Prediction Models for Oral Health–Related Quality of Life in Patients with Temporomandibular Joint Osteoarthritis 1 and 6 Months After Arthrocentesis with Hyaluronic Acid Injections

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Aims: To develop models for prognostic prediction of oral health–related quality of life (OHRQoL) for patients with temporomandibular joint osteoarthritis (TMJ OA) at 1- and 6-month follow-ups after arthrocentesis treatment with hyaluronic acid (HA) injections once a week for 4 weeks. **Methods:** From a cohort of 522 adult patients with TMJ OA treated with arthrocentesis with HA injections, 510 and 463 adult patients were included in the 1- and 6-month follow-ups, respectively. Patient characteristics and history, clinical examinations, and questionnaires were recorded as potential predictors at start of treatment, and all patients underwent an identical treatment protocol. Patients' OHRQoL values at 1 and 6 months after completing the treatment were used as outcome measures. Logistic regression methods were used to develop prediction models, and the performance and validity of these models were evaluated according to state-of-the-art methods, including receiver-operating characteristics curve for the discrimination of the models and calibration plots for the calibration of the models. **Results:** History of mental disease, maximal protrusion of the jaw, muscular pain with palpation, joint pain with palpation, awake bruxism, chewing-side preference, and low OHRQoL at baseline were significantly associated with OHRQoL at the 1-month follow-up, while age, pain in other joints, history of mental disease, joint pain with palpation, sleep bruxism, awake bruxism, chewing-side preference, and low OHRQoL at baseline were significantly associated with OHRQoL at the 6-month follow-up. While the performance of both models was found to be good in terms of calibration, discrimination, and internal validity, the added predictive values of the 1-month and 6-month models for ruling in the risk of low OHRQoL were 19% and 31%, respectively, while those for ruling it out were 28% and 15%, respectively. **Conclusion:** Several predictors were found to be significantly associated with patients' OHRQoL after treatment. Both prediction models may be reliable and valid for clinicians to predict a patient's risk of low OHRQoL at follow-up, so the models may be useful for clinicians in decision-making for patient management and for informing the patient. *J Oral Facial Pain Headache 2019;33:54–66. doi: 10.11607/ofph.2044*

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Over the last decade, oral health–related quality of life (OHRQoL) has gained increased attention in the field of temporomandibular disorders (TMD).[1–4] It has been shown that patients with TMD suffer from a significantly reduced OHRQoL.[5] Temporomandibular joint osteoarthritis (TMJ OA) has also been reported to have a negative effect on patients' OHRQoL.[6] TMJ OA is an inflammatory condition within the joint that results from a degenerative condition of the joint structures, defined as the presence of arthralgia with either crepitus in the TMJs or bony changes in radiographic examinations, including flattening, erosion, or sclerosis of joint surfaces or osteophyte formation.[7] Chronic pain is the main symptom of TMJ OA.[8] Its prevalence is estimated to be about 4% in the general population,[9,10] while in TMD patients it ranges up to 22%.[11–13] Orofacial pain, comorbid headache and body pain, functional limitation, parafunctional habits, age, and psychological factors are thought to negatively affect OHRQoL in patients with TMD.[1,12,14,15] However, studies specifically focusing on the risk factors for low OHRQoL in patients with TMJ OA are scarce.[16]

OHRQoL is regarded as a multidimensional construct that reflects people's wellbeing in general; their comfort when eating, sleeping, and engaging in social interaction; their self-esteem; and their satisfaction with respect to their oral health.[17] It is associated with functional, psychological, and social factors, as well as with experience of pain or discomfort.[17] Over the past 30 years, the use of biopsychosocial indicators in dental epidemiology has been widely advocated because single measures of clinical disease do not truly reflect the full impact of oral disorders.[18] Assessment of OHRQoL allows for a shift from traditional assessment of disease to evaluation of health and care, with a focus on the patient's social and emotional experiences and physical functioning in defining appropriate treatment goals and outcomes.[19]

OHRQoL is a highly relevant summary measure of individual wellbeing and outcome of oral health care. Its evaluation, particularly for predicting the risk of low OHRQoL in patients with TMJ OA, may provide important information for decision-making for patient management in health care and for informing the patient. As such, the aim of this study was to establish the optimal models for predicting OHRQoL in patients with TMJ OA at 1 month and 6 months after completing a standardized treatment of arthrocentesis with hyaluronic acid (HA) injections once a week for 4 weeks.

Materials and Methods

Study Design

This study was designed as a cohort study with OHRQoL as the observational outcome at follow-up. The cohort was comprised of 522 patients with TMJ OA who sought treatment at the Orofacial Pain Clinic, West China Hospital of Stomatology, Sichuan University, between January 2013 and January 2014. This study was approved by the Ethics Committee of the West China Hospital of Stomatology at Sichuan University (WCHSIRB-CT-2013-077). The experiments were undertaken with the understanding and written consent of each participant and according to ethical principles, including the World Medical Association Declaration of Helsinki.

Participant Enrollment

The inclusion and exclusion criteria for patients are presented in Table 1. Study participants provided informed consent before data collection. Thereafter, each included patient received an identical and standardized treatment: arthrocentesis with HA injections (2 mL per cartridge; Shipeite, Bausch Freda) once a week for 4 subsequent weeks. All patients were treated by the same experienced clinician (S.Z.), who has practiced oral and maxillofacial surgery for more than 20 years and performed arthrocentesis with HA injection for 5 years.

Table 1 Inclusion and Exclusion Criteria

Inclusion criteria
Age > 18 y
A diagnosis of TMJ OA according to the RDC/TMD (Axis I, group IIIb)
A treatment plan of receiving arthrocentesis with HA injections for TMJ OA complaints
Exclusion criteria
Allergy to HA
Taking any medication in the preceding 4 weeks that could interact with HA or confound its effect
Participation in another clinical trial(s) in the previous 3 months
A history of TMJ surgery
Condylar fracture or jaw trauma
Rheumatic disease or polyarthritis
Severe systemic comorbidity, such as cardiovascular, hepatic, nephritic, or systemic blood disease
Could not be followed up within 6 months

TMJ OA = temporomandibular joint osteoarthritis; RDC/TMD = Research Diagnostic Criteria for Temporomandibular Disorders; HA = hyaluronic acid.

Potential Predictors

The potential predictors, which were selected based on previous literature[1,2,5,14,15,20–25] and group discussions, are presented in Table 2. All the included predictors were collected by the same clinician mentioned above (S.Z.) and classified hierarchically into three blocks: patient characteristics and history; clinical examinations; and questionnaires.

Study End Point

The study outcomes—OHRQoL scores at 1 month and 6 months after the fourth HA injection—were assessed using the Chinese version of the 14-item Oral Health Impact Profile (OHIP-C14).[26] Each item on the OHIP-C14 is scored on a 5-point scale: 0 = never; 1 = hardly ever; 2 = occasionally; 3 = fairly often; and 4 = very often or every day, with scores of 3 and 4 indicating a negative impact.[27–30] The OHIP summary score (OHIP-SC) for each patient was calculated as the number of items with a response indicating a negative impact; so, the OHIP-SC ranges from 0 to 14. An OHIP-SC > 0 indicates that patients report at least one negative impact among the 14 items of the OHIP; this was considered essentially impaired[27–30] and regarded as low OHRQoL. OHRQoL assessment of each patient at follow-up was completed via email or postal mail, or the responses were documented via telephone or a face-to-face meeting.

Missing Data

Possible differences in distributions across predictors between patients who were available at the

1-month and 6-month follow-ups and patients who were lost to the follow-ups were assessed using the chi-square test.

Statistical Analyses

Screening of Potential Predictors and Modeling. The chi-square test was used to test the univariate associations of each potential predictor and OHRQoL at the follow-up, and predictors with a *P* value ≤ .20[31] were selected for the subsequent multivariate analyses. The candidate predictors were then selected for the final multivariate logistic regression model using hierarchical modeling procedures. Hierarchical modeling is a sequential process involving the entry of predictors in steps. The order of the entry of predictors into the analysis is based on a priori knowledge of theory and previous studies rather than on computer software.[32] During the hierarchical modeling, the predictors fell into three hierarchical blocks: Block A (patient characteristics and history); Block B (clinical assessment); and Block C (questionnaires). A first multivariate logistic regression analysis was done for all the predictors in Block A. Then, a second logistic regression analysis was done for all the predictors in Block B together with the remaining predictors in Block A that had a *P* value ≤ .20 in the first logistic regression analysis. Finally, a third logistic regression analysis was done for all the predictors in Block C together with the remaining predictors from the second logistic regression analysis with a *P* value ≤ .20.

Internal Validation. A model that has been developed from a dataset in which the data fit easily can result in overoptimism when applied to a new dataset.[33,34] To guard against such overfitting (ie, to improve the internal validity of the models), the regression coefficients of the predictors in the models were multiplied by a shrinkage factor.[33,34] This factor, which ranged from 0 to 1, was derived using a bootstrapping procedure with 300 replications.

Discrimination. Discrimination is the ability of a model to differentiate between those with and those without the outcome event.[35] The outcome event in the present study was low OHRQoL. The area under the receiver-operating characteristic curve (AUC) was used to assess the performance of the models in terms of accuracy of prediction.[36] An AUC of 0.5 indicates no discrimination above chance, whereas an AUC of 1.0 indicates perfect discrimination.[36]

The optimal cutoff for the predicted probability of the models was defined as the predicted probability with the maximum sum of sensitivity and specificity in the receiver-operating characteristic curve (ROC).

Calibration. Calibration refers to the agreement between observed outcomes and predicted outcomes.[35] Calibration of the models was assessed by plotting the predicted individual probability against the observed actual probability. For this, study members were grouped into deciles according to their predicted probability for low OHRQoL at follow-up according to the models. The prevalence of that end point within each decile represents the observed probability.

The calibration of the multivariate models was also evaluated using the Hosmer-Lemeshow goodness-of-fit statistic test (HL test). A *P* value of > .10 in the HL test indicates that the model fits the observed data.[37]

Clinical Values. Clinical values of the models, based on the optimal cutoffs for predicted probability, were assessed using the prevalence, positive predictive values (PPV), and negative predictive values (NPV) of patients with low OHRQoL at follow-up. PPV was defined as the risk of presence of low OHRQoL based on the models in patients with low OHRQoL, and NPV was defined as the risk of absence of low OHRQoL based on the models in patients without low OHRQoL. The (added) predictive value of the models at the certain cutoff for predicted probability for ruling in an increased risk of low OHRQoL at the follow-up was defined as PPV minus prevalence, while that for ruling out an increased risk of low OHRQoL was defined as NPV minus complement of prevalence (1 minus prevalence).

Scoring System. A clinical prediction rule was developed for low OHRQoL in patients with TMJ OA to provide an estimate for individual patients of their absolute risk of having low OHRQoL. For the final multivariate logistic regression models, the probability (P) of low OHRQoL is predicted with the formula:

$$P = 1 - 1/[1 + \exp(\text{constant} + \beta 1X1 + \ldots + \beta iXi)]$$

. . . where β is the regression coefficient of a predictor in the models. The status of a patient for any dummy or binary variable included in the models can be expressed as either 0 or 1.

To facilitate application of the prediction models in practice, the final regression models were converted to a score chart on which an individual's absolute risk for low OHRQoL could be examined by adding the score's weight for predicting. Then, the models were transformed into line charts. The x axis of the line charts represents the total scores of individual patients, while the y axis represents the predicted probability for low OHRQoL of individual patients.

The discrimination, calibration, clinical values, and scoring system of the two models were all assessed based on the shrunken regression coefficients. All the statistical analyses were performed with SPSS software 21.0 (IBM) and R software 3.2.3 (R Development Core Team).

Table 2 Descriptions of Coding Criteria and Distributions of Potential Predictors at 1-Month (n = 510) and 6-Month (n = 463) Follow-ups

Predictors	Description of coding	Patient at 1-mo follow-up, n (%)	Patients at 6-mo follow-up, n (%)	Patients lost to follow-up at 1 mo (n = 12), n (%)	Patients lost to follow-up at 6 mo (n = 59), n (%)	*P* value
Patient Characteristics and history						
Gender	0: Male	129 (25)	121 (26)	3 (25)	11 (19)	.670
	1: Female	381 (75)	342 (74)	9 (75)	48 (81)	
Age[6] (y)	1: < 45 y	321 (63)	290 (63)	5 (42)	36 (61)	.398
	2: 45–60 y	127 (25)	117 (25)	3 (25)	13 (22)	
	3: > 60 y	62 (12)	56 (12)	4 (33)	10 (17)	
Pain in joints other than TMJ, including knees, ankles, shoulders, wrists, elbow joints, hips, and phalangeal joints	No	382 (75)	348 (75)	6 (50)	40 (68)	.151
	Yes	128 (25)	115 (25)	6 (50)	19 (32)	
History of mental disease, such as depression or anxiety	No	472 (93)	430 (93)	12 (100)	54 (91)	.776
	Yes	38 (7)	33 (7)	0 (0)	5 (9)	
Clinical examination						
Maximal unassisted opening of the jaw[7,24] (mm)	Normal: ≥ 40	248 (49)	228 (49)	5 (42)	25 (42)	.749
	Abnormal: < 40	262 (51)	235 (51)	7 (58)	34 (58)	
Maximal laterotrusion of the jaw to the left[7,24] (mm)	Normal: ≥ 7	225 (44)	209 (45)	4 (33)	20 (34)	.356
	Abnormal: < 7	285 (56)	254 (55)	8 (67)	39 (66)	
Maximal laterotrusion of the jaw to the right[7,24] (mm)	Normal: ≥ 7	163 (32)	152 (33)	4 (33)	15 (25)	.722
	Abnormal: < 7	347 (68)	311 (67)	8 (67)	44 (75)	
Maximal protrusion of the jaw[7,24] (mm)	Normal: ≥ 7	244 (48)	225 (49)	4 (33)	23 (39)	.403
	Abnormal: < 7	266 (52)	238 (51)	8 (67)	36 (61)	
Pain on active movement of the jaw during opening of the jaw to the maximum, protrusion of the jaw to the maximum, and laterotrusion of the jaw to the left and right[7,24]	0: No pain on movement;	110 (22)	102 (22)	1 (8)	9 (15)	.819
	1: Pain on 1 movement	89 (17)	80 (17)	3 (25)	12 (20)	
	2: Pain on ≥ 2 movements	311 (61)	281 (61)	8 (67)	38 (64)	
Muscular pain with palpation on posterior temporalis, middle temporalis, anterior temporalis, superior masseter, middle masseter, inferior masseter, and posterior mandibular region and submandibular region of both sides[7]	0: No pain in any site	283 (56)	256 (55)	7 (58)	34 (58)	.947
	1: Pain in 1–3 sites	99 (19)	87 (19)	2 (17)	14 (24)	
	2: Pain in 4–6 sites	75 (15)	69 (15)	2 (17)	8 (14)	
	3: Pain in 7 or more sites	53 (10)	51 (11)	1 (8)	3 (5)	
Joint pain with palpation on lateral and posterior joints of both sides[7,24]	0: Pain in 1 site	194 (38)	176 (38)	3 (25)	21 (35)	.946
	1: Pain in 2 sites	180 (35)	161 (35)	5 (42)	24 (41)	
	2: Pain in 3 or 4 sites	136 (27)	126 (27)	4 (33)	14 (24)	
TMJ click on opening, closing, or horizontal excursion[24]	Absent	321 (63)	291 (63)	8 (67)	38 (64)	.989
	Present: TMJ click in 1 or both joints	189 (37)	172 (37)	4 (33)	21 (36)	
TMJ crepitus on opening, closing, or horizontal excursion[24]	0: TMJ crepitus in 1 joint	485 (95)	440 (95)	11 (92)	56 (95)	.976
	1: TMJ crepitus in both joints	25 (5)	23 (5)	1 (8)	3 (5)	
Questionnaires						
Sleep bruxism: Clench or grind teeth when asleep, based on any information you may have (from OBC)[25]	No: None of the time	421 (82)	382 (83)	11 (92)	50 (85)	.833
	Yes: < 1 night/mo; 1–3 nights/mo; 1–3 nights/wk; 4–7 nights/wk	89 (18)	81 (17)	1 (8)	9 (15)	
Awake bruxism: Clench teeth or grind teeth together during waking hours (from OBC)[25]	No: None of the time	402 (79)	362 (78)	10 (83)	50 (85)	.683
	Yes: A little of the time; some of the time; most of the time; all of the time	108 (21)	101 (22)	2 (17)	9 (15)	
Chewing-side preference (from OBC)[25]	No: None of the time	155 (30)	139 (30)	3 (25)	19 (32)	.964
	Yes: A little of the time; some of the time; most of the time; or all of the time	355 (70)	324 (70)	9 (75)	40 (68)	
OHRQoL at baseline (from OHIP-C14)[26]	Normal OHRQoL: OHIP-SC = 0	157 (31)	141 (30)	3 (25)	19 (32)	.604
	Low OHRQoL: OHIP-SC > 0	353 (69)	322 (70)	9 (75)	40 (68)	

TMJ = temporomandibular joint; OBC = Oral Behavior Checklist; OHRQoL = Oral health–related quality of life; OHIP-C14 = Chinese version of 14-item Oral Health Impact Profile; OHIP-SC = summary score of OHIP-C14.

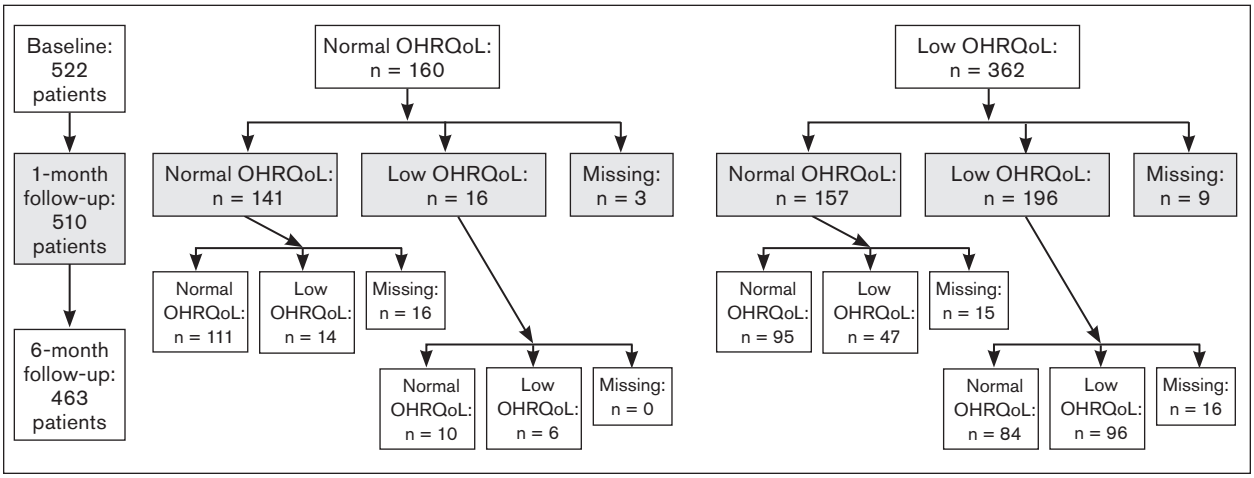


Fig 1 Flowchart showing the number of patients with normal oral health–related quality of life (OHRQoL), number of patients with low OHRQoL, and number of patients lost to follow-up from baseline to 6 months.

Results

A total of 510 patients who completed the 1-month follow-up were included in the analyses; the follow-up rate at 1 month was 98%. Of the 510 included patients, 381 (75%) were female and 129 (25%) were male. The mean age ± standard deviation (SD) was 39 ± 16 years for women and 38 ± 16 years for men.

A total of 463 patients completed the 6-month follow-up and were included in the analyses; the follow-up rate at 6 months was 89%. Of the 463 included patients, 342 (74%) were female and 121 were male (26%). The mean age was 39 ± 16 years for women and 37 ± 16 years for men.

The distribution of the potential predictors is presented in Table 2. Twelve patients were lost to follow-up at 1 month and 59 patients at 6 months because they changed their phone numbers, gave incorrect email addresses or phone numbers, or moved and therefore could not be contacted. However, the differences in distributions of potential predictors between patients who were available at the 1- and 6-month follow-ups and patients who were absent at the follow-ups were not statistically significant. Figure 1 shows the flowchart regarding the relationships of number of patients with normal OHRQoL, number of patients with low OHRQoL, and number of patients lost to follow-up over time from baseline to the 6-month follow-up. The number of patients with low OHRQoL at the 1-month follow-up and at the 6-month follow-up were 212 (42%) and 163 (35%), respectively.

The univariate associations between the potential predictors and the outcome for both 1- and 6-month follow-ups are presented in Table 3. Table 4 shows the predictors included in the final models based on hierarchical modeling in the multivariate logistic regressions. It shows that more sites of joint pain with palpation, the presence of awake bruxism, the presence of a chewing-side preference, low OHRQoL at baseline, and a history of mental disease were important, accurate, and valid predictors for lower OHRQoL in TMJ OA patients at both the 1- and 6-month follow-ups after arthrocentesis treatment.

The shrinkage factors of the models for the 1- and 6-month follow-ups were 0.91 and 0.89, respectively, showing good internal validity for both models. The AUCs of the two models were 0.80 (95% confidence interval [CI]: 0.77 to 0.84) and 0.80 (95% CI: 0.76 to 0.84), respectively (Fig 2). The calibration plots showed that there was good fit between the predicted probability and actual probability of low OHRQoL in both models (Fig 2), indicated by the fact that most plotted points were lying close to the diagonal line. With resulting values for the HL tests of 0.86 and 0.73, the goodness of fit of the two models was good.

The cutoffs for predicted probability of low OHRQoL in patients with TMJ OA in the two models were 0.38 and 0.43, respectively. The sensitivity, specificity, PPV, NPV, false positives, and false negatives of the two models at the cutoffs are presented in Table 5. The added value of the model at the 1-month follow-up for ruling in the patients with low OHRQoL was 0.19 (95% CI: 0.12 to 0.25), while that for ruling out the patients with low OHRQoL was 0.28 (95% CI: 0.22 to 0.35). The added value of the model at the 6-month follow-up for ruling in the patients with low OHRQoL was 0.31 (95% CI: 0.22 to 0.39), while that for ruling out the patients with low OHRQoL was 0.15 (95% CI: 0.09 to 0.21).

To enhance clinical usefulness of the models, the final regression models were transformed into a score chart and line charts (Fig 3). The cutoffs of the sum scores of the two models for low OHRQoL are 145 and 141, respectively.

Table 3 Univariate Analyses of the Potential Predictors Based on OHRQoL of Patients at 1-Month (n = 510) and 6-Month (n = 463) Follow-ups (Chi-Square Test)

	Model 1 (1 mo)			Model 2 (6 mo)		
Variables	No. of patients with low OHRQoL (n = 212, 42%)	No. of patients with normal OHRQoL (n = 298, 58%)	*P* value	No. of patients with low OHRQoL (n = 163, 35%)	No. of patients with normal OHRQoL (n = 300, 65%)	*P* value
Patient characteristics and history						
Gender, n (%)			.897			.895
Female	159	222		121	221	
Male	53	76		42	79	
Age (y)			.001*			< .001*
< 45	116	205		79	211	
45–60	58	69		49	68	
> 60	38	24		35	21	
Pain in joints other than TMJ			.106 *			< .001*
No	151	231		105	243	
Yes	61	67		58	57	
History of mental disease			< .001*			< .001*
No	182	290		138	292	
Yes	30	8		25	8	
Clinical examination						
Maximal unassisted opening of the jaw			.046*			.525
Normal (≥ 40 mm)	92	156		77	151	
Abnormal (< 40 mm)	120	142		86	149	
Maximal laterotrusion of jaw to the left			.317			.289
Normal (≥ 7 mm)	88	137		79	130	
Abnormal (< 7 mm)	124	161		84	170	
Maximal laterotrusion of jaw to the right			.595			.919
Normal (≥ 7 mm)	65	98		54	98	
Abnormal (< 7 mm)	147	200		109	202	
Maximal protrusion of jaw			.016*			.532
Normal (≥ 7 mm)	88	156		76	149	
Abnormal (< 7 mm)	124	142		87	151	
Pain on active movement of jaw			.023*			.066*
No pain on movement	39	71		26	76	
Pain on 1 movement	29	60		30	50	
Pain on ≥ 2 movements	144	167		107	174	
Muscular pain with palpation			< .001*			< .001*
No pain in any site	82	201		67	189	
Pain in 1–3 sites	44	55		33	54	
Pain in 4–6 sites	44	31		34	35	
Pain in > 6 sites	42	11		29	22	
Joint pain with palpation			< .001*			< .001*
Pain in 1 site	56	138		33	143	
Pain in 2 sites	71	109		54	107	
Pain in 3 or 4 sites	85	51		76	50	
TMJ click			.301			.911
No click in either joint	139	182		103	188	
Click in 1 or both joints	73	116		60	112	
TMJ crepitus			.133*			.394
Crepitus in 1 joint	198	287		153	287	
Crepitus in both joints	14	11		10	13	
Questionnaires						
Sleep bruxism			.155*			.007*
No	169	252		124	258	
Yes	43	46		39	42	
Awake bruxism			< .001*			< .001*
No	146	256		107	255	
Yes	66	42		56	45	
Chewing-side preference			.001*			.035*
No	48	107		39	100	
Yes	164	191		124	200	
OHRQoL at baseline			< .001*			< .001*
Normal OHRQoL	16	141		20	121	
Low OHRQoL	196	157		143	179	

OHRQoL = Oral health–related quality of life; TMJ = temporomandibular joint. **P* < .20.

Table 4 Multivariate Binary Logistic Regression Analyses of the Potential Predictors Based on OHRQoL in Patients at 1-Month (n = 510) and 6-Month Follow-up (n = 463)

	Model 1 (1 mo)			Model 2 (6 mo)		
Variables	β (SE)	Shrunken β	OR (95% CI)	β (SE)	Shrunken β	OR (95% CI)
Age (y)						
< 45				Reference		
45–60				0.592 (0.269)	0.530	1.807 (1.066, 3.063)
> 60				1.275 (0.362)	1.141	3.580 (1.760, 7.281)
Pain in joints other than TMJ						
No				Reference		
Yes				0.664 (0.259)	0.594	1.942 (1.169, 3.227)
History of mental disease						
No	Reference			Reference		
Yes	1.246 (0.471)	1.136	3.478 (1.382, 8.752)	1.524 (0.487)	1.364	4.590 (1.768, 11.917)
Maximal protrusion of jaw						
Normal (≥ 7 mm)	Reference					
Abnormal (< 7 mm)	0.446 (0.213)	0.406	1.562 (1.029, 2.369)			
Muscular pain with palpation						
No pain in any site	Reference					
Pain in 1–3 sites	–0.179 (0.279)	–0.163	0.836 (0.484, 1.446)			
Pain in 4–6 sites	0.077 (0.313)	0.071	1.080 (0.585, 1.995)			
Pain in > 6 sites	1.329 (0.397)	1.211	3.776 (1.733, 8.225)			
Joint pain with palpation						
Pain in 1 site	Reference			Reference		
Pain in 2 sites	–0.099 (0.260)	–0.090	0.906 (0.544, 1.508)	0.560 (0.284)	0.501	1.751 (1.003, 3.056)
Pain in 3 or 4 sites	0.512 (0.282)	0.466	1.668 (0.960, 2.900)	1.595 (0.308)	1.428	4.929 (2.694, 9.019)
Sleep bruxism						
No				Reference		
Yes				0.574 (0.296)	0.514	1.776 (0.993, 3.176)
Awake bruxism						
No	Reference			Reference		
Yes	0.549 (0.263)	0.500	1.731 (1.034, 2.898)	0.560 (0.277)	0.502	1.751 (1.017, 3.017)
Chewing-side preference						
No	Reference			Reference		
Yes	0.648 (0.240)	0.590	1.911 (1.194, 3.059)	0.330 (0.258)	0.296	1.391 (0.839, 2.307)
OHRQoL at baseline						
Normal OHRQoL	Reference			Reference		
Low OHRQoL	1.989 (0.321)	1.813	7.308 (3.892, 13.724)	0.555 (0.310)	0.497	1.743 (0.949, 3.198)
Constant	–2.979 (0.354)	–2.715		–2.804 (0.346)	–2.510	

β = regression coefficient; SE = standard error; OR = odds ratio; CI = confidence interval; TMJ = temporomandibular joint; OHRQoL = oral health–related quality of life.

Discussion

At the 1-month follow-up, low OHRQoL at baseline was the strongest predictor of OHRQoL, while at the 6-month follow-up, joint pain with palpation was the strongest predictor of OHRQoL.

Moreover, some predictors in the present study were only important for prediction of OHRQoL at either the 1- or 6-month follow-up. For example, muscular pain with palpation and maximal protrusion of the jaw only played a role in predicting OHRQoL at the 1-month follow-up, while age, pain in joints other than the TMJ, and sleep bruxism only played a role in predicting OHRQoL at the 6-month follow-up. HA can alleviate jaw pain by reducing the levels of inflammatory mediators in the joint and has a positive effect on joints even when the HA itself has been metabolized[38,39]; that is, the effectiveness of HA is long-acting after treatment, and the symptoms of TMJ OA can be increasingly improved over time. So, the effectiveness of HA for pain relief and for improvement of jaw function in the long term may be better than that in the short term. This may explain why patients with more severe muscular pain and abnormal maximal protrusion of the jaw at baseline are more likely to have low OHRQoL at the 1-month follow-up, but not at the 6-month follow-up.

Furthermore, TMJ OA is an age-related disease.[40] Older patients are more likely to have more severe TMJ OA,[40] which may be more difficult to cure and more likely to be recurrent after treatment. In addition, patients with generalized muscle and joint pain are more likely to be associated with changes in the peripheral and central nervous systems.[41] These patients are more sensitive to pain and may feel higher intensity of long-lasting pain.[42] Arthrocentesis with

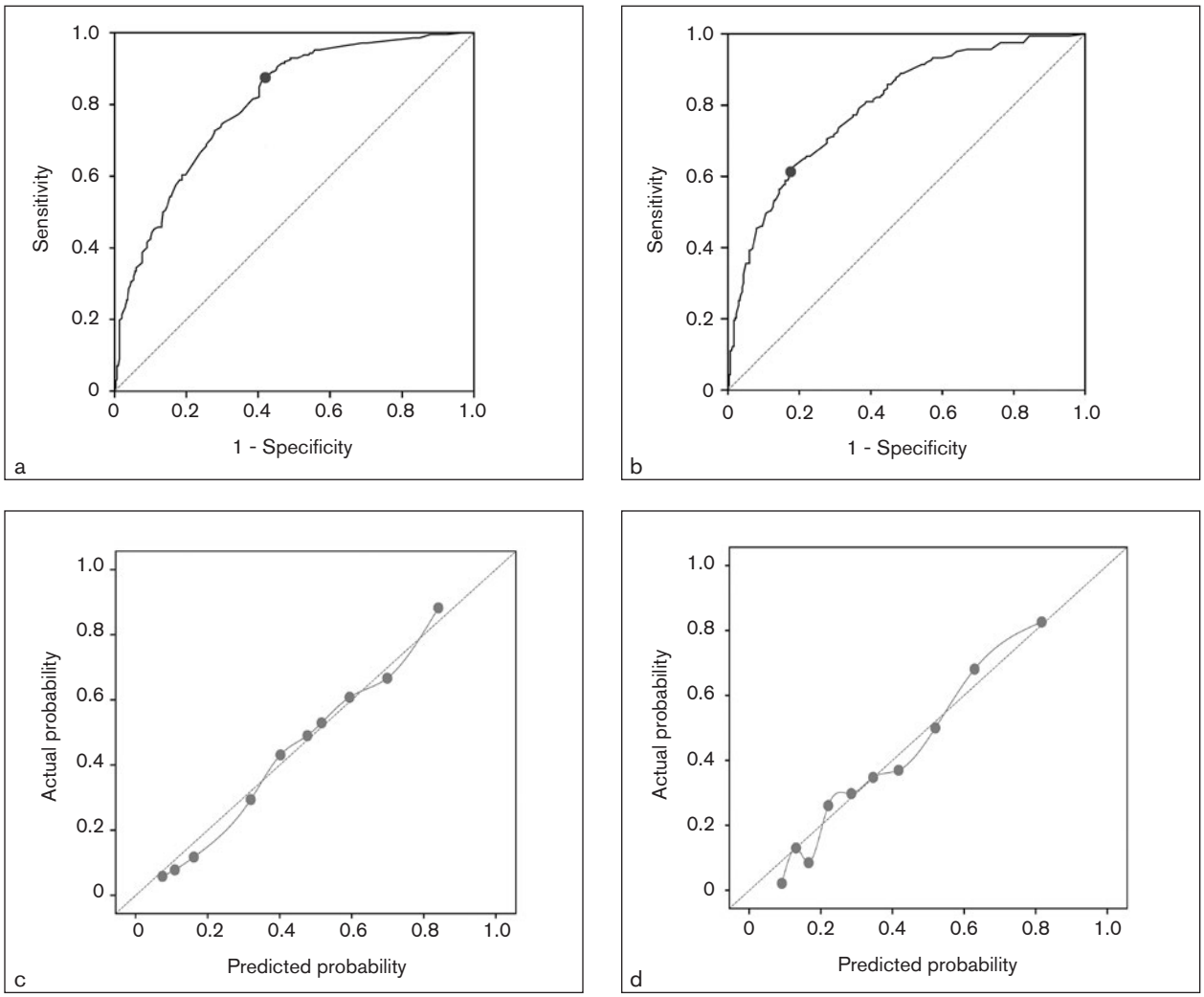


Fig 2 **(a, b)** Discrimination and **(c, d)** calibration of the final models for prediction of low oral health–related quality of life (OHRQoL) in patients with temporomandibular joint osteoarthritis (TMJ OA) at the **(a, c)** 1-month and **(b, d)** 6-month follow-ups. **(a, c)** Diagonal line represents a model with no discrimination, with an AUC of 0.50. The dot indicates 38% predicted probability (cutoff point) of low OHRQoL with sensitivity of 0.87 and specificity of 0.59 in the model at **(a)** 1-month follow-up and 43% predicted probability (cutoff point) of low OHRQoL with sensitivity of 0.62 and specificity of 0.83 in the model at **(b)** 6-month follow-up. **(c, d)** Diagonal line represents the predicted probability of the model is the same as the actual probability of the model, and the prediction is neither underestimated nor overestimated. The dot represents the deciles of the study members based on the predicted probability.

Table 5 Predictive Characteristics of the Two Models at Cutoff for Predicted Probability

Model	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	FP (95% CI)	FN (95% CI)
Model 1 (1 mo)	0.87 (0.82, 0.91)	0.59 (0.53, 0.64)	0.60 (0.55, 0.65)	0.87 (0.81, 0.91)	0.24 (0.21, 0.28)	0.05 (0.04, 0.08)
Model 2 (6 mo)	0.62 (0.54, 0.69)	0.83 (0.78, 0.87)	0.66 (0.58, 0.73)	0.80 (0.75, 0.84)	0.11 (0.09, 0.14)	0.13 (0.11, 0.17)

PPV = positive predictive value; NPV = negative predictive value; FP = false positives; FN = false negatives; CI = confidence interval.

HA injections may be transiently effective for pain relief in TMJs in the short term for these patients, but in the long run, pain in the TMJs may be recurrent because the problem in the nervous system still exists. That may explain why patients at older ages and having presence of pain in other joints are more likely to have low OHRQoL at the 6-month follow-up, but not at the 1-month follow-up. Furthermore, sleep bruxism may cause orofacial pain due to eccentric muscle contractions and overloading of the TMJs.[43,44] In the short term, patients with sleep bruxism may have less pain due to HA injection after treatment; however, HA injection does not resolve bruxism, and the presence of persistent sleep bruxism may exacerbate the pain in the orofacial area. This may explain why patients with presence of sleep bruxism are more likely to have low OHRQoL at the 6-month follow-up but not at the 1-month follow-up.

Model 1		
Predictors	Value	Score
History of mental disease	No	0
	Yes	74
Maximal protrusion of jaw	≥ 7 mm	0
	< 7 mm	27
Muscular pain with palpation	No pain/pain in 1–6 sites	0
	Pain in > 6 sites	79
Joint pain with palpation	Pain in 1–2 sites	0
	Pain in 3 or 4 sites	30
Awake bruxism	No	0
	Yes	33
Chewing-side preference	No	0
	Yes	39
OHRQoL at baseline	Normal OHRQoL	0
	Low OHRQoL	118
Total score		400

Model 2		
Predictors	Value	Score
Age	< 45 y	0
	45–60 y	33
	> 60 y	72
Pain in joints other than TMJs	No	0
	Yes	38
History of mental disease	No	0
	Yes	86
Joint pain with palpation	Pain in 1 site	0
	Pain in 2 sites	32
	Pain in 3 or 4 sites	90
Sleep bruxism	No	0
	Yes	32
Awake bruxism	No	0
	Yes	32
Chewing-side preference	No	0
	Yes	19
OHRQoL at baseline	Normal OHRQoL	0
	Low OHRQoL	31
Total score		400

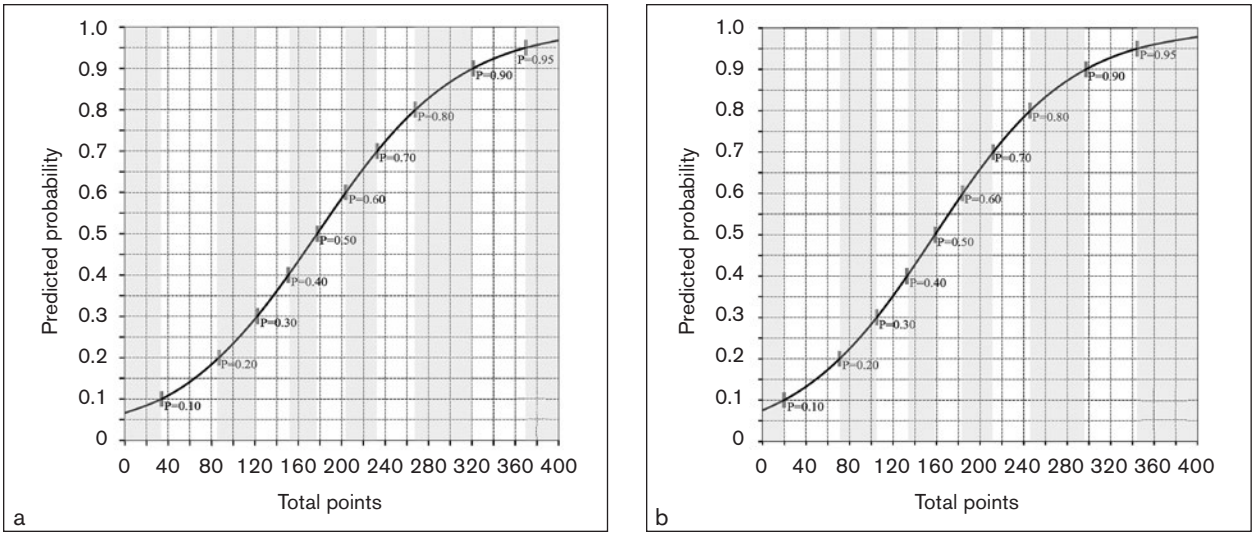


Fig 3 **(a)** Score charts for the risk of low oral health–related quality of life (OHRQoL) in patients with temporomandibular joint osteoarthritis (TMJ OA) and line charts for reading the predicted probability of total points for the model at **(b)** 1-month follow-up and **(c)** 6-month follow-up. Instructions: If a predictor is scored positively in the score chart, a given weighted score is assigned. The scores of each predictor are added to calculate the sum score of that model. From the line charts below the score chart, the exact risk (or predicted probability, %) of low OHRQoL for an individual patient (y axis) can be determined based on the total points (x axis) and the curve.

In the present study, based on several common and easily obtainable variables of patients that were treated with arthrocentesis with HA injections for their TMJ OA, two models have been derived to predict low OHRQoL at 1 month and 6 months post-treatment. To the authors' knowledge, these are the first prediction models for low OHRQoL in oral health care to be presented, and in patients with TMJ OA in particular.

For dentists, it is important to know the risk of low OHRQoL in patients after completing a series of HA injections. Based on the reported models, dentists can predict a patient's OHRQoL at 1 month and 6 months after the injections before such treatment is initiated. This provides the dentist with information for decision-making at the patient's first visit on whether to start HA injection by assessing whether HA injections have sufficient benefits to improve the patient's OHRQoL, and, if not, whether other treatments (such as psychological and social support or other types of physical treatments) are needed. Moreover, the reported models may help shape patient expectations of their OHRQoL at 1 month and 6 months after HA injections.

Patient profile

Demographic characteristics

Age: 65 y | Gender: Female

History

Mental disease: no | Pain in other joints: Yes

Clinical examination

Maximal protrusion of jaw: 5 mm | Muscular pain with palpation: 2 sites | Joint pain with palpation: 2 sites

Questionnaires

Awake bruxism: No | Sleep bruxism: Yes

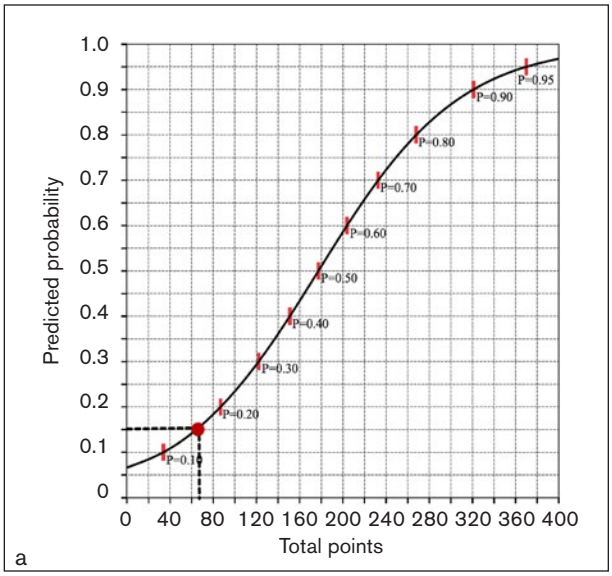
Chewing-side preference: Yes | OHRQoL at baseline: Normal

Model 1 (1-month follow-up)

Predictors	Value	Score
History of mental disease	No	**0**
	Yes	74
Maximal protrusion of jaw	≥ 7 mm	0
	< 7 mm	**27**
Muscular pain with palpation	No pain/pain in 1–6 sites	**0**
	Pain in > 6 sites	79
Joint pain with palpation	Pain in 1–2 sites	**0**
	Pain in 3 or 4 sites	30
Awake bruxism	No	**0**
	Yes	33
Chewing-side preference	No	0
	Yes	**39**
OHRQoL at baseline	Normal OHRQoL	**0**
	Low OHRQoL	118
Total score		**66**

Model 2 (6-month follow-up)

Predictors	Value	Score
History of mental disease	No	**0**
	Yes	86
Pain in joints other than TMJs	No	0
	Yes	**38**
Age	< 45 y	0
	45–60 y	33
	> 60 y	**72**
Joint pain with palpation	Pain in 1 site	0
	Pain in 2 sites	**32**
	Pain in 3 or 4 sites	90
Sleep bruxism	No	0
	Yes	**32**
Awake bruxism	No	**0**
	Yes	32
Chewing-side preference	No	0
	Yes	**19**
OHRQoL at baseline	Normal OHRQoL	**0**
	Low OHRQoL	31
Total score		**193**



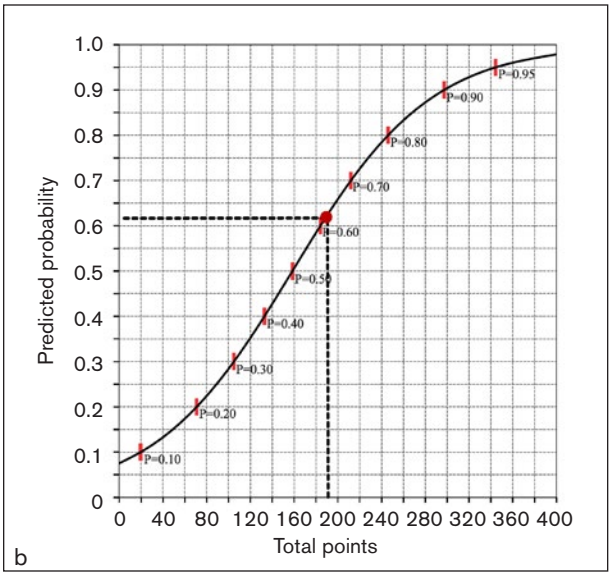


Fig 4 An example of how to use the prediction models in clinical practice. **(a)** The predicted probability for low OHRQoL at 1 month is 15% based on line chart A, which is lower than the cutoff of the predicted probability (38%), so the patient is not likely to have a low OHRQoL at 1 month following treatment. **(b)** The predicted probability for low OHRQoL at 6 months is 62% based on line chart B, which is higher than the cutoff of predicted probability (43%), so the patient is likely to have a low OHRQoL at 6 months following treatment. Clinical implications: Because the patient is likely to have low OHRQoL at 6 months, clinicians should re-evaluate the patients regularly and pay more attention to the patient's psychosocial status during follow-up. If necessary, psychosocial support should be adopted to improve the patient's psychosocial status. Physical treatment can be used to treat the patient's sleep bruxism. Also, clinicians can suggest the patient avoid the chewing-side preference and seek treatment for pain in other joints.

It is important to determine the optimal cutoff for predicted probability for risk stratification. It is the point at which the sum of sensitivity and specificity is at its maximum and where misclassification is lowest. The present models regarded 0.38 and 0.43 as the cutoffs for predicted probability of low OHRQoL at the 1-month and 6-month follow-ups, respectively, because the sum of sensitivity and specificity at both points were maximum in each model. Hence, when the sum scores of patients were over 145 and 141 in the two models, respectively, patients were most accurately predicted to have low OHRQoL at 1 month or 6 months after the HA injections.

In the present study, the added predictive values of the two models for ruling in low OHRQoL were 0.19 and 0.28, respectively, while those for ruling it out were 0.31 and 0.15, respectively. This indicates that if a patient with TMJ OA has a predicted probability of low OHRQoL of more than the cutoff of 0.38 (score > 145) in the model at the 1-month follow-up or more than the cutoff of 0.43 (score > 141) in the model at the 6-month follow-up, the posterior risk of low OHRQoL of this patient can be increased by 0.19 and 0.28, respectively, when compared to the prevalence of low OHRQoL at both follow-ups. Similarly, if a patient with TMJ OA has a predicted probability of low OHRQoL of less than 0.38 in the model at the 1-month follow-up or less than 0.43 in the model at the 6-month follow-up, the posterior probability of normal OHRQoL of this patient can be increased by 0.31 and 0.15, respectively, when compared to the prevalence of normal OHRQoL (complement of the prevalences of low OHRQoL) at both follow-ups. For the defined cutoff of the two models, the added values are considerable, so they add to accurate prediction of low OHRQoL.

In addition, it should be noted that with a false positive prediction, a patient who may not need more comprehensive treatments or more frequent follow-ups for re-evaluations is likely to receive this anyway, and therefore false positives give rise to an increase in financial and psychological burdens and waste resources. Moreover, with a false negative prediction, a patient who may need more comprehensive treatment or regular follow-ups for re-evaluations is unlikely to receive this, and this may result in less desired health outcomes. The risk of a false positive or false negative prediction of low OHRQoL, however, is 0.05 and 0.24, respectively, in the model at 1-month follow-up, and is 0.13 and 0.11, respectively, in the model at the 6-month follow-up. The risk for false positives and false negatives therefore can be considered relatively small.

The present study prospectively followed a cohort to collect outcome data and deviated from the conventional multivariate approach to data analyses of causal research. The two prediction models derived for low OHRQoL are multivariate but descriptive in nature; that is, claims of causation between included predictors and the outcome were avoided, and control for confounders was achieved by multivariate adjustment for covariates. Moreover, the relative contributions of the different predictors to the risk of low OHRQoL were weighted. This weight was included in the score charts, which can be used to calculate a risk of low OHRQoL for an individual. Figure 4 presents an example of how to use the prediction models in clinical practice.

Furthermore, in the derivation of the model, the study clearly deviated from using the conventional *P* value of .05 as the threshold for statistical significance. A less stringent threshold in the chi-square tests was used in the selection and exclusion of variables and in the multivariate regression analyses to minimize false negatives in the final model to avoid false negative findings in both modeling stages, which could lead to unjustified exclusion of independent predictors from the final model.[45]

A small number of events relative to the high number of potential predictors is a common limitation in many studies. An events per variable (EPV) value of 10 is widely advocated for multivariate logistic regression analyses to obtain a reliable outcome.[46,47] In the present model, there were 10 predictors included in the model at both follow-ups for multivariate analysis. The study was able to achieve this conventional threshold criterion with 21 EVP in the model at the 1-month follow-up and 16 EVP in the model at the 6-month follow-up.

Conclusions

In the present study, patient history of mental diseases, maximal protrusion of the jaw, muscular pain with palpation, joint pain with palpation, awake bruxism, chewing-side preference, and OHRQoL at baseline were significantly associated with low OHRQoL at the 1-month follow-up, while patient age, pain in other joints, history of mental disease, joint pain with palpation, sleep bruxism, awake bruxism, chewing-side preference, and OHRQoL at baseline were significantly associated with low OHRQoL at the 6-month follow-up. The added predictive values of the two models at cutoff for predicted probability may be considered sufficient for both ruling in and ruling out the risk of low OHRQoL at 1-month and 6-month follow-ups in decision-making. The score chart and line charts based on these models may assist clinicians in risk stratification of patients with TMJ OA and low OHRQoL. As such, both prediction models may aid decision-making for patient management in

health care and informing the patient. The performance of the models still needs to be tested in other populations of patients with TMJ OA to enable valid and reliable use of the score charts in clinical practice.

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