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Abstract

Background

Patients undergoing resection of a pulmonary nodule face uncertainty about a possible lung cancer diagnosis, yet the trajectories of anxiety, depressive symptoms, and pain across this perioperative transition are poorly characterized. This prospective cohort study characterizes these trajectories from before surgery to 6 months after pulmonary nodule resection and compares them between patients whose nodules proved benign versus malignant.

Methods

We enrolled 638 consecutive patients undergoing pulmonary resection for clinically suspected early lung cancer; after exclusions, 608 (34 benign, 574 malignant) were included. Pain (Faces Pain Scale–Revised [FPS-R]) and anxiety intensity (Visual Analog Scale for Anxiety [VAS-A]) were assessed preoperatively, on postoperative days (POD) 1, 3, and 7, and at 3 and 6 months; depressive symptoms (Patient Health Questionnaire-9 [PHQ-9]) and generalized anxiety (Generalized Anxiety Disorder-7 [GAD-7]) were assessed preoperatively and at 3 and 6 months. Pathological results were disclosed at a median of 4 days (IQR 4–6) postoperatively. Trajectories were modeled with linear mixed-effects models using time as a categorical factor, reporting estimated marginal means (EMMs) and 95% confidence intervals.

Results

Pain peaked on POD1 and declined thereafter, whereas anxiety and depressive symptoms decreased steadily from baseline. Trajectories did not differ between benign and malignant groups (all group

and group × time effects P > 0.05). Preoperatively, 12.0% (73/608) screened positive for depressive symptoms (PHQ-9 ≥ 5) and 11.8% (72/608) for anxiety symptoms (GAD-7 ≥ 5). Among patients with malignant nodules, the proportion screening positive at 3 and 6 months was 8.0% (26/325) and 2.7% (7/264) for depression, and 5.9% (19/325) and 2.3% (6/264) for anxiety; no patient with a benign nodule screened positive postoperatively.

Conclusions

After pulmonary nodule resection, pain rose acutely then recovered toward baseline, whereas anxiety and depressive symptoms improved steadily, with parallel trajectories regardless of benign or malignant pathology. Because depression and anxiety were not measured during the immediate postoperative period, these data cannot attribute symptom improvement to diagnostic disclosure; it likely reflects surgical recovery and a standardized perioperative pathway.

Trial registration

ChiCTR2400092948

November 26, 2024

(https://www.chictr.org.cn/historyversionpub.html?regno=ChiCTR2400092948).

Keywords

Pulmonary Nodules, Pulmonary resection, Cohort study, Patient-Reported Outcomes, Anxiety, Depression, Pain

1 Background

The widespread application of low-dose computed tomography (LDCT) in lung cancer screening

has markedly increased in the detection rate of pulmonary nodules[1]. Because a considerable proportion of pulmonary nodules are benign or indolent, clinical guidelines generally recommend active surveillance with follow-up for indeterminate nodules[2-5]. The observation period is, however, often psychologically challenging. Uncertain pulmonary nodules frequently evoke sustained concern for cancer, producing clinically significant anxiety or depressive symptoms. The detection rates of anxiety symptoms among patients with pulmonary nodules range from approximately 9.9%-47.8%, while depressive symptoms ranges from roughly 14.6%-44.2%, significantly exceeding rates in the general population[6-8]. This psychological burden is not static but fluctuates dynamically across the diagnostic and management pathway. Surgical intervention, a critical modality in the diagnosis and management of pulmonary nodules, is itself a stressor: patients commonly worry about surgical safety and pain before the operation, and must subsequently confront the pivotal psychological transition of receiving a definitive pathological diagnosis after the procedure. Detection rates of anxiety and depressive symptoms in newly diagnosed lung cancer patients have been reported as high as 56.1% and 53.1% respectively[9]. A lung cancer diagnosis can constitute a dual burden—coping with the diagnosis itself while also facing treatment-related and prognostic uncertainty[10, 11] which may compromise quality of life and interfere with treatment adherence, potentially influencing disease outcomes[12].

Many patients and some clinicians still assume that small pulmonary nodules are asymptomatic; however, symptoms encompass both physical and psychological dimensions[5, 13, 14]. Research on the dynamic changes in depression and anxiety from preoperative suspicion through postoperative pathological diagnosis in patients with small pulmonary nodules at high clinical suspicion of lung cancer remains limited. Most studies focus either on the psychological state of

patients with pulmonary nodules or on the distress of those with confirmed lung cancer, while the psychological adaptation during the transition from "suspected cancer" to "definitive diagnosis" is seldom examined. Furthermore, although psychological interventions—such as positive-emotion guidance, individualized psychological care, and dialectical behavior therapy—have shown efficacy in alleviating negative emotions in cancer patients, their optimal timing requires more precise evidence regarding the critical points at which patients' psychological states change[15].

To guide this investigation, we adopt two complementary perspectives on psychological adaptation to pulmonary nodule management. The disease-label perspective holds that receiving a cancer diagnosis is a discrete psychological "watershed" that would produce a divergent—and worse—trajectory in patients whose nodules prove malignant. The alternative common-factor perspective emphasizes experiences shared by all surgical patients—the stress of surgery, acute postoperative pain, symptom relief, the certainty of a definitive pathological result, and standardized follow-up—which would produce parallel trajectories of recovery regardless of the final diagnosis. These perspectives generate competing, testable hypotheses: (H1) pain rises acutely in the immediate postoperative period and then declines toward baseline by 6 months in both groups; (H2) anxiety and depressive symptoms decline from the preoperative assessment to 6 months postoperatively in both groups; and (H3) the trajectories of patients with malignant versus benign pathology diverge (disease-label perspective) rather than run parallel (common-factor perspective).

Accordingly, this study aims to characterize the trajectories of anxiety, depressive symptoms, and pain from the preoperative assessment through 6 months postoperatively in patients undergoing pulmonary resection for nodules, stratified by final pathological diagnosis (malignant [lung cancer] versus benign), using multiple instruments (APAIS, FPS-R, VAS-A, PHQ-9, and GAD-7) at pre-

specified time points, and to test whether the two groups' trajectories differ. The findings are intended to identify the timing of psychological distress in this population and to inform timely, appropriately targeted psychological support, advancing patient-centered integrated physical and mental healthcare. This cohort study is reported in line with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement [16].

2 Methods

2.1 Study Design and Patients

All participants provided written informed consent before enrollment. Patients scheduled for pulmonary resection for detected pulmonary nodules highly suspected of lung cancer were consecutively enrolled from the Department of Thoracic Surgery, Huaxi Tianfu Hospital, Sichuan University, between November 2024 and August 2025. Inclusion criteria were as follows: (1) age ⩾18 years; (2) pulmonary nodules with a diameter ranging from 0.5 cm to 3 cm and being highly suspected of lung cancer; and (3) conscious with adequate cognitive and communication abilities. Exclusion criteria were: (1) a history of psychiatric disorders or cognitive impairment precluding questionnaire completion; (2) a previous history of lung cancer or other malignancy; and (3) age ⩾ 85 years. Of the 638 consecutively enrolled patients, 12 were excluded because the maximum diameter of the surgically resected nodule fell outside the 0.5–3.0 cm range, and 18 were excluded because they had missing data at three or more time points. The remaining 608 patients (34 benign, 574 malignant) were included in the final analysis (Fig. 1).

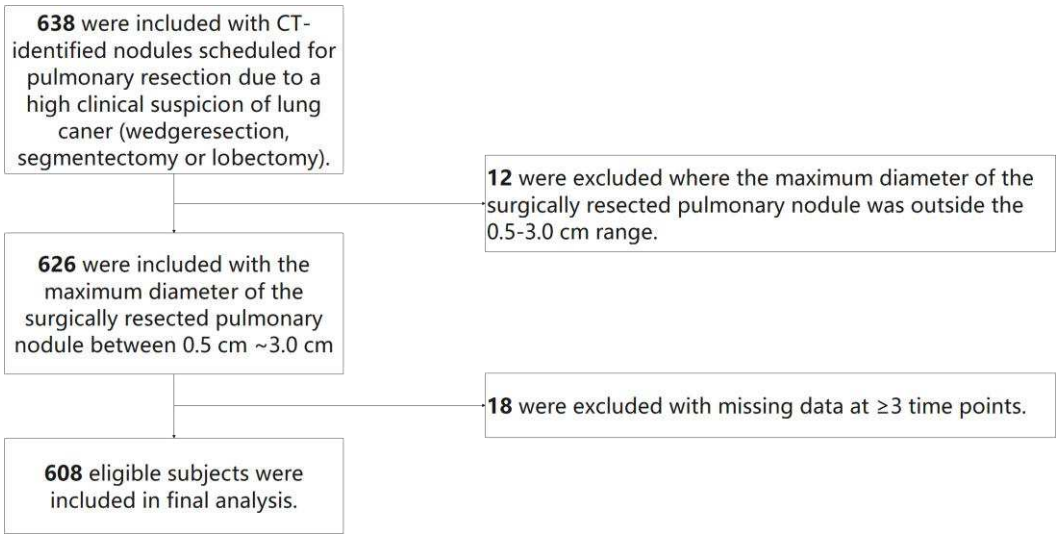

Fig. 1 Flowchart of Study Patient Selection.

2.2 Study Groups and Data Collection

Patients were divided into two groups according to the final postoperative pathological diagnosis: the benign group (benign nodules, e.g., granuloma, hamartoma, fibrous focus) and the malignant group (primary lung cancer, including adenocarcinoma, squamous cell carcinoma, etc.). The date on which each patient was informed of their pathological diagnosis was recorded to establish the timing of diagnostic disclosure relative to the postoperative assessments. Baseline characteristics were collected from the electronic medical record system, including age, sex, body mass index (BMI), smoking history, comorbidities, nodule imaging characteristics (size, location), surgical approach (wedge resection, segmentectomy, lobectomy, or other), length of hospital stay (LOS), and adjuvant treatment.

Data collection occurred at six pre-specified time points: preoperative (Pre-op), POD1, POD3, POD7, 3 months postoperatively, and 6 months postoperatively. Face-to-face follow-ups were conducted by uniformly trained researchers in the wards or outpatient clinics using standardized questionnaires. Sociodemographic information (education, ethnicity, marital status, employment,

income, insurance, living arrangements, medication history, and family history of lung cancer) was collected using a brief study-specific questionnaire developed for this study; an English-language version is provided as Additional file 1. The specific time windows for each outcome measure are illustrated in Fig. 2.



Fig. 2 Schematic Diagram of the Primary Outcome Measures Assessment Timeline

2.3 Study Tools and Measurements

2.3.1 Preoperative anxiety and information need

Amsterdam Preoperative Anxiety and Information Scale (APAIS) [17]: administered at the Pre-op time point to assess surgery- and anesthesia-related anxiety and the need for information before surgery.

2.3.2 Anxiety

Visual Analog Scale for Anxiety (VAS-A) [18]: a straight 0–10 line (0 = "no anxiety", 10 = "extreme anxiety") on which patients mark their current anxiety level, providing an intuitive measure of momentary anxiety intensity at all six time points.

Generalized Anxiety Disorder 7-item (GAD-7) Scale [19]: administered at Pre-op, 3 months, and 6 months to assess generalized anxiety symptoms over the preceding two weeks. Seven items are each

scored 0–3 (total 0–21); a score ≥ 5 suggests the presence of clinically relevant anxiety symptoms.

2.3.3 Pain

Wong-Baker FACES Pain Rating Scale-Revised (FPS-R) [20]: administered at all six time points. It consists of six facial expressions corresponding to scores from 0 to 10, with higher scores indicating greater pain intensity.

2.3.4 Depression

Patient Health Questionnaire-9 (PHQ-9) [21]: administered at Pre-op, 3 months, and 6 months to assess depressive symptoms over the preceding two weeks. Nine items are each scored 0–3 (total 0–27); a score ≥ 5 suggests the presence of clinically relevant depressive symptoms.

2.4 Statistical Analysis

Analyses were performed in R (version 4.6.0). A two-sided $P < 0.05$ was considered statistically significant. Continuous variables were summarized as mean ± standard deviation (SD) or median (interquartile range [IQR]) according to the Shapiro-Wilk test (test level $\alpha = 0.05$). Categorical variables were summarized as frequency (percentage). Baseline comparisons. Independent-samples t-tests (with variance homogeneity verified by Levene's test) were used for normally distributed variables, while the Mann-Whitney U test was applied for non-normally distributed variables. Chi-square tests were used for comparisons of categorical variables between groups. When the conditions for the chi-square test were not met (e.g., more than 20% of cells had expected counts < 5), Fisher's exact test was employed.

Longitudinal Analysis of Outcome Indicators

Because the observed pain and anxiety trajectories were markedly nonlinear (pain peaked on POD1),

time was modeled as a categorical factor in the primary analysis, and estimated marginal means (EMMs) with 95% confidence intervals (CIs) were computed for each time point by group and are displayed in Figs. 4–6. Models included fixed effects for group, time (categorical), and their interaction, with subject-level random intercepts; parameters were estimated by restricted maximum likelihood, and 95% confidence intervals were computed using the normal approximation. The sensitivity of results to this specification was assessed in two ways: (i) modeling time as a continuous variable with a natural cubic spline, with model fit compared by Akaike information criterion (AIC) (Supplemental Table 9); and (ii) adding surgical approach as an additional covariate (Supplemental Table 10). Model diagnostics (residual Q–Q plots, residuals-versus-fitted plots, and residual histograms) are presented in Supplemental Figures 1–4.

Binary outcomes. The proportion screening positive for depressive symptoms (PHQ-9 $\geqslant$ 5) and for anxiety symptoms (GAD-7 $\geqslant$ 5) was analyzed with logistic regression models (fixed effects for group, time, and their interaction) with likelihood-ratio tests. Because no benign-group participant screened positive at 3 or 6 months (complete separation), a subject-level random intercept could not be reliably estimated; between-group differences in the binary outcomes were therefore tested at each time point with Fisher's exact test. These proportions were calculated among participants who completed the questionnaire at each time point (per-timepoint denominators), not against the full baseline sample, to avoid misstating the proportion screening positive under attrition.

Between-group comparisons at each time point. Between-group differences in continuous scores at individual time points were derived from the linear mixed-effects models as contrasts of estimated marginal means; raw descriptive statistics and per-timepoint between-group P values (contrasts of estimated marginal means) are provided in Supplemental Tables 2–7. Missing data. Follow-up at 3

and 6 months was conducted during routine postoperative outpatient visits; missing assessments mainly reflected loss of contact or declined further follow-up, and no participant died during the study period. No imputation was performed; linear mixed-effects models used all available observations via restricted maximum likelihood, which provides valid estimates under a missing-at-random assumption. To examine this assumption, baseline symptom scores (PHQ-9, GAD-7, FPS-R, and VAS-A) were compared between participants with and without 3- and 6-month follow-up, and the primary models were refitted among participants with complete 3- and 6-month data as a sensitivity analysis. The number of participants completing each assessment at each time point is reported (Supplemental Table 8).

3 Results

3.1 Patient characteristics, attrition, and diagnostic disclosure

A total of 638 patients were enrolled, of whom 608 (34 benign, 574 malignant) were included in the final analysis: 34 (5.6%) with benign and 574 (94.4%) with malignant pathology, consistent with the high positive predictive value of the preoperative clinical assessment. Most demographic and clinical characteristics did not differ between the groups (all $P > 0.05$), including age, sex, education, ethnicity, marital status, employment, income, insurance, living alone status, medication history, family history of lung cancer, smoking history, anthropometric measurements (height, weight, and BMI), blood pressure, routine blood parameters, and tumor biomarkers (Table 1). The maximum diameter of surgically resected pulmonary nodules was similar between the benign and malignant groups (0.97±0.49 cm vs. 1.05±0.52 cm; $P = 0.3578$). The total number of resected pulmonary nodules did not differ (1.12±0.54 vs. 1.21±0.53; $P = 0.3463$), and the distribution of single versus multiple nodules was comparable ($P = 0.1073$) (Table 1). Pathological results were disclosed at a

median of 4 days after surgery (IQR 4–6; range 3–7); the timing was similar in both groups. Accordingly, the POD1 and POD3 assessments generally preceded diagnostic disclosure, whereas the POD7 assessment generally followed it. Median length of hospital stay was 8 days (IQR 7–9; range 3–54), and only five patients (0.8%, all malignant) received adjuvant therapy. The distribution of surgical approach differed between groups ($P = 0.018$, Fisher's exact test): wedge resection 366 (60.2%), segmentectomy 193 (31.7%), lobectomy 45 (7.4%), and other 4 (0.7%) overall (Table 1). Follow-up completion declined over time. Of 608 participants assessed preoperatively, 594 were assessed on POD1, 606 on POD3, 604 on POD7, 349 (57.4%) at 3 months, and 283 (46.5%) at 6 months (Supplemental Table 8). At 3 and 6 months, completion was 24/34 (70.6%) and 19/34 (55.9%) in the benign group versus 325/574 (56.6%) and 264/574 (46.0%) in the malignant group. The higher attrition at 3 and 6 months is addressed as a limitation.

Table 1. Patient Characteristics.

Factor		All(n=608)	Benign (n = 34)	Malignant (n =574)	*P* value
Demographics					
Age (years)	Mean±SD	51.54±13.13	50.68±11.91	51.59±13.21	0.6949
Sex	Male, n (%)	170(27.96%)	10(29.41%)	160(27.87%)	0.8461
	Female, n (%)	438(72.04%)	24(70.59%)	414(72.13%)	
Education	No formal education or Primary school, n (%)	67(11.02%)	0(0%)	67(11.67%)	0.0904
	Junior secondary school, n (%)	125(20.56%)	9(26.47%)	116(20.21%)	
	Senior secondary school (includes general and vocational), n (%)	110(18.09%)	3(8.82%)	107(18.64%)	
	Associate degree, n (%)	127(20.89%)	9(26.47%)	118(20.56%)	
	Bachelor's degree, n (%)	152(25%)	11(32.35%)	141(24.56%)	
	Master's degree or above, n (%)	27(4.44%)	2(5.88%)	25(4.36%)	
Ethnicity	Han Chinese, n (%)	585(96.22%)	33(97.06%)	552(96.17%)	1.000*

	Other ethnic minorities (includes Tibetan, Hui, Manchu, Mongol, Tujia and Yi), n (%)	23(3.78%)	1(2.94%)	22(3.83%)	
Marital Status	Married, n (%)	554(91.12%)	29(85.29%)	525(91.46%)	0.2132*
Employment Status	Employed, n (%)	360(59.21%)	22(64.71%)	338(58.89%)	0.1912
	Student, n (%)	3(0.49%)	1(2.94%)	2(0.35%)	
	Unemployed, n (%)	47(7.73%)	1(2.94%)	46(8.01%)	
	Retired, n (%)	198(32.57%)	10(29.41%)	188(32.75%)	
Monthly Household Income (RMB)	Low Income (<3000 RMB), n (%)	15(2.47%)	2(5.88%)	13(2.26%)	0.2017*
	Lower-Middle Income (3000-9999 RMB), n (%)	194(31.91%)	13(38.24%)	181(31.53%)	
	Upper-Middle Income (10000-19999 RMB), n (%)	91(14.97%)	3(8.82%)	88(15.33%)	
	High Income (>=20000 RMB), n (%)	49(8.06%)	5(14.71%)	44(7.67%)	
	Refused, n (%)	68(11.18%)	4(11.76%)	64(11.15%)	
	Unknown, n (%)	191(31.41%)	7(20.59%)	184(32.06%)	
Health insurance coverage	No health insurance coverage, n (%)	4(0.66%)	0(0%)	4(0.7%)	1.000*
	Public Health Insurance (Basic Medical Insurance for Urban Employees/Basic Medical Insurance for Urban and Rural Residents), n (%)	567(93.26%)	32(94.12%)	535(93.21%)	
	Private Health Insurance , n (%)	37(6.09%)	2(5.88%)	35(6.1%)	
Living alone	YES, n (%)	32(5.26%)	1(2.94%)	31(5.4%)	1.000*
Medication history	Antihypertensive Drugs, n (%)	84(13.82%)	3(8.82%)	81(14.11%)	0.6070*
	Antidiabetic Drugs, n (%)	30(4.93%)	0(0%)	30(5.23%)	0.4020*
	Lipid-Lowering Drugs, n (%)	21(3.45%)	0(0%)	21(3.66%)	0.6231*
Family history of lung cancer (First-degree relative (parent, sibling, child))	YES, n (%)	101(16.61%)	8(23.53%)	93(16.2%)	0.2647
Current smoker	YES, n (%)	57(9.38%)	3(8.82%)	54(9.41%)	1.000*

Anthropometrics and clinical measures					
Height (cm)	Mean±SD	160.69±7.52	162.1±6.82	160.6±7.56	0.2536
Weight (Kg)	Mean±SD	59.79±10.43	60.62±10.21	59.74±10.45	0.6343
BMI (Kg/m^2)	Mean±SD	23.08±3.2	22.93±2.51	23.09±3.24	0.7727
SBP (mmHg)	Mean±SD	123.61±15.82	125.4±15.64	123.5±15.84	0.5099
DBP (mmHg)	Mean±SD	80.05±9.66	81.56±9.11	79.96±9.69	0.3492
RBC (10^{12}/L)	Mean±SD	4.41±0.53	4.48±0.71	4.4±0.52	0.3905
Hb (g/L)	Mean±SD	131.93±16.06	134.7±21.12	131.8±15.71	0.3052
WBC (10^9/L)	Mean±SD	6.29 ± 3.80	5.16 ± 1.92	6.36 ± 3.87	0.4623
NEUT%	Mean±SD	59.29 ± 13.12	55.67 ± 9.81	59.50 ± 13.27	0.2850
ALT (U/L)	Mean±SD	21.43±15.49	21.71±15.71	21.41±15.5	0.9153
AST (U/L)	Mean±SD	23.87±10.64	23±6.65	23.92±10.83	0.6263
Cr (umol/L)	Mean±SD	62.27±14.52	62.88±14.92	62.23±14.51	0.7999
FPG (mmol/L)	Mean±SD	5.06±1.04	4.87±0.62	5.07±1.06	0.2602
AFP (ng/mL)	Mean±SD	3.21±1.78	4.04±3.21	3.18±1.69	0.0516
CEA (ng/mL)	Mean±SD	1.61 ± 1.16	1.45 ± 0.74	1.62 ± 1.17	0.7542
CYFRA 21-1 (ng/mL)	Mean±SD	2.32±4.46	1.9±0.53	2.34±4.57	0.6479
NSE (ng/mL)	Mean±SD	19.8±7.67	18.14±6.34	19.89±7.73	0.2872
SCC (ng/mL)	Mean±SD	1.38±2.2	1.78±2.6	1.36±2.17	0.3685
CA125 (U/mL)	Mean±SD	30.94±39.17	24.7±24.08	31.37±40.08	0.7154
FEV1 (L)	Mean±SD	2.8±1.85	2.78±0.68	2.8±1.9	0.9380
FVC (L)	Mean±SD	3.32±0.77	3.39±0.78	3.32±0.77	0.6005
PEF (L/s)	Mean±SD	7.13 ± 1.84	7.45 ± 1.90	7.11 ± 1.84	0.5648
Surgical and nodule characteristics					
Surgical approach	Wedge resection, n (%)	366 (60.20%)	20 (58.82%)	346(60.28%)	0.0180*
	Segmentectomy, n (%)	193 (31.74%)	8 (23.53%)	185 (32.23%)	
	Lobectomy, n (%)	45 (7.40%)	4 (11.76%)	41 (7.14%)	
	Other, n (%)	4 (0.66%)	2 (5.88%)	2 (0.35%)	
Length of hospital stay (days), median (IQR)	Median(IQR)	8 (7–9)	7.5 (7–10)	8 (7–9)	0.9540
Maximum diameter (cm) of surgically resected pulmonary nodules	Mean±SD; Median(IQR);Range	1.05±0.52;0.9(0.7-1.3);0.5-3.0	0.97±0.49;0.9(0.6-1.1);0.5-2.7	1.05±0.52;0.9(0.7-1.3);0.5-3.0	0.3578

Total number of surgically resected pulmonary nodules	Mean±SD; Median(IQR);Range	1.2± 0.53;1(1-1);1-5	1.12± 0.54;1(1-1);1-4	1.21± 0.53;1(1-1);1-5	0.3463
Grouping by number of surgically resected pulmonary nodules	1, n (%)	513(84.38%)	32(94.12%)	481(83.80%)	0.1073
	⩾2, n (%)	95(15.63%)	2(5.88%)	93(16.20%)	

Abbreviation

SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; RBC, Red Blood Cell Count; Hb, Hemoglobin; WBC, White Blood Cell Count; NEUT%, Neutrophil Percentage; ALT,Alanine Aminotransferase; AST, Aspartate Aminotransferase; Cr, Creatinine; FPG, Fasting Plasma Glucose; AFP, Alpha-fetoprotein; CEA, Carcinoembryonic Antigen; CYFRA 21-1, Cytokeratin 19 Fragment; NSE, Neuron-specific enolase;SCC, Squamous Cell Carcinoma Antigen; CA125, Cancer Antigen 125; FEV1, Forced Expiratory Volume in the 1st second; FVC, Forced Vital Capacity; PEF, Peak Expiratory Flow; IQR, Interquartile Range.

**, Fisher exact test.*

3.2 Assessment results of the Amsterdam Preoperative Anxiety and Information Scale

Based on APAIS results (Fig. 3 and Supplemental Table 1), preoperative anxiety and information need scores did not differ significantly between the benign (n=34) and malignant (n=574) groups for anesthesia-related anxiety (median [IQR]: 2 [2-3] vs 2 [2-4]; $P>0.05$, Fig. 3A), surgery-related anxiety (3 [2-5] vs 2 [2-4]; $P>0.05$, Fig. 3B), total anxiety score (6 [4-8] vs 4 [4-8]; $P>0.05$, Fig. 3C), or information need score (2 [2-5] vs 2 [2-5]; $P>0.05$, Fig. 3D). (all $P > 0.05$, Mann–Whitney U test).

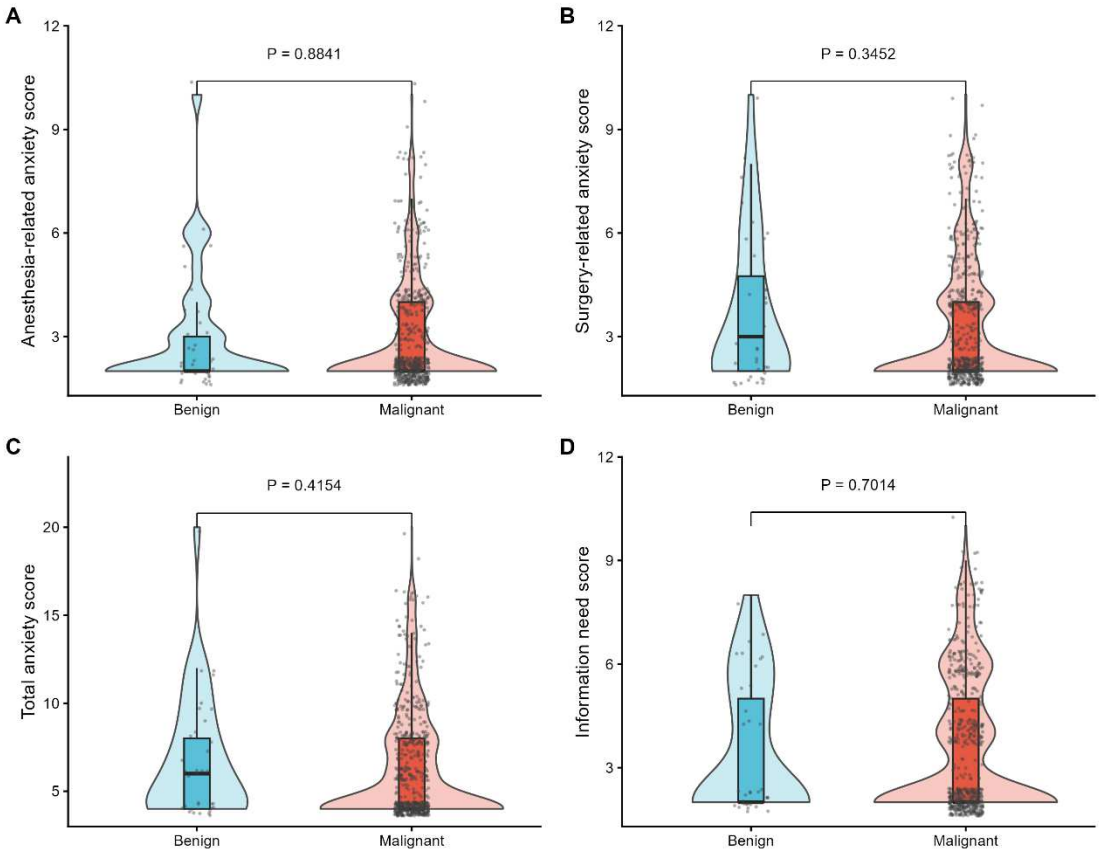

Fig. 3 Distribution of APAIS scores in Benign and Malignant group.

3.3 Pain and anxiety trajectories (FPS-R and VAS-A).

Longitudinal analysis (Fig. 4 and Supplemental Tables 2–3) showed significant temporal variation in both pain (FPS-R) and anxiety (VAS-A) in both groups (FPS-R time effect: $P < 0.0001$; VAS-A time effect: $P < 0.0001$), but no significant group effect (FPS-R P = 0.9930; VAS-A $P = 0.1815$) and no significant group × time interaction (FPS-R $P = 0.2561$; VAS-A $P = 0.5377$), indicating parallel trajectories between groups. Estimated marginal means (with 95% CIs) for each instrument are shown in Fig. 4.

Post-hoc tests demonstrated that FPS-R scores at all postoperative time points were significantly higher than preoperative levels in both groups (all $P < 0.05$), rising sharply on POD1 (EMM, 3.53 [95% CI, 3.12–3.94] in the benign group and 3.43 [95% CI, 3.32–3.53] in the malignant group) and

declining gradually thereafter. A transient between-group difference was noted at POD7 (EMM, 2.65 [95% CI, 2.24–3.06] in the benign group vs. 2.22 [95% CI, 2.12–2.32] in the malignant group; $P = 0.0463$) but did not persist.

For anxiety, the malignant group showed marginally higher VAS-A scores at 3 months (EMM, 0.98 [95% CI, 0.80–1.16] vs. 0.30 [95% CI, −0.36 to 0.97] in the benign group; $P = 0.0532$), a trend that diminished by 6 months (EMM, 0.68 [95% CI, 0.48–0.88] vs. 0.43 [95% CI, −0.31 to 1.17] in the benign group); no other time point differed between groups. These isolated single-timepoint differences should be interpreted cautiously given the absence of an overall group effect.

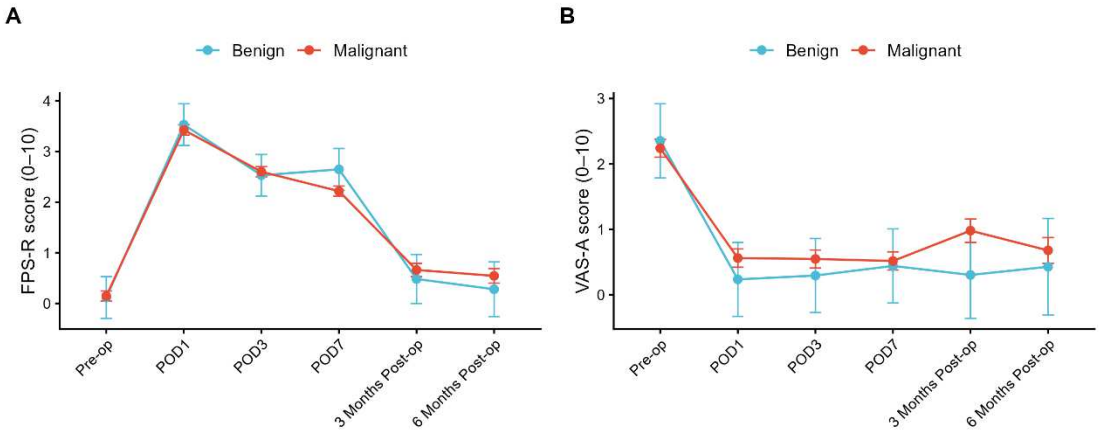

Fig. 4 FPS-R Score and VAS-A Score Trajectories in Benign vs Malignant Cases. Points represent estimated marginal means from linear mixed-effects models; error bars indicate 95% confidence intervals.

3.4 Depressive and anxiety symptoms (PHQ-9 and GAD-7)

Depressive symptoms improved significantly over time (Time P-value = 0.0001, Fig. 5A). Preoperatively, the PHQ-9 scores and the proportion screening positive were similar between groups

(Score P = 0.8824, Fig. 5A; screening-positivity P = 1.0000, Fig. 5C). At 3 months, PHQ-9 scores tended to be higher in the malignant group than in the benign group, although this difference did not reach statistical significance (EMM, 1.19 [95% CI, 0.89–1.49] vs. 0.08 [95% CI, −1.02 to 1.18]; P = 0.0559, Fig. 5A), and was no longer present at 6 months (EMM, 0.59 [95% CI, 0.26–0.92] vs. 0.38 [95% CI, −0.85 to 1.61]; P = 0.7475, Fig. 5A). The proportion screening positive for depressive symptoms fell from 11.8% (4/34) preoperatively to 0% (0/24 at 3 months and 0/19 at 6 months) in the benign group, and from 12.0% (69/574) preoperatively to 8.00% (26/325) at 3 months and 2.65% (7/264) at 6 months in the malignant group (Fig. 5C). Neither the group effect nor the group × time interaction was significant for scores (group P = 0.2682; group × time P = 0.2301) or for the binary screening outcome (group P = 0.2459; group × time P = 0.1579). See Supplemental Tables 4–5 for further details.

Anxiety symptoms likewise improved over time (Time P-value < 0.0001, Fig. 6A; Time P-value < 0.0001 for screening positivity). Preoperatively, there were no significant differences in GAD-7 scores (P = 0.7946) or in the proportion screening positive (P = 1.0000) (Fig. 6C). At 3 and 6 months, scores did not differ between groups (3 months: EMM, 0.82 [95% CI, 0.57–1.08] in the malignant group vs. 0.08 [95% CI, −0.86 to 1.02] in the benign group; 6 months: EMM, 0.43 [95% CI, 0.15–0.70] in the malignant group vs. 0.12 [95% CI, −0.92 to 1.16] in the benign group; P = 0.1335 and P = 0.5811, respectively). The proportion screening positive for anxiety symptoms fell from 11.8% (4/34) preoperatively to 0% (0/24 at 3 months and 0/19 at 6 months) in the benign group, and from 11.8% (68/574) preoperatively to 5.85% (19/325) at 3 months and 2.27% (6/264) at 6 months in the malignant group (Fig. 6C). Neither the group effect nor the group × time interaction was significant for scores (group P = 0.2557; group × time P = 0.5345) or for the binary screening outcome (group

P = 0.3489; group × time P = 0.2288). See Supplemental Tables 6–7.

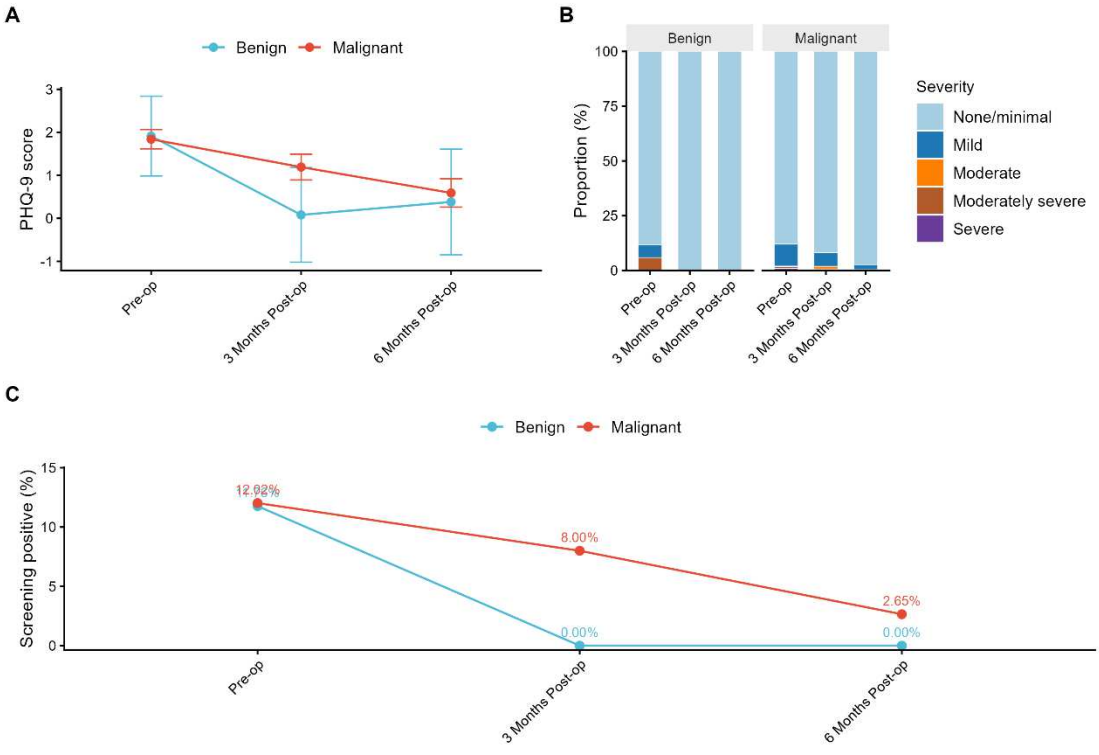

Fig. 5 PHQ-9 score (A), distribution of PHQ-9 severity grades (B), and proportion screening positive for depressive symptoms (C) by group and time point. In panel A, points represent estimated marginal means with 95% confidence intervals from linear mixed-effects models.

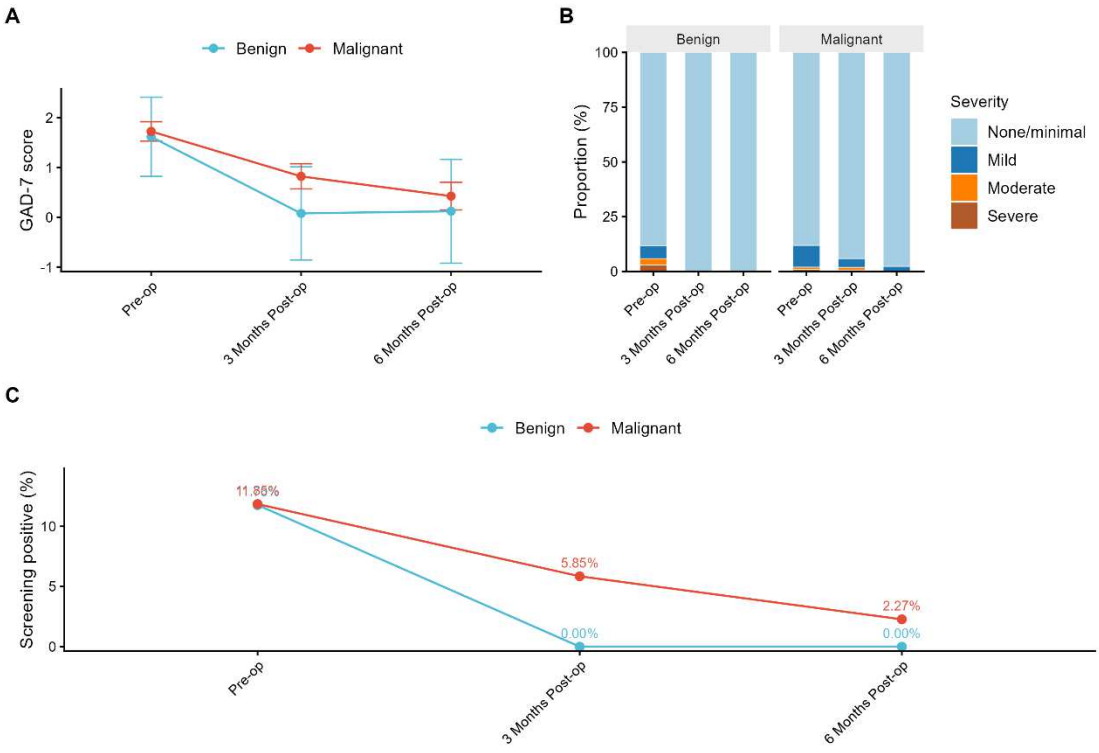

Fig. 6 GAD-7 score (A), distribution of GAD-7 severity grades (B), and proportion screening positive for anxiety symptoms (C) by group and time point. In panel A, points represent estimated marginal means with 95% confidence intervals from linear mixed-effects models.

3.5 Sensitivity analyses

Modeling time as a continuous variable with a natural cubic spline improved fit over the linear-time specification for VAS-A (AIC 11797.7 vs. 12140.0) and FPS-R (AIC 11140.8 vs. 11684.3), confirming the nonlinearity of these trajectories (Supplemental Table 9); spline models were not estimable for PHQ-9 and GAD-7, which were measured at only three time points. Adding surgical approach as a covariate did not materially change the group, time, or interaction effects for VAS-A, FPS-R, or PHQ-9; surgical approach was significant only for GAD-7 (F = 2.76, P = 0.042) (Supplemental Table 10). To assess the influence of attrition, baseline symptom scores did not differ significantly between participants with and without 3- or 6-month follow-up (all P > 0.05), except

for a non-significant trend toward higher baseline GAD-7 scores among 3-month non-completers (mean 1.85 vs. 1.62; P = 0.088). Refitting the primary models among the 267 participants with complete 3- and 6-month data left the conclusions unchanged (significant time effect and non-significant group and group × time effects for all four outcomes [Supplemental Table 11]).

4 Discussion

In this prospective cohort of 608 patients undergoing pulmonary nodule resection, anxiety and depressive symptoms followed broadly parallel, improving trajectories over six months, whereas pain rose acutely after surgery before returning toward its preoperative baseline regardless of whether final pathology was benign or malignant.

This pattern is more consistent with the common-factor perspective than with the disease-label perspective, at least over the first six postoperative months. Several aspects of the design and context are important for interpreting this finding.

First, the timing of diagnostic disclosure clarifies what the assessment schedule can and cannot establish. Pathological results were disclosed at a median of 4 days postoperatively; the POD1 and POD3 assessments therefore largely preceded disclosure, and the immediate rise in pain on POD1 is best understood as a surgical-recovery phenomenon rather than a response to the diagnosis itself. Because PHQ-9 and GAD-7 were administered only preoperatively and at 3 and 6 months, depressive and anxiety symptoms were not measured during the immediate postoperative period in which a disclosure effect would most plausibly occur. Our conclusion is therefore deliberately limited: the data show that the two groups' trajectories did not diverge over six months, not that diagnostic disclosure had no psychological effect.

Second, our findings engage the existing literature in two directions. On one hand, many studies

emphasize persistent psychological stress following a cancer diagnosis[22-24], including fear of cancer recurrence (FCR), which is strongly associated with anxiety and depression and may intensify over the first year[25, 26]. This contrasts with the generally improving symptoms in our cohort. The discrepancy likely reflects differences in populations and follow-up windows: we studied early-stage lung cancer and benign lesions assessed within six months of surgery, whereas studies emphasizing longer-term distress often include more advanced disease or the sustained uncertainties of systemic therapy. On the other hand, our results are partially supported by work showing that depressive and anxiety symptoms also decreased over time in patients with stage IV non-small cell lung cancer[27], suggesting that some degree of psychological adaptation occurs even in advanced disease. Similarly, psychological resilience in newly diagnosed lung cancer patients follows distinct longitudinal trajectories shaped by clinical and psychosocial factors[28], further supporting the notion that psychological adaptation is a meaningful and variable process in this population. Several nursing studies also support the value of universal psychological support, consistent with our observation that the diagnosis itself was not associated with a divergent short-term trajectory[29-34]; a randomized trial showed that systematic nursing intervention based on a stress-induced situation, affective, bodily, and cognitive reactions (SABC) framework alleviated anxiety and depression in patients undergoing lung cancer surgery[35].

Third, the high positive predictive value of the preoperative clinical assessment (574/608, 94.4%) is relevant context: most patients in this cohort received a definitive, usually early-stage, diagnosis and a standardized treatment pathway, which may itself be reassuring. The surgical approach distribution differed modestly between groups (P = 0.018), with more lobectomies and "other" resections in the small benign group; however, including surgical approach as a covariate did not

alter the main trajectory findings (except for a marginal association with GAD-7), suggesting that the imbalance did not drive the observed similarities.

These results have clinical implications. They suggest that low-intensity psychoeducation addressing common surgical concerns could be offered to all patients undergoing pulmonary nodule surgery—rather than reserving support exclusively for those with confirmed malignancy—combined with routine screening so that targeted psychological intervention is directed toward the minority who screen positive (approximately 12% preoperatively); a standardized perioperative pathway could make such tiered support cost-effective. Existing literature indicates that stepped psychological education and counseling around six months after diagnosis may help prevent or alleviate later exacerbations of FCR and emotional distress. Our data support routine psychological screening during the early postoperative phase (e.g., around discharge) and at the three-month follow-up, with targeted support for those who screen positive; however, because depression was not assessed during hospitalization, our data do not empirically identify discharge as a depression-specific intervention window, and the three-month recommendation rests primarily on the anxiety and pain trajectories. For patients with malignant nodules, monitoring should extend to at least six months postoperatively.

This study has several limitations. First, the benign group was small (n = 34), and its severe imbalance relative to the malignant group (n = 574) limits statistical power to detect subtle between-group differences; the absence of significant group or group × time effects cannot be taken as evidence of strict equivalence. This imbalance also meant that no postoperative screening-positive cases were observed in the benign group, precluding stable binary comparisons. Second, follow-up was restricted to six months, and loss to follow-up was substantial (42.6% at 3 months and 53.5%

at 6 months), with higher attrition in the malignant than the benign group; although baseline symptom scores did not differ significantly between completers and non-completers and a complete-case analysis yielded similar results (Supplemental Table 11), we cannot exclude informative dropout, and if loss to follow-up depended on unmeasured factors the observed trajectories could be biased. Third, the design could not measure the immediate psychological response to diagnostic disclosure, since depressive and anxiety symptoms were not assessed during hospitalization, and all participants underwent surgery, so the relative contributions of surgery versus diagnosis cannot be separated; postoperative complications were likewise not systematically recorded, so their potential influence on symptom trajectories could not be examined. Fourth, the instruments capture distinct constructs—surgery/anesthesia-related anxiety (APAIS), momentary anxiety intensity (VAS-A), and two-week generalized anxiety (GAD-7)—and a score ≥ 5 on PHQ-9 or GAD-7 represents screening positivity, not a clinical diagnosis; accordingly, we report the proportion screening positive rather than the prevalence of depression or anxiety. Fifth, the study was conducted at a single high-volume regional center, which may limit generalizability. Finally, the observational design cannot establish causality; randomized trials are needed to evaluate targeted psychological interventions.

Conclusions

Patients undergoing pulmonary nodule resection showed parallel trajectories over the six months following surgery—anxiety and depressive symptoms improved, whereas pain returned toward its preoperative level after an early postoperative peak—irrespective of a benign or malignant final diagnosis. Rather than supporting the view that pathological diagnosis is an absolute psychological

watershed, these findings underscore the shared influence of the surgical episode and subsequent recovery on short-term psychological adaptation. The results also delimit what the study design can establish, given that depressive and anxiety symptoms were not measured during hospitalization. Future research should extend follow-up, expand the benign cohort, measure the immediate post-disclosure period, and evaluate universal psychological interventions developed from this evidence.

List of abbreviations

Abbreviation	Full Term
AFP	Alpha-fetoprotein
ALT	Alanine Aminotransferase
APAIS	Amsterdam Preoperative Anxiety and Information Scale
AST	Aspartate Aminotransferase
BMI	Body mass index
CA125	Cancer Antigen 125
CEA	Carcinoembryonic Antigen
Cr	Creatinine
CYFRA 21-1	Cytokeratin 19 Fragment
DBP	Diastolic Blood Pressure
EMM	Estimated marginal mean
FCR	Fear of cancer recurrence
FEV1	Forced Expiratory Volume in the 1st second
FPG	Fasting Plasma Glucose
FPS-R	Wong-Baker Faces Pain Scale-Revised
FVC	Forced Vital Capacity
GAD-7	Generalized Anxiety Disorder-7
Hb	Hemoglobin
IQR	Interquartile Range
LDCT	Low-dose computed tomography
LOS	Length of hospital stay
NEUT%	Neutrophil Percentage
NSCLC	Non-small cell lung cancer
NSE	Neuron-specific enolase
PEF	Peak Expiratory Flow
PHQ-9	Patient Health Questionnaire-9

POD	Postoperative day
RBC	Red Blood Cell Count
SABC	Stress-induced situation, affective, bodily, and cognitive reactions
SBP	Systolic Blood Pressure
SCC	Squamous Cell Carcinoma Antigen
SD	Standard deviation
VAS-A	Visual Analog Scale for Anxiety
WBC	White Blood Cell Count

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Review Committee of West China Tianfu Hospital, Sichuan University (approval no. 2024(046)). Moreover, this study complied with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for research involving humans. Written informed consent was obtained from all participants prior to data collection.

Consent for publication

Not applicable. This manuscript contains no individual person's data in any form.

Availability of data and materials

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

Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Authors' contributions

YL contributed to conceptualization, resources, supervision, validation, and the writing of the original draft, as well as review and editing. RL contributed to funding acquisition, resources, supervision, validation, and the writing of the original draft, as well as review and editing. TB contributed to conceptualization, formal analysis, project administration, validation, visualization, and the writing of the original draft, as well as review and editing. Yuan Z contributed to data curation, investigation, validation, and the writing of the original draft. Yue Z contributed to data curation, investigation, and the writing of the original draft. MP contributed to data curation, investigation, and the writing of the original draft. BL contributed to formal analysis and software. CM contributed to investigation, validation, and the writing of the original draft. BF contributed to investigation, validation, and the writing of the original draft. All authors read and approved the final manuscript.

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