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Autologous chondrocyte implantation versus microfracture for knee cartilage injury: a prospective randomized trial, with 2-year follow-up

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Abstract The objective was to evaluate the functional performance over a 2-year period following autologous chondrocyte implantation (ACI) in an open knee procedure compared to microfracture. Objective functional outcome was studied as secondary analysis in a subgroup of patients, in a randomized clinical trial, with concealed allocation and independent evaluators. Sixty-seven patients with local cartilage defect, with a mean size of 2.4 cm^2 (SD 1.5) of the femoral condyle of the knee were included. Thirty-three patients underwent the microfracture and 34 the ACI procedure. An identical rehabilitation protocol was implemented for both groups. Active knee flexion and extension range, anterior laxity, knee extension strength (concentric at 60°/s) and single leg hop performance (single hop, crossover triple hop and 6 m timed hop test) were evaluated pre-surgery and at 6, 9,12 and 24 months post-surgery. We calculated the symmetry index for individual and four performance tests pooled. Mixed linear model analyses were used with confidence interval set at 95%. The change over 2 years for the pooled performance-based tests was comparable between the two treatment arms. At 2 years, 70% (38/54) of all patients returned to >85% symmetry in overall functional performance. A decrease in functional performance at 6 months following ACI resulted in slower recovery at 9 and 12 months compared to microfracture. Rehabilitation following both cartilage repair procedures is a lengthy process. At 2 years after surgery, ACI patients have similar overall functional outcome compared to microfracture patients.

Keywords Cartilage · Exercise · Knee · Physical therapy · Surgery · Treatment outcome

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Introduction

Current scientific evidence on the objective functional outcome after cartilage repair in the knee is lacking [13]. Little is known about the influence of cartilage repair procedures such as autologous chondrocyte implantation (ACI) and microfracture on the recovery of patients. These two procedures have different direct physical impact on the patient's knee [36]. Microfracture is an arthroscopic procedure, while ACI is a two-step open knee procedure. Ferruzzi et al. [5] observed a slower functional recovery of open ACI compared to an arthroscopic procedure. Noyes et al. [29] also observed a different recovery period for open versus arthroscopic procedures for an anterior cruciate reconstruction. These studies suggest a potential slower functional recovery following open knee surgery.

Patients suffering from a local cartilage defect in the knee, encounter a wide variety of problems including recurrent knee pain, giving way, muscle weakness or difficulties with sitting, walking, jumping and running [7].

Functional outcome is mainly evaluated with patient-reported outcome scales such as the Lysholm, the modified Cincinnati, the knee injury and osteoarthritis outcome score (KOOS) and the International Knee Documentation Committee (IKDC) form. These patient-reported outcome measures provide a unique and important perspective on how patients feel and function. The subjective functional outcome results of the cartilage repair studies, with use of different surgical techniques, have varied from good to excellent [2, 5, 13, 23, 24, 37, 42]. Despite the long history of cartilage repair surgery in the knee, limited research with objective outcomes has been done [13]. Only the IKDC adds an objective evaluation form to a subjective questionnaire. As a result, a minority of studies following cartilage repair reported objective outcome measures [5, 9]. The objective evaluation of the IKDC has seven knee-specific domains: effusion, passive range of motion, harvest site pathology, ligament evaluation, compartment and radiographic findings and last the symmetry index of single hop performance as functional test. So even if the IKDC is used, information of the functional performance of the patient contributes only partially to the reported objective outcome [11].

Different authors suggested that objective measures may be informative on the functioning of patients, in particular when a patient or athlete prefers to return to work-related activities or do potentially injurious sports [1, 15, 25, 40, 41]. Objective measures are widely used after other surgical knee interventions [1, 15, 40, 41]. Isokinetic strength testing, standard goniometry and anterior drawer test have been shown to be reliable and valid measures for, respectively, quadriceps strength, active knee range of motion and anterior knee laxity [6, 18, 34, 43]. Standardized single leg hop tests are frequently used to assess the functional performance of the lower limb. These tests are designed to mimic the greater demands imposed on the knee in the everyday environment [27, 30]. Furthermore, the single leg hop tests offer benefits of providing between-leg and within subject comparisons without the need to rely on population-specific normative data [27].

Therefore, the aims of this secondary analysis are to compare the objective functional outcome in patients treated with ACI versus microfracture up to 2 years after surgery and to evaluate the progress in functional recovery over time for both groups, within a randomized trial. The hypotheses of the present study are:

1. The recovery of functional performance following ACI in an open knee procedure is slower compared to an arthroscopic microfracture.
2. The overall functional performance at 2 years after ACI with an open knee procedure is superior when compared to the arthroscopic microfracture treatment.

Methods

Participants

This clinical study involved a subgroup of patients ($N = 67$) of the 118 patients enrolled in the multicenter randomized prospective trial conducted by Saris et al. (Fig. 1). The 67 patients were enrolled by the two major recruiting centers: University Medical Hospital, Utrecht, in the Netherlands and the University Hospitals of Leuven in Belgium. The study conformed to the Declaration of Helsinki and was conducted according to the International Conference on Harmonization Guidelines for Good Clinical Practice. Informed consent was obtained from all patients and the study protocol was approved by the ethics review board at both centers. Eligible patients were aged between 18 and 50 years, had a symptomatic single cartilage lesion of the femoral condyles between 1 and 5 cm^2 and agreed to actively participate in a strict rehabilitation and follow-up program (Table 1). Patients with recent osteochondritis dissecans, advanced osteoarthritis, complex ligamentous instability of the knee and malalignment exceeding 5°, patients enrolled by centers who were not able to do the objective outcome measures were excluded [36].

Intervention

Study procedure

Patients randomly allocated to the microfracture group and ACI group were treated according to the surgical technique described by Steadman et al. and Brittberg et al. [2, 39]. The ACI was performed using characterized chondrocytes (CCI), ChondroCelect® (TiGenix N.V., Haasrode, Belgium). After surgery, both groups were enrolled in an identical standardized rehabilitation program. Since surgical intervention was not blinded, two independent physical therapists were instructed and trained at the investigational sites to objectively assess the patients.

Rehabilitation program

All patients started the standardized rehabilitation protocol on the day following hospital discharge. During the

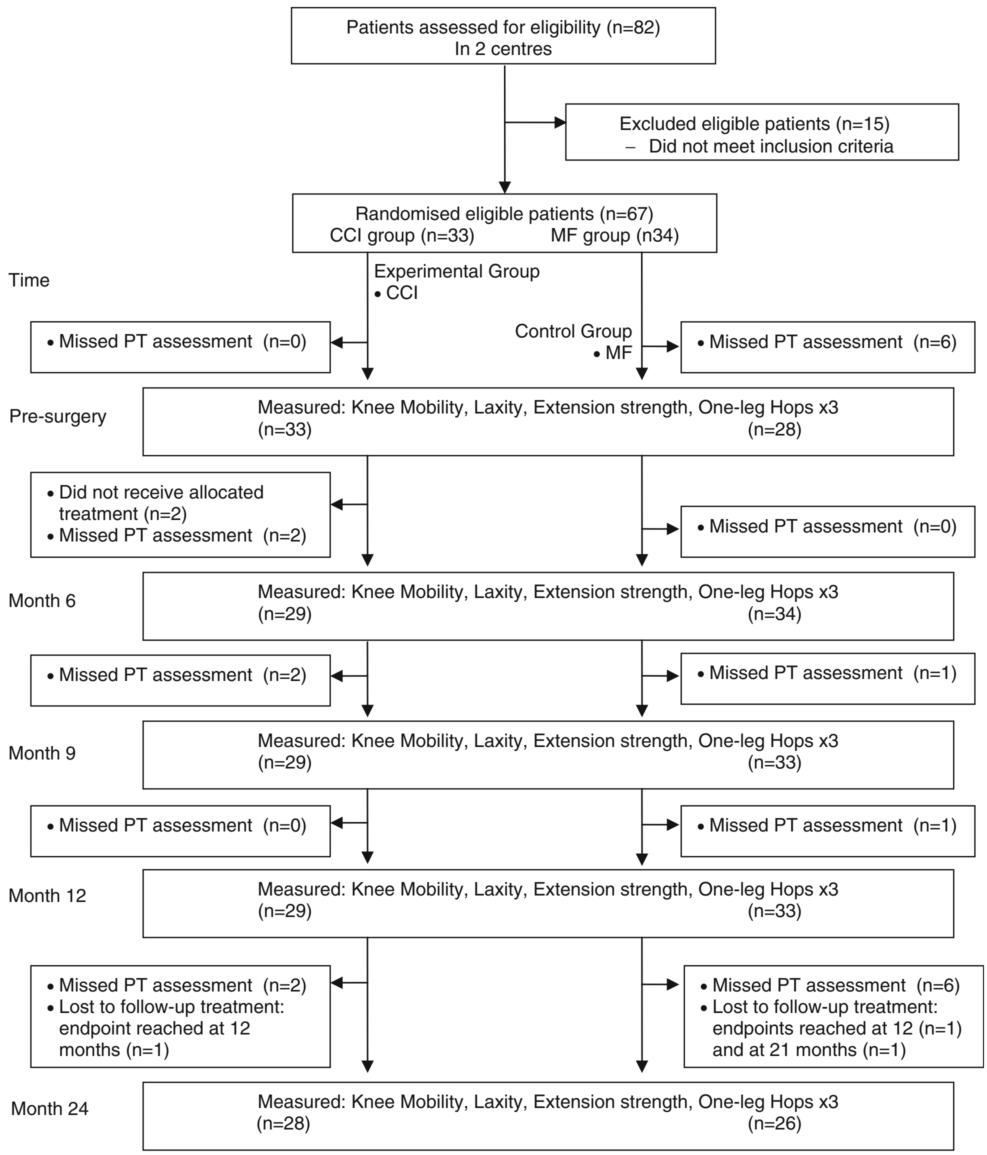


Fig. 1 Design and flow of patients through the trial. *PT* physiotherapy, *MF* microfracture, *CCI* ACI with characterized chondrocytes

3–5 days of the hospital stay, the ACI-treated patients received relative bed rest with continuous passive motion for 2–3 h each day and quadriceps setting exercises in full extension. The rehabilitation program was based on guidelines for rehabilitation following microfracture and ACI [31, 38, 39] and on the different phases of wound healing, with special focus on graft protection and wound control [12]. Restrictions on mobility and weightbearing were described in detail. Briefly, only non-weightbearing exercises were allowed during the first 2 weeks. After 2 weeks, weightbearing could be started with 10–15 kg. Subsequently, an increase of 10–15 kg loading per week was allowed. All patients wore a custom-made unloader brace (unloader XT®, Generation-II Orthotics, Canada) during the first 8 weeks [3, 16, 20, 33]. Crutches were used during the first 5 weeks and patients were allowed to reduce the use of crutches gradually from week 6 if the gait pattern was normal and swelling, pain and proprioception were optimal. Joint circulation exercises, such as heel slides, stationary cycling or rowing without resistance were recommended to be performed for up to 1 h each day as soon as motion was permitted. Stationary bicycle training as well as static and dynamic bilateral closed chain exercises was introduced at 6 weeks. The duration, frequency and intensity of specific exercises were not strictly imposed, but could be adapted to the patient's needs.

Strength training in the first 2 weeks consisted of isometric m. quadriceps settings in varied knee positions for muscle re-education. No open chain exercises were allowed. Proprioception and neuromuscular control were

Table 1 Characteristics of patients and centers

Characteristic	Randomized ($n = 67$)		Lost to follow-up ($n = 13$)	
	CCI ($n = 33$)	MF ($n = 34$)	CCI ($n = 5$)	MF ($n = 8$)
Patients				
Age (year), mean (SD)	31 (8)	31 (8)	33 (6)	33 (10)
Gender, *n* (%) males	22 (66)	24 (70)	3 (60)	4 (50)
Female	11 (33)	10 (30)	2 (40)	4 (50)
Height (cm), mean (SD)	179 (10)	177 (8)	179 (11)	176 (9)
Body mass index, (kg/m^2), means (SD)	24 (3)	25 (3)	27 (3)	25 (4)
Knee condition at baseline				
Duration since onset (year), mean (SD)	4 (4)	3 (3)	8 (5)	4 (4)
Symptoms onset category, *n* (%) gradual	15 (45)	12 (35)	2 (40)	3 (37)
Acute	18 (55)	22 (65)	3 (60)	5 (62)
Previous knee surgery, *n* (%) 1	19 (58)	18 (53)	2 (40)	3 (37)
≥2	8 (24)	7 (21)	3 (60)	2 (25)
No	6 (18)	9 (26)	0 (0)	3 (37)
Normal opposite knee, *n* (%)	19 (58)	28 (82)	2 (40)	6 (75)
Knee condition at baseline arthroscopy				
Defect size on femoral condyle post-debridement (cm^2), means (SD)	2.5 (1)	2.3 (1)	2.0 (1)	2.1 (1)
Concomitant lesions (ACL/ML) treated during study *n* (%)	3 (1)	2 (1)	0 (0)	0 (0)
Centers: patients treated, *n* (%)				
Center 1	19 (58)	17 (50)	2 (40)	2 (25)
Center 2	14 (42)	17 (50)	3 (60)	6 (75)

CCI Characterized chondrocyte implantation group, *MF* microfracture group, *SD* standard deviation, *ACL* anterior cruciate ligament, *ML* medial collateral ligament

the primary goals for strength training during weeks 3–6. Progressive closed chain exercises were started. After 3 months, strength training was intensified by an increase in work load, and after 6 months, by increasing resistance and decreasing the number of repetitions. During the final phase of the rehabilitation (10 months after surgery), impact training was initiated, as were heavier weight training and sport-specific exercises. During the final phase, low-impact activities could be started depending on sports discipline and sports level of the patient. High-impact activities were allowed at 16 months and after approval of a medical specialist.

Outcome measures

Objective functional outcome was investigated within three domains: mobility, strength and hop performance. Following assessments were done: active knee flexion and extension, anterior knee laxity, concentric quadriceps strength at 60°/s and performances on three different hop tests including single hop for distance (*single hop*), the triple crossover hop for distance (*crossover hop*) and the 6-m timed hop (*timed hop*). For the four performance-based tests (strength and 3 hop tests) the symmetry index scores were calculated for each patient and at each time point. Additionally to evaluate the overall functional recovery, the symmetry indexes of the four tests were combined (pooled) by calculating the mean [32]. To interpret results for the overall functional recovery, a change over time for the pooled symmetry index of more than 7.05% was considered to be a relevant change [32].

All tests were performed pre-surgery and at 6, 9, 12 and 24 months post-surgery.

Statistical analyses

To compare the total study group, ACI and microfracture, at baseline ($n = 67$) and at 24 months ($n = 54$) with the patient population of Saris et al. ($n = 118$), a median one-way analysis was used for continuous variables and a two-tailed Fisher's exact test for categorical variables with the significant level set at $P < 0.05$.

Descriptive statistics (means and SD) were calculated for the outcomes measures performed: the symmetry index and pooled symmetry index. Changes from baseline were calculated for each time point. To account for dependence of repeated outcome measures on the same subject and missing data, all analyses on patient outcome relied on a mixed linear model, with subjects as random variables, group and visit as dependent categorical variables and confidence interval (CI) set at 95%. Contrast analyses were performed to test consecutive time points within each treatment group [19, 26].

Results

Sixty-seven patients were enrolled in the study and randomized to ACI ($n = 33$) and microfracture ($n = 34$, Fig. 1). Characteristics of the patients at baseline ($n = 67$) and lost to follow-up ($n = 13$) are summarized in Table 1. The study group at baseline and at 24 months did not differ on any demographic, knee condition or lesion parameter from patients of the total population in the RCT conducted by Saris et al. [36].

Active knee flexion improved over time in both treatment groups (95% CI microfracture 4.5–11.9; ACI 4.5–12.3). At 2-year follow-up, active knee flexion averaged 141° (SD 10.7, Table 2). Active knee extension and anterior laxity remained unchanged over time and were similar for both groups. The overall mean active extension for the target knee was 2.6° (SD 2.5) and 2 of all the patients showed an abnormal knee laxity.

No significant group effect (95% CI −1.0–19.9) and visit effect (95% CI −11.5–3.2) were observed. Between pre-surgery measurements and 6 months, the symmetry index for knee extension strength showed a significant decrease of 11% for the microfracture (95% CI −18.2 to −4.1) and 19% for the ACI group (95% CI −20.8 to −6.3). Between 6 and 24 months the knee extension strength symmetry index improved 19% in microfracture patients (95% CI 9.2–24.3) and 23% in ACI patients (95% CI 10.3–25.2). Solely at 9 months the microfracture group showed a significant improvement for the extension strength symmetry index compared to ACI patients (95% CI −19 to −1; Table 3). Before surgery, quadriceps weakness (>20% deficit) was observed in 50% of all patients. At 1 year an extension strength deficit was observed in 33% of the patients and at 2-year follow-up in 26% of the patients.

A significant group effect was observed for the symmetry index *single hop* (95% CI 1.1–19.8). At 6, 12 and 24 months the microfracture group showed a significant improvement of the symmetry index for the single hop compared to ACI patients (Table 3). The ACI patients showed a decrease of 9% up to 2 years after surgery (95% CI −15.1 to −1.7), whereas microfracture patients improved with 10% (95% CI 0.4–15.0).

Results for the symmetry index of the *crossover hop and the timed hop* showed no significant group effect. The microfracture group showed only at 9 months a significant improved symmetry index for both tests compared to ACI patients (Table 3). Performance of the opposite leg improved significantly over 2 years in both groups for the

Table 2 Mean (SD) for each group and mean (95% CI) between-group difference for all outcomes of operated knee

Outcome	Groups										Difference between groups			
	Month 0		Month 6		Month 9		Month 12		Month 24		Month 6	Month 9	Month 12	Month 24
	CCI ($n = 32$)	MF ($n = 28$)	CCI ($n = 29$)	MF ($n = 34$)	CCI ($n = 29$)	MF ($n = 33$)	CCI ($n = 31$)	MF ($n = 33$)	CCI ($n = 28$)	MF ($n = 26$)	CCI minus MF	CCI minus MF	CCI minus MF	CCI minus MF
Knee strength														
Extension (N m)	180 (66)	181 (67)	147 (73)	174 (61)	166 (67)	195 (61)	179 (64)	204 (61)	196 (70)	214 (60)	−27 (−60 to 6)	−29 (−61 to 3)	−25 (−56 to 6)	−21 (−53 to 17)
One–leg hops														
Single hop (cm)	133 (43)	134 (59)	121 (45)	131 (51)	130 (59)	140 (51)	131 (56)	148 (49)	137 (57)	163 (44)	−10 (−34 to 14)	−10 (−37 to 17)	−17 (−43 to 9)	−26 (−53 to 1)
Crossover hop (cm)	360 (127)	315 (145)	356 (135)	360 (138)	364 (152)	422 (123)	374 (159)	410 (143)	400 (153)	442 (138)	−4 (−72 to 64)	−59 (−126 to 10)	−36 (−110 to 38)	−42 (−120 to 36)
Timed hop (s)	3.6 (1.9)	3.6 (1.4)	3.7 (1.4)	3.6 (1.1)	3.6 (1.2)	3.0 (0.7)	3.5 (1.2)	3.1 (1.0)	3.2 (1.1)	2.6 (0.6)	0.1 (−0.5 to 0.7)	0.6* (0.1 to 1.1)	0.4 (−0.1 to 0.9)	0.6* (0.1 to 1.1)
Knee mobility														
Extension (°)	2 (3)	3 (2)	3 (2)	2 (2)	2 (3)	2 (2)	2 (1)	2 (2)	2 (2)	3 (2)	1 (0.0 to 1.9)	0 (−1.3 to 1.3)	0 (−0.8 to 0.8)	−1 (−2 to 0.1)
Flexion (°)	131 (8)	133 (12)	135 (9)	135 (7)	138 (9)	138 (5)	140 (7)	138 (6)	141 (11)	141 (10)	0 (−3.9 to 3.9)	0 (−3.6 to 3.6)	2 (−1.2 to 5.1)	0 (−5.6 to 5.6)

CCI Characterized chondrocyte implantation group, *MF* microfracture group, *SD* standard deviation, *CI* confidence interval, 95% CI's noted in table are based on the difference between two sample means

* Significant difference with CI set at 95%

Table 3 Symmetry index (SI) of knee extension strength, one-leg hops, tests pooled and tests pooled change from baseline, mean (SD) for each group and mean (95% CI) between-group difference

Outcome	Groups										Difference between groups			
	Month 0		Month 6		Month 9		Month 12		Month 24		Month 6	Month 9	Month 12	Month 24
	CCI (*n* = 32)	MF (*n* = 28)	CCI (*n* = 29)	MF (*n* = 34)	CCI (*n* = 29)	MF (*n* = 33)	CCI (*n* = 31)	MF (*n* = 33)	CCI (*n* = 28)	MF (*n* = 26)	CCI minus MF	CCI minus MF	CCI minus MF	CCI minus MF
Knee strength														
SI extension	78 (19)	87 (25)	66 (22)	76 (22)	73 (21)	83 (16)	79 (20)	85 (14)	83 (20)	92 (19)	−10 (−21 to 1)	−10* (−19 to −1)	−6 (−14 to 2)	−9 (−19 to 1)
One-leg hops														
SI single hop	88 (15)	87 (20)	73 (13)	83 (17)	78 (20)	84 (15)	79 (18)	89 (12)	83 (20)	96 (12)	−10* (−18 to −2)	−6 (−15 to 3)	−10* (−17 to −3)	−13* (−22 to −4)
SI crossover hop	88 (15)	94 (18)	81 (17)	86 (17)	83 (12)	93 (11)	82 (21)	90 (13)	90 (13)	95 (8)	−5 (−13 to 3)	−10* (−17 to −3)	−8 (−16 to 1)	−5 (−11 to 1)
SI timed hop	86 (14)	88 (15)	78 (16)	84 (19)	79 (13)	93 (17)	80 (18)	88 (16)	89 (13)	92 (11)	−6 (−15 to 3)	−14* (−22 to −6)	−8 (−16 to 0.3)	−3 (−9 to 3)
Tests pooled														
If >2 tests performed	CCI (*n* = 32)	MF (*n* = 28)	CCI (*n* = 18)	MF (*n* = 20)	CCI (*n* = 23)	MF (*n* = 21)	CCI (*n* = 24)	MF (*n* = 24)	CCI (*n* = 22)	MF (*n* = 16)	CCI minus MF	CCI minus MF	CCI minus MF	CCI minus MF
SI of tests pooled	82 (15.8)	87 (17.9)	68 (23.1)	78 (19.1)	74 (19.0)	86 (12.5)	76 (18.0)	87 (11.5)	85 (17.1)	95 (15.5)	−10 (−23 to 3)	−12* (−22 to −2)	−11* (−18 to −3)	−11 (−23 to 1)
Change from baseline			−11.4 (12)	−7.2 (18)	−2.4 (13)	+1.2 (20)	−3.5 (20)	−0.1 (18)	+1.6 (12)	+6.5 (14)	−4.2 (−14 to 5)	−3.6 (−13 to 6)	−3.6 (−14 to 7)	−4.9 (−13 to 3)

CCI Characterized chondrocyte implantation group, *MF* microfracture group, *SD* standard deviation, *CI* confidence interval, 95% CI's noted in table are based on the difference between two sample means

* Significant difference with CI set at 95%

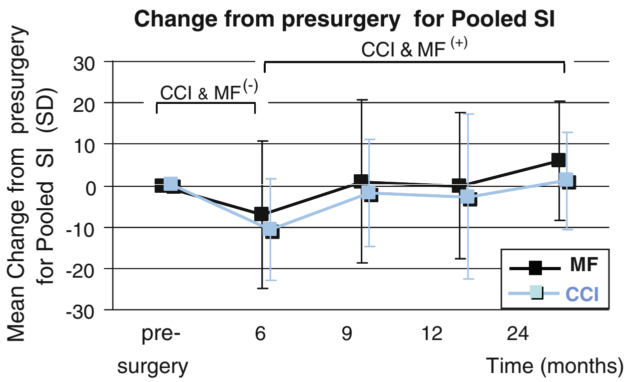
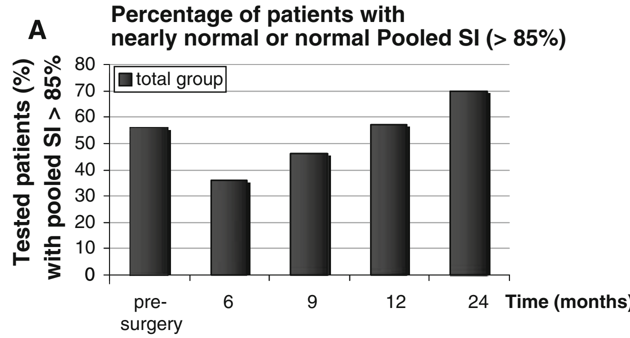


Fig. 2 Changes from pre-surgery for pooled symmetry index scores for both treatment groups: microfracture (*MF*) and ACI with characterized chondrocytes (*CCI*) over 2-year period, with significant differences (of >7.0%) illustrated (− decrease and + increase), using mixed linear model analysis and significance level at $P < 0.05$

single hop (95% CI 1.5–14.5) for the crossover hop (95% CI 2.7–65.0) and timed hop (95% CI 1.9–49.5).

The overall functional recovery was defined as the mean change from pre-surgery for the pooled symmetry indexes. Analysis showed no significant difference between microfracture and ACI at 2 years (95% CI −3.8 to 17.3, Fig. 2; Table 3). At 6 months, both groups showed a significant decrease in functional performance, with 7% for the microfracture group (95% CI −17.8 to −4.1) and 11% for the ACI group (95% CI −26.7 to −12.8). Functional performance of both groups improved significantly between 6 and 9 months (95% CI microfracture 1.5–15.6 and ACI 3.5–17.6). The microfracture patients showed an average improvement for this period of 8% and ACI patients of 9%. Since the decrease in functional performance at 6 months was less pronounced in the microfracture group, the microfracture group recovered to pre-surgery levels of functional performance at 9 months (Fig. 2). At 9 and 12 months the microfracture group showed a significant improved pooled symmetry index compared to ACI patients (Table 3). Both groups showed a small but significant improvement between 12 and 24 months, respectively, 5% for the ACI group (95% CI 0.2–17.9) and 6% for the microfracture group (95% CI 0.3–15.7). In the total study group, 'nearly normal' to 'normal' values for overall functional performance (pooled symmetry index >85%) were observed in 70% (38/54) of the patients at 2 years (Fig. 3a). Of the patients with nearly normal to normal symmetry at 2-year follow-up, 17 patients originated from the microfracture group and 19 from the ACI group. At 6, 9 and 12 months after surgery, less ACI patients demonstrated nearly normal or normal symmetry in overall functional performance compared to microfracture patients (Fig. 3b).



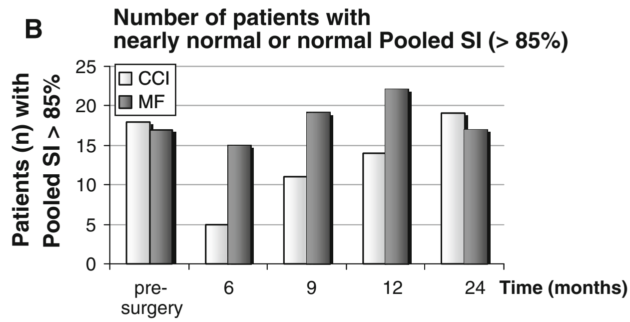


Fig. 3 **a** Percentage in total study group and **b** number of patients in each treatment arm with nearly normal or normal symmetry for overall functional performance or pooled symmetry index (SI) >85%. ACI with characterized chondrocytes (*CCI*) and microfracture (*MF*)

Discussion

The most important finding of the present study was that the functional recovery at 2 years is comparable for both groups. The results show no superiority of ACI over microfracture at 2 years. Recently, Ferruzzi et al. [5] reported slower recovery the first year following ACI with open knee surgery compared to the arthroscopic procedure. Similar differences were identified in the present study. More patients in the microfracture group recovered overall functional performance at 9 and 12 months. When considering changes from pre-surgery to 2-year follow-up no significant group effect was observed for overall functional recovery (95% CI −3.8 to 17.3). Saris et al. [36] concluded a structural superiority of cartilage repair following ACI with characterized chondrocytes over microfracture at 12 months. As a result ACI patients may have more potential capacity to adapt and withstand functional training compared to microfracture patients. The similar recovery between 1 and 2 years in both groups does not support this assumption. On the other hand, at 2 years after surgery 79% ($n = 22$) of the patients assessed in the ACI group could perform more than 2 of 4 tests and withstand the test procedure, compared to 62% ($n = 16$) of the microfracture patients.

Within the field of cartilage repair, no studies so far have reported on strength. Comparing the present study results with reports on strength following anterior cruciate ligament reconstruction, we detect a comparable decrease in extension strength symmetry at 6 months and recovery at 1 year [4, 8, 14, 35]. However, the mean age of patients in anterior cruciate ligament reconstruction studies is significantly younger (27.2 years) and the mean time period between injury and surgical intervention is shorter (3–12 months). Furthermore, the surgical procedure in all these anterior cruciate ligament reconstruction studies was arthroscopic, whereas in the present study half of the patients were treated with ACI in a two-step open knee procedure [4, 14, 17, 25].

For the *single hop test*, 51% (33/64) of the patients had a 'nearly normal' to 'normal' symmetry index at 1 year. This increased to 68% (37/54) at 2 years. Single hop symmetry index after anterior cruciate ligament reconstruction varies from 57% to 95% at 1 year [17, 21, 25]. Patients in the study showed a slower recovery for *crossover hop and timed hop* symmetry indexes compared to symmetry index after anterior cruciate ligament reconstruction surgery. For these two hop tests combined 63% (30/47) and 77% (34/44) of the study patients reached nearly normal to normal symmetry index at, respectively, 1 and 2 years, whereas anterior cruciate ligament reconstruction studies report overall normal or nearly normal symmetry index at 1 year [4, 10, 25]. In summary, the results show that functional hops, which are characterized by intense 'push of and landing', are only partially recovered at 1 and 2 years after cartilage repair surgery. When taking the minimal detectable change [32] into account, both microfracture and ACI patients showed that overall functional performance restored to pre-surgery levels at 2-year follow-up. Significant improvements of 13.7 and 13.0% were observed for the microfracture and the ACI patients between 6 month and 2-year follow-up (95% CI 12.9–27.5). These results suggest that functional training also in the long-term rehab follow-up is needed and appropriate for a number of patients following cartilage repair.

Noyes et al. and Mattacola et al. considered a symmetry index score of <85% as abnormal and did not recommend resuming sport activities with an impact on the knee joint [21, 28]. Overall, 57% of the patients following cartilage repair reached an acceptable pooled symmetry index of >85% at 1 year. At 2 years after surgery, 70% of the patients regained acceptable symmetry levels and could be advised to train for specific demanding sports activities [27].

Compared to the 'good to excellent' subjective outcome results reported in previous cartilage repair studies, the present study results on objective functional outcome are complementary [13]. The majority of patients regained a pre-surgery performance level and a minority improved. Mithöfer et al. [24] concluded that only 15% of recreational-level soccer players returned to play after ACI, although the majority (72%) had 'good to excellent' subjective outcomes. Additionally Mithoefer et al. [22] observed a decline in sports participation at 2 years after microfracture surgery. The authors could not identify the reason for this decline. As a result of these differences between subjective outcomes and effective return to demanding activities, we assume that objective outcomes in the present study are helpful to explain this phenomenon. The performance tests identify possible functional deficits and may clarify an underlying reason why patients following cartilage repair do not return to previous sport participation. However, the objective outcomes need to be read also with caution since they partially represent patient's intrinsic factors such as fear, motivation and coping. In order to reduce the risk of re-injury continuous functional strength training in a long-term rehabilitation phase is recommended. We propose clinicians to concentrate on improving functional performance in particular in patients with symmetry deficits at 1 or 2 years after cartilage surgery.

Although independently trained physical therapists conducted the assessments, a limitation of this study is that neither patients nor physical therapists were blinded to the treatment allocation. The methodological design with use of independent evaluators may not have been sufficient to overcome this limitation. In future studies blinding of the assessors could be realized by instructing patients to cover both knees with a simple sock prior to the functional assessments.

Insight in objective functional outcome measures that are clinically relevant in these patient populations is limited. This study provides detailed information on objective functional outcome over a 2-year period following the two most reported cartilage repair procedures. To date, comparisons with other cartilage repair studies are impossible.

Conclusion

The present study shows that the functional recovery following cartilage surgery is a lengthy process. The impact of the two-step surgical procedure influenced the recovery pace in the ACI group. Both cartilage repair groups reached comparable overall functional symmetry at 2 years post-surgery.

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