A commentary by Matthew J. Matava, MD, is linked to the online version of this article.

Long-Term Outcomes of Arthroscopically Verified Focal Cartilage Lesions in the Knee

A 19-Year Multicenter Follow-up with Patient-Reported Outcomes

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Background: Focal cartilage lesions (FCLs) are frequently found during knee arthroscopies and may impair quality of life (QoL) significantly. Several treatment options with good short-term results are available, but the natural history without any treatment is largely unknown. The aim of this study was to evaluate patient-reported outcome measures (PROMs), the need for subsequent cartilage surgery, and the risk of treatment failure 20 years after diagnosis of an FCL in the knee.

Methods: Patients undergoing any knee arthroscopy for an FCL between 1999 and 2012 in 6 major Norwegian hospitals were identified. Inclusion criteria were an arthroscopically classified FCL in the knee, patient age of ≥18 years at surgery, and any preoperative PROM. Exclusion criteria were lesions representing knee osteoarthritis or "kissing lesions" at surgery. Demographic data, later knee surgery, and PROMs were collected by questionnaire. Regression models were used to adjust for and evaluate the factors impacting the long-term PROMs and risk factors for treatment failure (defined as knee arthroplasty, osteotomy, or a Knee injury and Osteoarthritis Outcome Score-Quality of Life [KOOS QoL] subscore of <50).

Results: Of the 553 eligible patients, 322 evaluated patients (328 knees) were included and analyzed. The mean follow-up was 19.1 years, and the mean age at index FCL surgery was 36.8 years (95% confidence interval [CI], 35.6 to 38.0 years). The patients without knee arthroplasty or osteotomy had significantly better mean PROMs (pain, Lysholm, and KOOS) at the time of final follow-up than preoperatively. At the time of follow-up, 17.7% of the knees had undergone subsequent cartilage surgery. Nearly 50% of the patients had treatment failure, and the main risk factors were a body mass index of ≥25 kg/m^2 (odds ratio [OR] for overweight patients, 2.0 [95% CI, 1.1 to 3.6]), >1 FCL (OR, 1.9 [CI, 1.1 to 3.3]), a full-thickness lesion (OR, 2.5 [95% CI, 1.3 to 5.0]), and a lower level of education (OR, 1.8 [95% CI, 1.1 to 2.8]). Autologous chondrocyte implantation (ACI) was associated with significantly higher KOOS QoL, by 17.5 (95% CI, 3.2 to 31.7) points, and a lower risk of treatment failure compared with no cartilage treatment, microfracture, or mosaicplasty.

Conclusions: After a mean follow-up of 19 years, patients with an FCL who did not require a subsequent knee arthroplasty had significantly higher PROM scores than preoperatively. Nonsurgical treatment of FCLs had results equal to those of the surgical FCL treatments except for ACI, which was associated with a better KOOS and lower risk of treatment failure. Full-thickness lesions, >1 FCL, a lower level of education, and a greater BMI were the main risk factors associated with poorer results.

Level of Evidence: Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

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Focal cartilage lesions (FCLs) are frequently found in patients undergoing knee arthroscopy[1,2]. They may cause impairment of quality of life equivalent to that associated with end-stage osteoarthritis scheduled for treatment with knee arthroplasty[3,4]. The hyaline cartilage of the knee joint is unable to heal naturally because of its avascularity[5]. Several treatment options are available, but the optimal treatment is still unknown[6,7]. In the 1990s and the first decade of the 2000s, several new cartilage treatment options became available[8-10]. Most patients with surgically treated lesions can now expect good results, but few regain normal knee function[6,7,11]. Several clinical studies on cartilage treatment have shown good to excellent short-term results, but there are concerns regarding the long-term results[7]. Newer generations of cell-based treatments have had increasing popularity despite a lack of evidence of their superiority[12]. Randomized controlled trials (RCTs) have failed to represent the heterogeneous group of patients with an FCL encountered in an orthopaedic practice[13]. Cartilage registries might contribute to our knowledge, but currently only short-term results are available[14]. The long-term natural history of a nonoperatively treated FCL is largely unknown[15-18].

The aims of the present study were to (1) evaluate long-term patient-reported outcome measures (PROMs) in patients with arthroscopically verified FCLs in the knee, in particular using the Knee injury and Osteoarthritis Outcome Score-Quality of Life (KOOS QoL) subscore, (2) examine the need for subsequent cartilage surgery, (3) identify risk factors for treatment failure after an FCL, and (4) compare long-term PROMs and risk of treatment failure after different treatment options, including nonoperative treatment.

Materials and Methods

The study was approved by the Regional Ethics Committee (2017/1387). Patients with arthroscopically verified FCLs were identified in the records of 6 major Norwegian hospitals between 1999 and 2012 (Fig. 1). These hospitals had a high volume of cartilage surgery and participated in several prospective cartilage studies during this period[1,19-21].

The inclusion criteria in this study were any arthroscopically verified and classified FCL in the knee, patient age of ≥18 years at the time of surgery, and availability of at least 1 preoperative PROM. Exclusion criteria were cartilage lesions assessed as osteoarthritis or as "kissing lesions" on apposing surfaces at the time of the arthroscopy (Fig. 1). The 553 eligible patients received a questionnaire regarding their current height, weight, level of education, and knee function, and any previous or later knee surgery. In addition, the patients were asked to complete the KOOS as well as any other PROM that had been used at the time of diagnosis[22]. The PROMs used preoperatively were the KOOS[22], Lysholm scale[23], and International Cartilage Regeneration and Joint Preservation Society (ICRS) visual analogue scale (VAS) for knee pain[24].

Patients identified as eligible for participation in the present study were contacted by mail. Patients registered in the Norwegian Population Register as deceased or emigrated were excluded. After informed consent was obtained, the participants' trial data and/or surgical report were made available to the principal investigator (T.B.). The following variables were retrieved: the characteristics of the FCL (location, size [measured using a standard 4-mm probe], and grade according to the ICRS classification[25]), type of surgical treatment, any concomitant procedures, and preoperative PROM score. Nine knees in 8 patients meeting the exclusion criteria at the index surgery were then identified and excluded. The final follow-up was performed between March 6 and December 31, 2020.

Failure was defined as subsequent knee arthroplasty, subsequent knee osteotomy, or a KOOS QoL of <50 at the time of final follow-up. A KOOS QoL of ≥50 is considered to be the patient acceptable symptom state (PASS) after cartilage surgery[26]. The details of the arthroplasty group have been published previously[27].

Patients with knee arthroplasty or osteotomy were excluded from the analysis of PROMs but included in the analysis of treatment failure.

Statistical Analysis

Multiple logistic regression models were used to identify risk factors for failure, and multiple linear regression models were used to evaluate the factors influencing the KOOS QoL. A graphical causal model (www.dagitty.net/dags.html) was used to identify variables to adjust for in the regression models, as suggested by Westreich and Greenland[28]. In a secondary analysis, a subgroup that excluded patients with patellofemoral lesions was also analyzed using the same model. The time since cartilage surgery was calculated as the time from the index cartilage surgery until the questionnaire follow-up for the KOOS analysis and until the end of the study on December 31, 2020, for the failure analysis. The Lysholm and ICRS pain VAS scores were recorded preoperatively in only 185 and 114 patients, respectively, and no patients had >1 preoperative PROM; however, all patients had the KOOS recorded at the time of final follow-up.

A paired-sample t test was used to evaluate the difference in PROM scores between preoperatively and the time of final follow-up. A pre-inclusion power analysis suggested that 64 patients in each group were needed to detect a difference of 10 points in the KOOS, given a standard deviation of 20 points, at an α level of 0.05 and a power of 0.8. All analyses were performed using SPSS Statistics (version 26; IBM) and STATA (version 17; StataCorp).

Results

Of the 553 patients identified, 507 patients (516 knees) were eligible and, of those, 322 (63.5%, 328 knees) consented to participate (Fig. 1). The characteristics of these patients (responders) and their knees are summarized in Table I and Appendix Supplementary Table 1. At baseline, the only significant difference between the responders and nonresponders was that the responders were a mean of 3.0 years older (p = 0.002). Most of the lesions were ICRS grade 3 or 4 (84.1%), and their mean size was 2.0 cm^2 (95% confidence interval [CI], 1.8 to 2.2 cm^2). The mean follow-up time was 19.1 years (95% CI, 18.8 to 19.5 years), and the mean age at the time of the index

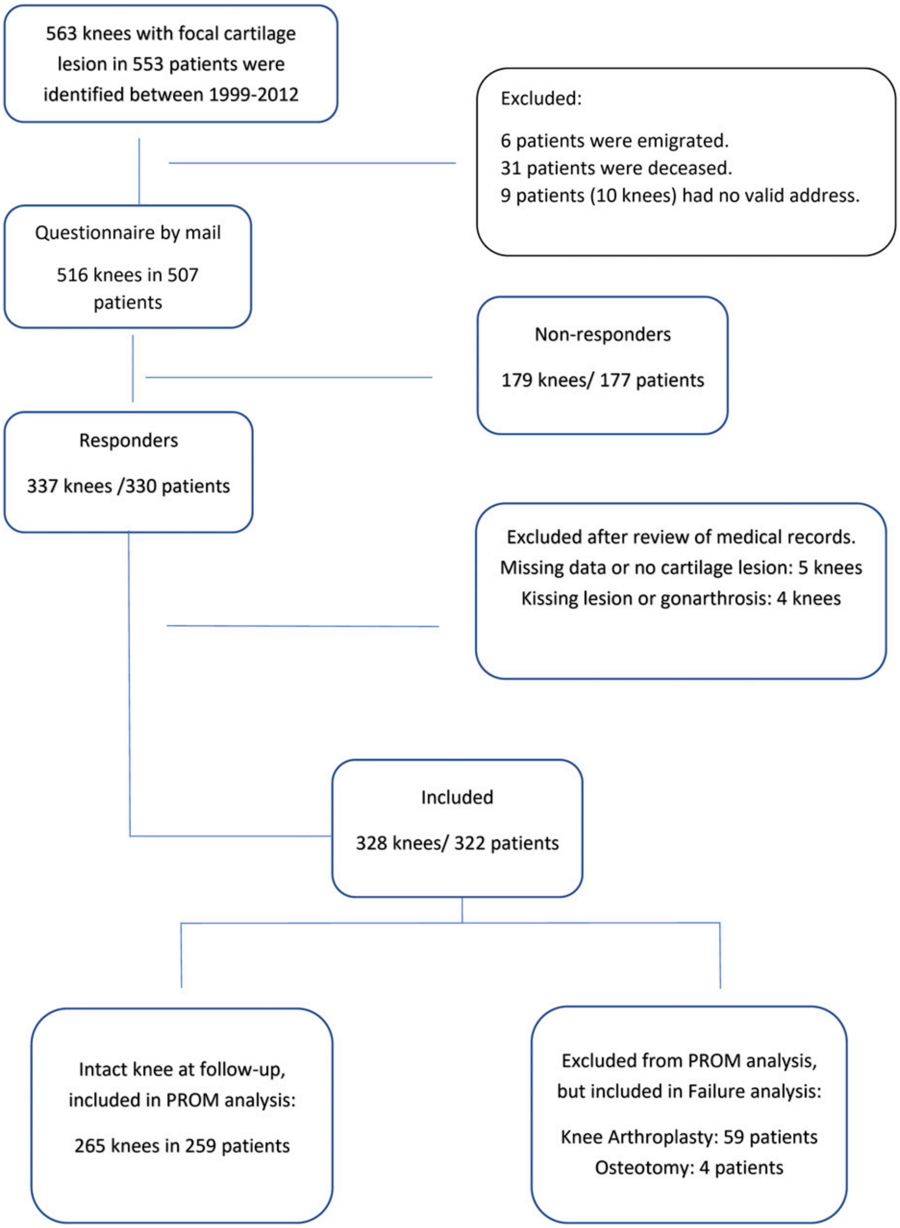

Fig. 1
Flowchart illustrating the inclusion of patients in the cartilage cohort.

surgery was 36.8 years. Fifty-nine patients (18%) had undergone knee arthroplasty and 4 patients (1.2%) had undergone femoral or tibial osteotomy by the time of follow-up. No patients had >1 preoperative PROM recorded, 8.8% had the KOOS recorded, 56.4% had the Lysholm score recorded, and 34.8% had the ICRS pain VAS recorded preoperatively. Most patients did not have any joint-space narrowing on their pre-enrollment weight-bearing radiograph.

Long-Term PROMs and Factors of Significant Influence

Mean PROM values preoperatively and at the time of final follow-up for the 254 patients (260 knees) without subsequent knee arthroplasty or osteotomy are presented in Table II and Figure 2; there was significant improvement in all PROM scores. Nine patients did not provide a PROM at the time of final follow-up. The mean KOOS subscores for all patients (n = 256, 262 knees) with an intact native knee at the time of final follow-up are presented in Table I. The unadjusted KOOS Sport/Recreation and KOOS QoL subscores at the time of final follow-up are presented by treatment group in Figures 3 and 4. In a multiple linear regression model (Table III), a higher level of education, treatment with autologous cartilage implantation (ACI), a higher preoperative Lysholm score, longer follow-up, and a lesion of the lateral compartment were associated with a better KOOS QoL subscore, while >1 lesion and ICRS grade-3 or 4 lesions were associated with a poorer score.

TABLE I Descriptive Statistics of the 328 Knees and 322 Patients with Focal Cartilage Lesions*

	No. (%) or Mean (95% CI)
Knees	328
Male/female	188 (57%)/140 (43%)
Right/left knee	173 (53%)/154 (47%)
Age at the time of surgery *(yr)*	36.8 (35.6, 38.0)
Time from index surgery to PROM follow-up *(yr)*	19.1 (18.8, 19.5)
Cartilage lesion ICRS grade 1-2/3-4	52 (16%)/276 (84%)
Size of cartilage lesion *(mm²)*	201.3 (178.9, 223.7)
Location of cartilage lesion†	
Patellofemoral	73 (22.3%)
Medial	204 (62.2%)
Lateral	51 (15.5%)
Type of index cartilage treatment	
None	93 (28.4%)
Microfracture	124 (37.8%)
Debridement	10 (3.0%)
ACI	30 (9.1%)
Mosaicplasty	53 (16.2%)
Other‡	18 (5.5%)
Level of education	
High school	155 (47.3%)
Bachelor's/master's degree	164 (50.0%)
Body mass index at end of study	27.4 (26.9, 27.9)
<25 kg/m²	100 (30.5%)
25-30 kg/m²	137 (41.8%)
>30 kg/m²	75 (22.9%)
ACL reconstruction in ipsilateral knee	50 (15.2%)
Yes	
At index surgery	15 (4.6%)
Before or after index surgery	35 (10.7%)
No	278 (84.8%)
Meniscal resection in ipsilateral knee	100 (30.5%)
Yes	
At index surgery	46 (14.0%)
Before or after index surgery	54 (16.5%)
No	228 (69.5%)
Knee arthroplasty	59 (18.0%)
Osteotomy	4 (1.2%)
KOOS at final follow-up in intact knees (n = 262§)	
KOOS Symptoms	72.7 (70.2-75.3)
KOOS Pain	73.9 (71.1-71.1)
KOOS Activities of Daily Living	81.0 (78.4-83.7)
KOOS Sport/Recreation	50.3 (46.5-46.5)
KOOS Quality of Life	58.1 (54.8-61.3)

*The lesions were diagnosed in 6 Norwegian hospitals between 1999 and 2012 All values are on a per-knee basis. When patients had >1 lesion, information on the largest lesion was used.CI = confidence interval, ICRS = International Cartilage Repair and Joint Preservation Society, ACI = autologous cartilage implantation. †Detailed location information by treatment group is given in Appendix Supplementary Table 1. ‡Trufit, Caritpatch, or MaioRegen. §Knees without arthroplasty or osteotomy.

Subsequent Cartilage Surgery

Forty-seven (17.7%) of the intact knees had undergone at least 1 subsequent cartilage surgery after the index surgery, as reported by the patients. The prevalence was 10.1% for knees with no operative treatment, 21.7% after microfracture, 18.2% after ACI, 26.6% after mosaicplasty, and 17.9% after other treatment. The differences between the treatment groups were not significant (p = 0.21; chi-square test). Most of the patients did not provide sufficient details regarding the subsequent surgery to classify that surgery.

Risk Factors for Treatment Failure

At the time of final follow-up, 162 knees (49.4%) were classified as failures (59 knee arthroplasties, 4 osteotomies, and 99 in patients reporting KOOS QoL < 50). The unadjusted and adjusted multiple logistic regression models of failure are summarized in Table IV. A body mass index (BMI) of 25 to <30 or ≥30 kg/m² increased the odds of failure at the time of follow-up, with odds ratios (ORs) of 2.0 (95% Cl, 1.1 to 3.6; p = 0.016) and 3.1 (95% Cl, 1.6 to 5.9; p = 0.001), respectively. A lower level of education had an OR of 1.8 (95% Cl, 1.1 to 2.8; p = 0.011) compared with patients with a bachelor's or master's degree. More than 1 cartilage lesion increased the odds of failure 1.9 times (95% Cl, 1.1 to 3.3; p = 0.035). ICRS grade-3 or 4 lesions had 2.5 times (95% Cl, 1.3 to 5.0; p = 0.009) higher odds of failure compared with ICRS grade-1 or 2 lesions. However, lesion size did not influence the odds of subsequent failure, nor did gender, age at the time of cartilage surgery, duration of follow-up, anterior cruciate ligament (ACL) reconstruction or meniscal resection, or the preoperative PROM score.

PROMs and Risk of Treatment Failure by Cartilage Treatment

The odds of treatment failure did not differ significantly between the group with no surgical treatment and the surgical treatment groups except for ACI treatment, which was associated with decreased odds of treatment failure (OR = 0.3) (Table IV). Moreover, ACI was associated with significantly higher mean KOOS QoL than no surgical cartilage treatment (p = 0.017) (Table III), but with an increased risk of arthroplasty[27]. Unadjusted KOOS QoL subscores are presented in Figure 4.

Discussion

Long-Term PROM Results

In the present study, we found a mean KOOS QoL of 58.1 at the time of final follow-up. In a series of 44 patients, Ossendorff et al.[29] found a KOOS QoL of 49 in patients with first-generation ACI treatment versus 64 in patients treated with microfracture. Furthermore, Kreuz et al.[30] and Niemeyer et al.[31] found KOOS QoL subscores of 58.0 and 54.3, respectively, in their studies. Even though the present study had considerably longer follow-up, the PROM results can likely be compared with those previous studies, as several previous studies have suggested stable results from mid- to long-term follow-up[30,32-34]. In contrast, Gobbi et al.[35] presented 15-year follow-up of 67 athletes with full-thickness lesions treated with microfracture in which the final KOOS QoL was 82.2. The higher KOOS value

TABLE II PROMs at the Time of Index Surgery and at the Time of Final Follow-up in the Patients without Subsequent Knee Arthroplasty or Osteotomy*

PROM	Preoperative†	Final Follow-up†	Improvement†	P Value
ICRS VAS‡ (n = 94)	58.0 (53-62.9)	71.1 (66.4-75.8)	12.4 (6.2-18.5)	<0.001
Lysholm (n = 140)	50.2 (47.4-53.0)	72.0 (68.6-75.4)	21.4 (17.7-25.2)	<0.001
KOOS Symptoms (n = 26)	50.0 (45.2-54.9)	70.1 (62.1-78.1)	20.0 (12.2-27.9)	<0.001
KOOS Pain (n = 26)	48.6 (42.6-54.6)	70.4 (60.4-80.4)	20.4 (11.0-29.7)	<0.001
KOOS ADL (n = 26)	61.1 (53.4-68.8)	77.7 (67.8-87.5)	16.5 (8.2-24.8)	<0.001
KOOS Sport/Recreation (n = 26)	23.5 (17.2-29.7)	41.7 (29.0-54.4)	18.3 (9.0-27.5)	<0.001
KOOS QoL (n = 26)	23.1 (18.2-28.1)	48.9 (38.1-59.7)	25.8 (17.0-34.6)	<0.001

*The values are given for the patients who answered the specific questionnaire both preoperatively and at the time of follow-up. PROM = patient-reported outcome measure, ICRS = International Cartilage Repair and Joint Preservation Society, VAS = visual analogue scale, ADL = Activities of Daily Living, QoL = Quality of Life. †The values are given as the mean with the 95% confidence interval in parentheses. ‡0 = no pain, 100 = worst pain imaginable.

might be due to a more active study population, as physical training has been shown to increase the KOOS in patients with an FCL[36]. Multiple lesions were associated with poorer KOOS QoL in our study. A possible explanation is that multiple lesions may alter knee homeostasis more than a single lesion would[37].

A lower level of education was associated with a poorer KOOS. An associated higher risk of heavy manual labor and a lower level of physical training might contribute to this. Furthermore, lower socioeconomic status is known to be associated with decreased self-reported general health[38].

Medial and lateral FCLs were associated with significantly better KOOS QoL compared with patellofemoral lesions. The poorer result for patellar lesions is consistent with previous studies[39-41]. Analysis of the subgroup without patellofemoral lesions using the same regression model gave the same overall results, indicating that the original model was able to adjust for the FCL location (see Appendix Supplementary Table 2).

Subsequent Cartilage Surgery

At the time of final follow-up, 47 (17.7%) of the knees had undergone subsequent cartilage surgery. In comparison, Niemeyer et al.[31] reported that 28.6% of patients treated with ACI required additional cartilage surgery and Ossendorff et al.[29] reported a 34% reoperation rate. The present study found no significant differences in the rate of subsequent cartilage surgery according to treatment, even though there was substantial variation in the rates. This could suggest that our analysis was underpowered. We also did not have detailed data on the nature of the subsequent cartilage surgical treatments, and the types of subsequent surgery could therefore have differed substantially among the different types of index surgery.

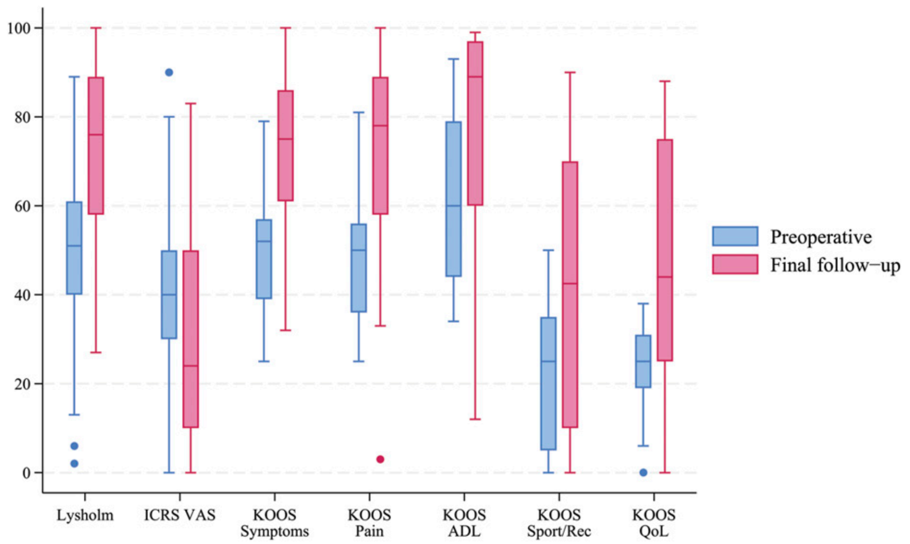

Fig. 2

Patient-reported outcome measures preoperatively (shortly before the index surgery) and at the time of final follow-up. The top and bottom of a box represent the interquartile range, the line within the box represents the median, whiskers represent the values within 1.5 times the interquartile range of the box, and circles represent outliers. For the ICRS, 0 = no pain and 100 = the worst pain imaginable. ADL = Activities of Daily Living.

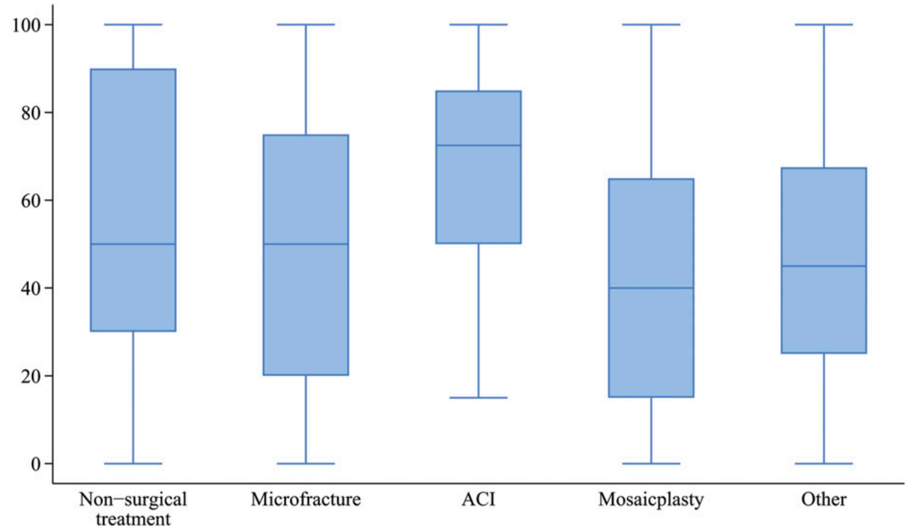

Fig. 3

Unadjusted KOOS Sport/Recreation subscores at the time of final follow-up, by treatment group, excluding patients with knee arthroplasty or osteotomy. The top and bottom of a box represent the interquartile range, the line within the box represents the median, and whiskers represent the values within 1.5 times the interquartile range of the box. Autologous chondrocyte implantation (ACI) differed significantly from mosaicplasty and from microfracture ($p < 0.003$). Nonsurgical treatment also differed significantly from mosaicplasty ($p < 0.05$). Other = debridement, MaioRegen (Finceramica, Italy), Cartipatch (Xizia, Hong Kong), or TruFit (Smith and Nephew).

Risk Factors for Treatment Failure

The rate of failure (defined as knee arthroplasty, osteotomy, or KOOS QoL < 50) was nearly 50%. Several other studies have defined any subsequent cartilage surgery as failure[31,34,35,42]. However, from a 20-year perspective, any subsequent surgery might not be the best failure measure. Knee arthroplasty is the final outcome of end-stage osteoarthritis and must be considered a failure in cartilage surgery. However, the risk of undergoing a knee replacement might vary considerably among countries as well as regions of a country[43,44]. To compensate for this, we also classified patients with a KOOS QoL subscore of <50 as having a treatment failure, as Chahal et al.[26] demonstrated this to be the PASS in patients with an FCL. The failure rate of nearly 50% seems high. Nonetheless, as previously discussed, the mean KOOS QoL in the present study is comparable with that in other long-term studies.

More than 1 FCL was associated with increased odds of failure, consistent with the results of Gobbi et al.[35]. An elevated

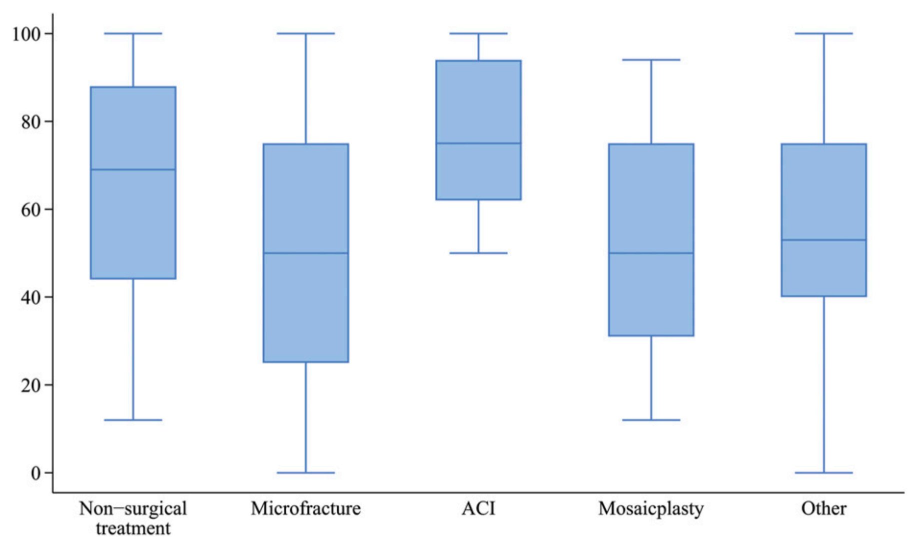

Fig. 4

Unadjusted KOOS Quality of Life (QoL) subscores at the time of final follow-up, by treatment group, excluding patient with knee arthroplasty or osteotomy. The top and bottom of a box represent the interquartile range, the line within the box represents the median, and whiskers represent the values within 1.5 times the interquartile range of the box. Autologous chondrocyte implantation (ACI) differed significantly from both mosaicplasty and microfracture ($p < 0.001$). Other = debridement, MaioRegen, Cartipatch, or TruFit.

TABLE III Factors Influencing the KOOS QoL at Final Follow-up of Focal Cartilage Lesions in the Knee*

	Unadjusted			Adjusted†		
	Mean Difference‡	95% CI	P Value	Mean Difference‡	95% CI	P Value
Gender§						
Male	Ref.					
Female	−2.7	−9.2, 3.8	0.418			
No. of cartilage lesions#						
1	Ref.			Ref.		
≥2	−6.4	−14.3, 1.4	0.111	−11.1	−19.5, −2.8	0.009
Cartilage lesion size**						
<2 cm^2	Ref.			Ref.		
≥2 cm^2	3.9	−2.9, 10.7	0.264	4.8	−2.1, 11.7	0.171
Age at index surgery§						
<30 yr	Ref.					
30-39 yr	−1.7	−9.7, 6.2	0.622			
≥40 yr	4.3	−4.3, 13.0	0.325			
BMI††						
<25 kg/m^2	Ref.			Ref.		
25-29 kg/m^2	−6.0	−13.4, 1.3	0.111	−5.4	−13.2, 2.4	0.178
≥30 kg/m^2	−8.2	−17.1, 0.7	0.072	−7.0	−16.1, 2.1	0.132
Level of education‡‡						
Bachelor's/master's degree	Ref.			Ref.		
High school	−7.9	−14.4, −1.4	0.018	−8.7	−15.2, −2.2	0.009
Ipsilateral ACL reconstruction§§						
No	Ref.			Ref.		
Yes	1.1	−8.1, 10.2	0.815	0.51	−8.7, 9.7	0.913
Ipsilateral meniscal resection##						
No	Ref.			Ref.		
Yes	−0.8	−7.9, 6.2	0.815	−2.5	−9.7, 4.8	0.505
ICRS grade***						
1-2	Ref.			Ref.		
3-4	−11.2	−19.5, −2.9	0.008	−9.8	−18.8, −0.9	0.032
Cartilage treatment at index surgery†††						
No treatment	Ref.			Ref.		
Microfracture	−11.2	−19.0, −3.4	0.005	−6.0	−15.9, 3.9	0.231
ACI	13.2	0.9, 25.5	0.036	17.5	3.2, 31.7	0.017
Mosaicplasty	−11.0	−20.8, −1.2	0.028	−9.4	−21.6, 2.8	0.129
Other‡‡‡	−10.1	−21.3, 1.1	0.078	−3.8	−17.7, 10.1	0.592
Location of cartilage lesion§§§						
Patellofemoral	Ref.			Ref.		
Medial compartment	7.8	0.1, 15.5	0.046	7.2	−0.8, 15.2	0.077
Lateral compartment	17.1	6.4, 27.7	0.002	17.6	6.9, 28.3	0.001
Time since index cartilage surgery### *(yr)*	0.9	0.0, 1.9	0.052	0.98	0.04, 1.93	0.040
Preoperative Lysholm score****	0.5	0.2, 0.7	<0.001	0.31	0.04, 0.57	0.023
Preoperative ICRS VAS††††	−0.2	−0.4, 0.1	0.183	−0.05	−0.32, 0.21	0.690

*Patients with ipsilateral knee arthroplasty or osteotomy prior to final follow-up were excluded. CI = confidence interval, OR = odds ratio, BMI = body mass index, ACL = anterior cruciate ligament, ACI = autologous chondrocyte implantation. †Mean difference adjusted according to a graphical causal model. ‡Mean difference in KOOS QoL subscore from reference. A negative number implies a lower mean score than the reference. §Not adjusted. #Adjusted for age at cartilage surgery, ACL reconstruction, BMI, gender, level of education, meniscal resection, size of cartilage lesion, and time from cartilage surgery to questionnaire follow-up. **Adjusted for age at cartilage surgery, BMI, meniscal resection, and time from cartilage surgery to questionnaire follow-up. ††Adjusted for age at cartilage surgery, gender, level of education, and time from cartilage surgery to questionnaire follow-up. ‡‡Adjusted for gender. §§Adjusted for gender, level of education, age at cartilage surgery, BMI, and time from cartilage surgery to questionnaire follow-up. ##Adjusted for age at cartilage surgery, BMI, ICRS grade, and time from cartilage surgery to questionnaire follow-up. ***Adjusted for age at cartilage surgery, BMI, meniscal resection, and time from cartilage surgery to questionnaire follow-up. †††Adjusted for age at cartilage surgery, ICRS grade, level of education, location of cartilage lesion, number of cartilage lesions, size of cartilage lesion, and time from cartilage surgery to questionnaire follow-up. ‡‡‡Debridement, Trufit, Caritpatch, or MaioRegen. §§§Adjusted for ACL reconstruction, age at cartilage surgery, gender, and meniscal resection. ###Adjusted for location of cartilage lesion, ACL reconstruction, age at cartilage surgery, gender, meniscal resection, BMI, cartilage treatment at index surgery, ICRS grade, level of education, number of cartilage lesions, and size of lesion. ****Adjusted for ACL reconstruction, age at cartilage surgery, BMI, gender, ICRS grade, level of education, location of cartilage lesion, meniscal resection, number of cartilage lesions, size of lesion, and time from cartilage surgery to questionnaire follow-up. ††††Adjusted for ACL reconstruction, age at cartilage surgery, BMI, gender, ICRS grade, level of education, location of cartilage lesion, meniscal resection, number of cartilage lesions, size of lesion, time from cartilage surgery to questionnaire follow-up, and cartilage treatment at index surgery.

TABLE IV Risk Factors for Treatment Failure*

		Unadjusted			Adjusted†		
	Failures	OR	95% CI	P Value	OR	95% CI	P Value
Total	162 (49.4%)						
Gender‡							
Male	87 (46.3%)	1					
Female	75 (53.6%)	1.3	0.8, 2.0	0.262			
Number of cartilage lesions§							
1	112 (45.9%)	1					
≥2	50 (59.5%)	1.9	1.2, 3.2	0.010	1.9	1.1, 3.3	0.035
Size of cartilage lesion#							
<2 cm²	110 (51.4%)				1		
≥2 cm²	52 (45.6%)	0.67	0.4, 1.1	0.119	0.8	0.5, 1.3	0.319
Age at time of index surgery‡							
<30 yr	36 (43.9%)	1					
30-39 yr	62 (49.2%)	1.2	0.7, 2.2	0.454			
>40 yr	64 (55.2%)	1.6	0.9, 2.8	0.119			
BMI**							
<25 kg/m²	37 (37.0%)	1			1		
25-29 kg/m²	70 (51.1%)	2.5	1.4, 4.4	0.001	2.0	1.1, 3.6	0.016
≥30 kg/m²	45 (60.0%)	2.6	1.4, 5.0	0.003	3.1	1.6, 5.9	0.001
Level of education††							
Bachelor's/master's degree	70 (42.7%)	1			1		
High school	87 (56.1%)	0.5	0.3, 0.8	0.003	1.8	1.1, 2.8	0.011
Ipsilateral ACL reconstruction‡‡							
No	139 (50.0%)	1			1		
Yes	23 (46.0%)	1.0	0.5, 1.8	0.916	1.1	0.6, 2.1	0.785
Ipsilateral meniscal resection§§							
No	110 (48.2%)	1			1		
Yes	52 (52.0%)	1.1	0.7, 1.8	0.574	1.3	0.8, 2.2	0.337
ICRS grade##							
1-2	17 (32.7%)	1			1		
3-4	145 (52.5%)	1.8	1.0, 3.5	0.061	2.5	1.3, 5.0	0.009
Cartilage treatment at index surgery***							
No treatment	40 (43.0%)	1			1		
Microfracture	71 (57.3%)	1.8	1.0, 3.1	0.038	1.2	0.6, 2.5	0.638
ACI	8 (26.7%)	0.5	0.2, 1.2	0.115	0.3	0.1, 1.0	0.040
Mosaicplasty	30 (56.6%)	1.7	0.9, 3.4	0.115	1.5	0.6, 3.9	0.369
Other†††	13 (46.4%)	1.1	0.5, 2.7	0.749	0.8	0.3, 2.7	0.752
Location of cartilage lesion‡‡‡							
Patellofemoral	42 (57.5%)	1			1		0.303
Medial compartment	98 (48.0%)	0.8	0.5, 1.4	0.513	0.7	0.4, 1.2	0.167
Lateral compartment	22 (43.1%)	0.7	0.4, 1.5	0.417	0.5	0.2, 1.1	0.82
Time since index cartilage surgery§§§		1.0	0.9, 1.0	0.442	1.0	0.9, 1.1	0.588
Preoperative Lysholm score###		0.98	0.96, 1.0	0.013	0.98	0.96, 1.00	0.107
Preoperative ICRS VAS****		1.03	1.01, 1.05	0.004	1.01	0.99, 1.04	0.190

*Failure was defined as ipsilateral knee arthroplasty, ipsilateral knee osteotomy, or KOOS QoL subscore < 50. OR = odds ratio, BMI = body mass index, ACL = anterior cruciate ligament, ACI = autologous chondrocyte implantation. †OR adjusted according to a graphical causal model. ‡Not adjusted. §Adjusted for number of cartilage lesions, age at cartilage surgery, ACL reconstruction, BMI, gender, level of education, meniscal resection, size of cartilage lesion, and time from cartilage surgery to the end of the study. #Adjusted for BMI, meniscal resection, and time from cartilage surgery to the end of the study. **Adjusted for age at cartilage surgery, gender, level of education, and time from cartilage surgery to the end of the study. ††Adjusted for gender. ‡‡Adjusted for gender, level of education, age at cartilage surgery, BMI, and time from cartilage surgery to the end of the study. §§Adjusted for age at cartilage surgery, BMI, ICRS grade, and time from cartilage surgery to the end of the study. ##Adjusted for age at cartilage surgery, BMI, meniscal resection, and time from cartilage surgery to the end of the study. ***Adjusted for age at cartilage surgery, ICRS grade, level of education, location of cartilage lesion, number of cartilage lesions, size of cartilage lesion, and time from cartilage surgery to the end of the study. †††Debridement, Trufit, Caritpatch, or MaioRegen. ‡‡‡Adjusted for ACL reconstruction, age at cartilage surgery, gender, and meniscal resection. §§§Adjusted for location of cartilage lesion, ACL reconstruction, age at cartilage surgery, gender, meniscal resection, BMI, cartilage treatment at index surgery, ICRS grade, level of education, number of cartilage lesions, and size of lesion. ###Adjusted for ACL reconstruction, age at cartilage surgery, BMI, gender, ICRS grade, level of education, location of cartilage lesion, meniscal resection, number of cartilage lesions, size of lesion, and time from cartilage surgery to the end of the study. ****Adjusted for ACL reconstruction, age at cartilage surgery, BMI, gender, ICRS grade, level of education, location of cartilage lesion, meniscal resection, number of cartilage lesions, size of lesion, time from cartilage surgery to the end of the study, and cartilage treatment at index surgery.

BMI was also associated with increased odds of failure, even in the general population[11,43].

Long-Term PROMs and Risk of Failure According to Cartilage Treatment Strategy

We found a higher KOOS QoL subscore in the patients treated with ACI compared with the other treatment strategies, including no surgical treatment. In contrast, Ossendorff et al.[29] found that patients treated with microfracture had significantly higher scores than patients treated with ACI. However, their analysis was not fully adjusted for significantly larger defects in the ACI group, and this might have introduced bias.

In a previously published study of the same cartilage cohort, we found ACI treatment to increase the risk of knee arthroplasty[27]. Thus, it was notable that ACI had the lowest risk of failure overall. Furthermore, the number of patients scoring their condition below the PASS was considerably lower than in the other treatment groups. The higher risk of knee arthroplasty is concerning. However, perhaps the patients treated with ACI had been more prone to undergo knee arthroplasty than the other patients in the event of a failure. Cartilage allograft is not available in Norway, and revision options in case of a failed ACI treatment that had involved a large area may be limited. This could at least partially explain the higher rate of knee arthroplasty.

The present study included a heterogeneous patient cohort. Our findings do, however, highlight the need for long-term follow-up of patients in RCTs, as was also suggested in a review by Orth et al.[18], as well as in cartilage-registry studies. Furthermore, including a sham-surgery arm in future RCTs should be considered.

Strength and Limitations

The main strength of the present study is the large number of knee FCLs that were evaluated arthroscopically in detail. Any concurrent knee injuries (including meniscal and ligamentous) were recorded. Even though the exact alignment of the legs remains unknown, due to the lack of a standardized preoperative radiographic protocol, all included patients had <5° of malalignment as that was an inclusion criterion of the previous clinical trials[19-21]. To our knowledge, this is the first study outside an ACL cohort that compares the PROM results of arthroscopically verified FCLs with no operative cartilage treatment and those of surgically treated lesions.

This study has several limitations. One hundred and fifty of the patients had participated in studies with previously published long-term results[32,33,42]. Therefore, they might not represent the average patient with an FCL[13]. The response rate of 65% might have introduced bias. The study was not an RCT, and the differences in the final PROM results should therefore be interpreted with caution. The number of participants suggested by the power analysis was not met in all of the subgroups, increasing the risk of a type-2 error in certain comparisons. Several of the patients did not provide sufficient details regarding any subsequent cartilage treatment after the index surgery. Three different PROMs were used preoperatively, and no patient had >1 preoperative PROM; because of list-wise deletion, this limited the adjustment of the regression models based on PROM data. Standardized preoperative radiographs were not available, nor was an activity scale.

Conclusion

At a mean 20-year follow-up, patients with an FCL without subsequent knee arthroplasty had significantly better PROM scores than preoperatively, even though nearly 50% of the knees could be classified as treatment failures. Nonsurgical FCL treatment had outcomes comparable with those of surgical treatments except for ACI treatment, which was associated with a better KOOS and lower risk of treatment failure, despite a greater risk of knee arthroplasty. More than 1 FCL, a full-thickness lesion, a lower level of education, a patellofemoral lesion, and an elevated BMI were the main risk factors predicting poorer results.

Appendix

eA Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJS/I181). ■

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