Related Factors and Risk Prediction of Chronic Pain after Knee Replacement

Ann. Ital. Chir., 2024 95, 5: 934–943
https://doi.org/10.62713/aic.3593

Jun Yang[1], Hui Gao[1], Canbin Wang[1], Jiangjun Zhou[2]

[1]Department of Orthopedics, Yingtan 184 Hospital, 335000 Yingtan, Jiangxi, China
[2]Department of Orthopedics, The 908th Hospital of Joint Logistics Support Force, 330000 Nanchang, Jiangxi, China

AIM: This study aimed to explore potential risk factors associated with chronic pain after total knee arthroplasty (TKA) and to establish the risk prediction model of chronic postoperative pain (CPSP).
METHODS: This study retrospectively analyzed the clinical data of 160 patients who underwent TKA in our hospital between January 2021 and January 2024. Relevant data such as the baseline characteristics, past medical history, CPSP condition, and pain numerical rating scale (NRS) were retrieved from the medical information system. Logistic regression analysis was performed on the risk factors affecting the postoperative CPSP of the patients. The identified risk factors were incorporated to develop a risk-prediction model.
RESULTS: Among the 160 patients, 67 (41.88%) had CPSP at or around the operation incision. The NRS pain score was significantly higher in the CPSP group than in the non-CPSP group during exercise preoperative and 3 months post-operation. Furthermore, the CPSP group had a higher NRS score than the non-CPSP group at rest 3 months after the procedure ($p < 0.05$). We observed that the preoperative NRS score, preoperative hospital for special surgery (HSS) score, postoperative functional training, and postoperative adverse events were the independent factors influencing the occurrence of CPSP after TKA ($p < 0.05$). Additionally, there was a significant positive correlation between preoperative NRS score, postoperative adverse events, and CPSP pain severity, and a significant negative correlation between preoperative HSS score, postoperative functional training, and CPSP pain severity ($p < 0.05$). The receiver operating characteristic (ROC) curve had excellent calibration and prediction capabilities for the predictive model of CPSP after TKA, with the area under the curve (AUC) of 0.868 (95% CI: 0.811–0.925).
CONCLUSIONS: In this study, the predictive model of CPSP risk for patients after TKA surgery was initially constructed, which can help medical staff predict the risk of CPSP in patients after surgery individually, thereby preventing the occurrence of CPSP.

Keywords: knee replacement; chronic pain; pain sensitization; risk factors; prediction model

Introduction

Total knee arthroplasty (TKA) is considered the most effective treatment for advanced knee osteoarthritis, especially in an aging population experiencing higher risk. Consequently, most of these patients are undergoing this surgery [1]. However, 10% to 34% of patients develop chronic postoperative pain (CPSP), which can last for several months or even years. The International Association for the Study of Pain defines chronic postoperative pain as pain lasting more than three months after surgery, excluding other causes such as infection, surgical failure, or recurrence of malignant tumor [2]. Chronic pain after knee joint replacement not only increases the pain experience of patients but also imposes a psychological burden, elevating the likelihood of anxiety, depression, and other mental health issues. Furthermore, it contributes to increased costs for patients. Therefore, chronic pain after knee joint replacement needs significant attention [3, 4].

In clinical practice, medical staff often focus on managing acute pain after TKA, while insufficient attention is given to CPSP after patient discharge. Moreover, there is no clear and effective treatment plan for CPSP after TKA. Although understanding the epidemiology of CPSP has improved, details about its risk factors remain limited. Current research on risk factors of CPSP after TKA surgery primarily focuses on various preoperative indicators, such as the severity and duration of knee joint pain, as well as pain in other areas. The incidence and severity of CPSP vary significantly, and only a few studies have evaluated the relationship between postoperative factors and chronic pain, including acute postoperative pain, anxiety, and other psychological factors [5, 6]. The risk factors assessed in various studies are inconsistent, resulting in different conclusions. For example, a study by Wylde *et al*. [7] indicates that preoperative anxiety affects pain levels in TKA patients one-year post-operation, but this effect will be improved within five years after surgery. It is considered that socio-

Submitted: 8 July 2024 Revised: 15 August 2024 Accepted: 23 August 2024 Published: 20 October 2024
Correspondence to: Jiangjun Zhou, Department of Orthopedics, The 908th Hospital of Joint Logistics Support Force, 330000 Nanchang, Jiangxi, China (e-mail: Zjjortho@163.com).

psychological variables are not risk factors for CPSP five years after surgery, and the negative impact of anxiety on CPSP does not persist longer. However, there are still unexplored factors that may lead to the development of CPSP after TKA. Therefore, further research is needed to determine whether it is possible to develop a limited and precise risk prediction tool to identify high-risk patients with CPSP after TKA and provide targeted interventions.

Therefore, by collecting the data of patients with CPSP after TKA, this study preliminarily explored the related risk factors in the perioperative period to enrich the knowledge about CPSP after TKA, carry out early intervention to prevent the disease from further progress, and facilitate the dynamic evaluation of patients in the later period. The purpose of this study is to provide evidence-based medical guidance for preoperative intervention and care in TKA, identify high-risk patients for CPSP, and investigate potential methods to reduce its incidence.

Materials and Methods

Research Participants

This study retrospectively analyzed the clinical data from 160 patients who underwent TKA in our hospital between January 2021 and January 2024. Among them, 44 patients were male, and 116 were female, with a mean age of 69.08 ± 5.34 years.

The inclusion criteria for study participants were set as follows: ① patients undergoing elective initial TKA; ② classified as American Society of Anesthesiology (ASA) grade I or grade II [8]; ③ uniform use of intravenous analgesia pump for postoperative analgesia management; ④ patients aged ≥18 years. However, exclusion criteria included: ① emergency TKA patients with data supplemented after surgery, potentially leading to recall bias; ② patients undergoing other surgical procedures or having trauma in other parts, which could affect recovery; ③ patients with abnormal liver or kidney function, which may affect the metabolism of narcotic drugs; ④ CPSP caused by other conditions could interfere the assessment of postoperative pain; and ⑤ those with incomplete clinical data or missing follow-up details.

This study is retrospective and does not involve new data collection and the signing of informed consent. During the research, we strictly followed ethical principles, obtained the approval of the Yingtan 184 Hospital ethics committee (2024012), respected patients' rights and interests, and protected patients' privacy and data security.

Anesthesia and Surgical Approaches

Patients undergoing spinal anesthesia were positioned on their sides with hips and knees bent. A 16-gauge puncture needle was used, targeting the second and third lumbar spaces of the puncture. The puncture needle was advanced from the epidural space to reach the subarachnoid space. After the cerebrospinal fluid flowed out smoothly, 1.6 mL of 1% ropivacaine (H20113381, Jiabo Pharmaceutical Co., Ltd., Guangzhou, China) was mixed with 0.5 mL of 10% glucose (H34020604, Global Pharmaceutical Co., Ltd., Bengbu, China), and intravenous injection was performed at a speed of 1 mL/10 s. After this, a catheter was then placed in the epidural space.

Patients receiving general anesthesia were kept fasting for 8 hours and avoided drinking for 2 hours before the procedure. After entering the operating room, electroencephalogram (EEG), blood pressure, blood oxygen saturation, and bispectral index of EEG were continuously monitored, and peripheral venous access was established in the upper limbs. Anesthesia was induced using intravenous injection of midazolam 0.05 mg/kg (H20067040, Renfu Pharmaceutical Co., Ltd., Yichang, China), etomidate 0.2 mg/kg (HJ20160234, B. Braun Melsungen AG, Melsungen, Germany), sufentanil 0.4 g/kg (H20054256, Renfu Pharmaceutical Co., Ltd., Yichang, China), rocuronium 0.8 mg/kg (EB1916, Xiancheng Pharmaceutical Co., Ltd., Taizhou, China). After achieving a sufficient depth of anesthesia, an appropriately modeled laryngeal mask was applied. Furthermore, anesthesia was maintained with contentious intravenous injection of propofol 4–8 mg/kg/h (H19990282, Nippon Pharmaceutical Co., Ltd., Xi 'an, China) and remifentanil 6–10 μg/kg/h (H20030199, Renfu Pharmaceutical Co., Ltd., Yichang, China). Blood pressure was kept below 20% of baseline values, and the bispectrum index of EEG was maintained between 45–60. Additionally, 0.05 mg/kg cisatracurium (H20060869, Hengrui Pharma Co., Ltd., Shanghai, China) was intermittently injected during the procedure.

All procedures were performed by the same group of surgeons. An anterolateral knee incision and a medial approach alongside the patella were used, with careful attention to stop bleeding at vessel ends, such as the lateral inferior genicular artery near the lateral meniscus. A balloon tourniquet was routinely used during the surgery, and the pressure was 300 mmHg. After osteotomy and soft tissue balance, the cancellous bone surface was washed with a pulse washing gun, and the prosthesis was fixed using high-viscosity bone cement. A posterior-stabilized prosthesis was used. After patella trimming, the wound was washed again, and after hemostasis, a drainage tube was placed, the joint capsule was sutured, and the incision was closed layer by layer. After the procedure, all patients were connected to a patient controlled intraavenous analgesia (PCIA) system. The PCIA formula included sufentanil 2 μg/kg (H20054256, Renfu Pharmaceutical Co., Ltd., Yichang, China), flurbiprofen axetil 100 mg (H20183054, Daan Pharmaceutical Co., Ltd., Wuhan, China), and normal saline to 100 mL. Overall, the settings included a loading dose of 2 mL, a background infusion rate of 2 mL/h, a single self-controlled additional dose of 2 mL, a locking interval of 10 min, and analgesia maintained for 48 hours.

Table 1. Baseline characteristics of the study participants.

Variables (n = 160)	n/$\bar{x} \pm$ s	Ratio/range
Gender		
Male	44	27.50%
Female	116	72.50%
Age (years)	69.08 $\pm$ 5.34	55–79
Basic diseases		
Hypertension	95	59.38%
Diabetes	48	30.00%
Preoperative HSS score (score)	55.51 $\pm$ 10.38	29–82
CPSP	67	41.88%

Note: HSS, hospital for special surgery; CPSP, chronic postoperative pain.

Data Collection

Relevant data, including demographic information such as age, gender, body mass index, comorbidity (e.g., diabetes, hypertension), and preoperative pain numerical rating scale (NRS) scores, were collected from the medical information system during the perioperative period of TKA. Perioperative details included knee joint function score, anesthesia method, operation time, intraoperative blood loss, postoperative NRS score of hospital for special surgery (HSS) before operation, postoperative function training, receipt of deep thermal therapy, occurrence of postoperative adverse events, and length of hospital stay. All study subjects were followed for 3 months, primarily through outpatient follow-up and telephone follow-up. These assessments were used to determine whether the patient developed CPSP. Patients were then divided into CPSP and non-CPSP groups based on the presence or absence of CPSP.

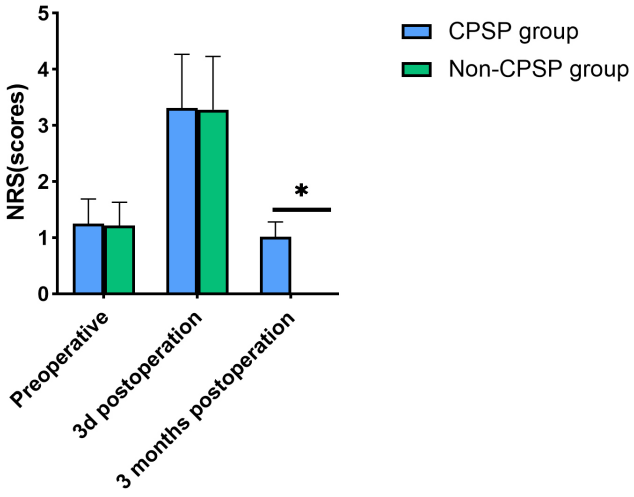

Fig. 1. Comparison of NRS score between the two groups of patients at different time points during rest. Note: compared with the CPSP group, $^{*}p < 0.05$; CPSP, chronic postoperative pain; NRS, numerical rating scale.

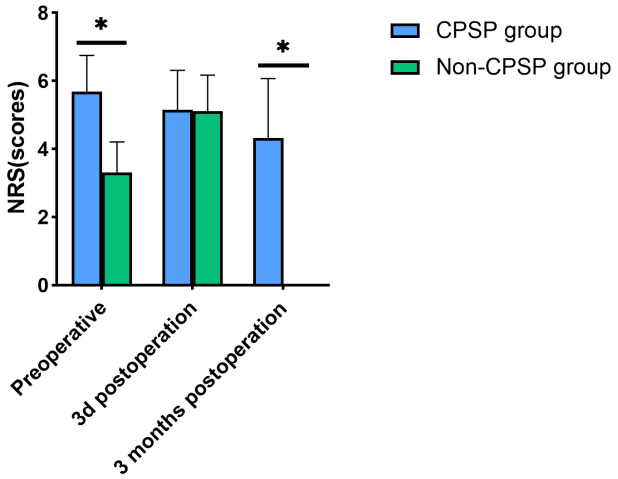

Fig. 2. Comparison of NRS score between the two groups of patients at different time points during exercise. Note: compared with the CPSP group, $^{*}p < 0.05$.

Evaluation Criteria

Evaluation of the study participants was performed based on the NRS score, HSS score, functional exercise, and CPSP judgment standard, as detailed below:

NRS score: The NRS score, ranging from 0 to 10 points, was divided into 4 categories: no pain (0 points), mild pain (1–3 points), moderate pain (4–6 points), and severe pain (7–10 points). A score of 0 indicated no pain, while a score of 10 represented severe pain, with higher scores indicating more severe pain [9].

HSS score: The HSS knee joint score is primarily used to assess the joint function before TKA. It determines various aspects, such as pain, functional activity, knee joint range of motion, knee flexion deformity, muscle strength, knee joint stability and other conditions of the patient. The overall knee joint function is assessed based on the total score: a score of $\geq$85 is considered excellent, 70–84 is considered good, 60–69 is rated medium and $\leq$59 is poor [10].

Functional exercise: The patients were engaged in physical activity three or more times per week, with each session lasting at least 30 minutes. Patients who exercised less than three times a week or for less than 30 minutes per session were categorized as having poor exercise adherence [11]. Postoperative adverse reactions included venous thrombosis of lower limbs, neuropathic pain, joint swelling, and chondrolysis.

CPSP judgment standard: CPSP was determined based on the following standards [12]: (1) New pain occurring at or adjacent to the surgical site after the procedure, with pain duration of $\geq$3 months and an NRS score of $\geq$1 point either at rest or during movement; (2) The nature of the current pain differs from pre-surgery pain, for example, pain exists at the operation site before surgery, but the nature of pain changes after TKA surgery; (3) Pain caused by other factors, such as recurrence of malignant tumor and chronic infection of incision, was excluded.

Table 2. Number and proportion of CPSP patients after TKA.

NRS score	NRS = 0	NRS 1–3	NRS 4–6	NRS 7–10	NRS 1–10
Patients	93 (58.13%)	21 (31.34%)	43 (64.18%)	3 (4.48%)	67 (41.88%)

Note: TKA, total knee arthroplasty; NRS, numerical rating scale.

Table 3. Comparison of NRS scores between the two groups at different time points.

Variables	Preoperative	3 days postoperation	3 months postoperation
Rest			
CPSP group (n = 67)	1.25 ± 0.44	3.31 ± 0.96	1.02 ± 0.26
Non-CPSP group (n = 93)	1.22 ± 0.41	3.28 ± 0.95	0
t-values	0.443	0.196	37.879
p-values	0.659	0.845	<0.001
Exercise			
CPSP group (n = 67)	5.69 ± 1.06	5.15 ± 1.16	4.33 ± 1.74
Non-CPSP group (n = 93)	3.31 ± 0.90	5.11 ± 1.06	0
t-values	15.311	0.226	24.028
p-values	<0.001	0.821	<0.001

Statistical Analysis

Statistical analysis was performed using SPSS 22.0 software (IBM SPSS Inc., Chicago, IL, USA). Measurement data were expressed as mean ± standard deviation ($\bar{x} \pm s$) and enumeration data were presented as percentages (%). A pairwise comparison of measurement data between groups was performed using the *t*-test, while analysis of variance (ANOVA) was utilized for multi-group comparison. Furthermore, categorical data were analyzed employing the χ^2 test. Logistic regression was used to identify the independent factors influencing CPSP after TKA in our study participants. The Spearman correlation coefficient was used to analyze the relationship between CPSP-related factors and pain severity. A receiver operating characteristic (ROC) curve was utilized to predict postoperative CPSP risk and determine the area under the curve (AUC). The Hosmer-Lemeshow test was employed to assess the goodness of fit of the risk prediction model. The test level was $\alpha = 0.05$, and $p < 0.05$ indicated that the difference was statistically significant.

Results

The Occurrence of CPSP after TKA

Among 160 patients, 67 (41.88%) experienced continuous CPSP at the joint site on the surgical side and around the surgical incision. Baseline characteristics of patients are shown in Table 1. Among these patients with CPSP, 21 (31.34%) experienced mild pain, 43 (64.18%) reported moderate pain, and 3 (4.48%) experienced severe pain (Table 2). Furthermore, 40 patients (59.70% of patients with CPSP) were affected by CPSP in their daily activities and 27 patients (40.30% of patients with CPSP) were affected by CPSP in their sleep.

Comparison of NRS at Rest and during Exercise between Two Groups at Different Time Points

The NRS pain scores in the CPSP group were significantly higher than those in the non-CPSP group during exercise preoperative and 3 months after the procedure. Furthermore, 3 months after the procedure, the CPSP group had a higher NRS score at rest than the non-CPSP group ($p < 0.05$). However, there was no significant difference in NRS scores between the two groups at rest preoperative and 3-day post-operation, nor during exercise at 3-day post-operation ($p > 0.05$). The comparison of NRS scores between the two groups is shown in Table 3 and Figs. 1,2.

Single Factor Analysis of CPSP after TKA

Univariate analysis demonstrated significant differences between the two groups regarding preoperative NRS score, preoperative HSS score, operation time, effective compression rate of the self-controlled analgesia pump, postoperative functional training, and the occurrence of postoperative adverse events ($p < 0.05$). However, there were no substantial differences in the effects of gender, age, comorbidities, anesthesia method, intraoperative blood loss, deep thermal therapy, and length of hospital stay on the onset of CPSP after TKA ($p > 0.05$). The single-factor analysis is summarized in Table 4.

Multivariate Analysis of CPSP after TKA

Multivariate analysis indicated preoperative NRS score, preoperative HSS score, postoperative functional training, and postoperative adverse events as the independent factors affecting the occurrence of CPSP after TKA ($p < 0.05$, Tables 5,6).

Table 4. Univariate analysis of CPSP after TKA.

Variables	CPSP group (n = 67)	Non-CPSP group (n = 93)	t/χ^2	*p*-value
Gender			0.319	0.572
Male	20 (29.85%)	24 (25.81%)		
Female	47 (70.15%)	69 (74.19%)		
Age (years)	69.52 ± 6.81	68.91 ± 7.05	0.548	0.584
Hypertension			0.065	0.799
Yes	39 (58.21%)	56 (60.22%)		
No	28 (41.79%)	37 (39.78%)		
Diabetes			0.148	0.700
Yes	19 (28.36%)	29 (31.18%)		
No	48 (71.64%)	64 (68.82%)		
Preoperative NRS score (score)	5.69 ± 1.02	3.15 ± 0.89	16.747	<0.001
Preoperative HSS score (score)	58.94 ± 10.62	50.28 ± 9.58	5.389	<0.001
Anesthesia method			0.167	0.682
Intraspinal canal	31 (46.27%)	40 (43.01%)		
General anaesthesia	36 (53.73%)	53 (56.99%)		
Operation time (min)			4.975	0.026
<150	22 (32.84%)	47 (50.54%)		
≥150	45 (67.16%)	46 (49.46%)		
Intraoperative blood loss (mL)			0.215	0.898
<50	18 (26.87%)	22 (23.66%)		
50–100	24 (35.82%)	35 (37.63%)		
>100	25 (37.31%)	36 (38.71%)		
Effective compression rate of self-controlled analgesic pump	71.46 ± 9.97	82.61 ± 9.55	7.153	<0.001
Postoperative functional training			4.528	0.033
Excellent	11 (16.42%)	29 (31.18%)		
Poor	56 (83.58%)	64 (68.82%)		
Deep thermotherapy			0.781	0.377
Yes	32 (47.76%)	51 (54.84%)		
No	35 (52.24%)	42 (45.16%)		
Postoperative adverse events			11.782	<0.001
Yes	23 (34.33%)	11 (11.83%)		
No	44 (65.67%)	82 (88.17%)		
Length of stay (d)			0.843	0.843
≤14	34 (50.75%)	54 (58.06%)		
>14	33 (49.25%)	39 (41.94%)		

Correlation Analysis between Independent Factors Affecting CPSP and Pain Severity

We observed a significant positive correlation between preoperative NRS score, postoperative adverse events, and CPSP pain severity (r = 0.670/0.443, $p < 0.05$). Conversely, a significant negative correlation was observed between preoperative HSS score, postoperative functional training, and CPSP pain severity (r = –0.522/–0.363, $p <$ 0.05). These findings are shown in Table 7.

Risk Prediction Model of CPSP Risk Factors

A predictive model for CPSP after TKA was established by incorporating the preoperative NRS score, preoperative HSS score, postoperative functional training, and postoperative adverse events. The model was evaluated by Calibration, and the Hosmer-Lemeshow ($\chi^2 = 1.627$, $p = 0.947$ >0.05) indicated that the model had good calibration ability. Furthermore, to evaluate the effectiveness of the prediction model, the ROC curve was plotted (Table 8, Figs. 3,4), and the AUC was calculated as 0.868 (95% CI: 0.811–0.925). The predictive model was considered to be effective when AUC >0.8.

Discussion

Previous systematic reviews have published that the incidence of CPSP after TKA ranges from 10% to 34%, with some studies indicating its probability as high as 48% [13, 14]. In our study, 67 (41.88%) patients out of 160 experienced continuous CPSP at the joint site or around the incision area. Among these patients, 21 (31.34%) patients experienced mild pain, 43 (64.18%) reported moderate pain, and 3 (4.48%) reported severe pain. The probability of oc-

Table 5. Multivariate logistic regression analysis of CPSP.

Factors	Variables	Assignment
Preoperative NRS score	X1	Continuous variable
Preoperative HSS score	X2	Continuous variable
Operation time	X3	Continuous variable
Effective compression rate of self-controlled analgesic pump	X4	Continuous variable
Postoperative functional training	X5	No = 0, yes = 1
Postoperative adverse events	X6	No = 0, yes = 1

Table 6. Multi-factor analysis of CPSP after influencing TKA.

Variables	*β*	*Standard error*	*Wald*	*p*-value	*Odds ratio*	95% CI	
						Lower limit	Upper limit
Preoperative NRS score	0.638	0.246	6.726	0.004	1.893	1.169	3.065
Preoperative HSS score	–0.398	0.125	10.138	0.002	0.672	0.526	0.858
Operation time	0.152	0.328	0.215	0.664	1.164	0.612	2.214
Effective compression rate of self-controlled analgesic pump	–0.294	0.517	0.323	0.541	0.745	0.271	2.053
Postoperative functional training	–1.256	0.617	4.144	0.017	0.285	0.085	0.954
Postoperative adverse events	1.074	0.539	3.970	0.023	2.927	1.018	8.419

Note: CI, confidence interval.

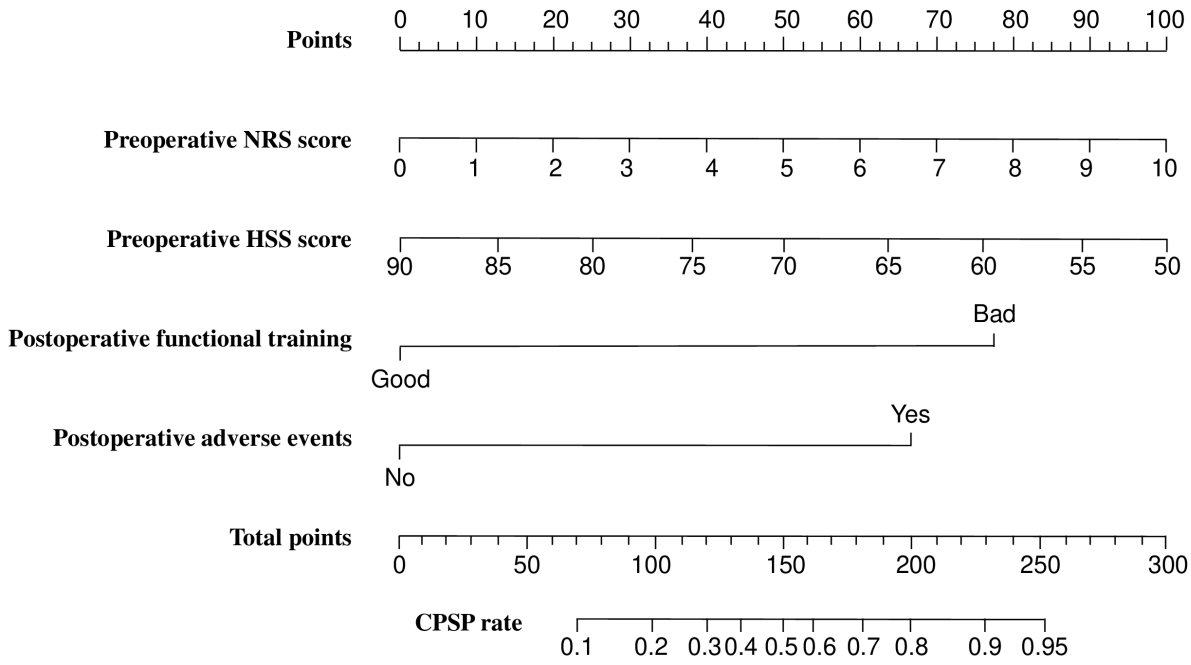

Fig. 3. Alignment diagram of CPSP after knee replacement. Note: The total score corresponds to a point on the CPSP risk axis below the nomogram, indicating the patient's corresponding risk of postoperative CPSP after knee replacement.

currence of CPSP is slightly higher than that in previous studies. These differences may be due to variations in inclusion and exclusion criteria and the definitions used for the timing of CPSP after surgery. This retrospective study evaluated CPSP based on patient assessment 3 months after TKA. Patients with an NRS score of $\geq$1, either at rest or during exercise, are divided into the CPSP group. The incidence of chronic pain after TKA surgery tends to alleviate over time, with the incidence of CPSP at six months being significantly lower than three months after surgery [15]. Additionally, a study indicates CPSP as moderate to severe pain, which differs from the present study's inclusion criteria for all levels of pain, such as mild, moderate, and severe [16]. This study also showed that CPSP caused patients with impaired daily activities and a high incidence of sleep disorders. These results indicate that the high in-

Table 7. Correlation analysis between independent factors affecting CPSP and pain severity.

CPSP pain severity	Preoperative NRS score	Preoperative HSS score	Postoperative functional training	Postoperative adverse events
r-value	0.670	–0.522	–0.363	0.443
p-value	<0.001	<0.001	0.003	<0.001

Table 8. Risk prediction model of CPSP risk factors.

AUC	95% CI		Sensitivity	Specificity	Youden's index	Cut-off value
	Lower limit	Upper limit				
0.868	0.811	0.925	80.6	78.5	0.591	>148

Note: AUC, area under the curve.

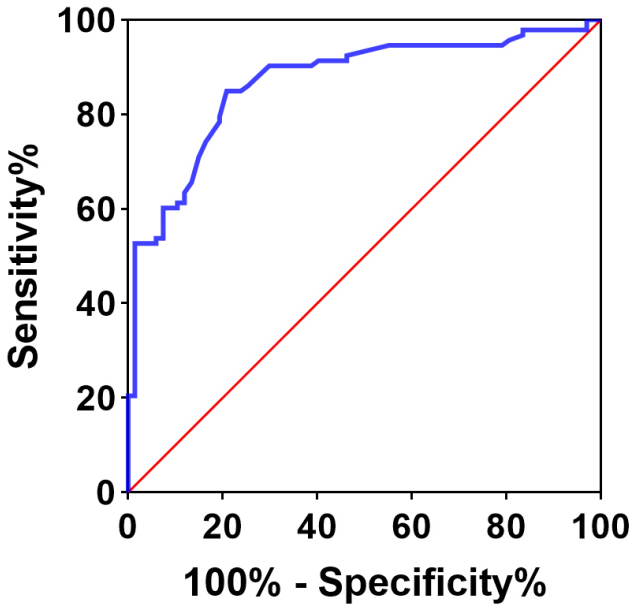

Fig. 4. Receiver operating characteristic (ROC) curve of CPSP risk prediction model.

cidence of CPSP after TKA has significantly affected postoperative rehabilitation and quality of life, underscoring the need for further attention and research.

In this study, we identified preoperative NRS score, preoperative HSS score, postoperative functional training, and postoperative adverse events as the independent risk factors influencing the occurrence of CPSP after TKA. Furthermore, we observed a positive correlation between preoperative NRS score, postoperative adverse events, and the severity of CPSP pain. Conversely, there was a negative correlation between preoperative HSS score, postoperative functional training, and CPSP pain severity. Similarly, previous research has indicated a strong correlation between preoperative pain intensity and the occurrence of CPSP after TKA. The probability of experiencing moderate to severe pain with significant knee joint activity 6 months after TKA is 10 times higher in patients with severe preoperative pain compared to those with low preoperative pain [17, 18]. Central sensitization, a common pathophysiological pain mechanism, is characterized by allodynia, hypoalgesia, an expended receptive field, and long-term pain after the stimulus is removed. This phenomenon is correlated with conditions like post-cancer pain, fibromyalgia, low back pain, and osteoarthritis. Long-term preoperative pain may increase the sensitivity of patients to pain, potentially elevating both the intensity and duration of postoperative pain [19, 20].

Postoperative chronic swelling of the knee joint and deep vein thrombosis in the lower limbs are common complications after TKA. Chronic joint swelling may be associated with local inflammatory edema or blood and fluid accumulation. It is speculated that postoperative pain can limit joint flexion-extension movements, leading to poor blood circulation, and can further aggravate joint swelling and pain, forming a vicious circle [21, 22]. Additionally, venous obstruction in the lower limbs impedes blood return, exacerbating postoperative pain. Deep vein thrombosis may affect the effective early postoperative functional exercise and increase the pain of these exercises [23, 24]. Therefore, enhancing the management of adverse reactions after surgery can help prevent CPSP after TKA.

Limited studies have explored the impact of preoperative knee joint function on postoperative pain. This study found that better knee joint function before TKA is associated with a lower incidence of postoperative CPSP and alleviated pain levels. Bin Abd Razak *et al.* [25] reported that knee joint function scores can better predict postoperative outcomes. For Asian patients undergoing their first TKA, those with lower preoperative knee joint function scores are more likely to suffer from pain and dysfunction than patients with higher preoperative scores. Post-TKA functional exercise is crucial for restoring knee joint function and range of motion. It can promote lower limb blood circulation, muscle strength recovery, and reduce complications associated with prolonged bed rest [26, 27]. Cai *et al.* [28] studied the incidence rate of motor fear in TKA patients and observed that negative pain coping strategies were a substantial risk factor for motor fear and also led to increased perception among 862 participants. The implantation of joint prosthesis during TKA treatment replaces diseased joints, and effective functional rehabilitation exercise after operation can prevent adhesion around the knee joint and prosthesis, thereby reducing the occurrence of CPSP.

Therefore, medical staff should conduct a range of motion training for patients as soon as possible after TKA to optimize the postoperative rehabilitation period and improve the recovery of knee joint function and pain management.

A study indicate that the risk of chronic pain is higher in women [29], while another study [30] found no significant difference in the incidence of CPSP between the sexes after adjusting the patients' preoperative mental and living conditions. In this study, no correlation was observed between the occurrence of CPSP and gender, leaving the impact of gender on the occurrence of CPSP still inconclusive. Notably, there is a substantial gender difference in this study. This could be due to the increased incidence of knee osteoarthritis in women than men (with a male-to-female ratio of about 3:10). Additionally, men and women may have different access to treatment, with women more likely to delay procedures until their joint functions are completely compromised.

A risk prediction model can quantify, graph, and visualize the results of logistic regression, achieving individualized prediction of adverse clinical events [31, 32]. In this study, we included independent factors affecting CPSP to establish a risk prediction model for CPSP after TKA. Our aim was to develop a reliable tool for predicting the CPSP in TKA patients. The results revealed that the prediction model has strong calibration and predictive capabilities, with an AUC of 0.868 (95% CI: 0.811–0.925). Internal validation within a cohort showed good discrimination and calibration capabilities, indicating its accuracy in predicting risk factors for chronic pain after knee replacement, making it a promising tool for clinical practice.

Besides its promising findings, this study has several limitations. As a retrospective study, there may be memory bias, and we did not collect anxiety and depression-related data of patients, thus missing the psychological influence on CPSP. Additionally, although univariate analysis revealed statistical differences between the two groups regarding operation time and the effective compression rate of the patient-controlled analgesia pump, multivariate analysis did not show these factors to affect CPSP. This variation may be due to the small sample size and potential bias. Further investigation, including multi-center and large-sample prospective research, is warranted to improve and validate these findings.

Conclusions

In summary, a high preoperative NRS score and the occurrence of postoperative adverse events are the risk factors for CPSP after TKA, while a high preoperative HSS score and good postoperative functional training serve as protective factors. In this study, we developed an initial predictive model for assessing the risk of CPSP in TKA patients, which can help medical staff predict the risk of CPSP in patients after surgery individually. At the same time, preoperative pain, postoperative adverse reactions and functional training can be improved in time, which provides a basis for formulating targeted individualized intervention programs. Timely intervention can improve patients' outcomes and reduce the probability of CPSP.

Availability of Data and Materials

The data and materials in the current study are available from the corresponding author upon reasonable request.

Author Contributions

JY, HG, CBW, and JJZ designed the research study. HG and CBW performed the research. JY and JJZ provided guidance and advice on the experimental design and execution. CBW analyzed the data. JY, HG, CBW, JJZ wrote the manuscript. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study is retrospective and does not involve new data collection and the signing of informed consent. During the research, we strictly followed conducted in accordance with the Declaration of Helsinki, obtained the approval of the Yingtan 184 Hospital ethics committee (2024012), respected patients' rights and interests, and protected patients' privacy and data security.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

References

[1] Gaffney CJ, Pelt CE, Gililland JM, Peters CL. Perioperative Pain Management in Hip and Knee Arthroplasty. The Orthopedic Clinics of North America. 2017; 48: 407–419.

[2] Saku SA, Madanat R, Mäkinen TJ. Reasons and risk factors for ninety day re-admission following primary total knee arthroplasty in a high-volume centre. International Orthopaedics. 2018; 42: 95–99.

[3] Murphy J, Pak S, Shteynman L, Winkeler I, Jin Z, Kaczocha M, *et al*. Mechanisms and Preventative Strategies for Persistent Pain following Knee and Hip Joint Replacement Surgery: A Narrative Review. International Journal of Molecular Sciences. 2024; 25: 4722.

[4] Vissers MM, Bussmann JB, Verhaar JAN, Busschbach JJV, Bierma-Zeinstra SMA, Reijman M. Psychological factors affecting the outcome of total hip and knee arthroplasty:

a systematic review. Seminars in Arthritis and Rheumatism. 2012; 41: 576–588.
[5] Lewis GN, Rice DA, McNair PJ, Kluger M. Predictors of persistent pain after total knee arthroplasty: a systematic review and meta-analysis. British Journal of Anaesthesia. 2015; 114: 551–561.
[6] Kluger MT, Lewis G, Rice D, McNair P. Psychological rather than pharmacological interventions for effective prevetion of pain after knee joint replacement? British Journal of Anaesthesia. 2016; 116: 150.
[7] Wylde V, Trela-Larsen L, Whitehouse MR, Blom AW. Preoperative psychosocial risk factors for poor outcomes at 1 and 5 years after total knee replacement. Acta Orthopaedica. 2017; 88: 530–536.
[8] Ament R. Origin of the ASA classification. Anesthesiology. 1979; 51: 179.
[9] Choudhury AK, Bansal S, Jain A, Raja BS, Niraula BB, Kalia RB. Conventional rehabilitation post-TKA achieves better knee flexion with higher resource utilization compared to application-based rehabilitation - a systematic review and meta-analysis. Journal of Orthopaedics. 2023; 44: 77–85.
[10] Irrgang JJ, Anderson AF. Development and validation of health-related quality of life measures for the knee. Clinical Orthopaedics and Related Research. 2002; 95–109.
[11] Zhou Y, Gao W, Gao S, Guo X, Liu M, Cao C. Pain Catastrophizing, Kinesiophobia and Exercise Adherence in Patients After Total Knee Arthroplasty: The Mediating Role of Exercise Self-Efficacy. Journal of Pain Research. 2023; 16: 3993–4004.
[12] Classification of chronic pain. Descriptions of chronic pain syndromes and definitions of pain terms. Prepared by the International Association for the Study of Pain, Subcommittee on Taxonomy. Pain. Supplement. 1986; 3: S1–S226.
[13] Shanthanna H, Aboutouk D, Poon E, Cheng J, Finley C, Paul J, *et al*. A retrospective study of open thoracotomies versus thoracoscopic surgeries for persistent postthoracotomy pain. Journal of Clinical Anesthesia. 2016; 35: 215–220.
[14] Fuzier R, Rousset J, Bataille B, Salces-y-Nédéo A, Maguès JP. One half of patients reports persistent pain three months after orthopaedic surgery. Anaesthesia, Critical Care & Pain Medicine. 2015; 34: 159–164.
[15] Sugiyama Y, Iida H, Amaya F, Matsuo K, Matsuoka Y, Kojima K, *et al*. Prevalence of chronic postsurgical pain after thoracotomy and total knee arthroplasty: a retrospective multicenter study in Japan (Japanese Study Group of Subacute Postoperative Pain). Journal of Anesthesia. 2018; 32: 434–438.
[16] Núñez-Cortés R, Chamorro C, Ortega-Palavecinos M, Mattar G, Paredes O, Besoaín-Saldaña Á, *et al*. Social determinants associated to chronic pain after total knee arthroplasty. International Orthopaedics. 2019; 43: 2767–2771.
[17] Pinto PR, McIntyre T, Ferrero R, Almeida A, Araújo-Soares V. Risk factors for moderate and severe persistent pain in patients undergoing total knee and hip arthroplasty: a prospective predictive study. PloS One. 2013; 8: e73917.
[18] Bruehl S, Billings FT, 4th, Anderson S, Polkowski G, Shinar A, Schildcrout J, *et al*. Preoperative Predictors of Complex Regional Pain Syndrome Outcomes in the 6 Months Following Total Knee Arthroplasty. The Journal of Pain. 2022; 23: 1712–1723.
[19] Petersen KK, Simonsen O, Laursen MB, Arendt-Nielsen L. The Role of Preoperative Radiologic Severity, Sensory Testing, and Temporal Summation on Chronic Postoperative Pain Following Total Knee Arthroplasty. The Clinical Journal of Pain. 2018; 34: 193–197.
[20] Kumar P, Bansal P, Rajnish RK, Sharma S, Dhillon MS, Patel S, *et al*. Efficacy of undenatured collagen in knee osteoarthritis: review of the literature with limited meta-analysis. American Journal of Translational Research. 2023; 15: 5545–5555.
[21] Nishimoto J, Shiraoka T, Takiguchi Y, Imamura R, Hirohama K, Tanaka S, *et al*. Derivation of a clinical prediction rule for chronic post-surgical pain after total knee arthroplasty considering biopsychosocial factors: A prospective cohort study. The Knee. 2023; 42: 364–372.
[22] Schindler M, Schmitz S, Reinhard J, Jansen P, Grifka J, Benditz A. Pain Course after Total Knee Arthroplasty within a Standardized Pain Management Concept: A Prospective Observational Study. Journal of Clinical Medicine. 2022; 11: 7204.
[23] Imai R, Nishigami T, Kubo T, Ishigaki T, Yonemoto Y, Mibu A, *et al*. Using a postoperative pain trajectory to predict pain at 1 year after total knee arthroplasty. The Knee. 2021; 32: 194–200.
[24] Götz JS, Leiss F, Maderbacher G, Meyer M, Reinhard J, Zeman F, *et al*. Implementing fast-track in total hip arthroplasty: rapid mobilization with low need for pain medication and low pain values: Retrospective analysis of 102 consecutive patients. Zeitschrift Fur Rheumatologie. 2022; 81: 253–262.
[25] Bin Abd Razak HR, Tan CS, Chen YJD, Pang HN, Tay KJD, Chin PL, *et al*. Age and Preoperative Knee Society Score Are Significant Predictors of Outcomes Among Asians Following Total Knee Arthroplasty. The Journal of Bone and Joint Surgery. American Volume. 2016; 98: 735–741.
[26] Çetinkaya F, Karakoyun A. The effects of elastic band exercise on the pain, kinesiophobia, functional, and psychological status after total knee arthroplasty: a randomized controlled trial. Clinical Rheumatology. 2022; 41: 3179–3188.
[27] Brown OS, Hu L, Demetriou C, Smith TO, Hing CB. The effects of kinesiophobia on outcome following total knee replacement: a systematic review. Archives of Orthopaedic and Trauma Surgery. 2020; 140: 2057–2070.
[28] Cai L, Liu Y, Xu H, Xu Q, Wang Y, Lyu P. Incidence and Risk Factors of Kinesiophobia After Total Knee Arthro-

plasty in Zhengzhou, China: A Cross-Sectional Study. The Journal of Arthroplasty. 2018; 33: 2858–2862.
[29] Liu X, Li N, Gao Y, Yin L, Zhang T, Li X, *et al*. Development and validation of a nomogram to predict chronic postoperative pain in elderly orthopedic patients. Annals of Palliative Medicine. 2021; 10: 11868–11883.
[30] Hawker GA, Wright JG, Coyte PC, Williams JI, Harvey B, Glazier R, *et al*. Differences between men and women in the rate of use of hip and knee arthroplasty. The New England Journal of Medicine. 2000; 342: 1016–1022.
[31] Pua YH, Poon CLL, Seah FJT, Thumboo J, Clark RA, Tan MH, *et al*. Predicting individual knee range of motion, knee pain, and walking limitation outcomes following total knee arthroplasty. Acta Orthopaedica. 2019; 90: 179–186.
[32] Tilbury C, Haanstra TM, Verdegaal SHM, Nelissen RGHH, de Vet HCW, Vliet Vlieland TPM, *et al*. Patients' pre-operative general and specific outcome expectations predict postoperative pain and function after total knee and total hip arthroplasties. Scandinavian Journal of Pain. 2018; 18: 457–466.