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Review article

Microfracture for the treatment of cartilage defects in the knee joint – A golden standard?

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ABSTRACT

The evidence for the effectiveness of the microfracture procedure is largely derived from case series and few randomized trials. Clinical outcomes improve with microfracture for the most part, but in some studies these effects are not sustained. The quality of cartilage repair following microfracture is variable and inconsistent due to unknown reasons. Younger patients have better clinical outcomes and quality of cartilage repair than older patients. When lesion location was shown to affect microfracture outcome, patients with lesions of the femoral condyle have the best clinical improvements and quality of cartilage repair compared with patients who had lesions in other areas. Patients with smaller lesions have better clinical improvement than patients with larger lesions. The necessity of long postoperative CPM and restricted weight bearing is widely accepted but not completely supported by solid data. Maybe new developments like the scaffold augmented microfracture[6] will show even more consistent clinical and biological results as well as faster rehabilitation for the treatment of small to medium sized cartilage defects in younger individuals.

All in all there is limited evidence that micro fracture should be accepted as gold standard for the treatment of cartilage lesions in the knee joint. There is no study available which compares empty controls or non-surgical treatment/physiotherapy with microfracture. According to the literature there is even evidence for self regeneration of cartilage lesions. The natural history of damaged cartilage seems to be written e.g. by inflammatory processes, genetic predisposition and other factors. Possibly that explains the large variety of the clinical outcome after micro fracture and possibly the standard tools for evaluation of new technologies (randomized controlled trials, case series, etc.) are not sufficient (anymore).

Future technologies will be evaluated by big data from international registries for earlier detection of safety issues, for detection of subtle but crucial co-factors for failure and osteoarthritis as well as for lower financial burdens affecting industry and healthcare systems likewise.

1. Introduction

The microfracture technique often is considered the golden standard therapy for the treatment of cartilage defects. The first results and the technique were published in 1994.[23] The microfracture procedure was originally designed for patients with post traumatic lesions of the knee that have progressed to full thickness chondral defects. Unstable cartilage that overlies the subchondral bone also is an indication for microfracture as well as degenerative changes in the knee joint with proper axial alignment. The technique has been developed by Steadman to enhance chondral resurfacing by providing an enriched environment for tissue regeneration and by taking advantage of the bodies own healing abilities.[27] For the surgical procedure 3 portals are recommended: for the inflow cannula; one each for the arthroscope and the working instruments. After assessing the full thickness articular cartilage lesion, the exposed bone is debrided of all remaining unstable cartilage. To debride the cartilage, the originating authors use a full-radius resector and/or a handheld curved curette. All loose or marginally attached cartilage from the surrounding rim of articular cartilage is also debrided to form a stable perpendicular edge of healthy vital cartilage around the

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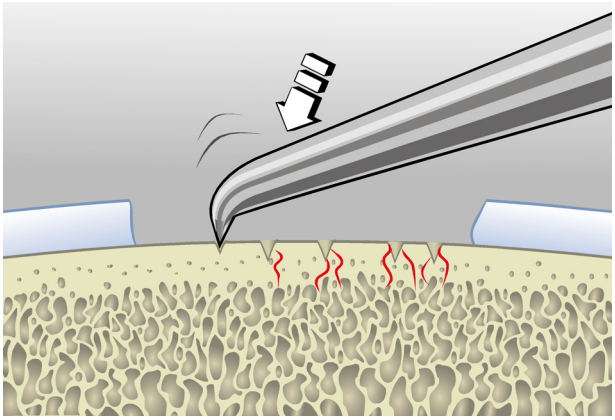

Fig. 1. Arthroscopic view of a medial femoral condyle after microfracture.

defect. This prepared lesion provides a pool that helps to hold the bone marrow clot as it forms. The calcified cartilage layer that remains as a cap to many lesions then is removed by using a curette. Thorough and complete removal of the calcified cartilage layer is extremely important according to Frisbie.[7] To avoid excessive damage to the subchondral bone, an arthroscopic awl then is used to make multiple perforations, or microfractures, into the exposed subchondral bone plate.[27] The holes should be placed 3–4 mm apart without breaking the subchondral bone plate between them. Fat emerging from the marrow cavity indicates the appropriate depth (2–4 mm) (Fig. 1). There is no thermal damage to be expected to the bone as seen with drills. When the blood flow from the bone marrow seems to be adequate in all areas of the defect after reducing the irrigation fluid pressure the procedure is terminated. Intraarticular drains are not recommended.

Steadman emphasizes the importance of an appropriate rehabilitation program after microfracture. The rehabilitation should be designed to promote the ideal physical environment in which the newly recruited mesenchymal stem cells from the marrow can differentiate into appropriate articular cartilage-like cell lines. Location of the defect, size and concurrently treated pathologies determine the postoperative plan. In general, continuous passive motion (CPM) is commenced in the recovery room with an increasing range of motion with usually one cycle per minute for 6–8 h per day.[27] Crutch-assisted touchdown weight bearing is prescribed for 6–8 weeks, depending on the size of the lesion. Elastic cord exercises and weight training are steps to full function and the return to more demanding sports not earlier than 4–6 months after microfracture.

Although the microfracture technique is performed by many orthopedic surgeons, clinical experience has shown that some patient populations may benefit more from microfracture than others. To identify factors which could possibly influence the outcome of microfracture this review study has been designed.

2. Literature search

In order to identify relevant publications a medline search was performed (PubMed April 29, 2016) which produced 432 hits using the keywords microfracture and knee. EMBASE and Google Scholar did not reveal any additional information. Additionally bibliographies from selected articles and pertinent journals from the last six months were searched for relevant citations.

Publications presenting previously unpublished original data regarding the clinical application of microfracture in human knee joints for the treatment of cartilage defects in adults were included in the study. From 42 studies fulfilling those requirements, 3 publications were excluded due to a combined treatment only with microfracture AND high tibial osteotomy[18,28] or to a duplication compared to a previous study.[10] A report about an already included cohort at a different time point was excluded from the study as well.[13] One study could not be evaluated since the original polish publication was not available.[4] A report about a mixed patient cohort with knee and ankle treatment was not selected for review as well.[22]

The remaining 36 publications (Table 1) were evaluated by 3 independent reviewers. The use of a specifically designed data extraction form enabled the standardized data collection regarding exact reference, objective of the study, study design, demographics of the participants, description of the intervention, possible control groups, outcome data and level of evidence according Journal of Bone and Joint Surgery criteria.[11] For selected studies a bias assessment was performed.

3. Results

The first studies were obviously published by Steadman and his co-workers beginning in 1994 by Rodrigo.[23] He examined 77 patients after microfracture treatment, all of them underwent second-look arthroscopy for various reasons. In a level III retrospective comparative series he compared one group with postoperative CPM treatment and a second group with no postoperative CPM with otherwise identical rehabilitation program. After a follow-up time of 64 weeks respectively 73 weeks macroscopic rating from 1 (excellent) to 5 (bad) showed an improvement of 2.67 grades for the CPM group in comparison to 1.67 grades for the non-CPM group. Rodrigo concluded that after microfracture treatment 8 weeks of postoperative CPM should be administered.

Blevins compared in 1998 the outcome of 48 professional athletes with 188 recreational athletes after microfracture.[3] The clinical outcome scores showed significantly better results in both groups from baseline to follow-up 3.7 respectively 4.0 years after operation. 31 of 48 professional athletes responded to the outcome questionnaire of which 23 returned to the same athletic level. The tapes of 26 second-look arthroscopies in the professional group were available for blinded evaluation versus 54 in the recreational athlete group. The examiner had no information whether the lesion was being viewed at the time of initial treatment or at second look. The cartilaginous findings were graded on a scale from I to IV adapted from Outerbridge. The average improvement in grades was 1.6 respectively for the professional athletes and 1.4 respectively compared to baseline. 35% in the recreational athlete group showed no improvement in lesion grading with the exposed subchondral bone visible compared to 8% showing no improvement in the professional group.

In 2003 already Steadman presented data with an average follow-up of 11 years after microfracture for traumatic chondral defects of the knee.[25] 68 patients (71 knees) younger than 45 years were questioned regarding their functional outcome after microfracture with details shown in Fig. 2.

In another series, Steadman reported about 25 national league football players of whom 19 returned back to play ±10 months after microfracture playing an average of 56 games.[26]

In the microfracture arm of his study Bachmann included 7 patients with a mean age of 33 years (±6) and found a clinical improvement using the Lysholm score from 45.5 to 74.2.[1] A complete defect fill in MRI was detected in 2/7 patients after 2 years.

A different set of patients was treated by Miller who presented outcome data 2.6 years (2–5) after microfracture of degenerative cartilage lesions.[19] All 81 patients were 40 years and older (40–70) and had an average defect size of 2.29 cm^2 (0.25–20). The Tegner score increased from 53.8 (19–85) preoperatively to 83.1 (44–100) at follow-up. Patients' satisfaction was measured with 8.2 (1–10)

Table 1
Publications on microfracture included included in this review.

Author	Year	Journal	Study design	Evidence level
Rodrigo[23]	1994	Am J Knee Surg	Retrospective comparative series	3
Blevins[3]	1998	Orthopedics	Case series	4
Steadman[26]	2003	J Knee Surg	Case series	4
Steadman[25]	2003	Arthroscopy	Case series	4
Miller[19]	2004	J Knee Surg	Case series	4
Bachmann[1]	2004	Radiologe	Case series	4
Gobbi[8]	2005	Knee Surg Sports Traumatol	Case series	4
Gudas[9]	2005	Arthroscopy	Prospective randomized trial	1
Mithoefer[20]	2005	J Bone Joint Surg A	Case series	4
Marder[16]	2005	Arthroscopy	Retrospective comparative series	3
Kreuz[14]	2006	Osteoarthritis Cart	Case series	4
Kreuz[15]	2006	Arthroscopy	Case series	4
Bae[2]	2006	Arthroscopy	Case series	4
Mithoefer[21]	2006	AJSM	Case series	4
Domayer[5]	2007	Osteoarthritis Cart	Case series	4
Knutsen[12]	2007	J Bone Joint Surg A	Prospective randomized trial	1
Matsunaga[17]	2007	Knee	Retrospective comparative series	3
Saris[24]	2008	AJSM	Prospective randomized trial	1
Namdari[46]	2009	AJSM	Case series	4
Cerynik[45]	2009	Arthroscopy	Case series	4
Van Assche[44]	2010	Knee Surg Sports Traumatol	Prospective randomized trial	1
Saris[44]	2009	AJSM	Prospective randomized trial	1
Solheim[42]	2010	Knee Surg Sports Traumatol	Case series	4
Basad[41]	2010	Knee Surg Sports Traumatol	Prospective randomized trial	1
Vanlauwe[40]	2011	AJSM	Prospective randomized trial	1
Mithoefer[39]	2012	Cartilage	Case series	4
Krych[38]	2012	J Bone Joint Surg Am	Retrospective comparative study	3
Gudas[37]	2012	AJSM	Prospective randomized trial	1
Salzmann[36]	2013	Arch Orthop Trauma Surg	Retrospective comparative series	3
Bae[35]	2013	Arthroscopy	Therapeutic case series	4
Anders[34]	2013	Open Orthop J	Prospective randomized trial	1
Gobbi[33]	2014	Knee Surg Sports Traumatol	Therapeutic case series	4
Harris[32]	2013	Orthop J Sports Med	Case series	4
Ulstein[31]	2014	Knee Surg Sports Traumatol	Prospective randomized trial	1
Saris[30]	2014	AJSM	Prospective randomized trial	1
Steadman[29]	2014	J Knee Surg	Case series	4

correspondent to an increase of the Tegner activity scale from 2.9 (1–6) to 4.5 (2–7). 5 failures were reported (total knee arthroplasty) as well as 13 re-arthroscopies due to pain. Miller concluded that arthroscopic microfracture can consistently achieve significant symptomatic and functional improvement in the degenerative knee.

At a mean follow-up time of 72 months (36–120) Gobbi evaluated a cohort of competitive athletes (26 professionals and 27 recreational) after microfracture.[8] A total of 33 males and

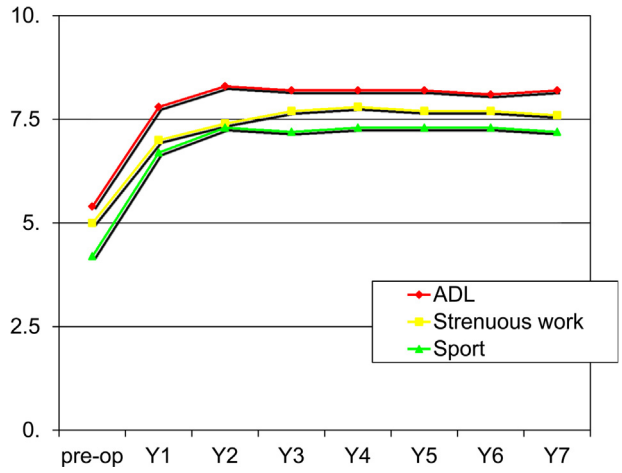

Fig. 2. Graph of function scores from preoperative to year 7 postoperative. 1, unable to perform activities; 10, no limitation in performing activities or strenuous work (from 25).

20 females with a mean age of 38 (19–55) showed large (mean 4.0 cm^2) grade III and IV cartilage lesions. Additionally to the scoring with Lysholm, IKDC and Tegner, which all showed a significant increase a follow-up, a clinical examination was performed with a functional test (one leg hop). 10% were not able to jump more than 50% of the distance covered using the normal leg whereas 70% performed normal or nearly normal. Two of three failures were treated with autologous chondrocyte implantation. Ten biopsies after second-look arthroscopy showed areas of fibromyxoid tissue with differentiation, a transition zone with some cartilage tissue in the areas with initial hyaline transformation. Another cohort with a average follow-up of 15.1 years suggested a benefit of micro fracture for small lesions in younger patients but deterioration was seen after as early as 2 years.[33]

In 2005 Gudas presented a prospective randomized clinical study of mosaic osteochondral autologous transplantation (OCT) versus microfracture (MFX). 30 patients in each group were randomly selected with comparable demographics.[9] No CPM was administered postoperatively. Different from the ICRS score at a follow-up time of 36 months, the mean HSS score indicates a decline after the first year in the microfracture group. 14 biopsies were obtained at 12 months postoperatively showing 8 cases of fibrocartilage and 6 cases of fibroelastic tissue or no coverage. Surprisingly 7 cysts were detected in 21 MRIs 12 months postoperatively in the microfracture group covered with an amount of tissue representing only 18% of the surrounding native cartilage. At 10 years follow-up the group after OCT published in 2012 showed a higher rate of return to and maintenance of sports at the preinjury level compared to MFX.[37]

Table 2
ICRS- and Cincinnati-score preoperative and after 36 months in 4 groups for 4 defect locations (femoral condyle, trochlea, tibia, patella). Patients of group 1 improved significantly more ($p < 0.02$) as patients in group 2, 3 or 4. 36 months after microfracture the Pearson coefficient of correlation between both scores (overall) was 0.81.[15]

Group	Average ICRS-score preoperative	Average ICRS-score after 36 months	Average Cincinnati-score preoperative	Average Cincinnati-score after 36 months
1 femoral condyle	3.53 ± 0.51	2.13 ± 0.75	4.0 ± 0.0	1.66 ± 0.87
2 trochlea	3.88 ± 0.34	3.06 ± 1.0	4.0 ± 0.0	2.94 ± 1.29
3 tibia	3.91 ± 0.3	3.0 ± 0.77	4.0 ± 0.0	2.55 ± 1.04
4 patella	3.64 ± 0.5	2.91 ± 0.83	4.0 ± 0.0	2.55 ± 0.93
Overall	3.69 ± 0.47	2.6 ± 0.92	4.0 ± 0.0	2.23 ± 1.13

Table 3
MRI 36 months after microfracture in 4 different compartments of the knee joint: the best defect filling could be detected in group 1 (femoral condyle) with significant difference to the other groups ($p < 0.02$). The Pearson coefficient of correlation between defect filling and subchondral edema was 0.89 and significant at the 0.01 level.[15]

Group	Defect filling	Subchondral edema	Cartilage signal	Effusion	Overall MRI-score
1 femoral condyle	1.69 ± 0.74	1.50 ± 0.62	1.63 ± 0.61	1.31 ± 0.47	1.78 ± 0.71
2 trochlea	2.56 ± 0.96	2.31 ± 0.96	2.31 ± 0.94	1.88 ± 0.62	2.56 ± 0.96
3 tibia	2.64 ± 0.92	2.55 ± 0.93	2.55 ± 0.93	2.36 ± 1.03	2.64 ± 0.92
4 patella	2.55 ± 0.93	2.45 ± 1.04	2.36 ± 0.92	2.18 ± 0.98	2.64 ± 1.03
Overall	2.17 ± 0.95	2.0 ± 0.93	2.04 ± 0.88	1.74 ± 0.81	2.23 ± 0.94

A prospective cohort study was published 2005 by Mithoefer following on 52 individuals (37 males and 11 females) who underwent microfracture due to persistent pain.[20] The patients were 48 years old (16 to 60) with a defect size of 4.8 cm^2 (2.4–20). After an average follow-up of 41 m (24–54), 48 patients answered the questionnaire indicating a good to excellent result in 32 cases versus 12 fair cases and 4 poor cases. 32 patients showed a decrease in IKDC after 24 months postoperatively. Patients with a BMI greater 30 seemed to do worse whereas patients with an age <30 do better after microfracture. Interesting was a persisting gap formation with the surrounding cartilage in MRI for 22 of 24 patients at 12 m.

The value of postoperative continuous passive motion after microfracture was studied by Marder in a retrospective comparative study 2005.[16] The study was defined to include 25 patients in each group with a cartilage lesion surface area less than 2 cm^2 with a circumferentially stable margin of intact cartilage. Postoperatively 25 patients were treated by continuous passive motion and touchdown weight bearing for 6 weeks and 25 patients were allowed to weight bearing as tolerated without CPM. After a follow-up time of 5.2 years (2–9) the mean Lysholm score increased from 37 to 81 in the CPM group and from 33 to 85 in the no CPM group. Correspondingly the pain sensations were much less in both groups without a significant difference. No failures were reported but 5 rearthroscopies due to pain.

Microfracture treatment on the femoral condyle shows better clinical outcome compared to other locations after 36 months (36–38 m) – this was concluded by Kreuz after a retrospective case series with 70 patients in 4 groups corresponding to 4 different locations in the knee joint (femoral, patella, trochlear, tibia).[15] Details of the clinical outcome in the MRI results after 36 m are displayed in Tables 2 and 3.

Another publication from Kreuz presented data examining the role of age for the outcome of microfracture in the knee joint.[14] 32 males and 37 females with cartilage defects ICRS grade 3 b and c were grouped for age under 40 years and over 40 years (18–55). Clinical examination and scoring according to Lysholm and ICRS as well SF36 was performed at 6, 18 and 36 months postoperatively. MR imaging was taken pre-operatively and at 18 and 36 m. ICRS scores suggest a deterioration between 18 and 36 m in the age group over 40. Patella and trochlear lesions showed more unfavorable results after 18 m. Details are shown in Fig. 3a–c.

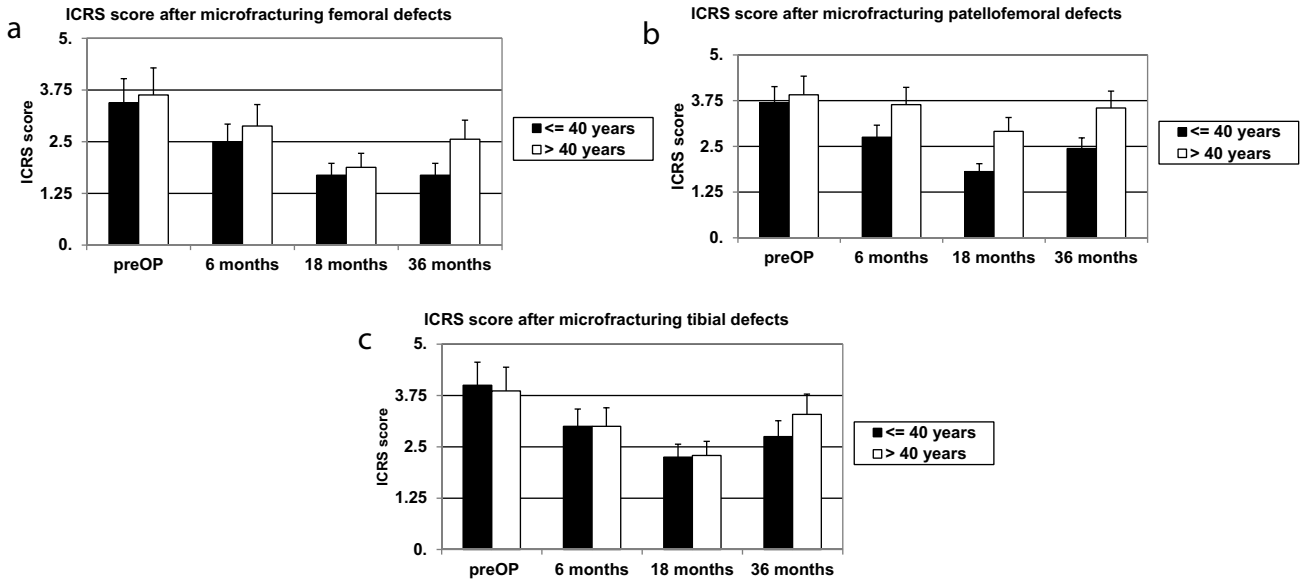

Fig. 3. (a) ICRS score after microfracturing femoral cartilage defects.[14] (b) ICRS score after microfracturing patellofemoral cartilage defects.[14] (c) ICRS score after microfracturing tibial cartilage defects.[14]

A challenging group of patients with osteoarthritic knees were treated by Bae with microfracture and cartilage healing was evaluated.[2] 46 patients the majority of whom was female aged 57 years (41–77) with a main defect size of 3.9 cm^2 (1–6) presented with persistent knee pain. At follow-up Baumgaertners knee scale rated 36% of the patients excellent; 53% good and 11% fair. Second-look arthroscopies were performed at 1 year (10–15 months) showing a cartilage healing >80% in 36 cases and less than 50% in 3 cases. Histological analysis including Western blotting and immunohistochemistry revealed a significantly reduced content of collagen II in the repair tissue with a mean of 44% comparing with a normal control tissue. 8 cases had more than 70% of the normal control group, 7 cases had collagen II in the range of 20–70% and only 6 cases showed less the 20% collagen II in the repair tissue. According to those findings a second cohort was studied more than 10 years after microfracture.[35] 51 knees out of 134 (38.1%) went to TKA implantation a mean of 6.8 years after the signature procedure and 6 knees were considered as clinical failures. The survival decreased over time to 67.9% at 10 years.

14 patients returned to sport, 8 on the same level, from a cohort of 32 high impact athletes (3% professional, 59% competitive and 38% recreational) after treatment by Mithoefer with microfracture.[21] After a minimum follow-up of 2 years this cohort with a large average lesion size of 4.9 cm^2 (2.4–20) showed significant improvement described by the Brittberg rating, the Tegner activity score and the Marx activity rating scale. 2 failures were reported.

The goal of a study by Domayer was to correlate clinical outcome after microfracture with MRI T2 mapping.[5] Therefore 24 patients aged 41 years (±14) and an average defect size of 2.0 cm^2 (0.825) were examined 29 m (±14) after microfracture both clinically and with MRI. All patients reported improvement after surgery with the mean Lysholm score of 80.6 (SD 18.5). The mean outcome of the subjective IKDC form was 70.0 (SD 23.8). In the IKDC rating the knee status was normal in 41.7%, nearly normal at 45.8% and abnormal in 12.5%. The average volume fill grade of the defect with regenerated tissue was above 75% in 66.7% of the cases in the MRI comparing to the adjacent native cartilage. In 4.1% the filling grade was below 25%. Since the T2 mapping index correlated with the outcome of the Lysholm score ($r = 0.641$) and the IKDC subjective knee evaluation form ($r = 0.549$) the authors suggested quantitative T2 mapping as a valuable tool to monitor the progress of cartilage repair.

The findings at 5 years after autologous chondrocyte implantation (ACI) and microfracture was presented by Knutsen after conducting a prospective randomized controlled trial.[12] 80 patients with an average defect size of 4.5 cm^2 after debridment (2–10) were randomly assigned to be treated either with ACI or microfracture. The procedures were performed in a standardized fashion with an identical rehabilitation program. Prior to the endpoint of the study at 5 years the patients were clinically examined at 12 and 24 months with a second-look arthroscopy at 2 years. At the time of the 5-year follow-up; there were 9 failures in each group. Clinical data on the patients who did not have a failure were collected at 5 years. The mean Lysholm scores and the mean scores on the visual analog pain scale remain significantly improved in both groups. Compared with the baseline values; 72% of the patients had less pain; 80% had improvement in the Lysholm score and 72% had improvement in the SF-36 physical component score. No significant difference between the treatment groups was found in the Lysholm score or the visual analog score at 5 years after treatment. Younger patients less than 30 years old had a significantly better clinical outcome than all the patients regardless of their treatment group after 5 years. Evaluation of second-look arthroscopies and histological analysis of the same patient population was presented in an earlier publication by Knutsen (2004).[13] The macroscopic findings of 35 patients after microfracture were graded as nearly normal. 39% of the biopsies specimens had at least some hyaline cartilage present. In contrast, 43 had fibrocartilage throughout most of their depth. Unscheduled second-look arthroscopy was necessary in 4 cases in the microfracture group.

The only study in this review with a control group was performed by Matsunaga comparing the repair of articular cartilage and clinical outcome after osteotomy with microfracture or abrasion arthroplasty for medial gonarthrosis.[17] In a retrospective comparative design 104 patients were assigned to 3 different therapeutic groups. 45 patients received a closing-wedge high tibial osteotomy with internal fixation combined with abrasion arthroplasty on the femoral condyle. In 25 patients abrasion arthroplasty was replaced by microfracture in combination with a high tibial osteotomy. No specific cartilage treatment was performed in 34 patients receiving only high tibial osteotomy serving as a control group. From day 2 postoperatively continuous passive motion exercise was performed for about 3 h daily for 4 weeks. Partial and full weight bearing was allowed from 4–6 to 8 weeks after surgery respectively. The same postoperative procedures were followed in all 3 groups. Repeat arthroscopy was done during removal of the hardware about 1 year after HTO. With an overall follow-up rate of 98% up to 5 years after surgery the clinical outcome was assessed using the Japanese Orthopaedic Association score (JOA) at 1, 3 and 5 years after surgery as displayed in Table 1. There was a significant improvement in all 3 groups after surgery and the clinical score did not deteriorate again within 5 years. There were no significant differences of the preoperative or postoperative JOA scores between the 3 groups at any time of assessment. At arthroscopy 1 year postoperatively cartilage repair on the medial femoral condyle was more extensive in the abrasion arthroplasty group than in the HTO group alone while there was no difference between the microfracture group and the HTO group. The authors concluded that abrasion arthroscopy combined with HTO is more successful in producing repair cartilage than microfracture combined with HTO, although neither procedure improved the clinical outcome within 5 years after surgery in comparison to HTO alone. Although it is generally assumed that covering exposed subchondral bone with repair cartilage should be relevant to the management of osteoarthritis the authors interpret their results in a way that it is impropriate to combine HTO with marrow stimulation techniques.

Another prospective randomized trial comparing microfracture with autologous chondrocyte implantation was published by Saris and co-workers.[24] 61 patients (41 males and 20 females) with a single defect on the femoral condyle measuring 2.4 cm^2 in the mean (±1.2) were treated in the microfracture arm of the study. The postoperative rehabilitation program was similar in both groups with partial weight bearing for 6 weeks and in unloading brace for 8 weeks. No detailed information was giving regarding the continuous passive motion. The follow-up time was 18 months for 51 out of 61 patients after microfracture. The KOOS score improved from an average of 59.53 (±14.95) to 75.04 (±14.50) postoperatively. 8 adverse events were considered to be serious. The KOOS overall score for the autologous chondrocyte implantation group was 56.3 (±13.61) at baseline compared to 74.73 (±17.01) postoperatively at 18 months. The adjusted mean overall histology assessment score was statistically significantly higher for the ACI treatment group than for the microfracture group. The authors contribute this significant histological difference of the regenerated tissue compared with microfracture to the use of characterized chondrocytes for the ACI technique. However; it was no difference detected in clinical outcome at 18 months. But, follow-up studies with a longer horizon and in comparison with matrix-applied chondrocytes showed a significant inferiority of the micro fracture technique.[30,40,43,44]

4. Discussion

A total of 36 articles reporting results from primary studies that examined the clinical use of microfracture for cartilage repair were included in this review according to the criteria detailed above. The preponderance of these articles on the use of microfracture report data from case series (evidence level IV).

Three retrospective comparative studies (evidence level III) evaluated the influence of different rehabilitation protocols[16,23] and high tibial osteotomies[17] on the outcome of the microfracture procedure.

Autologous chondrocyte transplantation[12,24,34,41,43,44] and mosaicplasty[9,31,37,38] were compared to microfracture in prospective randomized trials (evidence level I) without blinding.

Only one article reported about a control group.[17] Matsunaga compared 3 patient cohorts after HTO and microfracture, HTO and abrasion chondroplasty and HTO alone.

The majority of the studies were comparative for rehabilitation,[16,23] sport participation,[3] age,[14] defect location,[15] alternative treatments (ACI,[1,12,24,34,41,43,44] OATS,[9,31,37,38] abrasion[17]) and diagnostic measures (MRI[5]) vs. 7 outcome oriented trials.

Regarding the intervention standard more than 50% of the publications report about one center with different surgeons performing the procedure in contrast to five centers[1,3,19,25,26] with only one operating surgeon on the study. Three studies had a multicenter design.[12,23,24]

Follow-up over a long period is hard to achieve a.o. due to mobility of the patients and institutional limitations. Therefore, a lot of the included studies[2,5,8,14,15,19–21,23,25,26,29,39] relied on an institutional database for data collection and evaluation. This allows for a multitude of questions to be answered regarding a certain procedure and each case can be included in various evaluations. Surely this limits the value of those studies in comparison to prospective randomized trials. Only 2 studies had a follow-up of almost 100%.[17,24] The only use of questionnaires for the recruitment of follow-up data ($n = 6$ in this review[3,19–21,25,26]) is convenient but carries a higher risk of inappropriate description of the medical/functional status after an intervention. A combination of questionnaires and clinical examination clearly represent a more accurate way of outcome evaluation.

Over time a multitude of scoring systems tried to capture the clinical status of individuals before and after treatment preventing easy comparison of clinical trials. *Return to sport* served as another criterium for the success of microfracture. In the field of cartilage repair the use of the ICRS score (International Cartilage Repair Society) should be used for future trials.

4.1. Durability of MFX

Clinical outcome data is reported in all of the 18 articles included in this review. The mean length of patient follow-up ranged from 12 months (no range reported) to 11.3 years (7–17 years). Functional and other clinical parameters significantly improved in patients who had a symptomatic cartilage defect in a stable knee 2 and 5 years after microfracture[12] and in patients with degenerative knee lesions 2.6 years after microfracture.[19] Consistent with these results are the observations of Steadman et al. of decreased pain and improved function over the first two years and of decreased swelling over the first three years, responses that which were maintained up to 7 years.[25]

In a study of patients with moderate osteoarthritis 25/47 (53%) of the cases had good, and 36% had excellent scores after an average follow-up of 2.3 years (24–44 m).[2]

In contrast did 6 studies in the review with a duration of 18 months and more show that initial improvements in patient outcomes may decline at later timepoints. In two studies by Kreuz et al.[14,15] clinical outcome deteriorated between the 18- and 36-month timepoints depending on the age of the patient and/or the lesion location. In an 48-months study,[20] Mithoefer and colleagues found that while activities of daily living, the international Knee Documentations Committee (IKDC) score and the SF-36 physical component score improved up to 24 months following microfracture, the IKDC follow-up score significantly worsened from 24 to 36 months and was no longer significantly different than preoperative by 48 months. In another study with athletes activity scores initially increased but later declined in almost half of the patients.[21] Correspondent results were reported from Gudas[9,37] as well as from Gobbi who demonstrated in a longer term study (mean follow-up up to 6 years) knee function improved significantly following microfracture with 70% of the patients being considered normal or nearly normal. However, strenuous sports activities improved in 80% of subjects after 2 years follow-up but gradually decreased to 55% of patients who improved from baseline by the time of final follow-up.[8,33]

4.2. Quality of cartilage repair tissue following microfracture

MRI was used in 6 studies[1,5,14,15,20,24] to determine the degree of defect filling at given timepoints. The quality of the repair tissue could not be sufficiently evaluated with MRI. Future developments might help to correlate MRI results with histological quality of regenerated tissue. In one study MRI findings correlated with the clinical outcome.[5]

6 studies in the review report about histology results[2,8,9,12,17,24] which show variable results. Limiting for the histological grading was in most cases the morphological structure and the absent/reduced content of collagen II. With the microfracture technique the normal, hyaline cartilage structure cannot be restored. However, the regeneration of a repair tissue with inferior quality within a cartilage defect might be beneficial for pain and joint function.

4.3. Does age or lesion location affect the outcome of microfracture

There is evidence from the described studies that younger patients under 30–40 years might benefit more from the microfracture technique.[14,15,23,26]

Kreuz et al. reported that patients with femoral condyle lesions had the best clinical improvement, quality of cartilage repair and defect filling with microfracture than patients with lesions on the trochlea, tibia and/or patella.[15] In contrast, lesion location was not found to influence Lysholm scores in a study of patients 40 years and over with degenerative knee lesions.[19] When lesions in the medial femoral condyle, lateral femoral condyle and trochlea were compared, defect location did not influence MRI parameters including repair cartilage signal, repair cartilage fill, repaired lesion morphology, peripheral cartilage repair integration and subchondral edema.[20]

4.4. Does lesion size influence outcome with microfracture

For the most part, studies show that patients with smaller lesions have better clinical outcomes and quality of cartilage repair tissue following microfracture than patients with larger lesions.[2,9,12,19,21,23,36] Patients who have only a single lesion treated with microfracture showed a lower pain score compared to multiple lesions.[42]

The results of Steadman in 2003,[25] indicating that larger lesion size was significantly associated with greater improvement in clinical scores at final follow-up, could be explained with the lower scoring at baseline leaving or room for improvement.

4.5. How important is post operative CPM and limited weight bearing

Extensive postoperative CPM and prolonged toe-touch weight bearing after microfracture is described to be essential for a successful clinical outcome by numerous authors based on the recommendations of Steadman and his colleagues. Rodrigo showed better results 64 weeks after microfracture with CPM 6–8 h a day for 8 weeks compared to a patient cohort 73 weeks after microfracture.[23] Most authors of the studies included in this review adhered more or less to this regimen with variations regarding duration of CPM and degree of weight bearing from toe-touch to partial.

However, in a study that examined the difference between patients who were toe-touch weight bearing and receiving CPM postoperatively and those who had no CPM and were allowed weight bearing as tolerated, clinical improvements were observed but were not affected by postoperative treatment.[16]

4.6. Return to sport

The results are conflicting since some studies show a low rate of return to sport[45] sometimes as low as 44%[21] while others show a successful and long continuation of the career after micro fracture[3,26,29,32,46] with a slightly reduced performance.

5. Conclusion

The evidence for the effectiveness of the microfracture procedure is largely derived from case series and few randomized trials. Clinical outcomes improve with microfracture for the most part, but in some studies these effects are not sustained. The quality of cartilage repair following microfracture is variable and inconsistent due to unknown reasons. Younger patients have better clinical outcomes and quality of cartilage repair than older patients. When lesion location was shown to affect microfracture outcome, patients with lesions of the femoral condyle have the best clinical improvements and quality of cartilage repair compared with patients who had lesions in other areas. Patients with smaller lesions have better clinical improvement than patients with larger lesions. The necessity of long postoperative CPM and restricted weight bearing is widely accepted but not completely supported by solid data.

Maybe new developments like the scaffold augmented microfracture[6] will show more consistent clinical and biological results as well as faster rehabilitation for the treatment of small to medium sized cartilage defects in younger individuals.

All in all there is limited evidence that microfracture should be accepted as golden standard for the treatment of cartilage lesions in the knee joint. There is no study available which compares empty controls or non-surgical treatment/physiotherapy with microfracture. According to the literature there is even evidence for self regeneration of cartilage lesions. The natural history of damaged cartilage seems to be written e.g. by inflammatory processes, genetic predisposition and other factors. Possibly that explains the large variety of the clinical outcome after micro fracture and possibly the standard tools for evaluation of new technologies (randomized controlled trials, case series, etc.) are not sufficient (anymore).

Future technologies will be evaluated by big data from international registries for earlier detection of safety issues, for detection of subtle but crucial co-factors for failure and osteoarthritis as well as for lower financial burdens affecting industry and healthcare systems likewise.

Conflicts of interest

The authors have none to declare.

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