Autologous Matrix-Induced Chondrogenesis for Treatment of Focal Cartilage Defects in the Knee

A Follow-up Study

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Background: Autologous matrix-induced chondrogenesis (AMIC) is a well-established treatment for full-thickness cartilage defects.

Purpose: To evaluate the long-term clinical outcomes of AMIC for the treatment of chondral lesions of the knee.

Study Design: Case series; Level of evidence, 4.

Methods: A multisite prospective registry recorded demographic data and outcomes for patients who underwent repair of chondral defects. In total, 131 patients were included in the study. Lysholm, Knee injury and Osteoarthritis Outcome Score (KOOS), and visual analog scale (VAS) score for pain were used for outcome analysis. Across all patients, the mean ± SD age of patients was 36.6 ± 11.7 years. The mean body weight was 80.0 ± 16.8 kg, mean height was 176.3 ± 7.9 cm, and mean defect size was 3.3 ± 1.8 cm^2. Defects were classified as Outerbridge grade III or IV. A repeated-measures analysis of variance was used to compare outcomes across all time points.

Results: The median follow-up time for the patients in this cohort was 4.56 ± 2.92 years. Significant improvement ($P < .001$) in all scores was observed at 1 to 2 years after AMIC, and improved values were noted up to 7 years postoperatively. Among all patients, the mean preoperative Lysholm score was 46.9 ± 19.6. At the 1-year follow-up, a significantly higher mean Lysholm score was noted, with maintenance of the favorable outcomes at 7-year follow-up. The KOOS also showed a significant improvement of postoperative values compared with preoperative data. The mean VAS had significantly decreased during the 7-year follow-up. Age, sex, and defect size did not have a significant effect on the outcomes.

Conclusion: AMIC is an effective method of treating chondral defects of the knee and leads to reliably favorable results up to 7 years postoperatively.

Keywords: chondral; knee; cartilage; repair; AMIC

Articular cartilage is a highly specialized connective tissue found in synovial joints, with the principal function of providing a smooth, lubricated surface for articulation and facilitating the transmission of loads with a low frictional coefficient.[9,36] An important aspect of articular cartilage is that it is not innervated but is avascular; therefore, the innate mechanisms of tissue regeneration, which are based on blood supply and recruitment of cells through the vascular system to the site of damage, do not occur in the articular cartilage.[16,28] Because articular cartilage does not possess effective repair mechanisms, meaning spontaneous healing is unlikely, defects in articular cartilage constitute a difficult medical problem.[30] Untreated full-thickness cartilage lesions may be associated with significant pain and, eventually, arthritis, which is a major cause of disability and represents a significant socioeconomic burden.[29]

In recent decades, a variety of surgical techniques have been developed with the goal of restoring the articular surface and thereby preventing joint degeneration.[6] Among these, regenerative, scaffold-based procedures have emerged as a potential therapeutic option for the treatment of focal osteochondral lesions.[11,22] The rationale for using a

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scaffold is to have a temporary 3-dimensional structure of a resorbable membrane that facilitates the attachment, proliferation, and differentiation of cells and can withstand the mechanical stress in the joint. In this light, scaffolds have been introduced in clinical practice to improve results previously achieved with the first-generation cell-based approaches, while overcoming the drawbacks and simplifying the procedure.[1] One of the procedures currently in use is autologous matrix-induced chondrogenesis (AMIC), which has been well-reported since its initial description in 2010.[3] AMIC is a matrix-assisted bone marrow stimulation technique combining microfracturing with the use of a type I/III porcine collagen matrix (Chondro-Gide; Geistlich Pharma). The matrix is able to stabilize and protect the bone marrow clot produced from the microfracture that yields mesenchymal stem cells.[1,13,14,31]

Previous studies that have investigated short- and medium-term follow-up cohorts suggest that AMIC in cartilage repair is a safe and effective treatment option that improves patient outcome measures and pain.[4,13,14,17,21,31,38] To assess extended effectiveness and reliability of the AMIC procedure as well as the durability of the repaired cartilage, long-term follow-up is essential. One study provided longer term data after an AMIC procedure, in which significant clinical and functional improvement was maintained over a 7-year follow-up, but this was a small cohort of 21 patients.[32] The present study evaluated long-term follow-up after AMIC procedures in the knee based on data contained in an ongoing patient registry.

The aim of the study was to evaluate whether the AMIC technique results in objective and subjective improvements during a period of up to 7 years postsurgically. In an earlier study, we presented clinical improvement after AMIC in a 3-year midterm follow-up.[13,14] However, given the young age of patients commonly treated for cartilage lesions, a longer duration of symptom relief would be of great importance. It remains questionable how the repaired tissue reacts during aging and how it follows the natural gradual development of osteoarthritis.

METHODS

Study Design

Study participants consisted of a cohort of patients who had been treated with AMIC using the Chondro-Gide and enrolled in the AMIC registry between 2003 and 2013. The registry is an ongoing, multicenter database designed to longitudinally track changes in function and symptoms by evaluating the Lysholm score, the Knee injury and Osteoarthritis Outcome Score (KOOS), and visual analog scale (VAS) score for pain. Documentation was made on electronic case report forms, with surgeons having access to the registry via a web interface. Surgeons had access to their own patients' data, whereas the summary and overall performance data were anonymized. All patients were educated in detail about the surgical technique as well as all alternative procedures, including the attendant advantages and disadvantages of each. Thereafter, the patients who chose to undergo the index surgical procedure (ie, AMIC) were enrolled in the registry. All patients signed an informed consent to participate in the registry, and all treatment and follow-up examinations followed the standard of care, with no additional visits imposed on the patients. The study was performed in compliance with regulations of the ethical review board of our institution. Because the registry has no provision for radiographic follow-up, data were not available regarding the development of radiographically verified osteoarthritis.

Patients

Patients were included in the analysis if they had an articular cartilage lesion that had been treated via AMIC. The indication for AMIC cartilage repair was a symptomatic, circumscribed cartilage lesion in the knee that was grade III or IV according to the Outerbridge classification. Data were collected at baseline and at each year, up to 7 years postoperatively. The main exclusion criteria were concomitant surgery at the time of the index procedure, advanced osteoarthritis, significant narrowing of the joint lines, underlying rheumatic disease, total meniscectomy, body mass index >30, or deviation of the mechanical axis of the affected compartment. Baseline data collection included surgical history, defect origin, lesion size and location, concurrent procedures, age, weight, and sex.

Treatment

The operative procedure was performed through a miniopen approach as described by Benthien and Behrens.[3] After debridement, a 1.2-mm drill was used to perforate the subchondral bone plate to a depth of 1 cm, thereby mobilizing bone marrow stem cells into the defect. Care was taken to leave areas of intact subchondral bone plate between the drill holes. The Chondro-Gide was then placed before a fibrin sealant was applied.

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Ethical approval for this study was obtained from the ethics review board of the University of Lübeck (file No. 19-178).

TABLE 1
Demographic Characteristics for Patients With Baseline and Follow-up Data

	Male (n = 80)	Female (n = 48)
Age, y mean ± SD	36.3 ± 10.6	37.3 ± 13.3
Body mass index, mean ± SD	25.7 ± 3.2	25.8 ± 5.7
Defect size, cm^2, mean ± SD	3.4 ± 1.8	3.2 ± 1.7
Underwent previous surgery, no. of patients	29	24

Outcomes Assessment

Therapeutic outcomes were assessed on the basis of 3 scores: VAS, Lysholm, and KOOS. Preoperatively and at each subsequent follow-up, patients rated their pain using the VAS, with 0 indicating no pain and 10 indicating the worst pain the patient has known. Functional outcomes were assessed using the Lysholm and KOOS scores, as these are well-validated functional scores.[5] Because the data from this study were based on a registry, which followed standard of care, there were no additional, predefined, clinical follow-up visits. Investigators and research assistants maintained contact with the patients, motivated them to adhere to the follow-up protocol, and sent follow-up questionnaires to patients. Patients were not financially compensated for their time in completing the data-collection forms.

Statistical Analysis

The 3 outcome variables, KOOS, Lysholm, and VAS, were analyzed via a factorial analysis of variance (ANOVA) across all 8 time points (preoperative and years 1 through 7). A Student-Newman-Keuls test was used for post hoc analysis of the ANOVA. Exploratory comparisons of the change in scores from baseline were conducted to test for difference in patient sex as well as previous surgery. Additionally, we conducted exploratory comparisons of the change in scores with respect to the age group, defect location, and defect size. For age, the patients were classified into 3 groups: $\leq$32 years, 33-46 years, and >46 years. Defects were assessed via a correlation between outcomes scores and defect size. The a priori alpha level was set at .05.

RESULTS

Demographic Characteristics

Overall, the registry contained data for 178 patients; at the time this analysis was conducted, data were available for 131 patients. The mean time of the maximal follow-up examination was 4.56 ± 2.92 years. The demographic characteristics of the patients are presented in Table 1. Because the sex of 3 patients had not been entered into the registry, Table 1 contains data for 128 patients. The anatomic location of the cartilage defects is presented in Table 2.

TABLE 2
Location of the Chondral Lesions

Location	n
Medial femoral condyle	52
Lateral femoral condyle	17
Trochlea	12
Patella	47
Tibia	3

Because this was a registry study with no additional, planned follow-up visits for data collection, patient numbers have steadily decreased over time. With a total of 178 patients in the registry for this particular surgery, data sets of only 131 patients were sufficient for analysis. Not all sites obtained the same baseline evaluations, an issue that has been rectified since the inception of the registry. The number of patients for whom Lysholm scores were available at each time point is presented in Table 3.

The mean Lysholm score increased significantly from 46.9 at baseline to 83.8 at year 1 ($P < .001$). This improvement was maintained over the entire length of follow-up, as there was no significant difference in Lysholm score between any of the postoperative follow-up evaluations. Figure 1 illustrates the development of the Lysholm score over time.

The mean KOOS increased significantly from 45 at baseline to 77 at year 1 ($P < .001$). This mean improvement was maintained at subsequent time points. Figure 2 depicts the summary of the improvement in the KOOS as aggregated according to the relevant time points.

The median VAS score decreased significantly from 5.5 at baseline to 2.3 at year 1 ($P < .001$), and this was generally maintained, with a slight but statistically insignificant increase, by year 7. The data are presented in Figure 3.

When the data were analyzed with regard to sex, no significant differences were seen between male and female patients for the Lysholm, KOOS, and VAS scores. Although the Lysholm scores improved over time, there was no difference in the scores when compared between sexes ($P = .73$). Likewise, the KOOS improved over time, but there was no significant difference between male and female patients ($P = .42$), as depicted in Figure 4. The VAS score decreased significantly over time in both female and male patients, and sex did not have an effect on the VAS ($P = .13$).

To determine the influence of patient age at the time of operation, patients were divided into 3 subgroups: patients age $\leq$32 years, 33-46 years, and >46 years. In all groups, a significant improvement was seen for both the Lysholm and the KOOS; however, there was no significant difference between the age groups. The data for the Lysholm scores are presented in Table 4. Although some of the scores exhibited a notable, apparent difference, the low numbers at some follow-up points precluded statistical significance. The results for VAS and KOOS scores showed similar magnitudes of change over time.

To investigate whether the score results were dependent on previous surgeries, the patients were divided into

TABLE 3
Patients With Lysholm Score Available in the Registry, Stratified by Study Period

	Year 0 (Baseline)	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
Lysholm score available, n	131	106	61	44	35	27	22	9

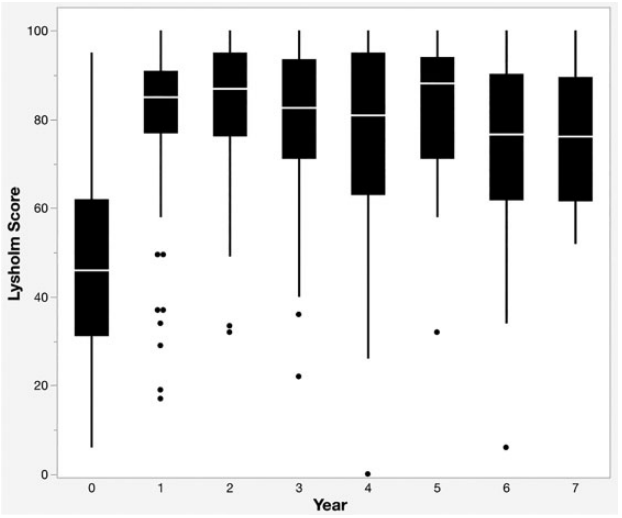

Figure 1. Lysholm scores over time. Treatment led to a significant ($P < .001$) improvement for up to 7 years compared with baseline. The preoperative and follow-up times are indicated. Scores are presented as means; the ends of the boxes define the 25th and 75th percentiles, and the whiskers depict the 1st and 4th quartiles. The dots depict the statistical outliers.

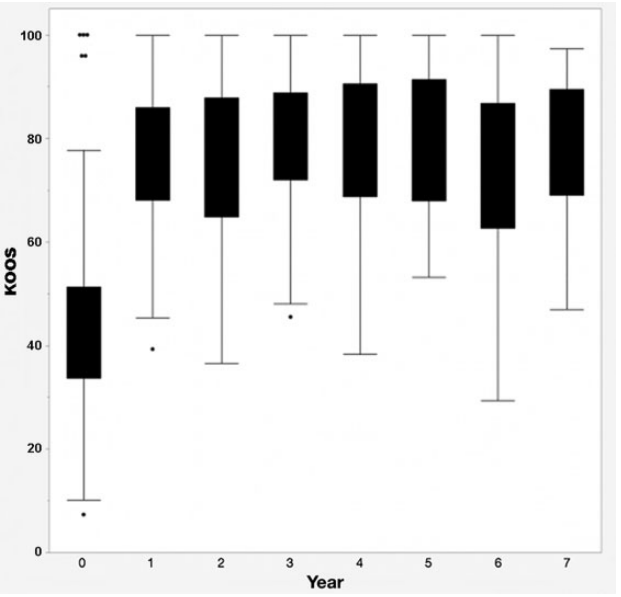

Figure 2. Knee injury and Osteoarthritis Outcome Scores (KOOS) over time. Treatment led to a significant ($P < .001$) improvement for up to 7 years compared with baseline. The preoperative and follow-up times are indicated. Scores are presented as medians; the ends of the boxes define the 25th and 75th percentiles, and the whiskers depict the 1st and 4th quartiles. The dots depict the statistical outliers.

2 subgroups: no previous surgery (NS) and previous surgery (PS). The previous surgeries included autologous chondrocyte implantation (ACI) (n = 1), matrix-associated ACI (n = 1), AMIC (n = 2), diagnostic arthroscopy (n = 7), drilling (n = 3), lavage with or without debridement (n = 27), and microfracture (n = 12). The Lysholm score did not exhibit a significant difference between the NS and PS groups ($P = .59$). The KOOS showed a trend toward improved scores in group NS at year 1 ($P = .09$) compared with group PS, but no further difference was seen between the groups. The VAS score showed no significant difference between the groups ($P = .39$). The outcome scores according to history of previous surgery are presented in Table 5.

The impact of cartilage defect location on the results was evaluated, with cases grouped as follows: medial femoral condyle, lateral femoral condyle, patella, trochlea, and tibial plateau. The Lysholm score improved significantly over time, but the location of the cartilage defect did not affect the results. This is presented in Table 6. Comparable changes were also seen for both VAS and KOOS, which both improved over time, while the localization of the defect did not demonstrate a significant difference.

Defect size was also an area of interest. We conducted a correlation analysis between the change in Lysholm score and defect size and noted no relationship between the 2 variables ($r^2 = 0.007$; $P = .39$), as shown in Figure 5.

DISCUSSION

The results of the present study indicated a significant improvement in all outcome scores analyzed as well as a significant decrease of pain up to 7-year follow-up. The positive effects of AMIC were seen at the 1-year postoperative visit, with clinically significant improvement in pain and functional outcomes. This improvement was stable without evidence of a tendency to deteriorate over time. Our results are in accordance with the results of a recent AMIC meta-analysis based on 12 studies (11 level 4 studies and 1 level 1 study) that included a total of 375 patients.[37] Most patients were very satisfied with the result of the index procedure and would choose to undergo the same procedure again, if needed. This is in agreement with our previous reported results at mid-term follow-up.[14]

Further, a randomized controlled trial confirmed the hypothesis that covering focal cartilage defects of the knee

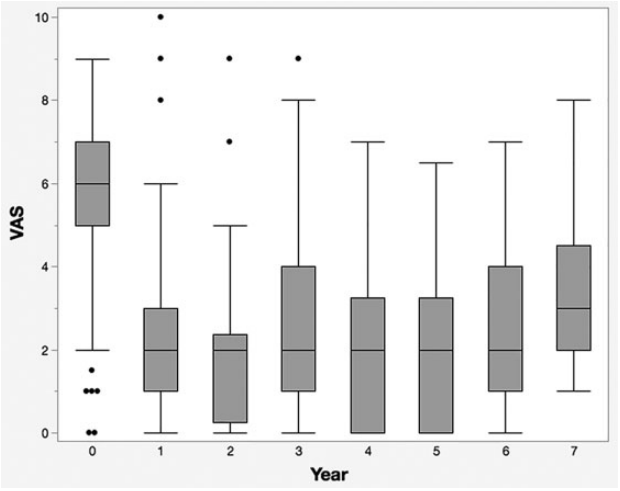

Figure 3. Visual analog scale (VAS) pain scores over time. Treatment led to a significant ($P < .001$) decline of the score values for up to 7 years compared with baseline. The preoperative and follow-up times are indicated. Scores are presented as medians; the ends of the boxes define the 25th and 75th percentiles, and the whiskers depict the 1st and 4th quartiles. The dots depict the statistical outliers.

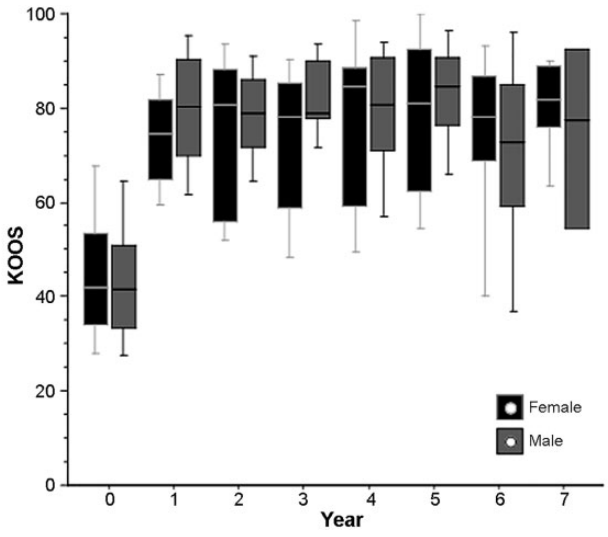

Figure 4. Differences in Knee injury and Osteoarthritis Outcome Scores (KOOS) over time, stratified by patient sex. Scores are presented as medians; the ends of the boxes define the 25th and 75th percentiles, and the whiskers depict the 1st and 4th quartiles. The dots depict the statistical outliers.

with a collagen I/III matrix (AMIC; Chondro-Gide) results in sustained benefit compared with microfracture alone.[38] This concurs with the literature, in which a beneficial effect has been shown by using several different scaffold-based approaches. Specifically, a case series presented good to excellent long-term clinical outcomes (mean 8 years of follow-up) of 1-stage cartilage repair in the knee with hyaluronic acid—based scaffold embedded with mesenchymal stem cells (sourced from bone marrow aspirate concentrate [BMAC]) in the treatment of small to large lesions.[15] Another prospective series with 28 patients that used a collagen type I scaffold (CaReS-1S; Arthro Kinetics) in large cartilage defects (mean defect size of 3.7 ± 1.9 cm^2) revealed clinical failure necessitating revision surgery in 5 of 28 patients (18%). Although the remaining patients showed good to excellent clinical results (on KOOS, VAS, Tegner score, and International Knee Documentation Committee score), the radiologic appearance of the repair tissue showed a reduction in the MOCART (magnetic resonance observation of cartilage repair tissue) score between the 2- and 5-year follow-up points.[33]

Validating earlier publications, we could not show a relationship between clinical results and patient age.[14,30] Further, in accordance with a recent study,[14] we could not show a significant impact of age on the results after AMIC at midterm follow-up. This is in accordance with data in the literature, showing no significant difference between younger (20-40 years) and older (40-60 years) groups after arthroscopic osteochondral autologous transplant.[26] Similarly, results after ACI showed a comparable failure rate in older patients compared with younger patients.[27] In contrast, older patients demonstrated a higher failure rate after microfracture or mosaicplasty when compared with younger cohorts.[35] Highlighting the patients' age, a prospective study involving patients treated with microfracture and ACI stated that the improvement in KOOS was significantly better for patients younger than 30 years compared with older patients.[8] This association between age and patient outcomes was also noted in a randomized controlled trial of 80 patients treated with ACI or microfracture.[18] Both of these studies concluded that the patient age influences the clinical outcome of ACI as well as microfracture, although our results after AMIC do not support their findings. Specific to ACI in comparison with AMIC, both procedures show comparable outcomes.[10] Although this was a fairly small study, with only 21 ACI patients and 20 AMIC patients, it seems that either treatment can achieve positive outcomes for patients.

In the present study, we found no sex-specific differences, as otherwise described for microfracture and mosaicplasty.[35] However, we demonstrated sex-related results after AMIC in a previous study.[14] Similarly, a follow-up study after ACI showed that female patients with patellar defects had worse prognostic factors than male patients.[19] Because little is known about sex-specific differences in cartilage repair, further studies should examine any sex-related differences in knee pathology, thus providing a knowledge base that may be used to refine related surgical treatments.

In our study, the defect size did not have a significant impact on the outcome. Both groups with small (<3 cm^2) and midsize (3-6 cm^2) defects showed significant improvements in all outcome scores along with a significant decrease in pain. Notably, the number of cases in the group of large defects (>6 cm^2) was too small for statistical analysis and thus broad generalization. The underlying reason for so few patients in the group with large defects stems

TABLE 4
Lysholm Scores for the Age Subgroups at Each Year of Follow-up[a]

Age Subgroup	Year 0	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
≤32 y	49.3 ± 20.3	80.6 ± 17.3	87.9 ± 12.8	77.6 ± 17.4	73.4 ± 29.3	83.9 ± 13.1	82.4 ± 13.6	81.0 ± 5.7
33-46 y	45.4 ± 18.9	85.0 ± 12.0	85.6 ± 11.4	79.6 ± 22.6	81.6 ± 14.4	82.2 ± 13.5	65.9 ± 33.7	79.3 ± 21.1
>46 y	42.3 ± 19.8	75.9 ± 22.4	72.1 ± 21.0	81.7 ± 15.9	72.4 ± 26.7	80.6 ± 22.3	71.7 ± 16.1	66.7 ± 12.9

[a]Data are reported as mean ± SD.

TABLE 5
Outcome Scores According to History of Previous Surgery[a]

	Lysholm		VAS		KOOS	
Year	NS Group	PS Group	NS Group	PS Group	NS Group	PS Group
0	46.9 ± 19.6	45.5 ± 20.1	5.4 ± 2.0	5.8 ± 1.6	42.7 ± 17.9	44.7 ± 11.5
1	83.8 ± 14.4	77.8 ± 19.3	1.8 ± 1.7	2.9 ± 2.1	79.1 ± 13.8	74.8 ± 12.4
2	85.2 ± 14.3	80.4 ± 17.7	1.4 ± 1.6	2.2 ± 1.9	77.6 ± 13.6	74.9 ± 16.1
3	81.6 ± 16.2	73.9 ± 22.3	2.2 ± 2.2	3.2 ± 2.6	79.6 ± 12.3	74.9 ± 16.2
4	77.2 ± 22.3	75.2 ± 26.5	2.0 ± 2.2	3.3 ± 2.9	76.7 ± 16.7	79.8 ± 15.8
5	84.5 ± 13.8	76.4 ± 22.1	1.8 ± 1.8	1.5 ± 1.5	82.6 ± 12.8	75.1 ± 16.3
6	73.7 ± 23.7	73.8 ± 22.3	2.8 ± 2.3	2.1 ± 2.0	76.8 ± 13.3	67.2 ± 25.1
7	77.0 ± 18.1	74.2 ± 16.3	3.5 ± 3.1	3.4 ± 1.3	80.7 ± 12.9	75.9 ± 18.3

[a]Data are reported as mean ± SD. KOOS, Knee injury and Osteoarthritis Outcome Score; NS, no previous surgery; PS, previous surgery; VAS, visual analog scale.

TABLE 6
Change in Lysholm Score for Each Defect Location Over the Follow-up Period[a]

	Year 0	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
Femoral condyle (lateral)	44.0 ± 15.8	82.2 ± 16.3	78.8 ± 15.4	61.5 ± 30.4	63.5 ± 42.9	75	80.4 ± 13.4	100
Femoral condyle (medial)	46.4 ± 20.1	83.0 ± 17.5	81.8 ± 19.3	92.4 ± 8.8	80.6 ± 19.7	85.9 ± 18.2	—	80.7 ± 11.7
Patella	43.7 ± 20.7	78.4 ± 17.6	84.1 ± 14.9	77.0 ± 15.6	79.2 ± 20.1	77.7 ± 13.8	70.3 ± 28.6	76.3 ± 9.0
Tibial plateau (lateral)	56.3 ± 32.0	72.3 ± 30.6	—	91	63	—	—	—
Trochlea	50.4 ± 12.7	84.9 ± 10.4	87.4 ± 12.7	95	80.5 ± 27.6	79.0 ± 16.9	62.0 ± 39.6	56

[a]Data are reported as mean ± SD. SDs are not provided for values with n = 1. Dashes indicate that no data were available for a lesion in that specific location at that time point.

from a former case series where patients with large defect size did not benefit from the AMIC procedure.[14] Therefore, patients presenting with a defect of this size are no longer scheduled for AMIC.

In the present cohort, no significant impact of the defect location on the results was observed. This is in contrast to the literature, where the concept has been brought forward that clinical outcomes and the incidence of complications are significantly influenced by defect location.[25] Respectively, cartilage lesions in the patellofemoral joint are generally regarded as more difficult to treat and lead to worse outcomes than lesions on the condyles.[20] Lesions treated with microfracture or mosaicplasty that did not involve the patellofemoral joint have been predicted to exhibit a good or excellent outcome.[35] Concerning ACI, an increased rate of hypertrophy was found for patellar defects, but no correlation was found for the occurrence of delamination, insufficient regeneration, and disturbed fusion.[25] In a prospective cohort study, de Windt et al[8] analyzed the prognostic value of defect location (medial vs lateral) on clinical outcome measures 3 years after treatment for a focal cartilage lesion using ACI and microfracture. The authors found a significantly better KOOS outcome for medial than for lateral lesions and therefore concluded that the defect location is related to clinical outcome of ACI and microfracture. A prospective cohort study by Kreuz et al[20] confirmed the effect of defect location on clinical outcome measures after microfracture procedures. However, our data are in contrast with the aforementioned studies, as we did not observe an impact of defect location on the outcome measures.

Clinical outcomes after cartilage restoration procedures might depend on addressing concomitant pathology. Although these additional procedures may affect the results, they are often part of the standard procedure. Therefore, to examine the outcomes that could be specific to the AMIC procedure, all cases with concomitant surgeries at the time of the index procedure were excluded from the present study. Similarly, other authors have excluded

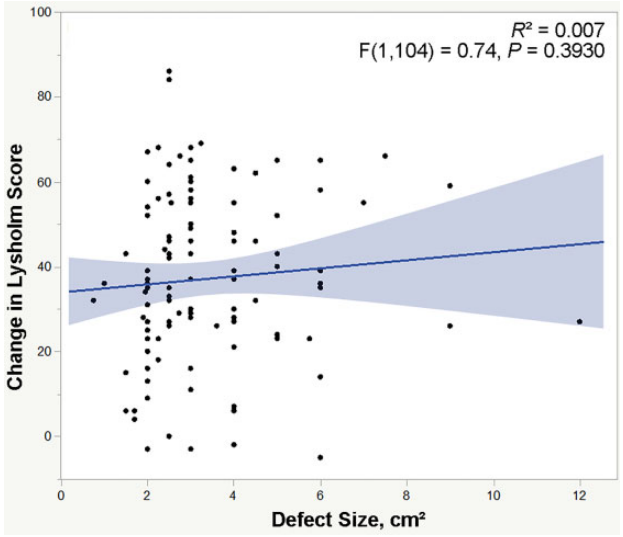

Figure 5. Correlation between defect size (in cm^2) and change in Lysholm scores. The dots in the graph depict the change of the score of each patient in relation to the defect size.

patients with malalignment, meniscal injury, and ligamentous instability.[34] Because patients were excluded when an additional treatment procedure was required (exclusion criteria), this might have introduced a patient selection bias versus the real standard of care, but this allowed us to minimize variables and focus on the AMIC outcomes.

Previous surgical procedures did not negatively influence the favorable follow-up results in our series. This is in contrast with the literature, where defects that had prior treatment affecting the subchondral bone failed at a rate 3 times higher than nontreated defects.[24] This may indicate that marrow-stimulation techniques may adversely affect subsequent cartilage repair via ACI. Therefore, careful planning is necessary if this technique is to be used for larger cartilage defects, which may need future treatment with ACI. This is in line with published data reflecting midterm results after matrix-associated autologous chondrocyte transplant.[2] Additionally, a recent study showed that the presence of bone marrow edema, detected by MRI after a prior marrow stimulation technique, was a predictive factor for graft failure among patients who then underwent second-generation ACI.[23]

A prospective, randomized clinical trial has addressed whether AMIC may benefit from association with other biological procedures, such as the addition of BMAC, to further stimulate the tissue repair ability of cells sourced from the microfracturing of the subchondral bone.[7] Both treatments (AMIC or AMIC+BMAC) provided improvements in function and pain lasting up to 100 months.[7] Our data support the fact that AMIC leads to reliable long-term results without an additional biological procedure (eg, BMAC). Modifications of the original AMIC technique may improve outcomes after chondral repair, but studies are required to confirm the initial results and reliability of modified AMIC techniques.

Although the results from the current study point to positive clinical outcomes resulting from the AMIC procedure, some limitations must be acknowledged. Some of these were previously mentioned by Gao et al,[12] who pointed to the need for further high-level studies. Although the recent data that were presented by Fossum et al[10] would certainly meet the criteria for a level 1 study, the use of data from a registry such as ours should not be discounted. The use of a registry provides real-world data among a diverse patient population, although this limits data collection because follow-up visits adhere to standard of care, whereas prospective studies will have predefined data collection points. Therefore, it is essential that a registry enroll the greatest number of patients possible. In our current registry-based study, the number of patients who had data at each postoperative time point decreased as time progressed from the baseline evaluation, which is a limitation of the registry that would have certainly decreased the power of the statistical analysis. With that in mind, it may also be necessary to adapt the statistical analyses to account for the gaps in data. Another confounding factor is that a multicenter registry may introduce variations in patient demographic characteristics or surgical technique that may influence outcomes. Therefore, continued enrollment to increase the numbers to be analyzed is essential to the provision of robust data.

In conclusion, AMIC is an effective and durable treatment, up to 7 years status postsurgically, for patients with Outerbridge grade III and IV cartilage defects in the knee. AMIC provides satisfactory results in terms of both pain relief and knee functional rehabilitation, which appear to be sustained in the majority of patients, according to our long-term follow-up results.

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