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Original Article

Risk factors and interaction effects in recurrent low back pain

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Abstract: Objectives: To identify risk factors for low back pain (LBP) recurrence and develop a clinically applicable predictive model, with emphasis on interactions between key factors. Methods: A retrospective cohort study was conducted, including 216 patients with newly-diagnosed LBP as the derivation cohort (January 2023-June 2024) and 46 as the external validation cohort (July-December 2024). Independent risk factors were screened through univariate, least absolute shrinkage and selection operator (Lasso), and multivariate logistic regression. Interaction effects were evaluated. A nomogram was constructed and validated. Results: The 1-month recurrence rate was 33.8%. Independent risk factors for recurrence included elevated white blood cell (WBC) count (OR=4.555, P<0.001), anxiety (OR=25.256, P<0.001), working >8 h/day (OR=8.748, P<0.001), and elevated interleukin-1β (IL-1β) (OR=3.356, P=0.008). Significant multiplicative interactions were observed between body mass index (BMI) and working hours, WBC and anxiety, and anxiety and working hours (all P<0.05). A positive additive interaction between WBC and anxiety was identified (RERI)=3.928). The nomogram demonstrated excellent discrimination (area under the receiver operating characteristic curve (AUC)=0.906 in the derivation cohort; 0.902 in the validation cohort), good calibration (Hosmer-Lemeshow P=0.06, 0.61), and optimal net benefit. Conclusion: Elevated WBC, IL-1β, anxiety, and prolonged working hours predict LBP recurrence, with notable interactions among these factors. The proposed nomogram aids personalized risk stratification and informs work-related and psychological interventions.

Keywords: Low back pain, risk factors, interaction, recurrence mechanism

Introduction

Low back pain (LBP) is a common musculoskeletal disorder characterized by lumbar pain, often accompanied by limited mobility, muscle stiffness, and other symptoms, which significantly affect patients' daily activities and quality of life [1, 2]. Its pathogenesis is complex, involving biomechanical imbalance, intervertebral disc degeneration, muscle strain, inflammatory response, and psychosocial factors [3, 4]. It has been reported that the lifetime prevalence of LBP in Germany is approximately 75%, with a point prevalence of 32% to 49%, and similar rates have been reported in other European regions [5]. Globally, chronic LBP is the leading cause of years lived with disability [6].

Current clinical interventions for LBP are diverse, including pharmacologic therapy, physical therapy, rehabilitation training, and psychological intervention [7-9]. However, most regimens mainly focus on relieving symptoms, failing to fundamentally prevent recurrence [10]. Recurrence of LBP has been linked to multiple risk factors, including aging, long-term poor posture, lack of exercise, obesity, psychological stress, and sleep disorders [11, 12]. Nevertheless, most existing studies have examined the effect of single risk factors, with limited attention to potential interactions among them. Moreover, the lack of validated clinical prediction models has hindered the quantitative assessment of individual recurrence risk, restricting the implementation of personalized

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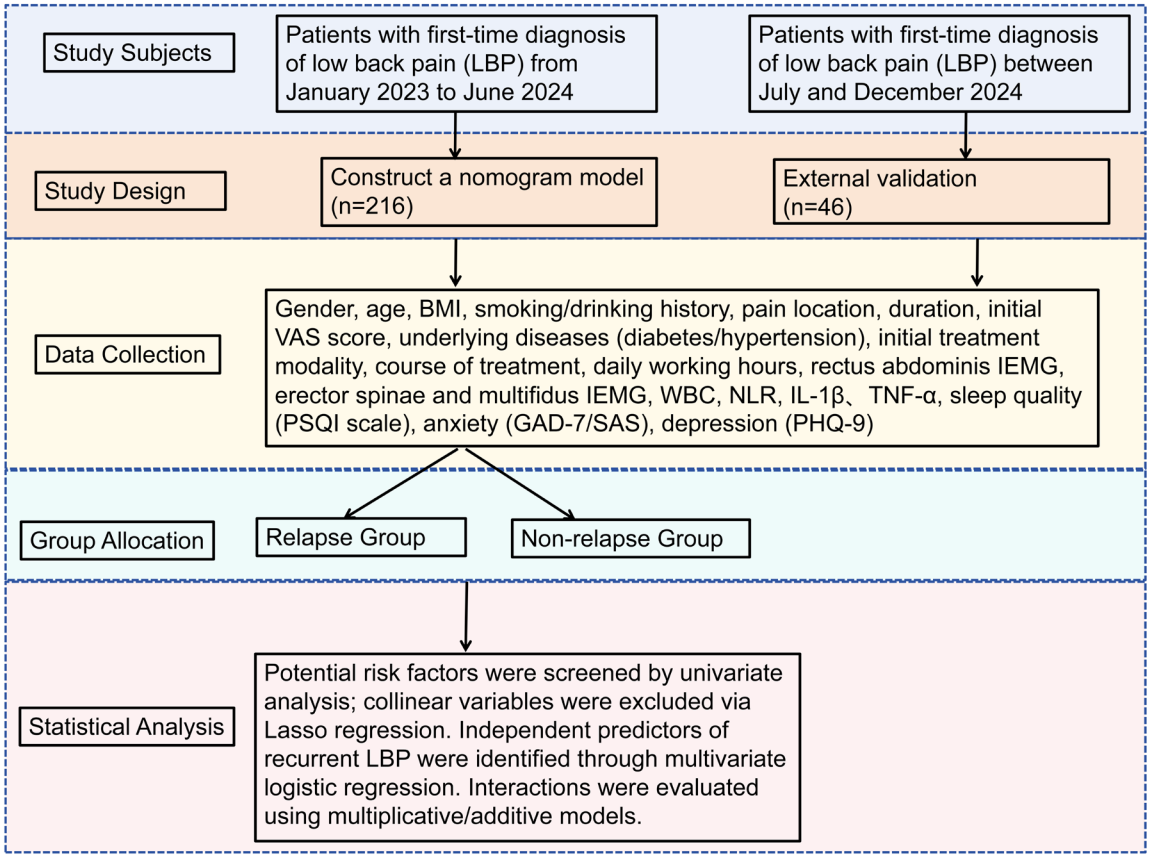

Figure 1. Study flow diagram.

preventive strategies. The underlying mechanisms of LBP recurrence remain incompletely understood, which severely constrains the development of precise and personalized clinical treatment plans.

This study employed multivariate analysis and interaction models to comprehensively investigate the risk factors and interaction mechanisms underlying recurrent LBP. A clinical prediction model integrating key risk factors was developed and externally validated to assess its efficacy. The research results will provide theoretical support for clinicians to formulate more targeted treatment strategies and a quantitative tool for individualized risk stratification. Moreover, the results offer scientific guidance for patients to optimize lifestyle habits and improve psychological well-being, thereby reducing the risk of chronic LBP recurrence and enhancing the quality of life of patients.

Patients and methods

Study cohort

A retrospective cohort study was employed. The derivation cohort comprised 216 patients with newly-diagnosed LBP who presented to the rehabilitation clinic or neurology departments of our hospital between January 2023 and June 2024. An external validation cohort included 46 patients diagnosed between July and December 2024 using the same inclusion/exclusion criteria, enabling assessment of the generalizability of the constructed prediction model. The research flow chart is shown in **Figure 1**.

Inclusion criteria

① Meeting the diagnostic criteria for LBP established by the International Association for the Study of Pain (IASP), i.e., presenting with low back pain symptoms while excluding other

organic diseases such as lumbar spinal stenosis and lumbar fracture [13]; ② Aged 18-35 years, regardless of gender; ③ First diagnosis of LBP, with no history of recurrent similar lumbodorsal pain.

Exclusion criteria

① Presence of severe organic spinal diseases, including spinal fracture, dislocation, tumor, tuberculosis, or severe lumbar disc herniation with imaging-confirmed nerve root compression. ② Coexisting chronic pain disorders in other regions, such as cervical spondylosis, knee arthritis, or fibromyalgia syndrome. ③ Incomplete medical records (e.g., missing details regarding initial treatment or recurrence time) or follow-up interrupted for more than 6 months without the possibility of obtaining supplementary information.

Ethics statement

This retrospective study was approved by the Ethics Committee of the 924th Hospital of the People's Liberation Army Joint Logistic Support Force (Approval No.: Guiyi [2023] No. 04). In accordance with the committee's approval, all patient data were anonymized (personal identifiers such as names, medical record numbers, and contact information were removed) to protect privacy, and the requirement for informed consent was waived. This study was conducted in compliance with the principles of the Declaration of Helsinki.

Sample size estimation

According to previous studies, the recurrence rate of LBP is 30%-40% [14]. Combining the main research objectives of this study and the expected effect size of risk factors, the sample size was calculated based on the average event per variable (EPV) principle. Taking EPV=10, assuming the LBP recurrence rate in this study was 30%, and expecting 6 variables to be included in the multivariate regression model, the sample size was calculated as follows: sample size = number of included variables × EPV/incidence rate =6×10/30%=180 cases. Considering a 20% dropout rate, the required sample size for this study was 216 cases.

For the external validation cohort, a sample size of 46 cases was determined based on two considerations: ① Clinical feasibility in a 6-month recruitment period; ② Statistical adequacy to assess model generalizability, as validation cohorts typically require 20%-30% of the derivation sample size. This sample size ensures sufficient events (expected recurrence cases: 46×30%=13.8) to evaluate model discrimination (e.g., ROC curve) and calibration.

Data collection

Data were collected through a retrospective review of electronic medical records, outpatient follow-up records, inpatient medical records, and community health archives. Two trained researchers independently extracted the data, with discrepancies resolved by third-party review. The collected data included the following categories:

(1) Demographic data: Gender, age, body mass index (BMI), smoking history, and drinking history.

(2) Clinical data: Pain location (e.g., paraspinal lumbar region, sacroiliac area, lumbosacral junction), pain duration (course of disease), pain intensity at first onset (assessed by Visual Analogue Scale [VAS], 0-10 points), and comorbidities (e.g., diabetes, hypertension).

(3) Treatment-related factors: First treatment modality (e.g., physical therapy, pharmacological therapy), treatment course, inflammatory marker levels from admission blood routine tests, and electromyographic indices. Inflammatory markers: white blood cell count (WBC) and neutrophil/lymphocyte ratio (NLR) were detected via standard automated hematology analyzer. For interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α): 5 mL of peripheral venous blood was collected on admission, centrifuged at 3000 rpm for 10 min at 4°C to separate serum, and stored at -80°C until analysis. IL-1β and TNF-α levels were determined by ELISA using commercial kits (IL-1β: Catalog No. GB20228; TNF-α: Catalog No. GB19301; both from Servicebio Technology Co., Ltd., Wuhan, China) with detection ranges of 1.56-100 pg/mL and 3.12-200 pg/mL, respectively (intra-assay CV <6%). Assays were performed according to manufacturer's instructions, with concentrations calculated from standard curves generated using recombinant standards. Absorbance was measured at 450 nm using a

microplate reader (Multiskan FC, Thermo Fisher Scientific).

(4) Electromyographic indices: Integrated electromyography (IEMG) of the rectus abdominis, erector spinae, and multifidus muscles.

(5) Lifestyle factors: Daily working hours and sleep quality (assessed by Pittsburgh Sleep Quality Index [PSQI], scored 0-21, with higher scores indicating poorer sleep quality).

(6) Psychosocial factors: Anxiety status (assessed by Generalized Anxiety Disorder Scale [GAD-7], scored 0-21, with higher scores indicating more severe anxiety) and depressive status (assessed by Patient Health Questionnaire-9 [PHQ-9], scored 0-27, with higher scores indicating more severe depression).

Research scales

The Self-Rating Anxiety Scale (SAS) was used for psychological assessment of anxiety, comprising 20 standardized items validated for identifying anxiety-related symptoms [15]. As an internationally recognized tool, the SAS has demonstrated satisfactory applicability in Chinese populations, with established psychometric properties, including acceptable test-retest reliability and criterion validity. The scale employs a four-level scoring system (1= rare occurrence, 4= frequent occurrence), with total raw scores converted via weighting (raw sum ×1.25) to yield final scores ranging 25-100. Per standardized classification: scores of 25-49 indicate normal status, 50-59 mild anxiety, 60-69 moderate anxiety, and ≥70 severe anxiety. The instrument showed excellent reliability, with internal consistency coefficient (Cronbach's α) reaching 0.88 in our cohort, exceeding the previously reported 0.82 in validation studies.

Depressive symptoms were evaluated using the Patient Health Questionnaire-9 (PHQ-9), a nine-item instrument based on the core diagnostic criteria for major depressive episodes in the *American Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) [16]. Each item is scored on a four-point Likert scale from 0 ("not at all") to 3 ("nearly every day"), yielding a total score of up to 27. The scoring reflects symptom frequency over the past two weeks: 0= never; 1= occasionally (about 1-3 days); 2= more than half of the days (about 4-10 days); and 3= almost every day (11-14 days). A total score of 0-4 points indicate no depression, 5-9 points mild depression, 10-19 points moderate depression, and 20-27 points severe depression.

The Pittsburgh Sleep Quality Index (PSQI) provides a multidimensional quantitative assessment of participants' sleep patterns over the preceding 30 days through seven core components: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleep medications, and daytime dysfunction. Each component is rated on a 4-point scale (0= no difficulty to 3= severe difficulty), and the global score (0-21) is obtained by summing the weighted domain scores, with higher values indicating poorer sleep quality. Sleep efficiency is calculated as the dynamic ratio of total sleep time to time in bed (>85% as normal, <65% as severe abnormality), while sleep latency integrates both time-to-sleep onset (>60 minutes scoring 3 points) and frequency of difficulty initiating sleep (≥3 times/week scoring 3 points) [17]. Clinically, total scores ≤5 indicate good sleep quality, whereas scores ≥16 indicate severe sleep disorders that necessitate medical intervention. Validated in Chinese populations, the PSQI demonstrates good reliability, with Cronbach's α ranging from 0.74-0.88, and serves as both a general screening tool and an adjunct diagnostic aid for sleep-related comorbidities along with depression and anxiety.

Study groups

Recurrence group: Patients whose pain recurred within 1 month after diagnosis of LBP and required repeated medical intervention (e.g., pharmacotherapy, physical therapy) due to pain severity; non-recurrence group: Patients remained symptom-free after 1 month of follow-up, and did not receive any treatment for LBP.

Model construction and validation

Based on independent risk factors identified through multivariate logistic regression in the derivation cohort of 216 patients initially diagnosed with LBP between January 2023 and June 2024, a clinically applicable nomogram model was developed to predict LBP recur-

Table 1. Univariate analysis of LBP recurrence in the derivation cohort (n=216)

	Recurrence group (n=73)	Non-recurrence group (n=143)	t/χ^2	*P*-value
Gender (n%)			1.661	0.198
Male	43 (58.90)	71 (49.65)		
Female	30 (41.10)	72 (50.35)		
Age (years, MD±S)	28.78±3.78	28.55±4.66	-0.387	0.699
BMI (kg/m^2, n %)			8.006	0.018
Normal	24 (32.88)	76 (53.15)		
Underweight	7 (9.59)	9 (6.29)		
Overweight	42 (57.53)	58 (40.56)		
Smoking history (n %)			0.086	0.769
Yes	7 (9.59)	12 (8.39)		
No	66 (90.41)	131 (91.61)		
Alcohol consumption history (n %)			0.038	0.845
Yes	10 (13.70)	21 (14.69)		
No	63 (86.30)	122 (85.31)		
Pain location (n %)			2.602	0.272
Paraspinal lumbar region	25 (34.25)	65 (45.45)		
Sacroiliac region	22 (30.14)	38 (26.57)		
Lumbosacral junction	26 (35.62)	40 (27.97)		
Disease duration (week, n %)			0.783	0.376
≤14	60 (82.19)	124 (86.71)		
>14	13 (17.81)	19 (13.29)		
Initial VAS score (score, n %)			0.799	0.371
≤6	44 (60.27)	95 (66.43)		
>6	29 (39.73)	48 (33.57)		
Hypertension history (n %)			0.191	0.662
Yes	14 (19.18)	24 (16.78)		
No	59 (80.82)	119 (83.22)		
Diabetes history (n %)			1.341	0.247
Yes	5 (6.85)	17 (11.89)		
No	68 (93.15)	126 (88.11)		
Daily working hours (n %)			4.793	0.029
≤8 hours	52 (71.23)	120 (83.92)		
>8 hours	21 (28.77)	23 (16.08)		
Treatment modalities (n %)			0.001	0.979
Physical therapy	42 (57.53)	82 (57.34)		
Pharmacotherapy	31 (42.67)	61 (42.66)		
Treatment duration (n %)			0.141	0.707
≤14 day	55 (75.34)	111 (77.62)		
>14 day	18 (24.66)	32 (22.38)		
Rectus abdominis IEMG (μs/V, MD±S)	523.34±89.31	516.60±87.66	-0.531	0.596
Erector spinae and multifidus IEMG (μs/V, MD±S)	584.02±96.49	566.23±100.68	-1.246	0.214
WBC (×10^9/L, n %)			17.016	<0.001
Normal range	31 (42.47)	102 (71.33)		
Elevated	42 (57.53)	41 (28.67)		
NLR (n %)			0.423	0.515
Normal range	50 (68.49)	104 (72.73)		
Elevated	23 (31.51)	39 (27.27)		

IL-1β (pg/mL, n %)			8.466	0.004
Normal range	41 (56.16)	108 (75.52)		
Elevated	32 (43.84)	35 (24.48)		
TNF-α (pg/mL, n %)			5.770	0.016
Normal range	34 (46.58)	91 (63.64)		
Elevated	39 (53.42)	52 (36.36)		
Anxiety (n %)			64.301	<0.001
None, SAS score ≤49	6 (8.22)	94 (65.73)		
Present, SAS score >49	67 (91.78)	49 (34.27)		
Depression (n %)			5.024	0.023
None, PHQ-9 score ≤4	15 (20.55)	51 (35.66)		
Present, PHQ-9 score >4	58 (79.45)	92 (64.34)		
Sleep quality (n %)			1.725	0.189
Good, PSQI score ≤5	21 (28.77)	54 (37.76)		
Poor, PSQI score >5	52 (71.23)	89 (62.24)		

Notes: BMI: body mass index; IEMG: Integrated electromyography; WBC: white blood cell; NLR: neutrophil-to-lymphocyte ratio; PHQ-9: Patient Health Questionnaire-9; PSQI: Pittsburgh Sleep Quality Index; Internal reference ranges (924th Hospital): NLR 0.88-4.00, WBC 3.5-9.5×10^9/L, IL-1β 0-5 pg/mL, TNF-α 0.1-8.1 pg/mL.

rence. Internal validation was performed using 500 bootstrap resamples to assess model stability. External validation was conducted in a cohort consisting of 46 newly diagnosed LBP patients recruited between July and December 2024 to evaluate the model's generalizability. The model's discriminative ability was assessed using receiver operating characteristic (ROC) curves and the area under the curve (AUC). Calibration was evaluated using calibration plots and the Hosmer-Lemeshow goodness-of-fit test. Clinical utility was assessed using decision curve analysis (DCA) to determine the net benefit across a range of threshold probabilities.

Statistical methods

All statistical analyses were performed using SPSS 26.0 and R 4.2.1 software, with α= 0.05 (two-sided) as the significance criterion. Measured data were expressed as mean ± standard deviation or median (25th, 75th percentiles) according to normality, and compared using independent-sample *t* tests or Mann-Whitney *U* tests, as appropriate. Counted data were presented as frequencies and percentages, with group differences assessed using the chi-square test or Fisher's exact test. Potential risk factors were initially screened by univariate analysis (P<0.05). After eliminating collinearity through least absolute shrinkage and selection operator (Lasso) regression, significant variables were entered into a multivariate logistic regression model, with backward stepwise selection used to identify independent risk factors. Multiplicative and additive interaction analyses were used to explore interactions among predictors of LBP recurrence, with relative excess risk (RERI), attributable proportion (AP), and interaction index (S) used to evaluate the significance of interactions (RERI and AP with 95% confidence interval (CI) excluding 0, or S with a 95% CI excluding 1 indicate significant interactions).

Results

Univariate analysis of LBP recurrence

There were no significant differences between the two groups in gender, age, smoking history, alcohol consumption history, pain location, disease course, initial VAS score, history of hypertension or diabetes, treatment modality, treatment course, rectus abdominis IEMG, erector spinae and multifidus IEMG, NLR, or PSQI (all P>0.05). However, significant differences were observed in several variables: the recurrence group had higher proportions of overweight individuals (57.53% vs. 40.56%, P<0.01), participants working >8 h/day (28.77% vs. 16.08%, P=0.029), patients with elevated WBC (57.53% vs. 28.67%, P<0.001), elevated IL-1β (43.84% vs. 24.48%, P=0.004), elevated TNF-α (53.42% vs. 36.36%, P=0.016), and higher rates of anxiety and depression (both P<0.05). Details are presented in **Table 1**.

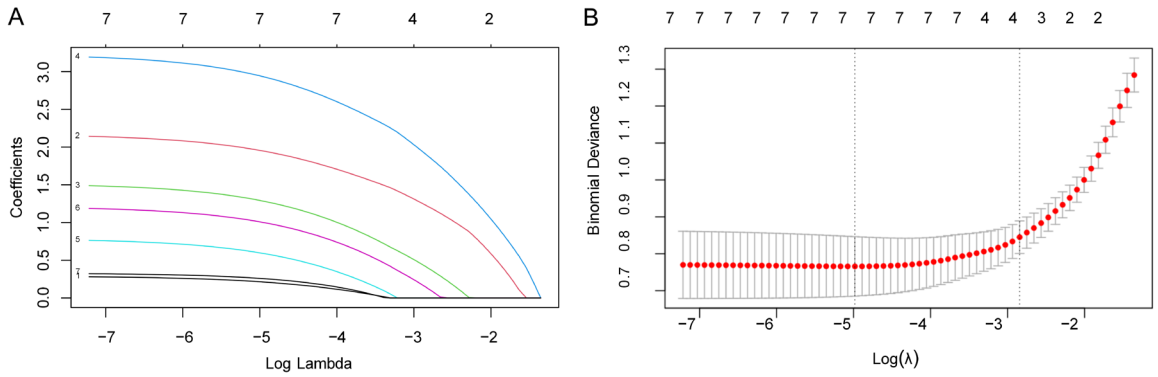

Figure 2. Lasso regression analysis of factors for LBP recurrence. A: Trajectory of variable coefficients across log(λ) values in Lasso regression; B: Binomial deviance versus log(λ) profile in Lasso regression.

Table 2. Multivariate logistic regression of intendent factors influencing LBP recurrence

Variable	*B*	*SE*	*Wald*	*P*-value	*OR*	*95% CI*
BMI	0.290	0.227	1.630	0.202	1.337	0.856-2.086
WBC	1.516	0.453	11.206	<0.001	4.555	1.875-11.066
Anxiety	3.229	0.556	33.732	<0.001	25.256	8.494-75.096
Working hours	2.169	0.485	20.012	<0.001	8.748	3.383-22.627
Depression	0.786	0.486	2.614	0.106	2.195	0.846-5.695
IL-1β	1.211	0.453	7.138	0.008	3.356	1.381-8.156
TNF-α	0.329	0.425	0.599	0.439	1.390	0.604-3.201

Notes: BMI: body mass index; WBC: white blood cells.

Multivariate logistic regression analysis and nomogram model construction

To identify independent risk factors for LBP recurrence, variables were first processed using Lasso regression to remove collinearity before multivariate logistic regression. Lasso regression penalizes regression coefficients, shrinking some coefficients to 0 to achieve variable selection and avoid collinearity interference.

As shown in **Figure 2**, with changes in Log Lambda, the coefficients of various variables displayed different trends. Variables such as BMI, WBC, anxiety, working hours, depression, IL-1β, and TNF-α retained stable coefficients, indicating greater potential influence on LBP recurrence, and all were included in the multivariate logistic regression.

The multivariate logistic regression results (**Table 2**) identified elevated WBC (*OR*=4.555, *P*<0.001), anxiety (*OR*=25.256, *P*<0.001), working hours >8 h/day (*OR*=8.748, *P*<0.001), and elevated IL-1β (*OR*=3.356, *P*<0.01) as independent risk factors for LBP recurrence. However, the effects of BMI (overweight) (*OR*=1.394, *P*=0.130), depression (*OR*=1.821, *P*=0.186) and elevated TNF-α (*OR*=1.390, *P*=0.439) on LBP recurrence did not reach significance.

Based on the independent predictors identified in multivariate logistic regression (elevated WBC, elevated IL-1β, anxiety, and working hours >8 hours/day), a nomogram model for predicting LBP recurrence was constructed (**Figure 3**). The model converts the regression coefficients of each risk factor into a visual scoring scale, and a risk score can be summed according to patient's WBC level, IL-1β level, anxiety status, and working hours. The total score can then be mapped to the predicted recurrence probability using the probability scale at the bottom of the nomogram.

Multiplicative interaction analysis of factors influencing LBP recurrence

The interactions between BMI and working hours, WBC and anxiety, as well as anxiety and working hours showed significant effects on

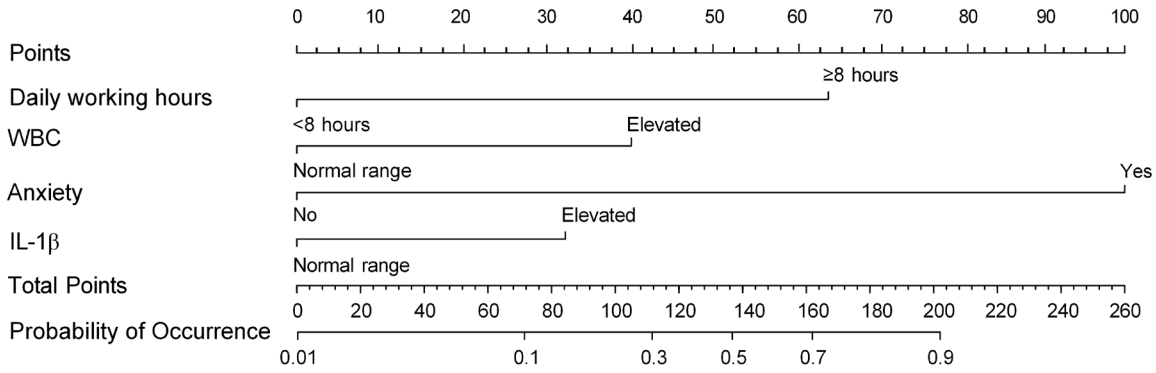

Figure 3. Nomogram for predicting the probability of low back pain recurrence based on independent risk factors.

Table 3. Multiplicative interaction analysis of factors influencing LBP recurrence

Variable Combination	*B*	*SE*	*Wald*	*P*	*OR*	*95% CI*
BMI-WBC	-0.411	0.332	1.528	0.216	0.663	0.346-1.272
BMI-Anxiety	-0.647	0.540	1.438	0.230	0.523	0.182-1.508
BMI-Working hours	1.002	0.380	6.963	0.008	2.725	1.294-5.738
BMI-Depression	0.538	0.364	2.181	0.140	1.713	0.839-3.497
BMI-IL-1β	0.618	0.339	3.326	0.068	1.855	0.955-3.605
BMI-TNF-α	-0.006	0.313	<0.001	0.985	0.994	0.538-1.836
WBC-Anxiety	3.289	1.215	7.330	0.007	26.808	2.479-289.901
WBC-Working hours	-1.012	0.695	2.121	0.145	0.363	0.093-1.419
WBC-Depression	-0.282	0.718	0.155	0.694	0.754	0.185-3.080
WBC-IL-1β	-0.315	0.643	0.240	0.625	0.730	0.207-2.574
WBC-TNF-α	0.414	0.616	0.452	0.501	1.513	0.452-5.061
Anxiety-Working hours	3.496	0.799	19.125	<0.001	32.980	6.883-158.012
Anxiety-Depression	0.390	0.993	0.154	0.695	1.476	0.211-10.342
Anxiety-IL-1β	-0.271	0.945	0.082	0.774	0.762	0.119-4.870
Anxiety-TNF-α	-1.156	0.970	1.421	0.233	0.315	0.047-2.107
Working hours-Depression	0.530	0.768	0.475	0.491	1.698	0.377-7.657
Working hours-IL-1β	1.260	0.910	1.916	0.166	3.526	0.592-20.995
Working hours-TNF-α	1.347	0.734	3.365	0.067	3.845	0.912-16.216
Depression-IL-1β	-0.780	0.729	1.145	0.285	0.458	0.110-1.913
Depression-TNF-α	0.269	0.686	0.154	0.695	1.309	0.341-5.017
IL-1β-TNF-α	0.403	0.642	0.393	0.531	1.496	0.425-5.264

Notes: BMI: body mass index; WBC: white blood cells.

LBP recurrence (all $P<0.05$), while interactions among other variables did not exhibit significant correlations (all $P\geq0.05$). Specifically, the interaction between BMI and working hours had an *OR* of 2.725 (95% CI: 1.294-5.738), indicating that long-term increased working hours in obese individuals significantly elevated the LBP recurrence risk by 2.73 times compared with single-factor effects. The interaction between WBC and anxiety showed an *OR* of 26.808 (*95% CI*: 2.479-289.901), suggesting that coexisting elevated inflammatory levels and anxiety could increase the recurrence risk by 26.8 times. The most prominent interaction was between anxiety and working hours (*OR*=32.980, *95% CI*: 6.883-158.012), indicating that prolonged work or sedentary behavior under anxiety could disrupt lumbar mechanical balance by increasing muscle tension, as detailed in **Table 3**.

Table 4. Additive interaction analysis of factors influencing LBP recurrence

Variable Combination	*RERI (95% CI)*	*API (95% CI)*	*S (95% CI)*
BMI-WBC	114.389 (-232.870-461.648)	0.937 (0.824-1.049)	18.158 (3.486-94.592)
BMI-Anxiety	88.588 (-310.784-487.971)	0.889 (0.612-1.165)	9.771 (0.917-104.07)
BMI-Working hours	10.296 (-18.217-38.808)	0.727 (0.345-1.109)	4.591 (1.143-18.438)
BMI-Depression	31.818 (-60.925-124.562)	0.864 (0.654-1.075)	8.954 (2.274-35.262)
BMI-IL-1β	0.354 (-2.677-3.367)	0.156 (-0.876-1.188)	1.400 (0.193-10.149)
BMI-TNF-α	34.909 (-71.607-141.425)	0.777 (0.450-1.104)	4.861 (1.162-20.342)
WBC-Anxiety	3.928 (0.971-6.884)	1.294 (0.983-1.606)	-1.073 (NA)
WBC-Working hours	1.417 (-14.577-17.410)	0.085 (-0.831-1.002)	1.100 (0.377-3.205)
WBC-Depression	7.679 (-1.670-17.027)	0.660 (0.357-0.962)	3.596 (1.202-10.759)
WBC-IL-1β	2.413 (-4.588-9.414)	0.295 (-0.354-0.944)	1.506 (0.516-4.398)
WBC-TNF-α	3.858 (-1.789-9.505)	0.519 (0.094-0.944)	2.499 (0.796-7.844)
Anxiety-Working hours	5.503 (-5.444-16.451)	0.446 (-0.193-1.085)	1.944 (0.515-7.345)
Anxiety-Depression	0.734 (-2.111-3.578)	0.201 (-0.555-0.958)	1.384 (0.326-5.883)
Anxiety-IL-1β	-1.153 (-5.584-3.277)	-0.335 (-1.654-0.984)	0.679 (0.186-2.478)
Anxiety-TNF-α	-2.082 (-6.709-2.544)	-0.651 (-2.043-0.741)	0.514 (0.173-1.525)
Working hours-Depression	32.732 (-20.292-85.756)	0.721 (0.386-1.056)	3.799 (1.093-13.197)
Working hours-IL-1β	40.196 (-32.661-113.054)	0.837 (-0.582-1.092)	6.884 (-1.347-35.183)
Working hours-TNF-α	17.172 (-5.957-40.302)	0.772 (0.500-1.044)	5.217 (1.349-20.178)
Depression-IL-1β	-2.170 (-8.190-3.850)	-0.357 (-1.504-0.790)	0.700 (0.259-1.893)
Depression-TNF-α	4.662 (-1.826-11.150)	0.565 (0.183-0.947)	2.801 (0.907-8.652)
IL-1β-TNF-α	3.266 (-2.369-8.901)	0.509 (0.022-0.996)	2.516 (0.682-9.289)

Additive interaction analysis of factors influencing LBP recurrence

Additive interaction analysis demonstrated a positive interaction between WBC and anxiety. The relative excess risk due to interaction (RERI) was 3.928, and its 95% confidence interval (CI) did not include 0, indicating statistical significance. The attributable proportion (API) was 1.294, indicating that 29.4% of the recurrence risk caused by the joint exposure could be attributed to the interaction effect. The synergy index (S) was -1.073. For other combinations, such as BMI × working hours (RERI=10.296, 95% CI: -18.217-38.808) and WBC × depression (API=0.660, 95% CI: 0.357-0.962), the confidence intervals included 0 or 1, indicating no significant additive interaction, as shown in **Table 4**.

Baseline characteristics and univariate analysis of the validation cohort

In the external validation cohort of 46 LBP patients followed for 1 month, 13 (28.3%) experienced recurrence, comparable to that of the derivation cohort. Univariate analysis revealed that the proportion of male patients in the recurrence group was higher than that in the non-recurrence group. Additionally, the proportions of overweight patients, those working >8 h/day, patients with elevated WBC, anxiety, and elevated IL-1β and TNF-α levels were also significantly higher in the recurrence group than in the non-recurrence group (all $P<0.05$). No statistical differences were observed between groups in age, smoking history, alcohol consumption history, lesion location, or disease duration ($P>0.05$). See **Table 5**.

Performance evaluation and external validation of the prediction model

The predictive performance of the LBP recurrence nomogram was evaluated using multiple indices. As shown in **Figure 4**, the nomogram achieved an AUC of 0.906 (95% CI: 0.861-0.0.952) in the derivation cohort, indicating excellent discrimination. The validation cohort yielded an AUC of 0.902 (95% CI: 0.805-0.999), demonstrating comparable performance and confirming the model's ability to effectively identify high-risk patients in an external population.

Table 5. Univariate analysis of low back pain recurrence in the validation cohort (n=46)

	Recurrence group (n=13)	Non-recurrence group (n=33)	t/χ^2	*P*-value
Gender (n %)			5.254	0.022
Male	10 (76.92)	13 (39.39)		
Female	3 (23.08)	20 (60.61)		
Age (years, MD±S)	27.00±5.31	27.12±4.02	0.084	0.933
BMI (kg/m^2, n %)			7.881	0.018
Normal	3 (23.08)	22 (66.67)		
Underweight	2 (15.38)	4 (12.12)		
Overweight	8 (61.54)	7 (21.21)		
Smoking history (n %)			0.043	0.836
Yes	3 (23.08)	5 (15.15)		
No	10 (76.92)	28 (84.85)		
Alcohol consumption history (n %)			0.036	0.849
Yes	1 (7.69)	5 (15.15)		
No	12 (92.31)	28 (84.85)		
Pain location (n %)			0.547	0.769
Paraspinal lumbar region	5 (38.46)	16 (48.48)		
Sacroiliac region	4 (30.77)	8 (24.24)		
Lumbosacral junction	4 (30.77)	9 (27.27)		
Disease duration (week, n %)			0.226	0.634
≤14	10 (76.92)	29 (87.88)		
>14	3 (23.08)	4 (12.12)		
Initial VAS score (score, n %)			3.344	0.067
≤6	5 (38.46)	24 (72.73)		
>6	8 (61.54)	9 (27.27)		
Daily working hours (n %)			7.481	0.006
≤8 hours	4 (30.77)	26 (78.79)		
>8 hours	9 (69.23)	7 (21.21)		
Treatment modalities (n%)			0.056	0.813
Physical therapy	9 (69.23)	24 (72.73)		
Pharmacotherapy	4 (30.77)	9 (27.27)		
Treatment duration (n %)			0.085	0.770
≤14 day	10 (76.92)	24 (72.73)		
>14 day	3 (23.08)	9 (27.27)		
Rectus abdominis IEMG (μs/V, MD±S)	529.65±97.12	495.44±92.21	-1.150	0.256
Erector spinae and multifidus IEMG (μs/V, MD±S)	581.16±107.80	588.37±101.30	0.213	0.832
WBC (×10^9/L, n %)			7.481	0.006
Normal range	4 (30.77)	26 (78.79)		
Elevated	9 (69.23)	7 (21.21)		
NLR (n %)			0.129	0.720
Normal range	9 (69.23)	21 (63.64)		
Elevated	4 (30.77)	12 (36.36)		
IL-1β (pg/mL, n %)			5.537	0.020
Normal range	6 (46.15)	28 (84.85)		
Elevated	7 (53.85)	5 (15.15)		
TNF-α (pg/mL, n %)			4.224	0.040
Normal range	6 (46.15)	27 (81.82)		
Elevated	7 (53.85)	6 (18.18)		

Anxiety (n %)			9.483	0.002
None, SAS score ≤49	3 (23.08)	24 (72.73)		
Present, SAS score >49	10 (76.92)	9 (27.27)		
Depression (n %)			4.060	0.044
None, PHQ-9 score ≤4	4 (30.77)	21 (63.64)		
Present, PHQ-9 score >4	9 (69.23)	12 (36.36)		
Sleep quality (n %)			0.003	0.953
Good, PSQI score ≤5	5 (38.46)	13 (39.39)		
Poor, PSQI score >5	8 (61.54)	20 (60.61)		

Notes: BMI: body mass index; IEMG: Integrated electromyography; WBC: white blood cells; NLR: neutrophil-to-lymphocyte ratio; PHQ-9: Patient Health Questionnaire-9; PSQI: Pittsburgh Sleep Quality Index; Internal reference ranges (924th Hospital): NLR 0.88-4.00, WBC 3.5-9.5×10^9/L, IL-1β 0-5 pg/mL, TNF-α 0.1-8.1 pg/mL.

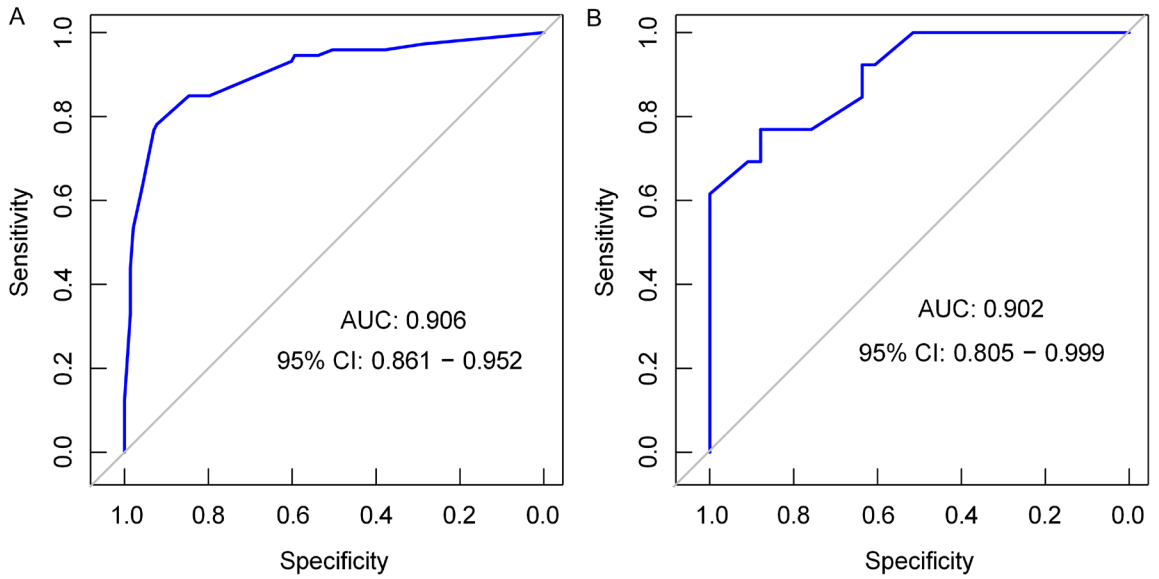

Figure 4. ROC curves for the prediction model in derivation and external validation cohorts. A: Derivation cohort (n=216); B: External validation cohort (n=46). Note: ROC: receiver operating characteristic.

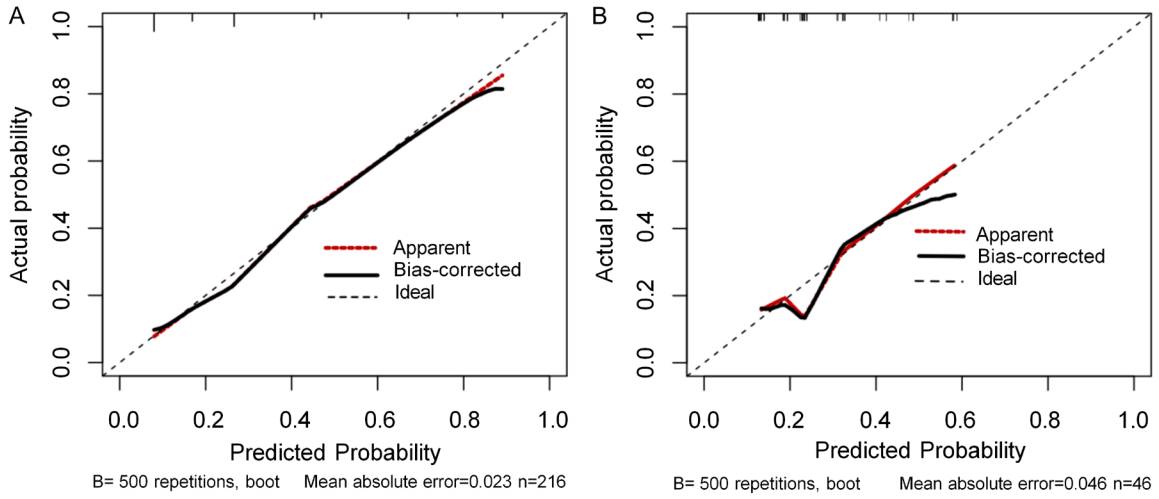

Figure 5. Calibration curves for prediction accuracy of the LBP recurrence prediction model. A: Derivation cohort (n=216); B: External validation cohort (n=46).

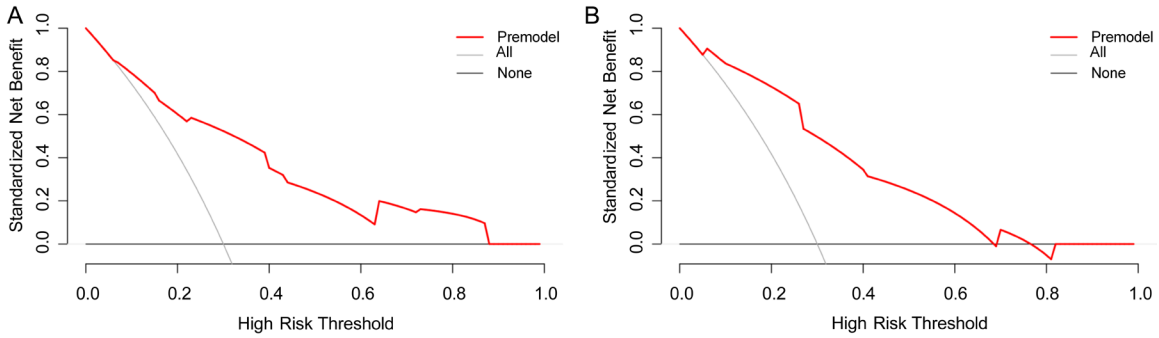

Figure 6. DCA for clinical utility evaluation of the LBP recurrence prediction model. A: Derivation cohort (n=216); B: External validation cohort (n=46). Note: DCA: decision curve analysis.

Calibration curves (**Figure 5**) demonstrated good agreement between predicted and observed recurrence probabilities. In the derivation cohort, the Hosmer-Lemeshow test yielded P=0.06, and the mean absolute error (MAE) from 500 bootstrap resamples was 0.023, indicating stable internal prediction accuracy. In the validation cohort, the calibration curve also demonstrated high consistency (Hosmer-Lemeshow test P=0.61), with a bootstrap MAE of 0.046, verifying the model's robustness in external data.

Decision curve analysis (**Figure 6**) showed that, across threshold probabilities of 0-80%, the model provided greater net benefit than the "all-patients-recur" or "no-patients-recur" strategies. The highest net benefit was observed at threshold probabilities of 15%-65%, indicating its clinical value in guiding individualized risk-based management decisions.

Discussion

This study showed that the 1-month recurrence rate of LBP after treatment was 33.8%, which is comparable to the reported recurrence rate after lumbar discectomy (3%-36%) [18-20]. LBP recurrence remains a major challenge in clinical practice, involving complex interactions among biological, psychological, and social factors. Although existing treatment methods can alleviate symptoms to a certain extent, recurrence rates remain high, underscoring the need for a deeper understanding of the underlying mechanisms of recurrence. By constructing a clinical prediction model that integrates biological, psychological, and social risk dimensions, this study aimed to elucidate the multidimensional mechanisms driving LBP recurrence and to provide a theoretical basis for precision interventions targeting the complex interplay of inflammatory, psychological, and occupational factors.

Analysis of independent risk factors for LBP recurrence

This study identified four independent risk factors for LBP recurrence by multivariate logistic regression: elevated WBC, elevated IL-1β, daily working hours >8 h, and anxiety, consistent with previous findings [21, 22]. As a classic marker of systemic inflammation [22], elevated WBC in LBP patients may be triggered by long-term lumbar mechanical stress or subtle local trauma. In the inflammatory microenvironment, WBCs release cytokines such as TNF-α and IL-1β [23], which directly stimulate lumbar nerve endings, enhance pain sensitivity, promote local tissue edema, and further compress surrounding nerves and muscles - ultimately increasing recurrence susceptibility. This mechanism also explains why elevated IL-1β (a key pro-inflammatory cytokine) emerged as an independent risk factor [24].

From a biomechanical perspective, prolonged sitting (a common manifestation of long working hours) increases lumbar intervertebral disc pressure to 1.7 times that of standing [25], accelerating nucleus pulposus dehydration and annulus fibrosus injury. Prolonged standing, another form of extended working posture, causes lumbar muscle fatigue and strain, reducing muscle elasticity and lumbar stability. Both postures ultimately elevate recurrence risk. Markova et al. [26] evaluated the relationship between LBP and prolonged sitting posture using photogrammetric images, posture-

angle calculations, machine-learning models, and questionnaire-based self-reports, confirming the adverse effects of prolonged labor on the lumbar spine.

Psychosocial factors also play a crucial role in LBP recurrence. Huang et al. [27] reported that anxiety was an independent risk factor for LBP recurrence. In an anxious state, the body releases substances such as cortisol and adrenaline, causing involuntary muscle tension, particularly in the lumbar muscles. This not only impairs local lumbar blood circulation, causing muscle hypoxia and metabolic product accumulation, but also reduces the pain threshold, making patients more sensitive to pain. In their cohort of 341 LBP patients, recurrence risk was significantly higher among those with anxiety.

Although previous studies [28-30] have identified advanced age as a risk factor for LBP recurrence, our study (focusing on 18-35-year-old population) found no significant association. This is likely because individuals in this age group are generally in a physiologically stable phase. During this period, significant degenerative changes in bones, muscles, and intervertebral discs are uncommon, and the cumulative effects of chronic conditions have not yet fully manifested. Consequently, age-related physiologic decline did not cause significant variation in our sample, resulting in the negligible influence of age on recurrence outcome.

Interaction analysis of factors influencing LBP recurrence

In addition to single risk factors, this study identified significant interactions among multiple factors, further elucidating the multifactorial synergistic mechanisms underlying LBP recurrence. Specifically, three multiplicative interactions and one positive additive interaction were detected, each with clear pathologic implications and clinical relevance.

The first significant multiplicative interaction was between BMI and daily working hours (OR=2.725). Individuals with high BMI often have weakened core muscle strength, while prolonged working hours (resulting in extended sitting or standing) further increase lumbar spine load. The coexistence of these two factors aggravates lumbar biomechanical imbalance. For example, in individuals with high BMI ($\geq$28 kg/m^2), long hours of desk work can increase intervertebral disc pressure to 2.5 times that of standing [31]. This compounded mechanical stress accelerates disc degeneration, aligning with the "prolonged work-poor posture-spinal degeneration" cascade reported by Escoto et al. [32] in subway workers with extended working hours. Abramowitz et al. [33] also noted that, among U.S. non-high-intensity workers, prolonged working hours may promote weight gain (causing high BMI) through the metabolic inhibitory effect of sedentary behavior, forming a secondary cycle that further increases the risk of LBP recurrence.

The second key interaction was between WBC and anxiety, demonstrating both significant multiplicative (*OR*=26.808) and positive additive interactions (*RERI*=3.928). This interaction reflects the bidirectional regulatory cycle between inflammatory response and psychological stress [34]. On the one hand, anxiety can activate the sympathetic nervous system, promoting the release of pro-inflammatory factors such as TNF-α and IL-6, while impairing the body's anti-inflammatory capacity; on the other hand, elevated systemic inflammation (marked by elevated WBC) can affect neurotransmitter metabolism through neuro-immune interactions, further exacerbating anxiety. This vicious cycle amplifies the local inflammatory response and pain sensitivity in the lumbar region, directly increasing the risk of LBP recurrence. The additive interaction results further showed that the attributable proportion (AP) of this interaction to recurrence risk was 1.294, meaning that 29.4% of the recurrence risk from combined elevated WBC and anxiety could be attributed to their interaction. Clinically, for patients with both elevated WBC ($\geq$10.0×10^9/L) and anxiety (SAS score >49), combining anti-inflammatory treatment with cognitive behavioral therapy or mindfulness meditation may help disrupt this vicious cycle and effectively reduce recurrence risk [35, 36].

The third significant multiplicative interaction was between anxiety and daily working hours (OR=32.980), which had the most prominent impact on LBP recurrence. Long working hours not only cause physical fatigue but also increase the mechanical pressure on the lumbar spine, whereas anxiety can induce persistent

tension in the lumbar muscles. The synergy of these two factors reinforces the "psychology-muscle-pain" pathway: muscle tension impairs local blood circulation in the lumbar spine, leading to the accumulation of metabolic by-products and reduced spinal stability, while work-related fatigue further weakens the body's resilience against lumbar discomfort. This finding suggests that in clinical practice, simply relieving pain symptoms without addressing anxiety (through psychological intervention) or adjusting work patterns (e.g., reducing working hours, optimizing work postures) is difficult to achieve effective prevention and control of LBP recurrence.

Clinical significance of the nomogram model for predicting LBP recurrence

The nomogram developed in this study integrates three categories of risk factors - inflammatory factors (elevated WBC and IL-1β), psychological status (anxiety), occupational exposure (daily working hours >8 h) - and shows significant advantages in predicting LBP recurrence. It provides a practical tool for individualized risk stratification in clinical practice.

First, compared to previous LBP recurrence prediction models, this model offers more comprehensive risk coverage. For example, Krause et al. [37] only included exercise and physical therapy patterns/frequency in their prediction model, while Gevers-Montoro et al. [38] only focused on urinary TNF-α as a potential biomarker for chronic primary LBP. In contrast, our model integrates biological, psychological, and social factors, aligning more closely with the complex, multifactorial pathogenesis of LBP recurrence and avoiding the limitations of single-dimension models. This multi-dimensional design enables clinicians to assess recurrence risk more holistically, rather than relying on a single type of indicator.

Second, the model demonstrated high predictive accuracy and good generalizability. In the derivation cohort (n=216), the AUC was 0.906 (*95% CI*: 0.861-0.952), indicating excellent discrimination. The Hosmer-Lemeshow test showed P=0.06, suggesting good consistency between the predicted and observed recurrence probabilities (calibration degree). In the external validation cohort (n=46), the model maintained an AUC of 0.902 (95% CI: 0.805-0.999) and a Hosmer-Lemeshow test *P*=0.61, confirming its stable predictive performance in external populations. These metrics surpass those reported for many existing LBP prediction models [39], meeting the requirements of precision medicine for the accuracy and generalizability.

Third, the model exhibits clear clinical utility. Decision curve analysis (DCA) showed that in the threshold probability range of 15%-65%, the net benefit of the model was significantly higher than the two extreme strategies. This means that, when clinicians apply this model to identify high-risk patients within this range, the clinical benefits (reducing missed recurrence and guiding timely intervention) outweigh potential harms (avoiding unnecessary intervention for low-risk patients). In addition, the weighted scoring system of the nomogram - highlighting anxiety as the strongest contributor - emphasizes the importance of incorporating psychological intervention into clinical practice. Alongside inflammation control and work-pattern adjustments, active psychological counseling or treatment for patients with anxiety can promote interdisciplinary, comprehensive management of LBP and further reduce recurrence [40, 41].

Study limitations and future directions

This study has several limitations: ① Its retrospective design may introduce selection bias, and the non-significant difference in treatment methods might be related to the limited sample size. The significant gender difference observed in the validation cohort (**Table 5**) was likely attributed to random variation in the small sample size (n=46), rather than selective inclusion, as gender was not associated with recurrence in the derivation cohort and did not affect model performance; ② The external validation cohort (n=46) was relatively small, necessitating large prospective studies to enhance generalizability; ③ The model lacks imaging indices (e.g., disc degeneration) and long-term follow-up data (only 1-month recurrence evaluated). Future research should adopt prospective design with larger samples (≥200) and incorporate imaging features to refine prediction accuracy; in addition, the model's long-term predictive efficacy and stratified interventions in real-world settings should also be explored.

Conclusion

Elevated WBC, elevated IL-1β, anxiety, and working hours >8 h/day were independent risk factors for LBP recurrence. Significant multiplicative interactions exist between BMI-work hours, WBC-anxiety, and anxiety-work hours. The nomogram demonstrates good discriminative ability (AUC=0.906/0.902) and clinical utility (15%-65% threshold), supporting its application in precision interventions that integrate anti-inflammatory, psychological, and biomechanical strategies. These findings emphasize the importance of synchronizing work-pattern adjustment and psychosocial management for patients with obesity, inflammatory activity, or anxiety to reduce recurrence risk.

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Disclosure of conflict of interest

None.

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