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Risk factors for unplanned reoperation after corrective surgery for adult spinal deformity

MACHINE LEARNING-BASED GAME THEORETIC APPROACH

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Aims

To determine the major risk factors for unplanned reoperations (UROs) following corrective surgery for adult spinal deformity (ASD) and their interactions, using machine learning-based prediction algorithms and game theory.

Methods

Patients who underwent surgery for ASD, with a minimum of two-year follow-up, were retrospectively reviewed. In total, 210 patients were included and randomly allocated into training (70% of the sample size) and test (the remaining 30%) sets to develop the machine learning algorithm. Risk factors were included in the analysis, along with clinical characteristics and parameters acquired through diagnostic radiology.

Results

Overall, 152 patients without and 58 with a history of surgical revision following surgery for ASD were observed; the mean age was 68.9 years (SD 8.7) and 66.9 years (SD 6.6), respectively. On implementing a random forest model, the classification of URO events resulted in a balanced accuracy of 86.8%. Among machine learning-extracted risk factors, URO, proximal junction failure (PJF), and postoperative distance from the posterosuperior corner of C7 and the vertical axis from the centroid of C2 (SVA) were significant upon Kaplan-Meier survival analysis.

Conclusion

The major risk factors for URO following surgery for ASD, i.e. postoperative SVA and PJF, and their interactions were identified using a machine learning algorithm and game theory. Clinical benefits will depend on patient risk profiles.

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Keywords: Unplanned reoperation, Game theory, Adult spinal deformity

Article focus

- We evaluated risk factors of unplanned reoperation after corrective surgery for adult spinal deformity (ASD) with interactions of perioperative radiological parameters using machine learning-based game theoretic approach.

Key messages

- Postoperative distance from the posterosuperior corner of C7, and the vertical line from the centre of the C2 body, as well as proximal junctional failure, were the major risk factors for unplanned reoperation following corrective surgery for ASD.
- Despite the black box characteristics of the machine learning model, clinically

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significant clues were found by analyzing the contribution of parameters using game theory, also confirmed with survival curve.

Strengths and limitations

- Since the biomechanics of the spine and the characteristics of ASD surgery have non-linear characteristics, machine learning capable of non-linear analysis has an advantage in terms of accuracy in predicting unplanned reoperation.
- Due to the heterogeneity of corrective surgery for ASD, with many requiring releases, osteotomies, and inter-body fusions at single or multiple levels, all patients fall into different clinical subgroups. However, we tailored the data and compared two groups with similar demographics, bone mineral density, and surgical plans.

Introduction

The prevalence of patients with symptomatic adult spinal deformity (ASD) is increasing, along with the proportion of the older population.[1] Corrective surgery for ASD to improve pain and disability is therefore critical for enhanced quality of life.[2] Various complications are reported with unsatisfactory results, despite optimized surgical planning based on the understanding of the deformed spine and surgical technique development.[1,3] Unplanned reoperations (UROs) for such complications have been performed in approximately 18% of postoperative patients with cumulative observations up to four years.[4] Therefore, although studies on ASD correction have been conducted, ASD remains challenging for spinal surgeons due to the spine's complex mechanical structure and clinical characteristics.[3]

Previously, many factors have been studied to predict surgical outcomes, per correction of ASD.[2,5,6] When such surgical risk factors related to prognosis accompany the clinical presentation, it is clinically important for surgical planning and postoperative management to determine whether conservative management with outpatient department follow-up is more appropriate. Otherwise, URO from severe pain and neurological deterioration should be anticipated. Until now, most recent studies reported risk factors using statistical analyses, such as *t*-tests, univariate analysis, multivariate analysis, and logistic regression.[7,8] However, considering the complex biomechanical and clinical characteristics of the spine, linear analysis is underequipped to inform personalized decision-making for such patients and to predict the reoperation risk; the accuracy of such methods will inevitably be low.[9]

Therefore, in recognizing and classifying data patterns to measure high-dimensional variables and to anticipate individual surgical outcomes, the non-linear method has a clear advantage.[10-13] To explain the high accuracy of the black box machine learning predictive model for URO, clinical characteristics and interactions between variables were analyzed through Shapley Additive Explanation (SHAP) values based on the concept of game theory.[14] SHAP values can be used to identify the most important variables in the model, to understand the relationship between the variables and the result, and to diagnose issues with the model's behaviour.

Since previous machine learning studies have reported limitations, such as data imbalance and overfitting, precluding proper estimation of the real-world performance of the predictive model, we applied the Synthetic Minority Over-sampling Technique (SMOTE) for data balance.[15] We also analyzed the clinical significance of risk factors through Kaplan–Meier survival curves and how they actually affected the URO risk over time.

Methods

Dataset and institutional review board approval. A dataset from two institutions of patients who underwent ASD surgery was applied to develop and externally validate a machine learning-based prediction tool for URO, and a game theory approach was used to explain the resulting prediction model. The use of patient data for research purposes was approved by the respective institutional review boards, and the patients provided written informed consent.

Inclusion and exclusion criteria. The inclusion criteria were patients: 1) undergoing spinal fusion and instrumentation for corrective surgery for ASD, involving four or more levels; 2) with at least one of the following radiological criteria preoperatively: sagittal vertical axis (SVA) > 5 cm, pelvic tilt (PT) > 25°, thoracic kyphosis (TK) > 60°, or coronal Cobb angle > 20°; and 3) with a follow-up period of more than two years. Patients were divided into two groups according to whether they underwent URO. It was documented whether proximal junctional failure (PJF) was observed. UROs were defined as revision surgery due to pain and neurological deterioration, with complications such as proximal junctional kyphosis/failure (PJK/F), rod breakage, and implant-related complications.

The exclusion criteria were patients: 1) with ASD secondary to other pathological conditions, such as autoimmune, infectious, malignant, post-traumatic deformity, or other syndromic conditions; 2) who underwent surgery for ASD involving fewer than four levels; and 3) whose follow-up period was less than two years.

Overall, 210 consecutive patients who underwent surgery for correction of sagittal imbalance arising from ASD met the study inclusion criteria (Figure 1). The patients were divided into two groups according to whether they underwent revision surgery (URO group, n = 58) or not (non-URO group, n = 152). Furthermore, it was explored whether postoperative PJF was present. Among patients who did not undergo revision surgery and were followed up as outpatients, 109 did not have PJF and 43 had PJF. Among patients who underwent revision, 18 did not have PJF and 40 did. In our institution, despite the occurrence of PJF, patients were followed up for as long as there were no neurological symptoms.

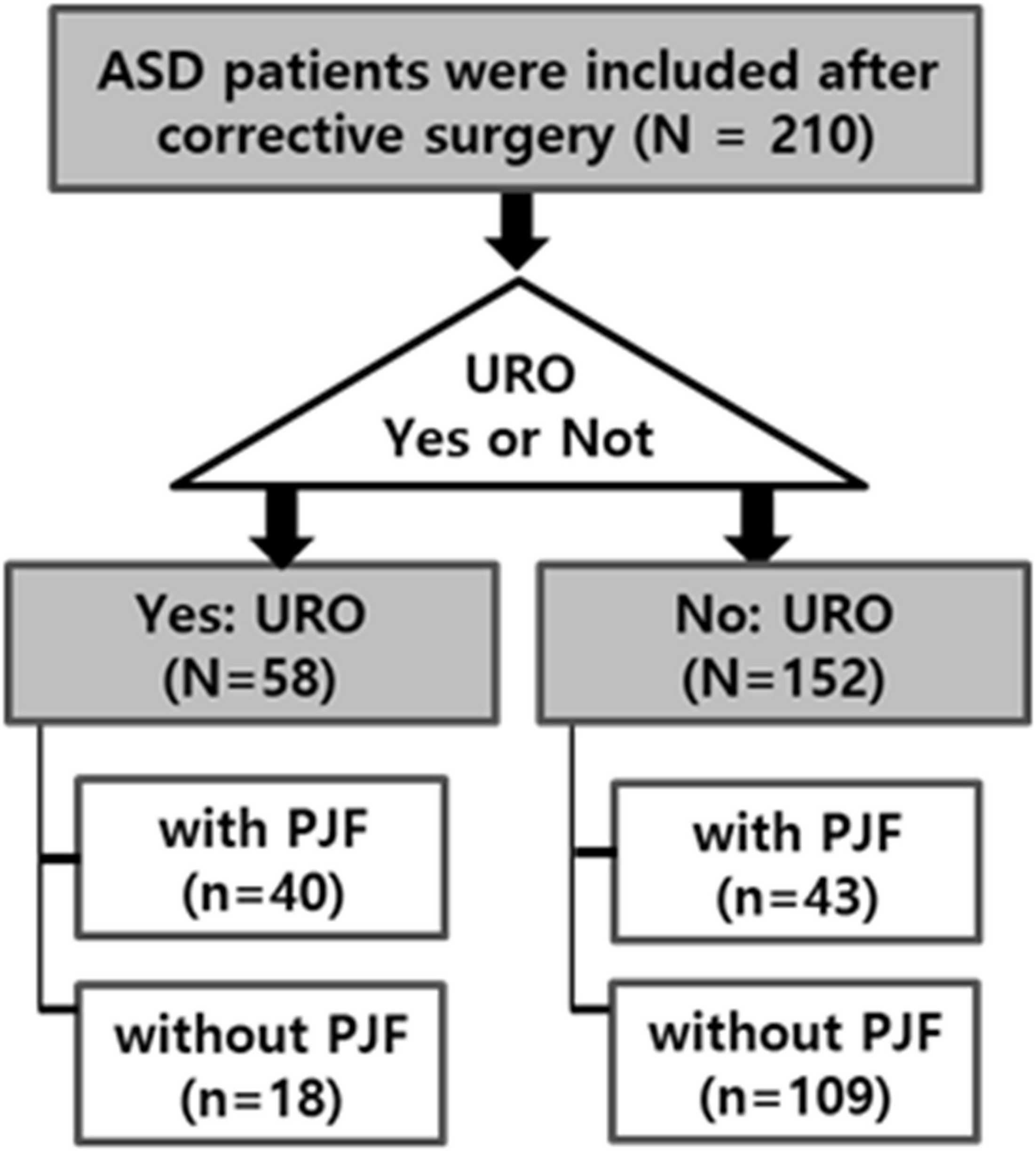

Fig. 1

Patient flow chart. Classification was based on whether proximal junction failure (PJF) or unplanned reoperation (URO) occurred. ASD, adult spinal deformity.

Table I shows demographic data; there were no statistical differences in terms of age ($p = 0.117$, independent-samples *t*-test), sex ($p = 0.289$, chi-squared test), follow-up period ($p = 0.419$, independent-samples *t*-test), BMI ($p = 0.222$, independent-samples *t*-test), and bone mineral density ($p = 0.561$, independent-samples *t*-test) between the groups.

Data collection. Each centre provided over two years of long-term follow-up data from prospective registries supplemented by retrospectively collected patient information. The clinical data collected were age, sex, surgical index level(s), height, weight, BMI, and history of spinal surgery.

The radiological parameters were collected from pelvic parameters to global parameters, which are described in Supplementary Table i. These were collected in the preoperative and immediate postoperative periods. Preoperative and postoperative differences in the variables were calculated and defined as δ values. The researcher who performed the machine learning analysis and spine surgeon who collected the data worked independently from each other.

PJK was defined as having a proximal junctional angle (PJA) between the uppermost instrumented vertebra (UIV) and vertebra level above the two vertebrae at the level of UIV (UIV + 2) > 10°, and PJF was defined as

Table I. Descriptive statistics for patients who underwent corrective surgery for adult spinal deformity; comparison between the unplanned reoperation and non-unplanned reoperation groups.

Parameters	URO (n = 58)	No URO (n = 152)	p-value
Mean age, yrs (SD)	66.9 (6.6)	68.9 (8.7)	0.117*
Sex, n			0.289†
Female	47	132	
Male	11	20	
Mean follow-up, mths (SD)	23.6 (20.3)	26.2 (21.4)	0.419*
Mean BMI, kg/m^2 (SD)	25.0 (3.7)	24.3 (3.4)	0.222*
Mean BMD, T-score (SD)	-1.9 (0.9)	-1.9 (1.1)	0.561*
Mean fused vertebrae, n (SD)	7.3 (2.2)	7.8 (2.1)	0.150*
Mean preop PT, ° (SD)	32.9 (12.3)	32.6 (11.9)	0.877*
Mean postop PT, ° (SD)	25.9 (10.6)	24.1 (13.2)	0.366*
Mean preop TK, ° (SD)	12.0 (16.8)	9.4 (16.6)	0.297*
Mean postop TK, ° (SD)	22.8 (13.6)	19.6 (15.1)	0.163*
Mean preop T1 slope, ° (SD)	24.1 (10.5)	23.2 (13.2)	0.637*
Mean postop T1 slope, ° (SD)	20.8 (9.3)	18.9 (8.9)	0.158*
Mean preop C7SVA, mm (SD)	102.3 (61.6)	104.4 (72.9)	0.893*
Mean postop C7SVA, mm (SD)	35.2 (33.1)	32.7 (34.3)	0.711*
Mean preop SVA, mm (SD)	13.4 (14.4)	15.5 (20.1)	0.471*
Mean postop SVA, mm (SD)	18.5 (11.9)	13.5 (11.1)	0.004*
Mean change of SVA, mm (SD)	5.1 (18.1)	-2.0 (23.1)	0.035*
PJF, n			< 0.001†
Yes	40	43	
No	18	109	
Scoring system			
Mean GAP score (SD)[18]	8.9 (3.5)	7.9 (3.9)	0.123*
Mean GAPB score (SD)[19]	87.9 (21.3)	82.3 (24.7)	0.129*

*Independent-samples *t*-test.
†Chi-squared test.
BMD, bone mineral density; C7SVA, C2-7 sagittal vertical axis, the distance from the posterosuperior corner of C7 and the vertical line from the centre of the C2 body; GAP, Global Alignment and Proportion; GAPB, Global Alignment and Proportion with bone mineral density; PJF, proximal junction failure; PT, pelvic tilt; SD, standard deviation; SVA, sagittal vertical axis is the length of a horizontal line connecting the posterior superior sacral end plate to a vertical plumbline dropped from the centroid of the C7 vertebra; TK, thoracic kyphosis; URO, unplanned reoperation.

symptomatic PJK, with postoperative PJA > 15°, associated with a possible requirement of revision such as in the case of fracture, soft-tissue failure, pullout of instrumentation at UIV, and/or sagittal subluxation.[16,17]

Cox proportional hazards regression, survival, and primary endpoint definitions. A Cox proportional hazards regression model was used to select URO-related risk factors. Event-free survival was defined as the primary outcome of interest and calculated as the time from the date of surgery to the date of URO occurrence. Follow-up times for patients without complications were censored at the last outpatient department visit. The proportional hazards assumption for the models was verified by examining the Kaplan-Meier survival curves. Cross-correlation function was performed with SPSS version 26 (IBM, USA). The results were compared with the risk factors, and their importance, per the SHAP value, was assessed using machine learning models to unravel the black box predictive model based on principles of game theory.[14]

Clinical data and machine learning-based prediction modelling. A total of 210 patients were randomly allocated into training (70% of the sample size) and test (the remaining 30%) sets to develop the machine learning algorithm. Variables were standardized by removing the mean and scaling to unit variance using Python (ver. 3.9; Python Software Foundation, USA) toolbox (sklearn.preprocessing.standardScaler). The SMOTE was applied to adjust for class imbalance.[15] We trained several machine learning model architectures (linear regression model, decision tree model, random forest model, and gradient boosting ensemble models of these architectures), and compared these with Python toolbox (sklearn.model_selection. RepeatedStratifiedKFold, n_splits = 10, n_repeats = 3, random_state = 1) and underwent external validation using a test dataset, which was separated from the beginning with Python toolbox (sklearn.model_selection. train_test_split, x, y, test_size = 0.3). Receiver operating characteristic and precision-recall curves were compared with each model. All analyses were performed in Python 3.9. A p-value less than 0.05 was considered statistically significant.

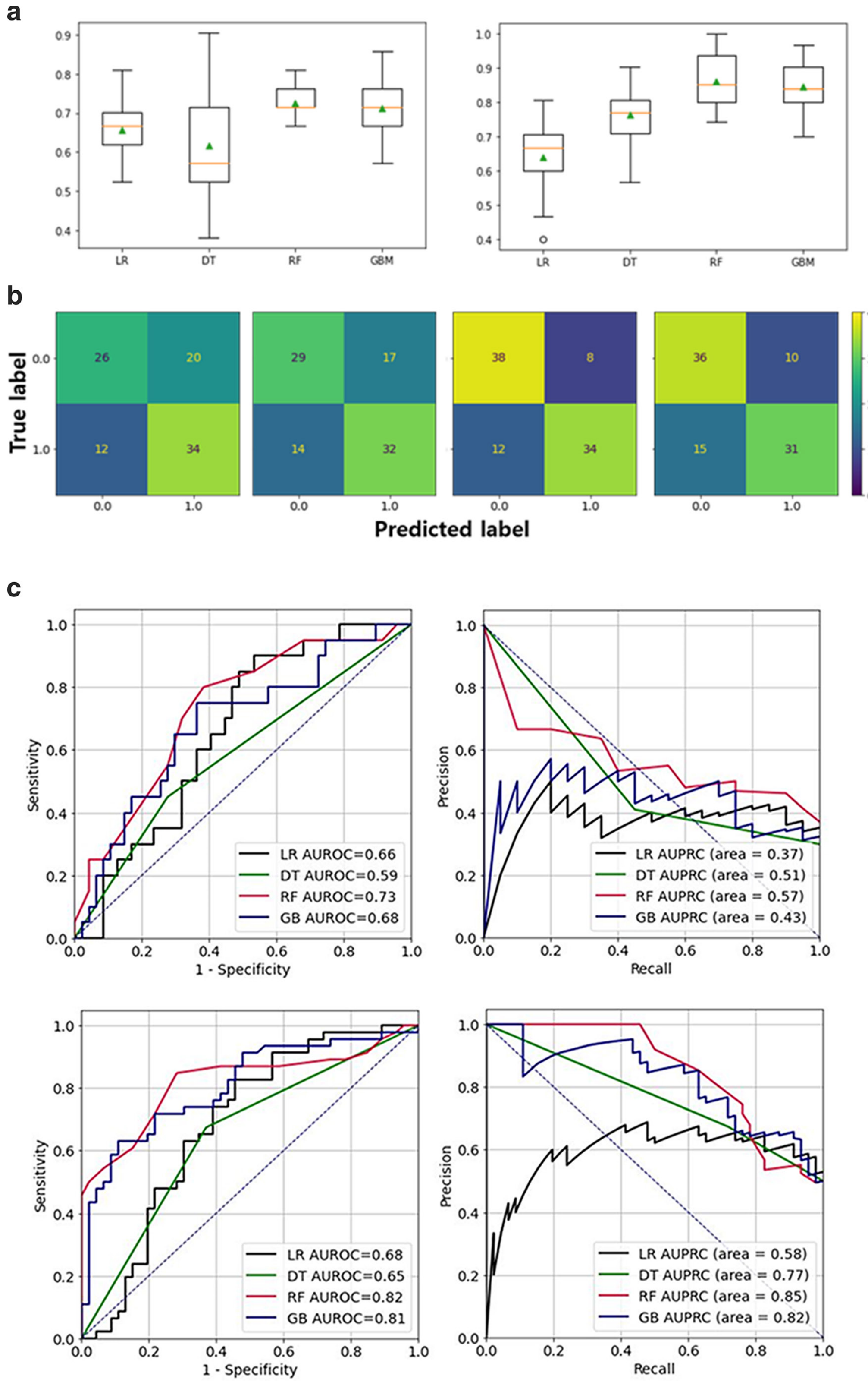

Fig. 2

Comparison of machine learning (ML) models for predicting revision surgery after corrective surgery for adult spinal deformity. a) Each ML model's mean accuracy and standard deviation (SD) were linear regression (LR), 0.656 (0.066); decision tree (DT), 0.617 (0.118); random forest (RF), 0.725 (0.034); and gradient-boosting model (GB), 0.713 (0.075). Each ML model's mean accuracy and SD with upsampling were LR, 0.640 (0.093); DT, 0.767 (0.071); RF, 0.868 (0.061); and GB, 0.847 (0.062). b) Each ML model's confusion matrix of test set. c) Receiver operating characteristic curve and precision-recall curves of LR, DT, RF, and GB with demographics and preoperative measurements (upper row) and the best model leveraging all the features (lower row).

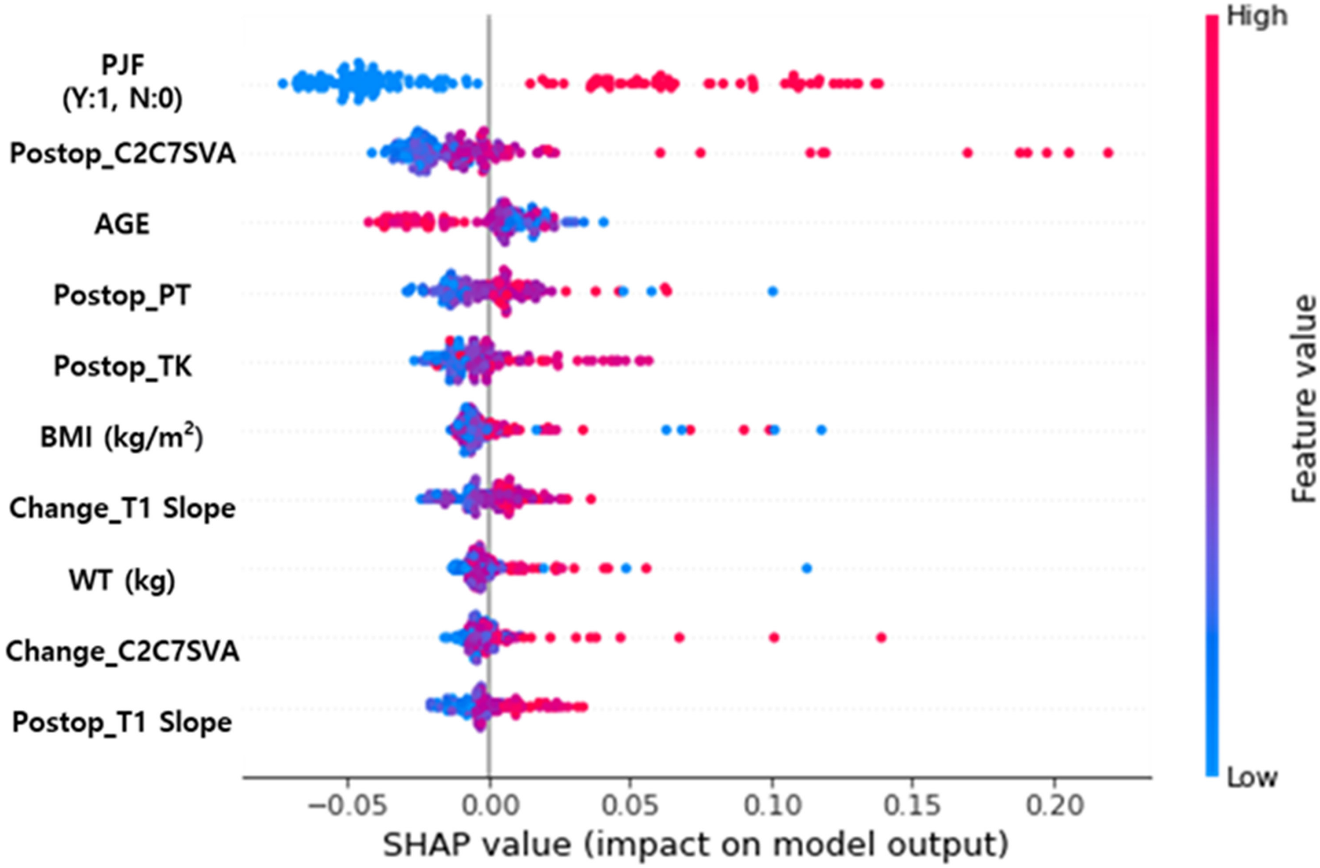

Fig. 3

Summary of risk factors' impacts on whether revision surgery would have to be performed following corrective surgery for adult spinal deformity. Shapley Additive Explanation (SHAP) was applied for interpretation of predictions of our random forest models in Figure 2. The top ten risk factors were plotted with the corresponding SHAP value. In order from first to tenth, risk factors include presence of proximal junction failure (PJF), postoperative sagittal vertical axis from the centroid of C2 (SVA), age, postoperative pelvic tilt (PT), postoperative thoracic kyphosis (TK), BMI (kg/m^2), change of T1 slope, weight (kg), change in SVA, and postoperative T1 slope.

Results

Sagittal parameters were analyzed with preoperative and postoperative radiological studies. There were significant differences in postoperative SVA ($p = 0.004$, independent-samples *t*-test) and change in SVA values ($p = 0.035$, independent-samples *t*-test).

Demographic and radiological parameters were put into a machine learning model to predict URO after corrective surgery for ASD. Each model's mean accuracy and standard deviation with repeated stratified ten-fold were plotted (Figure 2a), and the confusion matrix of the test set also showed that random forest (RF) had the best accuracy (Figure 2b). Receiver operating characteristic curve showed the diagnostic ability of our classifier model. Moreover, precision-recall curves showed the trade-off between the true positive rate and the positive predictive value for our machine learning prediction performance. The RF showed the best model performence with AUROC and AUPRC (Figure 2c).

To reveal the contributions of risk factors, we used the game theory approach, employing SHAP values. Since the RF model showed the best accuracy in Figure 2, the SHAP value for each risk factor was calculated for interpretation of our RF models. The top ten risk factors' SHAP values are plotted in Figure 3. Major significant factors were, in order, the presence of PJF, postoperative SVA, age, postoperative PT, postoperative TK, BMI (kg/m^2), change of T1 slope, and weight (kg).

In Figure 4, we further analyzed the RF model with the corresponding SHAP interaction value to assess the factors' inferred main effect of the postoperative radiological risk for predicting URO with PJF. There is a positive correlation between an increase in postoperative SVA and the occurrence of PJF. This suggests that as the postoperative SVA value increases, the risk of PJF also increases. Additionally, the data in Figure 4 imply that an increase in postoperative SVA has a corresponding effect of increasing the revision surgery in patients who have undergone spinal surgery. Increments of postoperative T1 slope increased the effect whereby revision surgery is predicted, and there was no clear correlation with PJF.

Figure 5 shows Kaplan-Meier revision-free survival curves based on whether PJF occurred and if postoperative SVA > 15 mm. There was a significant difference based

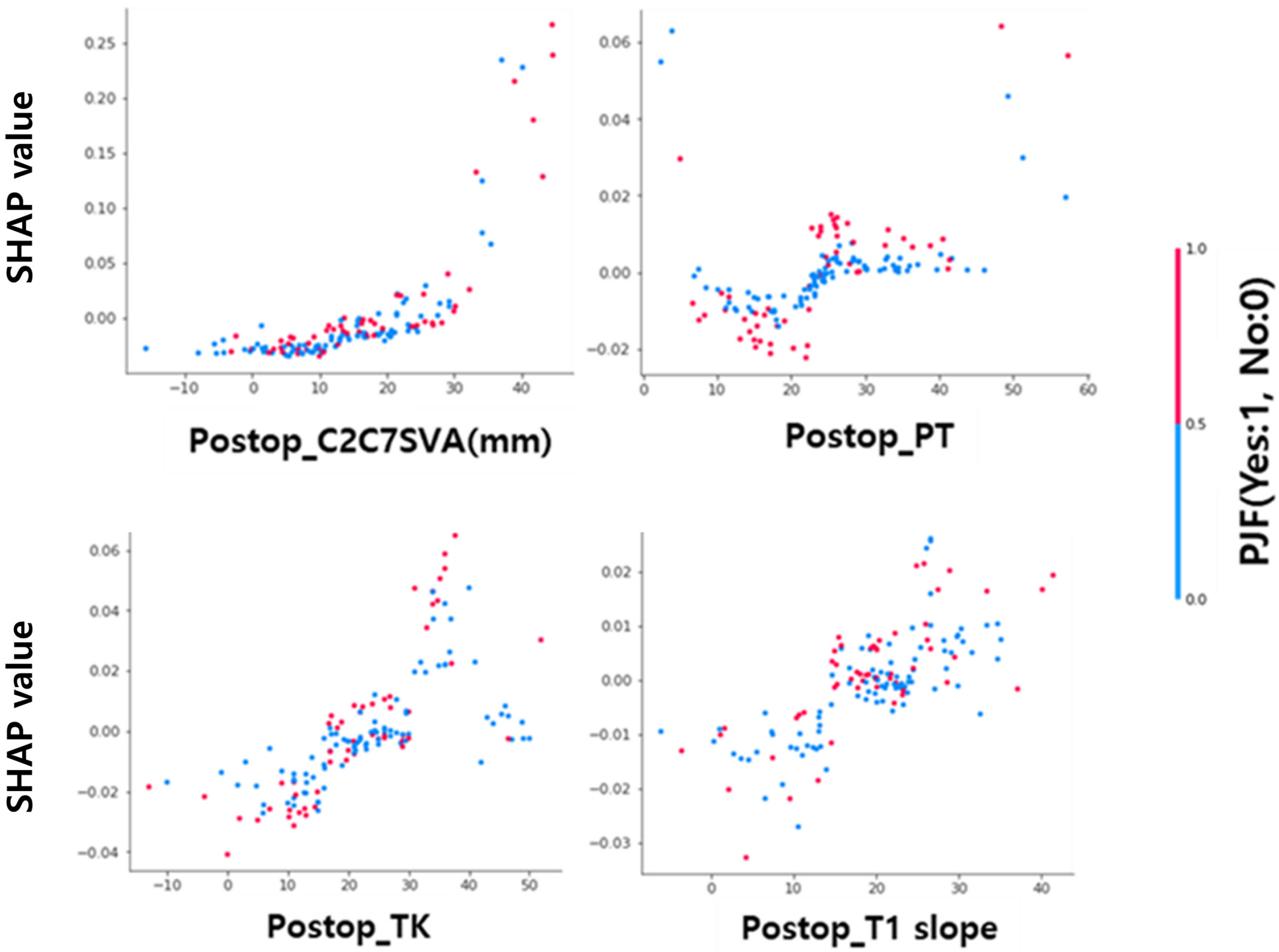

Fig. 4

Postoperative radiological risk factors' inferred main effects for predicting unplanned reoperations upon proximal junction failure. Each dot is a single prediction (row) from the postoperative radiological risk factors, and colour represents proximal junction failure (PJF) (red) or not (blue). The x-axis is the value of the postoperative radiological risk factors. The y-axis is the Shapley Additive Explanation (SHAP) value for the corresponding risk factors, which represents how much that risk factor's value changes the output of the model for that sample's prediction. Elongation of postoperative SVA correlated with PJF and increased the likelihood of revision surgery. Postoperative pelvic tilt (PT) is higher and lower than 25°; the SHAP values are aggregated depending on whether PJF exists. Increments of postoperative T1 slope increased the effect of predicting revision surgery, and there was no clear correlation with PJF. A postoperative thoracic kyphosis (TK) angle > 30° with the presence of PJF indicates a likelihood to undergo revision compared with a postoperative TK angle < 30° with the presence of PJF.

Table II. Cox proportional hazards regression model (forward Wald method) for the risk factors for unplanned reoperation.

Variable	B	SE	Wald	df	Sig.	Exp(B)	95% CI for Exp(B)
PJF	1.173	0.288	16.599	1	< 0.001	3.233	1.838 to 5.684
SVA (> 15 mm)	0.669	0.281	5.672	1	0.017	1.952	1.126 to 3.385

B, the regression coefficient; CI, confidence interval; df, degrees of freedom; PJF, proximal junctional failure; SE, standard error; SVA, sagittal vertical axis.

on whether PJF occurred (part a, $p < 0.001$), and between postoperative SVA > 15 or ≤ 15 mm (part b, $p = 0.008$). Among the absence of PJF and SVA ≤ 15 mm (group 1), absence of PJF and SVA > 15 mm (group 2), and presence of PJF and SVA > 15 mm (group 3), significant differences were observed (group 1 vs group 2, $p = 0.038$; group 1 vs group 3, $p < 0.001$; group 2 vs group 3, $p = 0.012$) (Figure 5c). Cox proportional hazards regression model showed that the odds ratios of PJF and SVA (> 15 mm) were statistically significant (Table II).

Discussion

Achieving appropriate balance, neural decompression, and improved quality of life are the main purposes of corrective surgery for ASD.[20] Although spine surgeons seek to avoid complications, PJF sometimes still occurs. Some

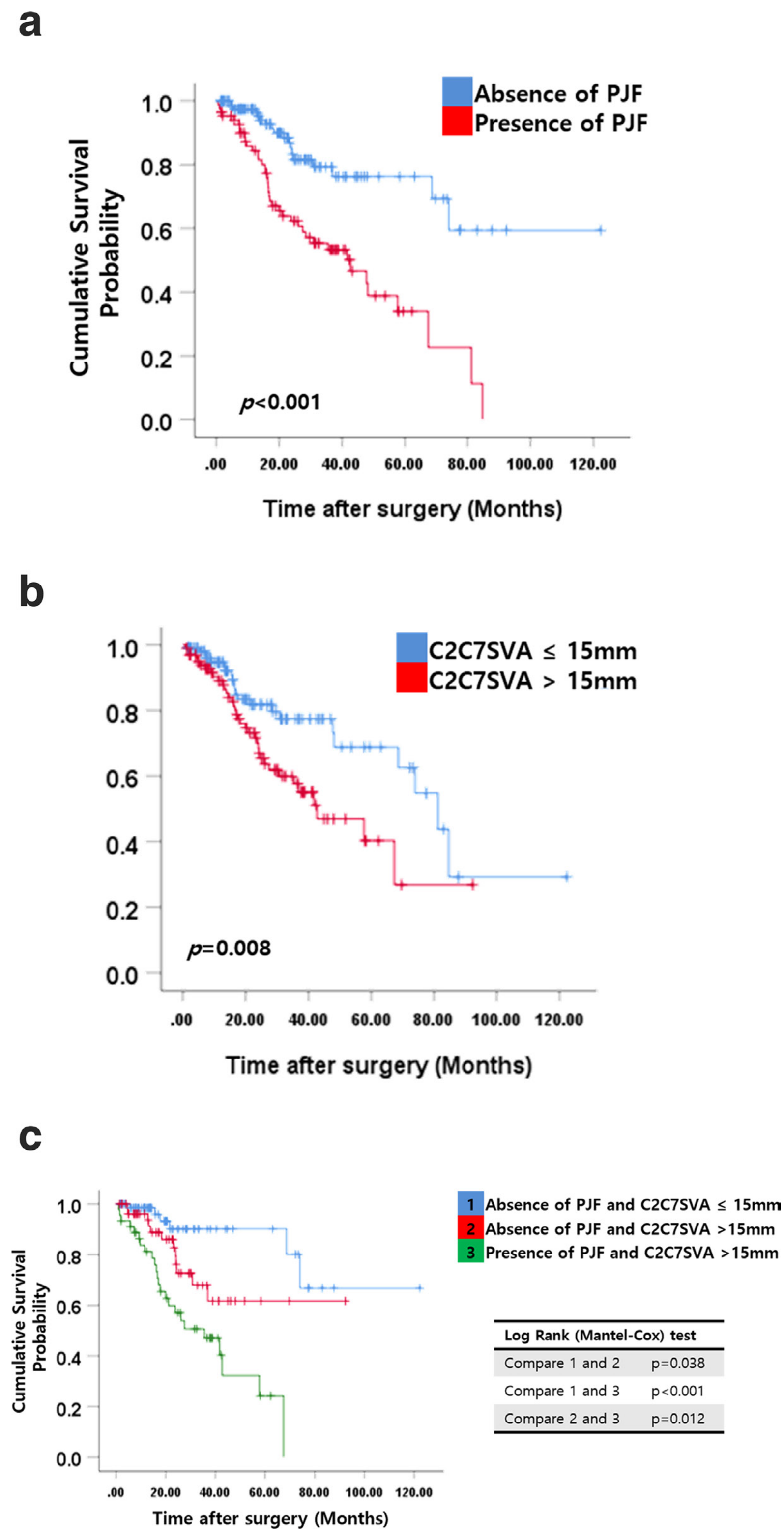

Fig. 5

Kaplan-Meier survival curves showing: a) presence or absence of proximal junction failure (PJF). Mean survival time with 95% confidence intervals (CIs) determined that absence of PJF showed 90.029 (95% CI 75.684 to 104.375) and presence of PJF showed 43.192 (95% CI 35.121 to 51.264) ;
b) postoperative sagittal vertical axis from the centroid of C2 (SVA) > 15 or ≤ 15 mm. Mean survival time with 95% CIs were that C2 (SVA) ≤ 15 mm showed 75.185 (95% CI 60.075 to 90.296) and C2 (SVA) > 15 mm showed 49.537 (39.553 to 59.521); and c) postoperative SVA > 15 or ≤ 15 mm with the absence of PJF and presence or absence of PJF with SVA > 15 mm. Mean survival time with 95% CIs determined that absence of PJF and C2 (SVA) ≤ 15 mm showed 100.441 (95% CI 83.798 to 117.083), absence of PJF and C2 (SVA) > 15 mm showed 65.530 (95% CI 52.839 to 78.222), presence of PJF and C2 (SVA) > 15 mm showed 35.741 (95% CI 27.488 to 43.993)

patients undergo URO for PJF, and others will continue their daily activities despite PJF.[2,4] Therefore, directly predicting whether URO will have to be performed after corrective surgery for ASD is as important as predicting PJF. Although many studies have reported on prediction with machine learning and risk factor analysis for PJF,[9,20–24] relatively few studies have directly predicted whether URO and investigated interactions among risk factors should be undertaken.[25,26]

Explaining complex systems using game theory has been applied in medicine after prior success in economics. In particular, game theory-based analysis is expanding from public medicine to the field of oncology.[27,28] Applications range from modelling mortality from COVID-19 to enhancing cancer therapy using game theory.[29,30] We were therefore inspired to apply the game theory methodologies to corrective surgery for ASD.

To the best of our knowledge, this study is the first report on using game theory to analyze risk factors, using machine learning models that directly predict the incidence of UROs following corrective surgery for ASD. Furthermore, our findings also include the identification of interactions between PJF and postoperative radiological risk factors that contribute to UROs.

The SMOTE, known as an upsampling method, was applied to overcome dataset imbalance, and it is generally known that application of this yields high performance.[9] Of the machine learning models, RF exhibited the highest accuracy and LR the lowest accuracy, at both preoperative features and all of the features (Figure 2). This is similar to previous results that predicted PJK/F, because modifiable non-linear analysis has higher accuracy than linear analysis regarding deformed spine.[9,20]

Reoperation risk for ASD based on whether PJF occurred is well known. Postoperative and δ SVA were significant in our study (Table I); additionally, it was ranked among the top in terms of feature importance (Figure 3). The SHAP value from the RF model revealed that the top ten most important prognostic indicators were PJF, age, weight, BMI, and six modifiable surgical parameters (postoperative SVA, δ SVA, postoperative PT, postoperative TK, postoperative T1 slope, and δ T1 slope; Figure 3). Some features were not significant (Table I). The potential role of postoperative sagittal alignment could not be ignored based on these findings. Cross-correlation function of PJF and postoperative SVA also showed clinical significance (Supplementary Figure a). Six modifiable parameters of the prediction model may further inform decision-making for preoperative surgical planning. Postoperative radiological parameters, including postoperative SVA, PT, TK, and T1 slope, had high SHAP values when accompanied with PJF as per the SHAP interaction analysis (Figure 4). To confirm whether those factors were important per real-world data, the statistically distinct curves were observed upon plotting Kaplan-Meier curves (Figure 5).

Insufficient correction of global imbalance in spinal deformity surgery is an indicator of the likelihood of subsequent mechanical complications.[31,32] Kim et al[33] reported an increase in cervical SVA when PJK was present in the upper thoracic region. The compensatory action of cervical curvature after ASD corrective surgery occurs over time in case of fusion of the middle or upper thoracic segments.[23,24,34] Le Huec et al[35] stated that anterior shifting of the centre of gravity biomechanically increased the lever arm force, resulting in a compression fracture of the spine, which is closely related to URO risk. Because screw fixation up to the upper and middle thoracic levels is performed for recent ASD corrective surgeries, postoperative SVA or δ SVA increases over a certain value independently modify the risk for undergoing URO.

Our study has some limitations. First, we developed our model using our institutional data; however, further validation studies are warranted for external validation with other institutions to confirm generalizability. Second, the sample size of this study was relatively small and imbalanced (URO, n = 58; non-URO, n = 152). To overcome this, we applied the SMOTE algorithm for machine learning analysis and even revision survival curves that unravelled statistically different real-world factors as observed with the original data, without upsampling. Third, we have concentrated on game theory details with some lacuna on clinical data; ASD patients are a very heterogeneous group, with many requiring releases, osteotomies, interbody fusions at single or multiple levels, and other different approaches. All these factors influence surgery outcomes, as all patients fall into different clinical subgroups. Despite this heterogeneity, we tailored the data and compared two groups within similar demographics and BMD (Table I). We also excluded acute URO cases due to surgical site infection and haematoma, and included the URO cases with severe pain or neurological deterioration at least six months after the first surgery. However, further studies will handle a more detailed comparison by subgrouping the surgical technique/approach/surgical scope/instrument/fusion level/decompression level and the type of osteotomy performed; external validation of a machine learning model is needed, with more balanced and larger sample data, to confirm these findings.

In conclusion, this study showed that postoperative C2C7SVA is an important risk factor for URO, as is PJF after corrective surgery for ASD. Our prediction model's explanation would affect operational planning and risk profile, to rule out the subsequent need to undergo URO. This will be meaningful from a clinical standpoint.

Supplementary material

ë Figure displaying cross-correlation function of postoperative proximal junction failure and postoperative sagittal vertical axis, and a table of abbreviations.

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