의학석사 학위논문

골 고정 기법을 통한 반월 연골판 이식술의 임상 및 객관적 장기 추시 결과: 최소 15 년 추적관찰

Long-term clinical and objective outcomes of meniscus allograft transplantation with bone fixation: Minimum 15-year follow-up study

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의 학 과

이 중 진

Long-term clinical and objective outcomes of meniscus allograft transplantation with bone fixation: Minimum 15-year follow-up study

지 도 교 수　　이 범 식

이 논문을 의학석사 학위 논문으로 제출함

2023 년 8 월

울 산 대 학 교 대 학 원

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이 종 진

이종진의 의학석사 학위 논문을 인준함

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2023 년 8 월

Abstract

Purpose: To investigate the clinical and objective outcomes of meniscal allograft transplantation (MAT) with bone fixation technique in patients with a minimum 15-year follow-up.

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

Methods: The 54 knees (52 patients) undergoing MAT with a minimum 15-year follow-up were retrospectively reviewed. Clinical outcomes were evaluated with the modified Lysholm score and clinical failure. Clinical failure was defined as a Lysholm score <65 or a need for additional surgery such as revision MAT or total knee arthroplasty. Objective outcomes were evaluated using the follow-up radiographs and MRI in 32 cases with a minimum of 15-year radiographic data. The progression of joint space narrowing and osteoarthritis using the International Knee Documentation Committee (IKDC) radiographic scale was evaluated with weight-bearing posterior-anterior radiographs at 45˚ of flexion. The status of associated cartilage and allograft was examined on MRI scans.

Results: The mean Lysholm score improved from 73.9 ± 17.5 preoperatively to 86.4 ± 15.6 with a mean follow-up of 17.5 ± 3.8 years ($P < 0.001$). The cumulative clinical survival rate was 87.0% (95% CI, 78.9%-96.1%). In objective evaluation, there was a significant decrease in absolute joint space width (JSW) from 4.96 ± 0.96 preoperatively to 3.47 ± 1.62 at the last follow-up. ($P < 0.001$) There was a significant progression of osteoarthritis in the IKDC radiographic scale ($P < 0.001$). On the last follow-up MRI, there was a significant progression of cartilage degeneration on the femoral and tibial sides, and 11 (34.4%) out of 32 cases had allograft tears involving more than 50% of the allograft. The patients with osteoarthritis progression had more meniscal allograft tears and extrusion

on the last follow-up MRI compared with those with non-progression.

Conclusions: Although there was a significant progression of joint space narrowing, osteoarthritis, and cartilage degeneration in objective evaluation, consistent favorable clinical outcomes were demonstrated after MAT with bone fixation technique at long-term follow-up.

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Introduction

In 1984, the first human meniscal allograft transplantation (MAT) was performed to prevent post-meniscectomy symptoms and restore biomechanics.[15] After that, favorable long-term outcomes of MAT using soft tissue or bone fixation technique have been reported in a minimum of 8 or 10 years of follow-up studies.[3,17,18] Therefore, MAT is established as an effective treatment choice for relieving symptoms in patients with post-meniscectomy syndrome.

To assess the value of a procedure, it is important to know its longevity through long-term clinical outcomes evaluated with patient-reported outcomes measures (PROM) or clinical survival rate.[7,8] In bone fixation technique MAT, the previous study reported a high 10-year clinical survival rate with a minimum 8-year follow-up, and the other reported significant improvement of PROM with a mean 12-year follow-up.[5,18] However, to our knowledge, there are no studies that reported the long-term clinical outcomes of bone fixation MAT with a minimum 15-year follow-up.

Several previous studies investigated the long-term objective outcomes of MAT and reported significant progression of joint space narrowing and osteoarthritis in the last follow-up radiographs after MAT.[3,22] However, these studies were performed only with follow-up radiographs. Therefore, little is known about the change of allograft status or cartilage degeneration on long-term follow-up MRI. In addition, no long-term studies compare the difference in allograft status between patients with progression of osteoarthritis and those with non-progression.

Therefore, this study aimed to investigate the clinical and objective outcomes of MAT with bone fixation MAT in patients with a minimum 15-year follow-up. We also compared the demographic factors and allograft status between patients with progression of osteoarthritis and those with non-progression.

Methods

Patient Selection

This study was approved by our institutional review board. A total of 79 consecutive primary medial or lateral MAT cases between December 1996 and January 2019 were retrospectively reviewed. Physically active patients with meniscus-deficient knees were eligible for MAT if they complained of persistent localized pain in the corresponding compartment. Patients having > 2 mm preserved joint spaces on the Rosenberg view were eligible.[16] Malalignment toward the affected compartment was corrected by osteotomy, and ligament insufficiencies were also stabilized by reconstruction before or during MAT. Localized International Cartilage Repair Society (ICRS) grade 3 or 4 cartilage lesions covered by the meniscal transplant were allowed for MAT; however, diffuse grade 3 or 4 degenerative arthritis was a contraindication.

The flowchart of the study population is presented in Figure 1. The inclusion criteria were as follows: (1) primary MAT with a minimum 15-year follow-up and (2) failure confirmed but < 15 years of follow-up. The exclusion criteria were as follows: (1) revisional MAT, (2) no MRI after MAT. Of the 79 knees, 23 cases with less than a 15-year follow-up and two cases without postoperative MRI were excluded. Finally, a total of 54 knees in 52 patients were enrolled in the study and evaluated for clinical outcomes. Because 22 patients were contacted by phone and had no radiographic data, the radiographic outcomes were assessed with 32 knees with a minimum 15-year objective follow-up. The patient characteristics are presented in Table 1. For data analysis, the cartilage lesions were categorized into low-grade (ICRS 0, 1, or 2) and high-grade (ICRS 3, 4).

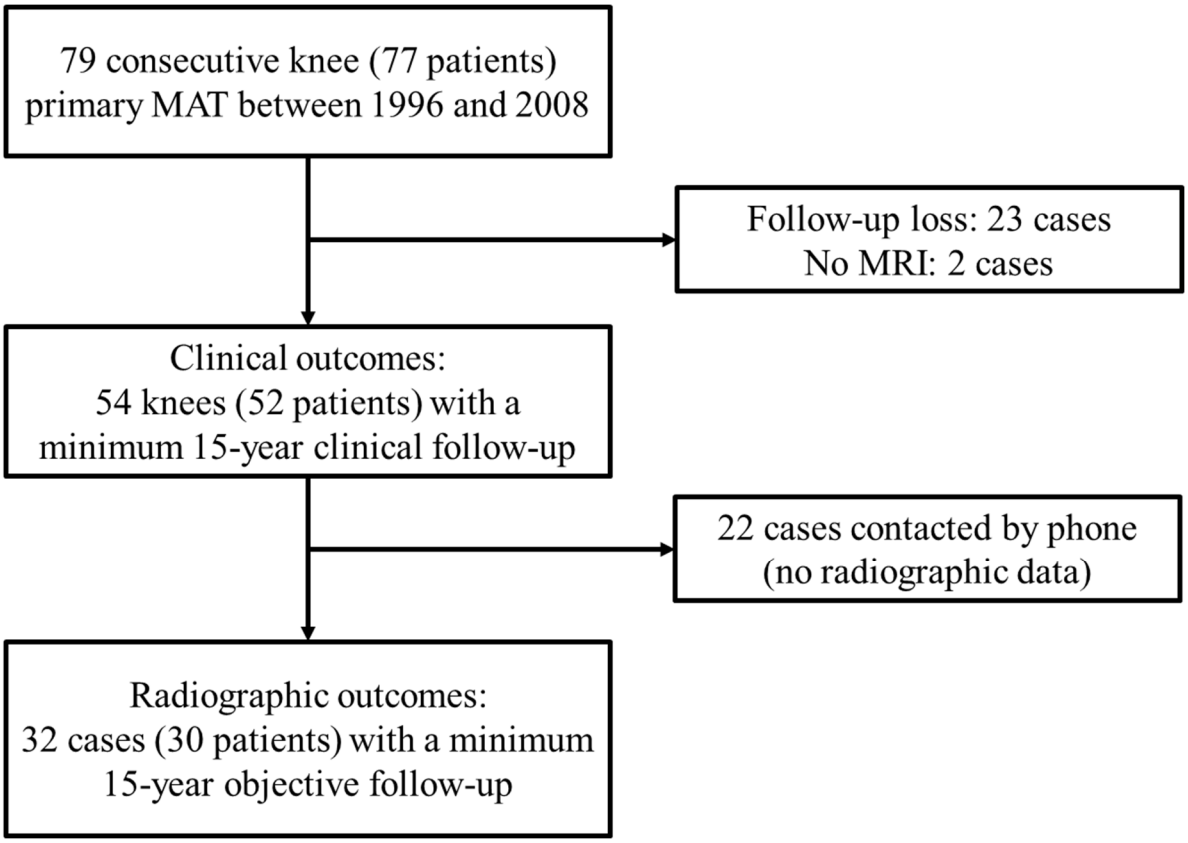


Figure 1. Flowchart of patient selection for this study. MAT, meniscal allograft transplantation; MRI, magnetic resonance imaging.

Table 1. Demographic characteristics of patients

Variable	Overall
No. of patients (knees)	52 (54)
Age, years, mean ± SD	32.6 ± 9.5
Sex, M:F, n	38:16
Side, right/left, n	29:25
BMI	23.6 ± 2.9
Alignment	1.1 ± 2.5
Time from meniscectomy, months, mean ± SD	39.0 ± 48.1
Cartilage status, ICRS grade	
Femur, low:high	29:25
Tibia, low:high	22:32
Follow-up MR period, years, mean ± SD	17.5 ± 3.8
Preoperative Lysholm score, mean ± SD	73.9 ± 17.5
Last follow-up Lysholm score, mean ± SD	86.4 ± 15.6

Surgical Technique and Rehabilitation

All MATs were performed with size-matched fresh-frozen allografts by a single senior surgeon. Medial MAT was performed using the double bone plug technique, whereas lateral MAT was performed using the keyhole technique. The status of the cartilage, ligaments, and meniscus was evaluated through an arthroscopic examination, following which all remaining host meniscus were resected. After preparing the tibial tunnel for the bone plugs of the medial menisci or the bone bridge of the lateral menisci, the allograft was introduced through anterior mini-arthrotomy. After confirming the optimal allograft position, we performed the traditional inside-out meniscal repair. Postoperatively, a range of flexion of 90° was gradually achieved within four weeks and 120° flexion by 6 to 8 weeks. Toe-touch weight-bearing was allowed during the first two weeks, and full weight-

bearing was allowed at 6 to 8 weeks postoperatively. Patients were advised to participate only in low-impact sports activities and light labor to avoid the deterioration of the meniscal allograft.

Assessment of clinical outcomes

The clinical outcomes were evaluated with modified Lysholm scores and clinical survival rates. Modified Lysholm scores were estimated immediately after and every 1 or 2 years postoperatively at follow-up visits or by phone. Clinical failure was defined as a poor Lysholm score < 65 or the requirement of additional surgery such as revisional MAT, realignment osteotomy, arthroplasty, and meniscectomy for more than 50% of the allograft.

Assessment of objective outcomes

The objective outcomes were evaluated by comparing preoperative and last follow-up radiographs, and MRI scans. The progression of joint space width (JSW) and knee osteoarthritis was evaluated with bilateral 45˚ weight-bearing posteroanterior (Rosenberg) radiographs. To minimize measurement error, images were acquired according to a standardized protocol. The images were acquired with 10˚ of internal rotation of the knee and centered midway between both knees at the level of the popliteal crease on a 14 X 17–inch (35.6 X 43.2–cm) film at a distance of 72 inches (182.9 cm) with the x-ray beam directed caudally at 10˚. The digital caliper in the picture archiving and communication system (PetaVision3D; Asan Medical Center) was used to measure the JSW values on radiographs. The absolute JSW value was measured at the center of the compartment using the midpoint method.[13] (Figure 2) To standardize the measurements, the relative JSW was calculated by dividing the affected absolute JSW by contralateral JSW. Two patients with bilateral knee operations were excluded from

the measurement of the relative JSW because the individual JSW values were different, and thus the extent of change might also have been different. The osteoarthritis grade was evaluated using International Knee Documentation Committee (IKDC) radiographic scale.[14] The absolute JSW and radiographic grade of osteoarthritis were compared between before surgery and long-term follow-up (>15 years after surgery).

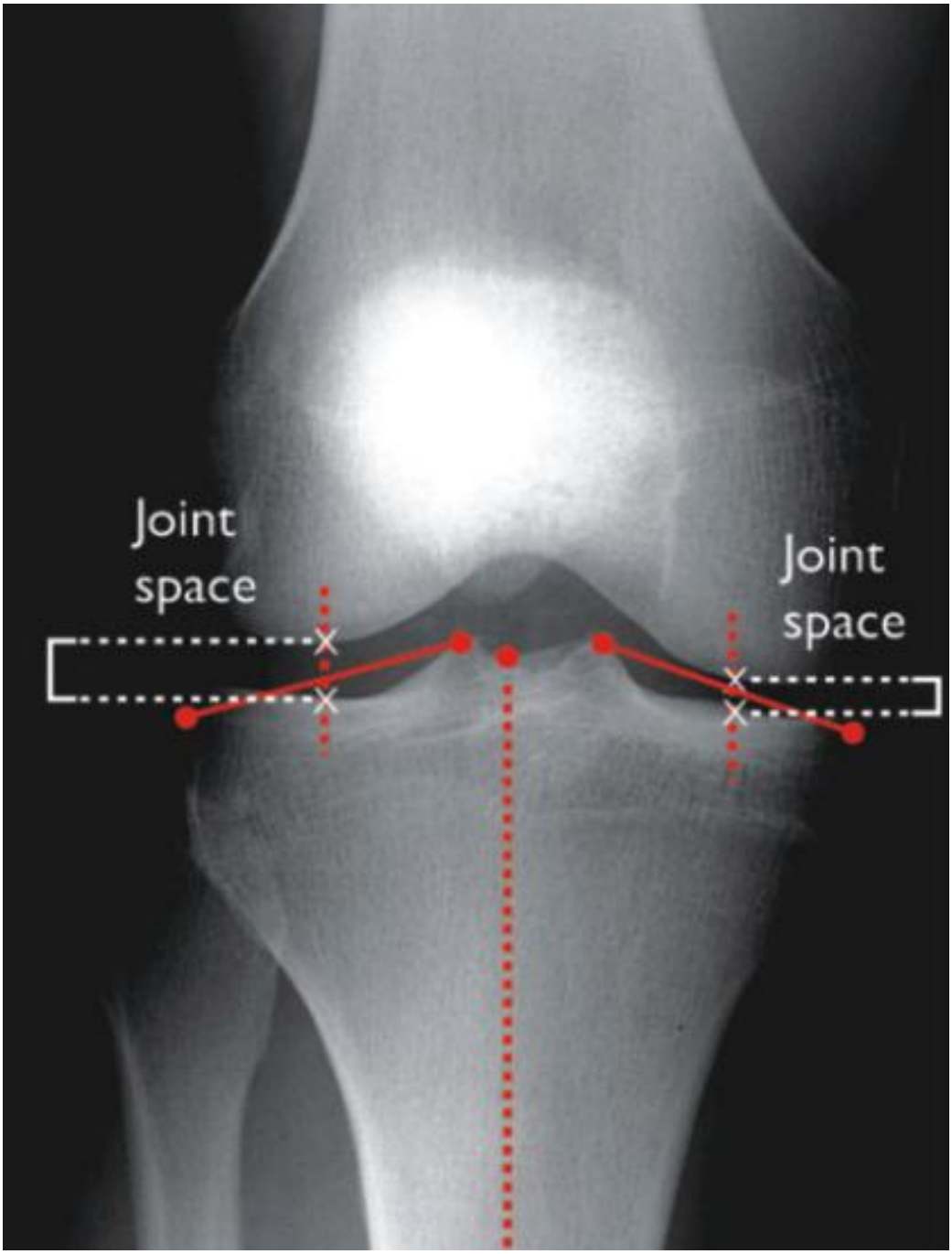


Figure 2. Midpoint method: The joint space widths (JSWs) for the medial and lateral compartments were measured between the tibial and femoral surfaces at the midpoints of the lines depicting each compartment and parallel to the long axis of the tibia.

The status of associated cartilage and allograft was examined on MRI scans. All MRI examinations were performed using a 1.5-T magnetic resonance scanner (Magnetom Vision, Siemens Medical Systems, Erlangen, Germany) using a dedicated knee coil or a 3-T magnetic resonance scanner (Gyroscan Achieva, Philips Medical Systems, Best, the Netherlands). The severity of articular cartilage was evaluated using the International Cartilage Repair Society classification.[6] The worst area of cartilage degeneration was taken to represent the overall status of the corresponding articular cartilage. The grade of cartilage status was compared between before surgery and the last follow-up. The allograft tears and extrusion were evaluated with a final follow-up MRI. The allograft tears were divided into no tears, tears involving less than 50% of allograft, and tears involving more than 50% of allograft. Based on the assessment of all coronal MRIs, the length of allograft extrusion was measured using the image showing maximum extrusion.[10] (Figure 3)

In addition, a comparison of demographic factors and radiographic features such as JSW and allograft tears was performed between patients with progression of osteoarthritis and those with non-progression of osteoarthritis.

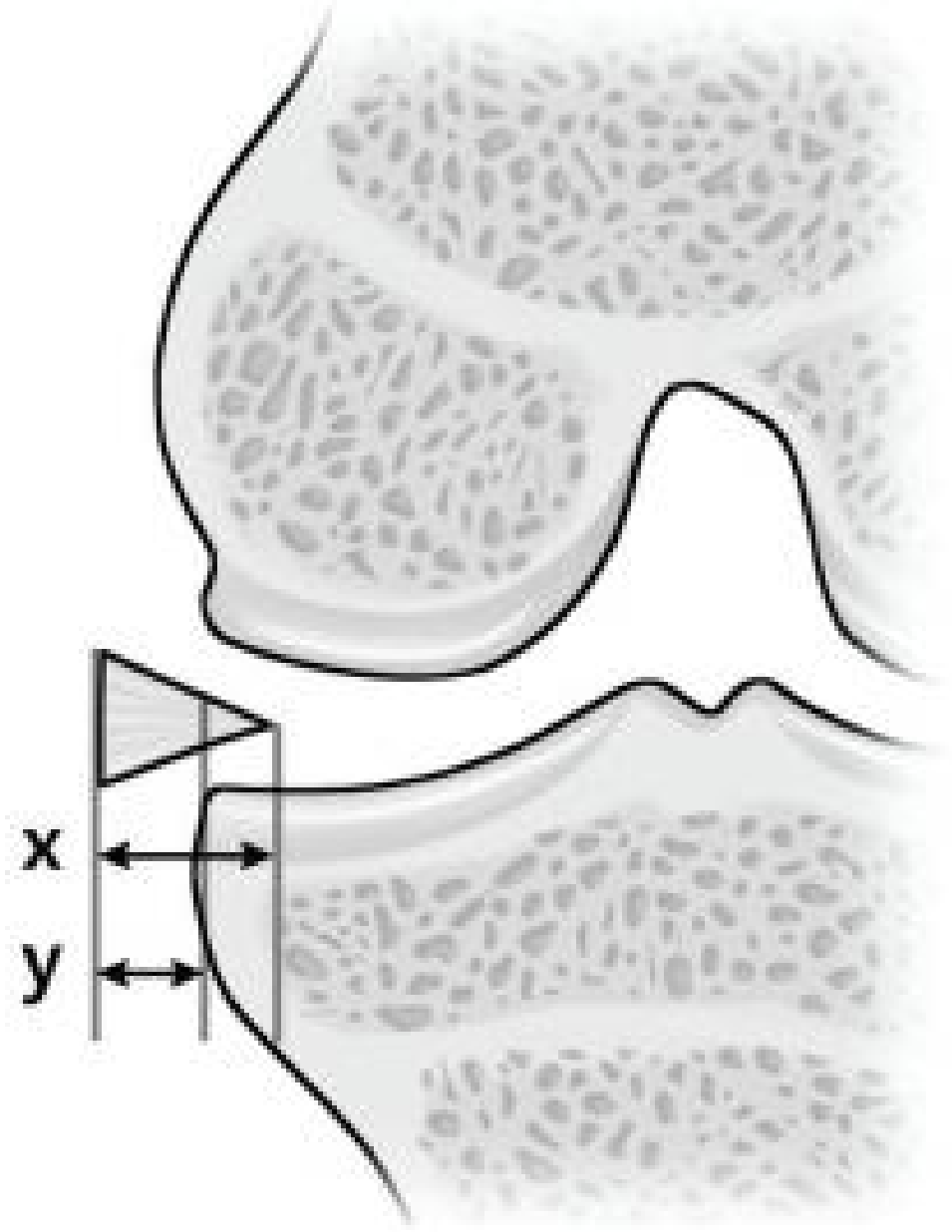


Figure 3. Measurement of meniscal extrusion. The absolute value of meniscal subluxation (y) was defined as the distance between the outer edge of the articular cartilage of the tibial plateau and the outer edge of the extruded meniscal rim.

Statistical Analysis

IBM SPSS statistics (version 27.0; SPSS Inc) was used for the statistical analyses with a *P* value of

< 0.05 considered statistically significant. Continuous data were compared with the independent *t* test or the Mann-Whitney test. The Chi-square or Fisher exact test was used to compare categorical data. The cumulative clinical survival rates were evaluated using a Kaplan–Meier survival analysis.

Results

Clinical outcomes

For all patients, at the last follow-up of a mean of 17.5 ± 3.8 years, the mean (±SD) Lysholm score significantly improved from 73.9 ± 17.5 preoperatively to 86.4 ± 15.6 at the last follow-up *(P*<0.001). The cumulative clinical survival rate was 87.0% (Figure 4). Of the 54 knees, seven cases underwent clinical failure. Two had a Lysholm score < 65, and five underwent additional surgery. Four underwent subtotal meniscectomy due to unstable peripheral rim, and one underwent cartilage restoration (mesenchymal stem cell).

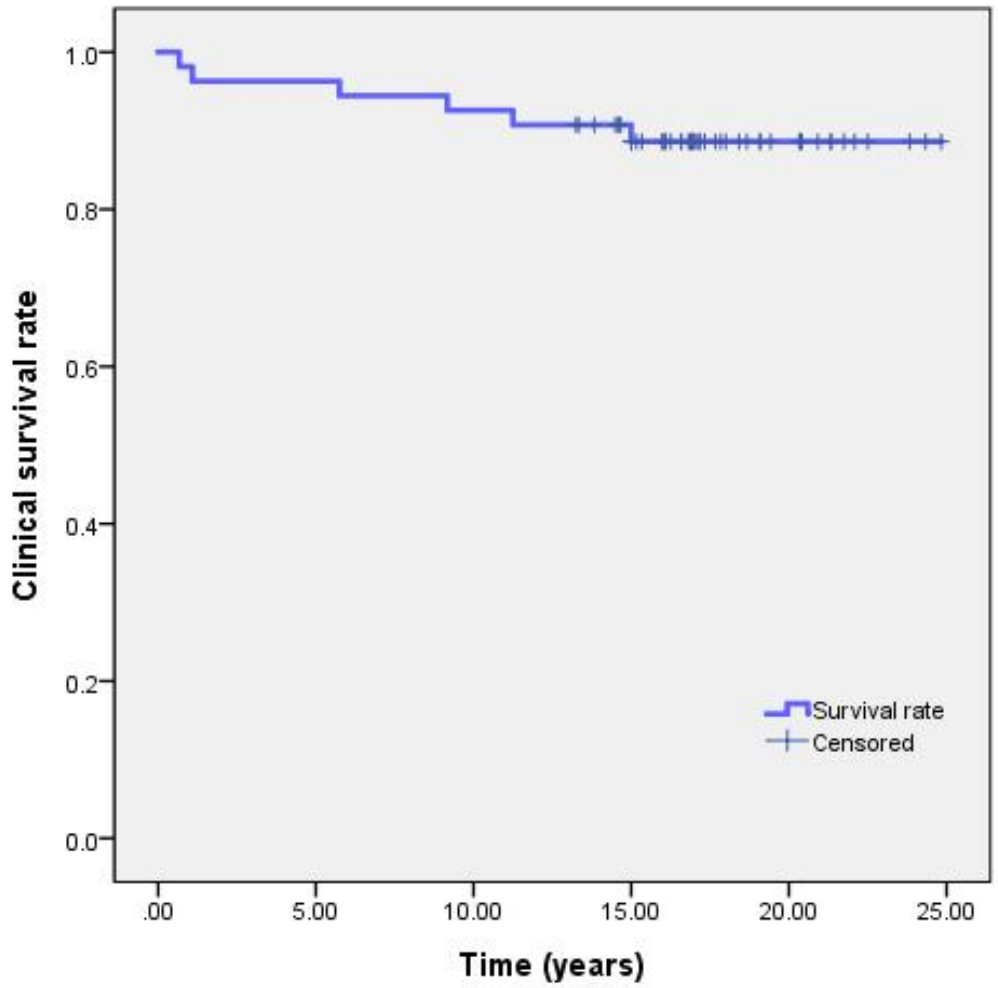


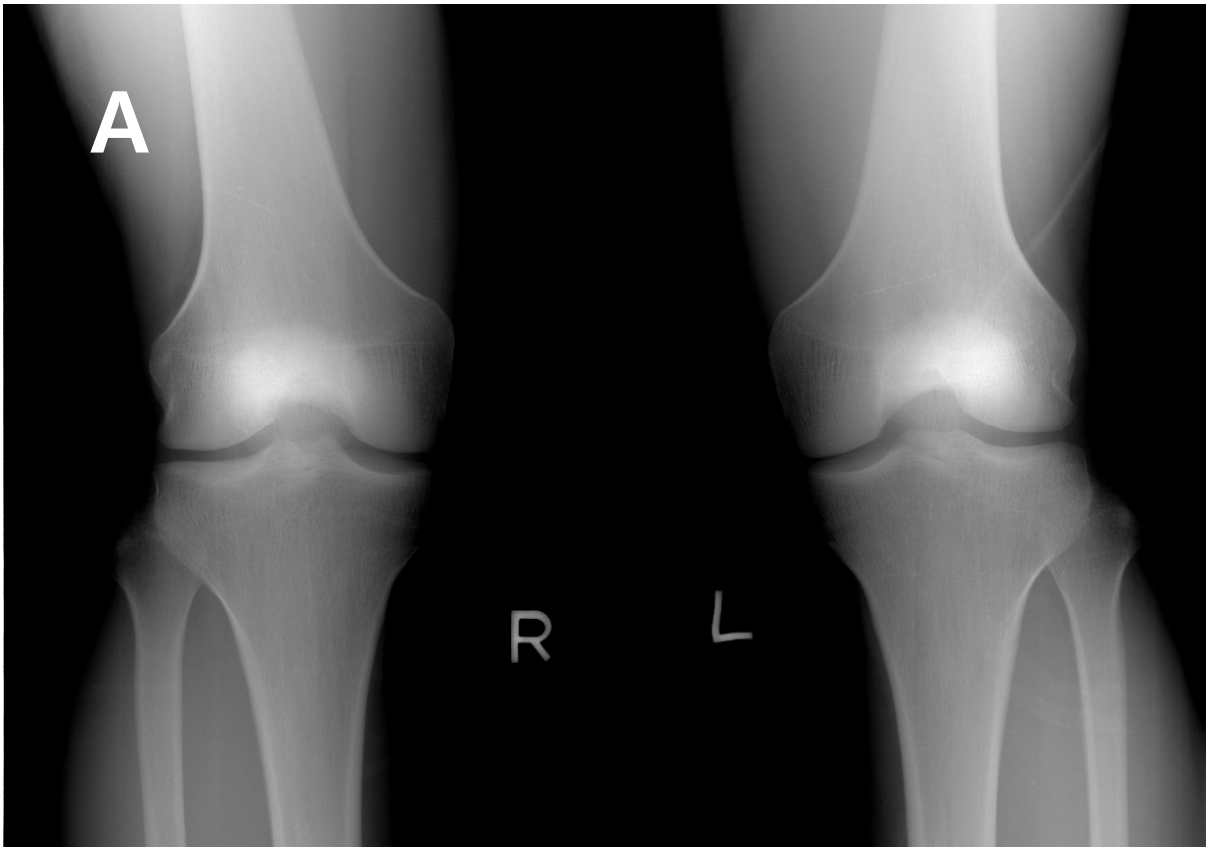
Figure 4. Kaplan-Meier curve of clinical survival rate

Objective outcomes

The preoperative, last follow-up JSW and grade of osteoarthritis are presented in Table 2. Contrary to the contralateral side without surgery, the absolute and relative JSW at the last follow-up significantly decreased compared with before surgery. In the IKDC radiographic grade, there was a significant progression of osteoarthritis compared with preoperative radiographs. Progression of osteoarthritis was noted in 20 cases (62.5%), and there was no change in 12 cases (Figures 5 and 6).

Table 2. The JSW and grade of osteoarthritis on weight-bearing posterior-anterior radiographs at 45° of flexion.

	Preoperative	Last follow-up (>15yr)	P-value
Absolute JSW, mm	4.96 ± 0.96	3.47 ± 1.62	<0.001
Contralateral JSW, mm	6.30 ± 1.33	5.77 ± 1.52	0.154
Relative JSW	0.81 ±0.23	0.63 ± 0.34	0.015
IKDC grade, A:B:C:D, n	9:15:8:0	3:11:11:7	<0.001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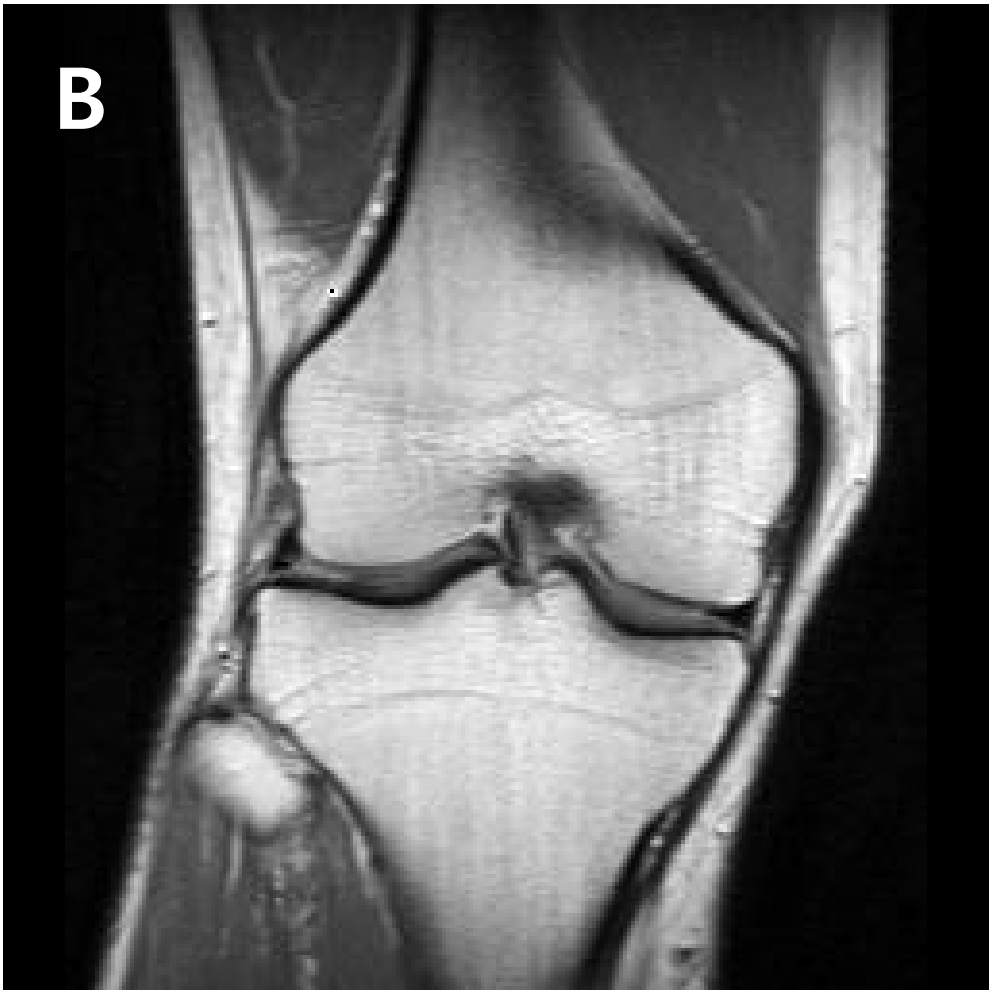
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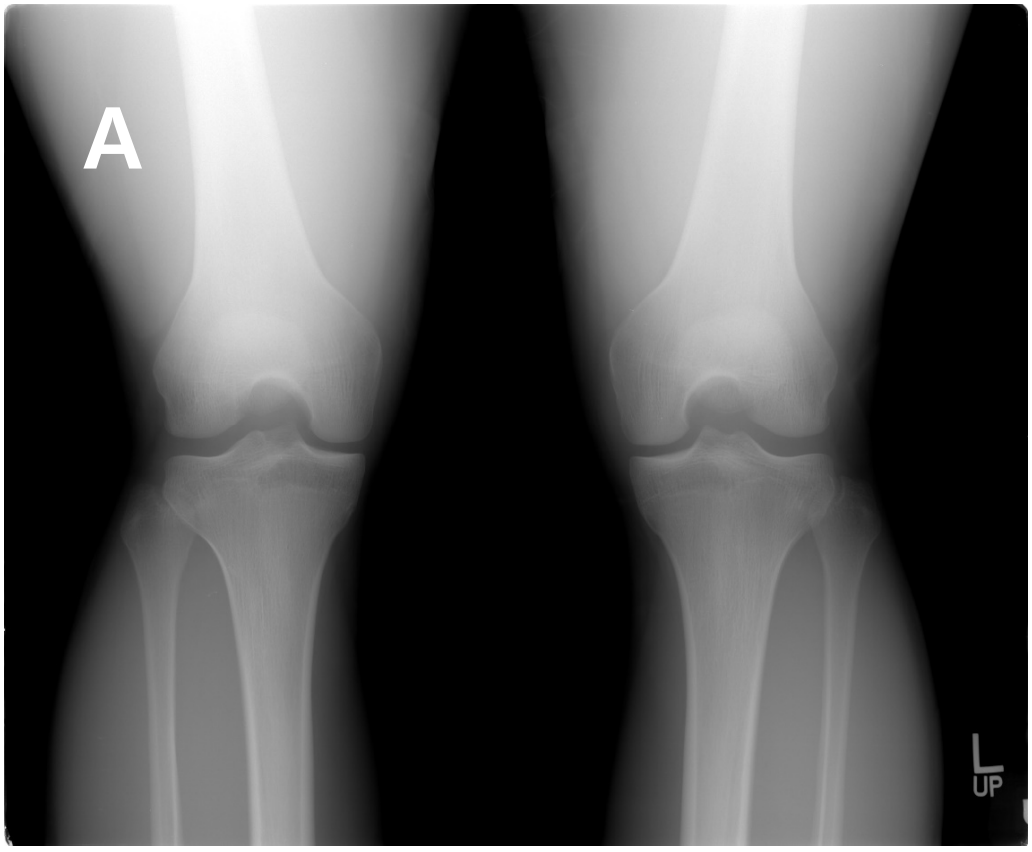
Figure 5. (A and B) A 21-year-old man underwent subtotal lateral meniscectomy on his right knee and suffered from post-meniscectomy syndrome. He underwent lateral meniscal allograft transplantation. (C and D) At the last follow-up of 15 years, there was no progression of osteoarthritis. On the last follow-up MRI, there were no allograft tears or extrusion.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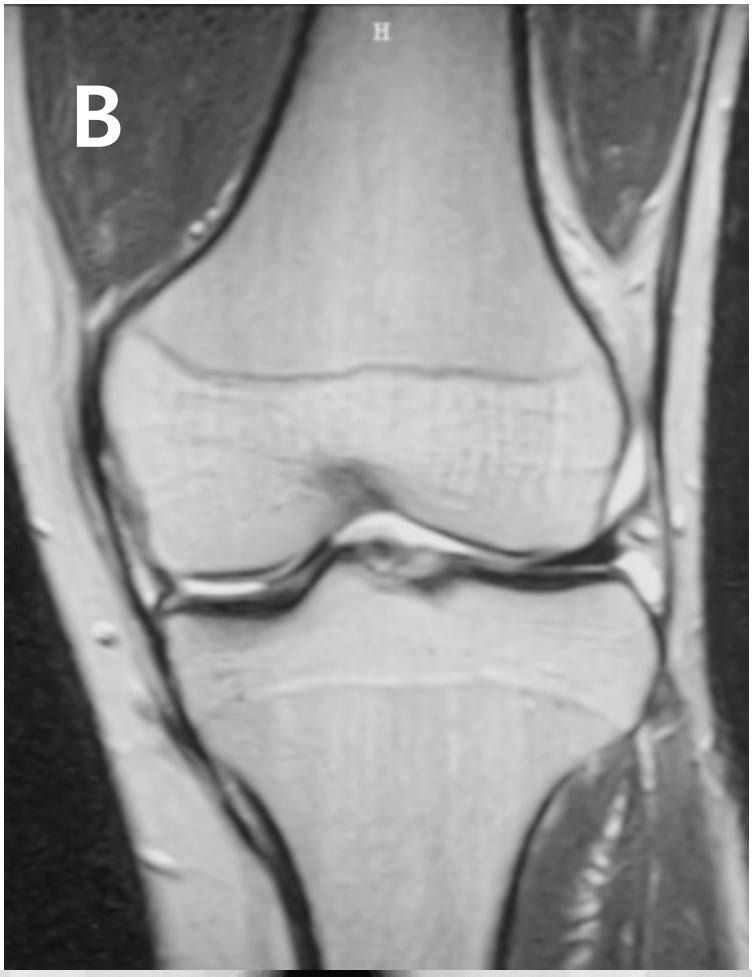
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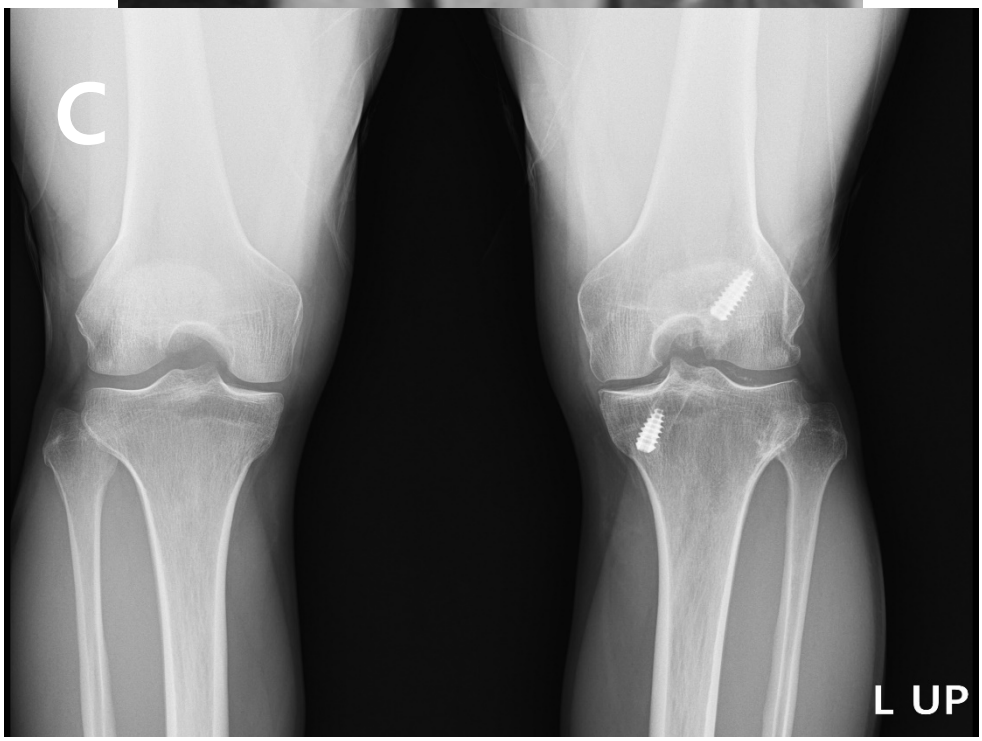
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Figure 6. (A and B) A 18-year-old man underwent subtotal medial meniscectomy on his left knee and suffered from the post-meniscectomy syndrome. He underwent medial meniscal allograft transplantation and anterior cruciate reconstruction. (C and D) At the last follow-up of 17 years, there was no progression of osteoarthritis. On the last follow-up MRI, there were no allograft tears or extrusion.

The cartilage status on preoperative and last follow-up MRI is presented in Table 3. There was significant degeneration of cartilage on both the femur and tibial sides. Progression of cartilage degeneration was observed in 20 cases (62.5%) on the femoral sides and 21 cases (65.6%) on the tibial sides. In the allograft tears on the final follow-up MRI, 11 cases had no tears; 10 cases had tears involving less than 50% of allograft; 11 cases had allograft tears involving more than 50%. The mean extrusion at the last follow-up MRI was 3.07 ± 1.25.

Table 3. The status of cartilage on preoperative and last follow-up MRI

	Preoperative	Last follow-up	P-value
Femur grade, 1:2:3:4, n	12:10:8:2	6:5:8:13	0.039
Tibia grade, 1:2:3:4, n	7:18:5:2	3:6:14:9	0.009

Analysis for patients with progression of osteoarthritis

The comparison was performed between patients with non-progression and those with osteoarthritis progression (Table 4). There was no significant difference in age, sex, BMI, preoperative cartilage status, and preoperative absolute JSW. However, in patients with osteoarthritis progression, the proportion of allograft tears and the mean of allograft extrusion was significantly higher than those with non-progression. In addition, the absolute JSW at the last follow-up was significantly lower.

Table 4. Comparison between patients with osteoarthritis progression and those with non-progression

Variable	Osteoarthritis non-progression	Osteoarthritis progression	*P*-value
No. of knees	12	20	
Age, years, mean ± SD	30.5 ± 9.0	31.5 ± 9.6	0.762
Sex, M:F, n	8:4	12:8	0.706
Compartment, medial: lateral	3:9	7:13	0.703
BMI	22.0 ± 2.0	23.3 ± 3.0	0.221
Preoperative cartilage status, ICRS grade			
Femur, low: high	8:4	10:10	0.471
Tibia, low: high	7:5	7:13	0.277
Allograft status on Last follow-up MRI			
No tear: minor tear: major tear	8:3:1	3:7:10	0.007
Allograft extrusion, mm	2.46 ± 1.31	3.41 ± 1.10	0.038
Preoperative absolute JSW	5.05 ± 0.85	4.91 ± 1.04	0.698
Last follow-up absolute JSW	4.69 ± 0.79	2.70 ± 1.55	< 0.001

Discussion

The most important finding in the present study was that favorable clinical outcomes were observed after the bone fixation technique MAT with a minimum 15-year follow-up. In objective evaluation, joint space narrowing, osteoarthritis, and cartilage degeneration significantly progressed. Patients with the progression of osteoarthritis were associated with allograft tears and extrusion compared with those with non-progression. Nevertheless, in clinical evaluation, the modified Lysholm score significantly improved at the long-term follow-up, and the cumulative clinical survival rate was favorable at 87.0%.

In the present study, patients with the progression of osteoarthritis had a higher proportion of allograft tears and allograft extrusion than those with non-progression. Lee et al.[11] compared patients with allograft extrusion with those with non-extrusion with a minimum mean 12.3-year follow-up. Similar to our study, they reported that the mean JSW in patients with allograft extrusion significantly decreased than in those with non-extrusion. Therefore, the prevention of allograft tears and extrusion may improve the long-term objective outcomes. Lee et al.[9] reported that the risk of graft extrusion increased as the axial plane through angle increased because it caused nonanatomic lateral placement of the graft. In addition, the nonanatomic position led to increased degeneration of the cartilage and allograft tears.[1,4] Therefore, meticulous anatomical positioning of allograft is needed to improve the objective outcomes when performing MAT.

MAT has been performed in two main surgical methods: bone fixation technique and soft tissue fixation technique. Grassi et al.[3] reported long-term outcomes and survivorship of MAT with soft tissue fixation with a minimum 10-year follow-up. They reported satisfactory clinical results for about 70% of patients; the overall survival rate was 87% at five years and 70% at ten years. Although it is almost impossible to compare the two techniques because of different inclusion and failure criteria, we considered that there were several advantages of MAT using the bone fixation technique. First, bone fixation MAT may provide more stability considering the tibiofemoral contact pressure in the

bone fixation technique was significantly reduced than the soft tissue technique in the cadaveric study.[12] Second, Winkler et al.[23] investigated the difference in allograft tears between the two techniques. They reported that meniscal allograft root tears, which could result in surgical repair or resection of allograft, were more frequently observed when using the soft tissue fixation technique. Third, the present study confirmed the relatively high clinical survival rate at 87.0% with a minimum 15-year follow-up.

In the present study, although the status of allograft and cartilage deteriorated in objective evaluation, clinical outcomes were still favorable at the last follow-up. The mismatch between clinical outcomes and objective outcomes has already been reported in previous studies.[2,7,20,21] It could be explained that the remaining tissue of failed allograft could partly perform normal meniscus functions to release pain in the meniscus-deficient knee. Considering that the average age for performing MAT is 29-39 years old,[17] it would be necessary to evaluate whether the clinical outcomes are maintained well in patients with poor status of objective outcomes, even in the long-term results for 20 years and 25 years or more.

This study had several limitations. First, its retrospective nature may have led to a selection bias. Second, in objective evaluation, the follow-up rate was low at 32 (40.5%) out of 79 cases. Third, considering the differences in the surgical methodology and the functions of the medial and lateral menisci, it would be better to analyze medial and lateral MAT independently. But it is difficult because of the small number of subjects. Finally, we used only the Lysholm score for the clinical outcome analysis. However, this is the most commonly used outcome measure for evaluation and has a high level of compliance, making it easy to obtain data over a long period.[19]

Conclusion

In conclusion, although there was a significant progression of joint space narrowing, osteoarthritis, and cartilage degeneration in objective evaluation, consistent favorable clinical outcomes were demonstrated after MAT with bone fixation technique at long-term follow-up.

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요 약 (국문)

목적: 골 고정 기법을 통한 반월 연골판 이식술 시행 후 최소 15년이상 추적 관찰한 환자를 대상으로 임상 및 객관적 결과를 알아보고자 한다.

연구 설계: 후향적 코호트 연구; Level of evidence, 3.

대상 및 방법: 연골판 이식술 후 최소 15년이상 추적관찰을 시행한 54개의 무릎 (52명의 환자)을 후향적으로 분석하였다. 임상 결과는 modified Lysholm score와 clinical failure로 평가하였다. Clinical failure는 Lysholm score가 65점 미만 또는 revision MAT와 같은 추가적인 수술을 시행했을 때로 정의하였다. 객관적 결과는 15년 이상 방사선학적으로 추적관찰한 32명 환자의 단순방사선사진과 MRI를 통하여 평가하였다. 단순방사선사진을 통하여 joint space width와 관절염의 진행여부를 평가하였다. MRI를 통하여 연골 상태와 이식물 상태를 평가하였다.

결과: 평균 17.5 ± 3.8년 추적 관찰에서 Lysholm 점수는 수술 전 73.9 ± 17.5에서 마지막 추적관찰 시 86.4 ± 15.6으로 유의미하게 향상되었다 ($P < 0.001$). 누적 임상 생존률은 87.0% 였다(95% CI, 78.9%−96.1%). 객관적 평가에서 absolute joint space width는 수술 전 4.96 ± 0.96에 비하여 마지막 추적 관찰에서 3.47 ± 1.62으로 유의미하게 감소하였다 ($P < 0.001$). 또한 유의미한 관절염 진행도 관찰되었다. 마지막으로 시행한 MRI상 대퇴골과 경골 측 무릎 연골의 퇴행성 변화가 확인되었다. 객관적 평가를 시행한 32명의 환자 중

11명(34.4%)의 환자에서 50%이상을 침범하는 이식물 파열소견이 관찰되었다. 관절염이 진행된 환자의 경우 이식물의 파열과 Extrusion이 관절염이 진행하지 않은 환자에 비하여 더 많았다.

결론: 연골판 이식술 후 장기 추적 시 객관적 평가상 관절염의 진행, 연골의 퇴행성 변화가 관찰되었지만, 임상적 결과는 양호한 것으로 확인되었다.