

HETEROGENEOUS CARTILAGE DAMAGE SEEN ON MRI AMONG KNEES WITH KELLGREN-LAWRENCE 2 & 3 OSTEOARTHRITIS: WHAT ARE THE IMPLICATIONS FOR CLINICAL TRIALS?

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BACKGROUND AND PURPOSE

- The most recent update of the Global Burden of Disease figures (GBD 2013) estimated that 242 million people were living in the world with symptomatic and activity-limiting osteoarthritis (OA) of the hip and/or knee.
- Many potential disease-modifying osteoarthritis drugs (DMOADs) have been investigated, but to date no DMOADs that slow or stop disease progression have been approved by the Food and Drug Administration (FDA) or the European Medicines Agency (EMA).
- A potential reason for the lack of demonstrated efficacy may be reliance on radiographs for defining structural inclusion and exclusion criteria for clinical trials, such as use of joint space width and Kellgren-Lawrence (KL) grade as surrogates for cartilage damage.
- Our objective is to estimate the distribution of cartilage damage seen on knee MRI in a sample of knees with radiographic KL 2 and 3 OA that would potentially qualify for a DMOAD trial.

METHODS

- Sample:** Knees from the Osteoarthritis Initiative (OAI), a longitudinal cohort study of knees with or at risk of developing symptomatic radiographic OA, that met common **structural inclusion criteria** for DMOAD trial enrollment at OAI baseline: knees with radiographs centrally graded as KL 2 or 3 and medial minimum joint space width (mJSW) \geq 1.5mm.
- Reader:** A musculoskeletal radiologist with 10 years of experience in MRI-based semiquantitative scoring of knee OA
- MR Images:** 3T coronal intermediate-weighted (IW) Turbo Spin Echo (TSE) & sagittal fat-suppressed IW TSE MR images.
- Scored feature:** Cartilage damage in the medial and lateral tibiofemoral and patellofemoral compartments using WORMS (Whole-Organ Magnetic Resonance Imaging Score).
- The WORMS cartilage scores were collapsed into 4 categories:
 - Normal:** No cartilage damage (WORMS 0 and 1)
 - Focal PT/FT:** focal partial or full-thickness cartilage damage (WORMS 2 and 2.5)
 - Diffuse PT:** Diffuse partial thickness cartilage damage (WORMS 3 and 4)
 - Diffuse FT:** Diffuse full-thickness cartilage damage (WORMS 5 and 6)

We estimated the prevalence of each category of cartilage damage in KL2 and KL3 knees; 95% confidence intervals (CI) accounted for clustering at the participant-level since some participants contributed two knees to the analysis.

RESULTS

- 2,372 participants contributing to 3,446 knees with radiographic OA (KL 2 and 3) and medial mJSW \geq 1.5mm.

KL2: 2,318 knees

KL3: 1,128 knees

- No cartilage damage in **any** compartment

KL2: 9.8% (95%CI: 8.5, 11.1)

KL3: 2.0% (95%CI: 1.1, 2.9)

- No cartilage damage in the **medial tibiofemoral** compartment

KL2: 52.4% (95%CI: 50.1, 54.6)

KL3: 14.4% (95%CI: 12.2, 16.6)

- No cartilage damage in the **lateral tibiofemoral** compartment

KL2: 61% (95%CI: 58.8, 63.2)

KL3: 53.6% (95%CI: 50.4, 56.7)

- No cartilage damage in **either tibiofemoral** compartment

KL2: 34.8% (95%CI: 32.7, 36.9)

KL3: 4.3% (95%CI: 3.0, 5.5)

- Diffuse FT cartilage lesions in the medial tibiofemoral compartment

KL2: 6.1% (95%CI: 5.0, 7.1)

KL3: 42.5% (95%CI: 39.4, 45.6)

Table 1. Cartilage damage seen on 3T MRI, by Kellgren-Lawrence grade. PT: Partial-thickness, FT: Full-thickness, TFJ: Tibiofemoral Joint, PFJ: Patellofemoral Joint).

Knee MRI Findings	Kellgren-Lawrence Grade			
	KL2 (n=2,318)		KL3 (n=1,128)	
	Percent	(95%CI)	Percent	(95%CI)
Medial TFJ				
Normal	52.4	(50.1, 54.6)	14.4	(12.2, 16.6)
Focal PT/FT	9.4	(8.2, 10.7)	2.6	(1.6, 3.5)
Diffuse PT lesion	32.1	(30.1, 34.2)	40.6	(37.5, 43.6)
Diffuse FT lesion	6.1	(5.0, 7.1)	42.5	(39.4, 45.6)
Lateral TFJ				
Normal	61.0	(58.8, 63.2)	53.6	(50.4, 56.7)
Focal PT/FT	16.4	(14.8, 18)	14.2	(12.1, 16.3)
Diffuse PT lesion	14.6	(13.1, 16.2)	12.1	(10.1, 14.0)
Diffuse FT lesion	7.9	(6.8, 9.1)	20.1	(17.6, 22.7)
Medial/lateral TFJ (maximum score)				
Normal	34.8	(32.7, 36.9)	4.3	(3.0, 5.5)
Focal PT/FT	15.1	(13.5, 16.6)	1.2	(0.6, 1.9)
Diffuse PT lesion	36.9	(34.8, 39.0)	35.4	(32.4, 38.4)
Diffuse FT lesions	13.3	(11.8, 14.8)	59.1	(56.0, 62.2)
PFJ				
Normal	22.0	(20.2, 23.9)	23.0	(20.3, 25.6)
Focal PT/FT	4.4	(3.5, 5.3)	3.9	(2.7, 5.1)
Diffuse PT lesion	24.9	(23, 26.9)	36.3	(33.3, 39.2)
Diffuse FT lesions	48.6	(46.2, 50.9)	36.9	(33.8, 40.0)
Whole knee				
Normal	9.8	(8.5, 11.1)	2.0	(1.1, 2.9)
Focal PT/FT	5.4	(4.4, 6.4)	1.0	(0.4, 1.5)
Diffuse PT lesion	28.8	(26.8, 30.8)	23.6	(20.9, 26.3)
Diffuse FT lesions	55.9	(53.7, 58.2)	73.4	(70.6, 76.2)
Number of compartments with diffuse FT lesions				
0	44.0	(41.7, 46.3)	26.6	(23.8, 29.4)
1	49.8	(47.5, 52.1)	48.9	(45.8, 52)
2	5.8	(4.8, 6.8)	22.9	(20.3, 25.5)
3	0.4	(0.2, 0.7)	1.6	(0.9, 2.3)
Number of TFJ compartments with diffuse FT lesions				
0	86.7	(85.2, 88.2)	40.9	(37.8, 44.0)
1 (medial or lateral)	12.5	(11.0, 13.9)	55.5	(52.5, 58.6)
2 (medial and lateral)	0.8	(0.4, 1.1)	3.5	(2.4, 4.7)

CONCLUSION

- There is a substantial percentage of knees with normal cartilage and diffuse full-thickness cartilage lesions in knees that would potentially qualify for DMOAD trial.
- MRI-based screening to define eligibility (ROAMES) may help in excluding knees without any cartilage damage (likely no effect of an anabolic compound) or widespread diffuse full-thickness damage (likely no effect of an anti-catabolic compound).
- Additional studies are needed to help analyze sub-strata of already completed trials.

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