Randomized Study of Long-term (15-17 Years) Outcome After Microfracture Versus Mosaicplasty in Knee Articular Cartilage Defects

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Background: Few comparative randomized long-term studies on microfracture versus mosaicplasty have been published, and only 2 studies reported a follow-up of 10 years.

Hypothesis/Purpose: The purpose was to compare the clinical outcome of microfracture versus mosaicplasty/osteochondral autograft transfer in symptomatic cartilage lesions. The null hypothesis was that the outcome was not statistically different at any point of time.

Study Design: Randomized controlled trial; Level of evidence, 1.

Methods: Forty patients with articular cartilage defects were randomized to undergo cartilage repair by either microfracture (n = 20) or mosaicplasty (n = 20). Inclusion criteria were as follows: age 18 to 50 years at the time of surgery, 1 or 2 symptomatic focal full-thickness articular chondral defects on the femoral condyles or trochlea, and size 2 to 6 cm^2. The main outcome variable was the Lysholm knee score recorded before the surgery and at 12 months, median 5 years, median 10 years, and minimum 15 years after the surgery.

Results: Forty patients were included in the study (28 men, 12 women; median age, 32 years; range, 18-48 years). Defects with a median size of 3.5 cm^2 (range, 2-5 cm^2) were treated. A significant increase in the Lysholm score was seen for all subjects—from a mean 53 (SD, 16) at baseline to 69 (SD, 21) at the minimum 15-year follow-up (P = .001). The mean Lysholm score was significantly higher in the mosaicplasty group than the microfracture group at 12 months, median 5 years, median 10 years, and minimum 15 years: 77 (SD, 17) versus 61 (SD, 22), respectively (P = .01), at the last follow-up. At all follow-up time points, the difference in mean Lysholm score was clinically significant (>10 points).

Conclusion: At short, medium, and long term (minimum 15 years), mosaicplasty results in a better, clinically relevant outcome than microfracture in articular cartilage defects (2-5 cm^2) of the distal femur of the knee in patients aged 18 to 50 years.

Keywords: microfracture; mosaicplasty; knee; articular cartilage defects; arthroscopy

Focal chondral lesions of the knee are debilitating and impair quality of life and clinical function to a similar degree or worse as for patients scheduled for knee replacement[15] or ACL reconstruction.[33] These lesions are commonly occurring, as displayed by the 19% incidence in a group of 1000 knee arthroscopies in a prospective study by Hjelle et al.[16] Årøen et al[1] and Solheim et al[33] found similar incidences in studies with a similar design.

Chronic articular cartilage lesions have little or no potential for spontaneous healing, and their treatment continues to pose a challenge for orthopaedic surgeons.[17] The last decades have seen a range of new treatment options, including microfracture[29,34] and autotransplantation of osteochondral cylinders (osteochondral autograft transfer [OAT] or mosaicplasty) from less weightbearing areas to the defect area.[12] Whereas the short-term results after cartilage repair procedures are acceptable for most patients, few regain normal pain-free function,[7,25] and the results seem to deteriorate with time.[6,23,31] So far, very few comparative randomized long-term studies on microfracture and mosaicplasty/OAT have been published; only 2 studies reported a follow-up ≥10 years.[9,36]

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The purpose of this randomized study was to compare the clinical outcome of microfracture versus mosaicplasty cartilage repair in articular defects of the knee at short term (12 months), midterm (median 5 years), and long term (median 10 years, minimum 15 years). The null hypothesis was that the outcome was not statistically different between the 2 methods at any time point after the surgery.

METHODS

Among patients treated at our institution from February 2000 to April 2002, 40 were enrolled in a randomized clinical study comparing microfracture and mosaicplasty cartilage repair surgery of articular cartilage defects of the knee (Figure 1). Randomization was done in the operating room after arthroscopic examination, debridement, and measure of the defects, via sequentially numbered opaque sealed envelopes in blocks of 20. The envelopes were kept in a locked container and opened by staff not otherwise involved in the study. Blinding of patients for type of treatment was not part of the protocol. Thus, the patients were blinded only during the surgery (and randomization procedure). After the surgery, the type of treatment received was revealed if/when the patient asked.

Inclusion criteria were as follows: age 18 to 50 years at the time of surgery and 1 or 2 symptomatic focal full-thickness articular chondral defects (International Cartilage Repair Society grade 3-4) on the femoral condyles or trochlea, with a total size 2 to 6 cm^2 (verified by arthroscopic examination). Exclusion criteria were as follows: joint space narrowing (to a space <4 mm) on standard anteroposterior radiographs, >5° varus or valgus malalignment, previous or concurrent realignment surgery, ligament instabilities, or the inability to follow the rehabilitation protocol.

The baseline data were acquired from a 2-page standardized form completed by the patient (page 1) and the surgeon (page 2). Page 1 contained details about preoperative symptoms and function, including the Lysholm knee score.[35] Page 2 contained perioperative findings and details about the surgery performed, including localization and size of the articular cartilage defect, similar to the system recommended by the International Cartilage Repair Society.[3] For the follow-up, the patients completed a 1-page form similar to the baseline questionnaire. Photographic images were captured by the surgeon (by use of the arthroscope) before and after the cartilage repair procedure.

At 12 months and yearly up to 5 years postoperatively, the patients completed the form when attending our outpatient clinic as routine check-ups. Later, every few years (in 2006, 2009, and 2012), we mailed the patients a questionnaire and asked them to fill in and return it. The last follow-up (minimum 15 years) was conducted from October 2016 to April 2017.

Among patients having undergone a knee replacement after the cartilage repair surgery, the most recent Lysholm score before the replacement procedure was recorded and used for the calculations. At the last follow-up, we asked the patients to answer (yes or no) if they would have gone through the surgery with their current knowledge of the outcome.

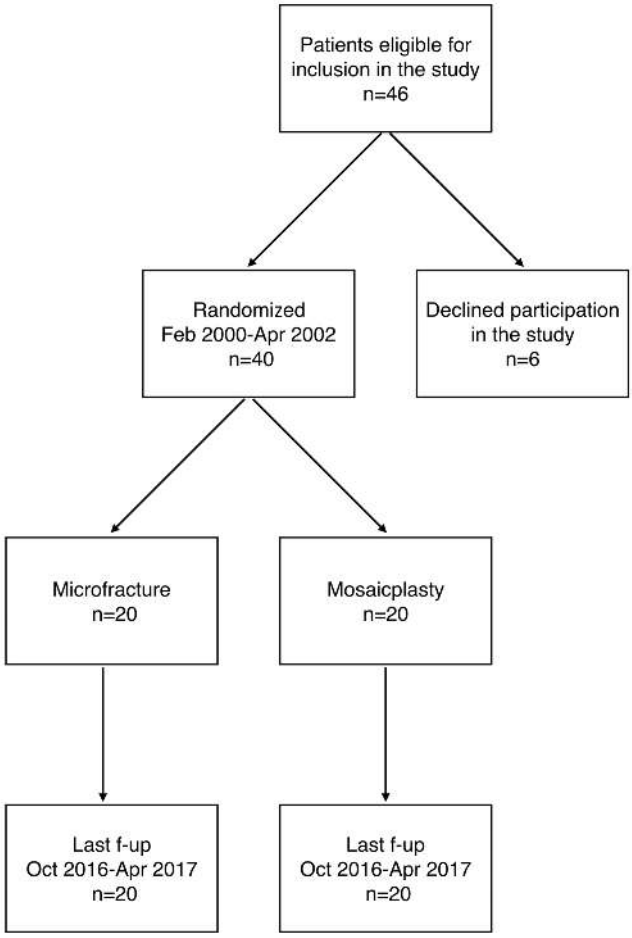

Figure 1. Flowchart showing patients eligible for inclusion, the randomization process, and the number available between the 2 groups for the last long-term follow-up (f-up; minimum, 15 years).

Independent researchers not involved in the treatment of the patients collected the data. The data were stored in a local database (Access; Microsoft Corporation). The regional committees for medical and health research ethics (REC; REC West, University of Bergen, Norway) reviewed and approved of the study (117.99) in February 2000. All patients gave their informed consent before inclusion in the study.

Surgical Techniques

After an arthroscopic evaluation, a microfracture or mosaicplasty procedure was performed. The lesion was debrided to subchondral bone and around the edges until healthy surrounding cartilage remained. The area of the lesion was calculated as centimeters squared after the lesion was measured with a meniscal probe.[16]

The microfracture procedure was performed as formerly described by Steadman et al.[34] Angled awls were used for making holes through the subchondral bone plate 3 to 4 mm apart. The inflow was stopped, and flow of marrow elements from the openings into the defect was verified.

The mosaicplasty procedure (Smith & Nephew Inc) was performed as described by Hangody et al.[12,13] Grafts were harvested from the periphery of the femoral condyles at the level of the patellofemoral joint and transplanted to corresponding bur holes in the defect. The procedure was performed with an arthroscopic approach or a mini-arthrotomy (allowing harvesting and transplanting through the same incision).

Rehabilitation

For both procedures, continuous passive motion was started within a few hours after the operation and was continued for 4 to 7 days (the duration of the stay in hospital). The patients were instructed in the use of crutches by a physiotherapist and maintained foot-touch weightbearing for 6 weeks; thereafter, full weightbearing was gradually introduced. Physiotherapy was commenced at the hospital and continued after the discharge. Initial exercises included stretching, straight-leg raise exercise, and passive motion—progressing gradually through active closed-kinetic-chain exercises, including stationary bicycling to dynamic weight training.

Statistical Analyses

The primary outcome measure was the Lysholm score,[2,22,35] reported as a number from 0 (worst) to 100 (best). Data were prospectively collected before the operation and at 12 months, median 5 years (range, 4-6 years), median 10 (range, 9-11 years), and minimum 15 years after surgery.

The study was planned as a multicenter study involving 2 other institutions and a total of 100 patients. As the other institutions were not able to complete their share of inclusion and we present only the patients recruited at our institution (n = 40), the statistical power is less than originally intended (>90%). A post hoc power analysis shows that with a total of 40 patients, based on a significance level of 0.05 and SD of 16, the probability (power) for detecting a treatment difference of 10 points at the Lysholm score is 80%. The minimal detectable change of the Lysholm score has been reported as 8.9.[2]

Statistical analyses were performed with the SPSS (v 23; IBM) on a personal computer. As measures of central location and spread of data, mean and SD or median and range were calculated. A 2-tailed paired *t* test compared the mean Lysholm score at the time of surgery with that of the long-term outcome. A 2-tailed unpaired *t* test compared the mean Lysholm score between subgroups of the patient population. For comparing binominal data of subgroups, the chi-square test was used. An a priori *P* value of .05 was used to denote statistical significance.

RESULTS

Out of a total of 158 cartilage repair operations performed at our institution during the designated period, 46 patients fulfilled the inclusion criteria, 6 of whom declined the offer to take part (before the randomization procedure in the operating theater) (Figure 1). Thus, 40 patients were included in the study: 28 men and 12 women. Twenty patients were treated by the microfracture technique, while 20 had a mosaicplasty performed. We managed to follow up most patients at multiple points after the surgery. The median age of the patients at the time of surgery was 32 years (range, 18-48 years), and the median follow-up time was 16 years (range, 15-17 years). At the time of surgery, median symptom duration was 36 months (range, 2-240 months). The right knee (60%) was treated more often than the left knee (40%). We treated defects with a median size of 3.5 cm^2 (range, 2-5 cm^2). In the mosaicplasty group, a median of 4 osteochondral grafts were used for the repair (Table 1).

TABLE 1
Demographic Data[a]

	Microfracture	Mosaicplasty	*P* Value
Male:female	14:6	14:6	>.999
Age at surgery, y	35 (9)	31 (7)	.145
Duration, mo[b]	58 (48)	52 (60)	.736
Knees, right:left	13:7	11:9	.452
Lesions, 1:2	18:2	18:2	>.999
Treated area, cm^2	3.6 (0.8)	3.4 (0.9)	.378
No. of grafts	N/A	4 (2-7)[c]	N/A

[a]Values are presented as No. or mean (SD) unless noted otherwise. None of the comparisons reached significance ($P < .05$). N/A, not applicable.
[b]Duration of symptoms before surgery.
[c]Median (range).

We recorded 3 cases of early complications (all in the mosaicplasty group): 1 case of wound rupture and superficial infection, 1 case of possible deep infection (treated by arthroscopic lavage and intravenous antibiotics), and 1 case of probable deep venous thrombosis. All complications were successfully treated without leaving any obvious long-term sequelae.

In the mosaicplasty group, the mean Lysholm score improved 21 points from baseline (56) to the last follow-up (77) at minimum 15 years ($P = .003$). The improvement in the microfracture group was 11 and above that of the determined minimal detectable change (9), and it approached statistical significance ($P = .064$) (Table 2). The mean Lysholm score was significantly higher in the mosaicplasty group than the microfracture group at 12 months, median 5 years, median 10 years, and minimum 15 years (Table 2). At all these time points, the difference in mean Lysholm score was clinically significant (>9 points).

During the follow-up period, 4 patients (10%) had already undergone a knee replacement in the ipsilateral knee or were scheduled for the procedure by the end of 2017: 3 in the microfracture group (15%) and 1 (5%) in the mosaicplasty group (Table 3). The microfracture group had a significantly higher frequency of poor outcomes (Lysholm score <64). The mosaicplasty group had a significantly higher frequency of good/excellent outcomes (Lysholm score ≥80) (Table 3). A significantly higher frequency of patients in the mosaicplasty group reported that they would have the surgery again, with their present knowledge of the outcome.

TABLE 2
Lysholm Score for Microfracture and Mosaicplasty at Different Time Points[a]

Time Point	Microfracture (n = 20)	Mosaicplasty (n = 20)	*P* Value
Baseline	50 (16)	56 (15)	.2
12 mo	72 (22)	85 (12)	.015[b]
Median, 5 y	67 (18)	83 (9)	<.001[b]
Median, 10 y	65 (22)[c]	81 (16)	.020[b]
Minimum, 15 y	61 (22)	77 (17)	.011[b]

[a]Values are presented as mean (SD).
[b]$P < .05$.
[c]Based on n = 19.

TABLE 3
Long-term Outcome (Minimum, 15 Years) for Microfracture and Mosaicplasty[a]

Time Point	Microfracture (n = 20)	Mosaicplasty (n = 20)	*P* Value
Good/excellent (Lysholm ≥80)	4 (20)	12 (60)	.010[b]
Poor (Lysholm <64)	13 (65)	4 (20)	.004[b]
Knee replacement	3 (15)	1 (5)	.292
Would have the surgery again	12 (60)	19 (95)	.008[b]

[a]Values are presented as No. (%).
[b]$P < .05$.

DISCUSSION

The most important finding of the present randomized study was that at the short, medium, and long term (median 10 years, minimum 15 years), the mosaicplasty procedure results in a statistically significant and clinically relevant (defined as a difference in Lysholm score >10 points)[2] better outcome than microfracture. Thus, the mosaicplasty (OAT) procedure offers a better clinical outcome in this type of lesions in the short-, medium-, and long-term scenarios.

The current study was planned to be part of a larger multicenter study involving 2 other institutions. After our institution had recruited our share of patients, it became clear that our partners struggled to include the planned numbers of patients. Thus, the multicenter cooperation was finally abandoned, and the number of patients presented here (n = 40) is less than what the multicenter study was supposed to produce (n = 100). Therefore, the statistical power (beta) of the study (80%) is less than originally planned (>90%), making it more vulnerable than intended for a type II error (failure to reject the null hypothesis when it is false). This would have been a problem had the statistical significance (alpha) $P < .05$ not been reached for the comparisons of mean Lysholm score (of the 2 methods) at all points of time (follow-up).

While the multicenter study was closed prematurely, we continued to follow up our patients regularly by using the Lysholm score,[35] which had been chosen as primary outcome measure. Many studies of cartilage surgery have used the Lysholm score, including those on microfracture and mosaicplasty/OAT articular cartilage repair.[4,18,20,30,32,36] The Lysholm score has demonstrated overall acceptable psychometric performance for outcome assessment of various chondral disorders of the knee.[22] In the original multicenter study design, we had planned to include several secondary outcome measures, including biopsy of the repair tissue and isokinetic muscle strength tests at 5 years after the surgery. These measures were abolished when the multicenter study was closed. This randomized study has never previously been reported. However, the study patients, being part of a large institutional cartilage defect database, have constituted small parts (of the study population) of previous reports.[30,32]

Whereas the short-term results after different cartilage repair procedures seem to be acceptable (in most patients), unfortunately, the clinical outcome seems to deteriorate with time.[6,23,31] Thus, long-term studies are warranted. Unfortunately, most of the previous randomized studies comparing the outcome after microfracture versus mosaicplasty/OAT have a follow-up period of 3 to 5 years,[8,10,11,24] which may be too short to adequately reflect the real long-term outcome. Only 2 previously published randomized studies on microfracture versus mosaicplasty/OAT reported a follow-up of about ≥10 years: median 9.8 years[36] and 9 to 11 years.[9] To our best knowledge, the present study offers a longer span of follow-up than any previous comparative study comparing microfracture and OAT in articular cartilage defects of the knee.

To our best knowledge, a total of 6 randomized studies have been published comparing microfracture and mosaicplasty/OAT in articular cartilage defects of the knee.[8-11,24,36] These studies concluded that mosaicplasty offers a better outcome than microfracture in the following respects: (1) better clinical outcome and better anatomic (arthroscopic) appearance of repair tissue in young athletes,[10] (2) better clinical outcome and magnetic resonance imaging results in children with OCD,[11] (3) higher rate of return to and maintenance of sports at the preinjury level at 10 years,[9] and (4) better International Knee Documentation Committee (IKDC) score among patients with combined ACL reconstruction and cartilage repair.[8] Two studies found no significant difference in outcome.[24,36] In the Ulstein et al[36] study, the reoperation rate was higher in the microfracture group (54%) than in the mosaicplasty group (36%). However, this seemingly clinically relevant difference did not reach statistical significance, probably because of the small study population (n = 25) and resulting low power. The better outcome by mosaicplasty (vs microfracture) shown in the present study and most other randomized studies[8-11] could be related to the quality of the tissue that eventually fills the former articular cartilage defects. The microfracture technique and other "marrow-stimulating procedures," such as drilling,[28] spongialization,[5] and abrasion,[19] rely on allowing the release of pluripotent mesenchymal stem cells from the bone marrow (by surgically inflicting wounds through the subchondral bone plate). Although this can theoretically lead to hyaline-like cartilage repair and indeed sometimes happens,[21] the procedure generally results in fibrocartilage or (worse) plain fibrous tissue,[21,38] which offers less mechanical protection of the underlying

pain fiber–innervated bone.[26] Furthermore, this type of scar tissue is less resistant to wear and tear and may disintegrate, revealing the original defect.

In contrast to the marrow-stimulating techniques, the mosaicplasty/OAT procedure does not rely on stem cell differentiation (into chondrocytes forming hyaline cartilage). When the surgical procedure has been completed, most of the former articular cartilage defect has already been replaced by a mosaic of transplants of normal autogenous hyaline cartilage and subchondral bone.[12,38] The mosaicplasty/OAT technique has been reported to result in a higher and faster return to sports than that after microfracture.[9,14,37] However, several factors could hamper the long-term outcome, including donor defects that heal with fibrocartilage or fibrous tissue, inadequate bonding between the cylinder grafts and native surrounding cartilage, and any less-than-ideal anatomic placement of any graft of the mosaic (including proud, low, or incorrectly angled cylinder grafts). All these factors could increase the risk of development of osteoarthritis in the long-term.[27,31,32]

The strengths of the current study include the following: a randomized design of 2 comparable groups of patients, a high follow-up rate at the last follow-up (100%), a long follow-up time (minimum 15 years), the inclusion of follow-up at several earlier time points (12 months, median 5 years, and median 10 years), the comparison of 2 common surgical treatments, and identical rehabilitation protocols.

The weaknesses include a small study group, the lack of secondary knee outcome scores and/or life quality scores, the lack of a routine second-look arthroscopy with biopsy of the repair tissue and isokinetic muscle strength tests, no follow-up magnetic resonance imaging examination (of donor site or repaired site), and no radiologic evaluation of the development of osteoarthritis.

CONCLUSION

At short, medium, and long term (median 10 years, minimum 15 years), mosaicplasty results in a better, clinically relevant outcome than microfracture in articular cartilage defects covering an area of 2 to 5 cm^2 of the distal femur of the knee in patients aged 18 to 50 years.

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