for overall survival according to (A) Different preoperative serum TBIL levels; and (B) Different preoperative serum DBIL levels.

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**Table 4.** Univariate and multivariate Cox's proportional hazards model analysis for overall survival

Characteristics	Univariate analysis			Multivariate analysis		
	HR	95% CI	P value	HR	95% CI	P value
Age			0.689			
≤60	1.000	Reference				
>60	1.083	0.731-1.606				
Gender			0.740			
Male	1.000	Reference				
Female	0.933	0.621-1.403				
Smoking history			0.019			0.095
Y	1.000	Reference		1.000	Reference	
N	0.592	0.381-0.919		0.683	0.437-1.069	
Stage			<0.001			0.401
I	1.000	Reference		1.000	Reference	
II	3.433	2.039-5.781		1.601	0.612-4.188	
III	5.528	3.452-8.852		2.147	0.679-6.793	
Tumor stage			0.010			0.884
T1-2	1.000	Reference		1.000	Reference	
T3-4	2.072	1.187-3.616		1.049	0.549-2.004	
Node stage			<0.001			<0.001
N0	1.000	Reference		1.000	Reference	
N1-3	4.471	2.976-6.717		3.275	2.142-5.007	
Histological type			0.736			
Squamous cell carcinoma	1.000	Reference				
Adenocarcinoma	0.998	0.639-1.558				
Large cell carcinoma	1.491	0.520-4.278				
TBIL (μmol/L)			<0.001			0.015
≤7.0	1.000	Reference		1.000	Reference	
>7.0	0.427	0.281-0.649		0.720	0.450-1.150	
DBIL (μmol/L)			<0.001			0.002
≤3.0	1.000	Reference		1.000	Reference	
>3.0	0.318	0.194-0.521		0.456	0.274-0.756	
ALP (U/L)			0.059			
≤114	1.000	Reference				
>114	1.464	0.986-2.174				
CEA (ng/mL)			0.236			
≤7.45	1.000	Reference				
>7.45	1.265	0.858-1.866				
NSE (ng/mL)			<0.001			0.169
≤21.97	1.000	Reference		1.000	Reference	
>21.97	2.169	1.457-3.228		1.663	1.106-2.501	
FER (μg/L)			0.051			
≤382.65	1.000	Reference				
>382.65	0.602	0.362-1.003				

TBIL, total bilirubin; DBIL, direct bilirubin; ALP, alkalinephosphatase; CEA, carcinoembryonic antigen; NSE, neuro-specific eno-  
lase; FER, ferritin; HR, hazard ratio; CI, confidence interval. Data were analyzed by Cox's proportional hazards model. *P*<0.05  
indicates significance.

### Discussion

The present retrospective study investigated association levels between preoperative serum

bilirubin levels, stage, and prognosis in patients with NSCLC. There were 3 main findings: 1) Preoperative serum levels of TBIL and DBIL were inversely correlated with NSCLC stage

(I-III); 2) Patients with low preoperative TBIL levels ( $\leq 7.0 \mu\text{mol/L}$ ) and low preoperative DBIL levels ( $\leq 3.0 \mu\text{mol/L}$ ) had poorer OS; and 3) Preoperative serum TBIL and DBIL levels can be used as potential independent prognostic factors for NSCLC patients.

The purpose of this study was to evaluate the significance of serum bilirubin levels (TBIL and DBIL) in NSCLC stage. Association levels between 17 clinical indices and NSCLC stage were examined. However, only 6 indicators, including TBIL and DBIL, were statistically significant. Results suggest that higher stages of NSCLC indicate lower levels of bilirubin. Present results are consistent with the research of Wei et al. [15] in gastric cancer. The etiopathogenesis of NSCLC is multifactorial. Disturbed redox status may be crucial to cancer progression [20]. Oxidative stress contributes to carcinogenesis. Thus, an imbalance in pro/antioxidant status may be important to proliferation of tumor cells [12, 21-23]. Bilirubin is protective against carcinogenesis, due to its anti-oxidation activity [9, 14]. It has been reported that, with the progression of NSCLC, a reduction in total antioxidant status leads to bilirubin levels that lower increasingly through stages I-III [20, 23-25]. Of importance in previous studies, inverse association levels between smoking and serum bilirubin levels have been suggested [26, 27]. Consequently, the smoking status of NSCLC patients may confuse these results. The current study showed no correlation between TBIL and DBIL levels and smoking status. Further research is necessary, however, to explore the relationship between serum bilirubin levels, smoking status, and cancer stage in NSCLC patients.

Moreover, the present study addressed the effects of preoperative serum bilirubin levels on prognosis in NSCLC. Results indicated that moderately elevated levels of preoperative serum TBIL and DBIL in NSCLC patients were related to favorable prognosis. Furthermore, preoperative serum TBIL and DBIL were shown to be independent prognostic biomarkers of NSCLC. These results are consistent with previous studies of Song et al. [28] and Li et al. [29] in NSCLC patients. Mechanisms underlying the correlation between preoperative serum bilirubin levels and survival outcomes of NSCLC remain unclear. In addition to being associated with cancer progression, possible mechanisms

linking serum bilirubin with lymph node metastasis have been elucidated by Deng et al. [30] in nasopharyngeal carcinoma. They suggested that oxidative stress can activate many molecules, such as Ras, PI3K/Akt, ERK1/2, p38 MAPK, and JNK1/2 [31], resulting in the up-regulation of activity and expression of matrix metalloproteinase (MMP) proteins related to cancer metastasis [32-34]. An antioxidant, serum bilirubin may inhibit ERK1/2 activation and MMP-2 expression, inhibiting metastasis of nasopharyngeal carcinoma cells [30]. However, whether the link between TBIL, DBIL, and prognosis in NSCLC patients is related to the above mechanisms requires further study. Some studies have also suggested that impaired antioxidant mechanisms of serum bilirubin in NSCLC may induce cisplatin resistance via redox disorder, resulting in poor prognosis [35, 36]. Further studies are necessary to determine the prognostic significance of preoperative serum TBIL and DBIL for NSCLC.

The current study had some limitations. First, as with most retrospective studies, data collection could not completely rule out the possibility of selection bias and inaccuracies. Second, the sample sizes of histological subtypes of NSCLC patients stages II and III or large-cell lung cancer were relatively small. It is necessary to collect more data of patients from other hospitals and conduct further investigations. Third, the current research failed to include data concerning indirect bilirubin. Therefore, present results require validation from future large-scale prospective studies and clinical trials.

In conclusion, serum bilirubin can be obtained conveniently via liver function examinations, employing rapid, economical, routine, and non-invasive methods. The current study demonstrated that preoperative serum TBIL and DBIL levels are inversely correlated with progression of NSCLC from stage I to III. Moreover, preoperative serum TBIL and DBIL were identified as independent prognostic factors for patients with stages I-III NSCLC in Jiangxi Province, China.

### Disclosure of conflict of interest

None.

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