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관절경하 내측 반월상 연골판 부분 절제술 후 관절의 장기 생존율 예측 모델

Development of a predictive scoring system for the long term joint survivorship following arthroscopic partial medial meniscectomy

울 산 대 학 교 대 학 원

의 학 과

송 주 호

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지 도 교 수 김 종 민

이 논문을 의학박사 학위 논문으로 제출함

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울 산 대 학 교 대 학 원

의 학 과

송 주 호

송주호의 의학박사학위 논문을 인준함

심사위원 김 종 민 (인)

심사위원 김 지 완 (인)

심사위원 이 동 호 (인)

심사위원 이 범 식 (인)

심사위원 인　　용 (인)

울 산 대 학 교 대 학 원

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Abstract

Background: The approach to treating degenerative medial meniscal tears (DMTs) has transitioned from a strategy that prioritized meniscectomy to one that emphasizes meniscus preservation whenever possible. However, not all patients respond to conservative treatment, and the symptom-relieving effect of arthroscopic partial medial meniscectomy (APM) is widely accepted in orthopaedic practice. Establishing appropriate surgical indications requires a prognostic prediction model incorporating numerous clinicoradiologic factors that interact with each other.

Purpose/Hypothesis: This study aimed to develop a predictive scoring system for the long-term joint survivorship following APM using a machine learning technique. It was hypothesized that selected preoperative factors could predict lower survival rates following APM when treating DMTs.

Study Design: Cohort study; Level of evidence, 3.

Methods: Patients who underwent APM for DMTs during 1999–2010 were retrospectively reviewed. The following inclusion criteria were applied: (1) diagnosis of DMTs on preoperative magnetic resonance imaging (MRI) scans, (2) no definite history of trauma, (3) follow-up duration >5 years. Joint survival rates were assessed with the endpoint being defined as conversion to arthroplasty (or realignment osteotomy) or progression to Kellgren-Lawrence grade 4. Investigated predictive factors included demographics, anatomic tibiofemoral angle (aTFA), posterior tibial slope (PTS), cartilage status of the medial and lateral compartments, medial meniscus tear pattern, preoperative subchondral bone marrow lesion (BML), and subchondral insufficiency fracture of the knee (SIFK) lesion. A scoring system was developed to stratify the survival rate following APM. Least absolute shrinkage and selection operator (LASSO)-based Cox regression was used to select the predictive factors of the scoring system, and assigned scores were determined based on the hazard ratio of each factor. Calibration plot was generated to compare the model-based predicted survival rates with the observed survival rates.

Results: A total of 633 knees were included, with a mean follow-up duration of 114.6 ± 47.4 months (range, 60–245 months). During that period, 151 cases experienced failure. The 10-year joint survival rate was 82.3% (95% confidence intervals [CI] 79.0–85.6%). After selection by LASSO-based Cox regression, the following factors (assigned scores) were incorporated into a scoring system: age ≥60 years (2 points), aTFA <2° (2 points), cartilage status of the medial compartment (2 points for grade 2 and 5 points for grade 3), cartilage status of the lateral compartment (1 point for grade 2 and 3 points for grade 3), preoperative subchondral BML (1 point for grade 1, 2 points for grade 2, and 3 points for grade 3), and SIFK lesion (2 points). The joint survivorship was assessed by dividing the total scores into five groups, and for scores of ≥9 points, the 10-year joint survival rate was 51.5% (95% CI, 40.7–61.2%). When comparing the predicted survival rates and observed survival rates in each of the five groups, the calibration plots generally demonstrated a linear pattern. Clinical outcomes were evaluated using the Lysholm scores.

Conclusion: The long-term joint survivorship following APM can be reliably predicted using the developed scoring system. The top scoring factor was grade 3 medial compartment cartilage status followed by grade 3 subchondral BML and grade 3 lateral compartment cartilage status. A total score of 9 points or higher resulted in a nearly 50% reduction in the 10-year joint survival rate. This scoring system provides a basis for an individual risk calculator to assess prognosis and determine indications for APM when treating DMTs.

Key terms: medial meniscus; degenerative tear; meniscectomy; machine learning

Contents

Introduction

The approach to treating degenerative medial meniscal tears (DMTs) has transitioned from a strategy that prioritized meniscectomy to one that emphasizes meniscus preservation whenever possible. This shift is driven by findings suggesting osteoarthritis progression following arthroscopic partial medial meniscectomy (APM).[4,22] Despite this transition, randomized controlled trials on APM have reported that 19–35% of patients did not respond to conservative treatments and thus opted for surgical intervention, where APM has been acknowledged for its symptom-relieving efficacy.[23] However, concerns persist regarding the potential of APM to exacerbate knee osteoarthritis and hasten the need for total knee arthroplasty (TKA).

Numerous factors influence the prognosis of APM. Alongside demographics typically found in large databases, significant prognostic factors include osteoarthritis severity,[2,20] limb alignment,[12,17] meniscal tear pattern,[9,15] and presence of subchondral bone marrow lesion (BML)[5,35] and subchondral insufficiency fracture of the knee (SIFK) lesion.[26] The variability in significant risk factors across studies reflects the diverse array of variables affecting APM prognosis, which often interact with one another. To establish appropriate surgical indications, it is imperative to develop a prognostic prediction model that incorporates multiple predictive factors.[27,31]

A large cohort is necessary to comprehensively investigate numerous variables. Healthcare databases are frequently utilized in research on APM for this purpose.[1,3] However, these databases lack individual information on factors such as the extent of cartilage wear, which can be assessed through magnetic resonance imaging (MRI), rendering analysis of these variables unfeasible. Additionally, long-term follow-up is necessary to comprehend the progression of osteoarthritis or the risk of TKA after APM. In this study, we analyzed a large cohort followed up for over 5 years post-APM from a single center. The study aimed to develop a predictive scoring system for the long-term joint survivorship following APM using a machine learning technique. It was hypothesized that selected preoperative factors could predict lower survival rates when treating DMTs.

Materials and Methods

Patients who underwent APM for DMTs during 1999–2010 were retrospectively reviewed after approval was obtained from our institutional review board. APM for DMTs was performed in cases where mechanical symptoms persisted conservative treatments, such as non-steroidal anti-inflammatory drugs and muscle strengthening exercises, for more than 3 months. Contraindications included advanced-stage medial osteoarthritis (Kellgren-Lawrence grade 4), diffuse full-thickness cartilage wear of the medial compartment, and severe varus alignment exhibiting thrust gait. Advanced age alone was not considered a contraindication for the surgery. The following inclusion criteria were applied: (1) diagnosis of DMTs on preoperative MRI scans, (2) no definite history of trauma, (3) follow-up duration >5 years.

All APM procedures were performed by a single senior surgeon, and arthroscopic findings, including the cartilage status of each compartment and medial meniscus tear pattern, were documented in a preformatted electronic database.[18] Torn meniscal fragments were carefully excised, with utmost care taken to preserve intact meniscal tissue. Following the procedure, the width of the remnant meniscus was measured using a probe, with meniscectomy resulting in a remaining rim less than 3 mm considered subtotal. Postoperative range of motion and muscle strengthening exercises were encouraged without limitation. Once mechanical symptoms had resolved, patients were followed up at 2–3 year intervals to assess osteoarthritis progression. Clinical outcomes were evaluated using the Lysholm scores.

Data collection

Joint survival rates were assessed with the endpoint being defined as conversion to arthroplasty (or realignment osteotomy) or progression to Kellgren-Lawrence grade 4. Investigated predictive factors included age, sex, body mass index (BMI), anatomic tibiofemoral angle (aTFA), posterior tibial slope (PTS), cartilage status of the medial and lateral compartments, medial meniscus tear pattern, preoperative subchondral BML, and subchondral insufficiency fracture of the knee (SIFK) lesion.

The aTFA, measured on 14×17-inch anteroposterior standing radiographs, indicated valgus angles as positive and varus angles as negative.[46] The PTS was determined by the angle between the medial tibial plateau and a line parallel to the mid-diaphysis of the tibia, using a previously validated method.[40] Cartilage status, assessed separately on the femoral and tibial articular sides based on the Outerbridge (OB) grading system, categorized lesions as follows: grade 1 for low-grade chondral lesions (OB grade 0, 1, or 2) on both sides, grade 2 for high-grade lesions (OB grade 3 or 4) on either side, and grade 3 for high-grade lesions on both sides.[37] Medial meniscus tear pattern included posterior root tear (PRT, located within 9mm of the root attachment),[16] radial (flap) tear, longitudinal tear, and bucket-handle tear. Based on the Whole-Organ Magnetic Resonance Imaging Score (WORMS) system,[30] preoperative subchondral BMLs were distinguished from subchondral cysts by their distinctively increased signal within the subchondral bone, lacking evidence of internal trabecular marrow tissue. Preoperative SIFK lesions, identified on MRI scans, showed a pathognomonic subchondral crescent line on T1 and potentially T2 sequences, along with focal epiphyseal contour depression and bone marrow edema.[34,36] Subchondral BMLs and SIFK lesions were categorized as grade 1 for presence on the femoral side, grade 2 for presence on the tibial side, and grade 3 for presence on both sides.

Selection of predictive factors using a machine learning technique

The least absolute shrinkage and selection operator (LASSO) method, tailored for high-dimensional data regression to reduce overfitting and simplify model complexity through L1 regularization, thus improving robustness, was applied.[33,38,42] This statistical technique identified the most informative predictive factors from the dataset. LASSO-based Cox regression shrank the coefficients of variables using a penalty function, effectively setting the coefficients of insignificant variables to zero and identifying crucial variables for subsequent analyses.[19,44]

The study population was randomly divided into training set (80%) and validation set (20%). The former set was used to develop a predictive model and the latter set was used to test its performance. The selected variables were included in a Cox regression analysis, and a time-dependent area under receiver operating characteristic curve was estimated for survival testing with the model.[6]

Development of a predictive scoring system

A predictive scoring system was developed to stratify the survival rate following APM. Assigned scores were determined based on the hazard ratio (HR) of each factor:[11] 1.0< HR <1.5 received 1 point, 1.5≤ HR <2.5 received 2 points, 2.5≤ HR <3.5 received 3 points, 3.5≤ HR <4.5 received 4 points, and 4.5≤ HR <6 received 5 points.[24] The HR intervals were adjusted if there was overlap among the categories of predictive factors with three or more grades. Continuous variables were categorized before performing survival analyses, and the intervals were redefined based on the results. For other categorical variables, if there were no distinct differences in survival rates between categories, the categories were merged and survival analyses were performed to verify the appropriateness of the defined grades.

The total scores were divided into five groups for survival analyses based on the number of cases corresponding to each score. To evaluate the performance of the scoring system in the validation set, the observed survival rate for each group was compared to the model-based predicted survival rate, and the differences were calculated. A calibration plot was then generated to confirm the accuracy, with a linear line having an intercept of 0 and a slope of 1 indicating perfect concordance between model predictions and observed frequencies.[21,39]

Statistical analysis

When assessing the joint survivorship, patients lost during follow-up were treated as censored at their last contact. The joint survival rate was estimated using Kaplan-Meier analysis. Continuous variables were analyzed using *t*-test and categorical variables using chi-square test. In LASSO-based Cox regression analysis, variable selection was conducted using the GLMNET package in R soft version 3.4.4 (R foundation for Statistical Computing, Vienna, Austria).[38] It was considered statistically significant when a two-sided $P < 0.05$.

Result

A total of 633 knees (mean age of 56.9 ± 7.7 years) were included, with a mean follow-up duration of 114.6 ± 47.4 months (range, 60–245 months). During that period, 151 cases experienced failure. 117 cases underwent TKA conversion at 90.7 ± 51.3 months postoperatively. The 10-year joint survival rate was 82.3% (95% confidence intervals [CI] 79.0–85.6%). The mean Lysholm score improved from 66.2 ± 16.1 preoperatively to 77.2 ± 20.3 at the latest follow-up. Patient characteristics are summarized in Table 1.

Table 1. Patient characteristics according to failure

	Overall	Failure (N = 151)	Non-failure (N = 482)	*P* value
Age, y	56.9 ± 7.7	59.3 ± 7.1	56.1 ± 7.8	<0.001
Male / Female, n	101/532	25/126	76/406	0.899
BMI, kg/m^2	25.7 ± 2.9	26.6 ± 2.9	25.5 ± 2.8	<0.001
aTFA,[b] deg	3.4 ± 2.9	2.3 ± 3.4	3.7 ± 2.9	<0.001
Posterior tibial slope, deg	10.5 ± 3.2	10.4 ± 3.2	10.5 ± 3.2	0.680
Medial cartilage status,[c] n (grade 1/grade 2/grade 3)	181/416/36	13/126/12	168/290/24	<0.001
Lateral cartilage status,[c] n (grade 1/grade 2/grade 3)	81/429/123	9/101/41	72/328/82	0.001
PRT, n	181	78	103	<0.001
Radial tear, n	107	35	72	0.019
Longitudinal tear, n	6	1	5	0.678
Bucket-handle tear, n	7	0	7	0.206
Subtotal meniscectomy, n	126	39	87	0.047
Subchondral BML,[d] n (grade 1/grade 2/grade 3)	53/48/108	14/18/67	39/30/41	<0.001
SIFK lesion,[d] n (grade 1/grade 2/grade 3)	58/33/71	29/22/33	29/11/38	<0.001
Preoperative Lysholm score	66.2 ± 16.1	66.1 ± 15.3	66.3 ± 16.3	0.909
Postoperative Lysholm score	77.2 ± 20.3	53.0 ± 22.3	82.9 ± 15.0	<0.001

BMI, body mass index; aTFA, anatomic tibiofemoral angle; PRT, posterior root tear; BML, bone marrow lesion; SIFK, subchondral insufficiency fracture of the knee

[a]Data are reported as mean ± SD unless otherwise indicated.

[b]A positive value indicates valgus alignment, whereas a negative value indicates varus alignment.

[c]Grade 1 = OB grade 0, 1, or 2 on both femoral and tibial articular sides; grade 2 = OB grade 3 or 4 on either side; grade 3 = OB grade 3 or 4 on both sides.

[d]Grade 1 = lesions identified on the femoral side; grade 2 = lesions identified on the tibial side; grade 3 = lesions identified on both femoral and tibial sides.

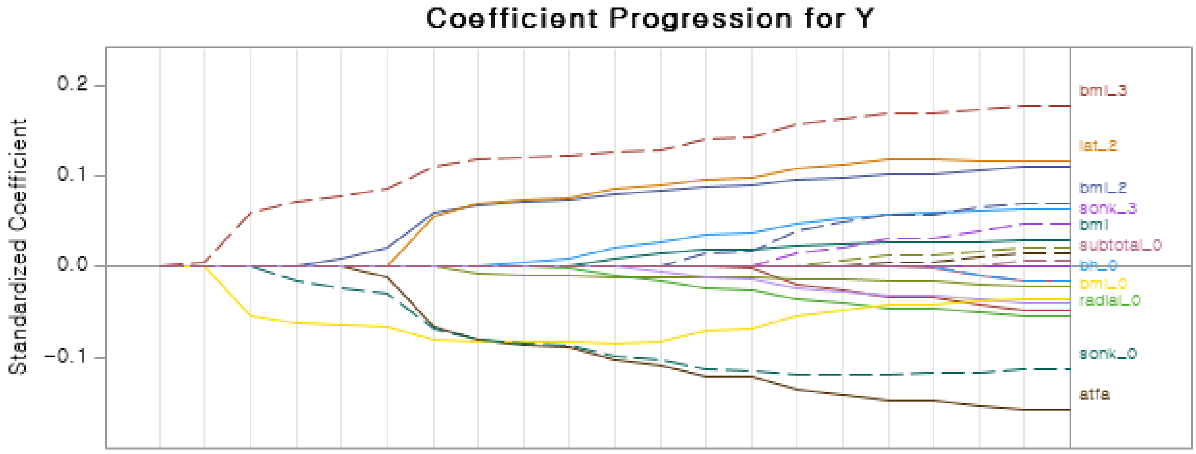
Selected predictive factors and assigned scores

14 variables were reduced to 6 variables by Lasso-based Cox regression. Selected predictive factors included age, aTFA, cartilage status of the medial and lateral compartments, preoperative subchondral BML, and SIFK lesion. LASSO coefficient profiles of the variables were presented as a plot (Figure 1).

To develop the scoring system, patient age was initially categorized into ≥40, ≥50, ≥60, and ≥70 years, and survival analyses were conducted. Based on these results, the age categories were redefined to ≥60 years and <60 years (Figure 2A, 2B). For aTFA, survival rates were compared between categories according to the quartiles of measurements, and the categories were merged based on an aTFA cutoff 2° according to the results (Figure 2C, 2D). Survival analyses were also performed for the other selected categorical factors. The grade of SIFK was simplified into two categories: presence or absence of the lesion (Figure 2E, 2F). The remaining categorical factors showed significant differences in survival rates according to their initial grades (Figure 2G, 2H, 2I).

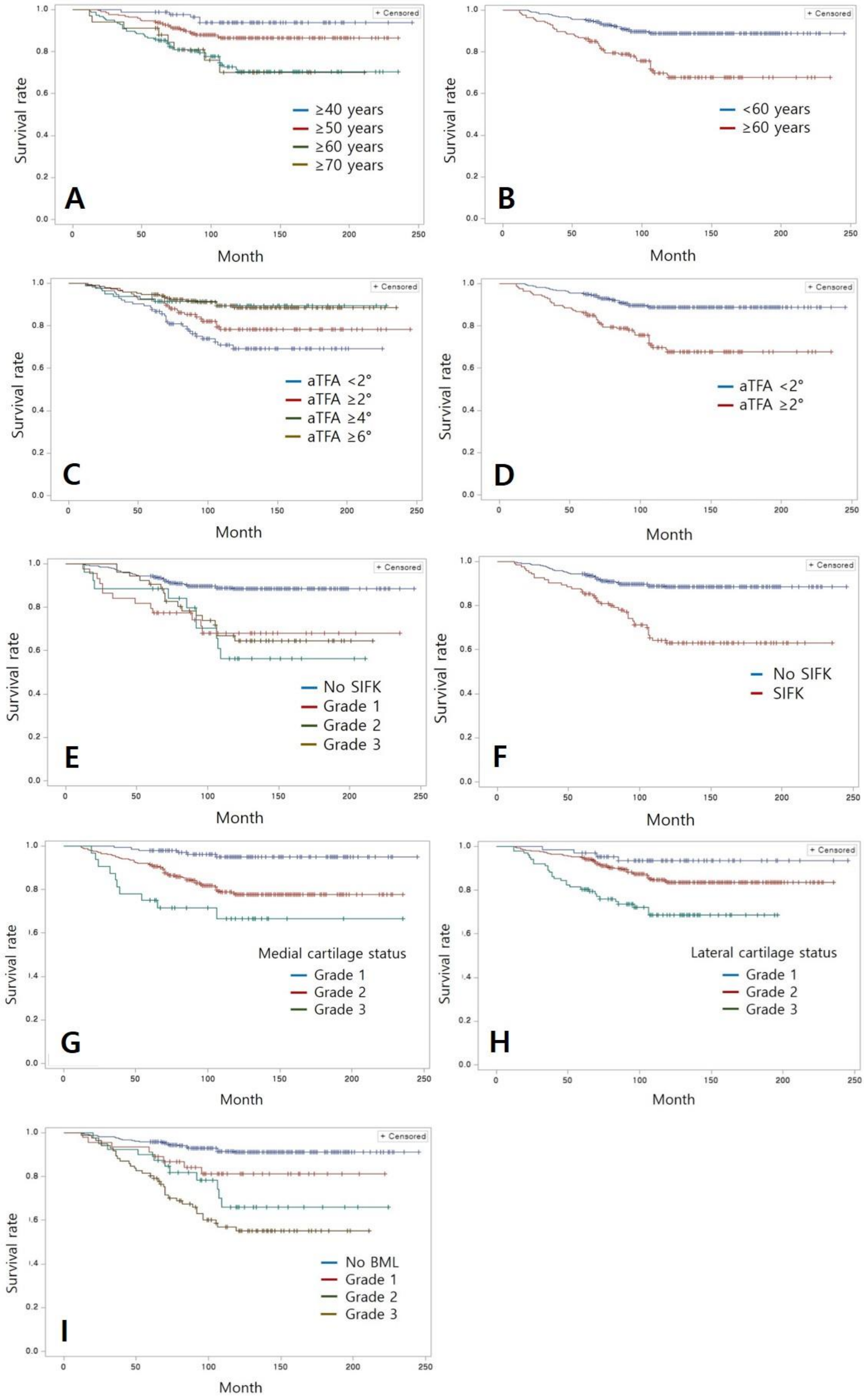
Cox regression analysis was performed with the selected factors of redefined intervals. As a result, the following factors (assigned scores) were incorporated into a scoring system (Table 2): age ≥60 years (2 points), aTFA <2° (2 points), cartilage status of the medial compartment (2 points for grade 2 and 5 points for grade 3), cartilage status of the lateral compartment (1 point for grade 2 and 3 points for grade 3), subchondral BML (1 point for grade 1, 2 points for grade 2, and 3 points for grade 3), and SIFK lesion (2 points). A time-dependent area under receiver operating characteristic curve was presented (Figure 3).

Figure 1. LASSO coefficient profiles of predictive variables



Selected predictive factors included age, aTFA, cartilage status of the medial and lateral compartments, preoperative subchondral BML, and SIFK lesion. LASSO, least absolute shrinkage and selection operator; aTFA, anatomic tibiofemoral angle; BML, bone marrow lesion; SIFK, subchondral insufficiency fracture of the knee.

Figure 2. Survival analyses of selected predictive factors



The categories of age (A, B), aTFA (C, D), and SIFK (E, F) were redefined based on survival analyses. The initial categories of cartilage status of the medial (G) and lateral (H) compartments and subchondral BML (I) showed significant differences in survival rates. aTFA, anatomic tibiofemoral angle; SIFK, subchondral insufficiency fracture of the knee; BML, bone marrow lesion.

Table 2. Assigned scores of selected predictive factors

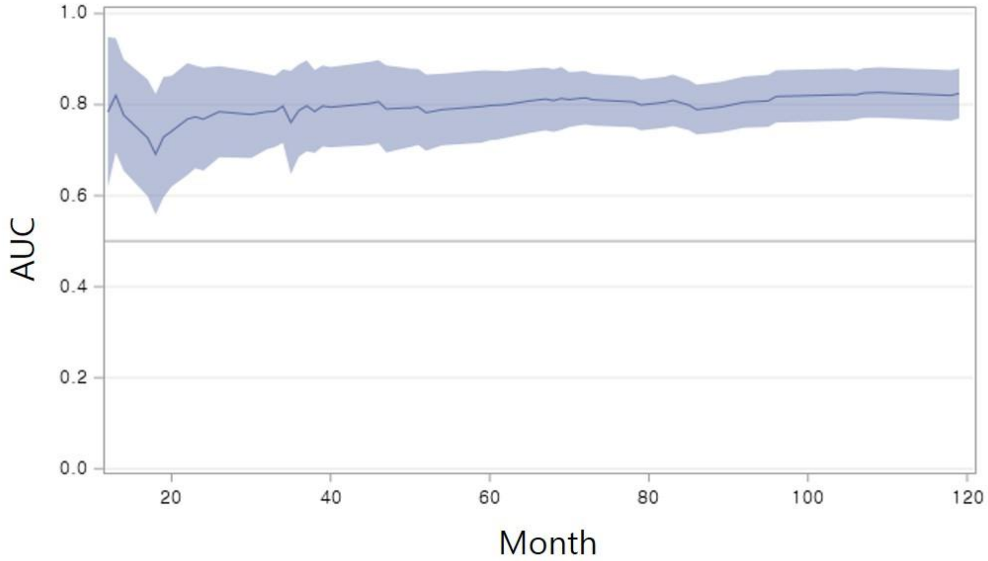
Predictive factor	Hazard ratio	95% CI	Assigned score
Age ≥60 years	1.90	1.20–3.03	2 points
aTFA <2°	2.19	1.35–3.55	2 points
Cartilage status, medial[a]			
grade 2	1.96	0.80–4.78	2 points
grade 3	5.55	1.80–17.1	5 points
Cartilage status, lateral[a]			
grade 2	1.47	0.49–4.43	1 point
grade 3	3.18	1.07–9.46	3 points
Subchondral BML[b]			
grade 1	1.71	0.72–4.03	1 point
grade 2	2.39	1.11–5.14	2 points
grade 3	3.26	1.76–6.05	3 points
SIFK lesion[b]	1.91	1.12–3.27	2 points

aTFA, anatomic tibiofemoral angle; BML, bone marrow lesion; SIFK, subchondral insufficiency fracture of the knee

[a]Grade 2 and 3 cartilage statuses were analyzed relative to grade 1.

[b]Subchondral BML and SIFK lesion were analyzed relative the absence of such lesions.

Figure 3. Time-dependent area under receiver operating characteristic curve

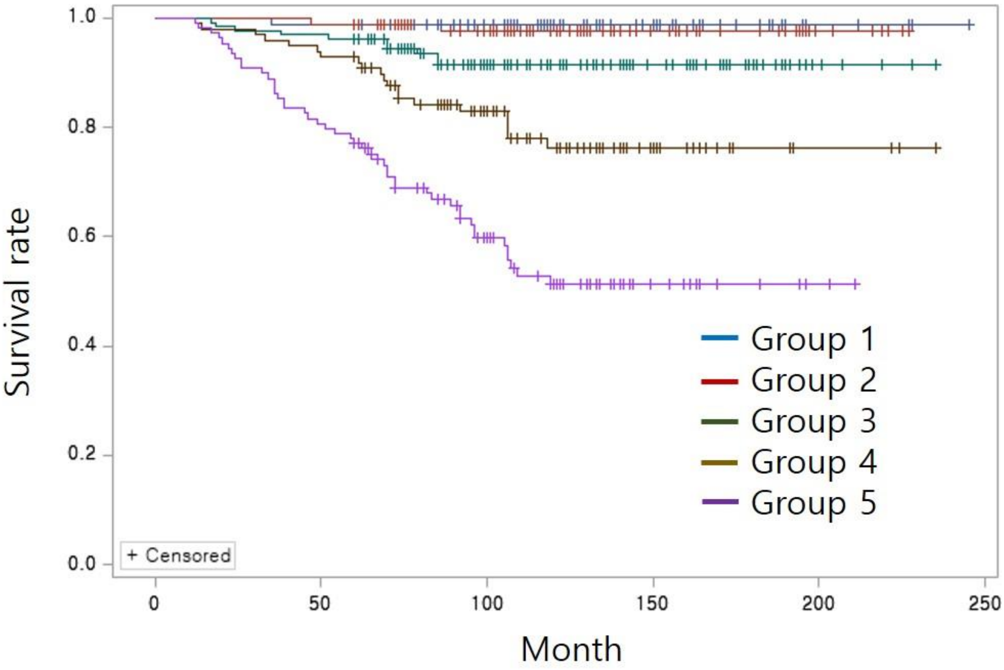


The predictive model was presented with the shaded area indicating the 95% confidence interval. AUC, area under curve.

Performance of the predictive scoring system

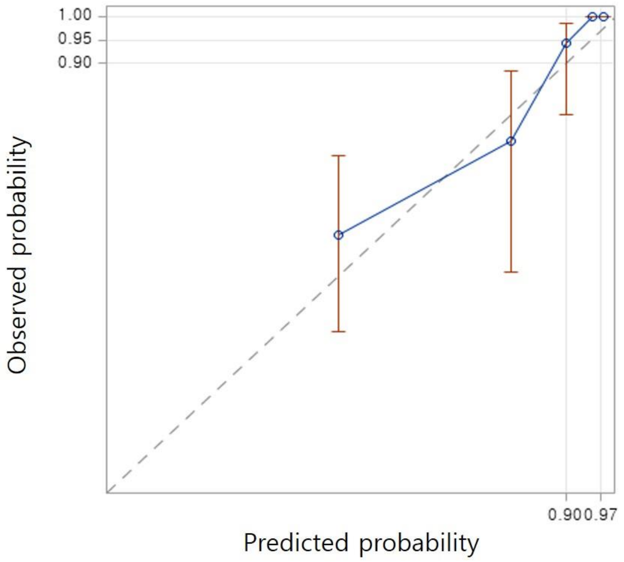
The five groups were defined as follows: Group 1, ≤2 points; Group 2, 3-4 points; Group 3, 5-6 points; Group 4, 7-8 points; and Group 5, ≥9 points. The 10-year joint survival rates for each group were as follows (Figure 4): Group 1, 98.7% (95% CI, 91.4–99.8%); Group 2, 97.5% (95% CI, 90.4–99.4%); Group 3, 91.4% (95% CI, 84.6–95.3%); Group 4, 76.2% (95% CI, 65.1–84.2%); and Group 5, 51.5% (95% CI, 40.7–61.2%). When comparing the predicted survival rates and observed survival rates in each of the five groups, the calibration plot generally demonstrated a linear pattern (Figure 5).

Figure 4. Survival analyses between five score groups



Survival graphs showed distinctively lower survival rates in group 4 and group 5.

Figure 5. Calibration plot comparing the predicted survival rates and observed survival rates



Calibration plot generally demonstrated a linear pattern. A linear line having an intercept of 0 and a slope of 1 indicating perfect concordance between model predictions and observed frequencies.

Discussion

The primary finding of the present study was that the developed scoring system could reliably predict the long-term joint survivorship following APM. The selected predictive factors by LASSO-based Cox regression included age ≥60 years, aTFA <2°, cartilage status of the medial and lateral compartments, preoperative subchondral BML, and SIFK lesion. The highest scoring item was grade 3 medial compartment cartilage status (5 points), followed by grade 3 subchondral BML and grade 3 lateral compartment cartilage status, each scoring 3 points. When the total score was ≥9 points, the 10-year joint survival rate decreased by nearly 50%.

In treating DMTs unresponsive to conservative treatments, APM has been one of the most commonly performed surgeries in orthopaedic practice, with its symptom-relieving effect well-documented.[23] However, concerns have been raised that APM might exacerbate knee osteoarthritis, leading to numerous recent studies evaluating the benefits and drawbacks of APM.[1,3,27,31] Addressing concerns about APM requires more than just examining short-term outcomes over 2–3 years; a long-term cohort capable of assessing joint survivorship in the context of osteoarthritis progression is necessary. Moreover, for individualized risk assessment, it is not sufficient to rely solely on healthcare databases, and comprehensive evaluation of various clinicoradiologic factors is essential. Therefore, this study analyzed patients who underwent APM with a follow-up of at least 5 years, considering all clinicoradiologic factors identifiable on preoperative radiographs and MRI scans to develop a predictive scoring system.

The highest scoring item was found to be grade 3 medial compartment cartilage status, which refers to an OB grade 3 or 4 observed on both femoral and tibial articular sides (5 points). This showed a significant difference in scores compared to cases where OB grade 3 or 4 was observed on either side (2 points). In this study, cartilage status was assessed based on intraoperative findings for accuracy. However, with the use of high-quality MRI, it can be evaluated preoperatively.[41] When applying the scoring system to a case with grade 3 medial compartment cartilage status, a total score of ≥7 points predicts a 10-year joint survival rate of 76.2% (compared to 91.4% for scores <6 points), indicating a substantial decline. Therefore, it is crucial to check for other predictive factors, such as age ≥60 years or aTFA <2°. Additionally, grade 3 lateral compartment cartilage status was also identified as a significant predictive factor, suggesting that the presence of pathology in both medial and lateral compartments is likely to cause poor long-term outcomes after APM. This underscores the importance of thorough preoperative evaluation to ensure that the DMT is indeed the cause of mechanical pain before proceeding with surgery.

Subchondral BML and SIFK, which can be identified on preoperative MRI scans, are also significant predictive factors. Numerous recent studies have demonstrated that both subchondral BML and SIFK reflect compromised biomechanics of the knee joint and are associated with poor prognosis.[8,10,28] While the score for subchondral BML varied depending on its grade, SIFK did not show such variation. Typically, high-grade SIFK indicates the presence of subchondral collapse in the literature;[34,36] however, this study investigated patients who underwent APM and had relatively less severe degenerative changes, making it difficult to apply such grading systems. This limitation might be reflected in the scoring system. Subchondral BML or SIFK can be caused by DMTs, but they also suggest that knee joint biomechanics are already impaired, affecting the subchondral bone. Therefore, it is essential to check for concurrent malalignment or severe cartilage wear.

The impact of patient age on the prognosis of APM has been reported with varying results in different studies. Some authors have associated older age with poor joint survivorship or subsequent TKA.[1,2] However, two issues can be raised with such conclusions. First, many studies fail to control for various prognostic factors that accompany the aging process. Second, using conversion to TKA as the sole measure of poor prognosis can be misleading due to the age-related indication for TKA, making it difficult to fairly assess the age effect. When the impact of age itself on the prognosis of APM, it has been reported that advanced age alone should not contraindicate APM.[37] The present study also showed consistent results, with a score of 2 points assigned to age ≥60 years, which alone did not significantly impact the 10-year joint survival rate (98.7% for total score ≤2 points). However, in actual practice, when deciding on APM for older patients, it is necessary to carefully evaluate the degenerative changes accompanying the aging process, such as cartilage wear, subchondral BML and SIFK.

The importance of alignment in the prognosis following APM has been demonstrated in several studies. Lee et al. analyzed 288 patients who underwent APM for medial meniscus PRT and reported favorable long-term survival in well-aligned knees [aTFA 2°–10°].[17] Subsequent studies have also shown that varus alignment is a poor prognostic factor for osteoarthritis progression after APM,[12,43] and many authors have defined varus alignment as an exclusion criterion in APM studies, opting instead for HTO.[14] Therefore, determining the acceptable degree of varus alignment and its impact is clinically relevant for APM-related decision-making in practice. In the present study, the patients were grouped based on the quartiles of alignment measurements, and survival analysis was performed. Categories with no clear difference in survival rates were merged to redefine alignment grades, resulting in a score of 2 points for aTFA <2° in the predictive scoring system. However, since varus alignment is involved in several prognostic factors identified in this study, such as medial compartment cartilage status,[25,32] subchondral BML,[13,45] and SIFK,[7,29] it should not be the sole consideration when determining the indication for APM.

Several limitations should be acknowledged. First, because the study included only patients who were followed for more than 5 years after APM, there might be a risk of selection bias. However, efforts were made to include patients who experienced failure (conversion to TKA or realignment osteotomy) regardless of the follow-up duration. Second, due to the nature of the study involving patients who underwent APM, cases with relatively severe predictive factors were not included. For instance, cases with severe varus malalignment, diffuse full-thickness cartilage wear, or collapse due to SIFK were not included as they were not candidates for APM. Third, alignment was measured on 14×17-inch standing anteroposterior radiographs, as long-standing hip-to-ankle radiographs were not performed preoperatively in some early cases. Thus, alignment analysis could not be conducted using the mechanical axis of the entire lower limb.

Conclusion

The long-term joint survivorship following APM can be reliably predicted using the developed scoring system. The top scoring factor was grade 3 medial compartment cartilage status followed by grade 3 subchondral BML and grade 3 lateral compartment cartilage status. A total score of 9 points or higher resulted in a nearly 50% reduction in the 10-year joint survival rate. This scoring system provides a basis for an individual risk calculator to assess prognosis and determine indications for APM when treating DMTs.

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