# Predicting the risk of non-specific low back pain in the young population: development and assessment of a new predictive nomogram

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**Abstract.** – **OBJECTIVE:** Non-specific low back pain is a common disorder that affects more than 80% of the world's population. But the potential risk factors remain unclear. The aim of this study is to develop a nomogram for the risk prediction of low back pain in young population.

PATIENTS AND METHODS: A total of 264 young participants (18-45 years old) were recruited and randomly divided into a training set (n=188) and a validation set (n=76) by a ratio of 7:3. The nomogram was developed based on the training set. The independent predictors of low back pain were identified by LASSO and logistic regression analysis. A nomogram was developed according to the predictors. To assess the reliability of the nomogram, the area under the curve (AUC), calibration curve, and decision curve analysis (DCA) were applied. The validation set was used to validate the results.

**RESULTS:** Sixteen factors were included in the characteristics of the eligible subjects. LAS-SO showed that five independent predictors including working posture, exercising hours per week, Tuffier's line, six lumbar vertebrae anomaly, and lumbar lordosis angle were the independent risk factors of low back pain in young population, which were identified by multivariate logistic regression analysis and were used to establish the nomogram. The AUC values of the nomogram were 0.867 (95% CI: 0.809-0.924) and 0.868 (95% CI: 0.775-0.961) in the training and validation set, respectively. The calibration curve revealed that the prediction model of the nomogram was greatly consistent with the actual observation. In addition, the DCA indicated that the nomogram was clinically useful.

CONCLUSIONS: Working posture, exercising hours per week, Tuffier's line, six lumbar verte-

brae anomaly, and lumbar lordosis angle are identified as independent predictors of non-specific low back pain in young population. And the nomogram based on the above five predictors can accurately predict the risk of low back pain in young people.

Key Words:

Non-specific low back pain, Tuffier's line, Nomogram, Risk factors, young population.

#### **Abbreviations**

LBP, low back pain; DCA, decision curve analysis; AUC, area under the curve; ROC, receiver operating characteristic curve; LSTV, lumbosacral transitional vertebra; BMI, body mass index; VAS, visual analogue scale; FLVA, four-lumbar-vertebra-anomaly; SLVA, six-lumbar- vertebra-anomaly; SS, sacral slope; LLA, lumbar lordosis angle; LASSO, least absolute shrinkage and selection operator; CI, confidence interval; OR, Odds ratio.

# Introduction

Low back pain (LBP) is a common medical problem, which affects more than 80% of the world's population<sup>1,2</sup>. It was reported that LBP is one of the most common causes of disability in people younger than 45 years old<sup>3</sup>. A cross-sectional survey<sup>2</sup> indicated that 33% of adolescents between 10 and 18 years old suffered from LBP. Of these, 26.3% had severe pain that is defined as pain intensity ≥7 in a 10-point scale (0, no pain;10, unbearable continuous pain). Researchers have found that chronic LBP is becoming more prevalent among younger individuals than

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before. Most people with chronic LBP have low back, lumbosacral and sacroiliac pain over 3 months, which usually requires long-term and costly treatment. The treatments of LBP should be adjusted according to specific pathogenesis of the disease. However, the specific pathogenesis and mechanism of LBP remains unclear. Generally, LBP can be resulted from a variety of factors including degenerative changes, spinal stenosis, neoplasm, infection, trauma, inflammation, abnormal development, and muscular strain<sup>4</sup>. But some people with LBP cannot be attributed to a currently recognizable pathology, which are described as non-specific LBP.

Abnormal anatomical structures of lumbosacral spine are usually observed in non-specific LBP populations. Tuffier's line refers to the horizontal line connecting the highest points of the iliac crests, which is considered to intersect the L4-L5 intervertebral space<sup>5,6</sup>. Lin et al<sup>5</sup> reported that the overall accuracy of determining the actual intervertebral level by using Tuffier's line was only 55.8%. Kim et al<sup>6</sup> reported that about 59% of the L4-L5 intervertebral space of the patients were correctly estimated by Tuffier's line, which indicated that a great number of people's Tuffier's lines were higher or lower than the L4-L5 intervertebral space. Therefore, abnormal Tuffier's line can be observed in some patients with LBP.

In addition to the abnormality of Tuffier's line, lumbosacral transitional vertebra (LSTV), a congenital vertebral anomaly including sacralization of the fifth lumbar vertebrae [four-lumbar-vertebra-anomaly, (FLVA)] or lumbarization of the first sacral vertebra [six-lumbar-vertebra-anomaly, (SLVA)], is responsible for disabling LBP<sup>7</sup>.

In the human body, the vertebral column plays a pivotal role in maintaining an upright posture. Biologically, bipedal hominids have five lumbar vertebrae, and this is associated with upright walking and makes it possible for people to perform daily activities. However, the increase or decrease of lumbar vertebrae can cause biomechanical changes and destroy the mechanical environment, thus leading to LBP or even a series of degenerative diseases ranging from intervertebral disc degeneration to spondylolisthesis. It was reported that L4-L5 spondylolisthesis may be associated with LSTV8. According to a recent research, increased stability between a sacralized L5 and the sacrum, which could be caused by LSTV, might lead to greater instability and disc degeneration of the L4-5 segment9. Thus, it is suggested that abnormal anatomical structures of lumbosacral spine may result in the so-called non-specific LBP. Predicting the risk factors of non-specific LBP in young patients under 45 years old would be helpful to prevent and reduce the occurrence of this disorder.

Notably, risk factors associated with LBP could be used for the accurate prediction. Besides Tuffier's line and LSTV, some other risk variables including body mass index (BMI), working posture, exercising hours, sacral slope (SS) and lumbar lordosis angle (LLA) were proved to be significantly associated with LBP<sup>10,16</sup>. However, researches about risk variables that can be used to predict non-specific LBP in young people are limited. And the analysis of risk variables of LBP in young population is still inadequate since a majority of research for risk variables of LBP were not specially designed for young people.

Therefore, we conducted this present study to develop a valid and simple prediction tool in order to predict LBP in young people. The results of this study indicated that working posture, exercising hours per week, Tuffier's line, six lumbar vertebrae anomaly, and LLA are independent risk factors of non-specific LBP in young population. The above risk factors are closely associated with LBP in young population and the nomogram based on the above five predictors can be used to predict the risk of LBP of young people. This study can provide useful reference for clinical practice, which also has implications for future research.

#### **Patients and Methods**

#### **Patients**

A total of 264 participants were recruited from five communities (126 citizens, in Shanghai) and one university (138 participants, came from all over China), from June 2021 to November 2021. Inclusion criteria: (1) non-specific LBP, which meant that despite a comprehensive diagnostic evaluation including a detailed medical history. physical examination, biochemical, and radiologic screening, no definite pathological cause could be found; (2) imaging including anteroposterior and lateral X-ray films and MRI of the lumbar spine was available; (3) the baseline data including age, sex, BMI, smoking, drinking, marital status, education level, working posture, working hours per day, and exercising hours per week were well documented; (4) people from 18 years old to 45 years old. Exclusion criteria: (1) patients with previous history of lumbar spine surgery; (2) patients with space-occupying lesions in vertebral body or pedicle; (3) patients with spinal trauma or low back injuries; (4) patients with degenerative condition in lumbar vertebra, such as lumbar spinal stenosis and lumbar intervertebral disc herniation; (5) spondylolisthesis; (6) inflammatory or infectious diseases related to LBP; (7) osteoporosis; (8) patients who were illiterate or had severe cognitive disorders. Informed consent from all participants were obtained. All participants completed questionnaires and had interviews with the researchers. Written informed consent was obtained from patients. This study was approved by the Institutional Review Board of Shanghai Changzheng Hospital. Written informed consent was obtained from all participants.

#### Data Collection and LBP Assessment

In the present study, 16 variables were initially included to estimate the risk of LBP, which included age, sex, BMI, smoking, drinking, marital status, education level, working posture, working hours per day, exercising hours per week, Tuffier's line, lumbosacral transitional vertebra that includes FLVA and SLVA, SS and LLA. The visual analogue scale (VAS) was used for the assessment of pain intensity of low back within the last 12 months. This numerical pain scale was divided into four categories: no pain (0), mild pain (1-3), moderate pain (4-6), and intense pain (7-10). To minimize the effect of subjectivity of participants, we required the participants whose VAS scores were 1-3 to estimate the reliability of their VAS scores: being reasonably reliable (Coefficient=1), being mildly reliable (Coefficient=1/2) or being not reliable (Coefficient=1/3). VAS-score' (real VAS-score  $\times$  Coefficient. Ultimately, participants whose real VAS-scores  $\geq 1$ were considered to have LBP.

# **Imaging Assessment**

The radiographic data were evaluated and analyzed in a blinded manner by three spine surgeons independently, and for further processing, the results were averaged. The Tuffier's line was defined as the line drawn between the tops of both iliac crests and it was measured on the anteroposterior X-ray film of the lumbar vertebrae. The L4-L5 intervertebral space was divided into three equal parts, and the L4 and the L5 vertebral bodies were both divided into four equal parts. The middle 1/3 part of the L4-L5 intervertebral space was named as "0" and it was regarded as the reference line. If the iliac crests line was located above

the reference line, it was orderly named as "1", "2", "3", "4", and "5"; similarly, if the iliac crests line was located below the reference line, it was orderly named as "-1", "-2", "-3", "-4", and "-5".

What's more, standing lumbar radiographs that included the lower thoracic vertebrae, lumbar vertebrae, and sacral vertebrae were graded according to Castellvi classification of LSTV. There exist many ways to categorize LSTV. The most common method is Castellvi classification of LSTV<sup>17,18</sup> which includes type I: dysplastic enlarged transverse process, type II: pseudoarticulation of the transverse process with the sacrum with increased sclerosis, type III: fusion with the sacrum, and type IV: unilateral LSTV type II with type III on the contralateral side. However, this method cannot differentiate the sacralization of the fifth lumbar vertebra and the lumbarization of the first sacral vertebra. To avoid obscuring the main concepts, the sacralization of the fifth lumbar vertebra and the lumbarization of the first sacral vertebra were named as FLVA and SLVA, respectively. What's more, to build a relatively reliable and practical model, type II, type III, and type IV were assigned into the same group and type I was set as a separate group, because it was reported that there was no fusion or pseudoarticulation in type I which might lead to significantly abnormal biomechanical forces<sup>19,20</sup>. The angle between the upper sacral endplate and the horizontal plane was known as the SS<sup>21</sup>. LLA, the angle between tangent lines to the superior endplate of L1 and superior endplate of S1, was assessed using the Cobbs method<sup>21,22</sup>.

# Statistical Analysis

Statistical analysis was performed using the R software (version 3.6.3, The R Foundation for Statistical Computing, Vienna, Austria). LASSO method was used to select the optimum predictive features of LBP in young people. Predictors with a p-value < 0.05 in the LASSO regression were included. Then, multivariable logistic regression analysis was applied to establish a predicting model. Variables with a p-value < 0.05 were included in the model. These potential predictors were used to establish a risk predicting nomogram for LBP in young people. Harrell's C-index was applied to quantify the performance of the nomogram. Then the nomogram was assessed by drawing the receiver operating characteristic curve (ROC) and calibration curve. Decision curve analysis (DCA) was conducted to determine the clinical usefulness of the predicting nomogram by quantifying the net benefits at different threshold probabilities. The net benefit was defined as benefit minus harm of the preventive model. Using bootstrapping validation, the corrected C-index, calibration curve, ROC curve, and DCA curve of the validation set were calculated.

#### Results

#### **Baseline Characteristics of Subjects**

A total of 264 eligible subjects were enrolled and randomly divided into a training set (n= 188) and a validation set (n= 76) by a ratio of 7:3. The characteristics of the participants were summarized (Table I). The baseline data were similar between the training set and the validation set. According to the results, 37.77% of the participants in the training set and 38.16% of the participants in the validation set had LBP. As shown in Table I, there were no statistical differences between the training set and the validation set (p > 0.05).

#### Feature Selection

Among the 16 characteristics, five potential predictors (working posture, exercising hours per week, Tuffier's line, SLVA, and LLA) were screened out through the LASSO regression model (Figure 1A, B). Multivariable logistic regression analysis based on the predictors was carried out in order to create the predicting model (Table II). In the results of the multivariable logistic regression analysis, the mobilized working posture (p < 0.05), 1.5-3 hours or >3 hours exercising per week (p <0.05), Tuffier's line at the level of 4, -4, 5, -5 (p <0.001), and LLA that was larger than  $50^{\circ}$  (p < 0.05) were independently associated with LBP in young people. Particularly, the risk of LBP in subjects with Tuffier's line at the level of 4 or -4 was 12.973-fold (95% CI: 3.404-57.034) higher and the risk of LBP in subjects with Tuffier's line at the level of 5 or -5 was 20.874-fold (95% CI: 5.082-102.403) higher when compared with that in subjects with Tuffier's line at the level of -1, 0, or 1.

# Construction and Assessment of the Nomogram

To predict the risk of LBP in young population, the nomogram was developed based on the results of the multiple logistic regression (Figure 2). The total score was obtained by adding the scores of each factor, and the predicted risk corresponding to the total score was the probability of LBP. Then the ROC analysis was performed. According to

the results of ROC analysis, the AUC value of the nomogram was 0.867 (95% CI: 0.809-0.924) in the training set (Figure 3A), indicating the good performance of the predicting nomogram. The calibration curve of the LBP risk nomogram showed good agreement between the prediction of the nomogram and the actual observation (Figur e 3B). In the training set, the C-index of the nomogram was 0.880 (95% CI: 0.827-0.933), showing good discrimination of the model. To evaluate the clinical usefulness of the nomogram, the DCA was performed in the training set by quantifying the net benefits at different threshold probabilities. The DCA curve of the training set indicated that the nomogram revealed clinical net benefit when the threshold probability was in the range of 2%-94% (Figure 3C).

To confirm the stability of the model, the nomogram was validated through the validation set and the C-index was 0.925 (95% CI: 0.852-0.998), suggesting that the model was well discriminated. In the validation set, the AUC of the nomogram was 0.868 (95% CI: 0.775-0.961) (Figure 3D), and the calibration curve for probability of LBP revealed good agreement between the nomogram prediction and the actual observation (Figure 3E). Furthermore, the DCA curve showed that net benefit could be achieved when the threshold probability was in the range of 1%-95% (Figure 3F). Therefore, the LBP risk nomogram represented a good prediction capability.

#### Discussion

LBP is a common symptom, which is the major cause of disability in both developed and developing countries. Many factors including degenerative changes, spinal stenosis, neoplasm, infection, trauma, inflammation, abnormal development, and muscular strain can result in LBP. Non-specific LBP is the most common form of LBP, which is defined if the pathoanatomical cause cannot be determined<sup>23</sup>. The diagnosis of non-specific LBP requires the exclusion of specific disorders affecting the lumbar spine<sup>24</sup>. In the past decade, there has been increasing awareness of LBP in childhood. A study<sup>25</sup> showed that about 37% of adolescents from 28 countries suffered from LBP monthly or more frequently, and the prevalence ranged from 28% (Poland, Lithuania, and Russia) to 51% (Czech Republic). A study<sup>26</sup> reported that those children who had LBP were more likely to have LBP as adults. LBP in young

**Table I.** Participants' characteristics in the training set and the validation set.

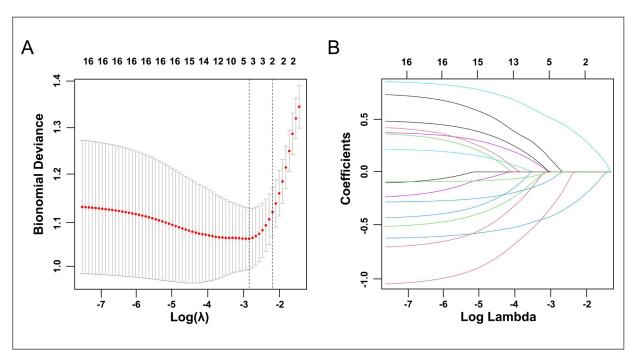
.,	No. (%)			
Variables	Training set (n=188)	Validation set (n=76)	C <sup>2</sup>	<i>p</i> -value
LBP				
No	117 (62.23)	47 (61.84)	0.004	0.953
Yes	71 (37.77)	29 (38.16)		
Age, year				
18-25	77 (40.96)	37 (48.68)	3.056	0.217
26-35	76 (40.43)	22 (28.95)		
36-45	35 (18.62)	17 (22.37)		
Sex				1
Male	93 (49.47)	42 (55.26)	0.727	0.394
Female	95 (50.53)	34 (44.74)		
Smoking				
No	92 (48.94)	39 (51.32)	0.123	0.726
Yes	96 (51.06)	37 (48.68)		,
Drinking	( )			,
No	95 (50.53)	37 (48.68)	0.074	0.786
Yes	93 (49.47)	39 (51.32)	/.	3.700
BMI	75 (.7)	55 (61.52)		
<18.5	28 (14.89)	13 (17.11)	2.317	0.509
≥18.5 and <24	65 (34.57)	19 (25.00)	2.317	0.507
≥24 and <28	64 (34.04)	29 (38.16)		
224 and <28 228	31 (16.49)	15 (19.74)		
Marital status	31 (10.47)	13 (17.74)		
Married	70 (37.23)	27 (35.53)	0.068	0.794
Other marital status	118 (62.77)	49 (64.47)	0.000	0.774
Education level, years	110 (02.77)	47 (04.47)		
<9	23 (12.23)	9 (11.84)	0.020	0.990
10-16	117 (62.23)	48 (63.16)	0.020	0.990
		·		
≥17	48 (25.53)	19 (25.00)		
Working posture	04 (44 (0)	29 (50 00)	0.616	0.422
Immobilized	84 (44.68)	38 (50.00)	0.616	0.433
Mobilized	104 (55.32)	38 (50.00)		
Working hours/day (h)	22 (12 22)	11 (14 47)	1 252	0.500
<5	23 (12.23)	11 (14.47)	1.353	0.508
5-8	116 (61.70)	41 (53.95)		
>8	49 (26.06)	24 (31.58)		
Exercising hours/week (h)	10 (0 ( 0 ( )			
≤0.5	49 (26.06)	23 (30.26)	3.673	0.299
>0.5 and ≤1.5	46 (24.47)	25 (32.89)		
>1.5 and ≤3	52 (27.66)	16 (21.05)		
>3	41 (21.81)	12 (15.79)		
Tuffier's line				
-1, 0, 1	53 (28.19)	16 (21.05)	2.662	0.616
-2, 2	41 (21.81)	21 (27.63)		
-3, 3	32 (17.02)	11 (14.47)		
-4, 4	29 (15.43)	15 (19.74)		
-5, 5	33 (17.55)	13 (17.11)		

Continued

**Table I.** Participants' characteristics in the training set and the validation set.

Variables	No. (%)		2	
	Training set (n=188)	Validation set (n=76)	C <sup>2</sup>	<i>p</i> -value
LSTV				
No	93 (49.47)	38 (50.00)	1.344	0.511
I	60 (31.91)	28 (36.84)		
II/III/IV	35 (18.62)	10 (13.16)		
SLVA				
No	145 (77.13)	61 (80.26)	0.310	0.577
Yes	43 (22.87)	15 (19.74)		
FLVA				
No	150 (79.79)	60 (78.95)	0.023	0.878
Yes	38 (20.21)	16 (21.05)		'
SS (°)				
<35	47 (25.00)	18 (23.68)	1.476	0.688
≥35 and <40	44 (23.40)	20 (26.32)		
≥40 and <45	51 (27.13)	24 (31.58)		
<u>≥</u> 45	46 (24.47)	14 (18.42)		
LLA (°)				
<40	39 (20.74)	18 (23.68)	3.667	0.453
≥40 and <45	38 (20.21)	16 (21.05)		
≥45 and <50	32 (17.02)	17 (22.37)		
≥50 and <55	40 (21.28)	9 (11.84)		
≥55	39 (20.74)	16 (21.05)		

LBP, low back pain; BMI, body mass index; LSTV, lumbosacral transitional vertebra; FLVA, four-lumbar-vertebra-anomaly; SLVA, six-lumbar-vertebra-anomaly; SS, sacral slope; LLA, lumbar lordosis angle.



**Figure 1.** Screening the potential predictors through LASSO regression model. **A**, Optimal lambda selection in the LASSO model. Dotted vertical lines were drawn at the optimal values. **B**, LASSO coefficient profiles of the 16 features.

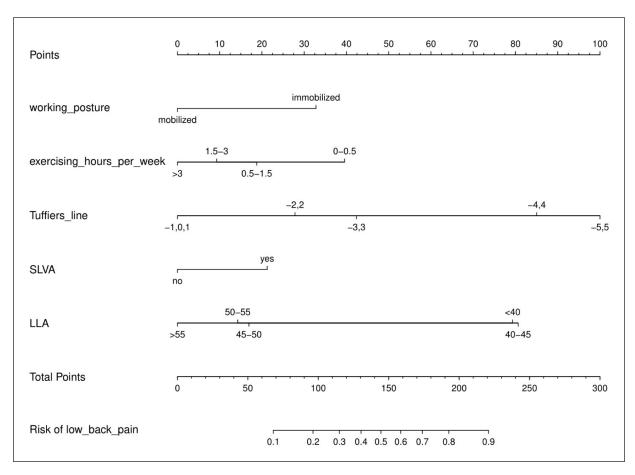
 Table II. Multivariable logistic regression analysis of the training set.

	Prediction model				
Intercept and variable	β	β OR (95% CI)			
Intercept	0.197	1.218 (0.208-7.167)	0.826		
Working posture					
Immobilized					
Mobilized	-1.116	0.328 (0.137-0.749)	0.010		
Exercising hours per week (h)					
≤0.5					
>0.5 and ≤1.5	-0.878	0.416 (0.128-1.289)	0.134		
>1.5 and ≤3	-1.282	0.278 (0.080-0.888)	0.036		
>31	-1.291	0.275 (0.079-0.892)	0.036		
Tuffier's line					
-1, 0, 1					
-2, 2	0.840	2.317 (0.635-9.076)	0.210		
-3,3	1.214	3.366 (0.999-12.403)	0.056		
-4,4	2.563	12.973 (3.404-57.034)	0.000		
-5,5	3.038	20.874 (5.082-102.403)	0.000		
LSTV					
No					
I	0.083	1.087 (0.391-3.029)	0.873		
II/III/IV	0.825	2.281 (0.693-7.627)	0.174		
SLVA					
No					
Yes	1.017	2.764 (0.944-8.262)	0.064		
FLVA					
No					
Yes	0.685	1.984 (0.637-6.336)	0.239		
SS					
<35					
≥35 and <40	-0.723	0.485 (0.147-1.540)	0.224		
≥40 and <45	-1.099	0.333 (0.095-1.099)	0.076		
<u>≥</u> 45	-0.447	0.639 (0.195-2.050)	0.452		
LLA					
<40					
≥40 and <45	0.491	1.633 (0.476-5.814)	0.439		
≥45 and <50	-1.336	0.263 (0.065-0.968)	0.050		
≥50 and <55	-1.327	0.265 (0.069-0.956)	0.047		
<u>≥</u> 55	-1.708	0.181 (0.040-0.738)	0.021		

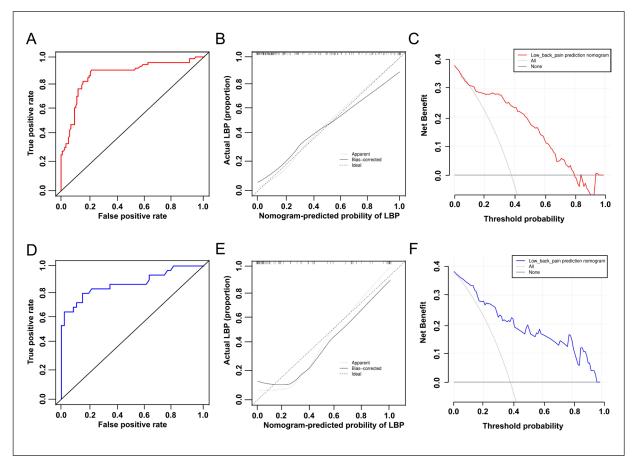
 $\boldsymbol{\beta}$  is the regression coefficient. CI, confidence interval; OR, odds ratio.

population often cannot be attributed to a specific cause, because they usually have no history of common causes of LBP. However, developmental abnormalities of spine can cause biomechanical alteration. And therefore, LBP in young population may be associated with abnormal development of spine. The treatment of LBP often leads to enormous socioeconomic burden. The best intervention to limit the negative effects of LBP is prevention. However, because the potential risk factors of non-specific LBP remain unclear, it is impossible to precisely prevent it. To establish a reliable predicting model for non-specific LBP in young population under the age of 45, a nomogram was constructed. We included some reported risk factors including age, sex, BMI, smoking, drinking, marital status, education level, working posture, working hours per day, exercising hours per week, Tuffier's line, lumbosacral transitional vertebra, SS, and LLA and recruited 264 participants ranging from 18 to 45 years old. The results revealed that LBP is closely related not only to lifestyles that include working posture and exercising hours per week but also to anatomy and structural anomalies including extremely higher or lower Tuffier's line and abnormal LLA.

With obesity, sedentary lifestyle, and smoking becoming increasingly prevalent, a great number of individuals are affected by LBP. There have been numerous scientific studies<sup>27</sup> that revealed that LBP was now more common among young people and that the age of onset tended to be young. According to this risk prediction model, people who maintain the immobilized working posture tend to have a higher risk of LBP. Previous studies showed that working periods that are longer than 7 h per day can significantly increase the risk of LBP<sup>28</sup>. In our study, although working hours per day is not significantly associated with LBP in the recruited people, we still believe that sustained detrimental postures could lead to LBP. The reason that working hours per day did not show a statistically sig-



**Figure 2**. Nomogram for LBP of young population. Each variable score was added together to give the total score at the bottom of the nomogram.



**Figure 3**. The ROC curves, calibration curves and DCA curves of the training set and the validation set. **A, D,** The AUC value of the nomogram was 0.867 (95% CI: 0.809-0.924) and 0.868 (95% CI: 0.775-0.961) in the training set (**A**) and validation set (**D**), respectively. **B, E,** In the calibration curves, the x-axis represented the predicted LBP risk. The y-axis represented the actual diagnosed LBP. The diagonal dotted line represented a perfect prediction by an ideal model. The solid line represented the performance of the nomogram, of which a closer fit to the diagonal dotted line represented a better prediction. **C, F,** In the DCA curves, the y-axis measured the net benefit. The dotted line represented the LBP risk nomogram. The thin solid line represented the assumption that all participants have LBP. Thin, thick solid line represented the assumption that no participants had LBP. **C,** The decision curve of the training set showed that if the threshold probability was in the range of 2%-94%, the nomogram revealed clinical net benefit. **F,** The decision curve of the validation set indicated that net benefit could be achieved when the threshold probability was in the range of 1%-95%.

nificant difference in this present study may lie in the fact that many participants in this study come from a military university and they usually do not have a sedentary lifestyle. It was reported that exercise could decrease the risk of LBP in the next year by 45%<sup>29</sup>. The exercising programs not only emphasize back-specific exercises, but also focus on the exercises of upper and lower limbs. It was suggested that exercising at least five days a week for half an hour can be beneficial to human body health<sup>30</sup>. In the present study, we found that those who exercised less than half an hour a week had a relatively high risk of LBP than those who had more than 3 hours exercise every week, which is in good agreement with literature reports<sup>30</sup>.

Human spines are among the most important parts of the body. Generally, there are 26 vertebrae in the human spine, which provide support for the body and protect the spinal cord<sup>31</sup>. Among all the vertebrae, the lumbar vertebra are the major load-bearing parts of the spine. However, the anatomy and structural anomalies may compromise the integrity of the lumbar spine, resulting in abnormal distribution of mechanical load imposed on the spine and causing destruction of the mechanical properties of the spine<sup>32</sup>. Tuffier's line is the line connecting the highest points of the iliac crests, which tends to intersect the L4-L5 intervertebral space<sup>5</sup>. Yet, it was reported that a large proportion of people's Tuffier's lines

were higher or lower than the L4-L5 intervertebral space<sup>5,6</sup>. According to a study, the distance between the conus medullaris and Tuffier's line was decreased with increased age, which might be resulted from vertebral deformities and the gradually decreased height of the vertebral body<sup>33</sup>. The higher or lower Tuffier's line not only can lead to false localization in surgery but also is responsible for the abnormal mechanical properties and load distribution imposed on the spine and pelvis, which can be closely related to non-specific LBP. In the present prediction model, we found that people with Tuffier's line at the level of 4, -4, 5 or -5, which remarkably deviates from the L4-L5 intervertebral space, have significantly higher risk of LBP. For people whose Tuffier's line is at the level of 2, -2, 3 or -3, the incidence of LBP is higher, but no significant difference was found. The results of this prediction model reveal that the Tuffier's line has a significant role in predicting LBP in young population. The mechanical characteristics of lumbar spine are largely depended on the structure of lumbosacral region, affecting the development of degenerative diseases. The coordinated connection among the ilium, the sacral vertebrae and the lumbar vertebrae is essential for both the stabilization and the mobilization of lumbosacral region. In this connection structure, Tuffier's line is an important indicator for measuring the structural stability of lumbosacral region. Both too high and too low Tuffier's line can negatively affect the mechanical characteristics of lumbar spine, resulting in early degenerative disorders and the dysfunction of lumbosacral structure and sacroiliac joints, which can subsequently lead to LBP. For those with higher or lower Tuffier's line, no obvious abnormality can be revealed by the radiological imaging. Thus, they tend to be diagnosed as non-specific LBP. With Tuffier's line, spine surgeons can assess the risk of LBP and partly explain the potential cause of the so-called non-specific LBP.

In addition to the great significance of Tuffier's line, sagittal spinal balance and proper sagittal alignment are also indispensable. FLVA, SLVA, and spinal sagittal alignment parameters including SS and LLA were used to assess the relationship between spinal sagittal alignment and LBP. In the present study, the results revealed that people with the anomaly of lumbar lordosis have significantly higher risk of LBP. Roussouly et al<sup>34</sup> held that SS was associated with lumbar curvature, and both were indispensable for maintaining the overall sagittal alignment. The lower

arc of lumbar lordosis is closely associated with the SS<sup>34</sup>. With SS increasing, both the lower arc and the global curvature of lumbar lordosis increases<sup>34</sup>. Evcik and Yücel<sup>35</sup> reported that people with chronic LBP were statistically more likely to have a less LLA. The loss of LLA that is often accompanied with the anterior shift of the sagittal vertical axis can cause the anterior shift of the gravity line which was reported to be closely associated with LBP<sup>36</sup>. The stability of spine is determined by the skeletal system and the neuromuscular system<sup>37</sup>. Lumbar instability resulted from disorders in one of the systems can be compensated by the other system. LLA tends to decrease with age. And researches have shown that maintaining lumbar lordosis can reduce spinal load<sup>38,39</sup>. When LLA is decreased, the load-carrying capacity of anterior and middle columns is reduced, and the posterior column is consequently subjected to greater axial spinal loading that is closely related to repeated injuries of spinal ligaments and facet joints. In addition, the flexibility of lumbar spine and the ability to withstand mechanical stress can also be reduced due to the decreased LLA, which requires the compensation of neuromuscular system. However, abnormal and repetitive loading will lead to excessive fatigue and impairment of neuromuscular system, which consequently require the compensation of the skeletal system through decreasing the SS and LLA. The vicious cycle between the lumbar skeletal system and the neuromuscular system can cause LBP.

What's more, according to the Castellvi classification, LSTV was divided into four types: type I (dysplastic enlarged transverse process), type II (pseudoarticulation), type III (fusion), and type IV (one transverse process fused and one with pseudoarticulation). But the Castellvi classification has a disadvantage: the sacralization of the fifth lumbar vertebra and lumbarization of the first sacral vertebra cannot be distinguished. Tokgoz et al<sup>40</sup> reported that people with LSTV had a higher risk of LBP. Apaydin et al<sup>41</sup> suggested that mechanical force in the lumbosacral vertebrae was changed by the lumbosacral anomaly, which could accelerate the degeneration of intervertebral discs and facet joints. For those with four lumbar vertebrae, the mechanical loading of each lumbar vertebra is increased. The formation of pseudoarthrosis and the fusion of transverse process with the sacral ala or iliac crest could make soft tissue swelling and this can subsequently compress nerve fibers. In our study, LSTV and FLVA did not show statistical significance for the prediction of LBP in young population, and we propose that this is probably due to the small sample size and a long-term prospective study with a large sample size is needed.

According to the present study, data show that Tuffier's line and LLA are important prediction factors of LBP. For people with developmental anomalies of these factors, it is advisable to avoid some occupations including military service, firefighting, and athletes. In addition, people who tend to have immobilized working posture or lack enough exercises should focus more on healthy lifestyles.

Although the present study included a total of 264 participants, further large-scale, multicenter studies are required to improve the accuracy of the nomogram. A more reliable and comprehensive risk prediction model for non-specific low back pain can be established through such studies.

#### Conclusions

The results of the study indicated that our nomogram could perform well in the prediction of LBP in young population. According to the nomogram, immobilized working posture, lack of exercises, too high or too low Tuffier's line, lumbarization of the first sacral vertebra and relatively lower LLA can increase the risk of LBP in young population. This study is anticipated to provide some references for clinical practice and prevention efforts.

### **Ethics Approval**

This study was approved by the Institutional Review Board of Shanghai Changzheng Hospital.

#### **Informed Consent**

Written informed consent was obtained from all participants.

## Availability of Data

The datasets are available from the corresponding author upon reasonable request.

# **Conflict of Interest**

We have no personal relationships or financial interests.

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#### **Authors' Contributions**

F.-D. Li and J.-G. Shi conceived and designed the study. F.-D. Li, Q.-J. Kong, B. Zheng, and K.-Q. Sun collected data. F.-D. Li and Y.-X. Wang analyzed the data and generated the figures and tables. F.-D. Li and Y.-X. Wang wrote the manuscript. K.-Q. Sun, B. Zheng, and J.-G. Shi were involved in the revision of the manuscript. The authors all read and approved the final manuscript.

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