



# Lesion size and varus malalignment are the major determinants leading to poorer clinical outcomes after combined microfracture treatment for focal cartilage lesions during anterior cruciate ligament reconstruction

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## Abstract

The purposes of this study were to evaluate the clinical effects of microfracture (MFX) performed for Outerbridge grade 3 or 4 focal cartilage lesion during the same surgery with arthroscopic anterior cruciate ligament (ACL) reconstruction and to analyze the major determinants of these potential effects on the clinical outcome. The clinical and radiographic data of 119 patients were evaluated. The mean follow-up time was  $32.6 \pm 6$  months. Isolated arthroscopic ACL reconstruction was performed in 70 patients (Group 1), whereas MFX for Outerbridge grade 3 or 4 chondral lesion during ACL surgery was performed in 49 patients (Group 2). Visual analogue scale (VAS) score, Lysholm knee score, and Tegner activity scale were the instruments used as outcome measures to evaluate the clinical status of the patients. Routine X-ray and MRI were also performed for all patients pre-operatively as well as at the latest follow-up visit. Linear regression analysis was performed to determine major factors predicting the poorer clinical outcome. Clinical outcomes were similar between isolated ACL reconstruction and combined procedure. On the other hand, according to linear regression analysis, cartilage lesion size  $> 2$  cm<sup>2</sup> and  $> 5$  degrees of varus alignment were detected as the major determinants leading to poorer outcomes in combined ACL reconstruction and MFX.

Level of evidence: III – Retrospective Comparative Study.

**Keywords** Cartilage lesion · Microfracture · ACL reconstruction · Arthroscopy · Knee ligaments

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## Introduction

The major focuses of the scientific research on ACL surgery have included anatomic reconstruction, biomechanical stability, and durability of the reconstruct without loosening or re-rupture. [1–3]. On the other hand, accompanying injuries of other intra-articular structures such as the menisci or cartilage may still lead to inferior clinical outcomes as well as poorer patient satisfaction despite of the excellent reconstruction techniques and flawless surgical procedures. Several authors mentioned that the concomitant cartilage lesions during the surgical management of ACL rupture not only impaired short-term and mid-term patient-reported outcomes but also increased the risk of subsequent progression to secondary degenerative arthritis [4–6]. Furthermore, disproportionate mechanical forces around the ACL-deficient knee during motion unfortunately create tendency to secondary cartilage injuries even though no lesion occurred at the time of trauma which resulted in ACL rupture [7, 8]. Therefore, accompanying cartilage lesions have become one of the most important concerns during the entire management process of a patient with ACL deficiency. Especially, Outerbridge grade 3 or 4 focal lesions diagnosed in young patients need intervention during the same surgery with ACL reconstruction [5, 9, 10].

Bone marrow stimulation has been the most widely performed surgical intervention as the treatment of chondral and osteochondral lesions since first introduced in 1950s [11]. In time, it has evolved as microfracture (MFX) and nanofracture (NFX) with technical development of the specially designed awls to provide more effective transfer of the pluripotent mesenchymal stem cells (MSCs) to the injured cartilage surface via blood flow [12]. As a well-established, cost-effective surgical treatment modality with reported good clinical outcomes by several studies, MFX still maintains its validity in the surgical management of focal cartilage lesions of the knee joint [7, 11]. On the other hand, the influences of bone marrow stimulation techniques for accompanying cartilage lesions during arthroscopic ACL reconstruction as well as the determinants of any potential influence has been controversial in the literature.

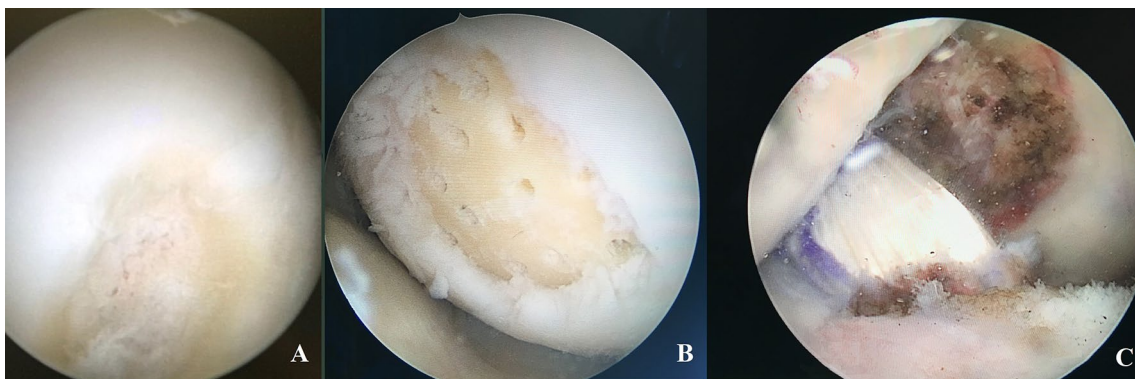
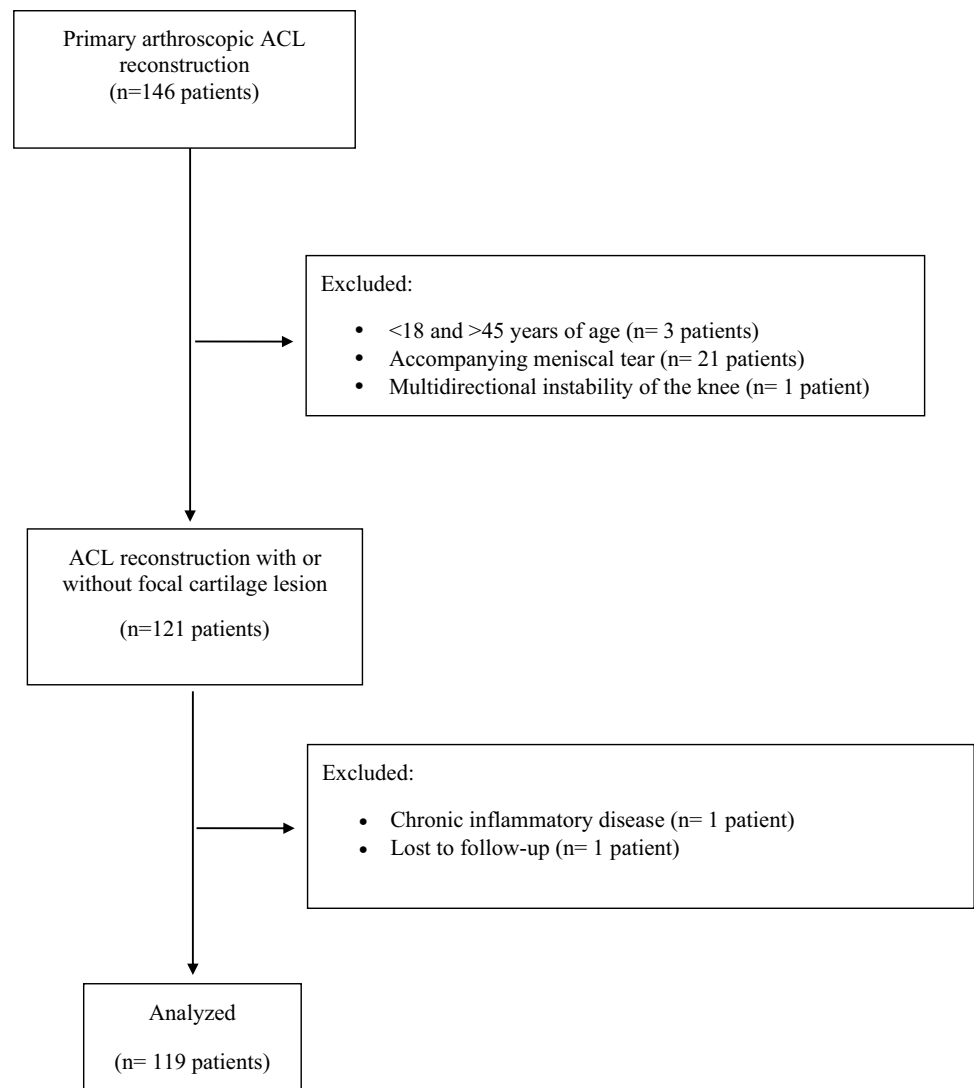
The purposes of this study were to evaluate the clinical effects of MFX performed for Outerbridge grade 3 or 4 focal cartilage lesion during the same surgery with arthroscopic ACL reconstruction and to analyze the major determinants of these potential effects on the clinical outcome. We hypothesized that the size of accompanying cartilage lesion would be the major factor for poorer outcome after combined ACL reconstruction and MFX surgery when compared to isolated ACL rupture cases.

## Materials and methods

The present study retrospectively evaluated the clinical and radiographic data of the patients who underwent surgical treatment for ACL rupture with or without concomitant cartilage intervention. The inclusion criteria were primary ACL reconstruction performed for symptomatic rupture leading to pain and instability, absence of any accompanying meniscal and/or ligamentous injury, age between 18 to 45 years at the time of surgical intervention, no radiographic signs of osteoarthritis (OA), and intact joint cartilage surface or Outerbridge grade 3–4 unifocal cartilage lesion in medial, lateral, or patellofemoral compartment of the knee joint according to arthroscopic evaluation during the ACL surgery. None of the patients had past medical history of chronic cartilage disorder before ACL surgery. Besides, the mean time from injury leading to ACL rupture to surgery was  $6.8 \pm 3$  weeks. Therefore, none of the cases included in the study had chronic or secondary degenerative chondral lesion and, all lesions treated via MFX during ACL reconstruction were acute lesions occurred due to the traumatic event that resulted in ACL rupture. Between January 2015 and January 2018, 146 patients were operated. The patients who were  $< 18$  and  $> 45$  years of age, with chronic inflammatory or rheumatologic disease, had a past medical history of intra-articular fracture or meniscectomy, underwent concomitant meniscal intervention such as partial excision or meniscal suture repair, had grade 1 or 2 cartilage lesion, and the ones who had incomplete or insufficient clinical records or lost to follow-up were excluded (Fig. 1). The clinical and radiographic data of 119 patients were evaluated after having approval from the institutional review board.

The patients were followed-up for at least 24 months. All patients had unilateral knee joint involvement. Pre-operative MRI was obtained for all knees to establish differential diagnoses and prove ACL rupture suspected on physical examination. Mechanical symptoms during daily-living activities were noted in all patients. None of our cases had intra-articular injection or physical therapy as conservative treatment measures during pre-operative period.

The patients were separated into two groups according to the treatment modality. Isolated arthroscopic ACL reconstruction for the knees without any cartilage lesion was performed in 70 patients (Group 1), whereas MFX for Outerbridge grade 3 or 4 chondral lesion during ACL surgery was performed in 49 patients (Group 2). All surgical procedures were performed by the same team who also determined the Outerbridge classification of lesions together intra-operatively. All lesions were either Outerbridge grade 3 or grade 4 with a mean size of  $1.7 \pm 0.8$  cm<sup>2</sup> (Fig. 2A). During the surgery, arthroscopic examinations were first performed to confirm the pre-operative diagnosis as well as to detect any

**Fig. 1** Flow chart demonstrating the excluded patients**Fig. 2** **A** Arthroscopic image of Outerbridge grade 4 chondral lesion during ACL reconstruction; **B** lesion area after microfracture procedure completed; **C** reconstructed anterior cruciate ligament

concomitant intra-articular pathologies. Following ACL procedure completed using anatomic single bundle reconstruction technique with a four-strand hamstring autograft, MFX was performed in cases with accompanying focal cartilage lesion (Fig. 2B, C).

A standard rehabilitation protocol focusing on early knee range of motion (ROM) and restoration of quadriceps function was utilized for all patients. Adjustable hinged ROM brace was routinely used during the first 4 weeks post-operatively. Active and passive motion exercises as well as the isometric quadriceps exercises were started at the first post-operative day however, maximum knee flexion did not exceed 90 degrees till the end of the 4th week after surgery. Continuous passive motion (CPM) was applied for a total of 2 h per day until discharge from the hospital. At the time of discharge, all patients were advised to continue active range of motion (ROM) and quadriceps strengthening exercises for at least 3 months post-operatively. The patients were not allowed weight bearing during the first month post-operatively. Then, progressive partial weight bearing was allowed starting from the end of the fourth week and after 6 weeks, full weight-bearing with full ROM. Low-impact sports activities such as swimming were allowed at the end of the 3rd month post-operatively; however, limited-contact sports activities such as football were not allowed until the end of the sixth month. After completion of 6 months, decision on the exact timing for return to low-impact sports activities left to the patient and the time passed from surgery to return to sports activities was noted for each patient.

### Data collection

All patients were followed clinically at least for 24 months post-operatively and the mean follow-up time was  $32.6 \pm 6$  months (range 24–48 months). Pre-operatively, age, body mass index (BMI), duration of symptoms up to decision of the surgical treatment, and radiographic measurement of alignment of the lower extremity which was evaluated by measuring the hip-knee-ankle angle (HKA) and defined as varus in case of a positive angular value were recorded. Visual analogue scale (VAS) score, Lysholm knee score, and Tegner activity scale were the instruments used as outcome measures to evaluate the clinical status of the patients pre-operatively, at 6 and 12 months post-operatively, and at the latest follow-up. The time from surgery up to return to non-impact sports activities was also noted for all patients. Routine X-ray and MRI were also performed for all patients pre-operatively as well as at the latest follow-up visit. Any radiographic sign of degenerative arthritis such as subchondral sclerosis, cystic degeneration, or osteophyte formation was recorded according to standing anteroposterior and lateral X-ray images. Magnetic resonance imaging evaluation was performed using a 1.5-Tesla MRI unit

(Philips, Amsterdam, Netherlands). Intra-articular effusion, edema or cyst formation in the subchondral bone, any progressive chondral damage to the joint surfaces, re-rupture of the reconstructed ACL, and any adhesions were evaluated on MRI scans.

### Statistical analysis

Statistical analyses were performed using paired *t* test and Wilcoxon signed-rank test to compare related data of pre-operative and post-operative periods and Mann–Whitney *U* test to compare independent interval data regarding differences of the patient groups. Linear regression analysis was performed to determine major factors predicting the poorer clinical outcome. The poorer clinical outcome was defined as having a Lysholm score  $< 84$  points and/or VAS score  $\geq 3$  at the latest follow-up. The level of significance was set at  $p \leq 0.05$ . Because of the retrospective nature of the study, we did not apply a priori calculation for the sample size; however, post hoc analysis was performed to determine the statistical power of the study.

### Results

Demographic data of the patients are demonstrated in Table 1. Progression of the clinical scores from pre-operative period through the entire follow-up is demonstrated in Table 2. Anterior drawer test and Lachman's test were positive in all patients pre-operatively. During the post-operative period, two knees from Group 1 and one from Group 2 became anterior drawer test positive; however, none of those was diagnosed with re-rupture of the reconstructed ACL according to MRI obtained at the latest follow-up visit. The mean VAS, Lysholm, and Tegner activity scale scores in both Groups were improved significantly from pre-operative to the latest follow-up ( $p < 0.001$ ). No statistically significant differences regarding clinical scores were detected between the two groups at any time interval during the clinical follow-up. On the other hand, nine patients with cartilage lesion size  $> 2 \text{ cm}^2$ , three patients with patellofemoral lesion, and five patients with  $> 5$  degrees of varus alignment pre-operatively in Group 2 had significantly lower VAS, Lysholm, and Tegner activity scale scores when compared to the others at the latest follow-up (Table 3). Therefore, these three variables were identified as potential predictors of the poorer clinical outcomes following combined arthroscopic ACL reconstruction and MFX procedure. These factors were included in linear regression analysis. Cartilage lesion size  $> 2 \text{ cm}^2$  and  $> 5$  degrees of varus alignment (HKA angle) were identified as the major determinants according to regression analysis (Table 4). The mean time from surgery to return to non-impact sports activities was  $7 \pm 1.5$  months

**Table 1** Demographic data of the patients

	Group 1 (n = 70)	Group 2 (n = 49)	p value
Mean age (years)	28 ± 6.9	30 ± 7.5	0.136
Gender			
Male	64	46	
Female	6	3	
Mean BMI (kg/m <sup>2</sup> )	23.3 ± 1.7	22.9 ± 1.5	0.187
Side			
Left knee	44	28	
Right knee	26	21	
Mean pre-op HKA angle (degrees)	1.3 ± 2.3	1.5 ± 2.8	0.67
Lesion location			
Medial femoral condyle	–	35	
Lateral femoral condyle	–	11	
Patellofemoral	–	3	
Mean time to surgery (weeks)	7 ± 3	6.5 ± 2	0.31
Mechanism of injury			
Contact	49	36	
Non-contact	21	13	

*p* < 0.05 means statistically significant

**Table 2** Progression of the Visual Analogue Scale (VAS) scores, Lysholm knee scores, and Tegner activity levels

		Pre-op	6 months	12 months	Latest follow-up
VAS	Group 1	3.6 ± 0.9	1.8 ± 1	1 ± 0.5	0.8 ± 0.7
	Group 2	3.5 ± 1.2	2 ± 1.3	1.1 ± 1	1 ± 1.1
	p value	0.604	0.345	0.473	0.228
Lysholm	Group 1	50 ± 8.8	84.1 ± 4.5	90.2 ± 5.1	91.8 ± 6.2
	Group 2	53 ± 10	83 ± 12	90 ± 10.1	90 ± 11.5
	p value	0.086	0.484	0.887	0.272
Tegner	Group 1	1.5 ± 0.5	1.7 ± 0.7	2.2 ± 0.6	3.1 ± 0.8
	Group 2	1.4 ± 0.7	1.7 ± 0.9	2.1 ± 1	2.9 ± 0.7
	p value	0.365	0.999	0.497	0.160

(*p* < 0.05 means statistically significant)

(range 6–12 months) in Group 1, 7.5 ± 2.2 months (range 6–12 months) in Group 2 (*p* = 0.142).

According to X-ray images obtained pre-operatively and at the latest follow-up visit, none of the patients had any radiographic signs of OA such as subchondral sclerosis, cystic degeneration, or osteophyte formation. Secondary cartilage lesion was not detected in any of the patients from Group 1 on post-operative MRI scans at the latest follow-up. In Group 2, according to the MRI scans at the latest follow-up, 14 patients had complete repair with the filling of the chondral defect, 24 had incomplete repair with > 50% the thickness of healthy adjacent cartilage tissue, and 11 knees had either a repair tissue < 50% the thickness of healthy adjacent cartilage tissue or no sign of defect filling. On the other hand, persistent edema of the subchondral bone was noted in five of the knees treated with MFX combined to ACL reconstruction. These five patients were among the

**Table 3** Comparison of the clinical scores according to lesion size, location of the lesion, and hip knee-ankle angle (HKA) at the latest follow-up in patients that underwent combined ACL reconstruction and MFX

	VAS	Lysholm	Tegner
Lesion size > 2 cm <sup>2</sup> (n = 9)	2.5 ± 0.5	74 ± 3	2 ± 1
Lesion size < 2 cm <sup>2</sup> (n = 40)	0.6 ± 1.5	94.5 ± 10	3 ± 0.9
p value	< 0.001	< 0.001	0.004
Patellofemoral lesion (n = 3)	2 ± 0.9	79 ± 5	2.1 ± 0.7
Lesion on medial or lateral femoral condyle (n = 46)	1 ± 0.8	91.7 ± 10	3 ± 0.8
p value	0.042	0.046	0.063
> 5 degrees varus alignment (n = 5)	3.3 ± 1	73 ± 4	2 ± 0.9
Normal or < 5 degrees varus alignment (n = 44)	0.8 ± 1.7	93 ± 12	3.1 ± 1
p value	0.002	< 0.001	0.023

*p* < 0.05 means statistically significant

**Table 4** Major determinants of the poorer clinical outcome according to linear regression analysis

Variable	Linear regression analysis			
	Coefficient	Standard error	<i>p</i> value	95% Confidence interval
Lesion size > 2 cm <sup>2</sup>	0.502	0.128	<0.001	0.242–0.762
Patellofemoral lesion	0.402	0.217	0.071	–0.035–0.840
HKA > 5 degrees	0.603	0.171	0.002	0.256–0.948

*p* < 0.05 means statistically significant

ones with lesion size > 2 cm<sup>2</sup> and had the lowest VAS and Lysholm scores. Intra-articular effusion, re-rupture of the reconstructed ACL, or any adhesions were not observed on MRI scans at the latest follow-up.

The overall complication rate of the present study was 4.2% (5 knees out of 119). Two patients in Group 2 had intra-articular hematoma which was treated via percutaneous drainage and primary wound care with 3 days hospitalization following surgery without need for secondary intervention. One patient from Group 1 and two from Group 2 had quadriceps atrophy and flexion contracture treated successfully by physiotherapy department. Septic arthritis, thromboembolism, adhesive arthropathy, or neurovascular complication was not detected in any of the patients.

## Discussion

The most important finding of the present study was that clinical outcomes were similar between isolated ACL reconstruction and combined MFX for focal cartilage lesion during an ACL reconstruction; however, cartilage lesion size > 2 cm<sup>2</sup> and > 5 degrees of varus alignment should be considered as the major determinants leading to poorer outcomes in patients underwent combined surgery. The prevalence of the concomitant full-thickness cartilage lesion at the time of ACL reconstruction was reported as 6.4% in the Norwegian and Swedish registries [13]. Cartilage lesions in ACL-deficient knee may play a crucial role as not only a potential factor negatively affects the healing process after surgical reconstruction in the means of individual's functional capacity but also a predisposing factor for the accelerated progression to premature degenerative arthritis [14, 15]. Cox et al. emphasized that articular cartilage injury was a significant predictor of IKDC and KOOS scores 6 years after ACL reconstruction [4]. On the other hand, Ulstein et al. demonstrated that concomitant full-thickness cartilage lesion present during the ACL reconstruction did not show to be a significant prognostic factor associated with patient-reported knee function 5–9 years after surgery [16]. Widuchowski et al. also noted that no statistically significant differences according to Lysholm and Tegner scale scores were observed at 10- and 15-year follow-up between the patients underwent ACL reconstruction without

any cartilage problem and the ones with an untreated focal lesion of 2.1 cm<sup>2</sup> mean size [17]. Several authors reported no negative effects of concomitant cartilage lesion on the clinical outcome of ACL reconstruction [18, 19], whereas some others strongly concluded that full-thickness cartilage lesions present at the time of ACL surgery predicted inferior outcomes [4, 6]. Treatment of accompanying focal cartilage lesion during primary arthroscopic ACL reconstruction as well as its clinical reflections has been controversial in the literature. Furthermore, the studies in the literature had heterogenous patient groups with wide variety of the lesion characteristics and without any standardized treatment modality. Therefore, the present study that was conducted with specific patient group, homogenous lesion characteristics, and standard intervention (young age, traumatic acute chondral lesion accompanied by ACL rupture, Outerbridge grade 3 or 4 unifocal lesion, standard treatment) evaluated the effects of MFX during ACL reconstruction and analyzed the major determinants of the poorer clinical outcome.

Røtterud et al. compared the clinical outcomes of 30 patients with full-thickness cartilage lesion during primary ACL reconstruction and 59 matched controls without cartilage lesion [5]. They reported worse outcomes and less improvement after ACL surgery in patients with cartilage lesion. However, only 7 of their 30 patients had cartilage procedure simultaneously with the ACL reconstruction whereas 23 left untreated. Therefore, they also mentioned that this might have influenced the results of the ones underwent cartilage procedure probably by improvement. According to a recent study evaluating the trends in incidence of ACL reconstruction and concomitant procedures among commercially insured individuals in the US between 2002 and 2014, the increase of concomitant MFX surgery was 75% over the study period [20]. This finding could represent an increase in propensity for performing cartilage restoration procedures to reduce the risk of posttraumatic osteoarthritis as well as the change in the clinical practice patterns. We also perform cartilage surgery during the ACL reconstruction and never leave any concomitant Outerbridge grade 3 or 4 lesion untreated.

As emphasized in a systematic review, because of considerable heterogeneity in patients, injuries, and surgical factors among different studies, it is impossible to directly compare the clinical effects of cartilage lesion as well as



its treatment during the same surgery with primary arthroscopic ACL reconstruction [21]. Ulstein et al compared MFX, debridement, and no treatment of concomitant full-thickness cartilage lesions in ACL reconstructed knees [22]. They reported no significant difference in patient-reported outcomes between MFX and leaving untreated. However, their study did not include any physician-oriented outcome measure and, any comparison to ACL surgery without cartilage lesion. Balain et al. concluded that no statistically significant differences were noted between MFX in ACL-intact knees and MFX in ACL-deficient knees regarding patient satisfaction as well as the functional outcome [23]. The present study not only comparatively evaluated the clinical outcomes in patients that underwent primary ACL reconstruction with or without concomitant focal cartilage lesion but also analyzed the factors leading to poorer outcomes of combined MFX and ACL procedures. According to our findings, in patients with concomitant cartilage lesion during ACL reconstruction, lesion size, and alignment of the lower extremity were the major determinants of clinical success.

Gobbi et al. reported that, as the surgical management of full-thickness cartilage lesion, MFX could offer good clinical outcomes at short- and long-term follow-up; however, the lesion size was a more important prognostic factor than age [12]. From the same point of view, the main hypothesis of the current study was that the size of accompanying cartilage lesion would be the major factor for poorer outcome after combined ACL reconstruction and MFX. On the other hand, MFX is a well-established first-line surgical treatment modality with lower cost than osteoarticular allografts or staged regenerative cartilage surgery. Blisard-Buddle mentioned that although some authors recommended MFX should only be performed for lesions  $\leq 2 \text{ cm}^2$ , lesion size should not be a limitation for MFX surgery of the knee [24]. Mithoefer et al. reviewed 28 studies including 3000 patients who underwent MFX surgery with the lesion size criteria as  $< 4 \text{ cm}^2$  for nonathletes and  $< 2 \text{ cm}^2$  for athletes [25]. They concluded that consistently improved knee function scores during the first 24 months after surgery were deteriorating between 2 and 5 years. Goyal et al. noted frequent progression to osteoarthritis in patients with lesions  $> 4 \text{ cm}^2$  5 years after the procedure [26]. The mean lesion size in our series was  $1.7 \text{ cm}^2$  with the largest defect was  $3 \text{ cm}^2$ . Since the patients with lesion size  $> 2 \text{ cm}^2$  had significantly worse outcome scores than the others, we recommend considering the lesion size as the major determinant leading to poorer outcomes during decision-making for MFX as well as pre-operative information given to such patients, in terms of the individual expectations regarding final outcome.

In the literature, although ACL injury and reconstruction have been reported as well-established risk factors for the development of tibiofemoral joint cartilage pathologies, patellofemoral cartilage problems accompanying or

secondary to ACL reconstruction has gone largely unrecognized [27]. Kreuz et al. mentioned that when comparing the use of MFX for different compartments in the knee, defects of the femoral condyles had significantly better healing than retro-patellar and tibial lesions [28]. Parallel to the developing scientific evidence, it has been demonstrated that the use of MFX alone for the cartilage lesions of the knee joint decreased significantly over the last years [29]. In the present study, patellofemoral location of the cartilage lesion was also identified as a potential factor that led to poorer outcomes according to univariate analysis; however, it was not among the major determinants according to linear regression analysis. It was not possible to reach an exact conclusion regarding whether it could have been a major determinant in case of more knees with patellofemoral lesion had been included. Therefore, clinical trials evaluating higher numbers of patients with concomitant patellofemoral cartilage lesion during primary ACL reconstruction are needed to reach a better understanding of the progress after such kind of combined surgical approach.

More than 5 degrees of pre-operative varus alignment of the operated knee was another determinant noted as leading to poorer outcome scores in our series. Five patients who had  $> 5$  degrees of varus malalignment but did not accept osteotomy for deformity correction during the same surgery with ACL reconstruction were included to test the effect of deformity as an independent variable. Pre-operative varus, as emphasized previously in the literature, may be a reason for progressive alterations in the patellofemoral and tibiofemoral morphology via further impairment in the gait biomechanics, which may explain how and why the clinical outcomes were worse [30]. Coronal malalignment may be more important prognostic factor than the degree of cartilage lesion regarding the progressive joint degeneration [31]. Cantin et al. reported that in all cases, the contribution of coronal plane alignment to varus-valgus knee stability must be carefully considered and addressed prior to ligament surgery [32]. According to our findings, we also strongly recommend that alignment of the lower extremity should be thoroughly evaluated during pre-operative planning in every single case to be operated for ACL deficiency and accompanying cartilage lesion because  $> 5$  degrees of varus alignment was identified as one of the two major determinants of poorer clinical outcomes.

## Limitations

The major limitation of the current study was the retrospective evaluation of prospectively followed patient groups. Second, the limited number of patients with relatively short follow-up time. The statistical power was 0.74 according to post hoc analysis with an alpha value of 0.05. Our study may be a reference for further clinical trials.

In conclusion, clinical outcomes after arthroscopic primary ACL reconstruction combined with MFX for Outerbridge Grade 3 or 4 focal cartilage lesion were not significantly different when compared to isolated ACL reconstruction without any accompanying cartilage lesion; however, orthopedic surgeons should consider lesion size  $> 2 \text{ cm}^2$  and  $> 5$  degrees of preoperative varus alignment of the lower extremity as the major determinants leading to poorer clinical outcomes in combined ACL reconstruction and MFX procedure.

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## Declarations

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** This study has been approved by the Institutional Review Board. This article does not contain any experimental studies with human participants or animals performed by any of the authors.

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