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Brief Report

How to define subregional osteoarthritis progression using semi-quantitative MRI Osteoarthritis Knee Score (MOAKS)

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SUMMARY

Objective: Recently, the MRI Osteoarthritis Knee Score (MOAKS), a new semi-quantitative magnetic resonance imaging (MRI) scoring tool, was introduced by a panel of experienced researchers in osteoarthritis (OA). The MOAKS is primarily applicable to quantify OA status, since the interpretation of change in the MOAKS features was not described. In order to enable longitudinal evaluation, we propose definitions for progression and improvement of the main MOAKS features.
Method: Clear definitions for progression and improvement of the main MOAKS features are given in this brief report. 687 baseline and 30 months follow-up MRIs of the knees of 348 overweight and obese middle-aged women, free of OA at baseline, were scored using the MOAKS. Baseline prevalence and the change of MOAKS features after 30 months follow-up, based on our definitions for progression and improvement, are presented.
Results: The proposed definitions showed 3% to 23% progression and 0% to 11% improvement in the MOAKS features during the 30 months follow-up. Overall, progression rates were higher in the medial than in the lateral tibiofemoral (TF) joint. Progression of bone marrow lesions (BMLs) and cartilage defects was highest in the patellofemoral (PF) joint. Inter-rater reliability of the MOAKS scores was moderate to nearly perfect (PABAK 0.77–0.88), with high percentage of agreement overall (89–94%).
Conclusion: This brief report presents definitions for progression and improvement of the main MOAKS features for the longitudinal evaluation of knee OA features on MRI. We advocate uniform usage of the proposed definitions across studies, but welcome suggestions for optimization.

Introduction

In recent years, magnetic resonance imaging (MRI) has demonstrated its relevance for the evaluation of structural changes during the development and progression of knee osteoarthritis (OA)[1]. Semi-quantitative scoring of MRI OA features has shown to be a valid tool for this evaluation[1]. For this purpose, several semi-quantitative scoring methods have been described, such as the KOSS[2], WORMS[3] and BLOKS[4].

Recently, a panel of experienced researchers on semi-quantitative MRI scoring of OA features re-evaluated all available scoring systems. The panel stated that: "these tools have undergone unpublished iterations that have made it difficult for the naïve reader to determine the differences between original instrument description and that which has been used"[5]. This effort resulted in the MRI Osteoarthritis Knee Score (MOAKS) which was advocated as an evolved semi-quantitative tool based on the authors' knowledge and experience[5].

The MOAKS, as published, is primarily applicable to quantify disease status. Since the interpretation of the change of the MOAKS features over time is not described by the authors, progression or improvement of MOAKS features is hard to quantify. However, change of MOAKS features seems to be an important measure for the monitoring of knee OA, since MOAKS is advocated to be the tool of choice for semi-quantitative analyses of knee OA. For proper comparison between studies and in order to enable future meta-

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analyses, it is important to reach consensus about the definition of change of the MOAKS features. These definitions need to be used consistently by all researchers reporting on the change of MOAKS features over time. Therefore, this work was conducted as an effort to propose clear definitions for the progression and improvement of the most important MOAKS features. We used baseline and 30 months follow-up data of a high-risk cohort of middle-aged overweight and obese women without knee OA at baseline to illustrate the numbers associated with these definitions.

Methods

Training

An experienced musculoskeletal radiologist (EO; 10 years of experience with musculoskeletal MRI in clinical and research settings) trained all five readers (JR, DS, BvM, PvdP and DvE) in the use of MOAKS. Before the training, the published MOAKS scoring system was discussed among our research team and additional information was obtained from the original authors for clarification of certain features. Next, all features were thoroughly discussed during four meetings. Between sessions, several MRIs of ongoing studies not presented here were scored by all trainees and these were evaluated at the next meeting. After completion of the training, MRIs of 20 randomly selected knees of these ongoing studies were scored by all trainees and the musculoskeletal radiologist in order to determine reliability of the scoring.

Definitions for longitudinal change

In addition to the published definitions of the main OA features of MOAKS[5], we defined and evaluated the definitions of the change of the main MOAKS features assessed per subregion, as listed in Table I. Contrary to structural features on radiography, improvement of structural features on MRI is possible. Therefore, both definitions of progression and improvement are given. Several MOAKS features were not taken into account in these definitions since progression/improvement will simply be the difference between baseline and follow-up scores (e.g., Hoffa's synovitis or effusion-synovitis) or their role in knee OA is uncertain[5].

Data collection

We applied the above mentioned definitions on knee MRI scans acquired at baseline and after 30 months follow-up within a high-risk cohort of middle-aged women with a body mass index (BMI) $\geq$ 27 kg/m^2, without knee complaints and radiographic knee OA (K&L $\geq$ 2) at baseline. The design of this intervention study has

Table I
Definitions of progression, improvement and unchanged status of main MOAKS features

Features described in MOAKS	Progression	Improvement	No change
BMLs without cyst at baseline	- Incidence of one or more cysts *or* - increase in the size of the BML *or* - an increase in the number of BMLs when there is no change in the size of the BML	No cyst at follow-up and: - a decrease in the size of the BML *or* - a decrease in the number of BMLs when there is no change in the size of the BML	- No cyst at follow-up *and* - no change in size of the BML *and* - no change in number of BMLs
BMLs with cyst at baseline	One or more cysts at follow-up and: - an increase in the size of the BML *or* - an increase in the percentage of the lesion that is BML when there is no change in the size of the BML *or* - an increase in the number of BMLs when there is no change in the size of the BML or percentage of the lesion that is BML	- No cysts at follow-up *or* - one or more cysts at follow-up and: - a decrease in the size of the BML or - a decrease in the percentage of the lesion that is BML when there is no change in the size of the BML or - a decrease in the number of BML when there is no change in the size of the BML or the percentage of the lesion that is BML	- One or more cysts at follow-up *and* - no change in size of the BML *and* - no change in percentage of the lesion that is BML *and* - no change in the number of BMLs
Cartilage defects	- an increase in the percentage of full-thickness cartilage loss *or* - an increase in the size of any cartilage loss when there was no change in the percentage of full-thickness cartilage loss.	- a decrease in the percentage of full-thickness cartilage loss *or* - a decrease in the size of any cartilage loss when there was no change in the percentage of full-thickness cartilage loss	- No change in the percentage of full-thickness cartilage loss *and* – no change in the size of any cartilage loss
Osteophytes	- an increase in score for an osteophyte scored $\geq$2 at baseline *or* - a score $\geq$2 at follow-up for an osteophyte with a score <2 at baseline	- a decrease in score for an osteophyte scored $\geq$2 at baseline	- a score <2 at baseline and follow-up *or* - no change in score for osteophytes scored $\geq$2 at baseline
Meniscal pathologies	- an increase in score of hypertrophy, cysts, partial maceration, complete maceration, progressive maceration, vertical tear, horizontal tear, complex tear, or root tear *or* - an increase in the score of signal when there is no improvement in any of the hypertrophy, cyst, maceration or tear scores*.	- a decrease in the score of hypertrophy when there is no increase in the cysts, maceration and tears scores *or* - a decrease in the score of cyst when there is no increase in the hypertrophy, maceration and tears scores *or* - a decrease in one of the maceration scores when there is no increase in hypertrophy, cyst, the other macerations and tear scores *or* - a decrease in one of the tear scores when there is no increase in hypertrophy, cyst, maceration and other tear scores *or* - a decrease in signal when there is no increase in hypertrophy, cyst, maceration and tear scores.	- No change in score of hypertrophy, cysts, partial maceration, complete maceration, progressive maceration, vertical tear, horizontal tear, complex tear, root tear, or signal
Meniscal extrusion	- an increase in extrusion score	- a decrease in extrusion score	- No change in extrusion score

* Since meniscal signal would then be regarded as a sequelae of the healing process..

been published previously[6]. At baseline and after 30 months, all subjects filled-in the WOMAC questionnaire and an MRI of both knees on a 1.5 T scanner was made. The MRI protocol included coronal and sagittal proton density weighted sequences (slice thickness 3.0 mm/slice gap 0.3 mm), a coronal T2-weighted Spectral Presaturation by Inversion Recovery (SPIR) sequence (slice thickness 5.0 mm/slice gap 0.5 mm), an axial dual spin-echo sequence (slice thickness 4.5 mm/slice gap 0.5 mm), and a sagittal 3D water selective (WATS) sequence with fat saturation (slice thickness 1.5 mm). MRIs were scored for baseline and follow-up time-points at the same time (order known) by JR and PvdP using MOAKS[5]. As part of the training process both readers and one additional trained team member (DvE) scored baseline and follow-up MRIs of one randomly assigned knee every 2 weeks (15 knees from 15 individuals in total) and discussed discrepancies in scoring until consensus was reached. To illustrate the frequencies of change associated with these definitions, we summed the change scores per feature (1 for progression, −1 for improvement and 0 for no change) into overall measures of change for the medial tibiofemoral (TF), lateral TF joint and patellofemoral (PF) joint.

Inter-rater reliability

To determine reliability of the change in MOAKS features, these MRIs were also scored by the experienced musculoskeletal radiologist involved (EO). Given the low prevalence of change of MOAKS features, prevalence-adjusted bias-adjusted kappa (PABAK) statistics[7], rather than regular kappa statistics, and percentage agreement were determined between the individual pre-consensus change scores of the two readers (JR and PvdP) and the musculoskeletal radiologist scores, averaged per feature over the subregions of MOAKS.

Results

Baseline and follow-up MRIs were available for 687 knees of 348 women (mean age 55.7 ± 3.2 years and mean BMI 32.4 ± 4.2 kg/m^2 at baseline). Their average baseline WOMAC scores (0–100; higher scores being worse) were 6.7 ± 11.4 for the pain subscale and 6.5 ± 11.0 for the function subscale. The summed overall baseline prevalence and the change of MOAKS features, based on our definitions, are given in Table II. Progression of the main MOAKS features ranged from 3% to 23%, with higher rates in the medial than the lateral TF joint. For progression of cartilage defects and bone marrow lesions (BMLs), the highest rates were found in the PF joint. Improvement was found in 0% to 11% of all knees, again with the highest rates in the PF joint.

The average PABAK values per feature showed 'substantial' to 'nearly perfect agreement'[8]; mean PABAK values for the change in BMLs were 0.88 (95% CI 0.81–0.96) and 0.86 (95% CI 0.79–0.93), with 94% and 93% agreement, respectively. Mean PABAK values for the change in cartilage defects were 0.85 (95% CI 0.74–0.95) and 0.79 (95% CI 0.65–0.93), with 92% and 90% agreement, respectively. Mean PABAK values for the change in osteophyte scores were 0.77 (95% CI 0.66–0.89) and 0.85 (95% CI 0.76–0.95), with 89% and 93% agreement, respectively. Mean PABAK values for the change in medial and lateral meniscal extrusion were 0.78 (95% CI 0.61–0.94) and 0.84 (95% CI 0.73–0.94), with 89% and 92% agreement, respectively.

Discussion

For proper comparison between studies, it is important to reach consensus on the definitions for change of OA status recorded with the currently most advocated semi-quantitative MRI scoring tool, MOAKS[5]. Since the original report of MOAKS did not include definitions for change, we here propose a set of definitions for the progression and improvement of the main MOAKS features. Improvement of MOAKS features was also defined, since it is known that several OA features seen on MRI can improve over time[9].

Table II
Baseline prevalence and change of MOAKS features over 30 months

MOAKS features	Medial TF joint	Lateral TF joint	PF joint
BMLs			
- Baseline prevalence	165/687 (24%)	87/687 (13%)	342/687 (50%)
- Progression	63/687 (9.2%)	42/687 (6.1%)	151/684 (22.1%)
- No change	580/687 (84.4%)	622/687 (90.5%)	458/684 (67.0%)
- Improvement	44/687 (6.4%)	23/687 (3.3%)	75/684 (11.0%)
Cartilage defects			
- Baseline prevalence	223/687 (32%)	116/687 (17%)	407/683 (60%)
- Progression	59/685 (8.6%)	41/686 (6.0%)	158/680 (23.2%)
- No change	617/685 (90.1%)	640/686 (93.3%)	502/680 (73.8%)
- Improvement	9/685 (1.3%)	5/686 (0.7%)	20/680 (2.9%)
Osteophytes			
- Baseline prevalence	295/687 (43%)	198/687 (29%)	354/686 (52%)
- Progression	79/686 (11.5%)	38/686 (5.5%)	53/683 (7.8%)
- No change	605/686 (88.2%)	644/686 (93.9%)	625/683 (91.5%)
- Improvement	2/686 (0.3%)	4/686 (0.6%)	5/683 (0.7%)
	Medial meniscus	**Lateral meniscus**	
Meniscal pathologies			
- Baseline prevalence	405/680 (59%)	164/681 (24%)	
- Progression	146/680 (21.5%)	77/681 (11.3%)	
- No change	520/680 (76.5%)	585/681 (85.9%)	
- Improvement	14/680 (2.1%)	19/681 (2.8%)	
Meniscal extrusion			
- Baseline prevalence	353/681 (51%)	43/684 (6%)	
- Progression	99/681 (14.5%)	22/684 (3.2%)	
- No change	564/681 (82.8%)	659/684 (96.3%)	
- Improvement	18/681 (2.6%)	3/684 (0.4%)	

The set of proposed definitions showed progression and improvement in a high risk population of women without radiographic and symptomatic knee OA at baseline. Although all subjects were free of radiographic and symptomatic knee OA at baseline, prevalence of OA features on MRI at baseline was relatively high. As expected, baseline prevalence and progression rates were higher in medial than in the lateral TF joint. Somewhat more notable was the high prevalence and the high progression rate of features within the PF joint. Prevalence of both cartilage defects and BMLs was approximately twice as high and these features progressed at double the rate within the PF joint compared to the TF joint. These data confirm a previous MRI study suggesting the PF joint to be the compartment predominantly affected by knee OA[10]. One should keep in mind that the data used originate from an intervention study, so the rate of change might not truly represent the rate of change in an open population. However, since no effects of the interventions on incidence of radiographic and clinical knee OA were found[11], this effect will be limited.

Despite the fact that the proposed definitions for longitudinal change of OA features on MRI can be used to evaluate the change of individual MOAKS features per subregion, we summed all change scores in order to obtain a concise description of the change of the MOAKS features over time. Obviously, summing the change of individual lesions does not reflect the true change over time in detail and does not discriminate between multiple low grade changes and a few high grade changes. However, showing the change of these features in a high-risk cohort was only a secondary objective in this brief report and developing a composite change score is beyond the scope of this report. Validation of the proposed definitions against clinical and other structural outcomes is warranted.

Previously, determining within-grade progression showed to have additional value in detecting longitudinal changes in semi-

quantitative scores[12]. This is particularly relevant for the MOAKS scoring system, in which certain feature grades reflect a wide range of severity (e.g., grade 2 for size and full-thickness percentage of cartilage defect: 10–75% of surface area). This leaves substantial possibility for progression or improvement remaining unreflected in the change in score over time. Moreover, without a within-grade progression score, a decrease in 'percentage of lesion that is BML' with unchanged 'size of the BML' can be interpreted as both increase in cyst size (progression) and a decrease in BML around a cyst (improvement). To assess the value of a within-grade progression score within the MOAKS, we will add a three-point scale to score overall change of the main MOAKS features over time in another ongoing cohort[13]. These data will also be used to validate the proposed definitions against the change in OA symptoms and radiographic features of OA.

In this brief report, we propose definitions for longitudinal semi-quantitative evaluation of OA features on MRI, assessed using the MOAKS. We advocate uniform usage of the proposed definitions across studies, but welcome suggestions for optimization; in order to enable proper comparison between future studies. Of course, other OA features not described in this brief report, such as effusion-synovitis or Hoffa's synovitis, might be valuable for longitudinal evaluation of OA features on MRI as well and could be evaluated along with the described definitions.

Contributions

All authors have made a substantial contribution to the concept and design of this study, interpretation of the data, drafting and revising the content of this article, and approved the final version being submitted. In addition, JR and EO have contributed to the collection and assembly of the reported data and take full responsibility for the integrity of the work presented.

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Competing interests

All authors declare no conflicts of interest.

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