Effects of denervation of the hip joint on results of clinical observations and instrumented gait analysis in dogs with sodium urate crystal–induced synovitis

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OBJECTIVE
To evaluate the effects of selective hip joint denervation on gait abnormalities and signs of hip joint pain in dogs.

ANIMALS
6 healthy adult hound-type dogs.

PROCEDURES
Minimally invasive denervation was performed on the right hip joint of each dog. Two weeks later, sodium urate was injected into the right hip joint to induce synovitis. Dogs were evaluated clinically and by use of instrumented gait analysis before and 2 weeks after minimally invasive denervation and 4, 8, and 24 hours after induction of synovitis. Dogs were euthanized, and necropsy and histologic examination were performed.

RESULTS
No kinetic or kinematic gait modifications were detected 2 weeks after minimally invasive denervation. Denervation did not eliminate signs of pain and lameness associated with sodium urate–induced synovitis. Results of histologic examination confirmed that denervation was an effective method for transecting the innervation of the cranio-lateral and caudo-lateral aspects of the hip joint capsule.

CONCLUSIONS AND CLINICAL RELEVANCE
In this study, minimally invasive denervation did not result in gait modifications in dogs. Denervation did not abolish the signs of pain and lameness associated with generalized induced synovitis of the hip joint. Further studies are required before conclusions can be drawn regarding the clinical usefulness of hip joint denervation for dogs with hip dysplasia. (Am J Vet Res 2016;77:1200–1210)

In a multi-institutional, 10-year study of almost half a million dogs in the United States, hip dysplasia was the most commonly identified hip joint condition, comprising 67.4% of all conditions described for that joint. Hip dysplasia is associated with joint pain and loss of joint function.

Sensory innervation of the hip joint in dogs consists of the cranial gluteal, sciatic, femoral, and obturator nerves, although the contribution of the obturator nerve may be inconsistent. It has been reported that the cranio-lateral area of the hip joint capsule is innervated by articular branches of the cranial gluteal nerve, the caudo-lateral area is innervated by articular branches of the sciatic nerve, and the ventral area is innervated by articular branches of the femoral nerve and articular branches of the obturator nerve. Articular branches innervate distinct areas of the joint capsule directly or indirectly via periosteal branches from the periarticular muscles covering the acetabulum.

The abundance of sensory nerve endings in the hip joint capsule provides the possibility that interruption of these fibers might eliminate pain in the joint.

Denervation of the hip joint capsule has been described as a treatment to alleviate pain associated with hip dysplasia and osteoarthritis in dogs. This technique is based on surgical removal of the periosteum in a semicircular manner, beginning at the cranio-dorsal margin (as far caudally as possible) of the acetabulum and progressing to the cranio-ventral margin (ventral aspect of the body of the ilium), thereby transecting the sensory nerve fibers (articular branches) innervating the hip joint. Originally, periosteotomy was achieved through a limited cranio-lateral open approach. However, percutaneous techniques involving the use of Steinman pins have also been described.

Denervation has resulted in clinical improvement in > 90% of treated dogs, as determined on the basis of owner assessment and results of observational gait analysis in various studies. The quality

ABBREVIATIONS
CV  Coefficient of variation
PVF  Peak vertical force
WD  Weight distribution

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of evidence yielded by most of these studies is diminished by the retrospective nature of the studies, lack of control subjects, small numbers of dogs in some studies, and subjective nature of the assessments. An additional limitation is that it is unclear whether the reported change in gait following denervation was a beneficial effect of the denervation procedure or a reflection of resolving lameness commonly seen in young dogs with hip dysplasia.

To our knowledge, the effect of denervation of the hip joint on objective gait characteristics has not been described for dogs. Dogs with hip dysplasia of various degrees of severity have been evaluated before and after treatment, but not before and after the onset of lameness. Gait characteristics are difficult to assess in dogs with naturally occurring disease, and a standardized method for induction of hip joint pain could help to determine the effect of denervation on gait and the efficacy of denervation in the treatment of joint pain.

In a recent study, investigators described the development of a novel method for inducing acute synovitis of the hip joint by intra-articular injection of sodium urate crystals. Observational and instrumented gait variables (temporospatial, kinetic, and kinematic) were recorded before and 4, 8, and 24 hours after induction of synovitis. Gait changes were similar to those reported for dogs with hip dysplasia. The inflammatory response after intra-articular injection of sodium urate crystals caused a detectable clinical effect and lameness after 1 to 2 hours, which reached maximal intensity at 4 hours and subsided by 24 hours after injection. That study highlighted the objectivity of instrumented gait analysis because it allowed the comparison of gait characteristics at various points.

The objective of the study reported here was to use the aforementioned synovitis induction method and assessment modalities to assess effects on gait characteristics of dogs. The hypotheses tested were that selective percutaneous denervation of the hip joint (defined as minimally invasive denervation) would not result in gait abnormalities and that selective denervation of the hip joint of dogs would abolish joint pain.

Materials and Methods

Animals

Six purpose-bred adult hound-type dogs (3 males and 3 females) that were free of orthopedic and neurologic disease were included in the study, which was conducted at Purdue University. Median body weight was 25.7 kg (range, 21.5 to 29.9 kg). These same dogs had previously been used in a study to develop a method for inducing synovitis in the hip joint. A routine clinical examination, CBC, and serum biochemical analysis were performed on each dog at the time it was enrolled in the present study; all dogs also received treatment for intestinal and cutaneous parasites. Complete orthopedic (including Barlow and Ortolani tests) and neurologic examinations were performed, and 2-view radiographs of the hip joint were obtained and examined to exclude orthopedic and neurologic diseases and confirm physiologic closure. Only clinically normal dogs were included in the study. Each dog was acclimated to leash walking and to the gait laboratory for 2 weeks prior to commencement of the study. The study protocol was approved by the Institutional Animal Care and Use Committee of Purdue University.

In preliminary experiments, 20 hip joints of 10 dogs euthanized for reasons unrelated to the present study were used to develop the techniques for intra-articular injection and minimally invasive denervation of the hip joint. Spinal needles were used to identify the dorsal joint space and location of the cranial, dorsal, and caudal aspects of the acetabular rim and to establish the spatial relationship between those bony landmarks and the greater trochanter and long axis of the femur. In 3 cadavers, injection of contrast material through the intra-articularly placed needles was monitored radiographically to ensure accurate injection. Finally, the needles were left in place in the hip joints and the joints were dissected; visible nerves coursing toward the joint capsule were dissected, recorded, and photographed. The cadaveric experiments resulted in technical refinement of the technique, and a repeatable and continuous area of juxta-acetabular periosteal scarification was consistently achieved. In addition to disruption of the periosteum, previously identified nerve branches from the cranial gluteal and sciatic nerves and the gluteal muscles appeared to be disrupted. Practice on the cadavers allowed us to perform the procedures with no additional damage to the adjacent joint area and minimal damage to the overlying gluteal muscles associated with the pin tract.

Study design

Instrumented gait analysis followed by visual gait analysis and clinical examination was performed on each dog at 5 points during the study. These evaluations included gait analysis performed 7 days after subsidence of the synovitis that had been experimentally induced in the right hip joint during a previous study (before denervation surgery in the present study; baseline), 12 to 14 days after unilateral denervation of the right hip joint, and 14 days later at 4, 8, and 24 hours after induction once again of synovitis in the right hip joint. Lameness was assessed by use of a numeric scale (0 = clinically normal; 1 = barely detectable lameness; 2 = mild lameness; 3 = moderate lameness; 4 = severe lameness, with limb not used during trotting; and 5 = non-weight-bearing lameness, with limb not used at any time) at 1, 2, 3, 4, and 24 hours after induction of synovitis. Peak extension, flexion, and abduction of the hip joint were measured manually by use of a goniometer at the same assessment points.

Instrumented gait analysis

Dogs were weighed, and 5 adhesive cutaneous reflective markers were affixed to each pelvic...
limb, as described elsewhere. Dogs were walked in a straight line at a comfortable velocity on a pressure-sensitive walkway. A valid trial was defined as walking in a straight line without stopping, hesitating, or pacing while maintaining a constant speed; no overt head movement; and inclusion of at least 2 gait cycles (8 sequential paw strikes). An integrated digital video camera was used to verify paw placement and pressure, and data were analyzed by use of designated software. Joint excursions and angles were measured by use of a 2-D kinematic system with a video camera. Six valid trials (3 in each direction [left to right and right to left]) to eliminate variability attributable to direction) were acquired and used for kinetic and temporospatial analysis. The 3 valid trials in the left to right direction were also used for kinematic analysis of the right pelvic limb, and the 3 trials in the right to left direction were used for kinematic analysis of the left pelvic limb.

Gait characteristics of each limb were determined through analysis of kinetic variables and temporospatial variables, which included PVF, PVF normalized for body weight, WD, gait cycle duration, stance phase duration, swing phase duration, stride length, and stride velocity. Symmetry index values (indicators of the difference between the limb of interest [right pelvic limb] and the contralateral limb) and intertrial variability (CV, which was an indicator of interstep variability) were calculated for all measured variables. Data were tabulated in spreadsheets.

For the analysis of kinematic joint-angle variables, video-recorded data were collected for 1 gait cycle during the same 6 valid trials, and joint angles and excursions were calculated by use of custom-written codes for 2-D kinematic software. Peak flexion, peak extension, and range of motion of the hip, stifle, and tarsal joints were obtained for right and left pelvic limbs at each assessment point and were recorded in spreadsheets. In addition, the symmetry index value and intertrial CV were calculated for each variable.

Minimally invasive denervation

All minimally invasive denervation procedures were performed by the same investigator (EAH). Each dog was premedicated with dexmedetomidine (0.005 mg/kg, IM) and butorphanol tartrate (0.1 mg/kg, IM). Anesthetic induction was achieved with propofol (6 mg/kg, IV, administered to effect), and anesthesia was maintained with isoflurane and oxygen (vaporizer setting, 1% to 3%). Cefazolin (20 mg/kg, IV) was administered after the induction of anesthesia.

Anesthetized dogs were positioned in left lateral recumbency and stabilized by use of a total hip replacement positioning board. A pillow was placed between the pelvic limbs to align the uppermost (right) limb parallel to the operating table. Adhesive tape was used to fix the right limb in slight adduction, with the stifle joint semiflexed and internally rotated. The skin was aseptically prepared for surgery.

A 3-inch-long, 20-gauge spinal needle was inserted 1 cm cranial and slightly dorsal to the greater trochanter and advanced to the dorsal aspect of the acetabular bone to provide orientation and ensure proper position of a stab incision. A stab incision was made in the skin, and a 4-mm Steinman pin was introduced through the incision (perpendicular to the skin and body of the ilium) and pushed through the gluteal muscles until the acetabular bone was reached. A protective sleeve was placed over the pin and advanced to the bone surface.

The periosteum was scarified by use of repeated semicircular movements while maintaining axial pressure on the pin. The uninterrupted arc was centered at the insertion point and extended cranially to the ventral aspect of the body of the ilium and caudally to the ventral aspect of the body of the ischium, parallel to the acetabular rim. The periosteal disruption bifurcated on either side of the tendon of origin of the rectus femoris muscle, which could be sensed through the pin. The intent was to cause destruction of the articular branches of the cranial gluteal nerve, the cranially located articular branches of the sciatic nerve, and the periosteal branches of the periarticular muscles. The subcutaneous fascia and subcuticular tissue then were apposed with 3-0 polyglactin 25 suture.

Hydromorphone (0.05 mg/kg, IV) was administered every 4 hours for 24 hours. Carprofen (2.2 mg/kg, IV) was administered at the time of surgery; carprofen was also administered (4.4 mg/kg, PO, q 24 h for 3 days) starting the day after surgery. Tramadol (2 to 4 mg/kg, PO, q 12 h for 3 days) was administered starting the day after surgery.

Induction of synovitis

Fourteen days after the denervation procedure, dogs were sedated with dexmedetomidine (0.008 mg/kg, IV). Oxygen was provided via a face mask. To induce synovitis, 1 mL of sodium urate suspension (20 mg/mL) was injected by use of ultrasonographic guidance into the right hip joint with a 25-gauge spinal needle, as described elsewhere. After the injection was completed, sedation was reversed with atipamezole hydrochloride (0.008 mg/kg, IM).

Necropsy and histologic examination

After the last gait analysis was performed 24 hours after induction of synovitis, all dogs were euthanized with pentobarbital (1 mL/5 kg, IV). Necropsy was performed immediately after dogs were euthanized. Tissues surrounding the right hip joint were examined for evidence of healing and tissue reaction, with particular attention to the pin tract through the muscles. The periosteum adjacent to the acetabulum was examined to determine the extent and completeness of scarring along the outer surface of the acetabulum. Visible remnants of...
nerve connections to the hip joint were recorded; signs of inadvertent damage to the joint capsule, femoral head, and sciatic nerve and the presence of extra-articular urate crystals were also recorded. Synovial fluid, if seen, was examined for discoloration. Acetabular articular cartilage as well as femoral articular cartilage was examined for erosions, ulcerations, and injuries. Joint capsule thickening and proliferation were recorded, as was the appearance of the ligament of the head of the femur. Joint margins were examined for evidence of osteophyte or enthesiophyte formation.

Both acetabula (denervated right hip joint and nondenervated left hip joint) were harvested and fixed in neutral-buffered 10% formalin. After fixation was achieved, sagittal bone cuts with a diamond saw were made parallel to the outer circumference of each acetabulum. Bone samples were decalcified in a solution containing 3.5 g of sodium formate/18 mL of formic acid, which was then diluted with 82 mL of distilled water. Nerve fibers were identified by silver impregnation with a 1% silver nitrate solution; pH was controlled by the addition of a buffer solution containing 0.5% borax–boric acid until a pH of 7.8 was obtained.

Statistical analysis

Descriptive statistics were used to summarize the distributions of the temporospatial, kinetic, and kinematic variables as well as the lameness scores over time. Lameness scores (ordinal data) were compared over time by use of commercially available software\textsuperscript{27}; data were analyzed by use of the Friedman test, followed by pairwise comparisons with the Dunn test and Bonferroni adjustment. Instrumented gait analysis data were analyzed with a linear mixed model that included time, limb (left vs right), and the time-by-limb interaction as fixed effects and dog as a random effect. Differences were considered significant at \( P < 0.05 \).

Results

Baseline gait variables

Limb velocity (range, 0.93 to 1.14 m/s) and percentage of the stride when the limb was bearing weight confirmed a walking gait in all 6 dogs prior to denervation surgery. No significant difference was identified between the left and right pelvic limb for any variables. Limb velocity at subsequent assessment points indicated that all instrumented gait analysis variables were measured during walking. All results were summarized (Tables 1 and 2).

Minimally invasive denervation

The procedure was easy to perform and could be completed rapidly (8 to 12 minutes) without any complications. All dogs were able to ambulate without obvious lameness within 2 to 4 hours after recovery from anesthesia. No postoperative complications were detected.

Effects of denervation on instrumented gait analysis

Denervation of the hip joint did not result in gait abnormalities, compared with results of baseline gait analysis. No differences in mean values for temporospatial, kinetic, and kinematic variables

\begin{table}[h]
\centering
\begin{tabular}{|l|l|l|l|l|}
\hline
Variable & Baseline & 4 & 8 & 24 \\
\hline
Limb velocity (m/s) & 0.98 ± 0.10 & 0.52 ± 0.40* & 0.54 ± 0.43* & 0.95 ± 0.09 \\
Stride length (m) & 0.78 ± 0.08 & 0.43 ± 0.34* & 0.42 ± 0.33* & 0.75 ± 0.07 \\
Gait cycle duration (s) & 0.80 ± 0.04 & 0.58 ± 0.48 & 0.50 ± 0.44* & 0.79 ± 0.06 \\
Stance phase duration (s) & 0.47 ± 0.02 & 0.28 ± 0.23* & 0.25 ± 0.25* & 0.45 ± 0.03 \\
Swing phase duration (s) & 0.32 ± 0.02 & 0.30 ± 0.25 & 0.24 ± 0.19 & 0.34 ± 0.03 \\
PVF (N) & 57.9 ± 10.8 & 26.5 ± 21.6* & 26.5 ± 25.5* & 51.0 ± 7.9 \\
PVF normalized for body weight (%) & 23.0 ± 4.3 & 10.5 ± 8.6* & 10.5 ± 10.1* & 20.2 ± 3.1 \\
W/D (%) & 19.8 ± 1.3 & 9.3 ± 7.8* & 9.3 ± 8.9* & 18.3 ± 2.9 \\
Hip joint & & & & \\
Peak extension (°) & 135.6 ± 8.7 & 124.4 ± 6.5 & 125.8 ± 7.4 & 130.4 ± 7.2 \\
Peak flexion (°) & 104.5 ± 6.5 & 105.4 ± 10.0 & 105.3 ± 7.0 & 99.9 ± 6.7 \\
Range of motion (°) & 31.2 ± 6.2 & 19.0 ± 6.0 & 20.5 ± 7.6 & 30.5 ± 6.0 \\
Stifle joint & & & & \\
Peak extension (°) & 149.9 ± 7.4 & 127.6 ± 23.0* & 130.4 ± 22.2 & 146.6 ± 9.0 \\
Peak flexion (°) & 112.4 ± 5.5 & 101.2 ± 15.3 & 99.7 ± 16.2 & 113.3 ± 3.5 \\
Range of motion (°) & 37.4 ± 6.6 & 26.4 ± 9.9 & 30.7 ± 11.5 & 33.4 ± 7.4 \\
Tarsal joint & & & & \\
Peak extension (°) & 154.5 ± 8.3 & 143.8 ± 12.4 & 143.7 ± 13.0 & 152.2 ± 6.5 \\
Peak flexion (°) & 125.0 ± 11.0 & 125.2 ± 11.9 & 120.4 ± 10.2 & 126.9 ± 6.4 \\
Range of motion (°) & 29.5 ± 6.3 & 18.7 ± 7.0 & 23.3 ± 9.6 & 25.3 ± 4.4 \\
\hline
\end{tabular}
\caption{Mean ± SD values of gait variables for the right pelvic limb of 6 dogs before (baseline) and 4, 8, and 24 hours after induction of synovitis by injection of sodium urate crystals into the hip joint.}
\end{table}

*Within a variable, value differs significantly (\( P < 0.05 \)) from the baseline value.
were identified between baseline and 2 weeks after denervation.

Clinical effects of synovitis after denervation

Prior to induction of synovitis (14 days after denervation surgery), no dogs had signs of lameness (lameness score, 0). One hour after induction of synovitis, 4 dogs had no signs of lameness (lameness score, 0) but 2 dogs had barely detectable lameness (lameness score, 1). Two hours after induction of synovitis, 2 dogs had barely detectable lameness (lameness score, 1) and 4 dogs had mild lameness (lameness score, 2). Three hours after induction of synovitis, the response differed among dogs, with a lameness score of 0.010, respectively. Three hours after induction of synovitis, 2 dogs had barely detectable lameness (lameness score, 0) but 2 dogs had barely detectable lameness (lameness score, 1).

A significant increase in lameness scores was identified between values at baseline and those at 3 (P = 0.047) and 4 (P = 0.001) hours after induction of synovitis as well as between values at 1 and 4 hours after induction (P = 0.004). Compared with results for the left pelvic limb, the right pelvic limb had significantly reduced values for extension and abduction, but not flexion, at 2 (P = 0.017 and 0.010, respectively), 3 (P = 0.006 and 0.032, respectively), and 4 (P = 0.012 and 0.007, respectively) hours after induction of synovitis.

Effects of synovitis after denervation on instrumented gait analysis

Effects of experimentally induced synovitis after denervation of the right hip joint were evaluated by use of instrumented gait analysis.

Temporospatial variables—Limb velocity, stride length, and stance phase duration of the right pelvic limb were all significantly decreased at 4 (P < 0.001, < 0.001, and 0.003, respectively) hours after induction of synovitis, compared with results for the same limb before induction of synovitis. A significant (P = 0.018) decrease in gait cycle duration was identified at 8 hours after induction of synovitis. Swing phase duration also decreased after induction of synovitis, but not significantly, compared with results before induction. There was no significant difference between values at baseline and 24 hours after induction of synovitis for any temporospatial variables of the injected limb. No differences were detected between assessment points for any temporospatial variables of the left pelvic limb.

Compared with values for the left pelvic limb, values for limb velocity, stride length, gait cycle duration, and stance phase duration of the right pelvic limb were significantly decreased at 4 (P = 0.003, 0.035, < 0.001, and 0.001, respectively) and 8 (P < 0.001, < 0.001, and 0.003, respectively) hours after induction of synovitis. Symmetry index values for all 5 temporospatial variables for both pelvic limbs were significantly (P < 0.001) increased at 4 and

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### Table 2—Mean ± SD values of gait variables for the left pelvic limb of 6 dogs before (baseline) and 4, 8, and 24 hours after induction of synovitis in the right pelvic limb by injection of sodium urate crystals into the right hip joint.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>4</th>
<th>8</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limb velocity (m/s)</td>
<td>0.99 ± 0.10</td>
<td>0.91 ± 0.23&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.04 ± 0.26&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.96 ± 0.10</td>
</tr>
<tr>
<td>Stride length (m)</td>
<td>0.78 ± 0.08</td>
<td>0.62 ± 0.08&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.64 ± 0.07&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.75 ± 0.07</td>
</tr>
<tr>
<td>Gait cycle duration (s)</td>
<td>0.80 ± 0.05</td>
<td>0.72 ± 0.22&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.67 ± 0.21&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.79 ± 0.06</td>
</tr>
<tr>
<td>Stance phase duration (s)</td>
<td>0.48 ± 0.02</td>
<td>0.47 ± 0.16&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.42 ± 0.15&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.48 ± 0.04</td>
</tr>
<tr>
<td>Swing phase duration (s)</td>
<td>0.32 ± 0.03</td>
<td>0.25 ± 0.06</td>
<td>0.26 ± 0.07</td>
<td>0.31 ± 0.02</td>
</tr>
<tr>
<td>PVF (N)</td>
<td>61.8 ± 7.9</td>
<td>81.4 ± 28.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>81.4 ± 26.5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>59.8 ± 7.9</td>
</tr>
<tr>
<td>PVF normalized for body weight (%)</td>
<td>24.5 ± 3.1</td>
<td>32.2 ± 11.3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>32.3 ± 10.5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>23.7 ± 3.1</td>
</tr>
<tr>
<td>WD (%)</td>
<td>21.2 ± 1.1</td>
<td>25.9 ± 4.5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>26.0 ± 5.2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>21.2 ± 2.4</td>
</tr>
</tbody>
</table>

<sup>a</sup>Value differs significantly (P < 0.05) from the corresponding value for the right pelvic limb in Table 1.
8 hours after induction of synovitis, compared with the baseline values (Table 3). Mean intertrial CV of the temporospatial variables of the affected limb of the 6 dogs ranged from 0.01 to 0.11 and did not differ significantly among assessment points.

**Kinetic variables**—Values for PVF, PVF normalized for body weight, and WD of the injected (right) pelvic limb were significantly decreased at 4 (P < 0.001, 0.029, and < 0.001, respectively) and 8 (P < 0.001, 0.027, and < 0.001, respectively) hours after induction of synovitis, compared with values before and at 24 hours after induction of synovitis. No differences in kinetic variables between assessment points were detected for the left pelvic limb. The PVF, PVF normalized for body weight, and WD differed significantly (P < 0.001) between the right and left pelvic limbs at 4 and 8 hours after induction of synovitis. In addition, range of motion for the hip and tarsal joint differed significantly (P < 0.001) between the left and right pelvic limbs at 4 and 8 hours after induction of synovitis.

Peak extension of the hip joint differed significantly between the left and right pelvic limbs at 4 and 8 hours after induction of synovitis. Range of motion of the stifle joint differed significantly (P = 0.036) between the left and right pelvic limbs at 24 hours after induction of synovitis. The symmetry index value for range of motion for the hip joint was significantly (P < 0.001) increased from baseline at 4 and 8 hours after induction of synovitis. Symmetry index values of peak extension, peak flexion, and range of motion for the stifle joint and range of motion for the tarsal joint also were significantly (P < 0.001) increased from baseline at 4 and 8 hours after induction of synovitis. Mean intertrial CV of the kinematic variables of the injected limbs of all dogs ranged from 0.01 to 0.25. Values of kinematic variables for the affected limb were summarized (Tables 1–3).

**Necropsy and histologic examination**

Minimal soft tissue reaction was identified over the acetabular area in 4 dogs, whereas a marked tissue reaction was identified in the remaining 2 dogs. The extent of the periosteal disruption could be clearly determined from tissue reaction over the ac-
etabular area, and it extended cranially to the ventral aspect of the body of the ilium and caudally to the ventral aspect of the body of the ischium in all dogs. No evidence of remnants of direct branches to the hip joint capsule was identified in any dog, nor was there visible damage to the sciatic nerve or the articular cartilage. Visible innervation to the ventral aspect of the hip joint capsule by branches of the obturator nerve was evident in 3 dogs. Synovial fluid was clear and scant in 1 dog, slightly turbid in 1 dog, hemorrhagic in 2 dogs, and not detectable in 2 dogs.

In the joints subjected to denervation surgery, the cranialateral, caudolateral, and ventral areas of the joint capsule had various (minimal to moderate) degrees of thickening of the synovial membrane, villous hypertrophy, and inflammation that in many instances extended through the superficial layers of the joint capsule into adjacent muscle. In most areas, thickness of the highly vascularized superficial joint capsule was increased as a result of inflammation; neutrophils, plasma cells, and histiocytes were the dominant cell types, with focal to coalescing areas of necrosis, multinucleated giant cells, and fibrosis. In general, compared with the dorsolateral aspect of the joint capsule, lesions in the ventral aspect of the joint capsule were more severe with regard to inflammation and fibrosis. No lesions were seen in the joint capsule of the unoperated hip joints.

Examination of sections of the right (denervated) acetabula stained by use of a silver impregnation technique consistently revealed fibrovascular repair tissue instead of periosteum along the entire dorsal aspect of the acetabulum. No nerve fibers were observed within the repair tissue (Figure 1). Ramifying nerve fibers were not observed between or within muscle bundles over the dorsal aspect of the acetabulum. Nerve fibers were seen in bone marrow cavities and on the ventral aspect of the acetabulum in densities similar to those of the left limb. Examination of sections of the left (nondenervated) acetabula revealed an intact periosteum with free nerve endings along the entire cranial-to-caudal dorsal aspect of the acetabular bone surface. As expected, nerve fibers were also seen in many bone marrow cavities away from the periosteum. Rami of nerve fibers were observed within the muscle bundles over the periosteum on the dorsal aspect of the acetabulum. A low density of nerve fibers was also seen in the ventral aspect of the acetabulum in both cranial and caudal directions. Nerve density was greater in the periosteum of the dorsal aspect of the acetabulum than on the ventral aspect of the acetabulum. Findings were similar for all 6 dogs.

**Discussion**

In the study reported here, minimally invasive denervation of the hip joint of healthy dogs did not induce temporospatial, kinetic, or kinematic gait abnormalities. In addition, denervation did not abolish the signs of pain and lameness caused by sodium urate crystal–induced synovitis.

There was a concern that joint denervation could result in laxity and instability of the hip joint with resulting gait abnormalities. Destruction of sensory afferent nerves from mechanoreceptors in the joint capsule may abolish or diminish reflexive contraction of periarticular hip muscles in response to distention or stretching of the joint capsule. This might lead to abnormal joint movement as well as leave an animal less able to protect the joint against abnormal or extreme movement. Such a mechanism has been described for the stifl e joint and has been hypothesized as a mechanism for hip dysplasia of dogs.28–30

Sensory integrity is particularly important in unstable stifl e joints and presumably unstable hip joints, as might be found in the early stages of hip dysplasia. In a study in which stifl e joints were monitored for 72 weeks after cranial cruciate ligament transection, dogs that had prior ipsilateral sensory interruption (dorsal root ganglionectomy) had much more severe osteoarthritis than did dogs with intact sensory in-
nerve. In that same study, a separate group of dogs that had undergone ganglionectomies and sham ligament transections did not develop osteoarthritis. In the study reported here, neither kinetic nor kinematic gait abnormalities were detected 2 weeks following denervation surgery, which suggested that denervation alone did not result in detectable gait abnormalities. Although kinematic analyses cannot directly identify focal sensory defects, they may suggest abnormalities through altered joint angles, and these were not identified in the present study. Thus, the hypothesis that selective hip joint denervation in dogs does not result in gait abnormalities was accepted.

Results of the present study indicated that hip joint denervation did not eliminate induced hip joint pain. The findings appeared to be in contrast to results of multiple previous studies in which investigators reported various degrees of pain relief and decreased lameness for dogs with hip dysplasia treated by use of hip joint denervation. A proposed explanation relates to the source of pain. The highest concentration of nerve endings is located in the dorsolateral area of the acetabular peristeum. This area is adjacent to the area of highest compression forces within the joint. Cases of hip dysplasia with craniodorsal subluxation of the femoral head would be affected in the region with the greatest number of capsular pain receptors. It has been suggested that sensory innervation of the caudolateral and ventral part of the joint capsule contributes only minimally to the pain sensation associated with hip dysplasia. Thus, denervation of the craniodorsal region of the joint capsule should be anticipated to have beneficial effects. In contrast, results for histologic examination of the joint capsule reported here and in other studies would suggest that sodium urate induces panarticular synovitis with more severe changes in the ventral part of the joint. Thus, clinical signs may not be ameliorated by this focal, partial denervation procedure.

Indeed, induced pansynovitis may not be a good method for inducing localized joint capsule pain such as that occurring early during development of hip dysplasia in young dogs with joint laxity. Approximately 4% to 9% of dysplastic dogs treated by denervation did not improve in other studies. A possible explanation might be that in these older dogs, the more severe arthritic changes had progressed to the medial joint capsule and painful stimuli from this region were not interrupted by denervation surgery. Indeed, necropsy in the study reported here revealed grossly intact internal obturator nerve branches to the medial joint capsule in 3 of 6 dogs. In addition, it may be that this method for induction of acute synovitis may not have accurately reflected chronic pain associated with long-lasting hip dysplasia with panarthrosis and nerve sensitization.

The source of pain in dogs with naturally occurring hip dysplasia is age dependent. In young dogs, pain reportedly results from severe laxity with stretching and tearing of the craniolateral region of the joint capsule, ligaments, and muscles and microfracture of the dorsal rim of the acetabulum. Denervation may be most effective in this patient category. Over time, reactive capsular fibrosis decreases joint laxity, and signs of pain often diminish or disappear spontaneously.

Clinical signs in older animals with chronic disease are attributable to osteoarthritic changes. The source of resurgence of pain is complex and poorly understood and probably originates from other articular and periarticular tissues in addition to the synovium. These patients have involvement of the entire hip joint, and it might be assumed that denervation would be less effective in patients without joint laxity but with osteoarthritis secondary to hip dysplasia. Thus, it is conceivable that the benefits of denervation may be temporal, depending on the stage of the disease and source of pain. Most reported clinical studies of hip joint denervation had no control group and relied on owner observations; therefore, it is reasonable to question whether, in some of the cases, the improvement observed was a result of the aforementioned spontaneous resolution or was the result of owner bias. Well-designed clinical studies targeting these 2 patient groups may elucidate such differences.

Instrumented gait analysis has been used to assess outcome following denervation in dogs with hip dysplasia. In 1 study, 13 dysplastic dogs (ages not reported) were treated with bilateral minimally invasive denervation and evaluated at 0, 4, 8, and 24 weeks by use of a visual analog scale for pain and lameness and a force plate for measurement of ground reaction forces. The ground reaction forces did not change significantly, but visual analog scale scores were significantly reduced in all dogs at 8 and 24 weeks. In another study, unilateral open denervation was performed in 10 dogs (8 months to 10 years old), and the response was evaluated by use of a force plate at 0, 4, and 12 weeks. There was moderate to marked improvement in subjective signs of lameness and owner perception in half of the dogs, but no or only mild improvement in the other half. Although half of the dogs had improvement in PVF in the operated limb, overall there was no significantly detectable improvement over time. Finally, in a study in which 9 dogs (7 months to 54 months old) underwent 16 open denervation procedures, owners judged there to be clinical improvement for 14 of 16 surgeries at an examination performed 12 weeks after the procedures. Instrumented gait analysis performed by use of a pressure-sensitive walkway at weeks 0 and 12 failed to detect a significant difference within dogs. Consistent among the aforementioned studies was an improvement in comfort and possibly range of motion but a lack of significant improvement in weight bearing in the treated limb. Findings for the present study that denervation did not prevent changes in gait variable values obtained through instrumented gait analysis may support those assumptions. A weak
correlation between results for subjective clinical assessment and objective instrumented gait analysis has been clearly established.\textsuperscript{36,37}

Minimally invasive denervation has the advantage that it is simpler and less traumatic than the original limited-open approach. It provides easier access to the caudalateral region of the acetabulum, compared with the original approach. However, the scarification process is not visible, with a greater potential chance for incomplete denervation than for open periosteal curettage. To our knowledge, efficacy of the open and closed techniques has not been compared. Necropsy in the present study failed to identify remaining extraperiosteal nerve branches to the joint capsule on the denervated side. In addition, histologic examination of tissue sections of the denervated acetabulum revealed complete disruption of the periosteum and absence of transiting nerves, compared with results for the unoperated side. This indicated that the minimally invasive denervation described here was effective in the craniolateral and caudolateral parts of the joint capsule. It should be mentioned that the dogs of this study did not have arthritic changes, and it is unknown how anatomic disturbances caused by secondary osteoarthritic changes related to dysplasia will influence the accuracy and effectiveness of denervation.

Advantages of denervation include its simplicity, the fact it can be performed without the need for sophisticated equipment, the short surgical and recovery times, and the relatively low cost.\textsuperscript{8} The procedure disrupts a minimum amount of tissue, which permits the subsequent use of additional procedures (eg, femoral head and neck ostectomy and total hip replacement), should denervation be unsuccessful.\textsuperscript{13} This may allow owners to choose a surgical treatment instead of long-term treatment with drugs and their associated adverse effects. A theoretical disadvantage of denervation treatment, compared with reconstructive techniques, is the fact that only clinical signs are being treated. Nonetheless, it has been suggested\textsuperscript{13} that the immediate cessation of pain via denervation breaks a vicious cycle of pain that causes muscle atrophy, which causes more pain, and so on. Thereby, denervation might lead to strengthening of the pelvic and femoral musculature and stabilization of incongruent hip joints.

As described in another study,\textsuperscript{20} the temporospatial and kinetic variables evaluated in the present study appeared to be almost equally effective for identifying hip joint lameness in walking dogs. Only the swing phase duration was similar to the baseline value throughout each trial and did not contribute to the recognition of lameness. The kinematic variables were less consistent for identification of lameness. Lameness was only associated with a change in the stifle joint peak extension at 4 hours after injection. In general, symmetry index values were different whenever the primary variable was different; however, selected symmetry index values were different when the primary variable was not abnormal (swing phase duration; range of motion for the hip joint; peak extension, peak flexion, and range of motion for the stifle joint; and range of motion for the tarsal joint). Thus, symmetry indices may be more useful than their primary variables for the detection of hip joint lameness.

The finding that joint-angle kinematic variables were not very effective for the detection of lameness should not lead to the conclusion that lameness is not associated with changes in peak extension, peak flexion, and range of motion of joints. It cannot be ruled out that this finding was primarily attributable to technical issues (eg, marker placement, marker size, and skin movement) and that more robust marker systems may improve the use of kinematic joint-angle analysis for detection of lameness in dogs.\textsuperscript{25,38} Clearly, more studies on kinematic gait analysis for the detection of lameness are needed.

We chose to always perform denervation on the same side that had been used during a previous synovitis study\textsuperscript{20} because we did not anticipate that effects from the previous study would persist and influence results of the present study. This assumption was based on the reported complete reversibility of urate-induced synovitis, repeated induction of synovitis at an interval of as little as 7 days in another study,\textsuperscript{39} return of all gait analysis variables to preinduction values in the previous synovitis study,\textsuperscript{20} and lack of gait alterations identified at the baseline gait analysis performed in the present study. We also opted to perform denervation surgery on the same limb to improve repeatability and consistency for the procedure and to avoid introducing technical variability.

The present study had other limitations. First, because of the study sample size, the possibility that some nonsignificant findings were the result of insufficient statistical power cannot be ruled out. Second, dogs were evaluated during walking, even though trotting is considered a more challenging gait than walking.\textsuperscript{40} Thus, it is possible that denervation could have had an effect had dogs been evaluated during trotting. We chose the walking gait because there was a greater chance that lame dogs would lift an affected limb off the ground while trotting than while walking. We believed that this would have been beneficial during the synovitis part of the study. Even during walking, 3 dogs had non-weight-bearing lameness. Finally, it is customary for gait analysis studies to include 5 or 6 valid trials. However, to our knowledge, there have been no studies conducted to validate this assumption, and it is unknown whether the different gait variables require the same number of trials. We limited the kinematic analysis to 3 valid trials/pelvic limb to control the number of trials for each dog.

In the present study, a standardized method for induction of synovitis and a repeatable and objective gait analysis technique were used. However, we were unable to detect adverse biomechanical effects or benefits of this denervation technique.
A number of questions remain unanswered. Prospective studies to determine the efficacy of the procedure in dogs with other clinical signs and at other stages of the disease will need to be undertaken to answer some of these questions. The goal of such studies would be to provide better understanding of the pain associated with hip dysplasia in dogs, define indications for denervation, identify patients that would benefit the most from denervation, improve information about the causes for failure, and establish the duration of efficacy, assuming that reinnervation may occur.

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Footnotes

b. 3/4-inch black LP SAT dots, Velcro USA Inc, Manchester, NH.


d. GL2-digital camcorder, Canon Inc, Melville, NY.


g. Microsoft Office Excel 2007, Microsoft Corp, Redmond, Wash.

h. MATLAB, version 7.10.0-499 (R2010a), MathWork Inc, Natick, Mass.

i. Torbutrol, Zoetis Inc, Kalamazoo, Mich.

j. Propofol, Abbott Laboratories, Abbott Park, Ill.

k. Isoflurane, Piramal Healthcare Ltd, Andhra Pradesh, India.

l. Cefazolin, Sandoz Inc, Princeton, NJ.

m. Positioning board assembly (10-010), BioMedtrix, Boontown, NJ.

n. Monocryl, Ethicon Inc, West Somerville, NJ.

o. Hydroxyapatite. HCL 2 mg/mL, Baxter Healthcare Corp, Deerfield, Ill.

p. Rimadyl 100-mg caplets, Zoetis Inc, Princeton, NJ.

q. Tramadol, Amneal Pharmaceuticals LLC, Bridgewater, NJ.

r. Beuthanasia-D Special, Intervet/Schering-Plough Animal Health Corp, Kenilworth, NJ.

s. Antisedan, Orion Corp, Espoo, Finland.

t. Reuthanasia-D Special, Intervet/Schering-Plough Animal Health Corp, Kenilworth, NJ.

u. SPSS, version 21.0, IBM Corp, Armonk, NY.

References


