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Meniscal allograft transplantation: long-term clinical results with radiological and magnetic resonance imaging correlations

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Abstract Long-term data on the clinical outcome and the fate of the meniscus allograft after transplantation are scarce. In this study we present the clinical, radiological and MRI outcome of the meniscus graft and the articular cartilage after 42 meniscus allograft transplantations in 41 patients with a minimum follow-up of 10 years. A total of 27 medial and 15 lateral meniscal allografts were transplanted. Eleven of the medial allograft procedures were associated with a high tibial osteotomy. The patients were evaluated clinically at the time of transplantation and at the final follow-up using the modified HSS scoring system. The knee injury and osteoarthritis outcome score (KOOS) was used as an evaluation tool for patient-related outcome at the final follow-up. Joint space width narrowing and Fairbank changes were radiological outcome parameters, which were available for 32 patients. Femoral and tibial cartilage degeneration, graft extrusion and signal intensity were scored on MRI scans obtained in 17 patients approximately 1 year after transplantation and at the final follow-up (> 10 years). For statistical analysis the patients were divided into three groups: lateral meniscal allograft (LMT), medial meniscal allograft transplantation with a high tibial osteotomy (MMT + HTO) and without (MMT). The modified HSS score revealed a significant improvement in pain and function at the final follow-up for all groups. Further analysis also revealed that an MMT + HTO procedure resulted in a greater improvement at the final follow-up when compared to MMT. Nonetheless, the KOOS scores obtained at the final follow-up revealed the presence of substantial disability and symptoms, in addition to a reduced quality of life. Radiographical analysis revealed no further joint space narrowing in 13/32 knees (41%). Fairbank changes remained stable in 9/32 knees (28%). MRI analysis showed no progression of cartilage degeneration in 6/17 knees (35%). An increased signal intensity of the allograft was present, as was partial graft extrusion in the majority of patients at the final follow-up. Seven cases had to be converted to a total knee arthroplasty during the follow-up; the overall failure rate was 18%. Long-term results after viable meniscus allograft transplantation are encouraging in terms of pain relief and improvement of function. Despite this significant improvement, substantial disability and symptoms were present in all investigated subgroups. Progression of further cartilage degeneration or joint space narrowing was absent in a considerable number of cases, indicating a potential chondroprotective effect. Level of evidence is therapeutic study, Level IV and retrospective analysis of prospectively collected data.

Keywords Meniscus · Allograft · Transplantation · MRI · Radiology

Introduction

The fibrocartilaginous menisci play an important role in the complex biomechanics of the knee joint. They improve joint stability, load distribution, shock absorption and articular cartilage lubrication. Surgical removal of this tissue can result in dysfunction and pain in the involved compartment and ultimately osteoarthritis [1–6]. These degenerative changes are the result of increased peak stresses on the articular cartilage due to a decreased contact area in the meniscectomized compartment of the knee. Therefore, meniscal tissue should be preserved whenever possible. Hence, in case of complete loss of the meniscus, substitution of the meniscus by an allograft will result in a decreased contact pressure on the cartilage surface compared to the meniscectomized knee [7–10]. Full restoration of the normal contact pressures by an allograft has nonetheless never been obtained in the in vitro setting, irrespective of the fixation method used [7–10]. In the late 1980s, clinical meniscal allograft transplantation appeared as a logical approach to improve function, relieve pain and prevent further articular cartilage degeneration [11].

Since then, numerous medium term but only few long-term reports on meniscal allograft transplantation have been published, showing a significant improvement in function and relief of pain [12–18]. However, it has not been substantiated in the literature that this procedure prevents or slows down cartilage degeneration [19].

The purpose of this prospective study was to report on the long-term clinical results of viable medial or lateral meniscal allograft transplantation (LMT) in 38 patients out of a total of the 41 (follow-up rate 93%) who had undergone this procedure more than 10 years ago. We also report on a specific subgroup of patients who had a medial allograft transplantation in combination with a high tibial osteotomy (HTO) to correct an initial varus malalignment of the lower limb. We hypothesized that viable meniscal allografting would significantly reduce pain and increase function of the involved joint in the long term.

To determine the clinical effectiveness, the preoperative modified Hospital for Special Surgery (HSS) score was compared with the score at final follow-up (>10 years) [20]. To ensure that this treatment also satisfied the need of the patient, the recently developed patient-related knee injury and osteoarthritis outcome score (KOOS) was included as a primary clinical outcome measurement tool at final follow-up [21].

A secondary goal of this study was to document possible graft failure or progressive degenerative changes in the articular cartilage using conventional radiology and magnetic resonance imaging as objective outcome measuring tools. When available, standing X-rays and MR images taken shortly after the meniscal allograft transplantation procedure were compared with images acquired at final follow-up. Changes of femorotibial joint space width as measured on standing X-rays have been recommended as the primary measure of biological effect in osteoarthritis by expert consensus [22]. MR imaging was used to visualize possible progression of degenerative changes in the articular cartilage and the transplanted meniscal tissue.

Patients and methods

Between 1989 and 1993, 42 meniscal allografts were transplanted in 41 patients (Table 1). The indication for meniscal allograft transplantation was the young or middle-aged patient who presented with moderate to severe pain due to a previous total meniscectomy. These patients were not considered for a knee arthroplasty because of the relatively limited and/or focal articular cartilage degenerative changes and their relatively young age. In case of axial malalignment of the lower limb or instability of the knee joint, a corrective osteotomy or stabilization procedure was performed at the time of transplantation.

The study group consisted of 35 men and 6 women, with an average age of 35.2 years (range 22–50 years) at the time of transplantation (Table 1). Three patients were lost to follow-up: one patient (lateral meniscus allograft) was lost immediately after the operation, two patients (medial meniscal allograft) died of unrelated causes during follow-up. This resulted in 38 patients (follow-up rate 93%) with 39 grafts who were available for follow-up in 2004 (mean follow-up time 12.1 years, range 10.0–14.8 years) (Table 1). Of these, seven patients (seven grafts) were converted to a total knee prosthesis after a mean follow-up of 6.5 years (SD 4.3 years) due to a progressive increase of pain and decrease of function. These patients were considered failures and were evaluated at the time of failure.

At the time of transplantation all articular cartilage degenerative changes were focal: two knee joints (5%) had Outerbridge grade I degenerative changes of the articular cartilage, 8 (19%) grade I–II, 4 (9.5%) grade II, 9 (21.5%) grade II–III, 3 (7%) grade III, 9 (21.5%) grade III–IV, and 7 (16.5%) grade IV, as documented visually during the arthrotomy [23].

The study protocol was approved by the Ethics Committee of the Ghent University Hospital and informed consent was obtained from each patient enrolled in this study.

Surgical technique

All patients underwent viable meniscal allograft transplantation. Donor allograft menisci were obtained from

Table 1 Overview of the different patient groups

	MMT ($N=16$) Mean ± 1 SD	MMT + HTO ($N=11$) Mean ± 1 SD	LMT ($N=15$) Mean ± 1 SD	Overall ($N=42$) Mean ± 1 SD
Age	33.1 ± 6.0	37.2 ± 5.2	35.7 ± 8.2	35.4 ± 6.7
Follow-up	11.9 ± 1.4	12.7 ± 1.8	11.8 ± 1.5	12.1 ± 1.6
Axial alignment	4.4 ± 2.7	6.3 ± 3.5	4.7 ± 3.6	5.1 ± 3.3
Outerbridge	2.5 ± 0.9	3.0 ± 1.1	2.7 ± 1.1	2.7 ± 1.0

Age age at the time of transplantation (years). *Follow-up* follow-up duration (years), excluding patients which were converted to a total knee arthroplasty, lost to follow-up or had died. *Axial alignment* femorotibial axis measured on standing X-rays after surgery. *Outerbridge* Outerbridge grading of cartilage degeneration at the time of transplantation. Mean values are given with standard deviation (SD)

the Ghent University Hospital Tissue Bank. The donors had died from a short disease; in the majority of cases the cause of death was a cerebrovascular incident or a car accident. A maximum age of 45 years was set for the donors. None had received corticosteroids or cytostatic drugs. The allograft was harvested within 24 h postmortem in aseptic conditions in the operating theatre and maintained in culture for 2 weeks in Dulbecco's Modified Eagle Medium (DMEM, Gibco Invitrogen Co., Merelbeke, Belgium) supplemented with 20% autologous serum prior to transplantation. Previous studies have demonstrated that meniscus cells remain viable and continue to synthesize their extracellular matrix molecules in this culture system [24]. During the meniscal tissue culture period, ample time was available to screen the donors for transmissible diseases.

All patients were operated on by the senior surgeon (R.V.). Access to the knee joint was achieved by a lateral or medial parapatellar arthrotomy. The insertion of the lateral collateral ligament and popliteus tendon or of the medial collateral ligament was detached through an osteotomy at the femoral side [25]. The osteotomy was later repositioned by screw fixation or stapling. The meniscal remnant was excised leaving only a bleeding, functional meniscal rim. The meniscal rim deserves surgical attention, as it serves as a strong envelope encapsulating the medial or lateral compartment of the knee. The rim should not be resected or transected during the operation. Doing so would lead to a breach in the envelope. The viable meniscal allograft was then securely sutured to this rim using horizontal polydioxanone surgical sutures (PDS II, Ethicon, Somerville, NJ, USA) every 5 mm in an all-inside fashion. Bone block fixation to the tibial plateau was not used to augment meniscal fixation. Instead the anterior and posterior horn of the transplanted meniscus was sutured to their remnant native horns on the tibia. The technical procedure has been published in detail [17].

Postoperative rehabilitation comprised 3 weeks of non-weight-bearing with mobilization of the knee within pain limits and limited to 60° of flexion. After 3 weeks, the patients were allowed to flex the knee to 90° and to start partial weight bearing. At 6 weeks, all patients were allowed to walk with one crutch.

Concomitant surgical procedures were judged essential in a few selected cases and included a HTO, femoral varus osteotomy (FVOS), or anterior cruciate ligament (ACL) reconstruction. Twenty-seven patients underwent a medial meniscal allograft transplantation (MMT). In 11 of these patients (41%) an HTO was associated to correct varus malalignment of the lower limb. ACL reconstruction at the time of transplantation had to be performed in three of the medial allograft cases and in none of the lateral allografts. ACL reconstruction was performed using an intra-articular double-loop tibialis posterior tendon allograft following a technique described previously [26]. The population analysed thus consisted of patients with stable knees or with knees stabilized prior to meniscal allografting. Fourteen patients underwent a LMT. In one of them an FVOS was associated to correct an obvious valgus malalignment. Another patient had a transplantation of the lateral meniscus in both knees.

Clinical evaluation

All patients were evaluated clinically preoperatively and at the final follow-up by an independent orthopaedic surgeon using the modified HSS score [20]. This scoring system evaluates pain, function, range of motion, flexion deformity, and instability of the involved knee (Table 2). Therefore, it is an indicator of the overall knee function [20]. This knee rating system has been used to determine knee function in previous reviews of meniscal allografting procedures and of fresh osteochondral allografting procedures in combination with meniscal allograft transplantation [17, 25, 27].

At the final follow-up (> 10 years), the modified HSS score was available for all patients ($N=31$). Twenty-five patients (81%) also performed KOOS self-assessment tests. The KOOS (Dutch version LK 1.0) is a 42-item self-administered knee-specific questionnaire based on the WOMAC Osteoarthritis Index [21]. KOOS was developed to be used for short- and long-term follow-up studies of knee injuries, and it comprises five subscales: pain,

symptoms, activities of daily living (ADL), sports and recreation function (S&R), and knee-related quality of life (QOL). A score ranging from 0 to 100, where 100 represents the best result, is calculated for each subscale. The questionnaire and scoring manual can be downloaded from http://www.koos.nu. KOOS is valid, reliable, and responsive in follow-up of meniscectomy, ACL reconstruction, and total knee replacement for osteoarthritis [3, 28, 29]. The participants completed the KOOS questionnaire answering questions on their operated knee.

In order to ascertain patient satisfaction, patients were also asked at the final follow-up if they would undergo the procedure again.

Those patients that were converted to a total knee arthroplasty (TKA) and were considered a failure ($N=7$) were evaluated separately using the modified HSS score at the time of failure. KOOS score was not available for these patients.

Radiology

For all patients, standing postero-anterior plain radiographs with 15° of flexion of the involved knee joint were taken within 6 months of the operation. Radiographic femoro-tibial alignment was thus recorded shortly after transplantation. Joint space narrowing of the medial and lateral compartment was graded using the International Knee Documentation Committee system (0, no narrowing; 1, < 50% narrowing; 2, > 50% narrowing; 3, obliteration of the joint space) [30]. Fairbank changes (narrowing of the joint space, flattening of the femoral condyle, bone spur formation) were also recorded [4].

At the final follow-up (> 10 years), 25 patients (81%) were available for standing radiographic examination of the index knee (9 MMT, 6 MMT + HTO, 10 LMT).

Standing radiographs of the index knees were also available for all failures just prior to the conversion to a TKA ($N=7$).

All plain radiographs were analysed and compared retrospectively by an experienced radiologist (K.V.) in a blinded fashion.

MRI evaluation

Twenty-five patients underwent an MRI examination on a 1.0 T magnet (Magnetom Expert, Siemens, Erlangen, Germany) of the operated knee joint within 1 year of the operation. Three millimetre sagittal proton-density and T2-weighted images, 2 mm coronal mixed T1–T2-weighted DESS-3D gradient-echo images and 1 mm sagittal fat suppressed T1-weighted 3D spoiled gradient-echo images were obtained for optimal visualization of all portions of the menisci and to assess the articular cartilage [31, 32]. Seventeen of them (6 MMT, 5

Table 2 Modified HSS scoring system

	Points
Knee score	
Pain	
None	50
Mild or occasional	45
Stairs only	40
Walking and stairs	30
Moderate	
Occasional	20
Continual	10
Severe	0
Range of motion (5° = 1 point)	25
Stability	
Anteroposterior	
< 5 mm	15
5–10 mm	5
10 mm	0
Mediolateral	
< 5°	15
6°–9°	10
10°–14°	5
15°	0
Subtotal	
Deductions	
Flexion contracture	
5°–10°	2
10°–15°	5
16°–20°	10
> 20°	15
Extension lag	
< 10°	5
10–20°	10
> 20°	15
Alignment	
5–10°	0
0–4°	3 points each degree
11–15°	3 points each degree
Other	20
Total deductions	
Knee score	
Function score	
Walking	
Unlimited	50
> 10 blocks	40
5–10 blocks	30
< 5 blocks	20
Housebound	10
Unable	0
Stairs	
Normal up and down	50
Normal up, down with rail	40
Up and down with rail	30
Up with rail; unable down	15
Unable	0
Subtotal	
Deductions	
Cane	5
Two canes	10
Crutches or walker	20
Total deductions	
Function score	

The system is subdivided into a knee score that rates only the knee joint itself (max. 100 points) with regard to pain (max. 50 points), range of motion (max. 25 points), and stability (max. 25 points). Flexion contracture, extension deficit, and malalignment are dealt with as deductions. Additionally, a daily functional score (max. 100 points) rates the patient's ability to walk (max. 50 points) and to climb stairs (max. 50 points), with deductions for walking aids

MMT + HTO, 6 LMT) were available for objective MRI analysis of the involved knee at the final follow-up (> 10 years). Cartilage degeneration of the femoral condyle and tibial plateau of the involved compartment was graded separately as described by Yulish with slight modifications (Table 3) [33]. For example, a lesion that was graded between grade III and IV was recorded as 3/4 and was given a nominative value of 3.5.

Signal intensity, extrusion, and tears of the meniscus allograft were recorded. Three grades of signal intensity were identified according to Thornton [34]. Grade I signal intensity is globular and not adjacent to either articular surface. A grade II signal is a linear signal within the meniscus. A grade III signal is a linear signal that extends to either the superior or inferior articular surface. Extrusion of the meniscus body was evaluated on the coronal sections as none (0), partial (1), or complete (2) [35]. If a tear of the graft was identified, the location (red, red on white, white zone) and the configuration of the tear were described (horizontal, vertical, or complex).

MRI data was unavailable for all failure cases.

Cartilage and allograft status of the involved compartment were compared to the initial MR scan. All MR images were analysed retrospectively by an experienced radiologist (K.V.) in a blinded fashion.

Statistical analysis

Statistical analysis was performed on subgroups of patients who had undergone (1) an MMT without a HTO ($N = 16$), (2) an MMT + HTO ($N = 11$), or (3) an LMT ($N = 15$ allografts in 14 patients) (Table 1).

SPSS version 11.0 for Windows XP was used as software for statistical analysis. Normality of distribution for the investigated clinical, radiological, and MRI parameters was tested within each subgroup using the Kolmogorov–Smirnov and Shapiro–Wilk test and was not achieved but in KOOS subscales. Therefore, statistical analysis was performed using non-parametric tests. Comparison of the postoperative to the preoperative clinical and radiological/MRI parameters was performed using the Wilcoxon signed rank test. Comparison among different patient groups was done using the Mann–Whitney test. Correlation studies between modified HSS and KOOS subscales and between specific radiological/MRI parameters and clinical outcome were performed using the Spearman's ρ two-sided test. These tests were performed on the overall data as well as on the different subgroups. Statistical significance was set at P value < 0.05.

Results

Clinical outcome

The preoperative mean modified HSS pain score was 14 ± 8.4, 13.3 ± 10, and 15.8 ± 7.9 for the MMT group, the MMT + HTO group, and the LMT group, respectively (Table 4; Fig. 1). These pain scores did not differ significantly at baseline. At the final follow-up, these values improved significantly when compared to the preoperative values: 35 ± 10.5 ($P = 0.01$), 45.5 ± 6.3 ($P = 0.011$), and 38.7 ± 14 ($P = 0.004$), respectively. The pain score of the MMT + HTO group was significantly higher than of the MMT group ($P = 0.017$) at the final follow-up.

Range of motion increased slightly in all groups, as did anteroposterior and mediolateral stability. Changes were, however, not significant.

The mean modified HSS walking score significantly improved at the final follow-up when compared to the preoperative score for all groups: 19.5 ± 16.1 to 44.0 ± 8.4 ($P = 0.007$), 24.4 ± 10.1 to 46.2 ± 5.2 ($P = 0.007$), 27.5 ± 10.6 to 49.1 ± 2.9 ($P = 0.002$) for the MMT, MMT + HTO, and LMT group, respectively. This was also true for the stair climbing ability score: 25.5 ± 15.4 to 44.0 ± 5.2 ($P = 0.011$), 35.6 ± 7.3 to 47.8 ± 4.4 ($P = 0.018$), 37.5 ± 8.7 to 46.7 ± 6.5 ($P = 0.009$), respectively. Details of the modified HSS score are presented in Table 4 and Fig. 1.

Table 3 Arthroscopic (Outerbridge) and MR (Yulish) classification system to grade cartilage lesions

Arthroscopic and MR classification of cartilage lesions			
Arthroscopic classification		MR classification	
Grade 0	Normal	Grade 0	Normal
Grade 1	Softening, without morphologic defect	Grade 1	Normal contour ± abnormal signal
Grade 2	Superficial blistering or fraying; erosion or ulceration of less than 50%	Grade 2	Superficial fraying; erosion or ulceration of less than 50%
Grade 3	Partial-thickness defect of more than 50% but less than 100%	Grade 3	Partial-thickness defect of more than 50% but less than 100%
Grade 4	Ulceration and bone exposure	Grade 4	Full-thickness cartilage loss

The KOOS scores at the final follow-up for the different groups are given in Table 4 and Fig. 2. The MMT + HTO group scored substantially higher on all subscales compared to the MMT and LMT group. These differences did not reach statistical significance (P values between 0.065 and 0.130, data not shown).

Further KOOS data analysis (see Appendix) revealed that, compared to the MMT group, the MMT + HTO group complained significantly less of swelling (question S1) and stiffness (question S7) of the knee. These patients also had significantly less frequent pain (question P1), had less difficulties with going up or downstairs (question P6), rising from bed (question A10), and getting in and out of bath (question A13). Additionally, these patients had more confidence in their knee (question Q3).

At the final follow-up, over 90% of all patients were satisfied with the outcome of the operation and would consider this procedure again if necessary.

Four MMTs (25%), 2 MMT + HTOs (18%), and 1 LMT (7%) were converted to TKA during follow-up (mean FU 6.5 years, SD 4.3 years) due to intolerable pain and loss of function. Thus, with conversion to TKA as an end point, the overall failure rate was 18% (7/39 grafts) in this series. At the time of conversion the mean pain, walking and stair climbing scores according to the modified HSS scale were 10 ± 14.1, 24.3 ± 12.7, and 15 ± 18.3, respectively, indicating a poor result. These scores were not included into the final follow-up (> 10 years) data.

Radiology

Plain radiographs of 13 knees out of 25 (52%) that were available at the final follow-up (12.0 ± 1.5 years) did not show any change in joint space width (Table 5). Progression of joint space narrowing was observed in 12/25 cases (48%): 8 knees were narrowed by 1 grade (32%), 3 by 2 grades (12%), and 1 by 3 grades (4%). Representative detailed magnetic resonance images are depicted in Fig. 3. Fairbank changes remained stable in 9 knees (36%). Progression was seen by 1 grade in 8 knees (32%) and by 2 grades in 8 knees (32%). Details are presented in Table 5. Representative detailed radiological images are depicted in Fig. 4.

All failure cases ($N = 7$, conversion to TKA) were characterized by progression in joint space width narrowing (2 by 1 grade and 5 by 2 grades) and Fairbank changes (6 by 1 grade and 1 by 2 grades).

Overall, considering both success and failure cases, joint space width remained stable in 13/32 cases (41%) in the course of the study. JSWN progressed by 1 grade in 11 cases (34%), by 2 grades in 7 cases (22%), and by 3 grades in 1 case (3%). Fairbank changes did not progress in 9 cases (28%). Fourteen cases showed progression by 1 grade (44%), and 9 cases by 2 grades (29%).

MRI evaluation

Absence of further degeneration of the femoral cartilage was noted in 8 knees (47%) out of a total of 17 that were

Table 4 Overview of clinical outcome at final follow-up (> 10 years)

	MMT			MMT + HTO		*P* value	LMT		
	Preop (Mean ± SD)	Postop (Mean ± SD)	*P* value	Preop (Mean ± SD)	Postop (Mean ± SD)		Preop (Mean ± SD)	Postop (Mean ± SD)	*P* value
Mod. HSS									
Pain	14.0 ± 8.4	35.0 ± 10.5*	0.01	13.3 ± 10.0	45.5 ± 6.3*	0.011	15.8 ± 8.0	38.7 ± 14.0	0.004
ROM	114.0 ± 11.5	120.5 ± 6.4	0.18	118.3 ± 9.0	121.1 ± 8.2	0.59	113.3 ± 12.5	118.0 ± 11.6	0.17
AP stab	5.0 ± 4.7	7.0 ± 4.2	0.16	7.8 ± 3.6	8.3 ± 3.5	0.70	7.5 ± 4.0	10.0 ± 0.0	0.04
ML stab	13.5 ± 4.7	15.0 ± 0.0	0.32	12.8 ± 5.0	15.0 ± 0.0	0.18	14.2 ± 2.0	15.0 ± 0.0	0.16
Walking	19.5 ± 16.1	44.0 ± 8.4	0.007	24.4 ± 10.1	46.2 ± 5.2	0.007	27.5 ± 10.6	49.2 ± 2.9	0.002
Stairs	25.5 ± 15.4	44.0 ± 5.2	0.011	35.6 ± 7.3	47.8 ± 4.4	0.018	37.5 ± 8.7	46.7 ± 6.5	0.009
KOOS									
Pain	N/A	68.6 ± 18.5		N/A	87.9 ± 10.2		N/A	76.1 ± 18.4	
Symptoms		57.6 ± 19.0			76.4 ± 17.1			55.8 ± 20.1	
ADL		72.5 ± 21.3			92.0 ± 8.9			79.1 ± 19.0	
S&R		44.4 ± 20.6			63.1 ± 24.2			44.5 ± 27.1	
QoL		41.4 ± 20.7			60.9 ± 28.5			39.9 ± 17.0	

Modified HSS subscales [pain, range of motion (ROM), anteroposterior stability (AP stab), mediolateral stability (ML stab), walking and stairs]. KOOS subscales [pain, symptoms, activities of daily life (ADL), sports and recreation (S&R) and quality of life (QoL)]. Mean preoperative and postoperative values are presented together with corresponding P value if applicable. Clinical outcome scores of the failure cases, i.e. conversion to TKA, are not included in the table

*Postoperative modified HSS pain score for the MMT + HTO was significantly more improved compared to the MMT group ($P = 0.017$)

N/A Not applied preoperatively

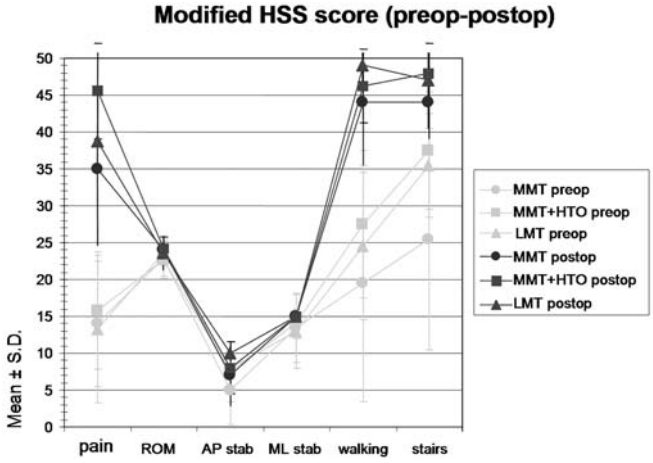

Fig. 1 Preoperative and postoperative subscales according to the modified HSS system. *Y*-axis: mean ± standard deviation (SD). *X*-axis: pain (max. 50), range of motion (*ROM*, max. 25), anteroposterior stability (*AP stab*, max. 10), mediolateral stability (*ML stab*, max. 15), walking (max. 50), stairs (max. 50). *MMT* medial meniscus transplantation, *MMT+HTO* medial meniscus transplantation combined with a high tibial osteotomy, *LMT* lateral meniscus transplantation. All subgroups improved significantly postoperatively when compared to the preoperative score. The MMT + HTO subgroup improved significantly more than the MMT subgroup

available for evaluation at the final follow-up (11.9 ± 1.4 years) (Table 6). One knee (6%) showed further degeneration by half a grade, 5 knees by 1 grade (29%), 2 knees by 1 and a half grade (12%), and 1 knee by 2 grades (6%).

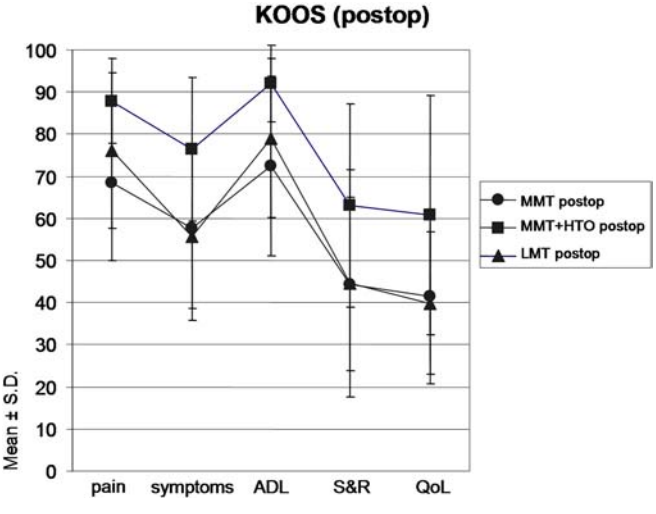

Fig. 2 Postoperative KOOS subscales. *Y*-axis: mean ± standard deviation (SD). *X*-axis: pain (max. 100); symptoms (max. 100); activities of daily life (*ADL*, max. 100), sports and recreation (*S&R*, max. 100); quality of life (*QoL*, max. 100). The MMT + HTO subgroup scored substantially better postoperatively than the MMT and LMT subgroup

No progression of tibial cartilage degeneration was observed in 7 knees (41%). Three knees (18%) showed progression by half a grade, 4 (23%) by 1 grade, 2 (12%) by 1 and a half grade, and 1 by 2 grades (6%). Six out of 17 (35%) knees did not show any progression of both femoral and tibial cartilage degeneration.

At the final follow-up, the signal intensity of the allograft was graded as grade III in ten allografts (59%) (5 MMT, 1 MMT + HTO, 4 LMT) and as normal or grade 0 in the remaining allografts. However, grade III signal intensity had already been observed in 5 MMTs, 1 MMT + HTO, and 1 LMT on the initial MRI scans, taken within 1 year of the procedure. Hence, no change in signal intensity was observed in 14/17 (82%) allografts. Grade I or II signal intensity of the allograft was never observed on the initial scans or at final follow-up. Normal signal intensity at baseline and at the final follow-up was most frequently observed in the MMT + HTO group. The MMT group without HTO showed grade III signal intensity on the initial MRI scans. These allografts, however, showed no increased signal intensity during follow-up. In contrast, the LMT group showed progressive grade III signal intensity in three grafts. Only two out of six grafts were graded as normal at the final follow-up.

At the final follow-up, the position of the allograft was evaluated as normal in 4 knees (24%) (1 MMT, 2 MMT + HTO, 1 LMT), and as partially extruded in 12 knees (70%) (5 MMT, 2 MMT + HTO, 5 LMT). Partial extrusion of the midbody and anterior horn of the allograft was most frequently observed. On the initial scans, the position of the graft was graded as normal in 15 knees (6 MMT, 4 MMT + HTO, 5 LMT) and as partially extruded in 2 knees (1 MMT + HTO, 1 LMT). Overall, the position of the graft did not change over 10 years in 6/17 knees (35%). The extrusion was progressive in 10/17 knees (59%). In one MMT + HTO knee, only a small remnant of the graft was present. Details are presented in Table 6.

In two knees, the allograft showed a tear of the posterior horn at the final follow-up. One MMT was diagnosed with a vertical tear in the red zone, while one LMT had a minor, horizontal tear in the white zone. Except for the graft with the vertical tear in the red zone, all grafts showed capsular ingrowth.

Correlation studies

The modified HSS pain, walking and stair-climbing subscales correlated significantly with each other (Spearman ρ test, range 0.465–0.675, $P < 0.007$).

Significant correlations were also found between the different KOOS subscales (Spearman ρ test, range 0.611–0.938, $P < 0.001$).

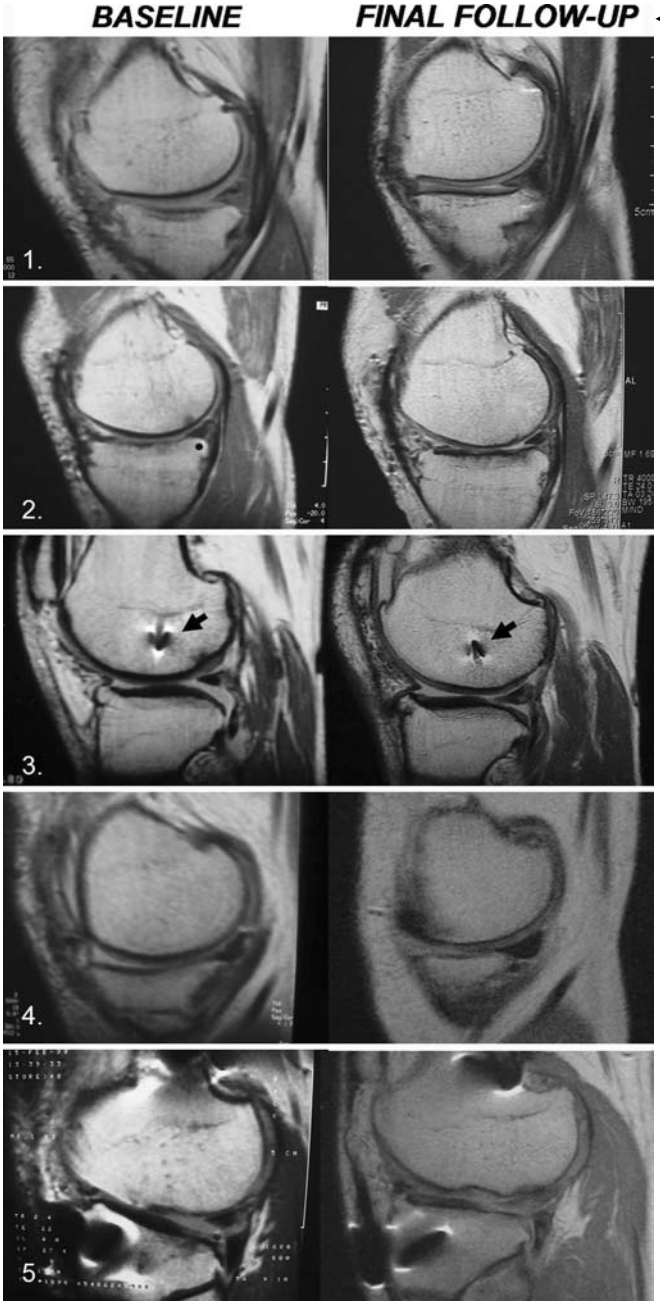

Fig. 3 Sagittal MR images of the involved compartment at baseline (within 1 year of the operation) and at the final follow-up (> 10 years) of five patients. Femoral and tibial cartilage degeneration was graded according to Yulish, meniscal allograft signal intensity was graded according to Thornton and tears of the allograft were documented. Images were selected to illustrate specific changes in MRI variables. *Patient 1* (MMT) showed no progression in cartilage degeneration. Grade 3 signal intensity of the allograft was observed at baseline and at the final follow-up. *Patient 2* (MMT + HTO) showed progression by 1 grade of both femoral and tibial cartilage degeneration during follow-up. Signal intensity of the allograft was normal. *Patient 3* (LMT) showed progression by 1 grade of femoral cartilage and by 1.5 grades of tibial cartilage degeneration. Signal intensity of the allograft changed from normal to grade 3 during follow-up. An artefact signal is observed in the femoral condyle due to a fixation screw (*arrow*). *Patient 4* (MMT + HTO) showed no progression of cartilage degeneration and allograft signal intensity. *Patient 5* (LMT) showed focal grade 4 cartilage lesions and a normal signal intensity of the graft at baseline. Focal grade 4 cartilage lesions were still observed at the final follow-up. Signal intensity of the graft was graded as 3 at the final follow-up. Complete capsular ingrowth was documented in each patient

The modified HSS pain, walking and stair-climbing subscales also correlated with the different KOOS subscales (Spearman ρ test, range 0.475–0.813, $P < 0.014$).

No significant correlations were found between any of the measured radiological or MRI parameters and the clinical subscales, nor did the status of cartilage degeneration correlate with any of the clinical subscales at the time of transplantation or at the final follow-up.

Axial alignment did not correlate with progression of femoral/tibial cartilage degeneration and signal intensity of the graft.

Discussion

Meniscal transplantation is still considered as an investigational procedure. Long-term follow-up data are scarce in the literature [18]. The comparison with published results remains troublesome due to the variety of associated procedures, preservation technique, graft fixation technique, clinical scoring systems, and duration of follow-up [15, 36]. Nonetheless, based on the available short- and medium-term data, it is generally accepted that meniscal allograft transplantation relieves pain and improves function in the symptomatic menisectomized knee [12–18, 36, 37].

The modified HSS scoring system, which was initially designed to evaluate the outcome of a TKA, was used as primary outcome measure in this study, because of the lack of a more appropriate measuring tool for the outcome of meniscus allograft transplantation in the late 1980s and early 1990s [20]. Since then, several scoring systems have been proposed and tested. However, compared to ACL reconstruction, 'meniscus reconstruction' has received little attention with respect to the functional outcome, in particular from the patient's perspective. At the final follow-up, the authors, therefore, included the patient-assessed KOOS score which has been shown to be sensitive and reliable for meniscus pathology [3, 21].

We were able to show that, after 10 years, patients had a significant improvement of function and relief of pain compared to the preoperative situation. In this study, the long-term clinical outcome after isolated medial or lateral transplantation was comparable. In contrast, others have noted a considerable difference between these two grafts. In that series, MMT were more prone to failure due to a higher number of patients

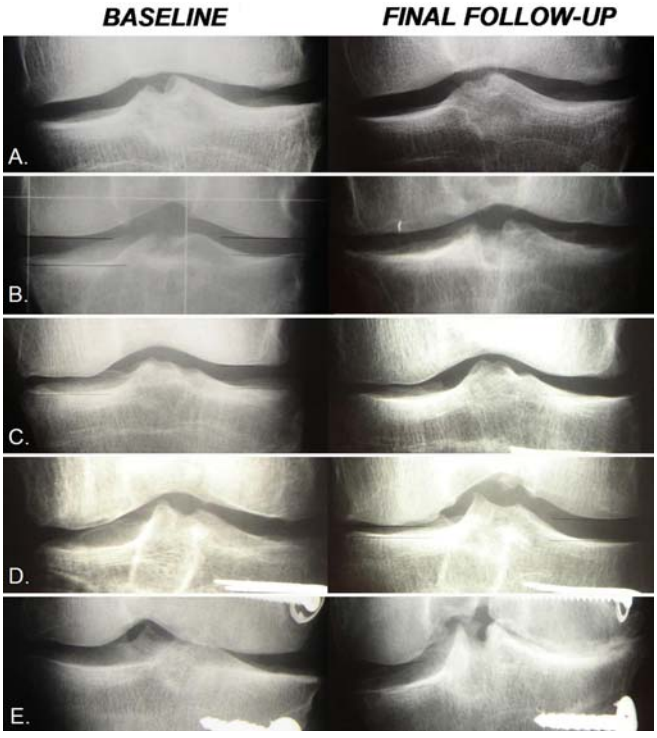

Fig. 4 Details of the joint space on standing postero-anterior plain radiographs at baseline (radiographs taken within 6 months of the transplantation) and at the final follow-up (> 10 years). Variable progression of joint space narrowing (graded according to IKDC) is seen during the follow-up. *Patient A* (LMT): no progression, *patient B* (MMT): minimal progression by one grade, *patient C* (MMT + HTO): progression by one grade, *patient D* (MT + HTO, previous ACL): progression by two grades, *patient E* (LMT): progression by three grades

with associated ACL laxity [38]. Increased anterior tibial translation due to a deficiency of the ACL is known to induce higher stress on the medial meniscus and therefore can induce secondary failure [38]. In our series all knees were stable at the time of transplantation or underwent a concomitant ACL reconstruction.

Further analysis also revealed that an MMT + HTO resulted in a significantly greater improvement of the modified HSS pain score at the final follow-up when compared to an MMT alone. We hypothesize that shifting the mechanical axis towards the lateral compartment by an osteotomy, results in unloading of the graft and the involved compartment. This makes them less prone to failure and degeneration, even though the articular cartilage was slightly more degenerated at the time of transplantation.

However, despite the significant improvement in pain and function for all investigated subgroups, substantial disability and symptoms in addition to a reduced quality of life and activity levels were evident at the final follow-up. This indicates that patients have difficulties with running, jumping, and squatting. Most knees also have a reduced range of motion compared to the contralateral knee, although flexion generally achieves more than 115°. The majority of patients are very well aware of their operated knee and adapt their lifestyle considerably. Nonetheless, when asked if they would undergo the procedure again, a vast majority answered positively, indicative of a high patient satisfaction rate at the final follow-up.

Cartilage degenerative changes at the time of transplantation are considered to be an important predictor of failure in the case of cryopreserved or irradiated meniscal allografts [14, 39]. In the presented series of viable meniscal allografts, however, we could not find any correlation between initial cartilage damage and clinical or radiological outcome parameters. This is in accordance with a previously published survivorship analysis of an identical but extended series of viable meniscal allografts where initial cartilage damage was neither able to predict clinical failure [17]. A possible explanation for this observation could be, firstly, that viable meniscal allografts are more resistant to mechanical failure compared to irradiated or cryopreserved grafts [14, 39]. The latter preservation techniques are known to render the graft acellular and may adversely affect the material properties [40–43]. In contrast, in vitro cultured menisci have been shown to remain viable and continue to produce extracellular matrix compounds, hence the term 'viable meniscal allograft' [24]. The cultured allograft is transplanted into the recipient knee after 14 days. The proportions of cells that survive and how long they survive in vivo are unknown. A DNA probe analysis in a goat model found that all donor cells were rapidly replaced by host cells over a period of 4 weeks [44]. However, a previous study in this department demonstrated the presence of donor DNA in the viable human meniscal allograft for as long as 64 months after transplantation, indicating that donor cells remain viable for a longer period and that this replacement process by host cells is probably slower in the human model [45]. The biomechanical function of the meniscal allograft not only depends on the quality of the surgical fixation technique, but also on the phenotype of the cell population of the allograft. It is not known if recipient meniscus-invading cells, probably derived from the synovial lining, have the same capacity to produce extracellular matrix as have native meniscus cells [46]. Secondly, the authors hypothesize that focal cartilage lesions have a less detrimental effect on the long-term outcome compared to generalized compartment degeneration. A high number of patients were transplanted with focal grade III and even focal grade IV cartilage lesions with exposure of the subchondral bone. In contrast, extended grade IV lesions are considered a contraindication for this type of surgery, because of the increased mechanical friction and decreased shock adsorption and as a consequence were excluded

Table 5 Overview of radiological parameters for the different patient groups at final follow-up ($N = 25$, > 10 years)

	Grade	MMT			MMT + HTO			LMT			Total
		Pre	Post	Δ grade	Pre	Post	Δ grade	Pre	Post	Δ grade	Δ grade
JSN	0	7	2	3	4	1	3	10	5	7	13
	1	3	3	4	3	3	2	1	1	2	8
	2	0	4	2	2	1	1	1	3	0	3
	3	0	0	0	0	1	0	0	1	1	1
Fairbank changes	0	3	1	1	2	1	4	3	1	4	9
	1	6	2	5	2	1	2	7	3	1	8
	2	1	2	3	2	2	0	1	1	5	8
	3	0	4	0	3	2	0	1	5	0	0

Preoperative (pre) and postoperative (post) values are presented as well as the number of patients presenting 0–3 grade changes in the different parameters considered during follow-up (Δ grade). Joint space narrowing (JSN) and changes according to Fairbank as measured on standing X-rays obtained in 25 patients. Radiological parameters for the failure cases, i.e. conversion to TKA, are not included in the table

from the study [14, 15, 36, 39]. Nowadays, focal cartilage defects would be treated in our institution with a chondrocyte transplantation, microfracture, or osteochondral plug transfer depending on its size. However, at that time, no such treatment was available in our institution and therefore these focal lesions were left untreated. This does not alter the fact that no significant correlation could be observed between the cartilage status at the time of transplantation and any clinical or radiological outcome parameter. The statistical analysis could have been influenced by the limited numbers.

Axial alignment is also considered as an important predictor of failure [12, 14, 39]. As previously published, we were able to show a significantly better clinical outcome at the final follow-up in the MMT + HTO group than in the MMT group [17]. This indeed shows that outcome is affected by axial alignment. However, the osteotomy was performed in case

Table 6 Overview of some magnetic resonance imaging parameters for the different patient groups ($N = 17$, > 10 years)

	Grade	MMT			MMT + HTO			LMT			Total
		Pre	Post	Δ grade	Pre	Post	Δ grade	Pre	Post	Δ grade	Δ grade
Femoral cartilage degeneration	0	2	1	2	0	0	2	1	1	4	8
	0–1	0	0	1	0	0	0	0	0	0	1
	1	0	0	1	0	0	2	0	0	2	5
	1–2	1	0	1	1	1	1	0	0	–	2
	2	1	1	1	1	0	–	1	1	–	1
	2–3	0	1	–	1	0	–	2	0	–	–
	3	2	0	–	1	1	–	0	0	–	–
	3–4	0	2	–	1	1	–	0	2	–	–
	4	0	1	–	0	2	–	2	2	–	–
Tibial cartilage degeneration	0	1	1	3	0	0	2	1	0	2	7
	0–1	0	0	–	0	0	1	0	0	1	3
	1	0	0	–	0	0	1	0	0	1	4
	1–2	1	0	1	0	0	1	0	0	1	2
	2	1	2	2	1	0	–	1	0	1	1
	2–3	1	1	–	2	1	–	2	1	–	–
	3	0	1	–	0	1	–	0	0	–	–
	3–4	1	0	–	2	1	–	0	3	–	–
	4	1	2	–	0	2	–	2	2	–	–
Meniscus signal intensity	0	1	1	6	4	4	5	5	2	3	14
	3	5	5	–	1	1	–	1	4	3	3
Meniscus position	Normal	6	1	1	4	2	3	5	1	2	6
	Part. extr.	0	5	5	1	2	2	1	5	4	11

Preoperative (pre) and postoperative (post) values are presented as well as the number of patients presenting × grade(s) changes in the different variables considered during follow-up (Δgrade)
Femoral and tibial cartilage degeneration (according to Yulish), meniscus signal intensity (according to Thornton) and meniscus position (coronal sections), as measured on MRI scans obtained in 17 patients

of varus malalignment and thus one might argue that a population consisting of symptomatic meniscectomized knees with varus malalignment and treated by an isolated osteotomy, i.e. without the meniscal transplant, would be a more appropriate control group. Long-term outcome data on HTO specifically for the treatment of symptomatic meniscectomized knees, however, are also lacking in the literature, making any comparison impossible for now. Nonetheless, in our series axial alignment did not significantly correlate with any of the investigated clinical and radiological or MRI parameters. A possible explanation for this observation could be that we corrected each varus aligned lower limb by an HTO, thereby eliminating this patient group—with a known risk factor for early failure, i.e. varus alignment—from the study.

Limited data is available on the progression of degenerative articular changes after this type of surgery. No previous medium- and long-term reports have indicated that meniscus allografting halts or slows down further degeneration. We have provided proof that progression of cartilage degeneration according to MRI and radiological criteria was halted in a number of patients, indicating a potential chondroprotective effect. Progressive articular cartilage degeneration changes are reported in the literature to occur in up to 89% of the cases after total meniscectomy, as radiographically observed in long-term follow-up studies [5, 6]. No such long-term follow-up studies exist using MRI criteria. The presented patient population here consisted of persons with total meniscectomized knees who eventually became symptomatic enough to warrant a meniscal transplantation. It is likely that this fraction of patients with symptoms and signs of excessive joint loading secondary to meniscal deficiency develops osteoarthritis faster than the asymptomatic subpopulation. The absence of further joint space narrowing in 41% at final follow-up (>10 years) in this series thus seems favourable to the previously published data on radiographical changes after total meniscectomy [5, 6].

The lack of a control group consisting of conservatively treated symptomatic postmeniscectomized patients in this study is a limitation observed in all studies published on meniscal allografting: ethically it is unacceptable to refuse any proven treatment—i.e. in this case a meniscal allograft, TKA or osteotomy—to a symptomatic patient.

Grade III signal intensity of the graft was frequently observed already on the initial scans, and showed little tendency to change over time. Although grade III signal intensity of the meniscus is generally described as a linear signal extending to the surface of the meniscus, the observed signal changes within the allograft meniscus were described as non-uniform patchy grey appearance and not linear [34]. Therefore, the authors hypothesize that these signal changes do not represent tears of the allografts, but rather changes in water content and extracellular matrix composition when compared to the normal meniscus. This phenomenon takes place quite rapidly after the transplantation procedure and could be induced by a repair or remodelling process. The exact biological and histological significance of this phenomenon remains unknown. Of note is the small number of grafts with grade III signal in the MMT + HTO group. The effect of the osteotomy on this phenomenon remains a focus of future research. Progression of graft extrusion was also frequently noted. Extrusion is considered a sign of ensuing joint degeneration by some authors [47, 48]. However, we did not find a statistical difference in progression of cartilage degeneration between those with and those without extrusion, possibly due to the small numbers within each group.

In this study, the MRI outcome did not correlate with the clinical outcome. This observation has already been published by several authors [31, 49]. The evaluation of the outcome after meniscus allograft transplantation should therefore primarily be a clinical one. Nonetheless, MRI is considered an objective tool to assess the cartilage and the meniscus, and should hence be included when possible [50].

The limited number of patients available for MRI analysis, however, could have influenced the statistical analysis.

In conclusion, long-term results are encouraging in terms of pain relief and improvement of function. Despite this significant improvement, substantial disability and symptoms were present in all investigated subgroups. Progression of further cartilage degeneration or joint space narrowing was absent in a considerable number of cases, indicating a potential chondroprotective effect.

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Appendix

Test statistics

Questions	Mann–Whitney U	Wilcoxon W	Z value	Asymp. Sig. (2-tailed)	Exact Sig. [2*(1-tailed Sig.)] P value
S1	11	47	−2.26977	0.023221	**0.028127**
S2	16.5	52.5	−1.67271	0.094385	0.104895
S3	20.5	56.5	−1.47162	0.141123	0.234499
S4	20	56	−1.84871	0.0645	0.234499
S5	19	55	−1.48342	0.137964	0.194872
S6	13	49	−2.0982	0.035888	0.049883
S7	12	48	−2.23607	0.025347	**0.037918**
P1	8	44	−2.59808	0.009375	**0.010412**
P2	16.5	52.5	−1.71169	0.086954	0.104895
P3	18	54	−1.80739	0.070701	0.160528
P4	31.5	67.5	−0.05576	0.955531	0.95913
P5	21.5	57.5	−1.20761	0.227195	0.278632
P6	12	48	−2.24733	0.024619	**0.037918**
P7	18	54	−1.65145	0.098648	0.160528
P8	11	47	−2.47717	0.013243	**0.028127**
P9	13	49	−2.16995	0.03001	0.049883
A1	19	55	−1.44743	0.147778	0.194872
A2	22	58	−1.11803	0.263552	0.328205
A3	22	58	−1.12938	0.258736	0.328205
A4	16	52	−1.87523	0.060761	0.104895
A5	28.5	64.5	−0.38651	0.699119	0.720901
A6	24	60	−0.97301	0.330549	0.441803
A7	14	50	−2.18282	0.029049	0.064957
A8	18.5	54.5	−1.49815	0.134094	0.160528
A9	15	51	−2.07379	0.038099	0.082984
A10	12	48	−2.56776	0.010236	**0.037918**
A11	15	51	−2.07379	0.038099	0.082984
A12	20	56	−1.5667	0.117185	0.234499
A13	12	48	−2.58199	0.009823	**0.037918**
A14	14	50	−2.19578	0.028108	0.064957
A15	16	52	−2.2188	0.0265	0.104895
A16	15.5	51.5	−1.83107	0.067089	0.082984
A17	15	51	−2.07379	0.038099	0.082984
SP1	27	63	−0.56662	0.57097	0.645377
SP2	14	50	−2.03984	0.041366	0.064957
SP3	18.5	54.5	−1.52597	0.127018	0.160528
SP4	13	49	−2.06815	0.038626	0.049883
SP5	25.5	61.5	−0.69983	0.484034	0.505361
Q1	26	62	−0.6475	0.517309	0.573737
Q2	27	63	−0.54339	0.586859	0.645377
Q3	11.5	47.5	−2.20886	0.027184	**0.028127**
Q4	17	53	−1.64054	0.100892	0.130381

Specific KOOS data analysis (Mann–Whitney U test) on specific questions rated within the subscales symptoms (S1-7), Pain (P1-9), activities of daily living (A1-17), sports and recreation (SP1-5), and quality of life (Q1-4) for medial allografts with or without a high tibial osteotomy. Significant P values, i.e. less than 0.05, are in bold

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