Clinical, radiographic, and magnetic resonance imaging findings of gastrocnemius musculotendinopathy in various dog breeds

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Gastrocnemius muscle, radiography, dog, musculotendinopathy, magnetic resonance imaging

Summary
Objectives: To describe clinical, radiographic, and magnetic resonance imaging (MRI) findings in 16 dogs diagnosed with gastrocnemius musculotendinopathy.
Methods: Retrospective evaluation of medical records, radiographs, and MRI results, as well as follow-up completed by telephone questionnaire.
Results: Most dogs had chronic hindlimb lameness with no history of trauma or athletic activities. Clinical examination revealed signs of pain on palpation without stifle joint instability. Seven dogs had radiographic signs of osteophyte formation on the lateral fabella. Magnetic resonance imaging revealed T2 hyperintensity and uptake of contrast agent in the region of the origin of the gastrocnemius muscle. Changes were found in the lateral and medial heads of the gastrocnemius. Conservative treatment resulted in return to full function in 11 dogs. Two dogs showed partial restoration of normal function, one dog showed no improvement. Two dogs were lost to follow-up.
Clinical significance: Gastrocnemius musculotendinopathy is a potential cause of chronic hindlimb lameness in medium to large breed dogs. A history of athletic activity must not necessarily be present. Magnetic resonance imaging shows signal changes and uptake of contrast agent in the region of the origin of the gastrocnemius muscle. A combination of T1 pre- and post-contrast administration and T2 weighted sequences completed by a fat-suppressed sequence in the sagittal plane are well-suited for diagnosis. Conservative treatment generally results in return to normal function.

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Introduction

Musculotendinopathy of the lateral head of the gastrocnemius muscle is a rare disease described in herding or athletic dogs (1, 2). Affected animals show chronic pelvic limb lameness and pain upon palpation of the lateral fabella, but no instability of the stifle joint. A history of trauma is usually not reported. Conservative treatment is the therapy of choice, and prognosis is good to excellent (1, 2).

The gastrocnemius muscle consists of lateral and medial heads, which arise from the lateral and medial supracondylar tuberosity of the femur, respectively. Both heads contain a fabella. The muscle bellies fuse distally and the gastrocnemius tendon inserts on the calcaneal tuber. The gastrocnemius muscle extends the tarsus and flexes the stifle joint (3). Repeated myotendinous strain during exercise is reported to cause microtrauma to the origin of the gastrocnemius muscle in that the tendon fibres become overstretched, and some of them tear (4).

Radiographically, visible signs of osteophyte formation on the lateral fabella and mineralizations at the origin of the gastrocnemius muscle can be detected. Magnetic resonance imaging (MRI) shows oedematous changes and uptake of contrast material in the region of the origin of the gastrocnemius muscle (1, 2).

This retrospective study describes clinical findings and radiographic and MRI features in 16 dogs of various breeds. None of the dogs were trained as herding dogs and two were explicitly sporting dogs.

To the authors' knowledge, there are only two other reports describing gastrocnemius musculotendinopathy in the dog (1, 2). Based on the findings of these reports, it might be assumed that gastrocnemius musculotendinopathy is a disease occurring almost exclusively in herding or athletic dogs, with the Border Collie to be the breed most commonly affected.

Thus, the purpose of this study was to go beyond existing knowledge of the disease and emphasize that gastrocnemius musculotendinopathy should be considered as a differential diagnosis for chronic hindlimb lameness in dogs regardless of athletic activity.

Materials and methods

Case selection

Medical records of 16 dogs that were presented to two referral centres (Small Animal Clinic, Justus Liebig University, Giessen, Germany and Tierklinik Lüneburg, Germany) from 2009 to 2014, and which were diagnosed with gastrocnemius musculotendinopathy, were reviewed. Therapy and outcome were evaluated by telephone questionnaire of owners, one to five years after diagnosis. A standard questionnaire developed for the study was used.

Radiographs and magnetic resonance imaging

Consensus review of the radiograph and MRI findings was performed by a board-certified radiologist (KP) and a first-year surgical resident (SK) using imaging software[a].

Radiographically, the fabellae and the stifle joint in general were examined for arthritic changes. The presence of joint effusion, subluxation of the tibia, abnormalities of the patella, and other changes were noted. A subjective scoring system (0 = no abnormality, 1 = mild changes, 2 = moderate changes, 3 = severe changes) was used for grading of the findings.

Magnetic resonance imaging of three patients was performed using a 1.0 Tesla scanner[b] and in 13 patients using a 0.2 Tesla scanner[c]. A solenoid coil was utilized. Slice thickness varied from 1 to 4 mm, adjusted to the size of the dog. Sagittal and dorsal slices were available in all cases, and transverse slices in 15 cases.

T1-weighted sequences pre- and post-intravenous application of contrast medium[d,e], T2, short tau inversion recovery (STIR), and proton density-weighted (PD) sequences were performed. Magnetic resonance imaging was performed under general anaesthesia. Patients were positioned in lateral, dorsal, or sternal recumbency.

The images were assessed using a subjective scoring system. Changes in signal intensity – relative to the surrounding muscle – were scored as iso-, hyper-, or hypointense, or mixed (both hyper- and hypointense). The extent of altered signal and contrast enhancement of the lateral and medial head of the gastrocnemius muscle was scored as not present, mild, moderate, or severe. Similarly, alterations of the lateral and medial fabellae, pathologies of the cranial and caudal cruciate ligament or the lateral and medial meniscus, the presence of joint effusion, and subjective changes in the volume of the gastrocnemius muscle were evaluated.

Statistical analysis

Descriptive statistics were performed for signalment (age, weight, sex, and breed), duration of lameness, affected side, initial trauma, clinical and imaging findings, therapy, and outcome.

To detect statistical correlations between imaging variables, rank correlation analysis was performed using commercially available software[f] to determine Spearman's rank correlation coefficient (r_s) and the corresponding p-value. P-values ≤0.05 were considered to be statistically significant.

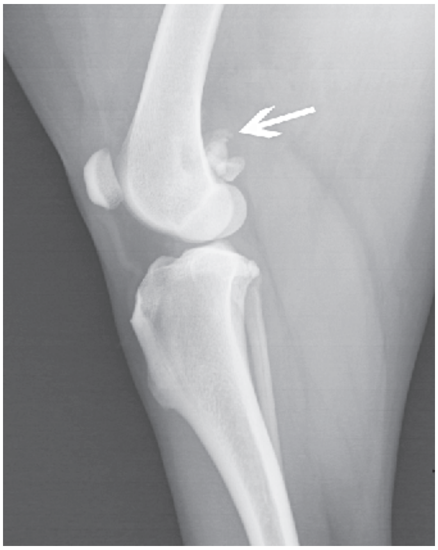

Figure 1 Mediolateral radiograph of the stifle of dog number 6. Note the moderate, mildly irregular, but smooth new bone formations surrounding the lateral fabella (arrow).

Results

Animals

From 2009 to 2014, 16 dogs were diagnosed with gastrocnemius musculotendinopathy using MRI; these included six Australian shepherds, two Bernese mountain dogs, and one of each of the following breeds: Labrador Retriever, Golden Retriever, Entlebucher Mountain Dog, Berger des Pyrénées, Cão da Serra de Aires, Airedale Terrier, Irish Soft Coated Wheaten Terrier, and mixed breed. Two of them were sporting dogs.

Six dogs were male (three neutered) and 10 were female (eight neutered). Mean age was seven years (range: 4–12 years) and mean body weight was 28.4 kg (range: 15–46.7 kg).

Dog number 12 had undergone a modified Maquet procedure surgery for a partial tear of the cranial cruciate ligament four months before diagnosis of gastrocnemius musculotendinopathy. An overview of the examined patients is given in ►Appendix Table 1 (Available online at www.vcot-online.com).

Anamnesis

Lameness before presentation was noted for up to one week in two dogs, up to two weeks in two dogs, up to four weeks in five dogs, and for more than four weeks in six dogs. In one dog, lameness was present for "several weeks" before presentation, but the exact duration was not noted. The left hindlimb was affected in nine dogs, and the right hindlimb in seven dogs. Initial trauma was noted in four dogs.

a OsiriX v.3.9.1.: Pixmeo Sarl, Geneva, Switzerland
b Gyroscan Intera: Phillips, Hamburg, Germany
c Vet-MR: Esaote, Köln, Germany
d Gadolinium-DTPA Dotarem 0.01 mmol: Guerbet, Sulzbach (Taunus), Germany
e Omniscan: GE-Healthcare, München, Solingen und Berlin, Germany
f SPSS software: IBM Deutschland GmbH, Ehningen, Germany

Table 1 Magnetic resonance imaging findings. **A)** Extension of the altered MRI signal of the gastrocnemius muscle, echogenicity of the altered signal, and uptake of contrast media. **B)** Further changes of the stifle joint.

A					
Lateral head of the gastrocnemius muscle	**Extension of signal**				
		No altered signal (n)	**Mild (n)**	**Moderate (n)**	**Severe (n)**
	T1, N = 16	0	10	6	0
	T2, N = 14	0	1	12	1
	STIR, N = 16	0	2	12	2
	PD, N = 4	0	2	2	0
	CM, N = 10	0	2	7	1
	Intensity				
		Isointense (n)	**Hyperin-tense (n)**	**Hypoin-tense (n)**	**Hyper- and hypointen se (n)**
	T1, N = 16	0	12	3	1
	T2, N = 14	0	12	1	1
	STIR, N = 16	0	15	1	0
	PD, N = 4	0	4	0	0
	Amount of contrast media uptake				
		No uptake (n)	**Mild (n)**	**Moderate (n)**	**Severe (n)**
	CM, N = 10	0	10	0	0
Medial head of the gastrocnemius muscle	**Extension of signal**				
		No altered signal (n)	**Mild (n)**	**Moderate (n)**	**Severe (n)**
	T1, N = 16	14	1	1	0
	T2, N = 14	6	6	1	1
	STIR, N = 16	10	3	2	1
	PD, N = 4	3	1	0	0
	CM, N = 10	9	1	0	0
	Intensity				
		Isointense (n)	**Hyperin-tense (n)**	**Hypoin-tense (n)**	**Hyper- and hypointen se (n)**
	T1, N = 16	14	2	0	0
	T2, N = 14	6	7	1	0
	STIR, N = 16	10	5	1	0
	PD, N = 4	3	0	1	0
	Amount of contrast media uptake				
		No uptake (n)	**Mild (n)**	**Moderate (n)**	**Severe (n)**
	CM, N = 10	9	1	0	0

N = number of dogs with available data; n = number of affected dogs. **MRI sequences:** T1 = MRI sequence T1; T2 = MRI sequence T2; STIR: short-tau inversion recovery; PD = proton density; CM = contrast medium.

B				
Changes of the lateral and medial fabella				
	No alteration	**Mild**	**Moderate**	**Severe**
Lateral fabella N = 16	11	4	1	0
Medial fabella N = 16	13	3	0	0
Changes of the cranial and caudal cruciate ligament				
	No alteration	Partial tear	Complete tear	
Cranial cruciate ligament N = 16	14	2	0	
Caudal cruciate ligament N = 16	15	1	0	
Changes of the lateral and medial meniscus				
	No alteration	Mild	Moderate	Severe
Lateral meniscus N = 16	15	1	0	0
Medial meniscus N = 16	15	1	0	0
Stifle joint effusion				
	Not present	Mild	Moderate	Severe
Stifle joint effusion, N = 16	13	1	2	0

N = number of dogs with available data; n = number of affected dogs.

Thirteen dogs had been treated previously by the referring veterinarian. In seven cases, non-steroidal anti-inflammatory drugs were used.

Clinical findings

At initial presentation, 13 dogs were clinically lame and three were not. Thirteen patients showed signs of pain on examination of the affected stifle joint; in the remaining three patients, this was not recorded. Seven patients had palpable joint effusion and four did not; in five patients, this was not recorded. The cranial drawer test and tibia compression test were negative in 12 patients, positive in two, and not recorded in two.

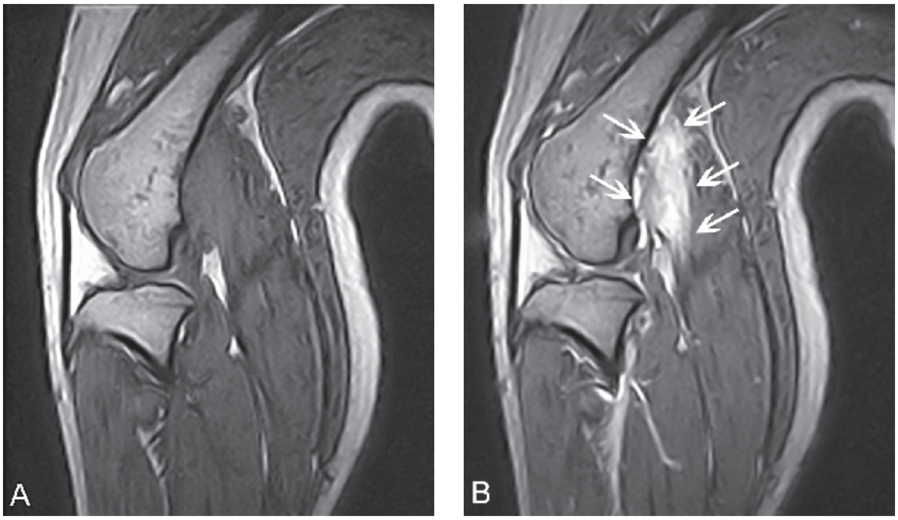

Figure 2 **A)** Pre- and **B)** post-contrast T1 weighted sagittal magnetic resonance image of the stifle of dog number 16. Extensive contrast uptake in the proximal aspect of the gastrocnemius muscle is visible (arrows).

Radiographs

In 14 dogs, mediolateral and craniocaudal radiographs were available. In dog number 4, no radiographs were obtained. In dog number 15, only a mediolateral radiograph was available.

Eight dogs had no abnormalities of the lateral fabella, while mild, moderate, and severe new bone formation was seen in four, two, and one dog, respectively (►Figure 1). Thirteen dogs showed no changes to the medial fabella, one dog showed mild changes, and one dog showed moderate changes. As to the stifle joint in general, 11 dogs had no arthritic changes, three had mild arthritis, and one had moderate arthritis. Two dogs showed mild radiographic signs of joint effusion, and one showed moderate signs. Subluxation of the tibia was not noted in any of the dogs. Alterations of the patella, such as the position on the lateral ridge of the femoral trochlea, were noted in three dogs.

Magnetic resonance imaging

The results of the MRI evaluations are summarized in ►Table 1.

With T1 imaging, before application of the contrast medium, a hyperintense signal was found in the lateral head of the gastrocnemius muscle in 12 dogs (►Figure 2A). The signal was hypointense in three dogs, and both hyper- and hypointense areas were found in one dog. The extent of the signal was mild or moderate. Fourteen dogs showed no altered signal in the medial head of the gastrocnemius muscle. In two dogs, a hyperintense signal of mild or moderate extent was found.

In 10 patients, MRI was also performed following intravenous application of a contrast medium (►Figure 2B). In all cases, mild uptake of the contrast medium was visible in the lateral head of the gastrocnemius muscle. The extent of contrast medium uptake was mild in two cases, moderate in seven cases, and severe in one case. In the medial head, mild uptake of the contrast medium was found in only one dog.

With T2 weighted imaging, 12 patients showed hyperintense signal in the lateral head of the gastrocnemius muscle (►Figure 3). One patient showed a hypointense signal, and another showed both hyper- and hypointense signal. The extent of the signal was mild in one, moderate in 12, and severe in one case(s). In the medial head, seven dogs showed a hyperintense signal, and one showed a hypointense signal.

A fat-suppressed short tau inversion recovery (STIR) sequence was performed in all patients, revealing a generally hyperintense signal with moderate extent in the lateral head (►Figure 4). In the medial head, the STIR sequence revealed hyperintensity in five dogs and hypointensity in one dog.

Four patients were also examined using a proton density (PD) sequence, which revealed hyperintense signal of mild-to-moderate extent in the lateral head of the gastrocnemius muscle. In the medial head,

Figure 3 T2 weighted sagittal magnetic resonance image of the stifle of dog number 16. The proximal aspect of the gastrocnemius muscle shows a diffuse and partially ill-defined moderate hyperintensity (arrows).

Figure 4 Short tau inversion recovery in sagittal orientation of the stifle of dog number 16. The proximal aspect of the gastrocnemius muscle shows a diffuse and well-defined severe hyperintensity (arrows).

one dog showed a hypointense signal in the PD sequence.

No changes in the volume of the gastrocnemius muscles were noted. A partial tear of the cranial cruciate ligament was found in two dogs, and alterations of the caudal cruciate ligament and of the medial or lateral meniscus were each found in one dog (▶Table 1B).

▶Table 2 shows the results of the rank correlation analysis that detected correlations between imaging variables.

Therapy

Owners were advised to restrict exercise for their dogs for various periods of time, to administer analgesics, and to perform physiotherapy. The following data concerning therapies performed at home were verified via telephone contact with the owners. Two owners (of dog numbers 1 and 2) could not be contacted via telephone; follow-up data were therefore not available. In dog number 14, a tibial tuberosity advancement was performed because of suspected rupture of the cranial cruciate ligament. Consequently, only the data concerning clinical examination and diagnostic imaging findings, but not the follow-up data, were included in the statistical evaluation.

One dog rested for up to one week, two dogs for up to four weeks, seven dogs for up to six weeks, and three dogs for more than six weeks. Seven dogs were treated with non-steroidal anti-inflammatory drugs, one with metamizole, and one with methocarbamole. Four dogs received no treatment with oral analgesics. Three owners administered oral analgesics as needed, and five owners administered them over specific periods of time (five days for one dog, and two to six weeks for four dogs). In five dogs, the exact time span of oral analgesics administration could not be evaluated. Professional physiotherapy was performed in nine dogs.

Outcomes

According to telephone consultations, 11 dogs returned to normal function, including canine sports, with no recurrence noted. Dog number 7 showed no improvement and was euthanatized 10 months after MRI of the stifle joint, but without further diagnostic evaluation, due to suspected concurrent intervertebral disc disease. Dog number 12 had previously undergone a modified Maquet procedure surgery four months before being diagnosed with gastrocnemius musculotendinopathy, and it continued to show intermittent lameness. Dog number 14 had tibial tuberosity advancement surgery, and it showed marked improvement but did not become completely free of lameness; this dog was euthanatized 12 months later due to unrelated disease. Two dogs (numbers 1 and 2) were lost to follow-up.

Table 2 Bilateral positive correlations between imaging variables detected by rank correlation analysis.

Variable x	Variable y	Spearman CC p-value Number
MRI: Lateral head of the gastrocnemius muscle, extension of signal, T2	**MRI:** Lateral head of the gastrocnemius muscle, extension of signal, STIR	0.817 0.000 14
MRI: Lateral head of the gastrocnemius muscle, extension of signal, STIR	**MRI:** Medial head of the gastrocnemius muscle, extension of signal, T2	0.606 0.022 14
MRI: Lateral head of the gastrocnemius muscle, extension of signal, STIR	**MRI:** Lateral head of the gastrocnemius muscle, extension of signal, T1	0.516 0.041 16
MRI: Medial head of the gastrocnemius muscle, extension of signal, T2	**MRI:** Medial head of the gastrocnemius muscle, extension of signal, STIR	0.619 0.018 14
MRI: Medial head of the gastrocnemius muscle, extension of signal, STIR	**MRI:** Joint effusion	0.613 0.012 16
MRI: Medial head of the gastrocnemius muscle, amount of contrast media uptake	**MRI:** Medial head of the gastrocnemius muscle, echogenicity, T1	1.000 0.000 10
MRI: Alterations of the lateral fabella	**MRI:** Joint effusion	0.730 0.001 16
Radiographs: Alterations of the lateral fabella	**MRI:** Joint effusion	0.615 0.015 15
Radiographs: Alterations of the lateral fabella	**MRI:** Alterations of the lateral fabella	0.645 0.009 15
Radiographs: Joint effusion	**MRI:** Joint effusion	0.661 0.007 15

MRI = magnetic resonance imaging; CC = correlation coefficient

Discussion

According to previous reports, musculotendinopathy of the gastrocnemius muscle is a disease occurring in athletic dogs, with Border Collies being the breed most commonly affected (1, 2). The disease also occurs in humans, most commonly due to sudden stop-and-go movement or turns during athletic activity (5–7).

In contrast, we diagnosed the disease in 16 dogs aged from four to 12 years and of various middle-to-large breeds, most of which were family dogs and not used for canine sport activities.

Inciting trauma was not observed in most of our patients. Palpation of the stifle joint was usually painful, but instability was not present in most cases. These findings are in accordance with the other reports in the literature (1, 2). Additionally, seven of our patients had palpable joint effusion.

Myotendinous strain due to excessive tension resulting in gastrocnemius musculotendinopathy can be acute or chronic (2). Four of our patients showed lameness for up to one or two weeks, and 12 were lame for a longer period of time.

Osteophyte formation at the lateral fabella and mineralizations at the origin of the gastrocnemius muscle have been described in affected dogs (1, 2). We found corresponding changes in seven dogs. Osteophyte formation at the medial fabella or arthritic changes of the stifle joint in general were uncommon among the dogs of this study, with only two and four dogs affected, respectively. Using MRI, mild or moderate alterations of the lateral fabella were found in five dogs, and mild alterations of the medial fabella were found in three dogs (▶Table 1B). These mineralizations or osteophyte formations indicated chronicity of the process (2). Periosteal reactions on the caudal aspect of the femur and the fabellae develop due to repeated microtrauma and avulsion of tendon fibres (8, 9). Dystrophic calcification due to mechanical stress can occur in the muscle next to the fabellae (8).

Magnetic resonance imaging examination of the gastrocnemius muscle revealed signs of inflammatory oedematous change that were subacute to chronic. In the T1 sequence, we found a hyperintense signal in the lateral head of the gastrocnemius muscle in 12 dogs, and a hypointense or a both hyper- and hypointense signal in four. Stahl and colleagues also found hyperintense T1 signal intensity in nine dogs (2). In contrast, Fiedler and colleagues described hypointense areas at the origin of the lateral gastrocnemius head (1). An explanation for this difference in signal intensity is stage of the disease. T1 hypointensity can indicate oedematous change, and thus represents a subacute process (1, 10). On the other hand, T1 hyperintensity can be due to fat cell infiltration, and thus represents a chronic process (1, 10). As most of the patients in the present study had a history of chronic lameness, the clinical findings fit well with the MRI findings.

As in cases described by others, we found uptake of contrast medium in the lateral head of the gastrocnemius muscle (1, 2). This can be interpreted as an active process, namely, a sterile inflammatory process (1, 2).

In the T2, STIR, and PD sequences, we generally found a hyperintense signal in the lateral head of the gastrocnemius muscle. This is compatible with the findings of other authors, and can be interpreted as oedematous change (1, 2, 10).

Peracute or chronic bleeding into a muscle is a potential differential diagnosis for hyperintensity in fluid-sensitive sequences and hypointensity in T1. If differentiation is necessary, a T2* sequence can be used (1). Another differential diagnosis for gastrocnemius musculotendinopathy due to myotendinous strain is muscle contusion secondary to direct trauma, leading to subcutaneous fluid accumulation. Differentiation via MRI might be difficult, as both conditions result in an increased signal intensity in fluid-sensitive sequences (2, 10).

The medial head of the gastrocnemius muscle was also examined. In individual patients, hyper- to hypointense signal intensity could be detected in all sequences performed. Uptake of the contrast medium was found in one dog. It was concluded that altered signal behaviour was not limited to the lateral head of the gastrocnemius muscle, and therefore that the medial head should be evaluated, as it can also be affected by the disease (although generally to a lesser extent). Rank correlation analysis revealed several correlations between the extent of the altered signal in different sequences. Similarly, positive correlations were found between the signal intensity in T1 sequences and the degree of enhancement on post-contrast sequences (▶Table 2). Thus, not all sequences performed in this study have to be carried out in order to diagnose gastrocnemius musculotendinopathy. If gastrocnemius musculotendinopathy is suspected in a clinical patient, we recommend a combination of T1- pre- and post-contrast administration and T2-weighted sequences, completed by a fat-suppressed sequence such as STIR to highlight changes in subtle cases.

Joint effusion detected by MRI was significantly correlated with alterations of the lateral fabella (▶Table 2) and can be interpreted as evidence for a fulminant course of disease. Importantly, no negative correlations were found between patient outcome and recurrence with clinical, radiographic, or MRI features.

Gastrocnemius musculotendinopathy develops because of repeated myotendinous strain to the origin of the gastrocnemius muscle (4). In general, musculotendinopathies can be categorzed as stretch injuries (grade I), partial tears (grade II), or complete tears (grade III). They can be classified clinically on the basis of the degree of muscle function loss or the extent of the lesion on MRI examination (11, 12). The dogs in this report showed lesions of grades I–II, which is in accordance with the results of others (1, 2).

As pathology of the cranial cruciate ligament and concurrent meniscal disease are differential diagnoses for gastrocnemius musculotendinopathy, MRI images were also investigated for abnormalities of these structures (▶Table 1B) (1).

An exact diagnosis of lameness is essential, as the appropriate therapy differs tremendously, with surgical procedures like tibia plateau levelling osteotomy or tibial tuberosity advancement being most commonly performed in cases of a ruptured cranial cruciate ligament (13).

Another differential diagnosis for gastrocnemius musculotendinopathy is avulsion of the lateral, medial, or both heads of the gastrocnemius muscle (9, 14, 15). In this case, dogs show severe lameness and often a plantigrade stance, and swelling can also be noted (9, 15).

As mentioned above, the therapy recommended to our patients consisted of exercise restriction, administration of analgesics like non-steroidal anti-inflammatory drugs, and professional physiotherapy. A limitation of our study is that the time span of restricted exercise and administration of analgesics varied, but most dogs for which follow-up was available rested for six weeks or longer. No recurrence of lameness and return to full function, including athletic activities, was noted in 11 out of 13 patients, for which follow-up was available (84.6%). These results are in accordance with other cases described in the veterinary literature (1, 2). In humans, a recurrence rate of only 0.7% after conservative therapy is reported (6). This study, however, included 720 human patients; thus, the recurrence rate cannot be directly compared to that in our rather small study population.

Obviously, the relatively small number of patients and the retrospective study design are limitations of the present study. As patients from two referral centres were included, different MRI imaging protocols were used, and images were obtained by two different magnetic resonance scanners. Patient anamnesis was heterogeneous, and details of treatment protocols varied between individuals. Due to these limitations, only descriptive statistical evaluations were possible. Altogether, further studies are necessary to overcome these restrictions.

In conclusion, gastrocnemius musculotendinopathy is a potential diagnosis in dogs with chronic hindlimb lameness. The most important differential diagnosis is cranial cruciate ligament rupture. Dogs of various middle-to-large breeds can be affected, and athletic activity is not a necessary cause. Both the lateral and the medial head of the gastrocnemius muscle can be involved, with emphasis on the lateral head. MRI shows oedematous changes and uptake of contrast agents in the region of the origin of the gastrocnemius muscle. Conservative treatment generally results in return to full function.

Conflict of interest

The authors confirm that they do not have any conflict of interest.

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