Development of a Multivariable Model Based on Individual Risk Factors for Recurrent Lateral Patellar Dislocation

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Background: Nonoperative treatment after first-time patellar dislocation is the standard of care. There is evidence that certain patients may be at high risk for recurrent instability. The aim of this study was to develop a multivariable model to guide management of patients based on their individual risk of recurrent dislocation.

Methods: A multivariable model was developed using 291 patients from 4 institutions to identify which patients were at higher risk for recurrent patellar dislocation within 2 years. This model was informed by a univariable logistic regression model developed to test factors based on the patient's history, physical examination, and imaging. The discriminatory ability of the model to classify who will or will not have a recurrent dislocation was measured using the area under the receiver operating characteristic curve (AUC).

Results: Age, a history of a contralateral patellar dislocation, skeletal immaturity, lateral patellar tilt, tibial tubercletrochlear groove (TT-TG) distance, Insall-Salvati ratio, and trochlear dysplasia were the most important factors for recurrent patellar dislocation. Sex, mechanism of injury, Caton-Deschamps ratio, sulcus angle, inclination angle, and facet ratio were not factors for recurrent dislocation. The overall AUC for the multivariable model was 71% (95% confidence interval [CI]: 64.7% to 76.6%).

Conclusions: Optimizing the management of lateral patellar dislocation will improve short-term disability from the dislocation and reduce the long-term risk of patellofemoral arthritis from repeated chondral injury. This multivariable model can identify patients who are at high risk for recurrent dislocation and would be good candidates for early operative treatment. Further validation of this model in a prospective cohort of patients will inform whether it can be used to determine the optimal treatment plan for patients presenting with an initial patellar dislocation. Until validation of the model is done with new patients, it should not be used in clinical practice.

Level of Evidence: Prognostic Level III. See Instructions for Authors for a complete description of levels of evidence.

The treatment of patients with lateral patellar dislocation (LPD) is variable, and there remains uncertainty over the optimal strategy. The current standard of care for managing first-time LPD is nonoperative treatment unless there is a need to address substantial osteochondral injuries¹⁻³. However, recurrent instability following first-time LPD is a growing concern, as recurrent dislocation rates have been reported to range widely from 15% to 88% of patients⁴⁻⁹. Thus, certain patients may benefit from surgery after the initial dislocation to prevent long-term morbidity, including decreased knee function and a >70%

rate of chondral/osteochondral injury¹⁰⁻¹². A Cochrane review showed that surgical treatment for first-time LPD resulted in a lower recurrent dislocation rate at 2 to 5 years compared with non-surgical intervention¹³. One economic analysis showed that, compared with delayed surgery or nonoperative treatment, immediate surgery provided the most benefits in terms of long-term quality of life of adolescents presenting with first-time LPD¹⁴.

Identification of risk factors may help classify patients for whom nonoperative treatment is more likely to fail and who would benefit from early surgical stabilization. Recent studies

Disclosure: The authors indicated that no external funding was received for any aspect of this work. On the **Disclosure of Potential Conflicts of Interest** forms, which are provided with the online version of the article, one or more of the authors checked "yes" to indicate that the author had a relevant financial relationship in the biomedical arena outside the submitted work (http://links.lww.com/JBJS/G334).

have identified risk factors for recurrent LPD, including age, skeletal immaturity, a history of patellar dislocation, contralateral patellar dislocation, patella alta, extensor mechanism malalignment, knee valgus, axial plane deformities, generalized ligamentous laxity, and trochlear dysplasia^{5,6,8,15,16}. Although attempts have been made to quantify thresholds for individual risk factors, they do not have a 1-to-1 relationship with clinical management decisions. A multivariable model can estimate a patient's probability of recurrence based on his/her unique combination of demographic, physical, and radiographic findings¹⁷.

The aim of this study was to develop a multivariable model that can accurately estimate the probability of recurrent patellar dislocation for each individual patient, thereby allowing orthopaedic surgeons to customize treatment to the patient rather than to the event or injury.

Materials and Methods

I nvestigators in 6 published studies on risk factors for recurrent LPD were contacted. Data sets were no longer available for 3 articles^{5,6,18} but were obtained for the remaining 3 articles^{8,19,20}, one of which consisted of 2 cohorts from 2 different centers^{16,19}. Thus, data were available from 4 "studies." The populations for each of the 4 studies and the potential predictor variables that were assessed are shown in Table I. Binary variables included sex, mechanism of injury, history of contralateral patellar dislocation, and skeletal immaturity. The Dejour classification (none, A, B, C, or D) was a categorical variable. All other variables were continuous.

Due to variability in the factors, multiple imputation was used for variables with missing data to prevent a reduction in statistical power²¹. In this procedure, a missing value is imputed using available data. A multivariable model is developed in which the missing variable is the dependent variable and the other variables (including the outcome variable) are the independent variables. This model is used to fill in the missing value based on the values of the other variables. For instance, measurements of lateral patellar tilt were not reported in 1 study. To impute the missing values, a linear regression model can be used since the dependent variable (lateral patellar tilt) is a continuous variable. The independent variables for this multiple imputation model would be any number of the variables that are listed in Table I plus the outcome regarding recurrent LPD.

To inform the model for multiple imputation, univariable logistic regression analysis was performed for all variables for which data were available, with recurrent dislocation as the outcome. Variables for which the p value was <0.15 were included in the multiple imputation model. This liberal cutoff was chosen to avoid overestimating the accuracy of the final model. Most models are overfitted, or overly optimistic, and do not perform as well for new patients when the standard p < 0.05 is used²².

Ten complete data sets were generated using multiple imputation by chained equations²³. Multiple data sets are necessary to reflect the uncertainty in effect estimates and not underestimate standard errors. The predicted values are only possible replacements for the missing values, not the true values. MULTIVARIABLE MODEL BASED ON INDIVIDUAL RISK FACTORS FOR RECURRENT LATERAL PATELLAR DISLOCATION

Each imputed data set was analyzed separately, and the point estimates and standard errors were combined using weighted averages to produce a single set of effect estimates.

To develop the multivariable model for recurrent LPD, the MAMI command was used in the statistical software R²⁴. This command performs a Bayesian model averaging (BMA) procedure on multiple-imputed data. The BMA procedure was chosen since all possible combinations of factors are considered and model selection is based on the Bayesian information criterion (BIC). In contrast to p values, the BIC has the advantage of not leading to overfitted models when validated on new patients²⁵. The multivariable model for recurrent dislocation was developed using logistic regression analysis in which the binary outcome was recurrent dislocation and the factors were the same variables that were used for the multiple imputation model. The BMA procedure gives the posterior effect probabilities, ranging from 0 to 1, that measure the importance of each variable²⁴.

The discrimination of the multivariable model, or its ability to distinguish between individuals who do and those who do not have a recurrent dislocation, was measured using the area under the receiver operating characteristic curve (AUC). The AUC is an overall measure of the model's accuracy and can be defined as the probability that, for each randomly selected pair of subjects consisting of 1 with the outcome and 1 without, the predicted probability will be higher for the subject with the outcome²⁶.

The coefficients from the final model can be added on the logarithmic scale and then transformed to calculate the predicted probability of recurrence. For easier calculations, the coefficients can be seen as the relative weight of each factor in a clinical scoring rule. From this set of weights, the coefficients were converted into integers by dividing all of the coefficients by the smallest value. Thus, each patient is assigned a total risk score based on his/her unique combination of factors.

Results

ata from 291 patients were available for developing the multivariable model (Table II); 163 (56%) experienced a recurrent patellar dislocation event within 2 years. The results from the univariable logistic regression analysis are shown in Table III. The factors that were significant at the p < 0.15 level were chronological age at the initial LPD, a history of contralateral patellar dislocation, skeletal immaturity (open physes), Insall-Salvati ratio, lateral patellar tilt, tibial tubercle-trochlear groove (TT-TG) distance, sulcus angle, and trochlear depth. The significant factors from the univariable analysis, plus the outcome recurrent LPD, were used to build the model for multiple imputation. The presence of trochlear dysplasia was categorized based on the Dejour classification, for which the most data were available, and trochlear depth. Despite being significant in the univariable model, the sulcus angle was >144° for 93% of the patients who had this measurement. This high proportion would prevent the model from discriminating between patients with and those without recurrence. Thus, trochlear dysplasia was a composite measure defined by a Dejour type-B, C, or D classification or trochlear depth of ≤ 3 mm.

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	Arendt et al. $(2018)^{16,19}$: Cohorts A (N = 37) and B (N = 108)	Balcarek et al. ²⁰ (2014) (N = 61)	Jaquith and Parikh ⁸ (2017) (N = 85)
opulation	Prospective study of consecutive patients from emergency rooms (Cohort A) or musculoskeletal clinics (Cohort B)	Case-control study of patients with and without recurrence	Retrospective review of pediatric patients from emergency room
Predictor			
Age	Years	Years	Years
Sex	M/F	M/F	M/F
Mechanism of injury	Contact/non-contact		Direct/indirect
History of contralateral patellar dislocation	Y/N	Y/N	Y/N
Caton-Deschamps ratio	Sagittal MRI on which patellar cartilage length was greatest: length of patellar tendon/length of patellar articular cartilage		Lateral knee radiograph: length from anterior-proximal corner of tibial plateau to most inferior point of patellar articular surface/length of patellar articular surface
Insall-Salvati ratio	Sagittal MRI on which patellar cartilage length was greatest: length of patellar tendon/length of patella	Sagittal MRI on which patellar cartilage length was greatest: length of patellar tendon/length of patella	
Skeletal immaturity	Open vs. closed/closing	Open vs. closed/closing	Open vs. closed/closing
Lateral patellar tilt	Axial MRI referencing an angle between posterior condyles at most inferior level of full posterior articular cartilage and greatest patellar width (may require 2 slices)	Measured by angle formed between transverse axis of patella and posterior condylar axis	
TT-TG distance	MRI axial length measurement between 2 points (requires 2 slices): (1) posterior condyles at most inferior level of full posterior articular cartilage, a point 90° to this baseline through lowest point of trochlear groove cartilage and (2) midline of patellar tendon insertion onto tibia	MRI axial length measurement between deepest point of trochlear groove and most anterior portion of tibial tubercle measured perpendicular to posterior condyle tangent	
Sulcus angle	Angled measurement of most proximal axial MRI cut with full anterior cartilage: measure cartilage surface, beginning at deepest part of trochlear groove and extending to highest points of lateral and medial trochleas		
Trochlear depth	Drop lines at 90° to baseline along posterior condyles at most inferior level of full posterior articular cartilage. Average lengths of medial and lateral trochlear facets, and subtract length of central trochlear groove		
Trochlear facet ratio	Measure on full articular cartilage across anterior aspect of femur from groove to edge of subchondral bone. Calculate ratio of medial trochlear facet length to lateral trochlear facet length		
Lateral trochlear inclination angle	Angle measurement on axial MRI using baseline of posterior aspect of femoral condyle at full articular cartilage. With line drawn across cartilaginous lateral facet		
Dejour classification	Modified Dejour using MRI only in Cohort A; none/modified Dejour using MRI only in Cohort B	A/B/C/D (transverse MRI)	None/A/B/C/D (lateral knee radiograph, confirmed by MRI as needed)

The following factors were incomplete and their data were imputed using multiple imputation: history of contralateral patellar dislocation (n = 4 missing), lateral patellar tilt (n = 93 missing), TT-TG distance (n = 85 missing), and Insall-Salvati ratio (n = 91 missing). Following multiple imputation, BMA was performed on the 10 imputed data sets. The posterior

TABLE II Demographics of 291 Patients Included for Development of the Clinical Prediction Model

Predictor				
Age* (yr)	16.5 (7.4)			
Female (no. [%])	153 (52.6)			
Mechanism of injury direct/contact (no. [%])	66 (29.6)			
History of contralateral patellar dislocation (no. [%])	45 (15.7)			
Caton-Deschamps ratio*	1.3 (0.2)			
Insall-Salvati ratio*	1.3 (0.2)			
Skeletal immaturity (no. [%])	122 (41.9)			
Lateral patellar tilt* (deg)	18.8 (6.8)			
TT-TG distance* (mm)	15.0 (4.2)			
Sulcus angle* (deg)	157.5 (10.9)			
Trochlear depth* (mm)	2.5 (1.2)			
Facet ratio*	0.46 (0.12)			
Inclination angle* (deg)	13.1 (5.4)			
Dejour B/C/D (no. [%])	72 (39.3)			
*The values are given as the mean and standard deviation.				

effect probabilities, or the relative importance of the variables, were: younger age (1.00), increased lateral patellar tilt (0.27), increased Insall-Salvati ratio (0.23), increased TT-TG distance (0.18), history of contralateral patellar dislocation (0.06), trochlear dysplasia (0.04), and skeletal immaturity (0.04). The

latter 3 variables, despite their low probabilities, were included

in the final multivariable model based on clinical judgment. Table IV displays the coefficients for the 7 variables included in the multivariable model. The coefficients were transformed to integers based on their weight relative to the smallest coefficient (TT-TG distance = 0.02). For instance, trochlear dysplasia contributed a score of 3 to the clinical risk score since its coefficient was 0.06 (0.02×3). The overall AUC for the multivariable model was 71% (95% confidence interval [CI]: 64.7% to 76.6%), indicating that, in 71 of 100 randomly selected pairs of patients, the multivariable model would assign a higher risk score to the patient with recurrent dislocation.

Discussion

The optimal management of patellofemoral instability in patients with first-time LPD is an area of clinical equipoise for orthopaedic surgeons. The current standard of care does not stratify by risk and remains nonoperative treatment for an initial dislocation without osteochondral fracture. However, recent evidence, including a Cochrane review¹³, shows that operative treatment may lead to lower recurrence rates and better patientreported outcomes. The ability to classify which patients are more likely to have a recurrent event and which are not without surgery is crucial for optimal clinical management. The use of mathematical modeling brings some quantifiable structure to MULTIVARIABLE MODEL BASED ON INDIVIDUAL RISK FACTORS FOR RECURRENT LATERAL PATELLAR DISLOCATION

overcome the influence of surgeon preference on treatment decisions. This multivariable model can determine which factors contribute most to an increased risk of recurrence.

We used a multivariable approach that considers all possible combinations of factors to develop a model that will help guide management of recurrent LPD. The 7 factors that were identified in our study align closely with those of the other published studies, whose data were not available for this study, that evaluated factors for recurrent LPD. One study showed that younger age, open physes, sports-related injury, patella alta, and trochlear dysplasia were predictive of recurrence⁵. Another study by the same investigators, of patients <18 years old, demonstrated that trochlear dysplasia was associated with recurrent instability within 2 years (p < 0.01) while several other factors approached significance, including sports-related injury (p = 0.06), skeletal immaturity (p = 0.06), and younger age $(p = 0.08)^6$. Our results are similar to those in a recent meta-analysis by Huntington et al. except for 2 variables²⁷. In their study, patients with a previous contralateral patellar dislocation had twice the odds of recurrence compared with those without such a history, and this effect approached significance (p = 0.11). In addition, lateral patellar tilt was evaluated in only 2 of the studies that they reviewed.

Our study has several strengths. While the meta-analysis by Huntington et al.²⁷ is the most comprehensive study on recurrent LPD, methodological flaw is the variability in follow-up duration across studies, ranging from less than a year to 20 years. It is reasonable to expect a higher cumulative likelihood of recurrence with increasing time. In our study, we developed a multivariable model for a finite period of follow-up (minimum, 2 years after the initial dislocation). In addition, 4 data sets were used that contained raw data at the patient level. This synthesis can be

TABLE III Results from Univariable Logistic Regression Analysis to Inform Multiple Imputation Model

Predictor	Coefficient (95% CI)	P Value
Age	-0.09 (-0.14, -0.05)	<0.001
Sex	-0.32 (-0.79, 0.15)	0.18
Mechanism of injury	-0.04 (-0.62, 0.53)	0.88
History of contralateral patellar dislocation	0.53 (-0.14, 1.20)	0.12
Caton-Deschamps ratio	0.05 (-1.27, 1.38)	0.94
Insall-Salvati ratio	1.85 (0.39, 3.32)	0.01
Skeletal immaturity	0.68 (0.20, 1.16)	0.01
Lateral patellar tilt	0.05 (0.01, 0.10)	0.02
TT-TG distance	0.06 (-0.002, 0.13)	0.06
Sulcus angle	0.04 (0.01, 0.07)	0.02
Trochlear depth	-0.22 (-0.50, 0.06)	0.13
Facet ratio	-0.52 (-3.19, 2.15)	0.70
Inclination angle	-0.03 (-0.09, 0.03)	0.30
Dejour none/A vs. B/C/D	0.16 (-0.47, 0.78)	0.62

TABLE IV Coefficients from Final Prediction Model and Converted Integers for Clinical Risk Score					
Predictor	Coefficient (95% CI)	Integer			
Age	-0.08 (-0.13, -0.03)	-4			
History of contralateral patellar dislocation	0.24 (-0.48, 0.96)	12			
Insall-Salvati ratio	1.39 (0.01, 2.76)	69.5*			
Skeletal immaturity	0.14 (-0.45, 0.72)	7			
Lateral patellar tilt	0.03 (-0.03, 0.08)	1.5			
TT-TG distance	0.02 (-0.07, 0.11)	1			
Trochlear dysplasia (Dejour B/C/D or depth ≤3 mm)	0.06 (-0.48, 0.61)	3			
Trochlear dysplasia (Dejour B/C/D or depth ≤3 mm)	0.02 (-0.48, 0.61)	3			

*While this integer may appear large, the Insall-Salvati ratios ranged from 0.8 to 1.9. Thus, the difference between 2 patients would not be as large.

considered an individual patient data meta-analysis, which is the gold standard for this study type and goes beyond the typical pooling of data at the study level²⁸. Investigators who calculate probabilities for recurrent LPD on the basis of multiple factors can make only generic statements (e.g., the presence of 2 risk factors predicted a risk of 51% to 60% whereas the presence of any 3 risk factors predicted a risk of 70% to 79%²⁷). The availability of patient-level data allowed calculation of individual risk scores in our study. Furthermore, factors were measured on a continuous scale, if applicable, to prevent the loss of information and to avoid the problem of variability in thresholds used across studies, which is an issue when dichotomizing values to pool odds ratios²⁷.

The multifactorial nature of recurrent LPD represents a "complex system" that requires more advanced methodological approaches to move the needle from identification of risk factors to risk prediction²⁹. Multiple imputation was used to fill in any gaps across the 4 data sets that were used in our study. A complete-case approach, which is the default for multivariable models, would have included only 194 patients (compared with 291). Multiple imputation is itself a form of prediction modeling, in which the missing data are predicted on the basis of values for all other variables. Our multivariable model for recurrent LPD was developed using mathematical modeling, and a few factors, such as trochlear dysplasia, were added post hoc based on expert opinion. While the low importance of trochlear dysplasia attributed by the BMA procedure may be surprising, the meta-analysis by Huntington et al. also showed that a Dejour classification of B, C, or D was not associated with higher odds of recurrence compared with Dejour type A²⁷. For prediction modeling, parsimony may be less important than model fit. In addition, given that clinicians are the ultimate users of clinical scoring rules, their judgment must be incorporated into the treatment algorithm. Both statistical significance and clinical relevance are important considerations.

This study also has several limitations. While our data came from multinational centers, they are a convenience

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sample of studies with available data sets that the investigators were willing to share. There may be a "selection bias" in the data that were available. While data were collected prospectively and retrospectively, this difference would not affect our results because developing the multivariable model requires a known outcome. The difference in study populations may even lead to improved external validity of the model. The variables were limited to those for which there were sufficient data across the 4 data sets. Some important risk factors such as ligamentous laxity (e.g., Beighton scores) could not be evaluated. In addition, some types of data were missing from the studies, including the role of coronal or axial plane alignment. Furthermore, the fact that the incidence of LPD varies widely across studies may be due to heterogeneity in the measurement of risk factors. There remains a lack of consensus on optimal thresholds and techniques that may affect the validity and reliability of the risk factors in the model. The model that we developed applies to first-time traumatic LPD and is not intended to extend across all types of patellofemoral instability.

Although there is no accepted threshold for adequate accuracy, the AUC value of 71% leaves room for improvement in the model's ability to discriminate between patients who will and those who will not have a recurrent dislocation. Setting a specific threshold will need to take into account how many misclassified patients clinicians are willing to accept. Missing data also precluded the ability to determine an optimal threshold across all risk scores, as this approach requires complete data on a new set of patients.

The lack of validation using an external data set remains the major limitation of our study. This work represents only the first step of developing a multivariable model of factors that are associated with recurrent LPD. External validation and then updating the model are crucial next steps before it can be implemented into routine clinical practice for patient management decisions^{30,31}. To the extent possible, we used methods in developing the multivariable model to avoid a reduction in accuracy at the validation stage, including conservative p values and BMA. However, external validation remains the ultimate test of a model's "goodness of fit."³² The development of our multivariable model provides directions for future research, including validation using external data sets and by independent investigators.

The Justifying Patellar Instability Treatment by Early Results (JUPITER) study is an ideal cohort for validating our multivariable model to identify patients who would benefit from surgical management after first-time dislocation. It is a multicenter, prospective cohort of patients with patellar instability from 12 institutions who are followed for a minimum of 5 years. Validating our model in the JUPITER cohort will help ensure that the final model is representative of the spectrum of patients who are seen in clinical practice. The model is not yet ready for use in clinical practice for management decisions. This work is a first step, for which external validation remains necessary by our group and other investigators. We intend to validate our model on patients in the JUPITER study who have reached the 2-year time point. Until

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validation of the model is done with new patients, it should not be used in clinical practice.

Once validated, the clinical utility of the model can be determined by the outcomes of patients who are at high risk, based on the model, and undergo surgery as well as those of patients who are at low risk and do not undergo surgery. In addition, as seen in Table I, data harmonization among the 4 studies proved challenging and made multiple imputation necessary. Similarly, the authors of a systematic review found inconsistencies in the reporting of preoperative and postoperative variables among 24 studies on isolated medial patellofemoral ligament reconstruction³³. They concluded that more consistency is needed to identify the optimal strategy for clinical decision-making and advance the field of patellar instability management. There has been growing interest in recent years among health researchers to implement minimum reporting requirements to improve the quality of published studies^{34,35}. Reporting standards in orthopaedics are sorely lacking. A checklist statement for authors as well as journal reviewers and editors may be useful to ensure that submitted manuscripts report sufficient detail to make meaningful contributions to the literature. Greater standardization of key variables and thresholds across studies will improve the quality of evidence and allow for future research studies to reduce the clinical equipoise on optimal treatment for recurrent LPD.

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