

Biological Knee Reconstruction With Concomitant Autologous Chondrocyte Implantation and Meniscal Allograft Transplantation

Mid- to Long-term Outcomes

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Background: Treating articular cartilage defects and meniscal deficiency is challenging. Although some short- to mid-term follow-up studies report good clinical outcomes after concurrent autologous chondrocyte implantation (ACI) and meniscal allograft transplantation (MAT), longer follow-up is needed.

Purpose: To evaluate mid- to long-term outcomes after combined ACI with MAT.

Study Design: Case series; Level of evidence, 4.

Methods: We performed a retrospective review of prospectively gathered data from patients who had undergone ACI with MAT between 1999 and 2013. A single surgeon treated 18 patients for symptomatic full-thickness chondral defects with meniscal deficiency. One patient was lost to follow-up. Thus, 17 patients (18 knees; mean age, 31.7 years) were evaluated over a mean 7.9-year follow-up (range, 2-16 years). A mean 1.8 lesions per knee were treated over a total surface area of 7.6 cm² (range, 2.3-21 cm²) per knee. Seventeen lateral and 1 medial MATs were performed. Survival was analyzed using the Kaplan-Meier method. The modified Cincinnati Knee Rating Scale, Western Ontario and McMaster Universities Osteoarthritis Index, visual analog scale, and Short Form-36 were used to evaluate clinical outcomes. Patients also self-reported knee function and satisfaction. Standard radiographs were scored for Kellgren-Lawrence (K-L) grade.

Results: Both 5- and 10-year survival rates were 75%. Outcomes for 6 knees were considered failures. Of the 6 failures, 4 knees were converted to arthroplasty and the other 2 knees underwent biological revision surgery. Of the 12 successfully operated knees, all clinical measures significantly improved postoperatively. Ten patients representing 11 of the 12 knees rated outcomes for their knees as good or excellent, and 1 rated their outcome as fair. Eight patients representing 9 of the 12 knees were satisfied with the procedure. There was no significant osteoarthritis progression based on K-L grading from preoperatively to a mean 5.9 years after surgery. Seven of the 12 knees (58%) required subsequent surgical procedures (5 arthroscopic alone, 2 both arthroscopic and open).

Conclusion: Combined ACI with MAT provided significant improvement in 65% of the operated knees over a mid- to long-term follow-up. This procedure can allow patients to retain their biological knees, delay or prevent rapid degeneration to osteoarthritis, and could be recognized as a bridge procedure before artificial knee replacement. However, careful discussion between the patient and surgeon is necessary before surgery to ensure realistic expectations.

Keywords: autologous chondrocyte implantation; meniscus allograft transplant; cartilage; meniscus; biological knee

Osteoarthritis (OA) in the knee joint is one of the most common chronic diseases causing pain and dysfunction among adults^{9,27,30,33,47} and affecting many health outcomes.^{8,10,20,32,49} Injury to the articular cartilage and

meniscus is a known major risk factor for OA.^{3,15,31,40,44,45} Moreover, a recent analysis of Osteoarthritis Initiative (OAI) data¹⁴ showed that injury rapidly accelerated joint disease; among participants without baseline knee joint OA, prior knee injury was associated with accelerated progression to end-stage radiographic knee OA within 48 months (odds ratio [OR], 9.22; 95% CI, 4.50-18.90). Regarding surgical treatment for cartilage lesions, autologous

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chondrocyte implantation (ACI) is a promising treatment that has recently been shown to have long-term durability.^{38,43} Similarly, meniscal allograft transplantation (MAT) for meniscal deficiency has been shown to result in significant clinical improvement over a long-term follow-up.^{16,26} Although successful clinical outcomes have been reported for each procedure in isolation, the combination of articular cartilage defects with meniscal deficiency remains a challenge for orthopaedic surgeons, especially when it occurs in young patients.

Historically, ACI and MAT have been contraindicated in meniscus-deficient knees and in patients with cartilage lesions, respectively. Although significant improvement in patient-reported outcomes has been reported over the short- to mid-term in patients undergoing combined ACI and MAT,^{2,18,23,25,46} the use of this combined surgery is controversial, and little is known about its mid- to long-term clinical outcomes. Additionally, whether it can prevent osteoarthritic changes remains to be determined.

The purpose of our study was to determine the mid- to long-term outcomes of combined ACI with MAT using validated outcome questionnaires and standard radiographs.

METHODS

Patient Demographics

The study was approved by our institutional review board. Informed consent was obtained from all patients at the time they were entered into the database, usually at the time of their index surgery. Between March 1999 and October 2013, a single surgeon treated a total of 18 patients with ACI combined with MAT for concomitant symptomatic full-thickness chondral defects and meniscal deficiency. One patient did not return for follow-up and was therefore excluded from this study (follow-up rate, 95%). Thus, 17 patients (18 knees) who had completed more than 2 years of follow-up by the time of data analysis were included in this study. There were 8 women and 9 men with a mean age (\pm SD) of 31.7 ± 10.8 years at the time of the index surgery (range, 16-56 years). Patients were observed after surgery for a mean of 7.9 ± 4.9 years (range, 2-16 years).

A total of 32 cartilage lesions (mean, 1.8 lesions per knee) were treated, representing a mean total surface area of 7.6 ± 5.3 cm² (range, 2.3-21 cm²) per knee. All knees had at least 1 cartilage lesion in the same compartment as the MAT. Bipolar (kissing) lesions were present in 7 of 18 knees. All bipolar lesions were located in the lateral compartment. Seventeen lateral and 1 medial MAT were performed (Table 1).

All but 1 patient had undergone previous surgery, including partial/total meniscectomy (16 knees), anterior cruciate ligament reconstruction (3 knees), MAT (1 knee),

TABLE 1
Patient Demographics^a

Age at surgery, y, mean \pm SD	31.7 \pm 10.8
Sex, male/female, n	9/8
Right/left knee, n	9/9
Body mass index, kg/m ² , mean \pm SD	26.5 \pm 3.4
Follow-up, y, mean \pm SD (range)	7.9 \pm 4.9 (2-16)
Duration between meniscectomy and index surgery, y, mean \pm SD	8.6 \pm 6.2
Cartilage lesions, n	
1	7
2	8
3	3
Received workers' compensation, n	1
MAT location, medial/lateral, n	1/17
Defects per knee, mean	1.8
Primary lesion size, cm ² , mean \pm SD	5.5 \pm 3.2
Overall lesion size, cm ² , mean \pm SD	4.3 \pm 2.9
Total defect surface area per knee at index surgery, cm ² , mean \pm SD	7.6 \pm 5.3
Defect location, n	
Lateral femoral condyle	17
Medial femoral condyle	2
Trochlea	3
Patella	2
Lateral tibial plateau	8
Medial tibial plateau	0
Unipolar/bipolar lesion, n	11/7
Bipolar lesion, medial/lateral, n	0/7

^aMAT, meniscal allograft transplantation.

Roux-Goldthwaite procedure (1 knee), and osteochondral autograft transplantation and distal femoral varus osteotomy followed by osteochondral allograft transplantation (1 knee). Two knees had severe cartilage lesions that produced excessive wear and extrusion of the meniscus, with a small nonfunctional meniscal remnant.

Patient Evaluation

Patients who underwent combined ACI with MAT were prospectively evaluated. Indications for surgery included 1 or more full-thickness chondral defect of the knee with meniscal deficiency in patients who had symptoms matching the defect location and who were resistant to nonoperative therapies, including physical therapy, injectable therapies, and/or the use of a custom unloader brace. All patients were evaluated by physical examination, radiography, magnetic resonance imaging (MRI), and arthroscopy before treatment with combined ACI and MAT was considered. Meniscal deficiency was defined by the presence of <5 mm of uninterrupted circumferential hoop fibers as determined by preoperative MRI and confirmed by diagnostic arthroscopy (Figure 1). Patients with lateral compartment pathology were more likely to undergo this

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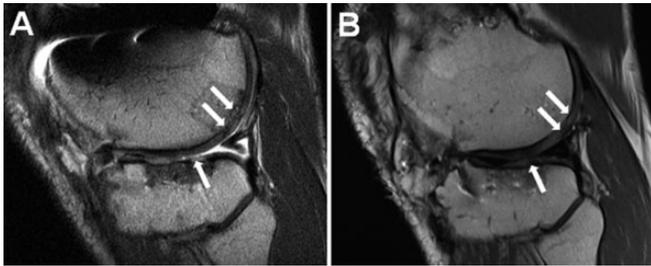


Figure 1. Pre- and postoperative sagittal magnetic resonance images of the involved compartment. This patient's previous surgeries included partial lateral meniscectomy, osteochondral allograft transplantation to the lateral femoral condyle (LFC), osteochondral autograft transplantation to the LFC, allograft transplantation to the lateral tibial plateau (LTP), distal femoral osteotomy, and autograft bone grafting to the LTP. Lateral meniscal allograft transplantation and autologous chondrocyte implantation to the LFC and LTP (lesion sizes, 100 mm² and 375 mm², respectively) were performed. (A) Preoperative image showing an irregular surface and chondral lesion defects in the LFC and LTP (arrows) with a remnant lateral meniscus. (B) Postoperative image showing normal signal intensity of the meniscal allograft and complete defect filling with a congruent articular surface 7 years postoperatively (arrows).

concurrent procedure because the lateral compartment tends to deteriorate much faster after meniscal deficiency than the medial compartment.^{12,42} Contraindications to treatment included inflammatory joint disease, unresolved or recent septic arthritis, metabolic or crystal disorders, body mass index >35 kg/m², and deficient soft tissue coverage. Tibiofemoral malalignment more than 2° to 3° from the neutral mechanical axis into the involved compartment was corrected with concomitant osteotomy and was therefore not considered to be a contraindication for surgery.

Presurgical Planning and Surgical Technique

ACI was performed as described in detail elsewhere.³⁶ Briefly, after an arthroscopic cartilage biopsy was performed at the initial surgery, chondrocytes were cultured, cryopreserved, and then thawed and recultured for definitive reconstruction after insurance approval. Three to 6 weeks after cartilage harvesting, the second surgery was performed for implantation with arthrotomy. Before May 2007, the periosteum was harvested from the proximal tibia or the distal femur (7 knees). After May 2007, a type I/III bilayer collagen membrane derived from porcine peritoneum and skin (Bio-Gide; Geistlich) was used (11 knees) instead of periosteum. The periosteum or collagen membrane was placed on the cartilage defect and secured using multiple 6-0 Vicryl sutures (Ethicon). The suture line was sealed with fibrin glue (Tisseel; Baxter Biosurgery), and the autologous chondrocytes were injected underneath the membrane.

Articular comorbidities, such as malalignment and patellar maltracking, were corrected at the time of surgery. Tibiofemoral malalignment more than 2° to 3° was corrected through osteotomy of the tibia or femur after

TABLE 2
Concomitant Procedures

Procedure	n
No concomitant procedure	10
Tibial tubercle osteotomy alone	1
Combined distal femoral osteotomy/tibial tubercle osteotomy	6
Sandwich technique	1

correcting the mechanical axis to neutral or zero degrees. Patellofemoral maltracking was addressed with anteromedialization tibial tubercle osteotomy (TTO) to centralize patellar tracking^{19,37} and proximal soft tissue balancing (lateral release, vastus medialis obliquus advancement) as necessary to centralize the extensor mechanism. Concomitant procedures included combined distal femoral osteotomy (DFO)/TTO in 6 and TTO alone in 1 patient. One patient underwent surgery using the "sandwich technique,"⁵¹ which involved the use of an autologous bone graft for the subchondral bone defect and ACI for the overlying cartilage defect, because this patient had a deep cystic lesion with the osteochondral injury. Ten patients did not require concomitant procedures (Table 2).

MAT was performed using a size- and side-matched graft with an attached bone block (bone block technique) for meniscal deficiency. Before 2004, MAT was performed using the keyhole technique.^{7,22} After 2004, it was performed using the bridge-in-slot technique.¹³ The meniscal remnant was removed to prepare a vascularized bed for the transplant. The majority of the menisci were fresh-frozen (15 knees), with some being cryopreserved (3 knees). Two of 3 cryopreserved allografts were sterilized by the BioCleanse chemical process (Regeneration Technology Inc), a low-temperature sterilization system that exposes the allograft to a variety of chemical solutions, including hydrogen peroxide and isopropanol.³⁹ All other grafts did not receive postharvest sterilization.

Postoperative Course

Postoperatively, a hinged knee brace was applied, and patients were not allowed to participate in weightbearing activities. Additionally, patients used a continuous passive-motion machine for 6 hours daily for 6 weeks. After 6 weeks, gradual progression to full weightbearing was allowed. Patients were allowed to return to most activities of daily living after 3 months and to return to nonimpact functional activities, including biking, treadmill walking, and progressing to an elliptical trainer after 4 to 6 months. After 12 months, patients' activities were progressed to in-line jogging. If a physical examination demonstrated return of full motion, muscle tone, and no effusion, and an MRI demonstrated complete isotonic graft appearance with a lack of bone marrow edema, full activities were allowed after 18 months.

Failure Definition

The outcome of failure was classified into 4 categories: (1) ACI and/or MAT graft failure with revision using partial or

Poor (1-2 points)	I have significant limitations that affect activities of daily living.
Fair (3-4 points)	I have moderate limitations that affect activities of daily living. No sports possible.
Good (5-6 points)	I have some limitations with sports but I can participate; I compensate.
Very good (7-8 points)	I have only a few limitations with sports.
Excellent (9-10 points)	I am able to do whatever I wish (any sport) with no problem.

Figure 2. Modified Cincinnati Knee Rating Scale for overall patient condition.

total knee arthroplasty, (2) ACI graft failure with revision cartilage repair, (3) MAT graft failure with revision MAT, and (4) graft survival but development of new defects elsewhere in the same knee necessitating additional surgery (disease progression).

Survival Analysis

The survival rate was evaluated using the Kaplan-Meier method with failure as the endpoint. Additionally, the survival rates of individual ACI grafts and MAT grafts were evaluated independently when case failures occurred and patients proceeded to arthroplasty or revision biological surgery.

Clinical and Radiographic Outcome Assessment

Patients were assessed for a range of functional scores, including the modified Cincinnati Knee Rating Scale,^{6,34} the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC),¹ visual analog scale (VAS), and the Short Form-36 (SF-36).⁴ The original Cincinnati Knee Rating Scale is based on a 0 to 100 continuous scale,⁴¹ whereas the modified Cincinnati Knee Rating Scale is based on a 1 to 10 categorized scale, with a 2-point change being considered clinically meaningful (Figure 2).^{6,34} Patients also answered questions regarding their self-rated knee function and satisfaction with the procedure. Scores were collected preoperatively and at yearly intervals postoperatively during an office visit or by mailed questionnaire. Standing long-alignment radiographs to include hip/knee/ankle as well as standing anteroposterior (AP), Rosenberg, and lateral radiographs were obtained. AP and lateral radiographs were scored in accordance with the Kellgren-Lawrence (K-L) grade²⁹ to evaluate the progression of OA before and after the index surgery.

Statistical Analysis

All statistical analyses were performed using Stata software (version 13; Statacorp LP). A subanalysis was performed by age (<30 vs >30 years), patient sex, cartilage defect size (<6 vs >6 cm²), type of cartilage lesion (unipolar vs bipolar), type of cover membrane (periosteum vs

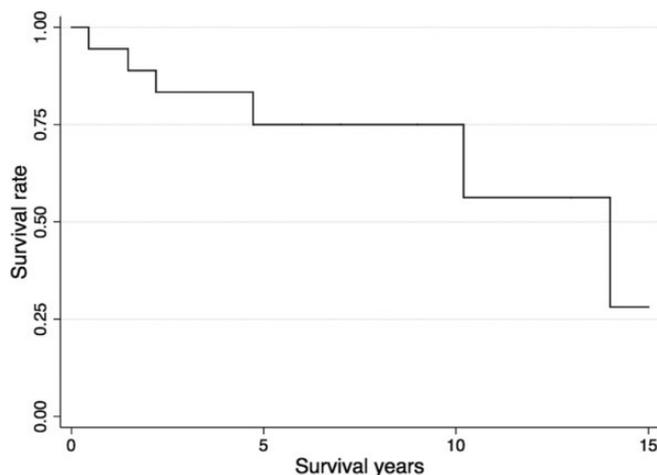


Figure 3. Kaplan-Meier survival curves. Failure was defined as the need for revision surgery due to ACI and/or MAT graft failure or as disease progression. ACI, autologous chondrocyte implantation; MAT, meniscal allograft transplantation.

Bio-Gide), sterilization method of meniscal allograft (no sterilization vs BioCleanse), and whether combined osteotomy occurred. The Wilcoxon signed-rank test was used to compare differences in functional scores (obtained from the VAS, WOMAC, SF-36, and modified Cincinnati) between the 2 time points (ie, preoperatively and at the different follow-up time points). Mann-Whitney *U* tests were used to compare the improvement in scores between different groups. Kaplan-Meier survival curves were used for survival analyses, followed by a log-rank analysis. The level of significance was set a priori at $P < .05$.

RESULTS

The outcome for 6 patients (6 knees) was considered to be failure. Self-reported satisfaction, functional scores, and results of radiographic evaluation in success and failure cases are reported independently. Of the 6 failures, 4 knees were converted to arthroplasty and the latest radiographs just prior to the conversion to arthroplasty were evaluated. The other 2 knees underwent biological revision surgery and were evaluated at the last follow-up.

Survival Analysis

Overall, survival was 75% (95% CI, 45%-90%) at both 5 and 10 years (Figure 3). Age ($P = .079$), sex ($P = .525$), type of cartilage lesion ($P = .218$), size of cartilage lesion ($P = .108$), type of cover membrane ($P = .77$), and presence of a combined osteotomy ($P = .194$) did not affect survival of the operated knee. However, sterilization methods of meniscal allografts affected survival of the operated knee ($P = .0066$). Survival was 88% (95% CI, 59%-97%) in no sterilization at both 5 and 10 years, whereas both patients with meniscal

TABLE 3
Satisfaction With the Procedure at Final Follow-up^a

Question	Operative Success (n = 12)	Operative Failure (n = 6)
Compared with before each surgery, how would you rate your operated joint now?		
Better	12	4
About the same	0	1
Worse	0	1
What is your overall satisfaction level with the joint surgery?		
Satisfied	9	3
Neutral	2	1
Dissatisfied	1	2
If you could go back in time and make the decision again, would you choose to have your joint surgery?		
Yes	11	5
Uncertain	1	1
No	0	0
How would you rate the results of your joint surgery?		
Good/excellent	11	2
Fair	1	3
Poor	0	1

^aData are presented as number of patients.

allografts sterilized by BioCleanse were considered failures in the study period.

Among 32 individual ACI grafts, 11 (34%) failed during follow-up. The survival rate was 80% (95% CI, 61%-91%) at both 5 and 10 years. Finally, among 18 MAT grafts, 6 (33%) failed during follow-up. Survival was 88% (95% CI, 61%-97%) at both 5 and 10 years.

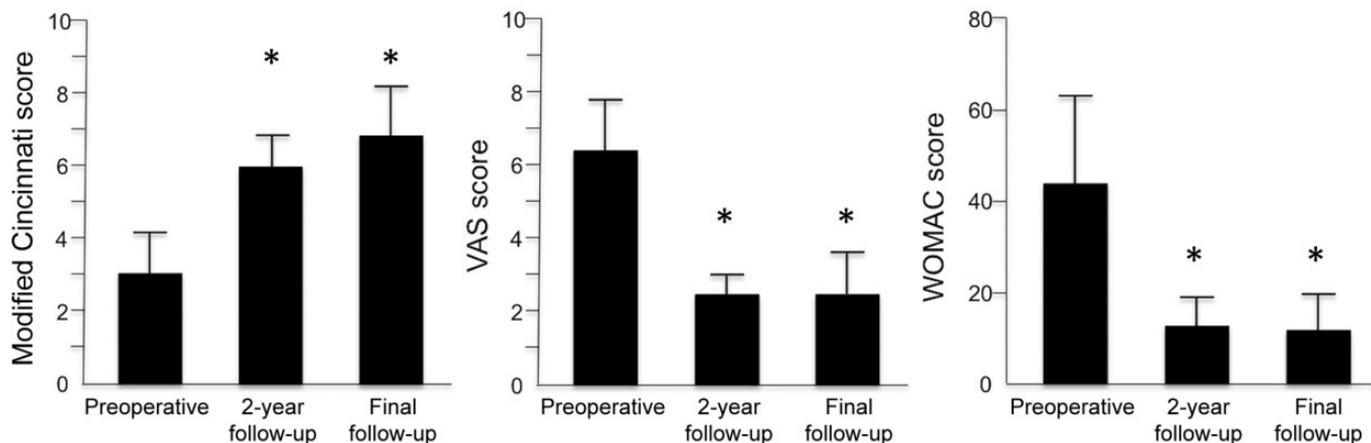


Figure 4. Mean scores for the modified Cincinnati Knee Rating Scale, VAS, and WOMAC preoperatively and at 2-year and final (mean, 7.9-year) follow-up for the 12 knees with retained MAT and ACI grafts. Error bars indicate SD. *There was a significant improvement from preoperative scores for all 3 functional measures ($P < .05$). ACI, autologous chondrocyte implantation; MAT, meniscal allograft transplantation; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

TABLE 4
Preoperative and Final Follow-up Clinical Outcomes^a

Rating System	Preoperative	Final Follow-up	P Value
Modified Cincinnati	3.1 ± 1.1	6.8 ± 1.4	.0024
VAS	6.4 ± 1.4	2.4 ± 1.2	.0024
WOMAC total	39.8 ± 18.9	13.3 ± 9.2	.0120
WOMAC–pain	9.6 ± 3.9	3.1 ± 2.6	.0047
WOMAC–stiffness	3.2 ± 2.1	1.5 ± 1.0	.0232
WOMAC–function	27 ± 15.1	8.8 ± 6.3	.0120
SF-36–PCS	38.4 ± 8.5	49 ± 5.2	.0037
SF-36–MCS	42.92 ± 7.9	49.6 ± 3.8	.0121

^aSuccessful knees, n = 12. Data are presented as mean ± SD. MCS, mental component score; PCS, physical component score; SF-36, Short Form–36; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Patient Satisfaction and Functional Outcome

All patients who did not have a failure reported that the knee improved after surgery. Almost all of these patients said they would choose to have this procedure again if they could go back in time and rated the results of the surgery as good to excellent. Two-thirds were satisfied with the procedure (Table 3).

Overall, for patients without failure, all functional scores improved significantly compared with preoperative scores (Table 4 and Figure 4). For patients with failure, WOMAC total and WOMAC function improved to a clinically and statistically significant level. Although the mental component score of the SF-36 improved statistically, it was not considered clinically significant. All other functional scores did not significantly improve (Table 5).

A subanalysis was performed to evaluate differences between specific groups. Differences were not significant based on age, sex, type of cartilage lesion, size of cartilage

TABLE 5
Preoperative and Final Follow-up (Prior to Failure)
Clinical Outcomes^a

Rating System	Preoperative	Final Follow-up	P Value
Modified Cincinnati	4.8 ± 1.5	4.7 ± 2.4	.5164
VAS	5.2 ± 1.0	4.5 ± 2.7	.9141
WOMAC total	41.8 ± 23.4	24.3 ± 20.4	.0464
WOMAC–pain	8.8 ± 6.7	5.5 ± 4.8	.666
WOMAC–stiffness	3.7 ± 1.5	3.3 ± 2.0	.7389
WOMAC–function	29.7 ± 18.3	15.5 ± 14.1	.0464
SF-36–PCS	42.8 ± 9.9	51.4 ± 3.8	.11
SF-36–MCS	43.4 ± 3.5	45.2 ± 3.9	.0464

^aOnly failures, n = 6. Data are presented as mean ± SD. MCS, mental component score; PCS, physical component score; SF-36, Short Form–36; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

lesion, type of cover membrane, or whether a combined osteotomy was used.

Radiographic Evaluation

Of 18 knees, 11 (including 6 successful knees and 5 failures) were available for radiographic evaluation at a mean (±SD) of 6.0 ± 2.2 years postoperatively (minimum, 2 years). The 5 failures included 3 knees undergoing arthroplasty and 2 knees undergoing biological revision surgery. Of 6 successful knees, OA grade did not increase in 5 knees. An increase of 1 point based on K-L grading was observed in 1 knee. There was no significant difference in the level of OA based on K-L grading before and after surgery (1.5 ± 0.8 preoperatively vs 1.7 ± 1.0 postoperatively, *P* = .31) (Table 6). Of the 5 failures, OA grade did not increase in 3. An increase of 1 point based on K-L grading was observed in 2 knees (Table 7).

Failures

A total of 6 knees were considered failures in this study period (Table 6). The mean time to failure after index surgery was 5.4 years (range, 0.4–14 years). Four patients (patients 1, 3, 4, and 6) were converted to arthroplasty due to progression of disease at a mean 7.8 ± 5.4 years after the index surgery. All except patient 6 had returned to all activities without significant complaints before arthroplasty. Patient 6 was the only patient who did not improve due to the index surgery. The other 2 patients (patients 2 and 5) underwent biological revision surgery after 5 and 17 months, respectively. Patient 2 injured his knee after revision ACI and underwent ACI with MAT 7 years after the index surgery; patient 5 underwent revision ACI with MAT. Patients 2 and 5 were involved in normal activities without any restrictions at 15 and 6 years later, respectively.

Subsequent Surgical Procedures

Overall, 12 of 18 knees required subsequent surgical procedures, including arthroscopic procedures in 10 knees and

TABLE 6
Preoperative and Postoperative
Kellgren-Lawrence Grading^a

	Successful Knees (n = 6)
Preoperative K-L grade	1.5 ± 0.8
Postoperative K-L grade	1.7 ± 1.0
<i>P</i> value, pre- vs postoperative	<i>P</i> = .31
Time to evaluation, y	5.9 ± 1.0
Increase in K-L grade, n	
+0	5
+1	1

^aMinimum 2 years postoperative (n = 6). Data are presented as mean ± SD unless otherwise indicated. K-L, Kellgren-Lawrence.

both arthroscopic and open in 2. Of 12 knees with retained grafts, 7 knees (58%) required subsequent surgical procedures due to arthrofibrosis in 5 knees, followed by ACI graft hypertrophy in 4 knees, MAT graft partial tears in 2 knees, painful hardware in 2 knees, compartment syndrome in 1 knee, and a new cartilage lesion in 1 knee. A total of 5 of 12 knees did not require subsequent surgical procedures. Of 6 failures, 5 knees required subsequent surgical procedures prior to being considered a failure resulting from MAT graft complications in 5 knees with 4 partial meniscal tears and 1 displaced meniscus, treatment of a new cartilage lesion in 3 knees, debridement for ACI graft partial delamination in 2 knees, lysis of adhesion in 1 knee, and removal of a loose body in 1 knee.

DISCUSSION

In this retrospective series of prospectively collected data, we analyzed data from 17 symptomatic patients (18 knees) who underwent ACI combined with MAT for concomitant cartilage lesions and meniscal deficiency. Our results showed a 75% survival rate at both 5 and 10 years postoperatively. Patients with retained grafts had significant and sustained improvement of all clinical outcomes, including the modified Cincinnati score, VAS, WOMAC, and SF-36 at a mean 7.9 years postoperatively. Although the failure rate was 33%, 4 of 6 failed patients could maintain their biological knee over 2 years (up to 14 years) with some functional scores being improved. Moreover, all patients with retained grafts rated their operated knee as better than before surgery, almost all answered that they would choose to have the same joint surgery, rated their operated knee as good or excellent, and 9 of 12 patients reported being satisfied with the procedure. It was unexpected that the overall satisfaction level was not high, given that almost all patients rated their operated knee as good or excellent. This observed discrepancy could be explained by the patient's high expectations before surgery and subsequent procedures needed after surgery. Sufficient discussion between patients and surgeons preoperatively is thus necessary to set realistic expectations and restrictions to avoid MAT failure, as this is a salvage or bridging procedure before

TABLE 7
Outcome Assessments in Failures^a

Patient	Age, y/Sex	Cartilage Lesion/Size, cm ²	MAT Location/ Graft Type	Unipolar or Bipolar	Concurrent Surgery	K-L Grade:		Revision or Arthroplasty
						Preoperative/Before Failure	Failure Reason	
1	46/M	LFC, LTP/15.3	Lateral/cryopreserved	Bi	No	N/A	Progression of disease	TKA at 14 y
2	30/F	LFC, LTP/8.7	Lateral/fresh-frozen	Bi	No	1/2	Delamination of ACI graft	Revision ACI at 5 mo
3	36/F	MFC/5	Medial/fresh-frozen	Uni	No	2/3	Progression of disease	UKA at 10 y
4	36/F	LFC, LTP/6.3	Lateral/cryopreserved	Bi	No	2/2	Progression of disease	TKA at 4.7 y
5	48/M	LFC, LTP, trochlea/16	Lateral/fresh-frozen	Bi	DFO	2/2	ACI and MAT graft failure	Revision ACI and MAT at 17 mo
6	35/F	MFC, LFC, trochlea/10	Lateral/fresh-frozen	Uni	DFO, TTO	2/2	Progression of disease	Bicompartment arthroplasty at 2.2 y

^aACI, autologous chondrocyte implantation; DFO, distal femoral osteotomy; F, female; K-L, Kellgren-Lawrence; LFC, lateral femoral condyle; LTP, lateral tibial plateau; M, male; MAT, meniscal allograft transplantation; MFC, medial femoral condyle; N/A, not available; TKA, total knee arthroplasty; TTO, tibial tubercle osteotomy; UKA, unicompartment knee arthroplasty.

arthroplasty. Hard pivoting sports/manual labor that involve repeated lifting and kneeling are discouraged to reduce the risk of reinjury.

After the first report of ACI by Brittberg et al⁵ in 1994, several studies have reported successful clinical outcomes in long-term follow-up. Minas et al³⁸ previously reported that ACI provided durable outcomes, with 71% survival at 10 years and improved function in 75% of patients with symptom cartilage defects of the knee a minimum of 10 years after surgery. Likewise, after the first performance of MAT by Milachowski et al in 1984 and the first report in 1989,³⁵ MAT has become a well-recognized procedure for treating pain and swelling in meniscus-deficient knee compartments.¹⁶ Recently, Kazi et al²⁸ reported good survival a mean 12.4 years prior to total knee arthroplasty in those requiring conversion, with 71% of allografts remaining in situ a mean 15 years postsurgery. Although each procedure alone has resulted in successful clinical outcomes, little is known about the mid- to long-term outcomes after concomitant surgery. To our knowledge, this is the first study to report the mid- to long-term outcomes of combined ACI with MAT. Our results showed that the survival rates at 5 and 10 years postoperatively were similar to those after each procedure alone.

Short- to mid-term clinical outcomes of ACI combined with MAT have been reported.^{2,18,46} These studies reported significant improvement of knee symptom and function after a mean 2- to 4.5-year follow-up. When compared with previous studies, we had a longer follow-up period, a higher rate of bipolar lesions, and larger cartilage lesions in patients. The previously reported failure rates ranged from 0% to 38%. Although the mean time to failure in our study was 5.4 years postoperatively, which was longer than the mean follow-up periods in previous studies, our failure rate (33%) was comparable to those reported in previous studies. The risk of failure remains unclear. Bhosale et al² reported data for 8 knees, including

6 knees with bipolar lesions after combined ACI with MAT with a mean 3.2-year follow-up. Their failure rate was similar to that in the present study. Therefore, bipolar lesions could be a risk factor for failure of this procedure. Although a subanalysis of survival in our study did not reach statistical difference between the unipolar and bipolar groups, further investigation with a larger sample size will allow more accurate interpretation.

MAT is a well-recognized procedure for treatment of pain and swelling in a meniscus-deficient knee.^{16,48} However, there has been very little research on human participants to assess its potential protective effects on articular cartilage, and controversy still exists regarding the chondroprotective effects of MAT. Our radiographic analysis showed that no K-L grade progression was observed in 73%, and there was no significant increase in K-L grade from before to after surgery. The results of our study were consistent with those of previous studies wherein only MAT was performed due to a lack of previous radiographic studies in the same series. In those studies, radiographic analyses based on K-L grade revealed no progression in OA grade in 50% to 78% of patients at a mean 2.6 to 8.8 years postoperatively.^{11,24,52} Moreover, Verdonk et al⁵⁰ reported that MRI analysis showed no progression of cartilage degeneration in 6 of 17 knees. Our results suggest that ACI with MAT has possible chondroprotective effects. However, further investigations using advanced imaging or second-look arthroscopy with larger sample sizes will be required for accurate evaluations and confirmation of this finding.

Our study included the 2 most commonly used types of menisci: fresh frozen (n = 15) and cryopreserved (n = 3). A very important difference between these is that the cryopreserved meniscus can maintain the viability of the cell.²¹ In animal studies, however, Fabbriani et al¹⁷ reported that there were no significant differences between fresh-frozen and cryopreserved grafts, and that even if cryopreservation enables maintenance of partial

cell viability in the tissue, this does not seem to improve the morphological and biochemical characteristics of the graft. In our study, 2 knees transplanted with cryopreserved grafts resulted in failure due to progression of disease at 4.7 and 14 years postoperatively. Although our study did not intend to compare these 2 grafts, it is worth investigating whether there is a difference in terms of protective effects on articular cartilage between the graft types with long-term follow-up. Regarding sterilization of meniscal allograft, subanalysis revealed that no poststerilization was better compared with chemical sterilization with BioCleanse. However, it should be noted that our study included only 2 meniscal allografts sterilized by BioCleanse and included both fresh-frozen and cryopreserved allografts. Therefore, this observation may have been influenced by graft type as well. A further study with a larger cohort is warranted to conclude the superiority of graft sterilization.

There were several limitations in our study. First, our study did not have a control group. However, it was difficult to set a control group in this limited treatment group. Second, our study had only 1 medial compartment pathology. This possibly introduced a selection bias based on the surgeon's decision, which addressed lateral compartment pathology more aggressively using MAT. We believe, however, that it was clinically an appropriate decision because the lateral compartment was highly vulnerable to deterioration after meniscal deficiency due to its unique anatomical structure of the lateral compartment having the round femoral condyle on the convex tibial plateau.^{12,42} In addition, a previous study showed no differences in clinical outcomes between medial and lateral meniscus allografts.¹⁸ Therefore, we believe that our results could represent outcomes of medial MAT as well. Thirdly, although we did not find any difference on subgroup analysis, the limited number of patients in our study may have hindered the detection of this difference. A larger patient cohort will be necessary for more rigorous subanalysis. Finally, we could not obtain radiographs at a minimum of 2 years' follow-up from all patients, despite our efforts.

In conclusion, our study showed that combined ACI with MAT for treating patients with both cartilage defects and meniscal deficiency had a 33% failure rate within a mean 7.9-year follow-up. For the remaining patients, however, the combined procedure provided successful clinical outcomes, based on a 75% survival rate in the mid- to long-term follow-up. This procedure allowed patients to maintain their biological knees, could delay or prevent rapid OA degeneration, and may be recognized as a bridge procedure before artificial knee replacement. However, it should be noted that 58% of patients with retained grafts required subsequent surgical procedures, although most were performed arthroscopically. Therefore, careful discussion between the patient and surgeon is necessary to manage patient expectations before surgery.

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