Do Focal Chondral Defects of the Knee Increase the Risk for Progression to Osteoarthritis?

A Review of the Literature

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Background: Focal chondral defects (FCDs) of the knee are believed to contribute to the development of osteoarthritis (OA), resulting in pain and dysfunction.

Purpose: To investigate whether untreated FCDs of the knee progress to radiographically evident OA over time.

Study Design: Systematic review; Level of evidence, 3.

Methods: A literature review was performed by searching the PubMed, Embase, and Cochrane Library databases to locate studies evaluating clinical and/or radiological outcomes of patients with FCDs that were diagnosed by arthroscopic surgery or magnetic resonance imaging (MRI) and were left untreated with a minimum 2-year follow-up. Additionally, studies were included if there was a radiographic assessment of OA. Search terms used were "knee," "focal," "isolated," "chondral," "cartilage," and "osteoarthritis." Studies were evaluated based on clinical/radiological outcomes and OA risk factors. The study methodology was assessed using the modified Coleman Methodology Score.

Results: Eight studies comprising 1425 knees met the inclusion criteria. All studies were of level 3 evidence. The risk of incident cartilage damage (enlargement of original FCDs or incidence of additional FCDs) at latest follow-up was assessed in 3 studies, while 1 study only reported the incidence of cartilage damage at follow-up. All 4 studies noted an increased progression of cartilage damage at follow-up. The progression of cartilage damage was most commonly seen in the patellofemoral joint and medial femoral condyle but was not associated with the development of knee OA based on the Kellgren-Lawrence grade. MRI of the FCDs revealed increased water content, cartilage deterioration, and proteoglycan loss within the medial and lateral compartments.

Conclusion: Patients with untreated FCDs of the knee joint are more likely to experience a progression of cartilage damage, although the studies included in this review did not demonstrate the development of radiographically evident OA within 2 years of follow-up.

Keywords: knee; focal chondral defect; cartilage; osteoarthritis

Focal chondral defects (FCDs) of the knee joint are common, occurring in over 60% of patients undergoing knee arthroscopic surgery.[1,7,9,13,18,26] FCDs have limited regenerative potential in response to injuries, as articular cartilage is relatively avascular and aneural.[12,13,26] Untreated FCDs within the knee joint can result in mechanical symptoms that impair function or cause pain and effusion, especially when located on weightbearing surfaces of the medial or lateral compartments.[13] In contrast, osteoarthritis (OA) of the knee joint is characterized by progressive loss of articular cartilage, osteophytes, subchondral cysts, joint space narrowing, and intermittent inflammation of the joint tissues.[30,32] Because FCDs can be seen in both radiographically healthy knees and arthritic knees, detecting their presence and progression is important for monitoring the natural disease course of these defects.[5,10,15] Some believe that FCDs progress to OA and cause permanent knee deterioration.[30] To date, there is a lack of knowledge regarding the correlation between the presence of an isolated FCD and possible eventual progression to OA. The purpose of this review was to determine if untreated FCDs of the knee joint result in radiographically evident OA changes within 2 years or if no such association exists.

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METHODS

Literature Search

A literature review of multiple databases was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Two independent reviewers searched PubMed, Embase, and the Cochrane Library up to October 9, 2017. The electronic search strategy used was the following: knee AND (focal OR isolated) AND (chondral OR cartilage) AND osteoarthritis. A total of 2512 studies were reviewed by title and/or abstract to determine study eligibility based on inclusion and exclusion criteria. Inclusion criteria included (1) studies that reported clinical and/or radiological outcomes of patients with untreated FCDs, (2) a radiological or arthroscopic diagnosis of FCDs, (3) studies that reported clinical and radiological outcomes with a minimum 2-year follow-up, and (4) studies that reported a radiographic assessment of OA. Exclusion criteria included (1) non-English publications, (2) studies unrelated to the knee, (3) patients with FCDs who underwent surgical treatment, and (4) studies with no radiographic assessment of OA at follow-up. Eight studies were determined to meet inclusion and exclusion criteria (Figure 1).

Reporting Outcomes

Radiographic and magnetic resonance imaging (MRI) scores, clinical outcome scores, and OA risk factors were recorded. Baseline OA risk factors included knee symptoms (pain, aching, or stiffness in or around the knee, or frequent use of pain medication for at least 1 month but not most days in the past 12 months), overweight or obesity, prior knee injury, prior knee surgery, history of knee replacement in a parent or sibling, Heberden nodes, frequent knee bending (repetitive activities involving bending, squatting, kneeling, climbing, or lifting), or radiographic OA (Kellgren-Lawrence grade $\geq$2).[16,20] Overweight was defined as a body mass index (BMI) between 25 and 29.9 kg/m^2, and obesity was defined as a BMI $\geq$30 kg/m^2.[20]

Study Methodology

The Modified Coleman Methodology Score (MCMS) was used to evaluate study methodology quality.[8] The MCMS has a scaled potential score ranging from 0 to 100. Scores ranging from 85 to 100 are excellent, 70 to 84 are good, 55 to 69 are fair, and $<$55 are poor.

Statistical Analysis

For continuous variables, means and SDs were calculated. Categorical variables were totaled and reported as percentages. Because of the significant heterogeneity of the included studies, statistical comparisons could not be made, and therefore, the data were primarily descriptive.

RESULTS

Literature Search

Eight studies[2,11,15,20,28-31] met the inclusion and exclusion criteria (all level 3 evidence). Table 1 shows the MCMS values from the 8 included studies. Five studies achieved a good score,[11,15,20,29,30] while 3 studies achieved a fair score.[2,28,31] The mean score was 70.9 ± 3.7.

Patient and Lesion Characteristics

Table 2 depicts the patient demographics from the included studies. A total of 1425 knees were included. The mean patient age was 47.6 ± 13.9 years, with a mean BMI of 26.8 ± 2.7 kg/m^2. The minimum follow-up ranged from 24 months[2,15] to 158.4 months.[30] Overall, there were a total of 1851 chondral lesions, 682 meniscal lesions, and 745 bone marrow lesions (BMLs) (Table 3). Table 4 presents the OA risk factors met by patients in the included studies.

A wide variety of imaging assessment tools was used in each of the studies (Table 5). The most commonly used imaging parameters were the Kellgren-Lawrence grade[19] (all 8 studies), the modified Whole-Organ Magnetic Resonance Imaging Score (WORMS)[25] (5 studies[2,15,20,28,29]), and MRI T2 values (4 studies[2,11,20,31]). The most commonly used outcome measure was the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)[3] (Table 6).

Three studies[2,20,29] examined middle-aged patients (45-55 years old) with OA risk factors, such as history of knee injury or surgery, but no radiographic OA from the Osteoarthritis Initiative (OAI) database. Two studies[15,28] assessed patients aged 50 to 79 years at baseline with or at high risk for knee OA using participants from the Multicenter Osteoarthritis Study (MOST). Of the 5 multicenter studies,[2,15,20,28,29] 3 studies[15,28,29] reported the risk of incident cartilage defects, while 1 study[20] only reported the incidence of cartilage damage at follow-up (Table 7).

One of the MOST studies[15] found that patients with baseline partial- and full-thickness FCDs had a significantly

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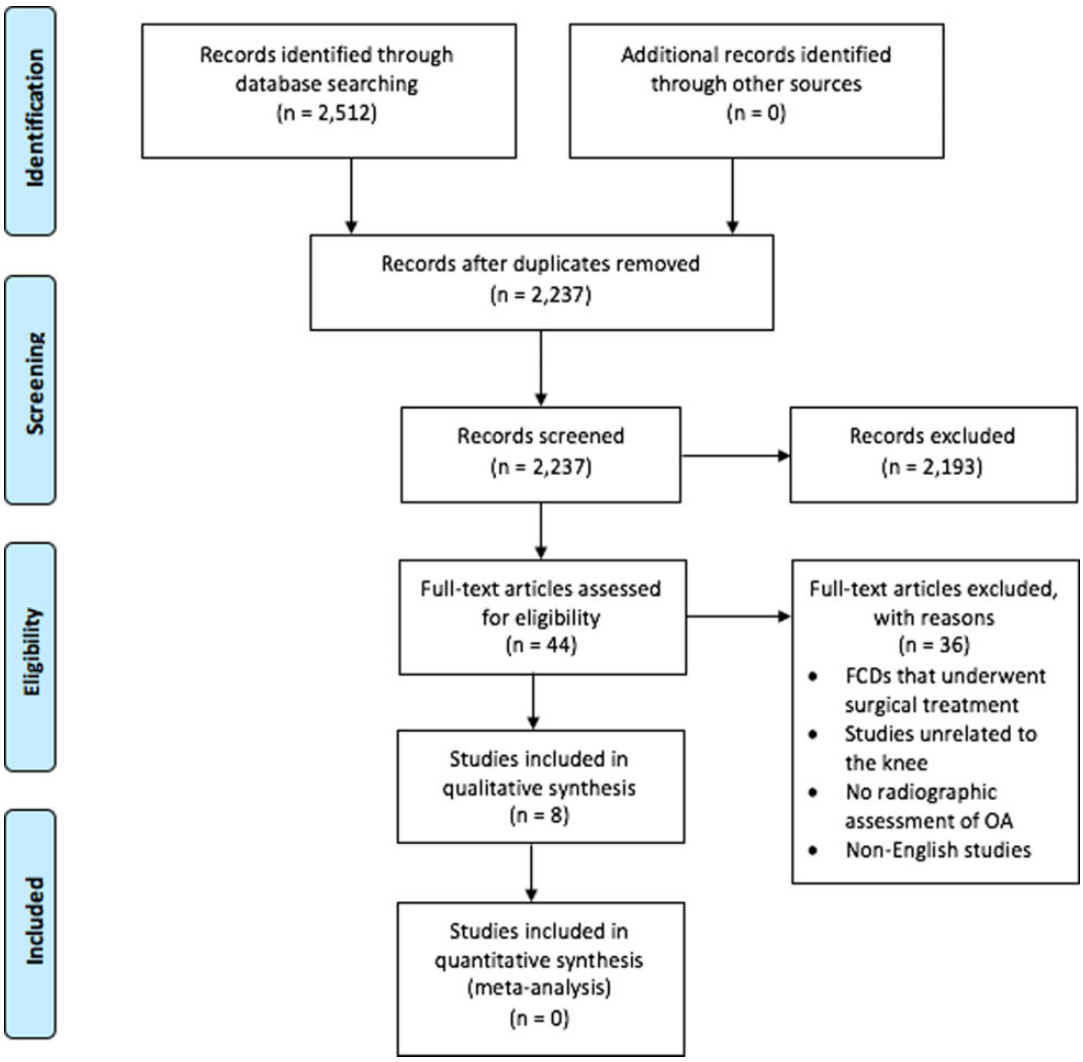

Figure 1. The electronic search strategy is outlined using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. FCD, focal chondral defect; OA, osteoarthritis.

TABLE 1
Modified Coleman Methodology Scores

Study (Year)	Score
Baum et al[2] (2012)	67
Engen et al[11] (2017)	71
Guermazi et al[15] (2017)	77
Laberge et al[20] (2012)	72
Stefanik et al[28] (2016)	68
Virayavanich et al[29] (2013)	70
Widuchowski et al[30] (2011)	75
Williams et al[31] (2010)	67
Mean	70.9 ± 3.7

higher risk of incident cartilage damage in other subregions within the same compartment of the tibiofemoral joint (TFJ), regardless of depth, over a 30-month follow-up. This study also found that partial- and full-thickness defects are similarly relevant to the development of cartilage damage in the OA disease process.[15] Another MOST study[28] found that compared to knees without full-thickness cartilage damage, those with isolated TFJ or patellofemoral joint (PFJ) full-thickness damage had 2.7 and 5.8 times the odds, respectively, of developing mixed full-thickness cartilage damage. Similarly, compared to patients without any BMLs, those with isolated TFJ or PFJ BMLs had 4.2 and 5.4 times the odds, respectively, of developing mixed BML damage.[28] Interestingly, this study found that in most knees that developed cartilage damage in multiple compartments, the damage was initially isolated to the PFJ at 7-year follow-up.[28] One study[29] found that patients who participated in frequent knee bending had a significantly higher risk of incident cartilage lesions, especially in the PFJ compartment, and had an increased risk of overall progression of cartilage damage and meniscal abnormalities over 36 months. Another study[20] found a statistically significant progression in the number of knees

TABLE 2
Population Demographics[a]

Study (Year)	Lesion Grade	n	Male/Female Sex, n	Mean Patient Age, y	Mean BMI, kg/m^2	Minimum Follow-up, mo
Baum et al[2] (2012)	WORMS >0	101	50/51	50.8 ± 2.9	24.0 ± 1.8	24
Engen et al[11] (2017)	ICRS ≥3	11	7/4	NR	25	120
Guermazi et al[15] (2017)	WORMS ≥2	265	127/138	61.3 ± 7.7	29.6 ± 4.5	24
	WORMS ≥2.5	94	35/59	61.3 ± 7.2	30.4 ± 4.8	
Laberge et al[20] (2012)	WORMS >0	137	81/56	50.9 ± 2.8	29.0 ± 3.5	36
Stefanik et al[28] (2016)	WORMS ≥2	317	NR	NR	NR	84
	WORMS ≥2.5	339	NR	NR	NR	84
Virayavanich et al[29] (2013)	WORMS >0	115	55/60	50.8 ± 2.9	24.1 ± 1.9	36
Widuchowski et al[30] (2011)	OB ≥3	37	24/13	24	28.79 ± 3.92	158.4
Williams et al[31] (2010)	NR	9	3/6	NR	NR	36
Total	—	1425	382/387	47.6 ± 13.9	26.8 ± 2.7	64.8 ± 50.7

[a]BMI, body mass index; ICRS, International Cartilage Repair Society[6]; NR, not reported; OB, Outerbridge classification; WORMS, Whole-Organ Magnetic Resonance Imaging Score.

TABLE 3
Baseline Lesion Characteristics[a]

Study (Year)	Lesion Grade	Chondral Lesion Location, n	Meniscal Lesion Location, n	BML Location, n
Baum et al[2] (2012)	WORMS >0	P: 62	MA: 3	P: 27
		T: 24	MB: 21	T: 10
		MFC: 18	MP: 46	MFC: 3
		LFC: 12	LA: 10	LFC: 3
		MTP: 10	LB: 8	MTP: 4
		LTP: 23	LP: 13	LTP: 7
Engen et al[11] (2017)	ICRS ≥3	NR	NR	NR
Guermazi et al[15] (2017)	WORMS ≥2	TFJ: 374	Any: 179	Any: 294
Laberge et al[20] (2012)	WORMS ≥0	P: 89	MA: 6	Any: 64
		T: 54	MB: 25	
		MFC: 33	MP: 76	
		LFC: 19	LA: 15	
		MTP: 11	LB: 21	
		LTP: 55	LP: 32	
Stefanik et al[28] (2016)	WORMS ≥2	PFJ: 179	NR	PFJ: 239
		TFJ: 138		TFJ: 94
	WORMS ≥2.5	PFJ: 187		
		TFJ: 152		
Virayavanich et al[29] (2013)	WORMS ≥1	PFJ: 79	MB: 57	NR
		MTFJ: 23	LB: 22	
		LTFJ: 35	Multi: 64	
		Multi: 87		
	WORMS ≥2	PFJ: 44	MB: 33	NR
		MTFJ: 18	LB: 9	
		LTFJ: 24	Multi: 39	
		Multi: 64		
Widuchowski et al[30] (2011)	OB ≥3	P: 11	Any: 3	NR
		TFJ: 26		
Williams et al[31] (2010)	NR	NR	NR	NR
Total	—	1851	682	745

[a]BML, bone marrow lesion; ICRS, International Cartilage Repair Society[6]; LA, lateral anterior; LB, lateral body; LFC, lateral femoral condyle; LP, lateral posterior; LTFJ, lateral tibiofemoral joint; LTP, lateral tibial plateau; MA, medial anterior; MB, medial body; MFC, medial femoral condyle; MP, medial posterior; MTFJ, medial tibiofemoral joint; MTP, medial tibial plateau; Multi, multiple locations; NR, not reported; OB, Outerbridge classification; P, patella; PFJ, patellofemoral joint; T, trochlea; TFJ, tibiofemoral joint; WORMS, Whole-Organ Magnetic Resonance Imaging Score.

with cartilage lesions of any grade in obese patients over a 36-month follow-up. However, obesity did not increase the relative risk of the progression of meniscal lesions or high-grade cartilage defects (Table 7). This study[20] suggested that this finding may be because of lower activity levels of very obese people.

TABLE 4
Baseline Osteoarthritis Risk Factors (n = 1167 Patients)[a]

Study (Year)	Symptoms	Prior Knee Injury	Prior Knee Surgery	Family History of Total Knee Replacement	Heberden Nodes	Activity Risk[b]	BMI of Overweight/ Obesity	Radiographic Knee Osteoarthritis[c]
Baum et al[2] (2012)	88	54	23	24	17	NR	0	0
Engen et al[11] (2017)	+	21	21	NR	NR	NR	+	0
Guermazi et al[15] (2017)	NR	NR	NR	NR	NR	NR	+	140
Laberge et al[20] (2012)	113	66	22	21	27	97	37/62	0
Stefanik et al[28] (2016)	+	+	+	NR	NR	38	+	+
Virayavanich et al[29] (2013)	0	50	27	25	22	84	NR	0
Widuchowski et al[30] (2011)	28	24	37	NR	NR	15	NR	0
Williams et al[31] (2010)	+	NR	NR	NR	NR	NR	NR	+
n (% of total)	229 (19.7)	195 (16.8)	130 (11.2)	70 (6.0)	66 (5.7)	234 (20.1)	99 (8.5)	140 (12.0)

[a]"+" indicates that the risk factor was present but that no exact number was available. BMI, body mass index, NR, not reported.
[b]Repetitive activities involving bending, squatting, kneeling, climbing, or lifting.
[c]Kellgren-Lawrence grade ≥2.

TABLE 5
Imaging Assessment Tools[a]

	WORMS							
Study (Year)	Cartilage	Meniscus	BMEP	KL Grade	T2 Values	dGEMRIC	ICRS	OB
Baum et al[2] (2012)	+	+	+	+	+	–	–	–
Engen et al[11] (2017)	–	–	–	+	+	+	+	–
Guermazi et al[15] (2017)	+	+	+	+	–	–	–	–
Laberge et al[20] (2012)	+	+	+	+	+	–	–	–
Stefanik et al[28] (2016)	+	+	+	+	–	–	–	–
Virayavanich et al[29] (2013)	+	+	–	+	–	–	–	–
Widuchowski et al[30] (2011)	–	–	–	+	–	–	–	+
Williams et al[31] (2010)	–	–	–	+	+	–	–	–

[a]"+/–" indicates that the outcome measure was/was not performed. BMEP, bone marrow edema pattern; dGEMRIC, delayed gadolinium-enhanced magnetic resonance imaging of cartilage; ICRS, International Cartilage Repair Society[6]; KL, Kellgren-Lawrence; OB, Outerbridge classification; WORMS, Whole-Organ Magnetic Resonance Imaging Score.

Using data from the OAI database, Baum et al[2] demonstrated that neither the presence of OA risk factors nor the presence of cartilage lesions at baseline were associated with increases in cartilage T2 values at 24-month follow-up. However, significantly increased cartilage T2 values were seen in the medial femoral condyle (MFC) of patients with OA risk factors. Additionally, patients with cartilage lesions had significantly higher T2 values compared to patients without cartilage lesions at both baseline and 24 months, but there was no accelerated T2 increase over 24 months. Furthermore, this study suggested that because elevated T2 values indicate increased water content and deterioration of the collagen network,[4,21] elevated T2 values may be a more sensitive biomarker for cartilage degeneration in the initial stages of OA.[2,24]

In a natural history study by Engen et al,[11] the authors evaluated the articular cartilage of 11 patients with untreated FCDs and 10 patients with FCDs that were treated with cartilage repair at a mean 12-year follow-up. Uninjured knees served as a control group. While there were no significant differences in delayed gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC) values between groups, this study found degenerative changes (Kellgren-Lawrence grade >0) in 13 of the 21 knees. However, these changes did not correlate with cartilage quality assessed using dGEMRIC and T2 values. The authors concluded that there were no more degenerative changes in the injured knees than in the uninjured knees based on dGEMRIC.

At a mean follow-up of 15.3 years, Widuchowski et al[30] found that among young, active patients with a single FCD on the weightbearing surface of the TFJ, tibiofemoral OA with coexisting patellofemoral involvement was common. However, there was no correlation between the presence of an FCD and coexisting OA when the FCD was located on the patella. Additionally, in patients with an FCD within the TFJ, there was no correlation between clinical outcome scores and lesion size, whereas in patients with an FCD in the patella, a significant negative correlation was observed in each outcome score. OA changes were found in 39% of the patients, with no difference in OA severity between knees with a full-thickness FCD and an uninjured knee. This study concluded that severe FCDs with no treatment have a limited influence on clinical outcomes and the development of OA.[30]

TABLE 6
Outcome Measures Used[a]

Study (Year)	WOMAC	Lysholm	Tegner	VAS	KOOS	PASE
Baum et al[2] (2012)	+	–	–	–	–	–
Engen et al[11] (2017)	–	+	+	+	+	–
Guermazi et al[15] (2017)	–	–	–	–	–	–
Laberge et al[20] (2012)	+	–	–	–	–	–
Stefanik et al[28] (2016)	–	–	–	–	–	–
Virayavanich et al[29] (2013)	+	–	–	–	–	+
Widuchowski et al[30] (2011)	+	+	+	–	–	–
Williams et al[31] (2010)	–	–	–	–	–	–

[a]"+/–" indicates that the outcome measure was/was not performed. KOOS, Knee Injury and Osteoarthritis Outcome Score; PASE, Physical Activity Scale for the Elderly; VAS, visual analog scale for physical function; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Finally, Williams et al[31] found that in patients with partial-thickness cartilage lesions, cartilage thickness within the TFJ decreased by 0.85% per year and that the most significant change was seen within the MFC, which decreased by 2.43% per year over a mean follow-up of 37 months.

DISCUSSION

This review of the literature is the first to investigate if untreated FCDs of the knee joint progress to OA or if no such association exists. Based on this review, patients with untreated FCDs are more likely to experience a progression of cartilage damage within the same joint compartment, especially when located in the PFJ and on the MFC. This is apparent based on the radiological findings at follow-up, which have demonstrated an increased incidence of cartilage damage and worsening T2 and dGEMRIC values. Additionally, more specific MRI analyses have demonstrated increased water content and deterioration of the collagen network as well as tissue swelling due to proteoglycan loss in patients with FCDs within the TFJ. These findings may be associated with the cartilage matrix degeneration seen in the initial stages of OA, although it is difficult to draw strong conclusions from the currently available data to determine whether untreated FCDs influence the development of knee OA.

There are distinct biochemical and mechanical properties of cartilage seen in the patella compared with that of the tibia and femur.[17,30] Femoral cartilage has been shown to have a higher compressive aggregate modulus, lower permeability, lower water content, and higher proteoglycan content than patellar cartilage.[14,17,27] Two studies[2,11] in this review demonstrated elevated T2 values in patients with FCDs located on the MFC compared to patients without FCDs, while another study[31] found an apparent lack of change in global measures of volume because of significant decreases in cartilage thickness, especially of the MFC region, as well as appreciable gains in thickness in other regions. The authors of these studies[2,11] suggested that because elevated T2 values indicate increased water content and deterioration of the collagen network,[4,21] these findings may be associated with the cartilage matrix degeneration and proteoglycan loss seen in the initial stages of OA. However, Williams et al[31] included patients with baseline radiographic OA. Although findings such as these are apparent in the initial stages of OA, these results may also be explained by the distinct biochemical and mechanical properties of the cartilage within the TFJ. Therefore, the presence of FCDs may have limited influence on the development of OA.

It is important to distinguish between FCDs and knee OA. FCDs are often isolated injuries that can range from small partial-thickness lesions to large full-thickness lesions.[9,23,25] While knee OA is associated with progressive loss of articular cartilage, OA is a pathological process that differs from isolated FCDs.[5,10,15] Radiographic evidence of knee OA is characterized by the formation of osteophytes, narrowing of articular cartilage associated with sclerosis of subchondral bone, appearance of subchondral cysts, and deformity of the bone contour.[19] In contrast, FCDs may be visualized as isolated regions of the knee joint with partial- or full-thickness loss of cartilage, with normal, undamaged cartilage in the surrounding regions. Over time, an FCD may worsen in the sense that the lesion may expand in terms of the surface area and/or depth, although the expansion of these isolated injuries differs from the disease process of OA.

Of the 8 studies included in this review, the knees with FCDs showed an increased progression of cartilage damage on the MFC,[2,11,31] the PFJ,[20,28,30] the same subregion of the medial or lateral compartments,[15] and the entire knee joint in obese patients.[20] Multiple studies demonstrated that specific risk factors in combination with FCDs, such as a high BMI,[20] frequent knee bending,[29] malalignment,[15] and knee symptoms or injury,[2,11,20,28,30] can have meaningful effects on the progression of cartilage damage.

There are several limitations to this review. Most importantly, the mean follow-up time of the included studies was 64.8 months, and it may often take longer than this for knee OA to develop after an injury.[22] Only 8 studies were included (all level 3 evidence), and the high heterogeneity of the included studies and population made it difficult to draw strong conclusions from the currently available data. Additionally, older patients who have an FCD are likely to have concomitant knee OA, and ideally, this review would have included exclusively younger patients. Although 1425 knees were included in this review, not all knees were evaluated using the same outcome measures, and therefore, sample sizes were limited when comparing outcomes between studies. The inconsistency of reporting

TABLE 7
Risk for Incident Cartilage Damage at Latest Follow-up[a]

Study (Year)	Baseline Cartilage Status	Follow-up Incident Cartilage Damage	Study Group	Study Group Incidence, n/N (%)	Reference Group Incidence, n/N (%)	Crude OR (95% CI)	Adjusted OR (95% CI)[b]
Guermazi et al[15] (2017)	WORMS = 2	Only 1 subregion of TFJ	Kellgren-Lawrence grade ≥2	26/235 (11)	107/1485 (7)	1.60 (1.01-2.54)[c]	1.59 (1.00-2.54)[c]
	WORMS = 2.5			12/82 (15)		2.21 (1.16-4.21)[c]	2.13 (1.08-4.20)[c]
Laberge et al[20] (2012)	WORMS ≥1	Any change in WORMS grade	BMI <25 kg/m^2	10/38 (26)[b]	NR	NR	NR
			BMI = 25-29.9 kg/m^2	9/37 (24)	NR	NR	NR
			BMI ≥30 kg/m^2	29/62 (47)[b]	NR	NR	NR
		New, higher grade lesions (WORMS ≥2)	BMI <25 kg/m^2	3/38 (8)	NR	NR	NR
			BMI = 25-29.9 kg/m^2	3/37 (8)	NR	NR	NR
			BMI ≥30 kg/m^2	2/62 (3)	NR	NR	NR
Stefanik et al[28] (2016)	WORMS ≥2: TFJ	WORMS ≥2: PFJ	NR	43/138 (31.2)	29/103 (28.2)	NR	1.2 (0.65-2.1)
	WORMS ≥2: PFJ	WORMS ≥2: TFJ	NR	80/179 (44.7)	40/103 (38.8)	NR	1.2 (0.75-2.1)
	WORMS ≥2: PFJ	WORMS ≥2: mixed	NR	80/179 (44.7)	11/103 (10.7)	NR	6.5 (3.2-13.1)
	WORMS ≥2: TFJ	WORMS ≥2: mixed	NR	43/138 (31.2)		NR	4.0 (1.9-8.4)
	WORMS ≥2.5: TFJ	WORMS ≥2.5: PFJ	NR	20/152 (13.2)	97/582 (16.7)	NR	0.80 (0.47-1.3)
	WORMS ≥2.5: PFJ	WORMS ≥2.5: TFJ	NR	48/187 (25.7)	112/582 (19.2)	NR	1.3 (0.89-2.0)
	WORMS ≥2.5: PFJ	WORMS ≥2.5: mixed	NR	48/187 (25.7)	31/582 (5.3)	NR	5.8 (3.6-9.6)
	WORMS ≥2.5: TFJ	WORMS ≥2.5: mixed	NR	20/152 (13.2)		NR	2.7 (1.5-4.9)
Virayavanich et al[29] (2013)	WORMS ≥1	Any change in WORMS grade: whole knee	FKB	29/84 (34.5)	4/84 (12.9)	4.12 (1.27-13.36)[c]	NR
		Any change in WORMS grade: PFJ		21/84 (25.0)	3/84 (9.7)	3.05 (0.81-17.21)	NR
		Any change in WORMS grade: medial TFJ		5/84 (6.0)	0/84 (0)	2.51 (0.33-inf)	NR
		Any change in WORMS grade: lateral TFJ		7/84 (8.3)	1/84 (3.2)	2.93 (0.34-140.19)	NR

[a]The reference group for 2 studies[15,28] was patients with no cartilage damage (WORMS = 0) at baseline, while the reference group for 1 study[29] was patients without FKB. BMI, body mass index; FKB, frequent knee bending; inf, infinity; NR, not reported; OR, odds ratio; PFJ, patellofemoral joint; TFJ, tibiofemoral joint; WORMS, Whole-Organ Magnetic Resonance Imaging Score.

[b]Statistical significance ($P < .05$) between the study groups.

[c]Statistical significance ($P < .05$) between the study group and reference group.

outcome measures is another limitation of the included studies. Furthermore, the overall quality of the currently available data on this topic was limited. Two studies[15,28] used data from the same multicenter study (MOST), while the authors of 3 studies[2,20,29] worked at the same research center and used data from the same multicenter OAI database. Therefore, it is likely that there is some overlap in patients, although this was not specified in these articles.

CONCLUSION

Patients with untreated FCDs of the knee joint are more likely to experience the progression of cartilage damage, although the studies included in this review did not demonstrate the development of radiographically evident OA within 2 years of follow-up.

REFERENCES

1. Aroen A, Loken S, Heir S, et al. Articular cartilage lesions in 993 consecutive knee arthroscopies. *Am J Sports Med*. 2004;32(1):211-215.
2. Baum T, Stehling C, Joseph GB, et al. Changes in knee cartilage T2 values over 24 months in subjects with and without risk factors for knee osteoarthritis and their association with focal knee lesions at baseline: data from the Osteoarthritis Initiative. *J Magn Reson Imaging*. 2012;35(2):370-378.
3. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol*. 1988;15(12):1833-1840.
4. Blumenkrantz G, Majumdar S. Quantitative magnetic resonance imaging of articular cartilage in osteoarthritis. *Eur Cell Mater*. 2007; 13:76-86.
5. Boegard TL, Rudling O, Petersson IF, Jonsson K. Magnetic resonance imaging of the knee in chronic knee pain: a 2-year follow-up. *Osteoarthritis Cartilage*. 2001;9(5):473-480.
6. Brittberg M, Winalski CS. Evaluation of cartilage injuries and repair. *J Bone Joint Surg Am*. 2003;85(Suppl 2):58-69.
7. Ciccotti MC, Kraeutler MJ, Austin LS, et al. The prevalence of articular cartilage changes in the knee joint in patients undergoing arthroscopy for meniscal pathology. *Arthroscopy*. 2012;28(10):1437-1444.
8. Coleman BD, Khan KM, Maffulli N, Cook JL, Wark JD. Studies of surgical outcome after patellar tendinopathy: clinical significance of methodological deficiencies and guidelines for future studies. Victorian Institute of Sport Tendon Study Group. *Scand J Med Sci Sports*. 2000;10(1):2-11.
9. Curl WW, Krome J, Gordon ES, Rushing J, Smith BP, Poehling GG. Cartilage injuries: a review of 31,516 knee arthroscopies. *Arthroscopy*. 1997;13(4):456-460.
10. Ding C, Garnero P, Cicuttini F, Scott F, Cooley H, Jones G. Knee cartilage defects: association with early radiographic osteoarthritis, decreased cartilage volume, increased joint surface area and type II collagen breakdown. *Osteoarthritis Cartilage*. 2005;13(3):198-205.
11. Engen CN, Loken S, Aroen A, Ho C, Engebretsen L. No degeneration found in focal cartilage defects evaluated with dGEMRIC at 12-year follow-up. *Acta Orthop*. 2017;88(1):82-89.

12. Flanigan DC, Harris JD, Trinh TQ, Siston RA, Brophy RH. Prevalence of chondral defects in athletes' knees: a systematic review. *Med Sci Sports Exerc*. 2010;42(10):1795-1801.
13. Frank RM, Cotter EJ, Nassar I, Cole B. Failure of bone marrow stimulation techniques. *Sports Med Arthrosc Rev*. 2017;25(1):2-9.
14. Froimson MI, Ratcliffe A, Gardner TR, Mow VC. Differences in patellofemoral joint cartilage material properties and their significance to the etiology of cartilage surface fibrillation. *Osteoarthritis Cartilage*. 1997;5(6):377-386.
15. Guermazi A, Hayashi D, Roemer FW, et al. Brief report: partial- and full-thickness focal cartilage defects contribute equally to development of new cartilage damage in knee osteoarthritis. The Multicenter Osteoarthritis Study. *Arthritis Rheumatol*. 2017;69(3): 560-564.
16. Guermazi A, Niu J, Hayashi D, et al. Prevalence of abnormalities in knees detected by MRI in adults without knee osteoarthritis: population based observational study (Framingham Osteoarthritis Study). *BMJ*. 2012;345:e5339.
17. Hinman RS, Crossley KM. Patellofemoral joint osteoarthritis: an important subgroup of knee osteoarthritis. *Rheumatology (Oxford)*. 2007;46(7):1057-1062.
18. Hjelle K, Solheim E, Strand T, Muri R, Brittberg M. Articular cartilage defects in 1,000 knee arthroscopies. *Arthroscopy*. 2002;18(7): 730-734.
19. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. *Ann Rheum Dis*. 1957;16(4):494-502.
20. Laberge MA, Baum T, Virayavanich W, et al. Obesity increases the prevalence and severity of focal knee abnormalities diagnosed using 3 T MRI in middle-aged subjects: data from the Osteoarthritis Initiative. *Skeletal Radiol*. 2012;41(6):633-641.
21. Liess C, Lusse S, Karger N, Heller M, Gluer CC. Detection of changes in cartilage water content using MRI T2-mapping in vivo. *Osteoarthritis Cartilage*. 2002;10(12):907-913.
22. Messner K, Maletius W. The long-term prognosis for severe damage to weight-bearing cartilage in the knee: a 14-year clinical and radiographic follow-up in 28 young athletes. *Acta Orthop Scand*. 1996; 67(2):165-168.
23. Outerbridge RE. The etiology of chondromalacia patellae. *J Bone Joint Surg Br*. 1961;43:752-757.
24. Park SY, Lee SH, Lee MH, Chung HW, Shin MJ. Changes in the T2 value of cartilage after meniscus transplantation over 1 year. *Eur Radiol*. 2017;27(4):1496-1504.
25. Peterfy CG, Guermazi A, Zaim S, et al. Whole-Organ Magnetic Resonance Imaging Score (WORMS) of the knee in osteoarthritis. *Osteoarthritis Cartilage*. 2004;12(3):177-190.
26. Richter W. Mesenchymal stem cells and cartilage in situ regeneration. *J Intern Med*. 2009;266(4):390-405.
27. Sharif M, Granell R, Johansen J, Clarke S, Elson C, Kirwan JR. Serum cartilage oligomeric matrix protein and other biomarker profiles in tibiofemoral and patellofemoral osteoarthritis of the knee. *Rheumatology (Oxford)*. 2006;45(5):522-526.
28. Stefanik JJ, Guermazi A, Roemer FW, et al. Changes in patellofemoral and tibiofemoral joint cartilage damage and bone marrow lesions over 7 years: the Multicenter Osteoarthritis Study. *Osteoarthritis Cartilage*. 2016;24(7):1160-1166.
29. Virayavanich W, Alizai H, Baum T, et al. Association of frequent knee bending activity with focal knee lesions detected with 3 T magnetic resonance imaging: data from the Osteoarthritis Initiative. *Arthritis Care Res (Hoboken)*. 2013;65(9):1441-1448.
30. Widuchowski W, Widuchowski J, Faltus R, et al. Long-term clinical and radiological assessment of untreated severe cartilage damage in the knee: a natural history study. *Scand J Med Sci Sports*. 2011;21(1): 106-110.
31. Williams TG, Holmes AP, Bowes M, et al. Measurement and visualisation of focal cartilage thickness change by MRI in a study of knee osteoarthritis using a novel image analysis tool. *Br J Radiol*. 2010; 83(995):940-948.
32. Wise BL, Niu J, Guermazi A, et al. Magnetic resonance imaging lesions are more severe and cartilage T2 relaxation time measurements are higher in isolated lateral compartment radiographic knee osteoarthritis than in isolated medial compartment disease: data from the Osteoarthritis Initiative. *Osteoarthritis Cartilage*. 2017; 25(1):85-93.