A simple nomogram for predicting osteoarthritis severity in patients with knee osteoarthritis

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Abstract

Objective: To explore the influencing factors of knee osteoarthritis (KOA) severity and establish a KOA nomogram model.

Methods: Inpatient data from our hospital's Department of Joint Surgery from January 2020-January 2022 were collected, and the least absolute shrinkage and selection operator (LASSO) methods were used to screen the factors for KOA severity to determine the best predictive index. Then, after combining the significant factors from the LASSO and multivariate logistic regressions, a prediction model was established. All potential prediction factors were included in the KOA severity prediction model, and the corresponding nomogram was drawn. The consistency index (C-index), area under the receiver operating characteristic (ROC) curve (AUC), GiViTi calibration band, net classification improvement (NRI) index, and integrated discrimination improvement (IDI) index evaluation of a model predicted KOA severity. Decision curve analysis (DCA) and clinical influence curves were used to study the model’s potential clinical value.

Results: Four hundred KOA patients were included. The nomogram's predictive factors were age, pulse, absolute value of lymphocytes, mean corpuscular haemoglobin concentration (MCHC) and blood urea nitrogen (BUN). The C-index and AUC of the model were 0.802. GiViTi calibration band (P = 0.065), NRI (0.091) and IDI (0.033) showed that the modified model can distinguish between severe KOA and nonsevere KOA. DCA showed that the KOA severity nomogram has clinical application value with threshold probabilities between 0.01-0.78.

Conclusions: A nomogram model for predicting KOA severity was established for the first time, can visually identify patients with severe KOA, and is novel for indirectly evaluating KOA severity by nonimaging means.

Key-points

The nomogram model our paper reported is novel for indirectly evaluating KOA severity by nonimaging means.

Introduction

Knee osteoarthritis (KOA) is the most common musculoskeletal disease in people over 60 years old[1, 2], and with the ageing of the population and the prevalence of obesity, the incidence of KOA is on the rise. The incidence of KOA is also on the rise among young people and physically active people[3, 4]. China's 2020 research report showed that the number of KOA patients increased from 26.1 million in 1990 to 61.2 million in 2017, and KOA was also the 24th most common cause of disability years in 2017, accounting for 1.08% of all disability years[5].

At present, there is no effective cure for patients with KOA. For a long time, the treatment strategies for KOA have mainly been analgesics and surgery. The complications associated with the available
treatments pose a huge hidden danger for elderly patients. Nonsteroidal anti-inflammatory drugs are the main drug therapy for osteoarthritis of the knee joint. However, a large number of randomized controlled clinical studies have confirmed that the long-term use of nonsteroidal anti-inflammatory drugs will significantly increase the risk of gastrointestinal bleeding, cardiovascular events and death[6]. Artificial joint replacement is an important method to treat the severe pain and joint deformities in late KOA, but it is not the best choice for patients with a poor economic status or relatively young people because of its high cost and the limited life span of artificial joints. In addition, Beswick AD et al reported that nearly 20% of KOA patients still had persistent pain after joint replacement[7]. The proportion of patients having revision surgery within 10 years is as high as 12%[8]. This suggests that it is necessary to explore the factors that affect the severity of knee osteoarthritis in order to improve the interventions given to patients with early knee osteoarthritis, improve the quality of life of patients, and reduce the social burden.

To date, many studies have focused on the treatment, pathogenesis and biomarkers of KOA [9–11]. However, there are few reports that have indirectly evaluated the severity of KOA by nonimaging methods [12]. In this study, the clinical data of inpatients from the Department of Joint Surgery of Chengde Medical University Affiliated Hospital were collected, and the related influencing factors of the KOA severity were analysed to establish a nomogram model to more easily identify patients with severe KOA and to effectively provide the basis for formulating more targeted intervention methods for KOA patients.

**Patients And Methods**

This study retrospectively collected data from a total of 642 patients who were initially diagnosed with KOA in the Department of Joint Surgery, Chengde Medical University Affiliated Hospital from January 2020 to January 2022. A total of 242 patients were excluded due to the lack of clinical data (n = 108), combined with osteoarthritis in other joints (n = 67), knee replacement, osteotomy and internal fixation for KOA and knee fracture (n = 32), active malignancy (n = 10), renal or liver failure (n = 10), rheumatic disease (n = 9), and active infection (n = 6). Finally, the clinical information of 400 KOA patients was collected. All clinical information collected in this study was obtained from the examination information of the patients when they were admitted to the hospital.

The clinical information that were collected from the patients included: sex, age, height, weight, physical illnesses, temperature, pulse, breathing rate, blood pressure, C-reactive protein, white blood cell count, red blood cell count, haemoglobin, haematocrit, platelet count, neutrophil ratio, lymphocyte percentage, monocyte percentage, percentage of eosinophils, percentage of basophils, absolute value of neutrophils, absolute value of lymphocytes, absolute value of monocytes, absolute value of eosinophils, absolute value of basophils, average volume of red blood cells, average haemoglobin content, mean corpuscular haemoglobin concentration (MCHC), coefficient of variation of red blood cell distribution width, red blood cell distribution width - SD value, average volume of platelets, distribution width of platelets, ratio of large platelets, thrombocytocrit, total protein, albumin, total bilirubin, prealbumin, alanine aminotransferase, aspartate aminotransferase, gamma glutamyltransferase, direct bilirubin, alkaline phosphatase, blood
glucose, total cholesterol, triglyceride, high-density lipoprotein cholesterol, apolipoprotein A1, apolipoprotein B, low-density lipoprotein cholesterol, potassium, sodium, chlorine, calcium, phosphorus, magnesium, α-hydroxybutyrate dehydrogenase, lactic dehydrogenase, creatinine kinase, creatine kinase isoenzyme, blood urea nitrogen (BUN), creatinine, uric acid, bicarbonate, β2 microglobulin, homocysteine determination, lipoprotein A, serum cystatin C determination, adenosine deaminase, serum total bile acid, estimated glomerular filtration rate, fibrinogen, prothrombin time, thrombin time, activity, international standardized ratio, activated partial thromboplastin time, fibrinogen degradation products, antithrombin III, erythrocyte sedimentation rate, blood type and the Kellgren-Lawrence (KL) grading were also collected.

The KL classification system is often used to classify the patient’s severity of osteoarthritis using the radiological findings. According to the severity of the imaging changes in the bones and joints and by using the KL classification system, KOA can be divided into grades 0, 1, 2, 3 and 4. If there is a classification difference between the patient’s knees, the most serious grade is the grading result of the patient [13]. In our study, the grade 4 KOA patients were classified into the severe group, while the others (grade 1, 2, 3 KOA patients) were classified into the nonsevere group.

Statistical analysis

All data in this study were analysed by R software (version 4.1.2; https://www.r-project.org/). In this study, the comparison of continuous variables between the two groups is expressed as the mean, standard deviation and difference. Student’s T test was used for normally distributed data, but the Mann–Whitney U test was used for nonnormally distributed data. The least absolute shrinkage and selection operator (LASSO) methods were used to screen the factors influencing the severity of KOA to determine the best predictive index. Then, by combining the factors obtained by the LASSO regression analysis and multivariate logistic regression analysis, the nomogram of the prediction model was established [14]. P < 0.05 indicated that the difference was statistically significant. All potential prediction factors were included in the KOA severity prediction model, and the corresponding nomogram was drawn. Harrell’s C statistic was used to calculate the consistency index (C-index) to evaluate the discrimination of the nomogram model. The receiver operating characteristic (ROC) curve was used to calculate the area under the curve (AUC) and evaluate the value of the index model in predicting the KOA severity [15]. The GiViTi calibration band was also utilized to illustrate the distinguishing ability of the prediction model. Net reclassification improvement (NRI) and comprehensive discrimination improvement (IDI) indexes were calculated to evaluate the predictive power of the model. Decision curve analysis (DCA) and clinical influence curves were used to study the potential clinical value of the model [16, 17].

Results

Characteristics of the KOA Patients
A total of 400 patients (110 males and 290 females) with an average age of 64 (58,69) years were included in this study. According to the KL grading system, the patients were divided into two groups: the KL 1–3 KOA group (206 cases) and the KL 4 KOA group (194 cases). The general situations, blood test results and knee osteoarthritis grouping of the two groups (severe group vs. nonsevere group) are shown in Table 1.
Table 1
Demographics and clinical characteristics of 400 patients with knee osteoarthritis.

| Variables                      | Total (n = 400) | KL 1–3 (n = 206) | KL 4 (n = 194) | P       |
|--------------------------------|----------------|------------------|----------------|---------|
| Sex, n (%)                     |                |                  |                | 0.19    |
| Female                         | 290 (72)       | 143 (69)         | 147 (76)       |         |
| Male                           | 110 (28)       | 63 (31)          | 47 (24)        |         |
| Age, Median (Q1,Q3)            | 64 (58, 69)    | 60 (54.25, 65)   | 66 (63, 71)    | < 0.001 |
| Height, Median (Q1,Q3)         | 160 (158, 167) | 162 (158, 168)   | 160 (158, 165) | 0.147   |
| Weight, Median (Q1,Q3)         | 70 (60, 75)    | 70 (62, 80)      | 69 (60, 75)    | 0.061   |
| Physical illnesses, n (%)      |                |                  |                | < 0.001 |
| No                             | 152 (38)       | 96 (47)          | 56 (29)        |         |
| Yes                            | 248 (62)       | 110 (53)         | 138 (71)       |         |
| Temperature, Median (Q1,Q3)    | 36.4 (36.2, 36.6) | 36.3 (36.2, 36.6) | 36.4 (36.2, 36.5) | 0.635 |
| Pulse, Median (Q1,Q3)          | 80 (74, 88)    | 80 (72, 87)      | 82 (74.5, 90)  | 0.004   |
| Breathing rate, n (%)          |                |                  |                | 0.77    |
| 16                             | 34 (8)         | 16 (8)           | 18 (9)         |         |
| 18                             | 256 (64)       | 135 (66)         | 121 (62)       |         |
| 20                             | 110 (28)       | 55 (27)          | 55 (28)        |         |
| Systolic pressure, Median (Q1,Q3) | 141 (130, 157) | 138 (128, 150)  | 146 (132.25, 160) | 0.003  |
| Diastolic pressure, Mean ± SD  | 83.05 ± 11.83  | 82.71 ± 12.06    | 83.41 ± 11.61  | 0.555   |
| C-reactive protein, Median (Q1,Q3) | 1.68 (0.81, 3.95) | 1.68 (0.83, 3.62) | 1.74 (0.8, 4.3) | 0.462   |
| White blood cell count, Median (Q1,Q3) | 5.64 (4.75, 6.49) | 5.64 (4.79, 6.42) | 5.65 (4.72, 6.64) | 0.807   |
| Red blood cell count, Median (Q1,Q3) | 4.33 (4.09, 4.65) | 4.39 (4.13, 4.71) | 4.24 (3.99, 4.56) | < 0.001 |
| Variables                                             | Total (n = 400) | KL 1–3 (n = 206) | KL 4(n = 194) | P       |
|------------------------------------------------------|----------------|------------------|---------------|---------|
| Haemoglobin, Median (Q1,Q3)                          | 132 (123, 142) | 134 (127, 144)   | 128 (120.25, 138) | < 0.001 |
| Haematocrit, Median (Q1,Q3)                          | 40 (37.9, 42.73) | 40.65 (38.52, 43.18) | 39.4 (37.25, 42.08) | < 0.001 |
| Platelet count, Mean ± SD                            | 225.93 ± 54.4  | 224.91 ± 52.99   | 227 ± 55.97    | 0.702   |
| Neutrophil ratio, Mean ± SD                          | 58.04 ± 8.96   | 57.21 ± 9.15     | 58.91 ± 8.69   | 0.057   |
| Lymphocyte percentage, Mean ± SD                     | 31.36 ± 7.9    | 32.29 ± 8.05     | 30.38 ± 7.63   | 0.015   |
| Monocyte percentage, Median (Q1,Q3)                  | 7.4 (6.4, 8.6) | 7.3 (6.4, 8.6)   | 7.5 (6.5, 8.78) | 0.285   |
| Percentage of eosinophils, Median (Q1,Q3)            | 2 (1.2, 3.1)   | 2.05 (1.2, 3)    | 2 (1.2, 3.1)   | 0.937   |
| Percentage of basophils, Median (Q1,Q3)              | 0.5 (0.4, 0.7) | 0.5 (0.4, 0.7)   | 0.5 (0.4, 0.7) | 0.337   |
| Absolute value of neutrophils, Median (Q1,Q3)        | 3.16 (2.59, 3.93) | 3.1 (2.63, 3.75) | 3.34 (2.55, 4.09) | 0.184   |
| Absolute value of lymphocytes, Median (Q1,Q3)        | 1.71 (1.38, 2.12) | 1.78 (1.43, 2.17) | 1.67 (1.35, 2.05) | 0.043   |
| Absolute value of monocytes, Median (Q1,Q3)          | 0.42 (0.34, 0.5) | 0.41 (0.34, 0.49) | 0.42 (0.34, 0.51) | 0.236   |
| Absolute value of eosinophils, Median (Q1,Q3)        | 0.11 (0.07, 0.17) | 0.11 (0.07, 0.17) | 0.11 (0.06, 0.18) | 0.845   |
| Absolute value of basophils, Median (Q1,Q3)          | 0.03 (0.02, 0.04) | 0.03 (0.02, 0.04) | 0.03 (0.02, 0.04) | 0.486   |
| Average volume of red blood cells, Median (Q1,Q3)    | 92.8 (89.8, 95.7) | 92.5 (90.23, 94.97) | 93.05 (89.5, 96) | 0.382   |
| Average haemoglobin content, Median (Q1,Q3)          | 30.6 (29.58, 31.6) | 30.9 (29.8, 31.8) | 30.45 (29.2, 31.4) | 0.011   |
| Mean corpuscular haemoglobin concentration(MCHC), Median (Q1,Q3) | 329 (322, 336) | 332 (324.25, 338) | 325.5 (320, 333) | < 0.001 |
| Coefficient of the variation of red blood cell distribution width, Median (Q1,Q3) | 12.6 (12.1, 13.1) | 12.5 (12, 13)    | 12.6 (12.12, 13.2) | 0.003   |
| Red blood cell distribution width -SD value, Median (Q1,Q3) | 42.9 (41, 44.9) | 42.2 (40.8, 44.4) | 43.45 (41.73, 45.5) | < 0.001 |
| Variables                                      | Total (n = 400) | KL 1–3 (n = 206) | KL 4(n = 194) | P   |
|------------------------------------------------|----------------|------------------|---------------|-----|
| Average volume of platelets, Median (Q1,Q3)    | 10.3 (9.7, 11) | 10.3 (9.6, 11)   | 10.3 (9.9, 11) | 0.258 |
| Distribution width of platelets, Median (Q1,Q3)| 11.7 (10.6, 13.4) | 11.7 (10.5, 13.4) | 11.7 (10.8, 13.35) | 0.537 |
| Ratio of large platelets, Median (Q1,Q3)       | 27.25 (22.4, 33.32) | 27.25 (21.83, 33.27) | 27.2 (23.58, 33.25) | 0.377 |
| Thrombocytocrit, Median (Q1,Q3)                | 0.23 (0.2, 0.26) | 0.23 (0.2, 0.26) | 0.24 (0.2, 0.27) | 0.505 |
| Total protein, Median (Q1,Q3)                  | 68.1 (64.65, 71.6) | 67.95 (65.2, 71.75) | 68.15 (63.9, 71.38) | 0.53 |
| Albumin, Median (Q1,Q3)                        | 38.8 (37, 40.73) | 39.2 (37.4, 41.08) | 38.4 (36.6, 40.48) | 0.006 |
| Total bilirubin, Median (Q1,Q3)                | 11.77 (9.44, 14.66) | 12.41 (9.72, 14.98) | 11.22 (9.13, 14) | 0.034 |
| Porealbumin, Median (Q1,Q3)                    | 250.45 (213.75, 287.82) | 254.1 (216.4, 291.65) | 241.7 (208.62, 284.35) | 0.093 |
| Alanine aminotransferase, Median (Q1,Q3)       | 15 (11.2, 21.38) | 15.4 (11.25, 21.28) | 14.1 (11.12, 21.48) | 0.244 |
| Aspartate aminotransferase, Median (Q1,Q3)     | 19.1 (16.28, 23.4) | 19.35 (16.83, 23.4) | 18.9 (16.1, 23.37) | 0.542 |
| Gamma glutamyltransferase, Median (Q1,Q3)      | 22.05 (15.9, 34.45) | 21.75 (15.72, 33.6) | 22.55 (16.52, 35.55) | 0.496 |
| Direct bilirubin, Median (Q1,Q3)               | 3.3 (2.5, 4.2) | 3.5 (2.5, 4.38) | 3.2 (2.4, 4) | 0.151 |
| Alkaline phosphatase, Median (Q1,Q3)           | 82.2 (69.7, 98.1) | 76.85 (67.53, 91.95) | 86.55 (72.9, 103.6) | < 0.001 |
| Blood glucose, Median (Q1,Q3)                  | 4.99 (4.55, 5.65) | 4.96 (4.58, 5.57) | 5.02 (4.52, 5.83) | 0.922 |
| Total cholesterol, Median (Q1,Q3)              | 4.63 (4.12, 5.35) | 4.62 (4.16, 5.43) | 4.64 (4.05, 5.3) | 0.366 |
| Triglyceride, Median (Q1,Q3)                   | 1.4 (1.05, 2.01) | 1.38 (1.04, 1.97) | 1.41 (1.11, 2.07) | 0.373 |
| High-density lipoprotein cholesterol, Median (Q1,Q3) | 1.21 (1.04, 1.4) | 1.23 (1.04, 1.44) | 1.17 (1.02, 1.36) | 0.207 |
| Variables                                                  | Total (n = 400) | KL 1–3 (n = 206) | KL 4(n = 194) | P     |
|-----------------------------------------------------------|----------------|-----------------|---------------|-------|
| Apolipoprotein A1, Median (Q1,Q3)                         | 1.19 (1.08, 1.33) | 1.21 (1.07, 1.37) | 1.18 (1.08, 1.3) | 0.493 |
| Apolipoprotein B, Median (Q1,Q3)                          | 0.88 (0.76, 1.04) | 0.89 (0.76, 1.03) | 0.88 (0.75, 1.05) | 0.952 |
| Low-density lipoprotein cholesterol, Median (Q1,Q3)       | 2.83 (2.46, 3.27) | 2.83 (2.48, 3.28) | 2.83 (2.4, 3.26) | 0.562 |
| Potassium, Median (Q1,Q3)                                 | 3.68 (3.45, 3.89) | 3.74 (3.46, 3.92) | 3.63 (3.44, 3.81) | 0.026 |
| Sodium, Median (Q1,Q3)                                    | 141 (139, 142)   | 140 (139, 141)   | 141 (139, 142)  | 0.019 |
| Chlorine, Median (Q1,Q3)                                  | 106 (105, 108)   | 106 (105, 108)   | 106 (105, 108)  | 0.439 |
| Calcium, Mean ± SD                                        | 2.26 ± 0.1       | 2.27 ± 0.1       | 2.25 ± 0.1     | 0.193 |
| Phosphorus, Median (Q1,Q3)                                | 1.12 (1, 1.26)   | 1.11 (1, 1.24)   | 1.12 (0.99, 1.28) | 0.777 |
| Magnesium, Median (Q1,Q3)                                 | 0.88 (0.83, 0.91) | 0.87 (0.82, 0.9) | 0.88 (0.83, 0.92) | 0.344 |
| α-hydroxybutyrate dehydrogenase, Median (Q1,Q3)           | 152 (135, 172.25) | 147 (131, 169)   | 154.5 (138, 174.75) | 0.004 |
| Lactic dehydrogenase, Median (Q1,Q3)                     | 178 (157, 200.25) | 172.5 (152, 198) | 183 (163, 203)  | 0.006 |
| Creatine kinase, Median (Q1,Q3)                           | 63.5 (48.68, 85.1) | 63.5 (49.92, 83.38) | 63.55 (47.12, 87.68) | 0.721 |
| Creatine Kinase Isoenzyme, Median (Q1,Q3)                 | 12 (9.75, 15)    | 12 (9, 15)      | 12 (10, 15)    | 0.571 |
| Blood urea nitrogen(BUN), Median (Q1,Q3)                  | 5.36 (4.48, 6.42) | 5.12 (4.3, 5.94) | 5.64 (4.7, 6.83) | < 0.001 |
| Creatinine, Median (Q1,Q3)                                | 56.7 (50.35, 66.3) | 56.95 (50.2, 67.22) | 56.4 (50.5, 66.25) | 0.98 |
| Uric acid, Median (Q1,Q3)                                 | 296.25 (248.43, 361.6) | 296.6 (250.3, 362.03) | 295.45 (245.6, 359.1) | 0.928 |
| Bicarbonate, Mean ± SD                                    | 25.88 ± 2.23     | 25.83 ± 2.32     | 25.94 ± 2.13   | 0.627 |
| β2 microglobulin, Median (Q1,Q3)                          | 1.63 (1.44, 1.91) | 1.53 (1.39, 1.78) | 1.72 (1.53, 2.06) | < 0.001 |
| Variables                                                  | Total (n = 400) | KL 1–3 (n = 206) | KL 4(n = 194) | P   |
|-----------------------------------------------------------|----------------|------------------|---------------|-----|
| Homocysteine determination, Median (Q1,Q3)                | 13.1 (11.38, 16.5) | 12.5 (10.9, 16.28) | 13.75 (11.9, 16.6) | 0.007 |
| Lipoprotein A, Median (Q1,Q3)                             | 13.05 (6.68, 28.23) | 11.65 (5.62, 26.82) | 14.75 (7.53, 29.23) | 0.077 |
| Serum cystatin C determination, Median (Q1,Q3)            | 0.64 (0.55, 0.77) | 0.6 (0.52, 0.7) | 0.67 (0.59, 0.8) | < 0.001 |
| Adenosine deaminase, Median (Q1,Q3)                       | 9.85 (8.5, 11.9) | 9.55 (8.3, 11.7) | 10.1 (8.7, 12.2) | 0.079 |
| Serum total bile acid, Median (Q1,Q3)                     | 3.5 (2.2, 5.7) | 3.45 (2.2, 5.77) | 3.6 (2.2, 5.5) | 0.918 |
| Estimated glomerular filtration rate, Median (Q1,Q3)      | 98.42 (90.7, 104.56) | 101.78 (94.04, 108.55) | 95.36 (87.9, 100.53) | < 0.001 |
| Fibrinogen, Median (Q1,Q3)                                | 2.57 (2.25, 2.96) | 2.49 (2.26, 2.94) | 2.62 (2.24, 2.96) | 0.309 |
| Prothrombin time, Median (Q1,Q3)                          | 11.2 (10.8, 11.7) | 11.2 (10.8, 11.7) | 11.2 (10.8, 11.8) | 0.693 |
| Thrombin time, Median (Q1,Q3)                             | 17.7 (17.1, 18.5) | 17.7 (17.1, 18.6) | 17.7 (17.1, 18.3) | 0.276 |
| Activity, Mean ± SD                                       | 93.33 ± 8.61 | 93.52 ± 8.17 | 93.12 ± 9.08 | 0.64 |
| International standardized ratio, Median (Q1,Q3)          | 0.97 (0.94, 1.02) | 0.97 (0.94, 1.02) | 0.97 (0.93, 1.03) | 0.666 |
| Activated partial thromboplastin time, Mean ± SD           | 26.08 ± 2.08 | 26.14 ± 2.12 | 26.02 ± 2.04 | 0.563 |
| Fibrinogen degradation products, Median (Q1,Q3)            | 2.5 (2.5, 2.5) | 2.5 (2.5, 2.5) | 2.5 (2.5, 2.5) | 0.103 |
| Antithrombin III, Median (Q1,Q3)                          | 87.7 (81.57, 97.73) | 87.75 (81.95, 97.18) | 87.7 (81.08, 97.85) | 0.935 |
| Erythrocyte Sedimentation rate, Median (Q1,Q3)             | 10 (6, 17) | 9 (5, 15) | 12 (6, 18) | 0.004 |
| Blood type ABO, n (%)                                      |                |                  |               | 0.766 |
| AB                                                        | 35 (9) | 20 (10) | 15 (8) | |
| A                                                         | 134 (34) | 72 (35) | 62 (32) | |
| B                                                         | 115 (29) | 57 (28) | 58 (30) | |
| O                                                         | 116 (29) | 57 (28) | 59 (30) | |
| Variables                      | Total (n = 400) | KL 1–3 (n = 206) | KL 4(n = 194) | P |
|-------------------------------|----------------|------------------|---------------|---|
| Blood type Rh, n (%)          |                |                  |               |   |
| negative                      | 2 (0)          | 1 (0)            | 1 (1)         |   |
| positive                      | 398 (100)      | 205 (100)        | 193 (99)      |   |

**Nomogram Variable Screening and Construction**

In the LASSO regression analysis, 400 patients had 81 features, which were reduced to 14 potential nonzero coefficient predictors related to KOA. These 14 factors are as follows: age, pulse, diastolic pressure, haemoglobin, absolute value of lymphocytes, MCHC, alkaline phosphatase, total cholesterol, potassium, α-hydroxybutyrate dehydrogenase, lactate dehydrogenase, BUN, β2 microglobulin, and ABO blood type. As determined by the multivariate logistic regression analysis of the above 14 factors, only the P values of age and MCHC were less than 0.05, and the P values of pulse, absolute value of lymphocytes, and BUN were less than 0.1. Finally, the above five factors were included in the nomogram model to predict the severity of KOA.

**Evaluation of the nomogram**

The C index and AUC were 0.802, which indicates that the nomogram has a good degree of discrimination for the severity of KOA (Fig. 2A). The GiViTi calibration curve (p = 0.065) in this study also consistently showed a good nomogram (Fig. 2B). The changes in the NRI and IDI were used to compare the accuracy between the nomogram and a model (age and MCHC). The NRI and IDI were 0.091 and 0.033, respectively (both P < 0.05). In addition, the AUC of the nomogram was higher than that of the model (0.802 vs. 0.783, P < 0.05). These indicators show that the nomogram is more accurate than the model.

**Clinical use of the nomogram**

This study predicts severe DCA of KOA, as shown in the figure. The DCA results show that the nomogram that was used to differentiate severe KOA in this study population is more beneficial than all of the patient intervention or nonintervention schemes because it has a threshold probability of 0.01–0.78 (Fig. 2C). In addition, the clinical impact chart shows that the predicted number of high-risk patients is always greater than the actual number of noncompliant patients, which seems to be accompanied by an acceptable cost–benefit ratio (Fig. 2D). These results indicate that the nomogram has high clinical application potential for determining the severity of KOA patients.

**Discussion**

KOA is a chronic disease occurring in the knee joint caused by the interaction of many factors; it is characterized by articular cartilage degeneration and secondary bone hyperplasia. As the most common
joint disease, it is estimated that 302 million people in the world are affected by KOA, and it has become one of the main causes of disability in the elderly [18–20]. Epidemiological survey data in China show that the prevalence rate of symptomatic KOA in China is 8.1% at present, and frequent knee pain affects the activity and quality of life of up to 25% of adults [21]. The high prevalence and disability rate of KOA have greatly affected the patients' quality of life and social and economic development. During the early stage of KOA, the articular cartilage still has a certain regenerative capacity, but during the late stage of KOA, the articular cartilage may permanently lose its regenerative capacity [22, 23]. According to the diagnosis and treatment of KOA, experts have divided KOA into early, middle stage and late stages. In the early stage, drug treatment is recommended, but while in the middle and late stages, invasive treatments such as repair and joint replacement are recommended [24]. Therefore, early identification of the severity of KOA plays an important role in the treatment and prognosis of KOA.

The nomogram model can visualize the results of logistic regression and can be directly used to predict the individual disease risk, which is easy to popularize and apply in the clinic. Studies at home and abroad have confirmed that nomogram models can be used to predict the prognosis of hepatocellular carcinomas, melanomas of the head and neck, gliomas, young patients with gastric cancer and the risk of anastomotic leakage after rectal cancer surgery [25–29]. In the field of KOA, the prediction accuracy and clinical value of nomograms have also been confirmed, and nomograms can be used to predict the probability of replacement surgery in the late stage of KOA and the probability of complications after joint replacement [30, 12]. However, there is little literature on the establishment of a nomogram model of KOA severity that is related to the clinical application of X-ray films to evaluate the KOA severity. Based on the abovementioned influencing factors of KOA severity, a nomogram model for predicting KOA severity was established for the first time, which realized visual and individualized prediction, helped to formulate strategies to prevent KOA, supplemented the shortcomings of imaging methods in evaluating the KOA severity, and proposed a new method for indirect evaluation of the KOA severity by nonimaging methods. In clinical work, the nomogram model of this study can be used in the primary medical units without access to imaging equipment (for example, community health service stations), in patients who are unwilling to receive radiation, in patients who cannot receive radiation (for example, pregnant women), and in patients who have been bedridden for a long time and have difficulty with X-ray examinations, etc.

A large number of studies have reported the relationship between age and KOA. Jurmain RD found that the incidence of osteoarthritis increased with age [31]. Calce SE et al found that most of the changes in KOA patients can be explained by age [32]. Deng L et al suggested that ageing is the key driving force of osteoarthritis [33]. Zhang B et al reported that osteoarthritis is an age-related arthritis and the main cause of chronic disability in the elderly [34]. This study is consistent with the above conclusions: it was found that age is an independent risk factor for patients with severe KOA. With increasing age, the severity of KOA increases.

There is no literature that directly supports the correlation between pulse and KOA severity. However, a large number of studies have proven that cardiovascular disease (CVD) is closely related to osteoarthritis, and there is a positive correlation [35–38]. Moreover, some studies have pointed out that vascular lesions
around joints are one of the pathogenesis of osteoarthritis, and these vascular lesions have been proven to be similar to CVD in pathology and are considered to be a manifestation of systemic metabolic abnormalities[39], which further verifies the close relationship between CVD and osteoarthritis. These considerations make it easier for us to understand the results of this study: pulse is an independent risk factor for patients with severe KOA, and with the acceleration of the pulse, the severity of KOA patients increases. Output per stroke is an important indicator of cardiac function. The greater the output per stroke, the better the cardiac function. Under the same cardiac output, the faster the pulse is, the smaller the stroke output; the slower the pulse, the larger the stroke output. However, CVD is positively correlated with osteoarthritis. It has been found that the faster the pulse and the smaller the output per pulse, the worse the heart function and the more severe the osteoarthritis, which could explain the results of our study.

BUN is a nitrogen-containing compound in the plasma, and is filtered out from the glomerulus and excreted. When renal insufficiency is decompensated, BUN will increase. Therefore, BUN is used as an index that is used to evaluate the glomerular filtration function in clinical work. There is no literature to support that BUN is directly related to KOA. However, the literature has proven that BUN increases with age [40], and age is closely related to KOA [31–34]. These conclusions can fully explain the results of our study, the higher the BUN is, the heavier the severity of KOA.

Many scholars have found that the absolute value of lymphocytes is inversely related to the severity of KOA [41–44]; that is, the smaller the absolute value of lymphocytes is, the heavier the severity of KOA. Also, the larger the absolute value of lymphocytes is, the lighter the severity of KOA. This is consistent with our research results.

Many studies have reported the importance of low MCHC in predicting the prognosis of diseases [45–47], including hepatectomy, chronic obstructive pulmonary disease and the development of cardiovascular diseases in dialysis patients. However, no literature has proven the relationship between MCHC and KOA. MCHC is defined as the amount of haemoglobin per litre of blood/haematocrit per litre of blood. There is a positive correlation between MCHC and haemoglobin, and it has been reported in the literature that haemoglobin tends to decrease with age [48], so MCHC also tends to decrease with age. Age is closely related to KOA [31–34]. This finding fully explains the results of this study, which showed that with a decrease in MCHC, the severity of KOA increases.

The C-index of KOA severity predicted by the nomogram model in this study was 0.802. The internal verification shows that the KOA severity predicted by this model is in good agreement with the actual KOA severity. The calibration curve further verifies that the model prediction has excellent discrimination and accuracy. In addition to excellent prediction accuracy, this study also confirmed that the nomogram model can effectively predict KOA severity by ROC curve analysis. By introducing a clinical decision curve and clinical influence curve to investigate the advantages and disadvantages of statistical inference results, the results further confirmed that this model has strong clinical practicability and high benefit.
The limitations of this study are as follows: (1) the sample size is small; (2) this study is a single-centre study; and (3) the nomogram for predicting KOA severity needs to be further verified by multicentre and large-scale case studies.

Conclusions

In this study, a nomogram model for predicting KOA severity was established for the first time by combining five influencing factors, including age, pulse, absolute value of lymphocytes, MCHC and BUN. Individualized prediction of KOA severity can be obtained, and these can help to directly identify patients with severe KOA, help to formulate strategies for preventing KOA, and may open up new ideas for indirectly evaluating the KOA severity by nonimaging means.

Declarations

Ethics approval and consent to participate

Ethical approval for the study was obtained.

Consent for publication

Not applicable.

Competing Interests

The authors declare that they have no competing interests.

Author contributions

Qingzhu Zhang and Pengcheng Wang designed the study. Qingzhu Zhang was responsible for preparation of the manuscript. Yinhui Yao and Jinzhu Wang contributed to the data collection. Yufeng Chen and Dong Ren played an important role in the analysis of outcomes. Yinhui Yao and Pengcheng Wang revised the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available because of restricted access to our hospital database but are available from the corresponding author upon reasonable request.
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Figures
Figure 1

Prediction factors for osteoarthritis severity were selected, and an osteoarthritis severity nomogram was developed in patients with knee osteoarthritis. (A, B) Least absolute shrinkage and selection operator (LASSO) coefficient profiles of the 14 prediction factors. (C) Logistic regression analyses of the 5 prediction factors in patients with knee osteoarthritis. (D) Nomogram prediction of the osteoarthritis severity in patients with knee osteoarthritis.
Figure 2

Evaluation of the KOA nomogram and its clinical use in patients with knee osteoarthritis. (A) ROC curve based on the predictive nomogram for osteoarthritis severity. (B) Calibration plots for predicting osteoarthritis severity. (C) Decision curve analysis for the osteoarthritis severity nomogram in patients with knee osteoarthritis. (D) Clinical impact plot for predicting the patient osteoarthritis severity.