Meniscal Allograft Transplantation Is an Effective Treatment in Patients Older Than 50 Years but Yields Inferior Results Compared With Younger Patients: A Case-Control Study

Prof. Stefano Zaffagnini, M.D., Alberto Grassi, M.D., Luca Macchiarola, M.D., Federico Stefanelli, M.D., Vito Coco, M.D., Prof. Maurilio Marcacci, M.D., Luca Andriolo, M.D., and Giuseppe Filardo, M.D., Ph.D.

Purpose: To evaluate the influence of age on midterm clinical outcomes and failures of meniscal allograft transplantation (MAT), aiming at investigating the efficacy of MAT in patients older than 50 years. **Methods:** In this case-control study, data on patients older than 50 years (older MAT [O-MAT] group) with at least 5 years of follow-up and a matched-pair group of patients younger than 30 years of age (younger MAT [Y-MAT] group) were extracted from a database of MAT procedures, performed with arthroscopic implantation of fresh-frozen meniscal allograft without bone plugs. **Results:** A matched-pair comparative analysis of midterm results and survival between 26 O-MAT patients and 26 Y-MAT patients was performed at a mean follow-up of 7.3 ± 2.2 years. All the clinical scores significantly improved from the baseline values in both the O-MAT and Y-MAT groups although with significantly lower scores in the O-MAT group. Two-thirds of O-MAT patients were able to return to a recreational level of sports activity. Only 2 patients in the O-MAT group underwent knee replacement, but the overall failure rate, also considering a clinical criterion, was 31% in the O-MAT group and 15% in the Y-MAT group ($P = .3244$). The mean survival time free from replacement or graft removal was 11.6 years in the O-MAT group and 12.3 years in the Y-MAT group ($P = .691$). **Conclusions:** MAT is able to provide symptom relief and functional improvement at midterm follow-up in patients older than 50 years although with inferior results and a higher failure rate compared with those younger than 30 years. MAT can be considered a viable option to treat patients older than 50 years. **Level of Evidence:** Level III, case-control study.

See commentary on page 2459

Meniscal allograft transplantation (MAT) can no longer be considered an experimental procedure[1]; it represents an established option, with a significant number of procedures performed every year,[2] to provide relief of compartmental pain in patients who have undergone meniscectomy. Because symptoms are thought to be caused by mechanical overload, the replacement of the damaged meniscus aims at protecting the knee from overload and from its detrimental consequences. In this light, the efficacy of MAT is gaining increasing evidence. In fact, good to excellent results have been shown in the general population, with function and pain improvement reported from short- to long-term follow-up studies.[3-5] Recently, a

From II Orthopaedic and Traumatologic Clinic (S.Z., A.G., L.M., F.S., V.C., L.A.) and Applied and Translational Research Center (G.F.), IRCCS Istituto Ortopedico Rizzoli, Bologna; and Department of Biomedical Sciences, Humanitas University, Humanitas Clinical and Research Center (M.M.), Milan, Italy.

Stefano Zaffagnini and Alberto Grassi equally contributed to this article.

The authors report the following potential conflicts of interest or sources of funding: S.Z. receives grant support from I+ srl, Springer, Fidia Farmaceutici Spa, CartiHeal (2009), IGEA Clinical Biophysics, Biomet, and Kensey Nash. M.M. receives grant support from Finceramica Faenza Spa, Fidia Farmaceutici Spa, CartiHeal (2009), IGEA Clinical Biophysics, Biomet, and Kensey Nash. G.F. receives support from Finceramica Faenza Spa, Fidia Farmaceutici Spa, CartiHeal (2009), EON Medica SRL, IGEA Clinical Biophysics, Biomet, and Kensey Nash. Full ICMJE author disclosure forms are available for this article online, as supplementary material.

Received August 29, 2018; accepted March 21, 2019.

Address correspondence to Luca Andriolo, M.D., II Orthopaedic and Traumatologic Clinic, IRCCS Istituto Ortopedico Rizzoli, Via Di Barbiano, 1/10-40136 Bologna, Italy. E-mail: lucas.andriolo@gmail.com

0749-8063/181054/$36.00
https://doi.org/10.1016/j.arthro.2019.03.048

significant improvement was confirmed compared with conservative treatment with physiotherapy.[6] Moreover, there is some evidence supporting the hypothesis that MAT may even reduce osteoarthritis (OA) progression.[7] To this regard, some controversial studies have pointed out that the heterogeneity of results may be a result of the treatment indications because the results of MAT also depend on the type of patient treated.[8]

The ideal candidate for MAT is a young patient (usually up to 50 years old)[9] with a history of total or subtotal meniscectomy in an otherwise stable and aligned knee, complaining of pain at the corresponding joint compartment and not responding to conservative treatment.[10] Moreover, caution is recommended if performing MAT in knees with moderate to severe radiographic OA (i.e., Kellgren-Lawrence grade $\geq$ 3) because of the higher reoperation rate and lower graft survivorship.[10] However, patients in clinical practice only seldom meet the criteria of the ideal candidate. In particular, the portion of the aging population remaining active is constantly increasing,[11] and clinicians frequently deal with patients older than 50 years, often presenting with some degree of OA, who wish to continue sports involvement and thus ask for non-prosthetic treatments. However, although a few series have investigated the effects of MAT in older patients,[12] clinical and subjective results in a homogeneous group of patients older than 50 years have never been reported. Therefore, there is a need for more solid data and evidence on the potential and limitations of MAT to consider when deciding the indications for MAT in such patients.

The purpose of this study was therefore to evaluate the influence of age on midterm clinical outcomes and failures of MAT, aiming at investigating the hypothesis that MAT would be effective in patients older than 50 years.

Methods

This case-control study is based on the Rizzoli Orthopaedic Institute's database of 175 consecutive MAT procedures performed between June 2006 and March 2013. Data on patients older than 50 years with at least 5 years of follow-up were extracted to form the treatment group (older MAT [O-MAT] group) based on an a priori sample size calculation. Chondral damage and concomitant procedures were not considered exclusion criteria. From the same database, data on a group of patients younger than 30 years at surgery, consecutively matched for follow-up, side of MAT, and sex, were extracted to form the control group (younger MAT [Y-MAT] group). The age cutoff values were selected to maximize the possible differences between the 2 groups. A matched-pair comparative analysis of midterm results and survival between 26 O-MAT patients and 26 Y-MAT patients was performed at a mean follow-up of 7.3 $\pm$ 2.2 years (minimum, 5 years).

The indications for MAT in both groups were unicompartmental pain due to a previous total or subtotal meniscectomy, grade I to III OA according to the Kellgren-Lawrence radiographic evaluation, no signs of contralateral-compartment and patellofemoral-compartment damage, and less than 5° of axial malalignment. In the case of greater than 5° of malalignment, a corrective osteotomy was performed to achieve neutral alignment. In the case of anteroposterior knee laxity and patient-reported subjective instability, a concomitant anterior cruciate ligament (ACL) reconstruction was performed. In patients with focal Outerbridge grade III or IV chondral lesions smaller than 2 cm^2, microfractures were performed, whereas in cases of larger focal Outerbridge grade III or IV lesions, an osteochondral biomimetic scaffold was implanted.[13] In the case of diffuse chondral damage or kissing lesions, no cartilage procedures were performed. All patients undergoing MAT were adequately counseled regarding the risks and benefits of the procedure and surgical alternatives, and in patients refusing surgery, conservative treatment was proposed as an alternative; in particular, in active patients older than 50 years who refused metal resurfacing, MAT was suggested as a salvage procedure to restore the knee anatomy and biomechanics. No patient refused MAT for ethical or religious reasons.

Surgical Technique

The surgical procedures were performed by 2 senior surgeons (S.Z. and M.M.) with experience treating knee conditions. Fresh-frozen (−80°) nonirradiated and non−antigen-matched allografts were used. The age criterion for donors was 15 to 35 years. Anthropometric parameters were used preoperatively to establish the correct size of the graft.[14] The transplantation was performed arthroscopically using a single-tunnel technique[15] or double-tunnel technique[16] depending on graft size mismatch and without bone plugs. Arthroscopically, the remnant of the native meniscus was removed up to the meniscal-capsular zone. A tibial tunnel directed to the posterior horn insertion was prepared to secure the suture corresponding to the posterior meniscal horn to the anterior tibial cortex. The previously prepared graft was inserted into the joint after a shuttle suture was passed through the posterior tunnel.[15] When the shuttle suture was pulled, the graft was located correctly and fixed to the capsule with all-inside stitches (No. 0 nonabsorbable Ultrabraid wire and poly-L-lactide bioabsorbable implants; Smith & Nephew, Andover, MA).

If the graft was determined to be the correct size, a second tibial tunnel, directed to the anterior horn attachment, was created, and the suture secured to the anterior horn graft was passed through the second tibial tunnel as performed for the posterior horn. Finally, the anterior horn of the transplanted meniscus was fixed to the remnant of the anterior horn of the native meniscus by an outside-in standard suturing technique using No. 2-0 PDS II (Ethicon, Somerville, MA). If the graft was not the correct size, creation of the anterior tibial tunnel was not performed. Rather, an additional arthroscopic portal was created at the same level as the end of the anterior horn of the graft, and the suture placed in the anterior horn was retrieved. Finally, the same suture was used to perform a stitch to fix the graft to the capsule using a free needle. The type of surgical procedure and the number of tunnels did not differ between the O-MAT and Y-MAT groups (Table 1). After checking for graft stability, the surgeon performed the required concomitant procedures. In the case of varus deformity, a lateral closing-wedge high tibial osteotomy fixed with a Krackow staple was performed during the same surgical stage. Valgus deformity was treated with a medial closing-wedge distal femoral osteotomy fixed with a blade plate. When needed, ACL reconstruction was performed with hamstrings using a single bundle plus a lateral-plasty technique during the same surgical stage.[17] Cartilage procedures, open or arthroscopic, were also performed after MAT. At this point, the skin was closed and a compressive bandage and full-extension brace were placed.

Table 1. Comparison of Baseline Characteristics and Scores Between O-MAT and Y-MAT Groups

	O-MAT Group (n = 26)	Y-MAT Group (n = 26)	*P* Value
Demographic characteristics			
Age at surgery, yr	55.3 ± 4.7	24.1 ± 4.4	<.0001*
Final follow-up, yr	7.1 ± 2.1	7.5 ± 2.3	.0706
Age at final follow-up, yr	62.4 ± 4.8	31.6 ± 5.0	<.0001*
Sex: male/female	18 (69)/8 (31)	23 (88)/3 (12)	.1744
BMI at surgery	25.1 ± 3.8	23.7 ± 2.0	.0683
Time from first meniscectomy, yr	16.1 ± 10.7	5.1 ± 3.5	<.0001*
Surgical characteristics			
Knee: right/left	15 (58)/11 (42)	13 (50)/13 (50)	.7809
Meniscus: medial/lateral	17 (65)/9 (35)	15 (58)/11 (42)	.7756
Concomitant procedures: yes/no	14 (54)/12 (46)	13 (50)/13 (50)	>.9999
No. of tunnels: 1 tunnel/2 tunnels	16 (62)/10 (38)	18 (69)/8 (31)	.7707
Clinical data			
VAS score for pain (0-100)	61.5 ± 28.2	58.0 ± 24.2	.4572
Lysholm score (0-100)	53.6 ± 17.5	55.9 ± 16.3	.5413
Tegner score (0-10)	2 (1-4)	3 (2-4)	.2299

NOTE. Data are presented as mean ± standard deviation, number of patients (percentage), or median (interquartile range).

BMI, body mass index; O-MAT, meniscal allograft transplantation in patients older than 50 years; VAS, visual analog scale; Y-MAT, meniscal allograft transplantation in patients younger than 30 years.

Rehabilitation

The postoperative rehabilitation protocol started with a 2-week period of immobilization and no weight bearing, followed by toe-touch weight bearing for the following 2 weeks, restriction of range of motion (0°-90° during weeks 3-4 and then free range of motion), isometric exercises, and closed-chain strengthening. At week 4 postoperatively, partial weight bearing was allowed, and at week 6 postoperatively, progression to full weight bearing was started; patients were also allowed to fully flex the knee. Sport-specific exercises were started after 3 months; a return to noncontact activities was not allowed until the fourth month. Patients were advised not to resume high-demand sports activities before 8 months postoperatively. Owing to the cautious nature of the rehabilitation protocol regarding knee mobilization and weight bearing, no substantial differences were present in the case of concomitant ACL reconstruction, osteotomy, or cartilage procedures.

Patient Evaluation

Demographic details were extracted from the patient's medical chart. Time from the first meniscectomy (in years) and the details of the surgical intervention and concomitant procedures were noted.

The preoperative evaluation was performed with the Lysholm score, the Tegner activity scale, and a visual analog scale for pain from 0 to 100. The final follow-up evaluation was performed using the same scores obtained preoperatively; moreover, a global satisfaction scale from 0 to 100 was administered. In addition, patients were asked whether they would repeat the procedure if needed. Details regarding sports practiced and the level of sport (competitive or recreational) before symptom onset and at final follow-up were registered, as was the time to return to sports activity. All procedures performed during the follow-up period were recorded. Failure was considered in the case of a revision procedure related to the initial MAT, such as total knee arthroplasty (TKA), unicompartmental knee arthroplasty (UKA), or meniscectomy owing to a graft tear or revision MAT, and in the case of a poor Lysholm score (<65 points).[18] In the case of failure as a result of a revision procedure, clinical scores were not administered and the time to revision was noted and used for survival analysis. A poor Lysholm score was not considered for the survival analysis because it was impossible to know the time of failure given the study's retrospective design. This study has been approved by the Local Ethical Committee of the Rizzoli Orthopaedic Institute, Bologna, Italy (Protocol No. 0021258).

Statistical Analysis

An a priori sample size calculation was performed with a power of 0.80 and an error rate of 5%, considering a difference of 8 ± 10 points in the Lysholm score between the 2 groups. On the basis of this calculation, we included 26 patients in each group.

Statistical analysis was performed with the MedCalc program (MedCalc Software, Oostende, Belgium). All continuous parametric variables were expressed as mean ± standard deviation, Tegner activity scale scores were expressed as median and interquartile range, and categorical variables were expressed as number and percentage. Comparison between preoperative and final follow-up values was performed with the paired-samples *t* test for continuous variables, whereas differences in Tegner activity scale scores were evaluated with the Wilcoxon test. Comparison between the 2 groups was performed with the paired-samples *t* test for continuous variables, whereas between-group differences in Tegner scores were analyzed with the Wilcoxon test. In the case of missing values for clinical scores owing to failure, the preoperative values were used to avoid overestimation of the clinical status. Differences in categorical variables were analyzed with the χ^2 or McNemar test. Kaplan-Meier curves were performed for the total series and for each subgroup using surgical failure data. The endpoints were MAT-related reoperations or MAT failures. The mean estimated survival times with 95% confidence intervals were also calculated from the Kaplan-Meier curves. Because of the limited numbers of patients in the O-MAT and Y-MAT groups, the log-rank test to assess differences in survival times and rates was not applied. Differences were considered significant at $P < .05$.

Results

The mean age at surgery of the 26 patients in the O-MAT group was 55.3 ± 4.7 years, whereas in the Y-MAT group, it was 24.1 ± 4.3 years ($P < .00001$). All the other demographic characteristics, surgical factors, and baseline clinical scores were comparable between the 2 groups, except time since first meniscectomy and MAT ($P < .00001$) (Table 1). The medial meniscus and lateral meniscus were involved in 17 and 9 cases, respectively, in the O-MAT group and 15 and 11 cases, respectively, in the Y-MAT group. In addition to medial or lateral meniscectomy, 27% and 54% of patients in the O-MAT and Y-MAT groups, respectively, had undergone a further procedure before MAT, mostly contralateral meniscectomy or ACL reconstruction ($P = .2513$) (Table 2).

Table 2. Previous and Concurrent Procedures in O-MAT and Y-MAT Groups

	O-MAT Group (n = 26)	Y-MAT Group (n = 26)	*P* Value
Previous procedures			.2513
1 procedure	19 (73)	12 (46)	
≥2 procedures	7 (27)	14 (54)	
Lateral meniscectomy	12	15	
Medial meniscectomy	18	19	
HTO	1	0	
ACL reconstruction	3	16	
PCL reconstruction	0	1	
Arthroscopic debridement	3	5	
ACI	0	1	
Concurrent procedure			.8476
Isolated MAT	12 (46)	13 (50)	
Concomitant procedures	14 (54)	13 (50)	
HTO	8	3	
DFO	1	1	
ACL reconstruction	4	5	
PCL reconstruction	0	1	
MCL reconstruction	1	0	
Osteochondral scaffold	0	3	
Microfracture	0	1	

NOTE. Data are presented as number of patients (percentage) or number of patients.

ACI, autologous chondrocyte implantation; ACL, anterior cruciate ligament; DFO, distal femoral osteotomy; HTO, high tibial osteotomy; MAT, meniscal allograft transplantation; MCL, medial collateral ligament; O-MAT, meniscal allograft transplantation in patients older than 50 years; PCL, posterior cruciate ligament; Y-MAT, meniscal allograft transplantation in patients younger than 30 years.

Clinical Scores

At a mean follow-up of 7.3 ± 2.2 years, all the clinical scores were significantly improved from the baseline values in both the O-MAT and Y-MAT groups (Table 3). However, the O-MAT group had a significantly lower Lysholm score (9.2 points), visual analog scale score, and Tegner score (2 points) (Fig 1, Table 3). Moreover, a significant difference between the 2 groups was found regarding the number of patients with excellent, good, fair, and poor Lysholm scores ($P = .0221$). In fact, 4 patients (18%) in the O-MAT group had poor Lysholm scores; these cases were therefore considered failures. Only 1 patient in the Y-MAT group (4%) had a poor Lysholm score (Fig 2). The surgical technique (number of tunnels) did not correlate significantly with the Lysholm scores at follow-up. Excluding patients with MAT removal, we found that only 36% of O-MAT patients were pain free compared with 74% in the Y-MAT group ($P = .0169$), but patient satisfaction was similar between groups (Table 3).

Sports Activity

At the final follow-up, 16 patients (62%) in the O-MAT group were able to practice sports, mostly noncontact activities such as jogging and cycling. In contrast, in the Y-MAT group, the 17 patients (65%)

Table 3. Comparison of Final Follow-Up Scores Between O-MAT and Y-MAT Groups

	O-MAT Group (n = 26)	Y-MAT Group (n = 26)	Difference	*P* Value
VAS score for pain (0-100)	31.2 ± 29.0*	16.2 ± 30.1*	+15.0 (SE, 8.2)	.0285*
Lysholm score (0-100)†	78.0 ± 17.2*	87.2 ± 13.7*	−9.2 (SE, 4.3)	.0402*
Excellent (91-100)	9 (41)	15 (65)		.0336*
Good (84-90)	1 (5)	4 (18)		
Fair (65-83)	8 (36)	3 (13)		
Poor (0-64)	4 (18)	1 (4)		
Tegner score (0-10)	3 (3-6)*	5 (4-7)*	−2	.0196*
Satisfaction (0-100)	78.1 ± 25.8	90.4 ± 15.8	−12.3	.0672
Reoperation	7 (27)	6 (24)	+1 (3)	.1000
Failure	8 (31)	4 (15)	+4 (16)	.3234

NOTE. Data are presented as mean ± standard deviation, number of patients (percentage), or median (interquartile range) unless otherwise indicated.

O-MAT, meniscal allograft transplantation in patients older than 50 years; SE, standard error; VAS, visual analog scale; Y-MAT, meniscal allograft transplantation in patients younger than 30 years.

*Significant improvement from baseline ($P < .0001$).

†For grading of the Lysholm score, only the patients who did not experience failure are accounted for (O-MAT group, n = 22; Y-MAT group, n = 23).

who returned to sports were involved in strenuous activities, especially soccer at both the recreational and professional levels. The mean time to return to sports was 8.1 ± 4.1 months in the O-MAT group and 9.3 ± 4.2 months in the Y-MAT group. The principal motivation for abandoning sports in both groups was "personal reasons" (Table 4).

Reoperations and Failures

In the O-MAT group, 7 patients (27%) underwent a subsequent surgical procedure during the follow-up period: 1 UKA and 1 TKA (8%), 1 graft removal and 1 graft meniscectomy (8%), 2 hardware removals (8%), and 1 arthroscopic arthrolysis (4%). However, only UKA, TKA, graft removal, and meniscectomy (15%) were considered failures. The overall failure rate in the O-MAT group, which includes the 4 patients with poor Lysholm scores (including 1 with hardware removal), was 31%.

In the Y-MAT group, 6 patients (24%) underwent a subsequent procedure: 3 graft meniscectomies (12%), 2 hardware removals (8%), 1 arthroscopic debridement not related to MAT (4%), and 1 previously planned autologous chondrocyte implantation (4%). Because only meniscectomies were considered failures and only 1 patient (who underwent hardware removal) had a poor Lysholm score, the overall failure rate in the Y-MAT group was 15%.

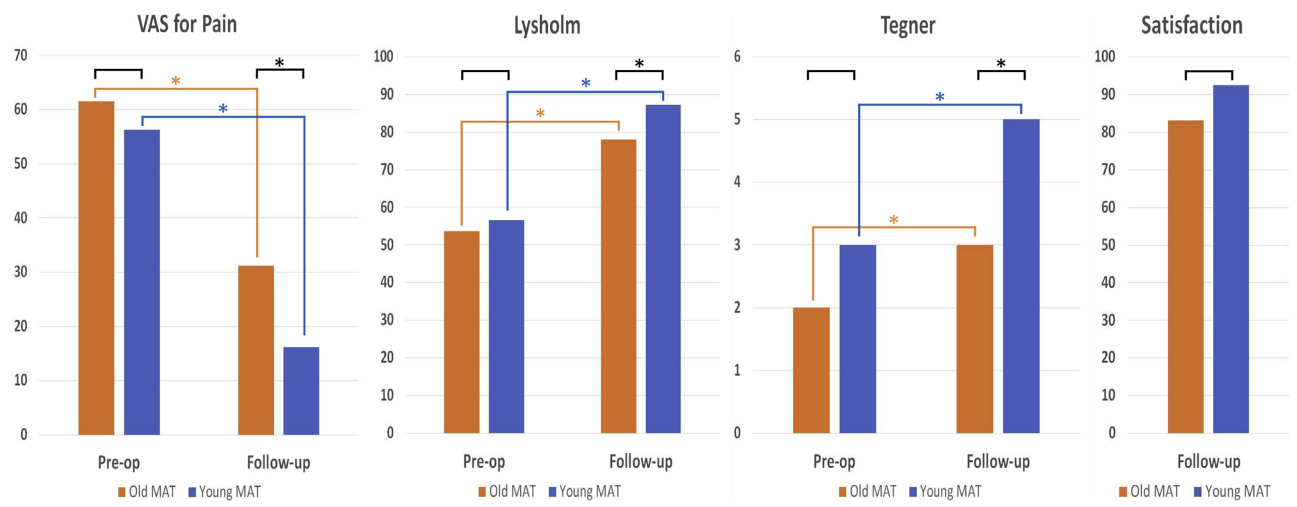

Fig 1. Preoperative (Pre-op) and follow-up clinical scores (visual analog scale [VAS] for pain, Lysholm, Tegner activity, and satisfaction) in older meniscal allograft transplantation (MAT) and younger MAT groups. Asterisks indicate statistically significant differences ($P < .05$). Comparison between preoperative and final follow-up values was performed with the paired-samples *t* test in the case of continuous variables, whereas differences in Tegner activity scale scores were evaluated with the Wilcoxon test. Comparison between the 2 groups was performed with the paired-samples *t* test for continuous variables, whereas between-group differences in Tegner scores were analyzed with the Wilcoxon test.

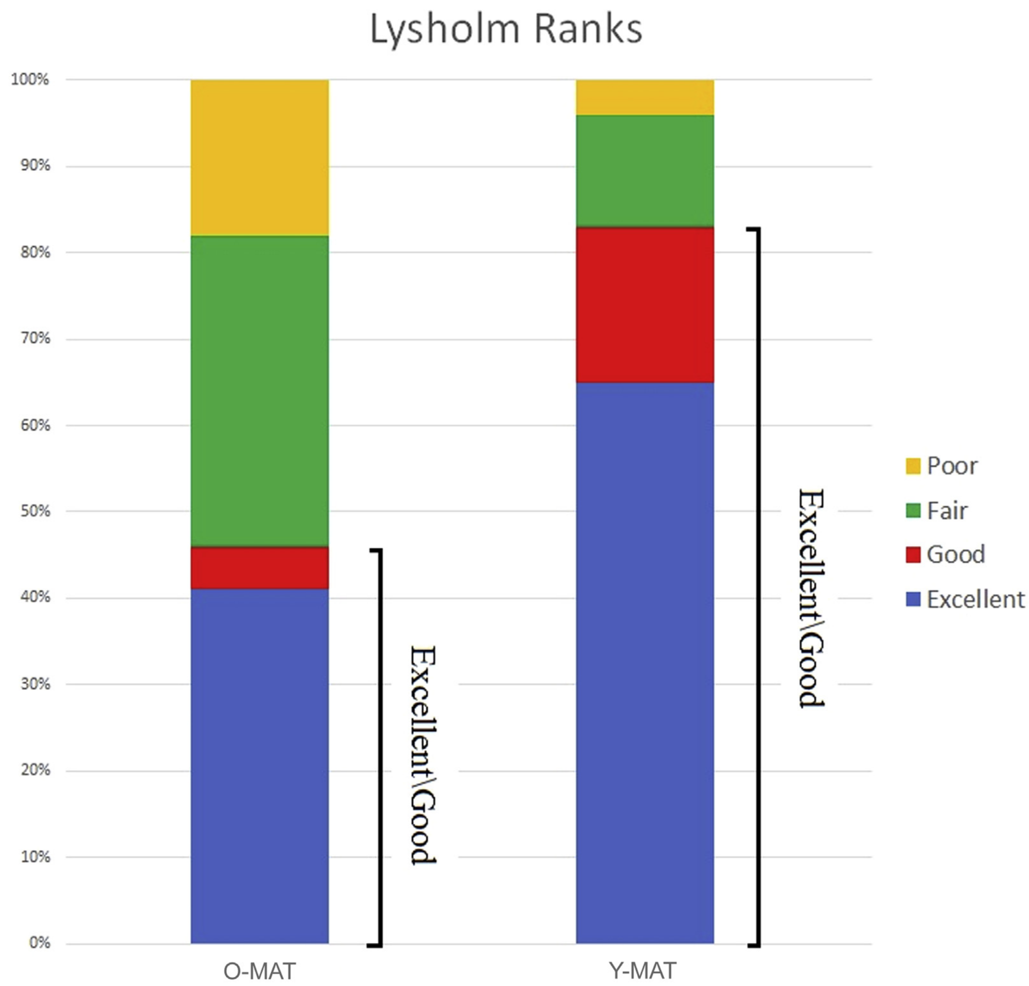

Fig 2. Lysholm score ranks in older meniscal allograft transplantation (O-MAT) and younger meniscal allograft transplantation (Y-MAT) groups.

Survival Analysis

The overall failure rate considering knee replacement or graft removal at final follow-up was 13%, and the mean estimated survival time predicted from analysis of the Kaplan-Meier curve was 12.0 years (Fig 3A). When the 2 subgroups were evaluated separately (Fig 3B), the mean estimated survival time free from replacement or graft removal was 11.6 years in the O-MAT group and 12.3 years in the Y-MAT group ($P = .691$, Table 5).

Discussion

The most important finding of this study is that MAT is able to provide symptom relief and functional improvement in active patients older than 50 years although with results inferior to those younger than 30 years. MAT is increasingly recognized as a valid treatment option, and interest in extending the indications for MAT is growing as well. The presence of concomitant cartilage damage is still a controversial aspect. Some studies have suggested that advanced cartilage damage is associated with unsuccessful MAT, with poor clinical improvement, a high reoperation rate, and a high failure rate.[19] Nevertheless, the occurrence of patients needing MAT and already showing cartilage degeneration is extremely frequent, and recent studies addressing this issue have reported satisfactory results even for these types of patients.[20-22] Kempshall et al.[20] compared the short-term results of MAT in young patients with or without advanced chondral damage and reported a higher failure rate in patients with advanced chondral damage but an overall clinical benefit similar to the ideal patient group. Similarly, Mahmoud et al.[21] reported an improvement at midterm follow-up in patients with a mean age of 35 years with cartilage lesions, although the survival rate was lower with respect to the control group. Saltzman et al.[22] reported no statistically significant differences in clinical scores, complications, and failures between young patients with chondral lesions treated concurrently with cartilage restoration procedures and those without chondral lesions at 4 years of follow-up. In addition, other authors have suggested that concurrent cartilage repair and MAT could successfully treat a meniscus-deficient knee with severe articular cartilage

Table 4. Comparison of Sports Activity Between O-MAT and Y-MAT Groups

	O-MAT Group (n = 26)	Y-MAT Group (n = 26)
Return to sports activity	16 (62)	17 (65)
Professional level	0 (0)	5 (19)
Recreational level	16 (100)	12 (81)
Sport		
Soccer	0	8
Basketball	0	1
Volleyball	0	1
Tennis	0	1
Jogging or running	3	3
Skiing	3	0
Cycling	4	2
Swimming	3	1
Hunting	2	0
Dancing	1	0
Time to return to sports, mo	8.1 ± 4.1	9.3 ± 4.2
Abandoned sports activity	10 (38)	9 (35)
Knee pain	4	1
Other health problems	0	1
Fear of reinjury	1	1
Personal reasons	5	6

NOTE. Data are presented as mean ± standard deviation, number of patients (percentage), or number of patients.

O-MAT, meniscal allograft transplantation in patients older than 50 years; Y-MAT, meniscal allograft transplantation in patients younger than 30 years.

damage.[12,13,20] In particular, in the study by Marcacci et al.,[13] patients with unicompartmental OA were shown to benefit from a combined biological approach involving realignment procedures, ACL reconstruction, osteochondral scaffold implantation, and MAT, supporting the use of MAT in patients with complex conditions as a salvage procedure to avoid metal resurfacing. Nevertheless, patients younger than 40 years still showed greater clinical improvement, suggesting a lower healing potential in older patients.

Thus, although concomitant cartilage lesions are being considered a contraindication less and less and although early MAT actually has recently been suggested in these cases even without marked pain to prevent further diffuse cartilage loss and to potentially yield a better long-term prognosis,[19] the limited healing potential of older patients remains a concern. Actually, age has been poorly investigated among factors influencing the outcome of MAT, probably because of the commonly accepted cutoff of 50 years as an indication for MAT,[9] and therefore, the evidence on older patients is limited in the literature. In our study, the analysis was focused, through a matched-pair comparative evaluation, on determining the opportunity to extend the indications for MAT to active adults older than 50 years.

The importance of this investigation derives from the constant increase in an aging population remaining active. These relatively young patients could benefit from a biological treatment approach to restore meniscal function and avoid or at least delay prosthetic resurfacing. In fact, patients aged 50 to 54 years are at a very high risk of undergoing revision surgery after knee arthroplasty, which can be quantified with a 35% risk of revision during the patients' lifetime,[23] and thus it is advisable to postpone replacement surgery as long as possible, taking advantage of biological treatment strategies such as MAT in the older active population.

Only a few studies have reported the results of MAT in patients older than 50 years, always within larger heterogeneous series and focusing marginally on the effect of age on the results and failures of MAT. In particular, Stone et al.[12] compared the failure rate of 53 patients older than 50 years with that of younger patients, finding a 2.9 higher risk of failure. However, they included patients with a broad follow-up period, ranging from 2 months to 12.3 years, and did not provide a stratification of patient reported outcome measures based on patients' age. In this regard, it is important to point out that results and survival values of MAT in less recent studies must be interpreted with caution, given that techniques were often significantly

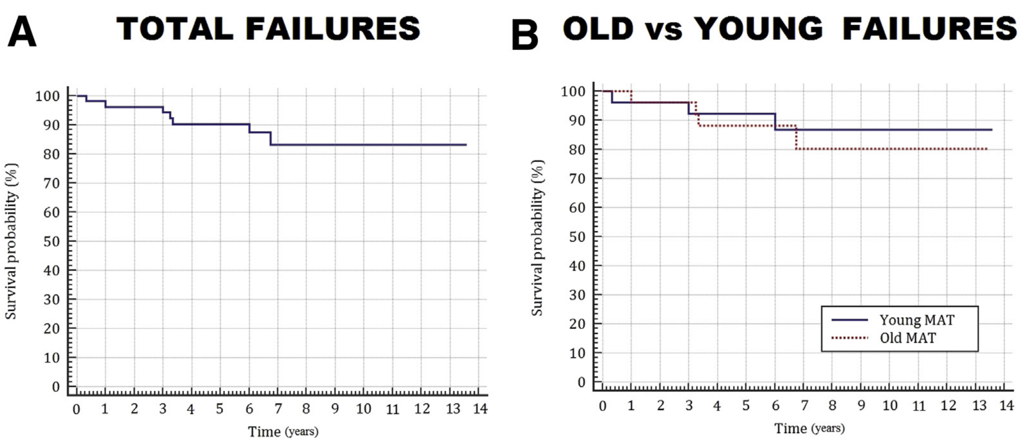

Fig 3. Survival curve until graft removal in overall survey (A) and for older meniscal allograft transplantation (MAT) and young MAT groups (B).

Table 5. Survival Analysis in O-MAT and Y-MAT Groups

	Survivorship Free From MAT Removal		
	O-MAT Group (n = 26)	Y-MAT Group (n = 26)	Overall (N = 52)
Mean time (95% CI), yr	11.6 (9.8-13.2)	12.3 (10.8-13.6)	12.0 (10.7-13.0)
2 yr (SE), %	96 (4)	96 (4)	96 (3)
4 yr (SE), %	88 (6)	92 (5)	90 (4)
6 yr (SE), %	88 (6)	87 (7)	87 (5)
8 yr (SE), %	80 (10)	87 (7)	83 (6)
10 yr (SE), %	80 (10)	87 (7)	83 (6)
12 yr (SE), %	80 (10)	87 (7)	83 (6)

CI, confidence interval; MAT, meniscal allograft transplantation; O-MAT, meniscal allograft transplantation in patients older than 50 years; SE, standard error; Y-MAT, meniscal allograft transplantation in patients younger than 30 years.

different from those currently applied.[24] In our study, indeed, the graft survival rate was higher: At a mean follow-up of 7 years, only 2 patients underwent knee arthroplasty, suggesting the possible efficacy of MAT as a bridge procedure. Moreover, considering both surgical failure and poor clinical outcomes, the percentage of patients with good results in the O-MAT group was 61%. This finding is actually in line with recent studies on younger patients, aged under 50 years, such as the study of Noyes and Barber-Westin,[25] who found a survival rate of 63% at 10 years. It is also important to underline that in these types of patients, who are willing to buy time delaying a joint replacement, symptom relief as well as an active lifestyle can be considered the primary goal.[24] Accordingly, our study confirmed the efficacy of MAT in improving patients' symptoms and allowing them to return to their desired activities.[26] In fact, two-thirds of these older patients were able to return to sports activity at a recreational level. Still, younger patients were more likely to return to competitive activities. This finding may be explained by the different sports requirements and aims of the different age groups. The return to competitive activities could be responsible for most of the surgical failures in the Y-MAT group, which were caused by graft lesions and occurred during a new trauma, and as such, the failure rate in young patients could have been overestimated. On the other hand, the reasonably

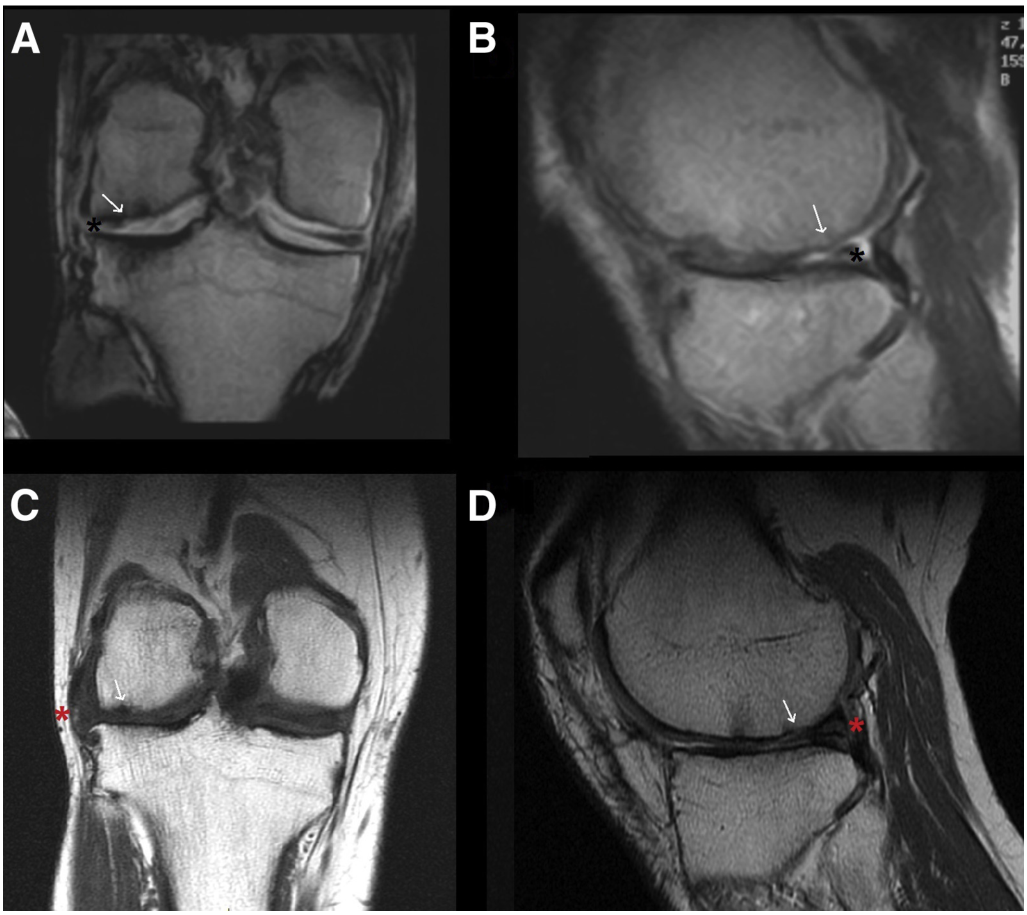

Fig 4. Preoperative magnetic resonance imaging of a 57-year-old male patient undergoing lateral meniscal allograft transplantation (A, B) and imaging at 5-year follow-up evaluation (C, D). The meniscal defects (black asterisks), meniscal allografts (red asterisks), and overlying femoral cartilage (white arrows) are highlighted.

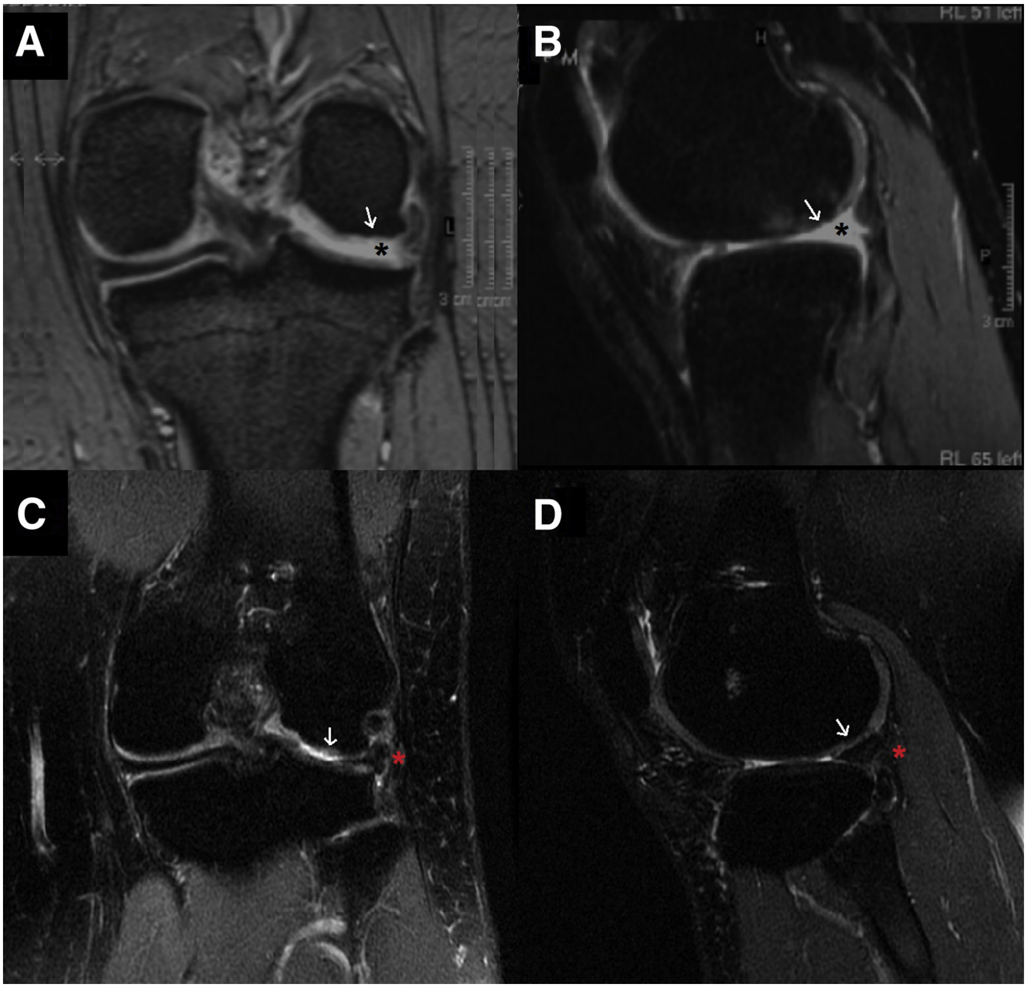

Fig 5. Preoperative magnetic resonance imaging of a 15-year-old female patient undergoing lateral meniscal allograft transplantation (A, B) and imaging at 5-year follow-up evaluation (C, D). The meniscal defects (black asterisks), meniscal allografts (red asterisks), and overlying femoral cartilage (white arrows) are highlighted.

higher failure rate of the implants in older patients could be explained by a lower healing potential of MAT. In older patients, in fact, the greatest challenge is represented by the unfavorable environment characterizing osteoarthritic joints, which was shown to significantly decrease the potential of regenerative procedures.[27] Another aspect that could contribute to an unfavorable environment is represented by the time since the articular damage occurred, which could be identified with the interval from the first meniscectomy. In fact, the loss of homeostasis consequent to the initial damage causes a chronic catabolic environment that can alter all the articular structures, eventually leading to an osteoarthritic knee.[28]

Limitations

Regarding study limitations, the matching process did not allow us to fully match the groups because of the number of patients available. In detail, the cartilage status could not be considered in the matching process because of the lack of a sufficient number of young patients with degenerated cartilage and old patients without some degeneration. Actually, this reflects the general population, thus allowing conclusions to be drawn on the most typical patients dealing with this pathology. This study presents some other limitations. First, although this was a comparative study based on a database case-control evaluation, the retrospective nature of patient selection may entail some bias. Moreover, although our study is one of the largest surveys focusing on this issue at midterm follow-up and despite our performance of a power analysis based on the Lysholm score, the number of patients may still be underpowered to perform a statistical analysis regarding the failure rate between the O-MAT and Y-MAT groups and also may be related to the lack of statistically significant differences between the 2 groups in the other outcomes evaluated; thus, these types of results should be considered cautiously. Moreover, the lack of a control group of patients older than 50 years undergoing alternative procedures to MAT or not undergoing surgery limits the power of the results and does not allow conclusions to be drawn on the superiority of

MAT over other procedures. Furthermore, our study included both medial and lateral MAT, as well as concomitant procedures in at least 50% of patients, and this reduces the homogeneity of the results, given that previous literature reported a lower survival rate in more medically complex patients[12,20,21]; patients should be advised about this risk. Moreover, the difference observed between the O-MAT and Y-MAT groups in the time elapsed between the first meniscectomy and MAT could be interpreted as a limitation of this study because it could influence the differences observed in the final results between groups. Furthermore, this study lacked a radiologic evaluation, which could generally be considered a meaningful aspect in MAT to quantify the progression of OA.[29] The number of magnetic resonance imaging scans available at midterm follow-up was not sufficient to perform a statistical comparison. The reason lies in the retrospective nature of the study based on a hospital database, for which no routine radiologic evaluation was considered for economic and ethical reasons. Magnetic resonance imaging examples from the O-MAT and Y-MAT groups are provided in Figures 4 and 5, showing the quite different scenarios in the 2 groups. Nevertheless, more than radiographic OA progression, in this category of older patients who already showed some degree of OA at the time of implantation, it is paramount to understand the improvement in pain symptoms and function because they are the most important determinant factors for the indications for knee arthroplasty. In this study, both clinical results and the need for surgical revision or arthroplasty were considered for the failure analysis. The definition of "surgical failure" used for the analysis may be a matter of argument because TKA and UKA are not equivalent to meniscectomies. Nevertheless, it is important to consider that failure in patients younger than 30 years cannot be treated in the same way as failure in patients older than 50 years. In fact, in younger patients, arthroplasty is not and should not be taken into account as an option, and every attempt should be made to preserve the graft, with a preference for meniscectomy and sutures over graft removal. In patients older than 50 years, on the other hand, MAT often already represents a salvage procedure, and in the case of failure, patients may undergo arthroplasty. Still, failures are an essential part both for performing scientific evaluations of the outcomes of surgical strategies[30] and for providing honest expectations and more appropriate indications to patients who are candidates for MAT, and a combined surgical and improvement-based definition of failure is crucial to properly evaluate its potential and limitations.

Conclusions

MAT is able to provide symptom relief and functional improvement at midterm follow-up in patients older than 50 years although with inferior results and a higher failure rate compared with those younger than 30 years. MAT can be considered a viable option to treat patients older than 50 years.

References

1. Elattar M, Dhollander A, Verdonk R, Almqvist KF, Verdonk P. Twenty-six years of meniscal allograft transplantation: Is it still experimental? A meta-analysis of 44 trials. *Knee Surg Sports Traumatol Arthrosc* 2011;19:147-157.
2. Cvetanovich GL, Yanke AB, McCormick F, Bach BR Jr, Cole BJ. Trends in meniscal allograft transplantation in the United States, 2007 to 2011. *Arthroscopy* 2015;31:1123-1127.
3. Myers P, Tudor F. Meniscal allograft transplantation: How should we be doing it? A systematic review. *Arthroscopy* 2015;31:911-925.
4. Samitier G, Alentorn-Geli E, Taylor DC, et al. Meniscal allograft transplantation. Part 2: Systematic review of transplant timing, outcomes, return to competition, associated procedures, and prevention of osteoarthritis. *Knee Surg Sports Traumatol Arthrosc* 2015;23:323-333.
5. Smith NA, MacKay N, Costa M, Spalding T. Meniscal allograft transplantation in a symptomatic meniscal deficient knee: A systematic review. *Knee Surg Sports Traumatol Arthrosc* 2015;23:270-279.
6. Smith NA, Parsons N, Wright D, et al. A pilot randomized trial of meniscal allograft transplantation versus personalized physiotherapy for patients with a symptomatic meniscal deficient knee compartment. *Bone Joint J* 2018;100-B:56-63.
7. Smith NA, Parkinson B, Hutchinson CE, Costa ML, Spalding T. Is meniscal allograft transplantation chondroprotective? A systematic review of radiological outcomes. *Knee Surg Sports Traumatol Arthrosc* 2016;24:2923-2935.
8. Van Der Straeten C, Byttebier P, Eeckhoudt A, Victor J. Meniscal allograft transplantation does not prevent or delay progression of knee osteoarthritis. *PLoS One* 2016;11:e0156183.
9. Verdonk R, Volpi P, Verdonk P, et al. Indications and limits of meniscal allografts. *Injury* 2013;44:S21-S27 (suppl 1).
10. Getgood A, LaPrade RF, Verdonk P, et al. International Meniscus Reconstruction Experts Forum (IMREF) 2015 consensus statement on the practice of meniscal allograft transplantation. *Am J Sports Med* 2017;45:1195-1205.
11. Vannini F, Spalding T, Andriolo L, et al. Sport and early osteoarthritis: The role of sport in aetiology, progression and treatment of knee osteoarthritis. *Knee Surg Sports Traumatol Arthrosc* 2016;24:1786-1796.
12. Stone KR, Adelson WS, Pelsis JR, Walgenbach AW, Turek TJ. Long-term survival of concurrent meniscus allograft transplantation and repair of the articular cartilage: A prospective two- to 12-year follow-up report. *J Bone Joint Surg Br* 2010;92:941-948.
13. Marcacci M, Zaffagnini S, Kon E, et al. Unicompartmental osteoarthritis: An integrated biomechanical and biological approach as alternative to metal resurfacing. *Knee Surg Sports Traumatol Arthrosc* 2013;21:2509-2517.

14. Van Thiel GS, Verma N, Yanke A, Basu S, Farr J, Cole B. Meniscal allograft size can be predicted by height, weight, and gender. *Arthroscopy* 2009;25:722-727.
15. Marcacci M, Zaffagnini S, Marcheggiani Muccioli GM, et al. Meniscal allograft transplantation without bone plugs: A 3-year minimum follow-up study. *Am J Sports Med* 2012;40:395-403.
16. González-Lucena G, Gelber PE, Pelfort X, Tey M, Monllau JC. Meniscal allograft transplantation without bone blocks: A 5- to 8-year follow-up of 33 patients. *Arthroscopy* 2010;26:1633-1640.
17. Zaffagnini S, Grassi A, Romandini I, Marcacci M, Filardo G. Meniscal allograft transplantation combined with anterior cruciate ligament reconstruction provides good mid-term clinical outcome [published online August 6, 2018]. *Knee Surg Sports Traumatol Arthrosc*. 10.1007/s00167-018-5078-0.
18. Zaffagnini S, Grassi A, Marcheggiani Muccioli GM, et al. Survivorship and clinical outcomes of 147 consecutive isolated or combined arthroscopic bone plug free meniscal allograft transplantation. *Knee Surg Sports Traumatol Arthrosc* 2016;24:1432-1439.
19. Kim JM, Lee BS, Bin SI. Editorial Commentary: Meniscal allograft transplantation: Still effective with poor cartilage, but much better with good cartilage-better done earlier. *Arthroscopy* 2018;34:1877-1878.
20. Kempshall PJ, Parkinson B, Thomas M, et al. Outcome of meniscal allograft transplantation related to articular cartilage status: Advanced chondral damage should not be a contraindication. *Knee Surg Sports Traumatol Arthrosc* 2015;23:280-289.
21. Mahmoud A, Young J, Bullock-Saxton J, Myers P. Meniscal allograft transplantation: The effect of cartilage status on survivorship and clinical outcome. *Arthroscopy* 2018;34:1871-1876.
22. Saltzman BM, Meyer MA, Leroux TS, et al. The influence of full-thickness chondral defects on outcomes following meniscal allograft transplantation: A comparative study. *Arthroscopy* 2018;34:519-529.
23. Schreurs BW, Hannink G. Total joint arthroplasty in younger patients: Heading for trouble? *Lancet* 2017;8:1374-1375.
24. Spalding T, Getgood A. Defining outcome after meniscal allograft transplantation: Is buying time a valid measure of success? *Knee Surg Sports Traumatol Arthrosc* 2016;24:1424-1426.
25. Noyes FR, Barber-Westin SD. Meniscal transplantation in symptomatic patients under fifty years of age: Survivorship analysis. *J Bone Joint Surg Am* 2015;97:1209-1219.
26. Chalmers PN, Karas V, Sherman SL, Cole BJ. Return to high-level sport after meniscal allograft transplantation. *Arthroscopy* 2013;29:539-544.
27. Filardo G, Vannini F, Marcacci M, et al. Matrix-assisted autologous chondrocyte transplantation for cartilage regeneration in osteoarthritic knees: Results and failures at midterm follow-up. *Am J Sports Med* 2013;41:95-100.
28. Rodrigo JJ, Steadman JR, Syftestad G, Benton H, Silliman J. Effects of human knee synovial fluid on chondrogenesis in vitro. *Am J Knee Surg* 1995;8:124-129.
29. Ahn JH, Kang HW, Yang TY, Lee JY. Risk factors for radiographic progression of osteoarthritis after meniscus allograft transplantation. *Arthroscopy* 2016;32:2539-2546.
30. Filardo G, Andriolo L, Balboni F, Marcacci M, Kon E. Cartilage failures. Systematic literature review, critical survey analysis, and definition. *Knee Surg Sports Traumatol Arthrosc* 2015;23:3660-3669.