Clinical effects of exercise on subchondral bone of carpal and metacarpophalangeal joints in horses

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Objective—To determine effects of treadmill exercise on subchondral bone of carpal and metacarpophalangeal joints of 2-year-old horses.

Animals—12 healthy 2-year-old horses.

Procedure—Horses were randomly assigned to the control (n = 6) or exercised (6) groups. Horses in the exercised group ran on a high-speed treadmill 5 d/wk for 6 months. Horses in the control group were hand walked for the same amount of time. Results of clinical, radiographic, nuclear scintigraphic, and computed tomographic examinations, and serum and synovial concentrations of biochemical markers of bone metabolism were compared between groups.

Results—Exercised horses were significantly lamer at the end of the study than control horses. Radionuclide uptake in the metacarpal condyles, but not in the carpal joints, was greater in exercised horses, compared with control horses. Exercised horses also had a higher subchondral bone density in the metacarpal condyles than control horses, but such differences were not detected in the carpal bones.

Conclusions and Clinical Relevance—None of the diagnostic techniques evaluated was sufficiently sensitive to detect all osteochondral damage. Computed tomography and computed tomographic osteoabsorptiometry were superior to conventional radiography for detecting small osteochondral fragments. Nuclear scintigraphy was a sensitive indicator of subchondral bone change but lacked specificity for describing lesions and discerning normal bone remodeling from damage. Newer techniques such as computed tomography may help clinicians better diagnose early and subtle joint lesions in horses prior to development of gross joint damage. (*Am J Vet Res* 2000;61:1252–1258)

Osteochondral diseases, including osteochondral fragmentation,[1,2,a] fracture,[3-7] and sclerosis,[8,b] are common in horses and can be career-ending and life-threatening conditions. Osteochondral diseases have largely been evaluated in retrospective studies of clinical cases,[1-8,a,b] and the pathogenesis of such diseases has been hypothesized on the basis of postmortem examinations.[9] The carpal and metacarpophalangeal joints are the 2 most common joints affected by osteochondral damage in racehorses. Osteochondral fragmentation can occur anywhere in the joints but is most common at the distal aspect of the radiocarpal bone and the proximodorsal aspect of the first phalanx.[1,2,a] Osteochondral fractures also can occur in any carpal bone (most commonly in the third carpal bone),[4,7] the third metacarpal condyle,[6] and the proximal sesamoid bones.[3,5] Some of these injuries can be catastrophic and life-threatening; affected horses often are euthanatized after reconstructive repairs have failed.[10] Some investigators have speculated that osteochondral damage in horses is the end result of a chronic process.[9] Signs of chronic disease, including formation of granulation tissue and necrotic subchondral bone at sites of disease and sites predisposed to disease, were detected by Pool[9] et al in postmortem specimens collected from racehorses. Stover et al[c] also have reported microdamage at sites predisposed to third metacarpal condylar fracture, at sites surrounding gross fractures, and at nonfractured sites in contralateral limbs.

Because there are few methods that can detect osteochondral disease early during disease development, subchondral bone damage is typically detected after the onset of joint disease. Consequently, damage to the articular surface usually develops prior to detection of the disease. Radiography is the most common diagnostic technique used to evaluate subchondral bone, yet it may be inadequate for detecting subtle damage. Radiography is useful only when damage to the joint is arthroscopically visible, and radiography often underestimates the amount of damage.[2] The purposes of the study reported here were to evaluate the ability of various diagnostic techniques to detect changes in the subchondral bone of treadmill-exercised and hand-walked horses and to identify techniques that may be used to discern pathologic and adaptive responses of subchondral bone.

Materials and Methods

Animals—Twelve 2-year-old Quarter Horse and Quarter Horse crossbred horses that weighed between 445 and 477 kg were included in the study. Horses were determined to be sound at a jog and unresponsive to distal limb and carpal flexion tests prior to the study. Results of radiography, nuclear scintigraphy, and arthroscopy of the carpal and metacarpophalangeal joints also were considered normal for all horses prior to the study. Each horse was randomly assigned to the exercised or control group (n = 6).[6] All pro-

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Experimental protocol—Lameness examinations, radiography, nuclear scintigraphy, and arthroscopy were performed (day 0) before an exercise program was instituted. Serum and synovial fluid also were obtained for determination of concentrations of biochemical markers of bone metabolism. On day 14, horses in the exercised group began an exercise program. Exercise consisted of running on a high-speed treadmill 5 d/wk for 6 months. Initial speeds and times were: 2 minutes at a trot (16 to 19 km/h [10 to12 mph), 3 minutes at a gallop (32 km/h [20 mph]), and 2 minutes at a trot. After 36 days of treadmill exercise, gallop speed was increased to 41.6 km/h (26 mph). Horses in the control group were hand walked for 7 minutes 5 d/wk for 6 months. Blood and synovial fluid were collected on days 44, 74, 104, 134, 164, and 194. Lameness examinations, radiography, and nuclear scintigraphy were performed on day 194. All horses then were euthanatized with an overdose of sodium pentobarbital. Forelimbs of each horse were removed at the proximal aspect of the radius and evaluated by use of computed tomographic osteoabsorptiometry. Carpal and metacarpophalangeal joints were dissected and photographed to record gross lesions.

Lameness examination—Lameness examinations were performed at the beginning (day 0) and end (day 194) of the study. All horses were monitored for lameness during the study, but semi-objective grading of lameness was reported only at the end of the study. We used the lameness grading system as described by the American Association of Equine Practitioners[11] to grade lameness at a jog as well as after carpal and distal limb flexion tests. Briefly, grade 0 indicated soundness at a jog; grade 1 indicated lameness that was difficult to observe and not consistently apparent regardless of circumstances (eg, weight-carrying, circling, incline, hard surface); grade 2 indicated lameness that was difficult to observe at a walk or during trotting in a straight line but consistently apparent under certain circumstances such as lunging; grade 3 indicated lameness that was consistently observable at a trot under all circumstances; grade 4 indicated lameness that was obvious; and grade 5 indicated that there was minimal weight-bearing while the horse was in motion.

Radiography—Radiography was performed at the beginning and end of the study. For evaluation of the carpal joint, lateromedial, flexed lateromedial, dorsolateral-palmaromedial oblique, dorsomedial-palmarolateral oblique, dorsopalmar, and dorsoproximal-dorsodistal (skyline) views were obtained.[12] For evaluation of the metacarpophalangeal joint, lateromedial, flexed lateromedial, dorsolateral-palmaromedial oblique, dorsomedial-palmarolateral oblique, and dorsopalmar views were obtained.[12] Radiographs were subjectively evaluated by a radiologist (RDP), who was unaware of treatment groups, for evidence of osteochondral damage such as osteochondral fragmentation, fracture, and subchondral bone sclerosis within joints. Particular attention was paid to the radial carpal, third carpal, and palmar condylar area of the third metacarpal bone. Subjective results were reported but not statistically analyzed.

Nuclear scintigraphy—Nuclear scintigraphy was performed at the beginning and end of the study. On the day of examination, each horse received technetium Tc 99 m-oxidronate[d] (0.36 mCi/kg of body weight, IV) and was evaluated 3 hours later, using a gamma camera.[13,e] Lateral and dorsal images were acquired of carpal and metacarpophalangeal joints. Each image was evaluated subjectively and quantitatively. For the subjective evaluation, 2 radiologists (RDP, PSS) who were unaware of treatment groups graded the intensity of radiopharmaceutical uptake in the proximal and distal rows of carpal bones, proximal sesamoid bones, third metacarpal condyles, and proximodorsal aspect of the first phalanx in the metacarpophalangeal joint. Grade 0 was defined as no difference in uptake between the area of interest and the surrounding areas. Grade 1 was defined as questionable increase in uptake in the area of interest, compared with the surrounding area. Grade 2 was defined as an obvious increase in uptake in the area of interest. Grade 3 was defined as an intense increase in uptake in the area of interest. The difference in grades at the end of the study from those obtained at the beginning (grade on day 194 – grade on day 0) was determined and compared between groups.

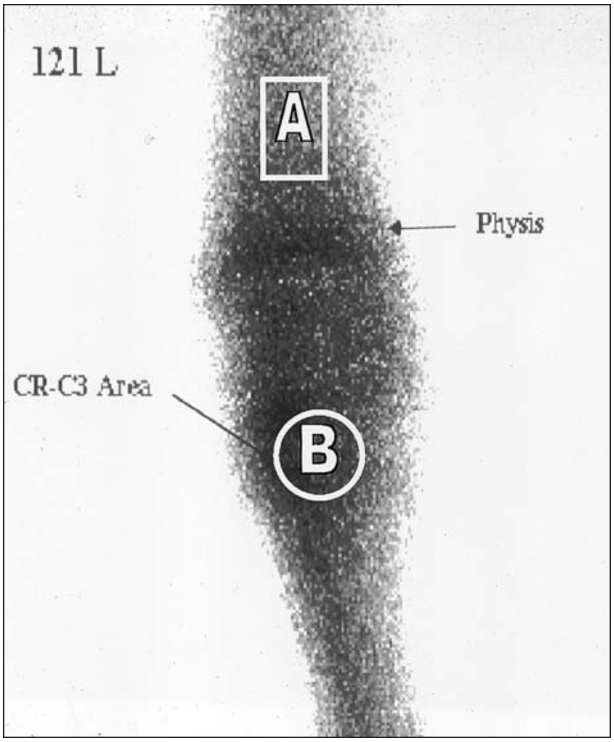

Figure 1—Nuclear scintigraphic image of a carpal joint of a healthy horse. Uptake of radiopharmaceutical per pixel in the target area (B) was divided by uptake per pixel in the nontarget area (A). CR-C3 Area = Area of the radiocarpal and third carpal bones.

For the quantitative evaluation, **regions of interest (ROI)** were drawn on a computer image of the images.[f] Uptake of radiopharmaceutical per pixel was determined in target and nontarget areas, and a ratio of target-to-nontarget uptake was calculated. Calculation of ratios allowed us to compare radioisotope uptake among horses without having to account for between-horse variation, as it is our opinion that there is considerable between-horse variation in intensity of whole-body uptake of radiopharmaceuticals.

For the carpal joint, the area of the radiocarpal and third carpal bones was identified as a target area and outlined on lateral and dorsal images. The distal aspect of the radius, approximately 2 cm proximal to the distal physis, served as the nontarget area (**Fig 1**). The uptake per pixel in the target area then was divided by the uptake per pixel in the nontarget area to normalize results to the overall uptake of the limb and horse.[14] The same approach was used for the metacarpophalangeal joint. The target areas were the proximal sesamoid bones and the distal third metacarpal condyles. Dorsal and lateral images were evaluated for uptake of radiopharmaceutical in the third metacarpal condyles, but only

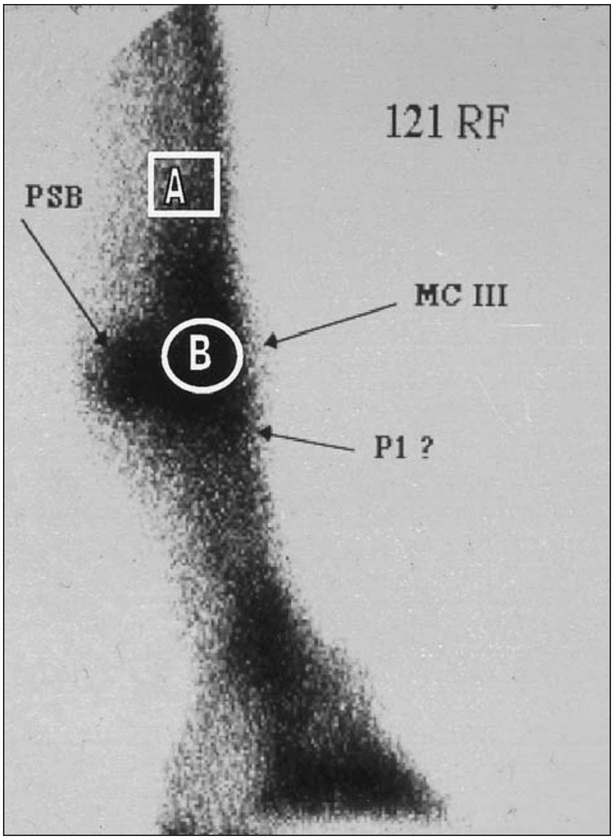

Figure 2—Nuclear scintigraphic view of a metacarpophalangeal joint of a healthy horse. Uptake of radiopharmaceutical per pixel in the target area (B) was divided by uptake per pixel in the nontarget area (A). PSB = Proximal sesamoid bone. MC III = Third metacarpal condyle. P1? = Presumed proximal phalanx.

the lateral images were evaluated for the proximal sesamoid bones. The nontarget area was the distal aspect of the third metacarpal bone, approximately 3 cm proximal to the proximal aspect of the proximal sesamoid bones (**Fig 2**). The difference in radiopharmaceutical uptake for each target area at the end of the study from the value obtained at the beginning (value on day 194 – value on day 0) was determined and compared between groups.

Arthroscopy—Arthroscopy of the carpal and metacarpophalangeal joints was performed only at the beginning of the study to ensure that visible abnormalities were not evident. To be included in the study, horses had to be free of visible lesions.

Prior to induction of anesthesia for arthroscopy, blood was withdrawn from the jugular vein for measurement of serum concentrations of markers of bone metabolism. Each horse was anesthetized, and each intercarpal and metacarpophalangeal joint was aseptically prepared for surgery. Synovial fluid was aspirated from each joint for biochemical analysis, and sterile saline (0.9% NaCl) solution was infused into each joint to cause distention. The intercarpal and metacarpophalangeal joints were arthroscopically explored as described.[15] Forelimbs were bandaged after surgery, and bandages were changed every 3 days for 14 days.

Computed tomographic osteoabsorptiometry—After horses were euthanatized on day 194, the carpal and metacarpophalangeal joints of each forelimb were evaluated by use of **computed tomography (CT)**. Each limb was placed hoof first into a CT scanner[g] and scanned at 2-mm-thick sections. The images were subjectively evaluated by an investigator (CEK) for evidence of osteochondral damage and subchondral bone sclerosis.

Images also were converted into 3 dimensions for computed tomographic osteoabsorptiometry.[16,17] Images from CT were imported into a software package[h] for 3-dimensional analysis. The radiocarpal and third carpal bones and distal third metacarpal condyle were considered ROI and outlined on each 2-mm-thick CT section. These ROI were configured into a 3-dimensional surface map of each bone. The relative density distribution, as represented by **Hounsfield units (HU)**, was determined on the distal radial carpal bone surface, proximal third carpal bone surface, and distal third metacarpal condyle surface. Three density ranges were represented by 3 colors, and the percentage of bone area represented by each color (each density range) was determined and compared between groups. White (low-density bone) represented a range from 800 to 1,199 HU, gray (medium-density bone) represented a range from 1,200 to 1,299 HU, and black (high-density bone) represented a range from 1,300 to 3,000 HU.

Determination of gross damage—After CT, the carpal and metacarpophalangeal joints were dissected and photographed to record gross lesions. Lesions such as wear lines, articular cartilage erosions, osteochondral fragments, and palmar metacarpal arthroses were graded from mild to severe. Scores of 0 (normal) to 3 (severe) were used for grading each type of lesion (**Appendix**). Gross lesions were graded for severity on each articular surface, and the total grade for each type of lesion and cumulative grade for all lesions were determined for each joint.

Measurement of serum and synovial fluid concentrations of biochemical markers—Blood and synovial fluid were centrifuged at 1,000 × *g* for 30 minutes, and sera or supernatants were frozen at -20 C and saved for subsequent analyses. Serum concentrations of **bone-specific alkaline phosphatase (BSAP)** and **C-terminus type-I procollagen (PICP)** were measured by use of ELISA kits.[i,j] Synovial fluid concentrations of **pyrodinoline (PYR)** and **deoxypyrodinoline (dPYR)** crosslinks also were measured by use of ELISA kits.[k,l] The **ratio of concentration of PYR to dPYR crosslinks (PYR:dPYR)** was calculated as a measure of articular cartilage damage.[18]

Statistical analyses—Because a split-plot design was used in which an individual horse's limb was placed within each treatment, an ANOVA was used to determine differences attributable to treatment and limb, using a statistical package.[m] Least-squares means were calculated to determine results that were significantly different between treatment groups. A repeated-measures design was used to evaluate biochemical marker data over time. Significance was determined at $P < 0.05$.

Results

None of the horses included in the study had abnormalities detected during lameness examinations, radiography, nuclear scintigraphy, or arthroscopy performed at the beginning of the study (day 0). One horse in the control group injured the suspensory ligament of its left forelimb on day 21, but results from this horse were included in the study because of financial considerations.

Lameness examinations—All exercised horses became lame during the study (**Table 1**). Most (4/6 horses) became lame approximately 3 months after beginning exercise. At the end of the study, there was not a significant ($P = 0.067$) difference in lameness

Table 1—Mean (± SEM) lameness scores before (lameness) and after carpal and distal limb flexion tests determined for 6 horses that were hand walked and 6 horses that were exercised on a treadmill 5 d/wk for 6 months

	Group	
Variable	**Hand walked**	**Treadmill**
Lameness	0.25 ± 0.25	1.17 ± 0.37
Carpal flexion	0.25 ± 0.18^a	2.38 ± 0.126^b
Digital flexion	0.29 ± 0.29^a	2.67 ± 0.18^b

[a,b]Within a row, values with different superscripts are significantly ($P < 0.05$) different.

Table 2—Mean (± SEM) differences* in radioisotope uptake determined for 6 horses that were hand walked and 6 horses that were exercised on a treadmill 5 d/wk for 6 months

	Group	
Variable	**Hand walked**	**Treadmill**
Subjective		
PSB	-0.46 ± 0.16^a	0.58 ± 0.30^b
MC3 condyles	-0.15 ± 0.11^a	1.38 ± 0.23^b
Proximal phalanx	-0.25 ± 0.17	0.25 ± 0.19
Carpus (proximal row)	0.00 ± 0.00	0.08 ± 0.06
Carpus (distal row)	-0.04 ± 0.19	0.17 ± 0.14
Quantitative		
PSB		
PSB/Can	-0.18 ± 0.18^a	0.53 ± 0.20^b
Third metacarpal condyle		
MC3/Can-Lat	-0.10 ± 0.19^a	0.95 ± 0.26^b
MC3/Can-Dor	-0.19 ± 0.21	0.42 ± 0.15
Carpus		
Carp/Rad-Lat	0.27 ± 0.13	-0.07 ± 0.14
Carp/Rad-Dor	0.14 ± 0.12	-0.14 ± 0.11

*Determined by subtracting day-0 value from day-194 value.

PSB = Proximal sesamoid bone. P1 = Proximal phalanx. MC3 = Third metacarpal condyles. Lat = Lateral. Dor = Dorsal. Can = Third metacarpal bone. Carp = Carpus. Rad = Radius.

See Table 1 for key.

scores between groups. However, when the lameness score for the injured control horse was removed from analysis, mean lameness score for the exercised group was significantly ($P < 0.001$) greater than for the control group. Horses in the exercised group were significantly ($P < 0.001$) lamer after distal flexion and carpal flexion tests than were control horses. All exercised horses had synovial effusion in the intercarpal and metacarpophalangeal joints beginning approximately 3 months after exercise was initiated. Effusions were mild to moderate in severity.

Radiography—Few abnormalities were evident on radiographs of the carpal and metacarpophalangeal joints. An osteochondral fragment was detected in the distal aspect of the radiocarpal bone of 1 exercised horse at the end of the study, but other lesions were not evident.

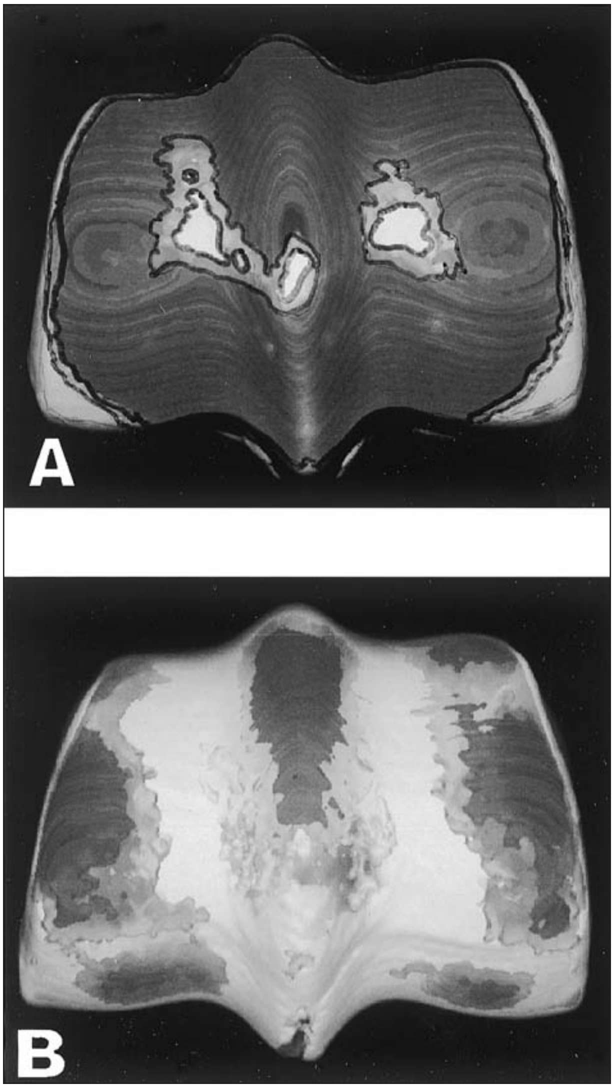

Figure 3—Computed tomographic osteoabsorptiometry images of the surface of the third metacarpal condyles of a horse exercised on a treadmill (A) and a hand-walked horse (B). Notice the increased density of subchondral bone (black areas) in the treadmill-exercised horse, compared with the hand-walked horse.

Nuclear scintigraphy—When nuclear scintigraphic images were evaluated subjectively, the mean difference between values for day 194 and day 0 for the proximal sesamoid bones and third metacarpal condyles was significantly ($P = 0.017$ and $P < 0.001$, respectively) greater in the exercised group, compared with the control group (**Table 2**). Significant differences were not detected in the carpus and first phalanx between groups.

When evaluated quantitatively, we detected significantly ($P = 0.035$) more uptake of radiopharmaceutical in the proximal sesamoid bones from exercised horses than in those from control horses (Table 2). Significantly ($P = 0.025$) more uptake also was detected in the distal third metacarpal condyle from exercised horses. However, differences between groups differed significantly only when lateral views were evaluated; evaluation of dorsal images did not reveal significant differences between groups. Regardless of view evaluated, significant differences were not detected in the carpus between treatment groups.

Computed tomographic osteoabsorptiometry—The exercised group had a significantly ($P = 0.008$) higher mean percentage of high-density bone and a sig-

Table 3—Mean (± SEM) results* of computed tomographic osteoabsorptiometry determined for 6 horses that were hand walked and 6 horses that were exercised on a treadmill 5 d/wk for 6 months

	Group	
Variable	Hand walked	Treadmill
Third metacarpal condyle		
White (800-1,199 HU)	0.34 ± 0.040[a]	0.12 ± 0.023[b]
Gray (1,200-1,299 HU)	0.30 ± 0.019	0.29 ± 0.024
Black (1,300-3,000 HU)	0.35 ± 0.039[a]	0.59 ± 0.035[b]
Third carpal bone		
White (800-1,199 HU)	0.22 ± 0.04	0.16 ± 0.01
Gray (1,200-1,299 HU)	0.21 ± 0.03	0.19 ± 0.02
Black (1,300-3,000 HU)	0.57 ± 0.07	0.65 ± 0.02
Radial carpal bone		
White (800-1,199 HU)	0.21 ± 0.05	0.15 ± 0.02
Gray (1,200-1,299 HU)	0.31 ± 0.027	0.29 ± 0.034
Black (1,300-3,000 HU)	0.48 ± 0.07	0.57 ± 0.04

*Expressed as the percentage of each range on the bone surface.
HU = Hounsfield units.
See Table 1 for key.

Table 4—Mean (± SEM) grades for gross joint lesions determined during necropsy of 6 horses that were hand walked and 6 horses that were exercised on a treadmill 5 d/wk for 6 month

	Group	
Variable	Hand walked	Treadmill
Metacarpophalangeal joint		
Cumulative*	0.167 ± 0.17[a]	4.25 ± 0.64[b]
Wear lines	0.00 ± 0.00	1.25 ± 0.71
AC erosion	0.167 ± 0.17[a]	2.00 ± 0.325[b]
OC fragment	0.00 ± 0.00[a]	1.00 ± 0.46[b]
Intercarpal joint		
Cumulative	0.00 ± 0.00	1.00 ± 0.53
Wear lines	0.00 ± 0.00	0.00 ± 0.00
AC erosion	0.00 ± 0.00	0.33 ± 0.33
OC fragment	0.00 ± 0.00	0.67 ± 0.47

*Cumulative grade is the summation of grades for all lesions in a given joint.
AC = Articular cartilage. OC = Osteochondral.
See Table 1 for key.

nificantly (P = 0.007) lower percentage of low-density bone on the surface of the third metacarpal bone than horses in the control group (**Fig 3** and **Table 3**). We did not detect significant differences in the percentage of bone area represented by each color in the radiocarpal and third carpal bones between groups.

Gross damage—We did not detect gross lesions in the carpal and metacarpophalangeal joints of control horses, except for a focal erosive lesion in the lateral proximal sesamoid bone of the horse injured on day 21. However, exercised horses had significantly greater grades of articular cartilage erosion and palmar metacarpal arthroses in metacarpophalangeal joints than control horses ($P < 0.001$ and $P = 0.043$, respectively). There were not any significant differences in gross damage grades for the carpal joints between groups. Although articular cartilage wear lines and erosion were rare in the intercarpal joints, osteochondral fragmentation was evident in the distal radial carpal bones of 1 horse in the exercised group. The osteochondral fragment of the right radial carpal bone was approximately 10 mm in width, whereas that of the left radial carpal bone was approximately 4 mm in width. Exercised horses had higher cumulative gross lesion grades in the intercarpal joints than control horses, but these grades did not differ significantly (P = 0.174; **Table 4**). However, exercised horses had significantly (P = 0.001) higher cumulative gross lesion grades in the metacarpophalangeal joints than control horses.

Concentrations of biochemical markers—We did not detect significant differences in serum BSAP or PICP concentrations between groups or over time. We also did not detect differences in synovial fluid concentrations of PYR or dPYR crosslinks or in the PYR:dPYR.

Discussion

Six months of exercising on a treadmill caused lameness in the 2-year-old horses in the study reported here. Distal limb and carpal flexion tests elicited signs of pain in both areas. This corresponds to the clinical condition in young racehorses in which signs of pain in these areas can consistently be elicited. It cannot be determined from our results whether signs of pain were attributable to soft-tissue or bone damage. Use of a soft-tissue phase during nuclear scintigraphy may have helped resolve this issue, but we did not use a soft-tissue phase because of financial constraints. Diagnostic nerve and joint blocks would have provided additional information on the specific site of pain, because distal limb flexion tests are not specific for pain localization.

Some osteochondral lesions were not detected by use of radiography. The 10-mm osteochondral fragment was seen radiographically, but the 4-mm fragment was not, nor was there radiographic evidence of gross articular cartilage damage. This lack of sensitivity has been reported previously; gross damage, as detected during arthroscopy, may be worse than impressions from radiographs.[2] The lack of sensitivity of radiography may be attributable to summation effects from superimposed structures that would hide evidence of osteochondral damage,[19] an inability to detect articular cartilage damage, or the fact that a 30 to 40% loss in mineral density is needed before lesions are radiographically detectable.[20] Therefore, the lack of sensitivity of radiography was expected and documents the lack of objective diagnostic capabilities that face veterinarians. Efforts are needed to discover and perfect diagnostic techniques that will increase the sensitivity of diagnosis of osteochondral disease.

Analysis of results of nuclear scintigraphy indicated that 6 months of exercising on a treadmill led to increased uptake of radiopharmaceutical in the metacarpophalangeal joints, particularly in the third metacarpal condyles and proximal sesamoid bones. This was evident from subjective and semiobjective evaluations. Nuclear scintigraphy is highly sensitive for detection of areas that are potentially diseased, but it lacks specificity for characterizing the disease process because of poor anatomic detail. We did not detect a scintigraphic sign that distinguished joints with gross pathologic changes from those without such changes. However, it appeared subjectively that uptake in the radial carpal area of the exercised horse with the osteochondral fragments was higher than in horses without fragments. Consequently, a normal bone response to exercise and a pathologic response may not be distinguishable by use of nuclear scintigraphy. It is difficult to explain the reason that the third metacarpal condyles and proximal sesamoid bones had increased radiopharmaceutical uptake, whereas the carpal bones did not. In a study by Forwood et al,[21] exercise of rats on a treadmill led to increased bone formation in the femurs but not in the tibias. Although our study evaluated cuboidal bones and not long bones, response of bone tissue was similar in both studies, suggesting that there is a regional difference in the response of bones to exercise. The lack of response in the carpal bones may have been attributable to the type of exercise; exercising on a treadmill may cause less stress to carpal bones than exercising on a racetrack. Additionally, the study may not have been of appropriate duration to induce carpal bone damage.

We did not detect a difference in sensitivity between results of the semiobjective and subjective evaluations of nuclear scintigraphic images. However, quantitative evaluation supplies continuous data that can be used for correlation analysis for comparison with other diagnostic techniques and histologic analyses.

Evaluation of joint surfaces by use of computed tomographic osteoabsorptiometry revealed that 6 months of exercise on a treadmill led to increased mineralization of subchondral bone in the distal third metacarpal condyles. Similar results have been obtained in studies evaluating human elbows in which differences in loading history led to changes in subchondral bone mineralization.[16,17] We did not detect increased mineralization of subchondral bone in the radial carpal and third carpal bone surfaces. It may be that the third metacarpal condyles react sooner to the stress of exercising on a treadmill than the carpal bones; Forwood et al[21] found that tibia and femora of rats respond differently to exercise. Furthermore, the computed tomographic osteoabsorptiometry analysis may not have been sufficiently sensitive to detect differences in the carpal bones between groups. The entire joint surface was imaged, and it is known that the dorsal surface of the radial carpal and third carpal bones are prone to damage. Therefore, use of a more precise area of interest may have revealed differences between groups. Also, the range of HU used in this study is large. Increasing the number of HU ranges also may increase the sensitivity of the technique for evaluation of carpal bones. Incongruent joint surfaces on the third metacarpal condyles were evident on computed tomographic osteoabsorptiometry images from control horses, because the densest bone was toward the periphery of the joint. The periphery of the joint surface will make contact before the center of the joint surface, and the flexibility of the subchondral bone will dissipate force in the joint.[16] However, a more congruent configuration to the joint surface was evident in images obtained from exercised horses. Therefore, exercise may cause a loss of incongruity in the metacarpophalangeal joint that leads to abnormal stress distribution across the joint surface.[16] Additional studies, using more precise measurement techniques and joint models, are needed to validate changes in joint congruence.

Six months of exercise on a treadmill lead to gross damage in carpal and metacarpophalangeal joints. Except for an osteochondral fragment in 1 exercised horse detected by use of radiography or CT and a small osteochondral fragment detected by use of CT, there did not appear to be a diagnostic test that aided in detection of all lesions. It appears that considerable articular cartilage damage can develop without detection by any available diagnostic test. **Magnetic resonance imaging (MRI)** is considered the best diagnostic test for detecting joint damage; however, higher magnet strengths and smaller magnet bores are needed to detect subtle changes in articular cartilage. Other diagnostic techniques such as dual energy x-ray absorptiometry and peripheral quantitative CT are highly sensitive and available for use. However, these 2 techniques only reveal bone mineralization, and results need to be correlated to gross damage. Structural changes in bone, such as osteochondral fragmentation, can be detected by sensitive imaging techniques such as CT, but at this time, highly sensitive MRI or more sensitive biochemical means are needed to detect articular cartilage damage.

We did not detect differences in serum or synovial fluid concentrations of biochemical markers between groups. Several factors may have influenced these results. Although the markers we measured in serum are indicative of bone function, concentrations can increase in response to bone formation and resorption.[22] Therefore, increased bone formation in 1 area (eg, the third metacarpal condyles) may be negated by increased resorption in another (eg, the third metacarpal cortical bone). Increased concentrations of a marker also may be a result of increased production (ie, bone formation) in 1 area and increased release (ie, resorption) in another area. Therefore, it is difficult to determine the relevance of an increase or decrease in serum concentrations of a particular marker.

Measurement of synovial fluid concentrations of PYR and dPYR crosslinks was considered a more specific diagnostic test than measurement of serum concentrations of markers of bone metabolism. Failure to detect significant differences in concentrations of PYR and dPYR crosslinks between or within groups may have been because we used an ELISA validated for use with human synovial fluid. There may be low cross-reactivity between human and equine PYR and dPYR.

If clinicians are to predict the onset of joint disease, they must be able to identify early pathologic changes in the joint. This includes identification of mineralization patterns that may lead to fracture or osteoarthritis, identification of articular cartilage signals by use of MRI that may be indicative of a poor matrix metabolic state, identification of nuclear scintigraphic patterns that may be used to discern adaptational processes from pathologic processes, and identification of loading patterns and muscle force patterns in limbs that may lead to joint disease. Furthermore, identification of reversible versus nonreversible pathologic processes would allow for more accurate prognoses. However, a single diagnostic technique may not be sufficiently sensitive to enable clinicians to identify early changes indicative of serious joint disease. Instead, a battery of tests may be necessary. We believe that additional studies must be performed in which several diagnostic tests are evaluated for early detection of a single disease process. In this way, a combination of tests may be identified that can be used to best diagnose the disease.

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[d] TechneScan HDP, Mallinckrodt Medical, St Louis, Mo.

[e] General Electric Maxi Camera, General Electric, Milwaukee, Wis.

[f] Nuclear Mac, Scientific Imaging, Littleton, Colo.

[g] General Electric Pace-3rd Generation, General Electric, Milwaukee, Wis.

[h] Cemax, Icon Inc, Fremont, Calif.

[i] Alkphase-B, Metra Biosystems, Mountain View, Calif.

[j] Prolagen-C, Metra Biosystems, Mountain View, Calif.

[k] Pyrilinks, Metra Biosystems, Mountain View, Calif.

[l] Pyrilinks-D, Metra Biosystems, Mountain View, Calif.

[m] SAS System, version 6.0, SAS Institute Inc, Cary, NC.

Appendix

Grades for gross lesions in the carpal and metacarpophalangeal joints of horses, detected during necropsy

Lesion	Grade	Description
Wear lines	0	None
	1	1 or 2 Partial-thickness wear lines/joint surface
	2	3 to 5 Partial-thickness or 1 to 2 full-thickness wear lines/joint surface
	3	> 5 Partial-thickness or > 2 full-thickness wear lines/joint surface
Erosions	0	None
	1	Partial-thickness erosion, < 5 mm in diameter
	2	Partial-thickness erosion, > 5mm in diameter
	3	Full-thickness erosion
Fragments	0	None
	1	Osteochondral fragments, < 2 mm in diameter
	2	Osteochondral fragments, 2 to 5 mm in diameter
	3	Osteochondral fragments, > 5 mm in diameter
Palmar arthroses	0	None
	1	Partial-thickness erosion, < 5 mm in diameter
	2	Partial-thickness erosion, purple discoloration, > 5 mm in diameter
	3	Full-thickness erosion, purple discoloration, > 5-mm in diameter

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