Osteoarthritis and Cartilage (2008) **16,** 1519–1525

doi:10.1016/j.joca.2008.04.015

Osteoarthritis and Cartilage

International Cartilage Repair Society

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Effects of exercise vs experimental osteoarthritis on imaging outcomes

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Summary

Objective: To identify changes in imaging outcomes in a controlled model of osteoarthritis (OA) vs exercise.

Method: Sixteen 2-year-old horses were randomly assigned to an exercise control ($n=8$) or an exercise OA ($n=8$) group. All horses had middle carpal joints arthroscopically explored and an osteochondral fragment was induced in one middle carpal joint of the OA group. All horses were treadmill exercised for the duration of the study (91 days). Clinical, radiographic, nuclear scintigraphic, computed tomographic and magnetic resonance imaging (MRI) examinations were performed and outcomes of these were compared between groups. Imaging results were correlated to clinical, biomarker and gross pathologic results.

Results: The OA group had significant increases in clinical outcomes and most imaging parameters. Specifically, the OA group showed significant increases in radiographic lysis and nuclear scintigraphic uptake. There was very little change in subchondral bone density, but a significant change in subchondral bone edema. Radiographic lysis, radial carpal bone edema and nuclear scintigraphy were strongly correlated with clinical changes and radial carpal bone edema was strongly correlated with changes in Type I and Type II collagen found in the synovial fluid.

Conclusions: OA induced significant changes in imaging parameters beyond the adaptation seen with exercise. Bone edema detected with MRI was closely correlated with collagen biomarkers detected in the synovial fluid.

Key words: Exercise, Experimental osteoarthritis, Imaging, Outcomes.

Introduction

Joint disease, specifically osteoarthritis (OA) due to repetitive trauma, is one of the most common causes of lameness in athletic horses, similar to athletes of any species[1]. This repetitive trauma usually starts in the osteochondral complex and follows cellular processes that are somewhat similar to normal adaptation to exercise[1–4]. Therefore, diagnostic methods that can be used to identify early pathologic changes are needed in order to improve diagnosis, discern adaptive from early pathologic change, and consequently improve monitoring and therapy of joint disease in the athlete.

Diagnostic imaging is the primary method used to characterize diseased joints and help in rendering a prognosis for treatment. However, in most instances gross pathologic changes, such as joint space narrowing, need to be present prior to seeing a change in imaging outcomes[5,6]. Although there has been shown to be modest correlation between radiographic signs and clinical signs of disease at best, imaging such as radiography is neither sensitive nor specific to the earliest changes of OA[5,7,8]. Changes in bone density, such as subchondral bone lysis and sclerosis, are commonly associated with joint disease in several species[1,6,8,9]. However, bone sclerosis is also seen in athletes such as racehorses, racing greyhounds and humans[1,8,10,11]. Computed tomography (CT) also displays some of the shortcomings in early diagnosis that radiography does, that is, it relies on physical abnormalities in order to characterize joint disease[12,13]. Nuclear scintigraphy can be useful, but it too suffers from the fact that there can be increased uptake in exercised animals that have no pain or physical defects in the joints[14–16]. Although magnetic resonance imaging (MRI) also relies on physical changes in joint tissues, it improves early diagnosis since changes in fluid distribution can be seen, and in some instances have been correlated with pathologic characteristics[17,18].

As diagnostic imaging techniques become more advanced, it sometimes becomes difficult to distinguish changes in joint tissues due to adaptation vs those that are truly pathologic[14]. Therefore, imaging techniques that can distinguish exercise related changes in joint tissues from pathologic change are needed in order to improve early diagnosis of joint disease, especially in athletes that undergo highly repetitive, impulsive loading of their limbs. This is particularly important in the human athlete,

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Received 7 February 2008; revision accepted 19 April 2008.

especially as diagnostic imaging techniques such as MRI expands in resolution and physiological imaging.

The purpose of this study was to identify changes in imaging outcomes in a controlled model of OA vs exercise in order to identify techniques that can help to distinguish changes in joints due to adaptation from those due to disease. This information can be translated to human medicine as experimental evidence for discriminating changes due to exercise from those due to OA.

Materials and methods

EXPERIMENTAL DESIGN

Following approval from the Colorado State University Animal Care and Use Committee, 16, 2-year-old horses free of lameness and radiographic changes of joint disease were used in the study. The horses were randomly assigned to either an exercise control ($n = 8$) or exercise OA ($n = 8$) group. Prior to induction of disease, all horses began treadmill exercise 5 days/week beginning on day 0. For each exercise day, the horses underwent trotting (16–19 km/h) for 2 min, galloping (approximately 32 km/h) for 2 min, followed by trotting (16–19 km/h) for two additional minutes to simulate the strenuous exercise of race training. On day 21, horses in the exercise control group had both middle carpal joints arthroscopically examined under general anesthesia. Horses in the exercise OA group had both middle carpal joints explored arthroscopically and OA induced in one middle carpal joint by creating an osteochondral fragment (OCF) on the distal aspect of the radial carpal bone[19]. The contralateral joint in each horse was sham operated. This created three groups of joints: both joints in exercise control horses were designated as EXC, the OA affected joint in the exercise OA horses was designated as OAF, and the sham operated joint in the OA affected horses was designated as OAC. All horses were housed in a stall between days 21 and 35, and beginning on day 35 all horses resumed exercise on a high speed treadmill using the above protocol until the end of the study on day 91.

CLINICAL ASSESSMENT

For each horse clinical examinations of both forelimbs were performed on days 0 and 91 by an experienced, blinded examiner. Lameness was graded on a scale of 0–5[19,20]. Response to flexion of the carpal joints and severity of middle carpal joint effusion were each graded on a scale of 0–4[19].

IMAGING ASSESSMENT

Radiographs

For each horse, a complete series of radiographs were obtained on days 0 and 91. A board-certified radiologist unaware of treatment groups assessed the radiographs for subchondral bone lysis, bone proliferation at the joint capsule attachment, and osteophyte formation. Each abnormality was graded on a scale of 0–3 for severity[19–22].

Nuclear scintigraphy

Each horse received 0.36 mCi/kg of technetium (Tc99) labeled with hydroxymethylene diphosphonate intravenously on days 0 and 91 for nuclear scintigraphic examination. Images were obtained of each carpus in both the lateral–medial and dorsopalmar directions. Each view was subjectively scored for severity of increased uptake[14]. In addition, the uptake per pixel in regions of interest in the carpus was determined and these were normalized to uptake per pixel in a non-target zone in the distal radius[14].

CT

On day 91, each carpus was individually scanned with a Picker PQ CT (Philips Medical, Barthow, WA, USA) at 140 kVp, with a slice thickness of 1-mm, 180 mm field of view and a 512×512 voxel matrix. Images were exported to a customized image analysis program (OsteoApp, Research Systems Inc., Boulder, CO, USA and Colorado State University, Fort Collins, CO, USA). The radial carpal and opposing third carpal bones were separately analyzed, and the volume of sclerotic bone in both the subchondral and trabecular bone areas (mm^3) of each bone were quantified by a board-certified radiologist (RDP). Correlation between CT derived density and bone volume has been proven to be good[13].

MRI

On day 91, each carpus was individually scanned in an MRI unit[a]. Images of 3-mm thickness were obtained in sagittal, dorsal and transverse planes using proton-dense and T1 fat saturation imaging sequences. Alterations in size, shape and signal intensity and distribution of signal intensity were considered when assigning a score from 0 (normal) to 10 (severely abnormal) for synovial effusion, synovial proliferation (irregularity and proliferation of the synovial membrane), joint capsule edema (thickening of the joint capsule with a concurrent signal intensity increase on fat saturated images), joint capsule fibrosis (thickening of the joint capsule with no concurrent signal intensity increase on fat saturated images and low signal intensity on proton density images), sclerosis of the radial carpal and third carpal bones (low signal intensity on proton density images) and radial carpal bone edema (increased signal intensity on fat saturated images).

SYNOVIAL FLUID COLLECTION AND ANALYSIS

Synovial fluid from each middle carpal joint was collected once weekly from each horse for routine synovial fluid analysis (total protein concentration, cytologic evaluation, and total WBC count) and biomarker analysis. Seven biomarker protein assays were performed on synovial fluid samples collected throughout the study and the results of this study have been previously submitted[b]. Briefly, markers included measurement of epitope CS846 (CS846) as a marker of aggrecan synthesis, epitope CPII (CPII) as a measure of Type II collagen synthesis, dimethylmethylene blue (DMMB) as a marker of cartilage matrix degradation, epitope Col CEQ (ColCEQ) as a marker of Type II collagen degradation, osteocalcin as a marker of bone formation, C-terminal of bone type I collage (CTXI) as a measure of Type I collagen, Col II – 3/4 C-Short for Types I and II collagen degradation and prostaglandin E2 (PGE2) as a measure of inflammation. The results are reported separately, but the correlation of results at day 91 to imaging parameters is reported here[b].

GROSS OBSERVATION OF JOINTS

At the end of the study (day 91) all horses were euthanized with an overdose of sodium pentobarbital (88 mg/kg) given intravenously. A necropsy examination was performed on both middle carpal joints and examined for degree and location of articular cartilage fibrillation and erosion and synovial membrane hemorrhage, the results of which have been reported[b]. Tissues were submitted for histologic and glycosaminoglycan (GAG) metabolism, which were reported elsewhere[b].

STATISTICAL ANALYSIS

The statistical analysis of limb related outcome parameters was performed. Specifically EXC, OAF, and OAC groups were evaluated using a split-plot design to evaluate dependent variables. The three groups were analyzed separately since an analysis of left vs right limbs in the OAC group using an analysis of variance (ANOVA) showed no significant differences[c]. A split-plot with repeated measures design was used as the statistical model to evaluate dependent variables over time (radiographs and nuclear scintigraphy). Outcome variables recorded at a single time point were subjected to a general linear model procedure ANOVA. Independent variables were analyzed for both the main and interaction effects on dependent variables. Proc Mixed was used to perform the general linear mixed model ANOVA for statistical comparisons. Independent variables in this model were day of sample collection and exercise and EXC, OAF or OAC. The random effect variable was subject within exercise/exercise OA, and in all analyses $P < 0.05$ was considered significant and reported. When there was a significant interaction effect the least square means test was used to make individual comparisons.

A Pearson correlation coefficient analysis was used to study the relationship between various dependent variables. Only those parameters that displayed either a moderate degree of correlation with correlation coefficients between 0.60 and 0.70 or a strong correlation with correlation coefficient values above 0.70 were reported.

[a]GE Horizon LX, 1.5 Tesla MRI Scanner.

[b]D. D. Frisbie, D.V.M., Ph.D.; F. Al-Sobayil, B.VSc., Ph.D.; R. C. Billinghurst, D.V.M., Ph.D.; C. E. Kawcak, D.V.M., Ph.D.; C. W. McIlwraith, B.VSc., D.V.M., Ph.D., D.Sc.. Changes in Synovial Fluid and Serum Biomarkers with Exercise and Early Osteoarthritis in Horses. *Osteoarthritis and Cartilage*, submitted.

[c]SAS, version 8e, Cary, NC, USA.

Results

CLINICAL ASSESSMENT

A significant increase in lameness, response to carpal flexion, and synovial effusion were demonstrated in OAF compared to EXC and OAC groups. In particular, this difference was strongest at day 91 between the groups. There was a trend for increased lameness in EXC horses at day 91 compared to day 0 ($P = 0.089$) and a trend toward lameness in EXC being worse than OAC at day 91 ($P = 0.057$). Although response to carpal flexion was worse in the OAF group compared to OAC and EXC at day 91, it was also noted that response to carpal flexion in the OAC group was significantly worse at day 91 compared to day 0. In addition, response to carpal flexion was significantly higher in the EXC group on day 91 compared to day 0. Synovial effusion was significantly higher in OAF than EXC and OAC groups on day 91.

IMAGING ASSESSMENT

Radiographs

Radiographic lysis was significantly higher in the OAF group at day 91 compared to the OAC and EXC groups. Radiographically evident proliferation was worse in the OAF group on day 91 compared to OAC and EXC groups. The same was found with radiographic evidence of osteophytes, that is it was worse in the OAF group at day 91 compared to OAC and EXC groups (Figs. 1 and 2).

Nuclear scintigraphy

The grade of nuclear scintigraphic uptake in the carpi was significantly higher at day 91 compared to day 0 in all three groups. The grade of nuclear scintigraphic uptake in the carpal joints was significantly worse in the OAF group at day 91 compared to the scores for the OAC and EXC groups. There was no significant difference in the uptake per pixel in the non-target areas between any of the groups. However, uptake per pixel in the target area of the carpus was significantly worse in the OAF group on day 91 compared to OAC and EXC. Consequently this resulted in a ratio (target/non-target) being worse in the OAF at day 91 compared to OAC and EXC (Fig. 3).

CT

The volume of sclerotic bone in the trabecular area of the radial carpal bone showed a trend ($P = 0.0552$) for being higher in the OAF compared to OAC and EXC groups. There was no significant difference between groups in volume of sclerotic bone in the subchondral area of the radial carpal bone or in the trabecular area of the third carpal bone. However, the volume of sclerotic bone in the subchondral area in the third carpal bone showed a trend ($P = 0.0757$) to be higher in the OAC group than the OAF group.

MRI

Synovial fluid volume showed a trend ($P = 0.0690$) to be higher in the OAF group than both the OAC and EXC groups. Synovial membrane proliferation was significantly higher in the OAF group compared to the OAC group, and showed a trend to be higher in the OAF group compared to the EXC group ($P = 0.097$). Joint capsule thickening was significantly higher in the OAF group compared to the OAC and EXC groups. Joint capsule edema was significantly higher in the OAF group vs the OAC group. Radial carpal bone edema was significantly higher in the OAF group compared to the OAC and EXC groups. Radial carpal sclerosis was significantly higher in the OAF group than the EXC group ($P = 0.010$), and showed a trend to be higher in the OAF group compared to the OAC group ($P = 0.0572$) (Fig. 4).

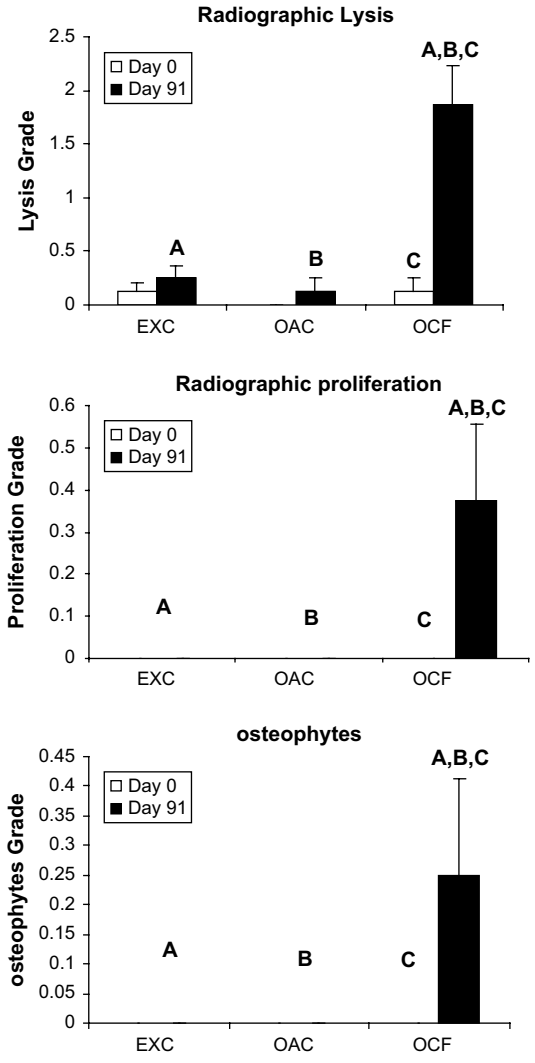

Fig. 1. Graphs showing significant increase in radiographic changes in limbs with OCFs compared to opposing non-fragmented limbs from the same horse (OAC) and exercise control horses (EXC). Similar letters reflect significant differences in data.

Correlations

Table I shows the significant correlations between imaging outcomes and other variables. To summarize, radiographic lysis, radial carpal bone edema as seen on MRI, and nuclear scintigraphy were strongly correlated with clinical changes due to disease. Specifically, radiographic lysis was strongly correlated with severity of lameness, radial carpal bone edema was strongly correlated with flexion response and effusion, and nuclear scintigraphic grade was strongly correlated with effusion.

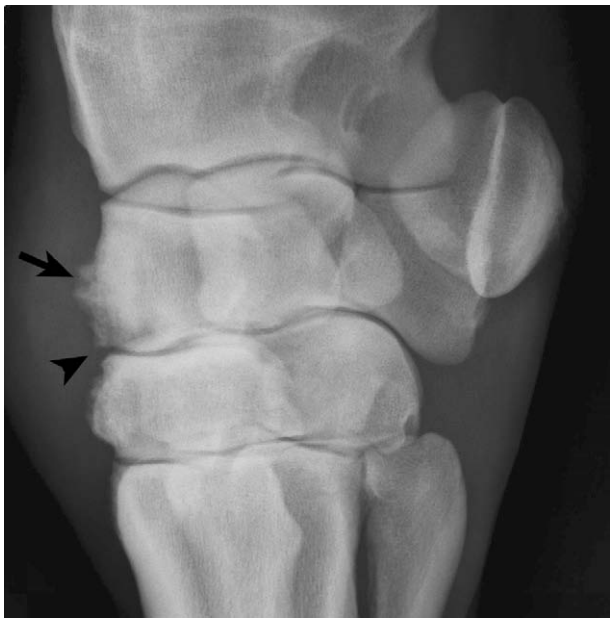

Fig. 2. Radiographic image of the carpus demonstrating grade 3 subchondral bone lysis (arrow head) and proliferation (arrow).

Radiographic lysis was strongly correlated with CPII, where radiographic proliferation was strongly correlated with PGE_2 and WBC. Radial carpal bone edema was strongly correlated with increases in both Col I and II, and nuclear scan grade was strongly correlated with Col II, CEQ, CPII, CS and WBC.

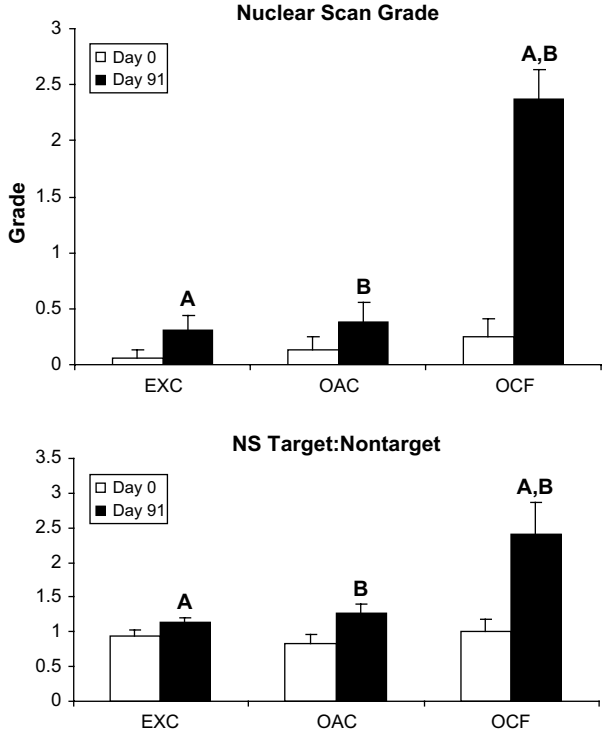

Fig. 3. Graphs showing significant increase in radioisotope uptake, measured subjectively and objectively, in limbs with OCFs compared to opposing non-fragmented limbs from the same horse (OAC) and exercise control horses (EXC). Similar letters reflect significant differences in data.

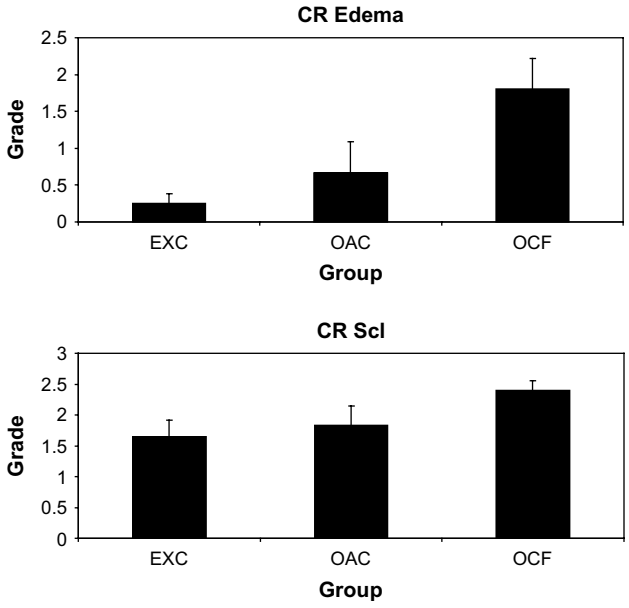

Fig. 4. Graphs showing significant increase in radial carpal bone edema and sclerosis detected on MRI, in limbs with OCFs compared to opposing non-fragmented limbs from the same horse (OAC) and exercise control horses (EXC). Similar letters reflect significant differences in data.

Discussion

The OCF model induced significant increase in lameness scores in the OAF vs the OAC and EXC groups with a significant increase in lameness over time. It was also interesting to note that there was a trend for increasing lameness in the EXC group between days 0 and 91 and vs the OAC group at day 91. However, lameness in the OAC group may have been less detectable than in the EXC group since the OAF limbs were usually the lamest, thereby overriding any less severe lameness in the OAC group. The model proved appropriate for inducing clinically relevant lameness even in the face of the trend of increased lameness due to exercise alone. Since the goal of this study was to identify parameters for characterizing pathologic change in the face of normal adaptation, the results show that this model could in fact be used to distinguish clinical signs in those two processes. This was further evident in the fact that response to carpal flexion and synovial effusion increased in all three groups between days 0 and 91, again demonstrating that a basal effusive response and response to flexion were evident due to exercise alone, but were worst in those joints with osteochondral disease. From a clinical perspective, this study is the first to demonstrate a basal level of gait abnormality that is common to athletic horses and compares this to horses with joint disease.

Radiographic evidence of joint disease was seen in the OAF group at the end of the study compared to the other two groups, specifically at the site of osteochondral fragmentation. There was no radiographic response to exercise. Therefore, although valuable in characterizing structural changes in diseased joints, radiography did not provide the ability to differentiate adaptive from pathologic changes in this model.

Table I
Significant correlation results showing both strong and moderate correlation coefficients of imaging data compared to clinical, pathologic and biomarker data

Imaging parameter	Outcome	R^2	*P*-value
Strong correlations			
Radiographic lysis	Lameness	0.72075	<0.0001
	CPII	0.77546	<0.0001
Radiographic proliferation	PGE_2	0.72767	<0.0001
	WBC	0.83710	<0.0001
MRI – radiocarpal bone (CR) edema	Flexion response	0.70032	<0.0001
	Effusion	0.72087	<0.0001
	Col I	0.72289	<0.0001
	Col II	0.73187	<0.0001
MRI – radiocarpal bone (CR) sclerosis	SF clarity	0.7043	<0.0001
NS grade	Effusion	0.70	<0.0001
	Col II	0.77046	<0.0001
	CEQ	0.70	<0.0001
	CPII	0.80	<0.0001
	CS	0.72862	<0.0001
	WBC	0.73476	<0.0001
NS ratio	Radiographicosteophyte	0.80849	<0.0001
Moderate correlations			
Radiographic lysis	Effusion	0.68382	<0.0001
	MRI – radiocarpal bone (CR) edema	0.62334	0.0019
	GAG	0.67087	<0.0001
	Osteocalcin	0.61581	0.0002
	Col I	0.63867	<0.0001
	PGE_2	0.60156	0.0003
	CS	0.60135	0.0003
	WBC	0.68188	<0.0001
Radiographic proliferation	Lameness	0.65903	<0.0001
	CS	0.60311	0.0003
Radiographic osteophytes	Flexion response	0.6444	<0.0001
MRI – synovial fluid	Col I	0.64514	0.0012
MRI – synovial proliferation	Total protein	0.61569	0.0023
MRI – CR edema	CEQ	0.61057	0.0025
	CPII	0.62341	0.0019
	Total protein	0.63447	0.0015
	WBC	0.68993	0.0004
NS grade	MRI – radiocarpal bone (CR) edema	0.68375	0.0005
	MRI – radiocarpal bone (CR) sclerosis	0.63158	0.0016
	Osteocalcin	0.62938	0.0001
	Col I	0.60123	0.0003
	PGE_2	0.62042	0.0002
	Total protein	0.61011	0.0002
	Neutrophils	0.61983	0.0002
NS ratio	MRI – radiocarpal bone (CR) edema	0.62233	0.002
	Col II	0.63063	0.0001
	CPII	0.63165	0.0001

There was a trend for increase in radioisotope uptake on nuclear scintigraphic images in EXC joints from day 0 to 91 showing there was a mild effect of exercise on basal levels of bone remodeling. There was a significant difference in the OAF group over time compared to the other groups. Therefore, the basal level of exercise in this group may not have been strong enough in clinical relevance to find nuclear scintigraphy to be of value in discerning adaptive from pathologic change using this model. In other words we expected to see significant increase in radioisotope uptake due to exercise alone, and although there was a trend, the differences were not significant. A previous study showed an effect of exercise alone on nuclear scintigraphic grade in the metacarpophalangeal joint of horses, and a lack of change in the carpal joints[14]. This may be due to a relatively larger joint surface area, and hence less pin-point loading to which nuclear scintigraphy may be more sensitive. There is concern that if there was significant effect of exercise on nuclear scan grade there may have been a diminished difference between adaptation and pathologic change. This would need to be investigated in future studies.

Although there were no significant differences in the volume of sclerotic bone in the radial carpal and third carpal

bones between the groups, there was an interesting trend in the pattern of sclerosis. In the radial carpal bone, for instance, there was a trend for increased sclerotic bone volume in the trabecular area of OAF horses compared to others, but no difference in the subchondral area. Since the OCF was created in the radial carpal bone of OAF horses, the trend for increased sclerosis of surrounding trabecular bone may have been a response to increased mechanical stress in areas around the fragment, or a change in joint loading due to pain. In addition, there was a trend for increased sclerotic bone volume in the subchondral area of the third carpal bone of OAC horses compared to OAF horses. This may reflect a decrease in mechanical stress on the bone surface opposite the OCF. This demonstrates the problem with evaluating subchondral bone density in these studies, as a reduction in weight-bearing or possible change in distribution of stress across the joint surface can induce changes in the bone response.

MRI provided useful information on the state of disease in the joint. The OAF joints showed a trend toward higher synovial fluid volume compared to the other two groups, a finding similar to the clinical situation. Synovial membrane proliferation was also higher in the OAF group compared to the OAC group, however; there was no difference between the EXC group and the others. This may be due to a relatively higher degree of synovial membrane proliferation in the EXC compared to OAC, although that conclusion could not be made from this study since no baseline data were obtained. Joint capsule edema and fibrosis were also higher in the OAF groups compared to others, as were edema and sclerosis in the radial carpal bone. These changes appear to adequately characterize the inciting events in the OCF model, as well as the subsequent changes, such as joint capsule edema and fibrosis, which represent a possible secondary change in the joint. MRI appears to best represent the pathologic changes that occur due to osteochondral fragmentation, however, because these were performed at the end of the study and not over time, we cannot characterize the effectiveness in using MRI to discern adaptive from pathologic states. This demonstrates a limitation of this study in that the model is induced acutely. A better model would be one that develops over time to allow for identification of imaging changes.

Radiographic lysis, radial carpal bone edema and nuclear scintigraphic grade correlated well with signs of clinical disease (lameness, response to flexion and synovial effusion). Therefore, these changes may be more indicative of symptoms compared to other findings. More information is needed on the sequential changes in MRI, and the effects of exercise alone on radial carpal bone edema. However, the associations shown in this study are strong and significant, leading to the conclusion that these imaging results may be useful for characterizing clinically painful disease from changes due to adaptation. Felson *et al.* showed an association between enlarging bone marrow lesions and development of knee pain in humans, yet Raynauld *et al.* did not find that association[18,23]. Therefore, the contribution of subchondral bone edema to pain is unknown, and at best in this current study can only be associated with pain.

Radiographic lysis was closely correlated with synovial fluid CPII, and also moderately correlated with synovial fluid WBC and several synovial fluid biomarkers, including GAG, osteocalcin, Col I, PGE_2, and CS. In previous reports[b] CPII was elevated in diseased joints and appeared to correlate well with severity of gross damage[b], the same is true for WBC and the other biomarkers. This appears to make radiographic lysis a strong indicator of the severity of joint disease once it is detected. The concern of using radiographic lysis as an imaging marker of disease is that between 30 and 50% change in bone mineral density is needed in order to observe the change, making it a diagnostic technique that can only characterize joint disease after the pathologic process has started.

Radiographic proliferation correlated closely with PGE_2 and WBC counts in the joints. It appears that bone proliferation may be associated with the degree of inflammatory response in the joint, which has been seen in another report[24].

Radial carpal bone edema detected using MRI correlated well with elevations in Col I and Col II in the synovial fluid. This strong association between bone edema and changes in collagen parameters is interesting in the fact that bone edema may represent an early indication of collagen damage due to trauma. The significance of bone edema in defining the pathologic state of bone and articular cartilage has yet to be studied in the horse, and in fact it is difficult to characterize its presence and significance on histologic specimens, but this study provides evidence that it may have a significant effect on collagen metabolism in the joint. In people, Pelletier *et al.* showed that the presence of bone hypersignal (edema) increased the risk of articular cartilage volume loss, and Raynauld *et al.* showed that subchondral bone edema was present in 90% of people with fast progression of knee OA and 54% of people with slow progression[23,25]. Therefore, it appears that the subchondral bone edema is associated with progression of joint disease and maybe even joint pain, but the exact mechanism of this interaction is unknown. The results of the present study support that edema may either be indicative of disruption to collagen metabolism or may stimulate such an event.

The severity of radioisotope uptake graded subjectively correlated well with synovial fluid WBC, Col II, CEQ, CPII and CS846. This association suggests that subchondral bone metabolism may affect articular cartilage metabolism to some degree. However, it was impossible in this study to determine the threshold of radioisotope uptake at which these articular cartilage markers would become significant or the point at which the change in these markers were considered pathologic.

This experimental study is the first to compare imaging changes due to exercise from OA. These same horses were used in a previously published study[b] which showed increases in specific biomarkers due to exercise and divergence from these concentrations due to OA. Considering humans can show changes in imaging outcomes with exercise such as enlargement of subchondral bone[26], it is important to be able to identify changes due to exercise from those due to disease. This will be especially important as imaging parameters gain higher resolution and better discrimination, for which this model may be effective for objective evaluation.

In summary, it appeared that the OCF model of OA was useful for distinguishing pathologic from adaptive responses in the joint using some imaging parameters. Changes in various imaging techniques provided close correlations to changes in clinical signs of disease; however, the pathologic states of the diseased joints were established early, limiting the usefulness of the model for fully discerning adaptive from pathologic changes. Subchondral bone edema, as detected on MRI, correlated with markers of Types I and II collagen degradation. This area of research deserves more attention, as it may provide insight as to the early detection of joint disease.

Conflict of interest

None of the authors have financial or personal relationships with other people or organizations that could inappropriately influence their work.

Acknowledgment

Funding provided as a charitable gift from the Thoroughbred Corp. The study sponsor did not play a role in study design, collection, analysis and interpretation of data or in writing and submission of this manuscript.

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