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Preoperative Risk Prediction Models for Short-Term Revision and Death After Total Hip Arthroplasty

Data from the Finnish Arthroplasty Register

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Background: Because of the increasing number of total hip arthroplasties (THAs), even a small proportion of complications after the operation can lead to substantial individual difficulties and health-care costs. The aim of this study was to develop simple-to-use risk prediction models to assess the risk of the most common reasons for implant failure to facilitate clinical decision-making and to ensure long-term survival of primary THAs.

Methods: We analyzed patient and surgical data reported to the Finnish Arthroplasty Register (FAR) on 25,919 primary THAs performed in Finland between May 2014 and January 2018. For the most frequent adverse outcomes after primary THA, we developed multivariable Lasso regression models based on the data of the randomly selected training cohort (two-thirds of the data). The performances of all models were validated using the remaining, independent test set consisting of 8,640 primary THAs (one-third of the data) not used for building the models.

Results: The most common outcomes within 6 months after the primary THA were revision operations due to periprosthetic joint infection (1.1%), dislocation (0.7%), or periprosthetic fracture (0.5%), and death (0.7%). For each of these outcomes, Lasso regression identified subsets of variables required for accurate risk predictions. The highest discrimination performance, in terms of area under the receiver operating characteristic curve (AUROC), was observed for death (0.84), whereas the performance was lower for revisions due to periprosthetic joint infection (0.68), dislocation (0.64), or periprosthetic fracture (0.65).

Conclusions: Based on the small number of preoperative characteristics of the patient and modifiable surgical parameters, the developed risk prediction models can be easily used to assess the risk of revision or death. All developed models hold the potential to aid clinical decision-making, ultimately leading to improved clinical outcomes.

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

Over the past 2 decades, there has been a substantial increase in the number of primary and revision total hip arthroplasties (THAs)[1,2]. In patients with osteoarthritis of the hip in whom conservative treatment approaches have failed, THA improves patients' quality of life, relieves pain, and restores physical activity[3-5]. Despite the high success and satisfaction rates, a substantial number of THAs can still result in adverse complications shortly after the primary operation. These complications include periprosthetic joint infection, aseptic loosening, periprosthetic fracture, and dislocation, and they all typically require a revision procedure[6-9]. The revision operations are always more demanding, and the charges are also markedly higher compared with primary THAs[6,10]. Therefore, due to the increasing number of primary THAs, even a small proportion of complications can lead to a substantial increase in the amount of individual difficulty and additional health-care costs.

Despite the considerable efforts made to identify individual risk factors for complications following THA, the

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Disclosure: Dr. Elo reports grants from the European Research Council ERC (grant number 677943), the Academy of Finland (grant numbers 296801, 310561, 314443, and 329278), and the Sigrid Juselius Foundation during the conduct of the study. Dr. Venäläinen reports a grant from the Academy of Finland (grant number 322123). The funders had no role in the study design, data collection and analysis, the decision to publish, or preparation of the manuscript. 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/JBJSOA/A246).

decision-making regarding the treatment is still largely based on the mean rates of risk for a diverse population of patients; these rates may not be accurate for an individual patient[11]. To obtain more accurate, patient-specific risk estimates and to better understand the cumulative effect of multiple risk factors, easy-to-use multivariable risk prediction tools are needed. Such tools would better inform both the surgeon and the patient about the expected outcomes, would engage the patients more in the decision-making process, and would help to avoid unnecessary risks. Although some risk prediction tools for THA already exist[12-14], they have not yet been adopted widely as part of clinical decision-making. Importantly, many previous risk prediction tools lack external validation, and, hence, their applicability to a larger population is not known[12]. Furthermore, the majority of the risk prediction models does not utilize information about surgery-related factors such as the components used and their properties. A type of risk prediction model that includes these factors would be instrumental in tailoring the primary THAs by matching the optimal surgical parameters with the characteristics of the patient and reducing the overall risk of adverse outcomes.

The aim of this study was to develop simple-to-use risk prediction models to assess the risk of the most common adverse outcomes after primary THA, based on patient and surgical data collected in the Finnish Arthroplasty Register (FAR). The FAR was thoroughly revised in 2014 to include new variables that offer the possibility to model and estimate the risk of revision using versatile data on the primary operation. The risk prediction models are aimed at helping surgeons to identify high-risk patients at an earlier point of care, thus leading to reduced revision rates and health-care costs. Despite being developed primarily for the FAR, our simple-to-use risk prediction models were designed to be applicable to any modern health-care setting.

Materials and Methods

Study Cohort

We extracted patient and surgical data collected in the FAR on all primary and revision THAs performed in Finland between May 2014 and January 2018. Overall, the initial data set, prepared and described in more detail in a previous study[15], contained information on 33,337 primary THAs. The register-based study was approved by the ethics committee of the Finnish Institute for Health and Welfare, Helsinki, Finland (Permission THL/506/5.05.00/2016).

In the present study, all operations with a minimum follow-up time of at least 6 months or resulting in a revision surgical procedure or death within the first 6 postoperative months were included. In the case of patients who were represented twice because of bilateral arthroplasties, only the first reported operation was included in the analysis. This left us with 25,919 primary THAs performed during the study period. Finally, for model training and validation, we applied the commonly used split ratio of 2:1[16-18] to randomly divide the data into a separate training cohort (n = 17,279; two-thirds of the data) and an independent test cohort (n = 8,640; one-third of the data). The patients in each cohort were unique, and no crossover of data was allowed at any stage of the model development and validation.

Included Variables and the Primary Outcome

For each operation, the primary outcome was the first reported adverse outcome, a revision surgical procedure due to any reason or death, occurring within the first 6 postoperative months. The candidate predictors for predicting the primary outcome included both patient demographic characteristics (e.g., age, sex, and body mass index [BMI]) and surgical variables (e.g., type of fixation, anesthesia, and bearing used). A complete list of all candidate predictors can be found in Appendix 1. During model development, the American Society of Anesthesiologists (ASA) physical status classification was tested both as categorical and numerical variables but eventually was selected to be treated as a numerical variable because of the improved model performance.

Model Development and Statistical Analysis

To construct multivariable models for predicting the individualized risk of revision or death, we applied penalized logistic regression to the patient and surgical data in the training cohort. Penalized regression is an effective method for creating simple-to-use risk models when the number of events is low compared with the number of predictors[19]. Here, the variable selection was performed using the least absolute shrinkage and selection operator (Lasso) penalty, and the amount of penalty applied to the coefficients was determined by maximizing the prediction accuracy estimated using fivefold cross-validation. To account for the effect of random subsampling during cross-validation and resulting model variability[20,21], we repeated the cross-validation 100 times and performed the final variable selection similarly to our previous study[22]. The discrimination performance of the risk assessment models was evaluated and optimized in terms of the area under the receiver operating characteristic curve (AUROC).

Among all of the candidate predictors, the number of missing values was relatively small. The BMI predictor had the highest number of primary THAs with missing values (10.8%). Therefore, we did not perform multiple imputation, but, because of the requirement of complete data for the penalized regression algorithm, we performed variable selection always only on the subset of patients with complete information on all candidate variables (n = 13,585 for the training cohort). The final models were constructed and evaluated using THAs with complete data on those variables identified as important by the iterative feature selection procedure.

The obtained penalized regression models allow the estimation of individualized risk scores based on the fitted regression coefficients and patient-specific data. To achieve this, raw risk estimates should first be calculated as a sum of patient-specific risk factors weighted with the regression coefficients. Finally, the individualized risk scores can be obtained as the

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inverse logit of the sum of the model intercept (constant term) and the raw risk score as:

$$\text{Risk} = \frac{1}{1+\exp(-[\text{Intercept}+\text{Raw score}])}$$

In addition to evaluating AUROC values based on individualized risk scores, we stratified patients into low-risk, intermediate-risk, and high-risk subgroups based on the risk scores in the training cohort. For each outcome, the stratification to low, intermediate, and high risk was done based on the tertiles of the risk score distribution. Finally, Cox proportional hazards regression was used to estimate hazard ratios (HRs), and Kaplan-Meier plots were used to perform a visual comparison of time to event between the groups.

All statistical analyses and mathematical modeling were performed using the R statistical computing environment (version 3.4.1; The R Foundation for Statistical Computing). The R package *glmnet*[23] was used for penalized regression, that for *survival*[24] was used for survival analysis, that for *ggplot2*[25] was used for the visualization of results, and that for *pROC*[26] was used for the evaluation of AUROC values.

Results

The most common outcomes within the first 6 postoperative months were revisions due to periprosthetic joint infection, dislocation, or periprosthetic fracture and death (Table I). Of the 25,919 hips included, 296 (1.1%) were revised for periprosthetic joint infection, 172 (0.7%) were revised for dislocation, and 124 (0.5%) were revised for periprosthetic fracture. For 172 (0.7%) of the primary THAs, the first reported outcome was death. Although the data set also included 102 primary THAs (0.4%) that were revised for various other reasons, we developed risk prediction models only for revisions due to periprosthetic joint infection, dislocation, or periprosthetic fracture and death, due to a greater accumulation of cases for applying the machine learning methodology.

The Lasso penalized regression identified 4 key variables increasing the risk of revision due to periprosthetic joint infection: male sex, higher BMI, higher ASA classification, and the use of general anesthesia (Table II). High ASA classification was also identified as an important risk factor for the other studied outcomes, but with different effect sizes. For the dislocation prediction, in addition to the ASA classification, the preoperative fracture diagnosis, previous contributing operations, 32-mm femoral head size (compared with other head sizes, mainly 36 mm), and posterior approach were found to increase the risk. In contrast, the only factors increasing the risk of revision due to periprosthetic fracture, in addition to the ASA classification, were advanced age and cementless fixation. Finally, for predicting the risk of death, Lasso penalized regression identified advanced age and preoperative fracture diagnosis as important risk factors in addition to the ASA classification.

By applying the obtained regression coefficients (Table II) to patient-specific data, risk estimates for each operation were calculated and were compared with the occurrence of actual outcomes. In terms of AUROC, the risk prediction model developed for death had the highest discrimination performance in both the training cohort (0.82 [95% confidence interval (CI), 0.78 to 0.86]) and the test cohort (0.84 [95% CI, 0.78 to 0.90]) (Table III). All the other models reached only moderate to good performance (AUROCs between 0.64 and 0.70). Among these, the performance of the model for periprosthetic joint infection was found to be the most consistent between the training cohort (AUROC, 0.70 [95% CI, 0.67 to 0.74]) and the test cohort (AUROC, 0.68 [95% CI, 0.62 to 0.74]), whereas the model for periprosthetic fracture showed the greatest reduction in performance in the test cohort (AUROC, 0.65 [95% CI, 0.58 to 0.72]) compared with the training cohort (AUROC, 0.70 [95% CI, 0.64 to 0.76]). Overall, the model for dislocation had the lowest discrimination performance in both the training cohort (AUROC, 0.65 [95% CI, 0.60 to 0.70]) and the test cohort (AUROC, 0.64 [95% CI, 0.56 to 0.72]).

The stratification of patients into different risk subgroups on the basis of the estimated risk scores revealed that

TABLE I Outcomes Reported Within the First 6 Postoperative Months

Outcome	All Patients* (N = 25,919)	Training Cohort* (N = 17,279)	Test Cohort* (N = 8,640)
Revision	789 (3.0%)	538 (3.1%)	251 (2.9%)
Periprosthetic joint infection	296 (1.1%)	204 (1.2%)	92 (1.1%)
Dislocation	172 (0.7%)	116 (0.7%)	56 (0.6%)
Periprosthetic fracture	124 (0.5%)	76 (0.4%)	43 (0.5%)
Other†	102 (0.4%)	73 (0.4%)	34 (0.4%)
Reason missing	95 (0.4%)	69 (0.4%)	26 (0.3%)
Death	172 (0.7%)	111 (0.6%)	61 (0.7%)

*The values are given as the number of events, with the percentage in parentheses. †This category includes the following revision reasons: breakdown of the liner; breakdown of the femoral head; free-floating, unstabilized femoral stem or non-ossified femoral stem; unclear pain; aseptic loosening of the femur; periprosthetic fracture of the acetabulum; unstabilized cup or non-ossified cup; repair of lower limb-length discrepancy; malposition of the femoral component; malposition of the acetabular component; aseptic loosening of the acetabular component; and miscellaneous.

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TABLE II The Variables Selected by Lasso Penalized Logistic Regression and Corresponding Coefficients for Predicting Each of the Outcomes*

Variable	Model			
	Periprosthetic Joint Infection	Dislocation	Periprosthetic Fracture	Death
Intercept	−8.576	−6.801	−9.138	−7.017
ASA class (per class)	0.387	0.459	0.404	0.491
Male sex (1 if yes, 0 if no)	0.444	—	—	—
Age (per 10 years)	—	—	0.244	0.104
BMI (per kg/m^2)	0.103	—	—	—
Preoperative diagnosis: fracture (1 if yes, 0 if no)	—	0.861	—	0.878
Previous contributing operations (1 if any, 0 if no)	—	0.675	—	—
Surgical approach: posterior (1 if yes, 0 if no)	—	0.606	—	—
Anesthesia: general (1 if yes, 0 if no)	0.636	—	—	—
Fixation: cementless (1 if yes, 0 if no)	—	—	1.479	—
Head diameter 32 mm (1 if yes, 0 if no)	—	0.355	—	—
Example calculations†				
Raw score (sum of patient value × coefficient)	4.681	2.844	4.350	3.058
Transformed score = $\frac{1}{1 + e^{-(\text{Intercept} + \text{Raw score})}}$	0.020 or 2.0%	0.019 or 1.9%	0.008 or 0.8%	0.019 or 1.9%

*The coefficients indicate the impact of 1-unit change in a predictor variable, given in parentheses, on the response variable when the other predictors are held constant. Fields without a numerical value indicate that the indicated variable is not needed for predicting the risk of the designated outcome (i.e., regression coefficient equals zero). †Example calculations are given for a 68-year-old female patient with ASA class III, BMI of 28 kg/m^2, preoperative fracture diagnosis, and no previous contributing operations for a surgical procedure performed using a posterior surgical approach, general anesthesia, and cementless fixation to install an implant with a head diameter of >32 mm.

belonging to a group with a higher estimated risk was also associated with higher observed rates of adverse outcomes (Table IV, Appendix 2). In general, these findings were consistent between both training and test cohorts, indicating good generalizability of the predicted risks and corresponding risk groups. The highest difference in hazard rates between high-risk and low-risk subgroups was observed for death (test cohort HR, 14.0 [95% CI, 5.6 to 35.3]; $p < 0.001$). Additionally, for periprosthetic joint infection (test cohort HR, 3.5 [95% CI, 2.0 to 6.2]; $p < 0.001$), dislocation (test cohort HR, 3.5 [95% CI, 1.4 to 8.5]; $p = 0.005$), and periprosthetic fracture (test cohort HR, 4.4 [95% CI, 1.9 to 10.0]; $p < 0.001$), significantly higher revision rates were observed in the high-risk subgroup compared with the low-risk subgroup.

Discussion

Preoperative risk prediction tools may help surgeons to identify patients at high risk for undergoing a revision at an

TABLE III Discrimination Performance of the Developed Models in Terms of the AUROC*

Model	Training Cohort (N = 17,279)			Test Cohort (N = 8,640)		
	No. of Primary Operations Available	No. of Corresponding Events	AUROC†	No. of Primary Operations Available	No. of Corresponding Events	AUROC†
Periprosthetic joint infection	15,127	199	0.70 (0.67 to 0.74)	7,506	86	0.68 (0.62 to 0.74)
Dislocation	15,907	109	0.65 (0.60 to 0.70)	7,929	51	0.64 (0.56 to 0.72)
Periprosthetic fracture	16,291	74	0.70 (0.64 to 0.76)	8,140	44	0.65 (0.58 to 0.72)
Death	16,466	109	0.82 (0.78 to 0.86)	8,226	56	0.84 (0.78 to 0.90)

*This table includes the number of primary operations available for predictions as well as the corresponding number of events in both the training and test cohorts. †The values are given as the AUROC, with the 95% CI in parentheses.

TABLE IV HRs for Different Risk Subgroups*

		Training Cohort		Test Cohort	
Risk Group*	Threshold	HR†	P Value	HR†	P Value
Periprosthetic joint infection					
Low	0.0%	Reference	—	Reference	—
Intermediate	0.8%	1.8 (1.1 to 3.0)	0.01	1.6 (0.8 to 3.2)	0.1
High	1.3%	4.8 (3.2 to 7.3)	<0.001	3.5 (2.0 to 6.2)	<0.001
Dislocation					
Low	0.0%	Reference	—	Reference	—
Intermediate	0.5%	1.8 (1.0 to 3.5)	0.05	2.0 (0.8 to 5.1)	0.1
High	0.8%	3.6 (2.0 to 6.5)	<0.001	3.5 (1.4 to 8.5)	0.005
Periprosthetic fracture					
Low	0.0%	Reference	—	Reference	—
Intermediate	0.3%	2.5 (1.1 to 5.8)	0.03	2.3 (0.8 to 6.4)	0.1
High	0.5%	5.4 (2.7 to 10.6)	<0.001	4.4 (1.9 to 10.0)	<0.001
Death					
Low	0.0%	Reference	—	Reference	—
Intermediate	0.5%	3.9 (1.5 to 10.1)	0.005	1.4 (0.4 to 5.0)	0.7
High	0.8%	21.3 (9.3 to 48.7)	<0.001	14.0 (5.6 to 35.3)	<0.001

*For each outcome, the thresholds for low, intermediate, and high risk were defined using tertiles of the risk score distribution in the training data.
†The values are given as the HR, with the 95% CI in parentheses.

earlier point of care and to ensure long-term survival. In the present study, we developed simple-to-use patient-specific preoperative risk prediction models for periprosthetic joint infection, dislocation, periprosthetic fracture, and death within 6 months after primary THA using patient demographic and surgical characteristics from the revised data contents of the FAR. Based on the obtained regression coefficients, all models can easily be applied to estimate the expected levels of risk and to enable more informed decision-making about the treatment.

Penalized Lasso regression identified male sex, higher BMI, higher ASA class, and general anesthesia as the most important factors increasing the risk of periprosthetic joint infection. Notably, all of these factors have also been previously reported as risk factors for periprosthetic joint infection[27-29]. Although previous analyses have also suggested that comorbid conditions may increase the risk of periprosthetic joint infection[30], we did not include them because of the unavailability of the comorbidity data. However, ASA class is a crude estimate of medical condition and hence was considered sufficient for representing patients' status.

The ASA class, fracture diagnosis, previous contributing operations, 32-mm femoral head size, and posterior approach were identified as important risk factors in our risk prediction model for dislocation. All these risk factors for dislocation have been widely described in the literature[31-35]. Patients who underwent a failed cephalomedullary nail treatment before the THA were at higher risk for dislocation and revisions due to dislocation[36]. Conversion THAs (after sliding hip screw and side plate devices or cephalomedullary nails) are more demanding and are associated with an increased risk for postoperative complications such as dislocation[37].

In our risk prediction model for periprosthetic fracture, advanced age, higher ASA class, and cementless fixation were identified as important risk factors for periprosthetic fracture. All of these risk factors for periprosthetic fracture have been widely identified in prior studies[38-41].

Finally, our risk prediction model for death identified advanced age, higher ASA class, and fracture diagnosis as important risk factors for death. These findings are consistent with prior studies, which have associated older age (≥80 years)[42], higher ASA class (≥III)[43], and femoral neck fracture diagnosis[44] as strong risk factors for death after THA.

When the patients were stratified into different risk subgroups (low, intermediate, and high), those who were predicted to belong to the high-risk subgroup were also observed to have a higher incidence of adverse outcomes. Although the predicted patient-specific risks were relatively low in general, the incidence of adverse outcomes was found to be up to 4 to 14 times higher in the high-risk subgroups compared with the low-risk subgroups. Therefore, from a clinical point of view, it may be most important to concentrate on the use of models developed to identify patients belonging to these high-risk subgroups. For these patients, the risk of adverse outcomes could potentially be reduced by optimizing the treatment-related modifiable risk factors with the aid of our risk prediction models. More intensive follow-up of high-risk

patients could also be considered. Finally, in addition to patient stratification, the risk prediction models can be used to estimate more detailed trends in risk, even within a certain risk subgroup.

Even though all of the developed models reached moderate to good performance and were able to stratify patients according to the predicted risk, it should be noted that some individuals may still be misclassified as having high or low risk for particular outcomes. The performance of some models, such as the model for periprosthetic joint infection, might still be improved, for example, by the inclusion of comorbid conditions, which were not available here but could be considered in the future when reevaluating the models with larger amounts of data. Another limitation in the present study was the absence of factors describing surgeon experience that could substantially reduce variability in the results. It is anticipated that, by considering these additional variables and retraining the models with a greater number of operations as more data become available, even more accurate risk predictions could be achieved. An important feature that is also still missing is the possibility of evaluating error bounds for the predictions, which could be associated with the models when robust tools for evaluating them in Lasso regression become available.

The strength of this registry-based study is a large, versatile, prospectively collected data set. However, the data completeness for revision THA in the FAR is 81%[45], meaning that not all of the revision data are updated regularly to the register. In particular, not all of the data of the debridement operations or revision operations during the on-call hours due to periprosthetic joint infection may have been reported to the FAR. Furthermore, the FAR did not have data on closed reductions after dislocations. Some of the dislocated hips may have stabilized after several closed reductions without a revision operation. It is possible that patients sustain 1 or 2 dislocations before the revision operation. In the present study, the incompleteness of revision data may have resulted in a slight underestimation of the risk of revision outcomes compared with the true incidence. For these reasons, it would be beneficial to further validate the performance of the developed models in additional patient cohorts.

In summary, the present study introduces simple-to-use risk prediction models for the most common adverse outcomes after primary THA, namely revisions due to periprosthetic joint infection, dislocation or periprosthetic fracture, and death. These models can be applied in clinical practice to identify patients at a higher risk for adverse outcomes and to help to select the most suitable surgical parameters and implant properties for an individual.

Appendix

eA 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/JBJSOA/A247). ■

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