

Predicting Anterior Cruciate Ligament Reconstruction Revision

A Machine Learning Analysis Utilizing the Norwegian Knee Ligament Register

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Background: Several factors are associated with an increased risk of anterior cruciate ligament (ACL) reconstruction revision. However, the ability to accurately translate these factors into a quantifiable risk of revision at a patient-specific level has remained elusive. We sought to determine if machine learning analysis of the Norwegian Knee Ligament Register (NKLK) can identify the most important risk factors associated with subsequent revision of primary ACL reconstruction and develop a clinically meaningful calculator for predicting revision of primary ACL reconstruction.

Methods: Machine learning analysis was performed on the NKLK data set. The primary outcome was the probability of revision ACL reconstruction within 1, 2, and/or 5 years. Data were split randomly into training sets (75%) and test sets (25%). Four machine learning models were tested: Cox Lasso, survival random forest, generalized additive model, and gradient boosted regression. Concordance and calibration were calculated for all 4 models.

Results: The data set included 24,935 patients, and 4.9% underwent a revision surgical procedure during a mean follow-up (and standard deviation) of 8.1 ± 4.1 years. All 4 models were well-calibrated, with moderate concordance (0.67 to 0.69). The Cox Lasso model required only 5 variables for outcome prediction. The other models either used more variables without an appreciable improvement in accuracy or had slightly lower accuracy overall. An in-clinic calculator was developed that can estimate the risk of ACL revision (Revision Risk Calculator). This calculator can quantify risk at a patient-specific level, with a plausible range from near 0% for low-risk patients to 20% for high-risk patients at 5 years.

Conclusions: Machine learning analysis of a national knee ligament registry can predict the risk of ACL reconstruction revision with moderate accuracy. This algorithm supports the creation of an in-clinic calculator for point-of-care risk stratification based on the input of only 5 variables. Similar analysis using a larger or more comprehensive data set may improve the accuracy of risk prediction, and future studies incorporating patients who have experienced failure of ACL reconstruction but have not undergone subsequent revision may better predict the true risk of ACL reconstruction failure.

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

The anterior cruciate ligament (ACL) is one of the main knee stabilizers, and its rupture can lead to pain, instability, and functional limitation¹. Injury rates have been rising globally, and surgical reconstruction of the ACL is often performed to restore normal biomechanics and to improve knee stability²⁻⁵. Recent studies have associated several

factors with an increased risk of failed surgical reconstruction⁶⁻¹⁴. However, due to the complex relationships between these various factors, accurate prediction and quantification of patient-specific risk are challenging.

A novel approach to health-care research, machine learning, has the potential to improve our predictive capability.

Disclosure: The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (<http://links.lww.com/JBJS/G758>).

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Machine learning refers to a set of techniques that model complex relationships between variables in order to predict an outcome. Relationships can be more complex than those assessed with traditional statistical techniques. Although applications of machine learning in sports medicine have been slow to develop, machine learning has broadly impacted the medical field, including within orthopaedic surgery^{15,16}. Established in 2004, the Norwegian Knee Ligament Register (NKLR) contains demographic, injury, surgical, and outcome data on >25,000 patients. The NKLR has produced many studies since its inception that have impacted our understanding of ACL injuries^{11,12,17,18}, and the application of machine learning presents the opportunity to further evaluate factors associated with outcome.

Previous studies into the risk factors for ACL reconstruction failure have assessed the strength of association (effect measure) and the probability of seeing results at least as strong as those that were observed if there is no true association between the independent and the dependent variables. This has resulted in the identification of numerous factors associated with outcome such as age, sex, graft choice, fixation method, body mass index (BMI), and return to pivoting sports^{11,12,19-21}. Although traditional statistical models require human selection of variables thought to be of importance, machine learning allows a computer to consider all possible combinations and interactions of variables contained in a data set and their relationships to the outcome of interest. The machine learning analysis can identify which factors from this much larger pool are focal in predicting the outcome. As with traditional methods, machine learning can develop an algorithm to predict the outcome for future patients. However, more complex interactions and relationships can be used in machine learning predictive algorithms, which may yield more accurate and patient-specific predictive capability.

An accurate predictive model for clinical outcome following ACL reconstruction would be beneficial for both the orthopaedic surgeon and the patient. This would allow patient and surgical information to guide shared clinical decision-making with regard to patient-specific management. There are currently no machine learning-driven models to predict outcome after ACL reconstruction based on national knee ligament registry data. The purpose of this study was therefore to use machine learning analysis of the NKLR to identify the most important risk factors associated with subsequent revision of primary ACL reconstruction and develop a clinically meaningful model for predicting primary ACL reconstruction revision. The hypothesis was that machine learning analysis would enable accurate prediction of revision risk for a patient undergoing a primary ACL reconstruction.

Materials and Methods

Data Preparation

Patients contained within the NKLR with primary ACL reconstruction surgery dates from January 2004 through December 2018 were included. Those with missing values for graft choice were excluded. All variables captured by the reg-

ister were considered for the analysis. We recoded or defined new variables for the following: years between the injury and the surgical procedure, meniscus injury identified at the surgical procedure, any additional injury identified at the surgical procedure, choice of graft (patellar tendon autograft, hamstring tendon autograft, other), and height and weight variables that combined data from patient and surgeon-reported variables. Time to revision was calculated as the number of years from the primary surgical procedure to revision. For assessing concordance at specific follow-up times, we considered patients with a revision at or prior to the time point as experiencing the event. We also created a predictor indicating if a patient was below the median score in all 4 Knee Injury and Osteoarthritis Outcome Score (KOOS) categories at the time of the primary surgical procedure and scaled predictors for KOOS Quality of Life (QoL) and Sports measures to a score of 10. The final list of predictor variables included for analysis is presented in Table I.

Model Creation

The primary outcome was the probability of revision ACL reconstruction within 1, 2, and/or 5 years. We randomly split the cleaned data into training sets (75%) that were used to fit the models and test sets (25%) that were used to evaluate the models. We used R (version 3.6.1; The R Foundation for Statistical Computing) to fit several machine learning models to the training data²². All models and their performance measures described below account for censoring of our time-to-event outcome. “Censoring” means that, at any given follow-up time, we do not have complete information on the outcome for all patients. This is because some patients have not been in the registry for the requisite number of years, and others have not yet experienced revision and it is unknown when or if they ultimately will. Four models intended for this type of data were tested: Cox Lasso, survival random forest, generalized additive model (GAM), and gradient boosted regression model (GBM). These models are among the most commonly used in machine learning. The Cox Lasso model is a semiparametric, penalized regression model that selects a subset of variables for inclusion²³. The survival random forest model is a tree-based, nonparametric method adapted for right-censored data such as ours²⁴. GBMs are also nonparametric, meaning that they do not require prespecification of a model structure, and iteratively improve the model fit using all available variables^{25,26}. GAMs allow for machine-selected nonlinear relationships among a prespecified group of variables²⁷. Further details on each model are included in Appendix A.

We applied the L1-regularized Cox model (“Cox Lasso,” package *glmnet*; lambda value selected via cross-validation) to select variables and retained those with nonzero coefficients, shown in the top left of Figure 1. We trained a survival random forest (function *rfsrc* from package *randomForestSRC*) with node size 200, 10 variables tried per split, 100 trees, and the full set of predictors (Table I). We trained a GAM (function *gam* from package *mgcv*) with those variables selected in the Cox Lasso, using a smooth term for the years from injury to surgery predictor. Finally, we trained a GBM (functions *gbm* and *basehaz.gbm*

TABLE I Characteristics of the Registry Population and Variables Considered for Machine Learning Analysis

Characteristic or Variable*	Values (N = 24,935)
Age	
At surgery† (yr)	28 ± 11
At injury† (yr)	27 ± 10
Missing data‡	1,251 (5%)
Sex‡	
Male	14,019 (56%)
Female	10,916 (44%)
BMI† (kg/m ²)	25.0 ± 3.8
Missing data‡	7,920 (32%)
KOOS QoL at primary surgery†	3.49 ± 1.86
Missing data‡	5,149 (21%)
KOOS Sports at primary surgery†	4.28 ± 2.73
Missing data‡	5,324 (21%)
Below median on all KOOS subscales‡	
Yes	3,972 (16%)
No	15,982 (64%)
Missing data	4,981 (20%)
Hospital geographic region‡	
Southeast	9,335 (37%)
West	3,974 (16%)
Central	2,162 (8.7%)
North	958 (3.8%)
Missing data	8,506 (34%)
Hospital type‡	
Public	16,429 (66%)
Private	8,506 (34%)
Injury‡	
Meniscus	13,145 (53%)
Cartilage	5,801 (23%)
Any	171 (0.7%)
Posterior cruciate ligament	398 (1.6%)
Medial collateral ligament	1,993 (8.0%)
Lateral collateral ligament	464 (1.9%)
Posterolateral corner	243 (1.0%)
Missing data	2,720 (10.9%)
Graft choice‡	
Bone-patellar tendon-bone autograft	9,891 (40%)
Hamstring autograft	14,481 (58%)
Unknown or other	563 (2.3%)
Tibial fixation device‡	
Interference screw	19,283 (77%)
Suspension or cortical device	2,367 (9.5%)
Unknown or other	3,285 (13%)

*continued***TABLE I (continued)**

Characteristic or Variable*	Values (N = 24,935)
Femoral fixation device‡	
Interference screw	8,287 (33%)
Suspension or cortical device	13,072 (52%)
Unknown or other	3,576 (14%)
Fixation device combination‡	
2 interference screws	8,086 (32%)
Interference or suspension	154 (0.6%)
2 suspension or cortical devices	1,809 (7.3%)
Suspension or interference	9,725 (39%)
Unknown or other	5,161 (21%)
Injured side‡	
Right	12,675 (51%)
Left	12,260 (49%)
Previous surgical procedure‡	
On contralateral knee	1,804 (7.2%)
On ipsilateral knee	4,213 (17%)
Time from injury to primary surgery† (yr)	1.63 ± 3.26
Missing data‡	1,255 (5%)
Systemic antibiotic prophylaxis‡	
Yes	24,769 (99%)
No	108 (0.4%)
Missing data	58 (0.2%)

*All variables represent patient demographic characteristics, injury, patient-reported outcome scores, or surgical details at the time of the primary ACL reconstruction. †The values are given as the mean and the standard deviation. ‡The values are given as the number of patients, with the percentage in parentheses.

from package *gbm*), using the full set of predictors, a shrinkage parameter of 0.001, and 6,550 trees (number of trees selected via cross-validation). To maximize accuracy for the tree-based methods, we used a finer grouping for fixation device variables (Supplementary Tables 1a, 1b, and 1c). To achieve a more direct comparison between the models using variable selection and those using the full set of predictors, we also trained the random forest and GBM using only predictors selected in the Cox Lasso. All 4 models were restricted to patients with complete data for the predictors used (see Table II and Missing Data section below).

Model Evaluation

We evaluated model performance by calculating predicted survival probabilities for the held-out test data using the trained models. Model calibration was assessed using a version of the Hosmer-Lemeshow statistic that accounts for censoring²⁸. Calibration refers to the accuracy of the risk estimates, comparing the expected outcomes with the actual observed outcomes. This statistic sums the average misclassification in each predicted risk

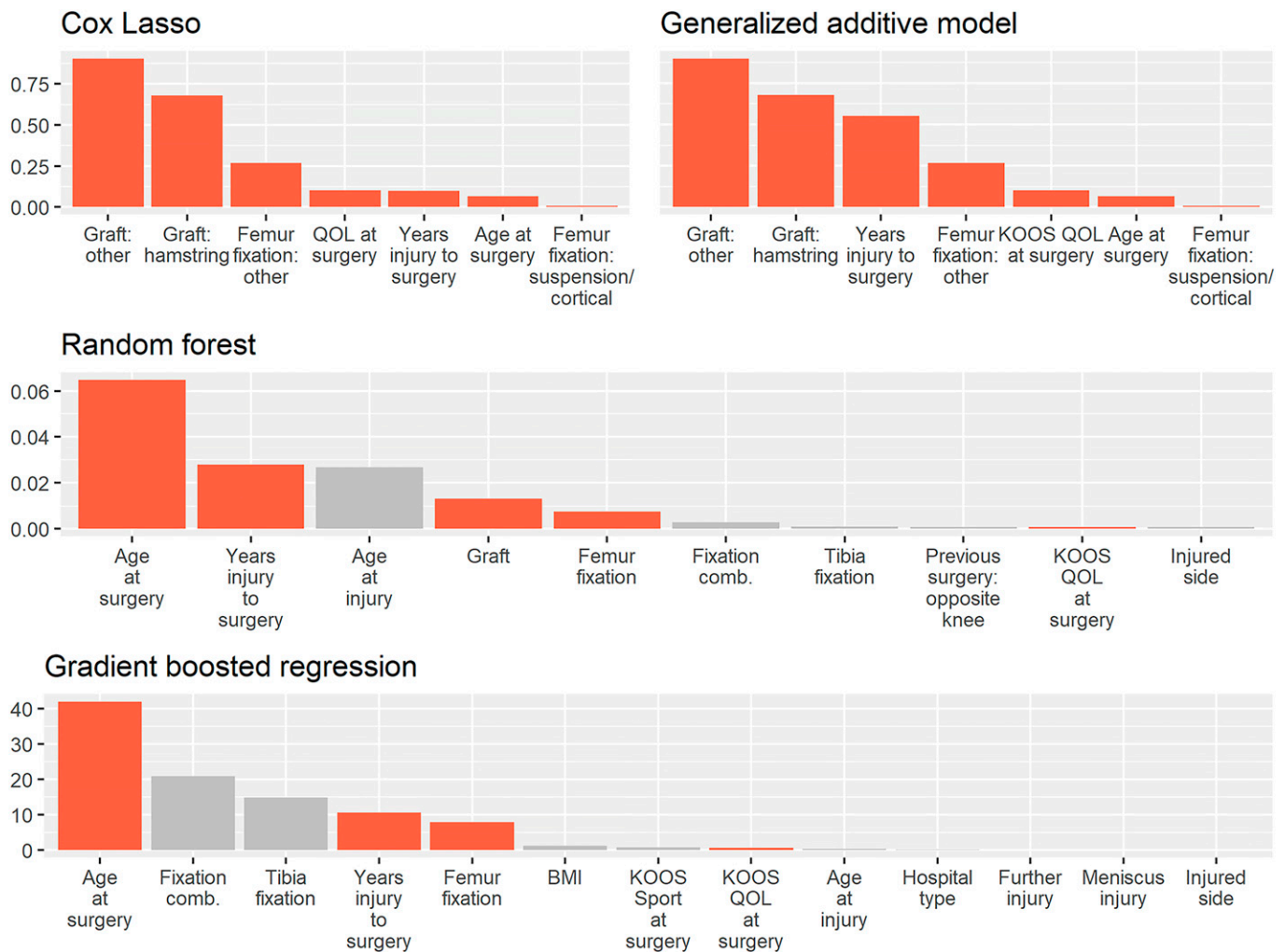


Fig. 1
Feature importance. The 4 plots show relative feature importance in each of the machine learning models. The highlighted bars indicate features selected into the Cox Lasso model. The random forest plot shows variables with importance of >0.0005 and the gradient boosted plot shows variables with importance of >0 , for readability. The orange bars represent variables selected as important in the Cox Lasso model, and the gray bars represent the other variables used in the models.

quintile and converts the sum into a chi-square statistic. Larger calibration statistics correspond to smaller p values, and significance means that the null hypothesis of perfect calibration is rejected. Concordance was calculated using the Harrell C-index²⁹ at 1, 2, and 5-year follow-up times. The C-index measures the proportion of ranked pairs of observations in which the predicted ranking corresponds with true outcomes. It is a generalization of the area under the curve (AUC) appropriate for censored data, where not all patients have completed the follow-up time. As with the AUC, the C-index ranges from 0 to 1, with 1 indicating perfect concordance.

Missing Data

To assess the impact of restricting data to complete cases, we retrained the models using multiple imputation. This common statistical technique fills in a patient's missing data values based on characteristics of other patients in the population. Because

our population had nontrivial missing data on several variables, multiple imputation allowed us to gauge the reasonableness of excluding these incomplete observations. We conducted multivariate imputation by chained equations (MICE) with 5 imputations on both training and test data (function *mice* from package *mice*). Using the variables with nonzero coefficients in the complete-case Cox Lasso, we refit the Cox model on

TABLE II Proportion of Complete Cases by Model

Model	Total Cases	Incomplete Cases	Complete Cases
Cox Lasso and GAM	24,935	6,048	76%
Random forest and GBM	24,935	11,663	53%

TABLE III Description of Censoring

Follow-up Time	Patients with Revision*	Patients with Complete Follow-up and No Revision*	Patients with Incomplete Follow-up and No Revision*†
1 year	190 (0.8%)	22,908 (91.9%)	1,837 (7.4%)
2 years	529 (2.1%)	20,703 (83.0%)	3,703 (14.9%)
5 years	999 (4.0%)	15,107 (60.6%)	8,829 (35.4%)

*The values are given as the number of patients, with the percentage in parentheses. †This category represents patients who have not yet reached the specified end point.

imputed data, averaging predictions over the 5 imputations. We similarly refit the GAM and the GBM. For the random forest model, imputation was done using the adaptive tree imputation algorithm of Ishwaran et al.²⁴, as implemented in the *rfsrc* function from the *randomForestSRC* R package. We maintained the default of 1 iteration of the algorithm for imputing training data. Supplementary Tables 2a through 2d show model performance with imputation on training data only and training and test data.

Source of Funding

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Results

Data Characteristics

Table I describes characteristics of the registry population at the time of the primary surgical procedure and the varia-

bles included for analysis. After data cleaning (5 patients were excluded for missing graft choice), 24,935 patients met the inclusion criteria; of these patients, 1,219 (4.9%) underwent a revision surgical procedure during a mean follow-up period (and standard deviation) of 8.1 ± 4.1 years. Table III presents the proportion of patients with complete follow-up at each of the 3 time points. The population was predominantly male (56%), with a mean age of 27 ± 10 years at the time of the primary injury and 28 ± 11 years at the time of the surgical procedure.

To assess the potential impact of missing data on our results, we compared covariate distributions between complete cases and the full data set (Supplementary Tables 1a, 1b, and 1c). Although the large sample size results in the complete cases and the full data set being significantly different ($p < 0.05$) on multiple variables, the magnitudes of the between-group differences were generally small and not clinically meaningful.

Model Performance

All 4 models were generally well-calibrated, with concordance in the moderate range (0.67 to 0.69). Only the 2-year

TABLE IV Model Performance Measures

Model	Concordance	Calibration Statistic	Calibration P Value
Probability of revision: 1 year			
Cox Lasso	0.686	4.89	0.18
Random forest	0.672	3.12	0.374
GAM	0.687	4.79	0.188
GBM	0.669	4.98	0.174
Probability of revision: 2 years			
Cox Lasso	0.684	11.35	0.01
Random forest	0.67	11.66	0.009
GAM	0.685	11.19	0.011
GBM	0.666	3.76	0.288
Probability of revision: 5 years			
Cox Lasso	0.683	6.19	0.103
Random forest	0.67	3.71	0.295
GAM	0.684	6.98	0.073
GBM	0.665	0.38	0.944

TABLE V Randomly Selected Example Patients from 3 Predicted 5-Year Risk Groups*

Variable	Low-Risk Patients	Medium-Risk Patients	High-Risk Patients
Age (yr)	39	15	15
KOOS QoL at primary surgery (points)	25	25	6
Graft choice	Hamstring autograft	Bone-patellar tendon-bone autograft	Hamstring autograft
Femoral fixation device	Suspension or cortical device	Interference screw	Suspension or cortical device
Time between injury and primary surgery (mo)	14	9	8
Risk of revision			
At 1 year	0.5%	1.2%	2.8%
At 2 years	1.4%	3.6%	8.5%
At 5 years	2.8%	7.2%	17.2%

*Low (<5%), medium (between 5% and 15%), and high (>15%). The patients' values for each variable used in the Cox model are given, along with the Cox model-predicted risk of revision at 1, 2, and 5 years.

Cox Lasso model, random forest model, and GAM had calibration p values between 0.01 and 0.05, suggesting modest evidence of miscalibration (Table IV). The GBM had a small edge in calibration for 2-year and 5-year follow-up times. However, concordance was slightly lower for the GBM and the random forest model at all follow-up times (0.67 compared with 0.68).

Imputing missing data did not significantly improve performance for any of the models (Supplementary Tables 2a through 2d). When the random forest model and the GBM were restricted to the Cox Lasso predictors, calibration worsened substantially when limited to complete cases and stayed about the same under imputation. Concordance was virtually unchanged (Supplementary Tables 3a and 3b).

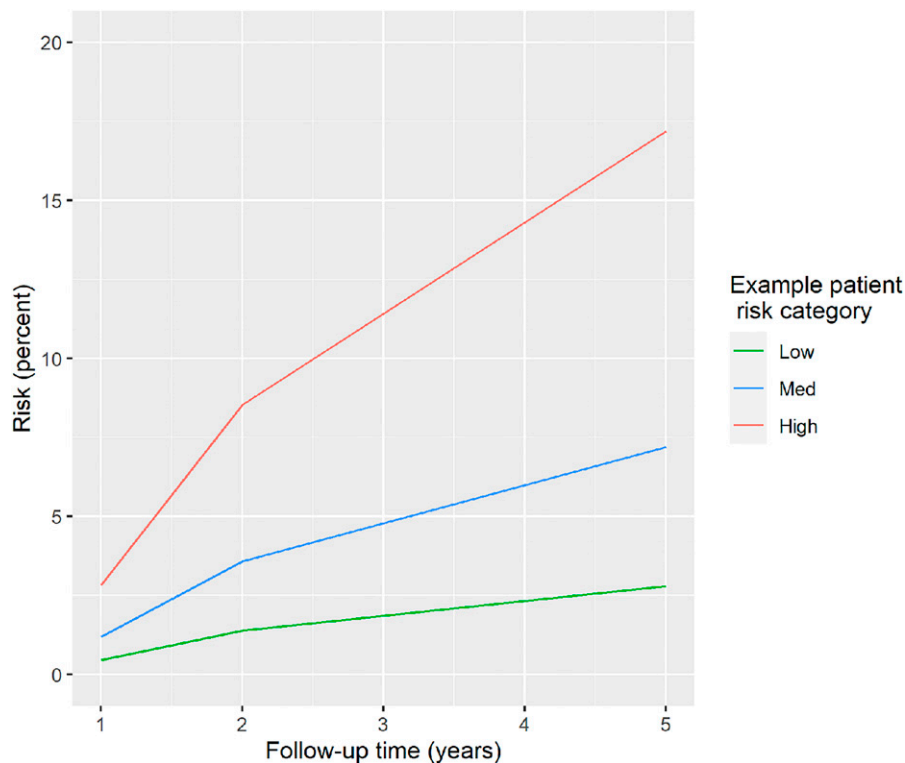


Fig. 2
Risk of revision ACL reconstruction in 3 randomly selected example patients corresponding with Table V.

Factors Predicting Outcome

The most important predictors for revision in the Cox Lasso model, in order, were graft choice, femoral fixation device, KOOS QoL at the time of the surgical procedure, years from the injury to the surgical procedure, and age at the time of the surgical procedure. In the random forest model, predictors in the top third by variable importance score also included age at the time of the injury, tibial fixation device, and fixation device combination. The most important features in both the GAM and the GBM were relatively similar to those in the Cox Lasso model. The Cox Lasso model and the GAM quantify feature importance in terms of effect size associated with the variable. The other models use the difference in the model error rate that results if the feature is removed (Fig. 1).

Risk-Prediction Calculator

The Cox Lasso model was selected to create an easy-to-use in-clinic calculator to predict the risk of ACL reconstruction revision (Revision Risk Calculator). Whereas the overall risk of revision in the registry was 4.9%, this calculator can quantify the risk at a patient-specific level, with a plausible range from near 0% for low-risk patients to 20% for high-risk patients at 5 years. Table V, Figure 2, and Video 1 demonstrate examples of the calculator's risk prediction using 3 sample patients.

Discussion

The most important finding of this study was that machine learning analysis of a knee ligament register allows the creation of a validated algorithm to predict a patient's risk of ACL reconstruction revision with moderate accuracy. Additionally, despite having 24 possible prognostic variables contained within the NKLR, the algorithm required only 5 factors for prediction: age and KOOS QoL at the time of the primary surgical procedure, graft choice, femoral fixation device, and the number of years between the injury and the primary surgical procedure. Using this algorithm, an in-clinic calculator was developed that can estimate revision risk.

This study represents the first machine learning-driven model for predicting the outcome of ACL reconstruction at a patient-specific level. Currently, the risk of a patient undergoing a revision ACL reconstruction is estimated on the basis of clinical experience and subjective consideration of the known risk factors. Although it is generally accepted that these factors influence the outcome, the ability to accurately quantify this risk has remained elusive. For the clinician, the introduction of an easy-to-use calculator can guide the patient-specific discussion surrounding the surgical options and realistic outcome goals.

Machine learning is a relatively new tool in the health-care research realm. In this study, 4 models were used to analyze the data and create algorithms predicting the risk of undergoing a revision ACL reconstruction. All models first identified which factors were predictive of a revision surgical procedure and then calculated the relative

weight of their influence on the risk of this outcome. Of all of the various factors contained within the registry, the Cox Lasso model identified only 5 variables necessary to predict outcome, and the other 3 models either used more variables without an appreciable improvement in accuracy or had slightly lower accuracy overall. For this reason, the Cox Lasso model was selected for creation of the in-clinic calculator.

It is interesting to note that several variables that have previously been considered important for predicting ACL reconstruction failure were not necessary for inclusion in the Cox Lasso machine learning model. Some examples include sex¹⁹, tibial fixation¹², and increased BMI²⁰. Variables were excluded from this model using the Lasso technique, which retains only those predictors adding significantly to the model's accuracy. Although these previously identified risk factors are no doubt associated with outcome, the Lasso method suggests that they are either less important than the factors selected by the Lasso or somehow represented in those factors. In comparison with the Cox Lasso model, the random forest model and the GBM included more variables. However, this inclusion did not significantly improve performance. The reason for this is similar: the information offered by these added variables is already contained within the few most important predictors, so adding the extra variables does not improve performance. All 5 of the variables that were found to be important for outcome prediction have previously been identified as being associated with an increased risk of revision ACL reconstruction^{11,12,14,17,20,21,30}.

Revision ACL reconstruction was selected as the primary outcome measure for this study because of the long follow-up and completeness of the data provided for this end point. This is in contrast to a study designed to predict ACL reconstruction failure based on revision surgical procedures and/or inferior patient-reported outcomes. Although this wider outcome would also capture patients who experience a failure but do not undergo a subsequent revision surgical procedure, the number of patients within the register with patient-reported outcome measures substantially drops over time. In contrast, the overall compliance with data entry in the register is 86%⁴. Machine learning analysis requires a large volume of robust data and we therefore chose this narrower outcome measure to maximize patient inclusion and model accuracy.


There were limitations to the current study. First, although we considered a variety of machine learning methods in this analysis, it is possible that a model not considered might have performed better. Second, there were substantial missing data in some predictors such as BMI (32%) and preoperative KOOS (21%), and we could not rule out that data were not missing at random. We noted that observations with complete data for all variables included in the random forest model and the GBM tended to be newer to the registry than incomplete observations, possibly reflecting improvement in data collection over time. Additionally, revision was a relatively rare outcome in these data (<5% of individuals), and most patients

were predicted as being at low risk for revision. For this large majority of low-risk patients, functional scores might have offered more clinical insight.

There were also limitations with regard to the clinical application of this analysis. Especially in the case of the random forest model and the GBM, our models used variables that may not have been readily available in a clinical setting. Clinical utility was greatest with the Cox Lasso model, which required only 5 variables and showed no significant difference in performance from the more complex models. Further, the results of this study may not be applicable to populations in other countries as they represented data from a single national register. Although national registers offer generalizability and real-world applicability³¹, the large number of surgeons included in the data collection may also have produced wide variability in surgical decision-making, skill, and technique. Finally, although the machine learning algorithm was well-calibrated, the concordance was moderate. The accuracy of the model would presumably be improved if a larger data set, such as one composed of combined data from multiple registries or one that included additional variables, was assessed. Potentially important variables may include coronal or sagittal alignment (tibial slope), physical examination findings, rehabilitation information, or surgical technique details such as tunnel position or graft size.

In conclusion, machine learning analysis of a national knee ligament register can predict the risk of ACL reconstruction revision with moderate accuracy. This supports the creation of an in-clinic calculator for point-of-care risk stratification based on the input of only 5 variables. Similar analysis using larger or more comprehensive data may improve the accuracy of risk prediction, and future studies incorporating patients who have experienced a failure of ACL reconstruction but have not undergone subsequent revision may better predict the true risk of ACL reconstruction failure.

Appendix

 Supporting material provided by the authors is posted with the online version of this article as a data supplement at [jbjs.org \(http://links.lww.com/JBJS/G759\)](http://links.lww.com/JBJS/G759). ■

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