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Magnetic Resonance Imaging Scoring Of An Experimental Model Of Post-Traumatic Osteoarthritis In The Equine Carpus

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Abstract

Magnetic resonance imaging (MRI) is the most sensitive imaging modality to detect the early changes of osteoarthritis. Currently, there is no quantifiable method to tract these pathological changes over time in the horse. The objective of this experimental study was to characterize the progression of MRI changes in an equine model of post-traumatic osteoarthritis using a semi-quantitative scoring system for whole-organ evaluation of the middle carpal joint. On day 0, an osteochondral fragment was created in one middle carpal joint (OCI) and the contralateral joint (CON) was sham-operated in 10 horses. On day 14, study horses resumed exercise on a high-speed treadmill until the completion of the study (day 98). High-field MRI examinations were performed on days 0 (pre-osteochondral fragmentation), 14, and 98 and scored by three blinded observers using consensus agreement. Images were scored based on 15 independent articular features, and scores were compared between and within groups. On days 14 and 98, OCI joints had significantly ($p = 0.05$) higher whole-organ median scores (29.0 and 31.5, respectively), compared to CON joints (21.5 and 20.0, respectively). On day 14, OCI joints showed significant increases in high signal bone lesion scores, and osteochondral fragment number and size. On day 98, high-signal bone lesions, low-signal bone lesions, osteophyte formation, cartilage signal abnormality, subchondral bone irregularity, joint effusion, and synovial thickening scores were significantly increased in OCI joints. Study results suggest the MRI whole-organ scoring system

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Competing interests

The authors have no competing interests.

reported here may be used to identify onset and progression of pathological changes following osteochondral injury.

Keywords

Equine; Carpus; MRI; Osteoarthritis; Semi-quantitative Scoring System

Introduction

Osteoarthritis is a multifactorial process characterized by changes in structure and function of the entire joint, and is the most common cause of lameness and decreased performance in the equine athlete.(1) A diagnosis of osteoarthritis is commonly made based on patient history, clinical examination, and diagnostic imaging findings. Conventional radiography is the most common imaging modality used to characterize the progression of structural changes associated with osteoarthritis, however, it lacks the sensitivity necessary to detect early changes associated with osteoarthritis and correlates poorly with clinical outcomes.(2-5) These limitations likely play a role in why it has been difficult to demonstrate treatment efficacy in osteoarthritis research as radiographically detectable osteoarthritis may represent a stage of osteoarthritis that is already too advanced for pharmacological intervention.(6,7) Identifying imaging modalities that are able to recognize changes associated with osteoarthritis starting at the onset of the disease process and correlating these imaging findings to clinical symptoms is critical to improving our understanding of osteoarthritis and for developing effective therapeutic interventions.

Magnetic resonance imaging (MRI) is a non-invasive, cross-sectional, multiplanar imaging modality that is increasingly being used for the assessment of musculoskeletal disorders in horses.(8,9) Recently, several case series have shown the ability of MRI to identify osteoarthritis-related structural changes related to equine lameness that could not be identified by radiography,(3,4,10-12) however, very little information is known regarding the significance and pathological progression of these imaging findings in the horse. Such information would be beneficial in determining the prognosis, as well as for case management.(13,14)

In people, semi-quantitative MRI whole-organ scoring systems have been shown to provide a reliable method to quantify the structural changes that occur in joints over time.(15,16) They have also been shown to relate clinical symptoms to pathological features and to identify risk factors for structural changes.(17-19) Several equine cadaver studies have evaluated the ability of MRI to assess pathological change in cartilage, bone and soft tissue structures,(20-28) however, studies using MRI to evaluate the joint as a whole-organ are lacking and could improve our understanding of the progression of this complex disease.

The carpal osteochondral injury-exercise model is a commonly utilized model of post-traumatic osteoarthritis in the horse, and several studies have evaluated imaging and pathological findings at the completion of these studies.(29-31) To the authors' knowledge, there are no studies evaluating the use of MRI to identify the progression of osteoarthritis-associated structural changes that occur over time following osteochondral injury using this

model. The objective of this study was to characterize the progression of MRI changes in a carpal osteochondral injury-exercise model of post-traumatic osteoarthritis using a semi-quantitative scoring system for evaluation of the equine middle carpal joint. We hypothesized that MRI would be able to detect osteoarthritis-associated structural changes 14 days following osteochondral injury and scores obtained from a semi-quantitative equine MRI osteoarthritis scoring system (EMOSS) would be higher in the osteochondral injured joints at both 14 and 98 days following osteochondral injury compared to baseline examination, as well as between osteochondral injured and control joints.

Materials and Methods

Experimental Design

The horses used in this experimental study were part of an independent project evaluating the therapeutic effects of a novel treatment for osteoarthritis. The MRI images used were from ten control (untreated) horses in that project. The study protocol was approved by the University of Florida Institutional Animal Care and Use Committee. Study horses were obtained from the University of Florida College of Veterinary Medicine Research Herd and included in the study if they were free of lameness and lacked clinical abnormalities in their carpi including effusion, periarticular soft tissue swelling, or decreased range of motion. Subjective gait analyses were performed by two evaluators using the American Association of Equine Practitioners' lameness grading scale(32), and confirmed using the Lameness Locator (Equinosis, LLC, St. Louis, MO) for objective gait analysis. Complete radiographic examination of each middle carpal joint [dorsopalmar, dorsal 45° lateral-palmaromedial oblique, dorsal 45° medial-palmarolateral oblique, lateromedial, lateromedial (flexed), dorsal 55° proximal-dorsodistal oblique (flexed), and dorsal 35° proximal-dorsodistal oblique (flexed) views] were obtained and horses were excluded from the study if there was presence of soft tissue swelling, osteochondral fragmentation, marginal osteophytosis, enthesophytosis, subchondral bone sclerosis, or subchondral bone lysis. Prior to the start of the study, all horses were exercised 5 days/week on a high-speed treadmill for 21 days. For each exercise day, horses underwent trotting (16-18 km/h) for 2 min, then galloping (30-32km/h) for 2 min, followed by trotting (16-18 km/h) for two additional minutes to simulate the exercise of race training.

Magnetic resonance imaging examinations were performed under general anesthesia with the horse placed in left lateral recumbency on days 0, 14, and 98. Both carpi were scanned individually with each carpus placed in partial flexion (15-25°) using a 1.5 Tesla high-field unit and a quadrature transmit/receive knee coil (Toshiba America Medical Systems, Tustin, CA) with one receiver channel. Magnetic resonance imaging sequences were selected to be clinically applicable and to allow timely completion to avoid a prolonged period of general anesthesia. Sequences included sagittal proton density (PD), axial PD, dorsal T2-weighted (T2), axial T2 short-tau inversion recovery (T2-STIR), sagittal proton density with fat suppression (PD-FS), dorsal PD-FS, and dorsal T2*-weighted spoiled gradient echo with fat suppression (SPGR-FS). (Table 1) Total acquisition time was approximately 80 minutes for all sequences on both limbs.

On day 0, immediately following the initial MRI examination, all horses were placed in dorsal recumbency and underwent bilateral arthroscopic examination of the middle carpal joints using the standard arthroscopic approach.(33) An osteochondral fragment was created at the distodorsal aspect of the radial carpal bone in one randomly selected middle carpal joint of each horse to simulate osteochondral injury. The osteochondral fragment was made by using an 8 mm curved bone gouge placed through the medial arthroscopic portal and directed perpendicular to the articular surface of the distal aspect of the radial carpal bone at the level of the medial synovial plica. The osteochondral fragment was allowed to remain adhered to the medial synovial plica and any osteochondral debris resulting from creation of the osteochondral fragment was left within the joint as previously described.(34) This joint was designated the osteochondral injured joint (OCI), the other middle carpal joint was sham-operated and designated the control joint (CON). The arthroscopic portals were closed with 2-0 polydioxanone in a simple, interrupted pattern and the limbs were bandaged routinely for recovery. Each horse received one dose of intravenous potassium penicillin (22,000 U/kg), gentamicin (6.6 mg/kg), and phenylbutazone (4.4 mg/kg) at the time of surgery, and phenylbutazone (4.4 mg/kg) intravenously once daily for 5 days following. All horses were housed in a 3.65 m × 3.65 m stall from day 0 to 10. During this time, the bandages were changed and horses were monitored daily for vital parameters and any complications following surgery. On day 10, sutures were removed and all horses were returned to paddock turnout. On day 14, all horses resumed exercise on a high-speed treadmill using the protocol described above until the end of the study on day 98.

Magnetic Resonance Imaging Assessment

All images were transferred and stored in Digital Imaging and Communications in Medicine (DICOM) format on a Picture Archive and Communication System (Merge Healthcare, Chicago, IL). Images were analyzed at the same time by three observers including a board-certified veterinary radiologist, a board-certified large animal surgeon, and a large animal surgery resident using a dedicated DICOM workstation equipped with three megapixel greyscale monitors. The observers were not aware of the identity of experimental groups. Images were scored by consensus agreement in which images with different scores assigned by one or more observers were reviewed again and scores discussed. A final score was then assigned by consensus of all three observers. All images were used to evaluate each feature, although certain sequences were more suitable for grading individual articular features than others and were reported accordingly.

Equine MRI Osteoarthritis Scoring System

A semi-quantitative whole-organ scoring system for use in the equine middle carpal joint was adapted from a previously described human knee osteoarthritis scoring system.(15) Images were scored ordinally based on fifteen independent articular features including presence of cartilage signal abnormalities, size and intensity of high-signal bone lesions; subchondral bone irregularity; low-signal bone lesions; marginal osteophytes; medial and lateral collateral, medial and lateral palmar intercarpal, and dorsomedial intercarpal ligament integrity; number and size of osteochondral fragment(s); synovial thickening; and joint effusion.

The six cuboidal bones that make up the middle carpal joint were divided into 9 sub-regions. (Figure 1) The radial carpal, intermediate carpal, and third carpal bones were each divided into two sub-regions based on the bone on the apposing articular surface with which it articulates. The radial carpal bone was divided into the second and third facets, the intermediate carpal bone was divided into the third and fourth facets, and the third carpal bone was divided into the radial and intermediate facets. The margins of each sub-region division were extended along a line perpendicular to the articular surface of the middle carpal joint to either the corresponding radiocarpal or carpometacarpal joint. The ulnar, second, and fourth carpal bones were evaluated as their own undivided sub-regions. Six of the articular features (cartilage signal abnormalities, high-signal bone lesion size and intensity, low-signal bone lesion, subchondral bone irregularity, and marginal osteophytes) were evaluated independently at the 9 different sub-regions in the middle carpal joint. Scoring was based solely on the middle carpal joint such that scored abnormalities originated and extended only from the articular surface of the middle carpal joint. Abnormalities within the bone originating from either the radiocarpal or carpometacarpal joint were not scored.

Cartilage signal abnormalities were scored based on changes in signal and morphology on SPGR-FS and PD-FS images and graded as: 0 = no abnormalities, 1 = single lesion < 5 mm, 2 = single lesion > 10 mm or multiple lesions < 5 mm, 3 = multiple lesions with at least one lesion > 10 mm. High-signal bone lesions were defined as poorly marginated areas of increased signal intensity in the normally hypointense trabecular or subchondral bone on both the PD-FS and T2-STIR images. The size of the high-signal bone lesion was based on the extent of regional involvement and graded as: 0 = none, 1 = < 25%, 2 = 25-50%, and 3 = > 50%. The intensity of increased signal for each high-signal bone lesion was subjectively graded based on severity of signal increase (0 = none, 1 = mild, 2 = moderate, 3 = marked) compared to the surrounding subchondral or trabecular bone on PD-FS and T2-STIR images. (Supplemental 1) Subchondral bone irregularity was scored based on severity and graded as: 0 = smooth and regular chondro-osseous junction, 1 = mild subchondral plate irregularity, 2 = marked subchondral plate irregularity with intact trabecular bone, 3 = bone irregularity extending to the trabecular bone with preservation of some bone trabecular pattern, 4 = cyst-like formation. Subchondral bone irregularity was differentiated from high-signal bone lesions by the presence of subchondral bone plate irregularity with progressive involvement of trabecular bone. Low-signal bone lesions were defined as reduced signal intensity on PD and T2-weighted images and graded as: 0 = <10% of region, 1 = 10-25%, 2 = 26-50%, 3 = >50%. Marginal osteophytes were graded according to size (0 = none, 1 = < 1 mm, 2 = 1 - 2 mm, 3 = >2 mm), and based on the largest osteophyte identified within each sub-region.

The soft tissue supporting structures associated with the middle carpal joint, including: the lateral and medial collateral ligament, dorsomedial intercarpal ligament, and lateral and medial palmar intercarpal ligament, were assessed independently and graded together as normal (0) or abnormal (1) based on changes in size and signal intensity. Synovial thickening and joint effusion were scored independently using T2-STIR and PD-FS images. Synovial thickening was recognized as tissue of moderate signal intensity protruding into the hyperintense synovial fluid and subjectively graded (0 = normal, 1 = mild, 2 = moderate, 3 =

marked) based on the intensity and distribution of synovium. (Supplemental 2) Joint effusion was graded from 0 - 3 and based on the estimated maximum distension of the synovial cavity: 0 = normal, 1 = <33% of maximum potential distention, 2: 33%-66% of maximum potential distention, 3 = >66% of maximum potential distention. Each joint was scored according to the number of osteochondral fragments present and by the size of the largest osteochondral fragment. The number of osteochondral fragments were graded as: 0 = none, 1 = 1 fragment, 2 = 2 fragments, 3 = >2 fragments. The dorsal to palmar depth and lateral to medial width of the fragment was measured using the longest dimensions on axial images, and the proximal to distal height was measured using the largest dimension on the sagittal images. The size of the largest osteochondral fragment was then graded based on the estimated volume of the osteochondral fragment (0 = none, 1 = <250 mm³, 2 = 250 - 500mm³, 3 = >500mm³). Final scores were totaled to determine a whole-organ score for the entire middle carpal joint (0-188).

Statistical Analysis

Statistical analysis was performed by the primary author (AS). Since the response was ordinal scale and non-normal, a nonparametric approach was considered. The experimental design was a split plot in time(35) with group (CON vs OCI joints within a horse) as the main plot factor and day as the sub-plot factor. The aligned-rank transform method (36) was applied to a split plot in time design (SAS Institute Inc, Cary, NC). Initially, a group-day interaction was tested followed by main effect tests for group (CON vs. OCI) and day (0, 14, and 98). These tests were followed with the nonparametric Wilcoxon Signed Rank Tests to determine which differences were significant between CON and OCI groups fixing the day or pairs of days (0 vs 14, 0 vs. 98, and 14 vs. 98) and fixing the group. Outcome ordinal data (scores) were reported as median (minimum, maximum) because the data were not normally distributed. The null hypotheses that median scores for pathological changes observed between groups (CON vs. OCI) on days 0, 14, and 98 were not different were tested by using the Wilcoxon Signed Rank Test (Statistix 9 for Windows, 2008, Analytical Software, Tallahassee, FL). The null hypotheses that median scores for total individual articular and total joint scores observed between groups (CON vs OCI) on days 0, 14, and 98 were not different were tested by using the Wilcoxon Signed Rank Test (Statistix 9 for Windows, 2008, Analytical Software, Tallahassee, FL). For these two hypotheses, values of $p < 0.05$ were considered statistically significant as only one comparison was made between each outcome variable.

Among OCI joints, the null hypotheses that median scores were not different between days 0, 14, and 98 was tested using the Wilcoxon Signed Rank Test (Statistix 9 for Windows, 2008, Analytical Software, Tallahassee, FL) for paired data (i.e., day 0 vs 14, day 0 vs 98, day 14 vs 98). Similarly, among CON joints, the null hypothesis that median scores were not different between days 0, 14, and 98 was tested by using the Wilcoxon Signed Rank Test (Statistix 9 for Windows, 2008, Analytical Software, Tallahassee, FL) for paired data. Because each outcome variable was tested against three time points (0, 14, and 98) in these two hypotheses, a Bonferroni-adjusted significance level of 0.0167 was calculated to account for the increased possibility of type-1 error.

Results

Ten thoroughbred horses (5 mares and 5 geldings) between 2 and 9 years of age (median: 4.0, min: 3.0, max: 9.0) that were free of lameness, and clinical and radiographic evidence of middle carpal joint disease were included in the study. Supplemental files 3 and 4 contain the aligned rank split plot in time analyses. In the majority of cases among the totals, there was a significant interaction between group and day indicating that the difference between CON and OCI scores changed over time. Furthermore, in every case there was a significant main effect for day and in all but one case a significant main effect for group. This meant that there were significant differences between days averaged over groups and significant differences between groups averaged over days.

Supplemental files 5 - 8 represent the median (min, max) scores for whole-organ assessment of the CON and OCI joints and their comparisons between group on days 0, 14, and 98. On baseline MRI examination (day 0), no significant differences were seen between CON and OCI joints in any of the 15 articular features evaluated or whole-organ scores. (Supplemental files 5 and 8) Low-grade pathology, however, was variably identified in each articular feature evaluated despite strict inclusion criteria excluding horses with radiographic abnormalities. (Supplemental files 5 and 8) When evaluating individual articular features, the third and fourth facets of the intermediate carpal bone, the intermediate facet of the third carpal bone, and the fourth carpal bone (Supplemental files 5 - 7); the lateral and medial collateral ligaments and the medial and lateral palmar intercarpal ligaments (Supplemental file 8) showed no significant osteoarthritis-associated structural changes throughout the study period in either the CON or OCI joints.

On day 14, osteochondral fragments of varying size ($p = 0.001$) and number ($p = 0.001$) were identified on all sequences in the OCI joints. (Figure 2) The osteochondral fracture planes were best identified on PD-FS, SPGR-FS, and T2-STIR sequences in the dorsal or axial images as distinct linear patterns of increased signal intensity that was continuous with the synovial fluid and communicated with the joint distally and exited proximally in the dorsomedial aspect of the third facet of the radial carpal bone. High signal bone lesions were also identified on PD-FS, SPGR-FS, and T2-STIR sequences and extended radially from the fracture plane in the third facet of the radial carpal bone in all of the OCI joints, and extended into the second facet of the radial carpal bone in 9 of 10 OCI joints on day 14. (Figure 2 & 3) Additionally, median dorsomedial intercarpal ligament scores ($p = 0.031$) were also increased in the OCI joints compared to CON joints on day 14.

On day 98, there was no longer a significant difference between osteochondral number or size between CON and OCI joints as a discrete osteochondral fragment was identified in only 3 out of the 10 OCI joints. The osteochondral fragments in the other 7 OCI joints were identified adjacent to their fracture bed on the third facet of the radial carpal bone and the previous areas of increased signal intensity was no longer continuous with the synovial fluid nor did it span across two cortices. (Figure 2) In 4 out of these 7 OCI joints, the trabecular bone along the previous fracture plane was of uniform low signal intensity with complete resolution of high signal intensity. In the other 3 OCI joints, a portion of the previous fracture line was still evident along a variable portion of its length as evidenced by a thin

line of intermediate to high signal intensity on PD-FS, T2-STIR and SPGR-FS sequences within the trabecular bone of the third facet of the radial carpal bone. The size and signal intensity of the high-signal bone lesions were also no longer significantly different between groups on day 98, however, median low-signal bone lesions ($p = 0.016$), cartilage signal abnormality ($p = 0.020$), and subchondral bone irregularity ($p = 0.004$) scores for the third facet of the radial carpal bone were significantly increased in the OCI joints. Median synovial thickening scores ($p = 0.028$) were also increased in the OCI joints compared CON joints on day 98. Finally, total joint scores for the OCI joints were increased on days 14 ($p = 0.014$) and 98 ($p = 0.014$) compared to CON joints. (Supplemental file 8)

Table 2 represents the median (min, max) scores for the second and third facet of the radial carpal bone, the second carpal bone, and the radial facet of the third carpal bone for both the CON and OCI joints and their corresponding within group comparisons on days 0, 14, and 98. On day 14, increases in high-signal bone lesion scores from baseline examination were identified in the second and third facets of the radial carpal bone of the OCI joints for both size (RC-2: $p = 0.010$, RC-3: $p = 0.001$) and signal intensity (RC-2: $p = 0.004$, RC-3: $p = 0.001$) (Fig 2 & 3). In both the CON ($p = 0.008$) and OCI ($p = 0.016$) joints, median joint effusion scores were also increased on day 14 compared to baseline examination. (Figure 4)

At the end of the study (day 98), no significant differences were found in any of the articular features evaluated in the CON joints compared to days 0 or 14. However, significant osteoarthritis-associated structural changes were identified in the OCI joints, the majority of which were in the third facet of the radial carpal bone. These changes included increases in median scores for high-signal bone lesion size ($p = 0.016$) and intensity ($p = 0.016$) (Figures 2 & 3), marginal osteophyte formation ($p = 0.008$) (Figure 5), cartilage signal abnormalities ($p = 0.004$) (Figure 6), and subchondral bone irregularity ($p = 0.004$). (Figure 6) Although the high-signal bone lesion median scores of the third facet of the radial carpal bone remained increased compared to day 0 in the OCI joints, they were decreased in both size ($p = 0.002$) and signal intensity ($p = 0.002$) compared to day 14. In addition to the osteoarthritis-related structural changes identified in the third facet of the radial carpal bone, median cartilage signal abnormalities scores ($p = 0.008$) were increased in the radial facet of the third carpal bone on day 98 compared to baseline exam. Marginal osteophyte formation was also identified on the second facet of the radial carpal bone ($p = 0.008$). Median joint effusion scores remained increased compared to day 0 in the OCI joints ($p = 0.023$), although there were no differences compared to day 14. Median synovial thickening scores were also increased in the OCI joints on day 98 compared to day 0 ($p = 0.008$). (Figure 3) Total joint scores for the OCI joints were increased compared to baseline on days 14 ($p = 0.001$) and 98 ($p = 0.002$), although no difference was noted between days 14 and 98.

Discussion

The Equine MRI Osteoarthritis Scoring System used in the current study allowed temporal assessment of the osteoarthritis-associated structural changes that occur following osteochondral injury in the equine middle carpal joint. This semi-quantitative whole-organ scoring system was adapted from the Whole-Organ Magnetic Resonance Imaging Score (WORMS)(15) knee scoring system used in people for use in the equine middle carpal joint.

The articular features included are considered to be important for whole-organ assessment of the joint in people(37) and considered clinically relevant to traumatic joint injuries in the equine athlete. The sequences selected for use in this study were similar to those used in the clinical evaluation of traumatic joint injuries in the horse and provided an efficient means of evaluating all structures of the joint in order to minimize anesthetic time. The equine carpal osteochondral fragment model was easily performed and provided a suitable model to study post-traumatic osteoarthritis pathology from the onset of osteochondral injury to the development of osteoarthritis.

The osteochondral fragments created on the third facet of the radial carpal bone were easily identified on all imaging sequences on day 14 in the OCI joints. In contrast, a distinct osteochondral fragment was no longer observed in 7 out of 10 OCI joints on day 98. In 3 of these 7 OCI joints, there was an intermediate to high signal intensity on PD-FS, T2-STIR and SPGR-FS sequences still present along a variable portion the fracture plane within the trabecular bone of the third facet of the radial carpal bone, which was not identified in the remaining 4 OCI joints. The differences in these findings likely represent variability in healing of the fractures. This is similar to what is seen clinically in horses, where resolution of high signal intensity on fat saturated sequences is associated with resolution of the fracture plane and the persistence of high signal intensity on PD-FS and T2-STIR images likely represents continued boney remodeling.(13)

In addition, there was also evidence of injury to the subchondral and trabecular bone of the second and third facet of the radial carpal bone identified on MRI as large, ill-defined areas of increased signal intensity on fat-suppressed sequences on day 14. These lesions have been referred to as “occult”, as they are not recognized by other imaging modalities.(4) Because MRI has the ability to provide both anatomic and physiological information, these lesions can be identified and characterized.(4) Lesions with a similar appearance have been identified on MRI examination of horses following a known traumatic joint injury and are typically associated with lameness.(3,4,38) Although the mechanism by which subchondral bone injury leads to osteoarthritis is controversial,(39) it is recognized that injury to the subchondral bone predispose horses to osteoarthritis.(40)

In the current study, all of the high-signal bone lesions present in the third facet of the radial carpal bone on day 14 showed at least 50% resolution in size on day 98 in the OCI joints. Of the 6 OCI joints with persistent high-signal bone lesions on day 98, the pattern of resolution was from the trabecular bone towards the articular surface with a focal, discrete area of mild to moderate signal intensity remaining within the subchondral bone on fat-suppressed sequences. Additionally, cartilage signal abnormalities were identified adjacent to these areas of high-signal bone lesion in all (6) of the OCI joints with persistent high-signal bone lesion and in 2 of the OCI joints without persistent high-signal bone lesions on day 98. Prior to this study, the presence and progression of these “occult” lesions were not well documented in the horse because of the lack of chronological, comparative MRI studies of these types of injuries.(3,10,12,27,38,41) In people, similar appearing high-signal bone lesions have been identified on MRI initially following traumatic knee injuries with similar patterns of resolution overtime associated with cartilage degeneration.(42-46) The findings in this current study suggest that cartilage degeneration may be associated with these

patterns of high-signal bone lesions following osteochondral injury in the horse as well. The use of MRI to evaluate these changes longitudinally over time will help us determine their significance in the pathological progression of post-traumatic osteoarthritis.(47)

In the current study, there is evidence that there is a continuum between low- and high-signal bone lesions. This was most evident in the third facet of the radial carpal bone where low-signal bone lesions scores developed in areas of previous high-signal bone lesions and adjacent to areas of resolving high signal bone lesions. In addition, there was a trend ($p = 0.06$) for an increase in high-signal bone lesion scores in the radial facet of the third carpal bone on day 98 within areas of persistent low-signal bone lesion. Although high-signal bone lesions are included in human knee semi-quantitative MRI scoring systems(15,48-50); low-signal bone lesions, or more commonly termed subchondral bone sclerosis, have not been included, despite being considered one of the hallmarks of osteoarthritis.(51,52) Several studies have shown a correlation between subchondral bone sclerosis and cartilage degeneration in veterinary medicine,(21,24,53-55) however, it is unclear if subchondral bone sclerosis is a cause or a result of cartilage injury,(51) or how it relates temporally in the development of osteoarthritis. Although cartilage signal abnormalities were identified on both third facet of the radial carpal bone and the radial facet of the third carpal bone, the difference in appearance and manifestation of high-signal bone lesions and low-signal bone lesions between these two sub-regions likely reflects differences in mechanism of injury.(56) If we consider that the differences in signal intensities between these two time points in both sub-regions likely represents a continuum of bone remodeling following a traumatic injury, it is likely that a relationship exist between high- and low-signal bone lesions identified on MRI and cartilage degeneration.

In addition to differences in size of the high-signal bone lesions, the intensity, or severity of signal also changed over time. This was most evident in the third facet of the radial carpal bone of the OCI joints between days 14 and 98. (Figures 2 & 3) Previous studies in people and dogs have documented that changes in signal intensity correlated with differences in histopathological findings.(57,58) Although histopathology was not performed in the present study, we speculate that the changes in signal intensity of high-signal bone lesions over time in the current study represents different levels of severity of bone injury and remodeling. A limited number of studies have correlated MRI and histopathology in the horse;(22,23,59) however, to the authors' knowledge there are no studies that have correlated MRI and pathological findings over time or at the early stages of disease. These comparisons would validate the findings identified on MRI in the current study and provide a better understanding of how these MRI findings relate to the pathological progression of post-traumatic osteoarthritis. Additionally, changes in the severity of high signal intensity over time may prove to be better associated with return to soundness than either the persistence or resolution of high signal intensity as neither have been shown to be an accurate predictor of return to soundness in a limited number of case reports.(10,38,60,61)

In addition to cartilage signal abnormalities, subchondral bone irregularities were identified in similar locations on the third facet of the radial carpal bone on day 98 in the OCI joints. We may have been biased when evaluating cartilage signal abnormalities because areas of subchondral bone irregularity were likely closely scrutinized for cartilage signal

abnormalities, which could explain their association. However, subchondral bone irregularity scores on MRI have been correlated to the presence of gross cartilage damaged previously. (62) These subchondral bone irregularities were also associated with the site of osteochondral fragmentation and could represent incomplete healing of the osteochondral fragment. However, it is more likely that these represent true lesions as most of the subchondral bone irregularities identified extended along the articular margin well beyond the original fracture line. Additionally, persistent high-signal bone lesions were present in only 3 of the 10 OCI joints at the articular aspect of the previous fracture line. It is in these 3 OCI joints that we believe there was evidence of incomplete healing of the osteochondral fragment at the articular surface.

Progressive marginal osteophyte formation was identified in the medial aspect of the OCI joints on the second and third facet of the radial carpal, surrounding the site of osteochondral injury. The formation of marginal osteophytes is commonly assessed when evaluating osteoarthritis-associated structural changes in the horse.(63) There are several proposed causes for osteophyte formation, but they all seem to result in progressive overgrowth of cartilage and subchondral bone along the borders of articulation.(64) In the current study, marginal osteophytes appeared isointense to cortical bone on all sequences, regardless of the time period, which would suggest that they represent mineralized tissue. In a canine anterior cruciate ligament transection model of osteoarthritis(2), however, osteophytes were identified as early as 4 weeks and were characterized as being marginally hyperintense to cortical bone on T1-weighted gradient echo sequences which would be consistent with cartilage and incomplete mineralization (i.e. chondrophyte). The differences in osteophyte appearance between the two studies may be explained by the different pulse sequence parameters used or by the timing of MRI examination. Osteophyte appearance may also have been affected by the study design and exercise regimens used or by species-specific pathologic changes occurring in osteoarthritis disease progression.

Joint effusion scores were increased compared to baseline in both the CON and OCI joints 14 days following initial arthroscopy. Although synovial fluid analyses were not performed, we assume that the increases in joint effusion scores in the CON joints were related to acute synovitis secondary to arthroscopy as no other procedures were performed and effusion scores returned to baseline by day 98. A study using a similar model of osteoarthritis reported an increase in total white blood cells and total protein in the control joints for up to two weeks following arthroscopic surgery which subsequently returned to baseline levels after two weeks.(31) Joint effusion and synovial thickening scores in the OCI joints were increased compared to both CON and OCI joints at baseline exam and to CON joints on day 98. These increases are likely a result of on-going synovitis in the OCI joints, as chronic synovitis may lead to both synovial thickening and concurrent increases in joint fluid production.(65) These results are similar to the previous study(31) that found a continued increase in both white blood cells and total protein for up to 10 weeks in experimental osteoarthritis joints. In another study using the carpal osteochondral injury-exercise model, MRI identified increases in synovial thickening but not joint effusion in the experimental osteoarthritis joints compared to controls at 10 weeks.

The PD-FS and SPGR-FS sequences were used in the current study to evaluate the articular cartilage because these sequences increase the contrast between articular cartilage and subchondral bone. Although, these sequences have demonstrated reasonably accurate detection of articular cartilage defects in cadaver studies(20,22,62), they do not accurately determine the size of the articular defect, particularly with respect to thickness.(20,62) In contrast to the cartilage in the knee of people, equine articular cartilage is much thinner and more difficult to assess using MRI.(30) As cartilage thickness decreases, the more important spatial resolution becomes to be able to delineate cartilage interfaces and minimize volume averaging. Although the sequence parameters used in the current study were improved to provide better cartilage imaging (Table 1) over the previously mentioned studies,(20,62) spatial resolution was still limited. We chose not increase our spatial resolution further, as it would result in lowering the signal-to-noise ratio and result in decreased image quality. Longer acquisition times would be required to maintain similar image quality,(66) which were not chosen in this study to avoid potential complications associated with prolonged anesthesia. Because of this, the authors elected to score the articular cartilage based on changes in cartilage signal only. This differs from how the articular cartilage is scored in the whole-organ assessment in people, where the score is based on changes in both cartilage signal and thickness.(37)

The identification of variable low-grade pathological abnormalities on baseline MRI examinations illustrates the inherent variability that exists in any study population, and highlights the limitations of radiography and the necessity for baseline MRI examinations. Every middle carpal joint in our study population showed some degree of low-grade pathology despite all horses included in the study being clinically sound and free of radiographic signs of carpal disease. The increased sensitivity of MRI to detect osteoarthritis-associated structural changes compared to conventional radiography has been previously demonstrated in the equine metacarpophalangeal joint with natural osteoarthritis(24) and canine stifles with experimental osteoarthritis.(2) Because scores were compared over time, differentiation between pre-existing low-grade pathology and pathology that resulted from the induction of post-traumatic osteoarthritis was possible.

A limitation of this study was the variability of the size and number of the osteochondral fragments that were created despite strictly adhering to the guidelines set forth by Foland et al.(34) The size of the osteochondral fragments created in the current study varied in both axial to abaxial dimensions as well as the proximal to distal dimensions. In addition, small, discrete osteochondral fragments were still present on MRI examination in 3 OCI joints on day 98. Differences in number, size and continued presence of a separate osteochondral fragment may contribute to the progression and severity of development of osteoarthritis in the OCI joints and may explain the variability in the osteoarthritis-associated structural features reported. Another limitation of this study was the use of consensus agreement to score the MRI images. Consensus agreement was used in this study to limit the subjectivity of the EMOSS scoring system and to apply the system accurately and consistently to all MRI evaluations. Although the number of times the three examiners disagreed was not recorded, it was not frequent. When a difference in score was encountered, the images were reviewed and discussed carefully until a consensus was achieved.

To the authors' knowledge, this was the first study to evaluate the osteoarthritis-associated structural changes that occur over time using a semi-quantitative MRI whole-organ scoring system in an established model of post-traumatic osteoarthritis in the horse. The EMOSS allowed temporal assessment of high-signal bone lesions, cartilage signal abnormalities, low-signal bone lesions, subchondral bone irregularity, marginal osteophytes, joint effusion, synovial thickening, and other soft tissue abnormalities. The ability of MRI to identify early osteoarthritis-associated structural changes, such as high-signal bone lesions, represents an advantage over other imaging modalities and should be further investigated to determine how these changes relate to clinical outcomes. In conclusion, this method of semi-quantitative analysis of osteoarthritis-associated structural changes may provide an effective and non-invasive way to study disease progression and measure the effects of future disease modifying drugs and therapies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Previous Presentations or Abstracts

- Magnetic Resonance Imaging Scoring of an Experimental Model of Osteoarthritis in the Equine Carpus. American College of Veterinary Surgeons Proceedings. San Diego, CA. October 2014.
- Magnetic Resonance Imaging Scoring of an Experimental Model of Osteoarthritis in the Equine Carpus. Osteoarthritis Research Society International Proceedings. Paris, France. April 2014.
- Magnetic Resonance Imaging Scoring of an Experimental Model of Osteoarthritis in the Equine Carpus. World Veterinary Orthopedic Conference. Breckenridge, Colorado. March 2014.

Figure 1.

Diagram of the 9 subregions that were evaluated using EMOSS. RC-2: second facet of the radial carpal bone; RC-3: third facet of the radial carpal bone; IC-3: third facet of the intermediate carpal bone; IC-4: fourth facet of the intermediate carpal bone; UC: ulnar carpal bone; 2C: second carpal bone; 3C-R: radial facet of the third carpal bone; 3C-I: intermediate facet of the third carpal bone; 4C: fourth carpal bone.

Figure 2.

Sagittal PD-FS (A-C) and PD (D-F) MRI images of an OCI joint at day 0 (A,D), 14 (B,E), and 98 (C,F) showing the progression of signal changes at the osteochondral fragmentation site in third facet of the radial carpal bone. An osteochondral fragment is present on day 14 that is delineated from the parent bone by a linear pattern of marked increased signal intensity within the fracture line in the PD-FS image (B) and an intermediate to decreased signal intensity on the PD image (E). There is marked increased signal intensity (grade 3 high-signal bone lesion) adjacent to the fracture line in the RC-3 in the PD-FS image (B). A separate osteochondral fragment can no longer be appreciated on day 98 in either image (C, F). The high-signal bone lesions have significantly decreased in size and signal intensity (grade 1 high-signal bone lesion) in the third facet of the radial carpal bone adjacent to and within the healing fracture fragment on day 98 on the PD-FS images (C), however, there is markedly decreased signal intensity (grade 3 low-signal bone lesion) on the PD image (F) on day 98.

Figure 3. Dorsal PD-FS (A-C) and Axial T2-STIR (D-F) MRI images of an OCI joint at day 0 (A,D), 14 (B,E), and 98 (C,F) showing the progression of high-signal bone lesions (A-F) and synovial thickening in the middle carpal joint (D-F). Note the focal, large region of increased signal intensity (grade 2 high-signal bone lesion - size, grade 3 high-signal bone lesion - signal intensity) on day 14 (B), with partial resolution at day 98 (C). Increase in synovial thickening is seen in the axial T2-STIR image on day 98 (F) dorsally as an increased amount of low and intermediate signal intensity synovial tissue within high signal intensity joint fluid.

Figure 4.

Sagittal PD-FS MRI images of an OCI joint at day 0 (A) and day 14 (B) showing the increase in joint effusion identified on day 14 (B) where increased volume of hyperintense joint fluid and cranial displacement of the joint capsule is seen within the middle carpal joint.

Figure 5.

Dorsal T2-weighted MRI images of an OCI joint at day 0 (A) and 98 (B) demonstrating the progression of low-signal bone lesions (a) and marginal osteophyte formation (arrow) in the third facet of the radial carpal bone. A large angular osteophyte (grade 3 marginal osteophyte) is present in the distomedial aspect of the third facet of the radial carpal bone with an adjacent area of low signal intensity (grade 3 low-signal bone lesion) (B).

Figure 6.

Dorsal SPGR-FS MRI images of an OCI joint demonstrating the progression of subchondral bone irregularity and cartilage signal abnormality on the third facet of the radial carpal bone on day 0 (A), 14 (B), 98 (C). On days 0 and 14, no subchondral bone irregularity or cartilage signal abnormalities are seen, however, the osteochondral fragment is evident on day 14 (B) by a linear intermediate signal intensity separating it from the parent bone. There is also increased signal intensity within the third facet of the radial carpal bone within and surrounding the fracture fragment. On day 98, a separate osteochondral fragment is no longer evident; however, there is a focal area of increased signal within a defect in the subchondral bone that is continuous with the joint fluid. This is an example of grade 3 subchondral bone irregularity and grade 2 cartilage signal abnormality.

Magnetic Resonance Imaging Parameters

Table 1

SEQUENCE	Acquisition type	SLICE THICKNESS/ INTERSLICE GAP(mm)	TE (msec)	TR (msec)	FA (deg.)	TI (msec)	NEX	FOV (cm)	MATRIX (Phase × Frequency)	Pixel Size (mm)	Time (mins)
Sagittal PD-FSE	2D	3.0/0.0	48	3827	90	n/a	1	19 × 16	256 × 336	0.74 × 0.47	4:48
Axial PD-FSE	2D	3.5/0.0	18	3500	90	n/a	1	17 × 17	288 × 336	0.59 × 0.51	4:19
Dorsal T2-FSE	2D	3.0/0.3	90	4600	90	n/a	2	16 × 19	256 × 320	0.63 × 0.59	3:37
Axial STIR- FSE	2D	3.5/0.0	60	8739	90	130	1	17 × 17	256 × 320	0.66 × 0.53	4:14
Sagittal PD-FS-FSE	2D	3.0/0.0	48	5142	90	n/a	1	19 × 16	256 × 320	0.74 × 0.50	4:23
Dorsal PD-FS-FSE	2D	3.0/0.3	48	4500	90	n/a	1	16 × 19	288 × 320	0.56 × 0.59	4:17
Dorsal SPGR-FS-GE	3D	2.0/0	7	42	20	n/a	1	16 × 19	280 × 288	0.57 × 0.66	9:32

TE, echo time; TR, repetition time; FA, flip angle; TI, inversion time; NEX, number of excitations; FOV, field of view; PD, proton density; FSE, fast spin echo; STIR, short tau inversion recovery; FS, fat saturation; SPGR, T2*-weighted spoiled gradient recalled echo; GE, gradient echo

Table 2

Median Scores (Min, Max) For Pathological Changes Observed Within 10 CON And 10 OCI Joints On Days 0, 14, And 98.

	Control Limbs				Osteochondral Injured Limbs			
	RC-2	RC-3	2C	3C-R	RC-2	RC-3	2C	3C-R
Cartilage Signal Abnormality								
Day 0	0 (0,0)	0 (0,1)	0 (0,0)	0 (0,2)	0 (0,0)	0 (0,0) ^A	0 (0,0)	0 (0,0) ^A
Day 14	0 (0,0)	0 (0,1)	0 (0,0)	0 (0,2)	0 (0,1)	0 (0,2) ^A	0 (0,0)	0 (0,0) ^A
Day 98	0 (0,0)	0 (0,1)	0 (0,0)	0 (0,1)	0 (0,2)	2 (0,2) ^B	0 (0,0)	1 (0,2) ^B
HSBL-Intensity								
Day 0	0 (0,1)	0 (0,0)	0 (0,1)	0 (0,1)	0 (0,1) ^A	0 (0,0) ^A	0 (0,1)	0 (0,0)
Day 14	0 (0,1)	0 (0,1)	0 (0,1)	0 (0,1)	2 (0,3) ^B	2.5 (1,3) ^B	0 (0,1)	0 (0,1)
Day 98	0 (0,0)	0 (0,1)	0 (0,0)	0 (0,1)	0 (0,1) ^A	1 (0,2) ^C	0 (0,0)	0 (0,1)
HSBL-Size								
Day 0	0 (0,2)	0 (0,0)	0 (0,3)	0 (0,1)	0 (0,2) ^A	0 (0,0) ^A	0 (0,1)	0 (0,0)
Day 14	0 (0,2)	0 (0,1)	0 (0,3)	0 (0,1)	1 (0,3) ^B	2 (1,3) ^B	0 (0,1)	0 (0,1)
Day 98	0 (0,1)	0 (0,1)	0 (0,0)	0 (0,1)	0 (0,1) ^A	1 (0,1) ^C	0 (0,0)	0 (0,1)
Subchondral Bone Irregularity								
Day 0	0 (0,1)	0.5 (0,1)	0 (0,1)	0 (0,2)	0 (0,1)	0 (0,1) ^A	0 (0,0)	0 (0,1)
Day 14	0 (0,1)	0 (0,1)	0 (0,1)	0 (0,2)	0 (0,1)	0 (0,2) ^A	0 (0,1)	0 (0,1)
Day 98	0 (0,2)	0 (0,1)	0 (0,0)	1 (0,1)	0 (0,2)	2.5 (1,4) ^B	0 (0,0)	1 (0,1)
LSBL								
Day 0	1 (0,2)	1 (0,2)	0 (0,3)	2 (0,3)	1 (0,2)	1 (0,2)	0 (0,1)	1 (0,2)
Day 14	1 (0,2)	1 (1,2)	1 (0,2)	2 (1,2)	1 (0,1)	1 (0,3)	0.5 (0,2)	1 (0,2)
Day 98	1 (0,2)	1 (0,2)	1 (0,2)	1 (0,3)	1 (0,2)	2 (1,3)	0 (0,1)	1.5 (0,2)
Marginal Osteophyte								

	Control Limbs				Osteochondral Injured Limbs			
	RC-2	RC-3	2C	3C-R	RC-2	RC-3	2C	3C-R
Day 0	1 (0,3)	1 (0,3)	0 (0,1)	1 (0,3)	1 (0,1) ^A	1 (0,3) ^{A,B}	0 (0,0)	1 (0,2)
Day 14	1 (0,2)	1 (0,2)	0 (0,1)	0 (0,2)	1 (0,2) ^B	0 (0,2) ^A	0 (0,1)	0 (0,2)
Day 98	1 (0,3)	1.5 (1,3)	0 (0,1)	1 (0,2)	1.5 (1,3) ^B	2 (1,3) ^B	0.5 (0,1)	0.5 (0,2)

RC-2 = second facet of the radial carpal bone; RC-3 = third facet of the radial carpal bone; IC-3=third facet of the intermediate carpal bone; IC-4=fourth facet of the intermediate carpal bone; UC=ulnar carpal bone; 2C=second carpal bone; 3C-R=radial facet of third carpal bone; 3C-I=intermediate facet of third carpal bone; 4C=fourth carpal bone; HSBL = High Signal Bone Lesion; LSBL = Low Signal Bone Lesion. Data are reported as median (min, max).

^AWithin each column, groups with different superscripts are significantly different (p = 0.0167).
^BWithin each column, groups with different superscripts are significantly different (p = 0.0167).
^CWithin each column, groups with different superscripts are significantly different (p = 0.0167).