Use of zoledronate for treatment of a bone fragility disorder in horses

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**Objective**—To assess clinical outcomes and scintigraphic findings in horses with a bone fragility disorder (BFD) treated with zoledronate (a nitrogen-containing bisphosphonate).

**Design**—Prospective uncontrolled clinical trial.

**Animals**—10 horses with evidence of a BFD.

**Procedures**—Signalment, history, and geographic location of horses’ home environments were recorded. Physical examinations, lameness evaluations, and nuclear scintigraphy were performed. Diagnosis of a BFD was made on the basis of results of clinical and scintigraphic examination. Each horse was treated with zoledronate (0.075 mg/kg [0.034 mg/lb, IV, once]) at the time of diagnosis. Horses were reevaluated 6 months after treatment.

**Results**—Affected horses were from the central and coastal regions of California and had ≥1 clinical sign of the disorder; these included scapular deformation (n = 2), lordosis (1), nonspecific signs of musculoskeletal pain (1), and lameness that could not be localized to a specific anatomic region (9). All horses had multiple sites of increased radiopharmaceutical uptake during initial scintigraphic evaluation of the axial skeleton and bones of 1 or both forelimbs. Six months after treatment, clinical improvement (defined as improvement in the lameness score, resolution of signs of musculoskeletal pain, or both) was detected in 9 of 10 horses; scintigraphic uptake was unchanged (n = 2) or subjectively decreased (8). No adverse effects attributed to zoledronate treatment were detected.

**Conclusions and Clinical Relevance**—Treatment with zoledronate appeared to be useful in improving clinical outcome and scintigraphic findings in horses with a BFD; however, future placebo-controlled studies are necessary to accurately determine efficacy and long-term safety. (J Am Vet Med Assoc 2012;240:1323–1328)

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In recent years, a debilitating, progressive BFD primarily affecting the axial skeleton and proximal aspects of the appendicular skeleton has been identified in horses in California.1–3 Clinical signs reportedly range from generalized stiffness, exercise intolerance, and intermittent lameness early in the course of the disorder to lordosis, lateral bowing of the scapulae, weight loss, severe lameness, and reduced range of motion in the cervical portion of the spine in advanced cases.1–3 Systemic osteopenia and pathological fractures are often detected in chronically affected horses that have severe clinical signs.1–3 This disorder was determined to have a specific regional distribution in the equine population, predominantly detected in the coastal regions of Northern California, with a geographic distribution similar to that of pulmonary silicosis in horses.1–3

Historically, treatment for this BFD has been largely symptomatic, relying on systemic administration of NSAIDs and corticosteroids, exercise restriction, and relocation to a different geographic region.1–3 Treatment has been generally unrewarding, with only transient improvement in clinical signs reported.1–3 In a recent retrospective study1 of 16 horses with this BFD, worsening of the condition was detected in all horses, and 11 of 16 were euthanized ≤7 years after diagnosis despite symptomatic treatment. The etiology of this BFD is not clearly understood, although recent publications have indicated a geographic distribution similar to that of pulmonary silicosis, and the disorder has frequently been diagnosed in horses with concurrent pulmonary silicosis, supporting the hypothesis that the 2 conditions may be linked etiologically.1–4 Pulmonary silicosis in horses has been attributed to the inhalation of the fibrogenic and cytotoxic cristobalite form of silicate, and cristobalite is considered to be a candidate for the etiologic agent directly responsible for this BFD.4 Alternatively, exposure to cristobalite may initiate a sequence of events that eventually results in the condition; a recent study4 of 9 horses with this BFD that underwent necropsy examination identified histopathologic evidence of osteoporosis and abnormal osteoclast-mediated bone resorption.4 Treatment targeting abnormal osteoclast activity

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**Abbreviations**

BFD  Bone fragility disorder
IRU  Increased radiopharmaceutical uptake
could aid in the treatment of horses with this disorder, and in the authors’ experience, there have been anecdotal reports of clinical improvement in affected horses for ≤ 6 months following treatment with tiludronate, a non-nitrogen–containing bisphosphonate.

Bisphosphonates inhibit bone resorption through their intracellular effects on osteoclasts. After uptake by endocytosis, bisphosphonates disrupt the normal function of these cells, decreasing resorption of bone and eventually causing osteoclast apoptosis. Zoledronate is a third-generation, nitrogen-containing bisphosphonate that has a high affinity for hydroxyapatite. Zoledronate is retained in bone tissue until it is taken up by osteoclasts. Within these cells, it inhibits farnesyl pyrophosphate synthase in the intracellular mevalonate pathway, preventing protein prenylation. Interference with this cellular pathway results in osteoclast apoptosis and inhibition of osteoclastic bone resorption.

Zoledronate was shown to decrease the risk of pathological fractures due to osteoporosis in women. In humans with Paget’s disease of bone, characterized by abnormal osteoclast-mediated bone resorption, clinical signs and serum biomarkers of bone resorption were decreased following treatment with zoledronate. Zoledronate has a longer duration of action and increased potency in humans when compared with tiludronate and other non-nitrogen–containing bisphosphonates. Because the proposed mechanism of the BFD in horses of the study reported here involves abnormal osteoclast-mediated bone resorption and because zoledronate was shown to have a role in improving human disorders characterized by pathological bone resorption and osteopenia, we hypothesized that zoledronate treatment would improve clinical outcome and scintigraphic abnormalities in horses with this condition. The objective of the study was to evaluate clinical outcomes and scintigraphic findings in horses with this BFD following treatment with zoledronate.

Materials and Methods

Animals—Horses evaluated at the University of California-Davis William R. Pritchard Veterinary Medical Teaching Hospital from May 1, 2008, to October 31, 2009, were included in the present study if they had a diagnosis of BFD made on the basis of clinical signs and bone-phase nuclear scintigraphic findings consistent with those of the BFD previously identified in horses in California. Horses were excluded if they had previously received a bisphosphonate drug or if they had received any medications (excluding NSAIDs) ≤ 7 days prior to or after zoledronate administration. The study was approved by the University of California-Davis Institutional Animal Care and Use Committee. Written owner consent was obtained for all horses prior to study enrollment.

Signalment and geographic location of the horses’ home environments were recorded. Clinical signs in affected horses included scapular deformation, lordosis, generalized stiffness, chronic lameness, and lameness not localizable with regional anesthesia. At the initial evaluation, a complete physical examination and video-recorded lameness evaluation were performed by 2 authors (SAK and RJWB). All horses were observed at the walk and trot in a straight line and in a circle on hard ground. Lameness was graded according to the American Association of Equine Practitioners lameness grading system (scale from 0 to 5, with 0 representing no detectable lameness and 5 representing non-weight-bearing lameness).

Diagnostic imaging—After aseptic preparation of the skin, a 14-gauge catheter was inserted into the left jugular vein by use of an aseptic technique. Horses received technetium Tc 99m methylene diphosphonate (0.3 mCi/kg [0.14 mCi/lb], IV) 4 hours prior to bone-phase nuclear scintigraphy. At the time of imaging, horses were sedated with detomidine hydrochloride (0.01 to 0.03 mg/kg [0.005 to 0.014 mg/lb], IV) and butorphanol tartrate (0.01 to 0.02 mg/kg [0.005 to 0.009 mg/lb], IV). Horses were positioned squarely with all 4 limbs bearing weight equally during image acquisition. For all horses, lateral images of the cervical vertebrae, forelimbs, ribs, and thoracic spine (cranial to the level of L1) were obtained. One-minute static acquisitions were acquired with a gamma camera, and a dedicated computer system was used to process and interpret the images. Subsequent to image acquisition, the left jugular IV catheter was removed. Multifocal areas of IRU identified in 1 or both scapulae, ribs, cervical or thoracic vertebrae, and sternum were considered supportive of a diagnosis of BFD. Additional sites of IRU identified within the forelimbs were also noted. Adjunctive radiography was performed at the time of diagnosis in some horses. Radiography was performed if an area of marked focal IRU was identified in a forelimb and was suspected to be associated with a pathological fracture that could progress to catastrophic failure. Scintigraphic and radiographic images were assessed by a board-certified radiologist (SMP), and a preliminary diagnosis of BFD was made on the basis of identification of abnormal IRU in the described regions.

Treatment with zoledronate—A 14-gauge catheter was inserted into the right jugular vein in an aseptic manner as described for the administration of technetium Tc 99m methylene diphosphonate. Because acute-phase reactions caused by transient increases in pyrogenic cytokines have been reported after IV administration of zoledronate in humans and because it was considered possible that similar adverse reactions could develop in horses, each horse was premedicated with flunixin meglumine (1.1 mg/kg [0.5 mg/lb], IV) 30 minutes prior to bisphosphonate administration. Zoledronate (0.075 mg/kg [0.034 mg/lb]) was dissolved in 50 mL of a 11.3 mg/mL sodium citrate solution and then further diluted in 500 mL of an isotonic solution consisting of 400 mL of sterile water and 100 mL of mannitol. Immediately following preparation, zoledronate was administered via IV infusion during a 30-minute period. The dose used was extrapolated from the label dose recommended for the treatment of osteoporosis and Paget’s disease in humans. Each horse was observed for adverse reactions during drug administration and for a minimum of 2 hours afterward. Because of the risk of pathological fracture in horses with this disorder, owners were advised to restrict exercise for all horses during the 6 months between treatment and...
follow-up examination. The recommended exercise restriction consisted of confinement to a box stall with a run or small paddock. A diet consisting of 50% alfalfa hay was recommended to increase calcium intake following treatment with zoledronate.

**Follow-up examinations and scintigraphy**—Horses were clinically reevaluated, and scintigraphy as previously described was repeated 6 months after zoledronate administration. Physical examination and lameness evaluation were conducted by 2 authors (SAK and RJWB) as previously described. Following assessment, results of the clinical examination were compared with initial findings. For the purposes of the present study, clinical improvement was defined as improvement in lameness grade or resolution of musculoskeletal pain. Clinical deterioration was defined as worsening of the lameness grade or continued evidence of musculoskeletal pain.

All scintigraphic images for each horse were interpreted by 2 authors (SAK and RJWB) who were blinded to patient identification and to whether the images were obtained before or after zoledronate treatment. A scoring system was not used for comparison, and author evaluations were independent of each other. Scintigraphic findings were considered to be improved if a subjectively determined decrease in radiopharmaceutical uptake was detected in ≥ 1 previously identified site of IRU and were considered stable if no additional sites of IRU were detected on follow-up scintigraphic images. Improvement or stabilization of scintigraphic findings was considered a positive outcome; detection of additional sites of IRU or apparent increases in radiopharmaceutical uptake in previously identified sites were considered a negative outcome.

**Statistical analysis**—Descriptive statistics were used to evaluate the data. Results are reported as mean ± SD and range.

**Results**

Ten horses (6 mares and 4 geldings) met inclusion criteria for the study. Mean age of affected horses was 13.3 ± 6.2 years (range, 5 to 25 years). Breeds included Lipizzaner, Arabian, and Quarter Horse (2 each) and Appaloosa, Thoroughbred, Connemara, and Icelandic Horse (1 each).

**Geographic distribution**—Four of 10 affected horses were from Carmel (Monterey County), and 2 were from Santa Rosa (Sonoma County). The remaining 4 horses were from 4 different locations in California (Napa [Napa County], Anderson [Shasta County], Oakland [Alameda County], and Ojai [Ventura County]). Periods that horses resided in these locations ranged from 2 to 20 years.

**Initial clinical evaluation**—Nine of 10 affected horses had a history of chronic intermittent lameness. Mean duration of lameness in these 9 horses was 2.9 ± 3.6 years (range, 2 months to 10 years), and 8 were lame at the time of initial clinical evaluation. Attempts had been made to localize the lameness with regional anesthesia in 6 horses prior to referral; the remaining 3 horses evaluated for lameness at the veterinary teaching hospital were referred specifically for scintigraphic evaluation. Scintigraphic evaluation was recommended by the referring veterinarians because they were aware of the possibility that these horses might have a BFD. One horse was evaluated for progressively worsening generalized stiffness, lordosis, and scapular deformation of 5 years’ duration in addition to chronic lameness. The final horse had no history of lameness and was evaluated for exercise intolerance and signs of discomfort while the girth was tightened during saddling. This was suspected to be related to pain in the region of the sternum and ribs at the cranioventral aspect of the thorax, although signs of pain were not elicited on palpation of this region. This horse had been previously examined for exercise intolerance and coughing and was treated for pharyngitis 8 months prior to the diagnosis of BFD.

Lameness at the time of initial evaluation was graded as 3/5 in 6 horses and 4/5 in 2 horses. Lameness involved the right forelimb only in 4 horses and the left forelimb only in 2 horses. In the remaining 2 horses, lameness that involved ≥ 1 limb was identified; 1 horse had bilateral forelimb lameness, and in the other horse, lameness involved the left forelimb and left hind limb. The 2 horses determined to be nonlame (sound) included 1 with a history of intermittent bilateral hind limb lameness and a previous diagnosis of pulmonary interstitial fibrosis and 1 that had no history of lameness.

**Initial scintigraphic findings**—At the time of initial evaluation, all horses had multiple sites of IRU involving the axial and appendicular skeleton. Increased radiopharmaceutical uptake in 1 (n = 3) or both (6) scapulae was evident in 9 of 10 horses examined; involved sites included the scapular spine (3), neck of the scapula (1), and cranial (2) and caudal (3) borders of the scapula. Two horses had signs of deformation and bowing of scapulae detected on the basis of results of scintigraphic evaluation. Additional sites of IRU in the axial skeleton included the ribs (n = 7), sternum (2), cervical spine (2), and thoracic spine (1). Additional sites within the appendicular skeleton included the proximal aspect of the humerus (n = 2), metacarpal bones (2), carpal bones (1), proximal sesamoids (1), proximal phalanx (1), and middle phalanx (1). No IRU was evident in the sternum or ribs at the cranioventral aspect of the thorax in the sound horse that was thought to have signs of pain referable to those regions.

**Radiographic findings**—A standard series of radiographic images of the right metacarpophalangeal joint in 1 horse was obtained, including dorsopalmar, dorsolateral-palmaromedial oblique, lateromedial, and dorsomedial-palmarolateral oblique projections. Evaluation of these images revealed osteoarthritis of the metacarpophalangeal joint with remodeling of the proximal sesamoid bones. No evidence of fracture was identified.

**Zoledronate treatment and 6-month follow-up examination**—Intravenous administration of zoledronate was well tolerated in all horses. No adverse effects were observed during or after drug administration. Although administration of NSAIDs was permitted, none of the horses received NSAIDs during the interval between zoledronate administration and the 6-month follow-up.
examination. Despite exercise restriction recommendations, owners returned all horses to their previous housing arrangements at the time of discharge from the hospital (ie, stalls with intermittent paddock turnout or full-time pasture turnout).

At the 6-month follow-up examination, clinical improvement was detected in 9 of 10 horses. Lameness grade was improved by 1 point on the 5-point scale in 5 of 8 horses that were lame at the time of initial evaluation and was improved by 2 points in the remaining 3 horses. Lameness was not completely resolved in any of these horses. The horse that had bilateral forelimb lameness during the initial evaluation had a 2-point improvement in lameness grade; on the basis of follow-up examination results, lameness was detected in the right forelimb only. One horse that had been evaluated for exercise intolerance and signs of discomfort during saddling had no evidence of clinical signs at the time of follow-up and had remained sound. The remaining horse that was determined to be sound during the initial evaluation but had a history of chronic intermittent hind limb lameness had a grade 2/5 bilateral forelimb lameness identified at the follow-up examination; this horse had been wearing horseshoes during the initial evaluation, and the shoes had been removed during the interval between zoledronate administration and the follow-up examination. Discussion with the owner revealed that this horse historically had bilateral forelimb lameness when it was not wearing shoes. This horse was considered to have clinical signs of deteriorating condition.

Posttreatment scintigraphic findings—Scintigraphic outcomes were considered positive in all 10 horses. The independent reviews were all in agreement as to whether there was improvement or stabilization of scintigraphic findings for each horse. Eight horses had improved scintigraphic findings at the time of follow-up evaluation; each of these had a generalized decrease in radiopharmaceutical uptake in all previously identified IRU sites. In the remaining 2 horses, scintigraphic findings were stable, with no additional sites of IRU identified; 1 had clinical improvement as indicated by a 1-point decrease in lameness grade at the time of follow-up examination, and the other was considered to have clinical signs of deteriorating condition because it had developed bilateral forelimb lameness after it was determined to be sound at the time of initial examination.

Discussion

In the study reported here, treatment with zoledronate appeared to be useful for improving the clinical and scintigraphic signs of a BFD identified in horses in California. Six months after drug administration, 9 of 10 affected horses had an improvement in lameness grade or resolution of clinical signs of musculoskeletal pain, compared with findings at the time of initial examination. In addition, 8 of 10 horses had subjectively decreased radiopharmaceutical uptake detected from results of follow-up scintigraphy in all sites that were determined to have IRU via initial scintigraphic evaluation.

As anticipated, similarities were identified between the population of horses with this BFD in a previous retrospective study and the population of horses in the study reported here. Fourteen of 16 horses in the previous study and 7 of 10 in the present study were from the Monterey-Carmel Peninsula, Sonoma County, or Napa County. All horses in the previous study and 9 of 10 in the present study were evaluated for lameness of various durations and severities. In addition, referring veterinarians had attempted to localize lameness with regional anesthesia in all horses of the previous study and in 6 of 10 horses of the present study without success. Lateral bowing of the scapulae and lordosis, believed to be characteristic of more advanced stages of this BFD, was detected in 2 horses of the study reported here and in 3 horses of the previous study.

Scintigraphic findings for horses of the previous study were also similar to those reported here, with the scapulae and ribs being the most prevalent sites of IRU. In the previous study, IRU was detected in the caudal appendicular skeleton (primarily in the pelvic bones) in 9 of 16 horses; however, scintigraphy was not performed caudal to the level of L1 in the present study because a full-body scintigraphic evaluation was not considered necessary for diagnosis. Diagnosis of BFD can be reliably made on the basis of clinical signs and scintigraphic evaluation of IRU sites in the cervical, thoracic, and appendicular skeleton. The disorder appears to be a progressive disease with sites of scintigraphically detectable IRU developing in several bones over a range of 1 to 24 months. In the previous study, 6 of 16 affected horses were euthanized at the time of diagnosis. Five of the remaining 10 horses had progressive lameness and were euthanized at a median interval of 2 years after diagnosis. Five horses in that study had follow-up scintigraphy performed (1 month to 2 years after diagnosis); with no treatment or with palliative treatment only, additional sites of IRU were detected in 3 of these horses and no change was evident in the number of IRU sites in the remaining 2 horses.

The eutiological of the BFD described in the horses of the present study and other studies has not been conclusively determined. However, 3 possible mechanisms have been proposed. These include exposure to high concentrations of the cristobalite form of silicate in the Monterey Formation region of California, causing chronic systemic inflammation; direct dissemination of silicate-laden macrophages to bone marrow secondary to pulmonary silicosis; and abnormal osteoclast-mediated resorption and remodeling of bone similar to Paget’s disease of bone in humans. Other causes of pathological bone resorption include chronic corticosteroid use, primary or secondary hyperparathyroidism, and calcium or vitamin D deficiencies; however, prolonged corticosteroid use has not been a historical finding in horses in which this BFD is diagnosed, and no consistent abnormalities in circulating concentrations of parathyroid hormone, calcium, or other standard biochemical variables have been identified in previous studies of horses with this disorder.
In a study that evaluated postmortem findings in 9 horses with a diagnosis of BFD, investigators identified histopathologic evidence of abnormal osteoclast-mediated bone resorption and pulmonary inflammation in all 9 horses as well as an association between pulmonary silicosis and concurrent generalized osteoporosis, suggesting that silicosis-associated osteoporosis may be responsible for the development of the BFD. In a recent retrospective study, 3 of 16 horses with scintigraphic evidence of BFD also had a diagnosis of pulmonary silicosis. In the study reported here, respiratory disease was a historical finding in 2 horses at the time of BFD diagnosis, and none of the other horses had clinical signs of respiratory disease; however, diagnostic tests to rule out evidence of subclinical pulmonary inflammation were not pursued in the remaining 8 horses.

Exercise restriction was recommended for all horses of the present study because of the risk of pathological fracture development. Although exercise restriction could have contributed to the improvement noted from results of follow-up clinical and scintigraphic evaluations, this was thought to be unlikely because all owners elected to allow their horses access to turnout and did not follow the recommended exercise restrictions.

Although no complications attributed to drug administration were encountered in the present study, hypocalcemia has been reported as an adverse effect of zoledronate administration in humans. In the authors’ experience, hypocalcemia also developed in 1 horse (a 3-year-old Thoroughbred) treated with zoledronate at the University of California-Davis Veterinary Medical Teaching Hospital for an orthopedic condition unrelated to BFD; this condition resolved following treatment with 23% calcium gluconate (50 mL/L) in a 10-L total volume of a balanced electrolyte solution. As a result of the development of hypocalcemia in the aforementioned horse, we routinely evaluate total and ionized serum calcium concentrations 10 to 14 days following bisphosphonate administration. Additionally, we recommend a diet consisting of ≥ 50% alfalfa hay to increase calcium intake following treatment with zoledronate.

Bisphosphonates can be categorized as non-nitrogen–or nitrogen-containing agents. The nitrogen-containing compounds have been reported as more potent inhibitors of bone resorption with a longer duration of action. Tiludronate is a non-nitrogen–containing bisphosphonate that exerts its effects on osteoclasts by incorporation into nonhydrolyzable analogues of ATP, which in turn induces cellular apoptosis. Tiludronate is currently licensed in several countries in Europe for IV use in the treatment of osteoarthritis in the distal tarsus and navicular disease in horses. However, tiludronate is not currently approved by the FDA, and import into the United States requires a special permit issued by that agency. Tiludronate has been used to treat some horses with BFD, but the response to treatment has reportedly been inconsistent and repeated treatment has been required. Zoledronate is a third-generation nitrogen-containing bisphosphonate that is incorporated into hydroxyapatite and causes osteoclast apoptosis as well as inhibition of osteoclastic bone resorption. Zoledronate is used in humans for the treatment of Paget’s disease of bone as well as for osteoporosis in postmenopausal women. Although there have been several recent studies investigating the clinical efficacy of tiludronate for the treatment of a variety of orthopedic conditions in horses, we elected to use zoledronate in the study reported here because of its increased potency and duration of action as compared with tiludronate in humans and because of its use for the treatment of conditions that appear to have similarities to this BFD in humans. To the authors’ knowledge, the use of zoledronate in horses has not been previously described. At the time of publication, no horses included in the present study had evidence of further clinical deterioration after treatment with zoledronate.

Limitations of the study reported here included the small number of horses and the lack of a placebo-control group to fully evaluate the efficacy of zoledronate. Because of the regional distribution and sporadic occurrence of the BFD described in horses of the present study, obtaining a large study group of naturally affected horses is difficult. In addition, this BFD is a progressive, debilitating disease, which suggests the need for treatment at the time of diagnosis in most situations. This is primarily because of the risk of pathological fractures developing in addition to other signs of clinical deterioration, which makes a long-term placebo-controlled trial difficult to justify to horse owners. Although an inherent bias was present in the current evaluations, investigators were blinded to patient information during interpretation of scintigraphic images, and scintigraphic improvement mirrored clinical improvement in the majority (8/10) of horses. Pharmacokinetic properties of zoledronate have not been fully assessed in horses, and future studies are necessary to determine absorption, distribution, elimination, and half-life of the drug.

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From this month’s AJVR

Cardiovascular and respiratory effects of incremental doses of dopamine and phenylephrine in the management of isoflurane-induced hypotension in cats with hypertrophic cardiomyopathy

Ashley J. Wiese et al

Objective—To determine cardiopulmonary effects of incremental doses of dopamine and phenylephrine during isoflurane-induced hypotension in cats with hypertrophic cardiomyopathy (HCM).

Animals—6 adult cats with severe naturally occurring HCM.

Procedures—Each cat was anesthetized twice (once for dopamine treatment and once for phenylephrine treatment; treatment order was randomized). Hypotension was induced by increasing isoflurane concentration. Cardiopulmonary data, including measurement of plasma concentration of cardiac troponin I (cTnI), were obtained before anesthesia, 20 minutes after onset of hypotension, and 20 minutes after each incremental infusion of dopamine (2.5, 5, and 10 μg/kg/min) or phenylephrine (0.25, 0.5, and 1 μg/kg/min).

Results—Mean ± SD end-tidal isoflurane concentration for dopamine and phenylephrine was 2.44 ± 0.05% and 2.48 ± 0.04%, respectively. Cardiac index and tissue oxygen delivery were significantly increased after administration of dopamine, compared with results after administration of phenylephrine. Cardiac index and tissue oxygen delivery were significantly increased after administration of phenylephrine, compared with results after administration of dopamine. Oxygen consumption remained unchanged for both treatments. Systemic and pulmonary arterial blood pressures were increased after administration of both dopamine and phenylephrine. Acid-base status and blood lactate concentration did not change and were not different between treatments. The cTnI concentration increased during anesthesia and infusion of dopamine and phenylephrine but did not differ significantly between treatments.

Conclusions and Clinical Relevance—Dopamine and phenylephrine induced dose-dependent increases in systemic and pulmonary blood pressure, but only dopamine resulted in increased cardiac output. Hypotension and infusions of dopamine and phenylephrine caused significant increases in cTnI concentrations. (Am J Vet Res 2012;73:908–916)