STANDARD ARTICLE

Journal of Veterinary Internal Medicine

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Grading of oligodendroglioma in dogs based on magnetic resonance imaging

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Abstract

Background: Oligodendroglioma (OG) accounts for 22% of primary brain tumors in dogs. Oligodendroglioma in dogs is graded as low-grade (II) or high-grade (III), based on the presence of microvascular proliferation and necrosis.

Objective: To investigate if magnetic resonance imaging (MRI) features differ between OG II and III in dogs.

Animals: Thirty-two dogs with histological diagnosis of intracranial OG and MRI.

Methods: Retrospective descriptive study. Histology was reviewed to grade OG according to the revised classification. Brain MRI results were reviewed following criteria including contrast enhancement (CE) pattern, presence of cystic structures, gradient-recalled-echo (GRE) signal voids, and necrosis based on signal intensity, as well as diffusion-weighted imaging characteristics. The MRI features were compared between OG II and III using Fisher's exact tests and logistic regression models.

Results: Histology identified 8 dogs with OG II (25%) and 24 with OG III (75%). All OG III showed moderate-to-marked CE including 18/24 (75%) with a ring pattern. These features were not seen in OG II. Heterogeneity, cystic structures, GRE signal voids, and necrosis were associated with OG III. No difference in diffusion characteristics was detected between OG II and III.

Conclusion and Clinical Importance: Moderate-to-marked CE and ring pattern were present in dogs with OG III but not in OG II. The presence of cystic structures, GRE signal voids, and necrosis was strongly associated with OG III. Although the importance of brain tumor grading in dogs with regard to prognosis and treatment options remains unknown, the results indicate that MRI reflects the histological features used for grading OG in dogs.

KEYWORDS
advanced imaging, central nervous system, dog, glioma, tumor grade

1 | INTRODUCTION

Oligodendroglioma (OG) is a type of glioma that accounts for 22% of primary brain tumors in dogs.[1] Boxers, French Bulldogs, and Boston Terriers have a significantly increased risk of OGs.[1] Boxers represent 36%[2] to 56%[3] and Boston Terriers up to 31%[3] of dogs with OG. Magnetic resonance imaging (MRI) is the imaging modality of choice for intracranial neoplasia.[4] Typically, MRI features of OG in dogs include the presence of a well-marginated, round or ovoid intraaxial mass lesion, with T1-weighted (T1w) hypointense and T2-weighted (T2w) hyperintense signal relative to gray matter, and variable degree of contrast enhancement (CE).[3,5-8] Additional inconsistent MRI features such as cystic structures, gradient-recalled echo (GRE) signal voids, and perilesional edema also are reported.[3,5-8]

According to the World Health Organization (WHO) classification, the biological behavior of gliomas correlates with the grade that is histologically defined.[9] In humans, low-grade gliomas have been associated with longer survival time[10] and better response to treatment.[11] In dogs, previous studies did not identify any MRI features that allow for clear differentiation between glioma types and grade,[3,6,7] and treatment routinely is carried out without histological confirmation.[12,13] In accordance with the WHO classification, recent revision of OG classification in dogs defined 2 grades based on histological characteristics: the low-grade or grade II (OG II), and the high-grade or grade III (OG III).[14] The presence of at least 1 of 2 key histological features, microvascular proliferation and necrosis, determines high-grade OG (OG III).[14] In the absence of these 2 features, high number of mitotic figures, nuclear pleomorphism, anisokaryosis, anisocytosis, or cellular atypia are used to define OG III.[14] Previous literature in humans suggested a correlation between the presence of vascular proliferation and CE on MRI.[15,16] In dogs, OG is more common than astrocytoma and its binary classification is simpler than for astrocytoma, which consists of 3 grades.[14] Presumptive diagnosis of OG may be attempted with the aforementioned imaging features and signalment. Finding reliable MRI criteria of high- or low-grade OG would allow future prospective studies grouping dogs based on a presumptive diagnosis and testing their response to treatment and survival time. In addition, information from MRI images serves as a surrogate for histopathology in cases involving brain biopsy specimens.[17] Knowledge about the association of MRI features and OG grading could be helpful, especially when the biopsy samples are inconclusive regarding tumor grade.

Our aims were therefore: (a) to describe MRI features of dogs with confirmed histological diagnosis of intracranial OG and (b) to investigate associations between MRI features and grading in intracranial OG in dogs. Our hypothesis was that CE would be an indicator of microvascular proliferation and, therefore, a discriminative MRI feature of high-grade OG.

2 | MATERIALS AND METHODS

2.1 | Case selection and inclusion criteria

The neuropathology database of Vetsuisse Faculty, Bern University Switzerland was searched for dogs with histological diagnosis of intracranial OG between November 2004 and December 2019. The inclusion criteria were: (a) a definitive histological diagnosis of intracranial OG based on biopsy or necropsy examination and (b) an available MRI examination of the brain. The study was conducted in accordance with the local ethical regulations.

2.2 | Neuropathology

Cases were reviewed by a board-certified veterinary pathologist (AO). Tumor type and grade were established according to the most recent glioma classification system.[9,14,18] Diagnosis of OG relied on key nuclear features: small round uniform hyperchromatic nuclei, and clear perinuclear halos giving a "fried-egg" appearance.[9,14,18] Additional architectural growth patterns (e.g., honeycomb arrangement of evenly spaced tumor cells, delicate branching capillaries resembling chicken-wire, mucinous background and lakes) also were used to facilitate the diagnosis of OG.[9,14,18] Diagnosis of OG III was based on the presence of necrosis, microvascular proliferation, or both.[14] In absence of these 2 criteria, tumors were graded as high-grade if a high number of mitotic figures (>6 mitoses per 10 high-power fields), overt nuclear pleomorphism, anisokaryosis, anisocytosis, cellular atypia or some combination of these features were present.[14]

2.3 | MRI features evaluation

Magnetic resonance imaging studies were randomized, anonymized, and independently reviewed by a board-certified radiologist (AD) who was aware that lesions were OGs but blinded to their histological grade. Open-source digital imaging and communications in medicine commercial viewing software (Horos v3.3.6) was used to review the MRI studies. A predefined list of MRI criteria adapted from previous literature with specific instructions for some criteria, was used to describe the OGs. It included tumor origin (intraaxial or extraaxial), border definition (ill-defined or well-defined), margins (smooth or irregular), and shape (ovoid or amorphous).[7] Tumor lateralization was described as right, left, or midline. Neuroanatomic location was recorded as: cerebrum, diencephalon, caudate nucleus, brainstem, or ventricle. When the neuroanatomic location was cerebrum, the affected cerebral lobes were specified (i.e., frontal, parietal, temporal, piriform), and >1 cerebral lobe could be affected. The predominant signal intensity of the tumor relative to gray matter on T1w, T2w, and fluid attenuated inversion recovery (FLAIR) was noted.[3] The tumor was considered heterogeneous if it had mixed signal intensity in any of the sequences. The predominant tumor signal intensity on diffusion-weighted imaging (DWI) was reported as hyperintense, isointense, or hypointense, and the apparent diffusion coefficient (ADC) was described as low or high, both relative to normal gray matter. Restricted diffusion was considered when areas of low ADC also showed hyperintensity in the b800 diffusion-weighted images. When applicable, the signal intensities of the tumor center and periphery were described separately.

Contrast enhancement was assessed on T1w sequences and, if available, subtraction images. The degree of CE was classified as none, mild, or moderate-to-marked, based on the most severely enhancing

portion of the tumor.[8] If CE was noted, its pattern was described as focal, uniform, nonuniform,[7] or as a ring pattern.[3,6] A ring pattern of CE was specified as partial or complete,[3,6] and its location was further described as central or peripheral.

Intratumoral cystic structures were reported when either single cyst or multiple intratumoral fluid accumulations were identified.[19] Peritumoral edema was defined as white matter T2w and FLAIR hyperintensity at the borders of the tumor, and subjectively graded as mild, moderate or marked. Signs of mass effect and increased intracranial pressure[20] were reported.

Signal voids in gradient-recalled-echo (GRE) T2*-weighted (T2*w) sequence consistent with hemorrhage or mineralization were recorded.[3] Presence of necrosis was decided based on an irregularly bordered component within the tumor with low signal on T1w and high signal on T2w, that did not enhance with contrast medium.[21] Local extension was assessed by the presence and degree of contact with and possible infiltration of the ventricles and meninges.[3,7]

Three criteria were considered as possible indicator for distant metastatic spread: distant ependymal enhancement, distant meningeal enhancement, and presence of syringomyelia. Other reported features were the presence of hydrocephalus internus, and adjacent bone changes.

2.4 | Topographical correlation between neuropathology and MRI

After histological grading and blinded MRI evaluation, histological slides were reviewed side-by-side with the MRI images, with special attention to the areas of CE on MRI and matching areas on the histological slides. For all areas with CE on MRI, it was noted if microvascular proliferation (central, peripheral incomplete, peripheral complete, multifocal), hypertrophic vessels, and Scherer structures (perineuronal, subarachnoidal, perivascular) were present.

2.5 | Statistical analysis

For our purpose, we considered the tumor grade (OG II vs OG III) determined by histology as the binary outcome variable and each MRI criterion (absence vs presence of each feature) as an explanatory variable. Contingency tables of the outcome variable and each MRI criterion were examined and tested for association using Fisher's exact tests (NCSS12 v12.0.9 www.ncss.com). For criteria with significant test results, odds ratios (OR) were calculated by means of logistic regression models. The significance level was set to $P < .05$.

3 | RESULTS

3.1 | Signalment

Thirty-two dogs, including 14 males (7 intact and 7 castrated) and 18 females (4 intact and 14 spayed), met the inclusion criteria. The mean age (years) was 7.8 ± 2.4 (range, 3.0-12.0). The most common breeds were French Bulldog (n = 10), Boxer (n = 7), and Labrador
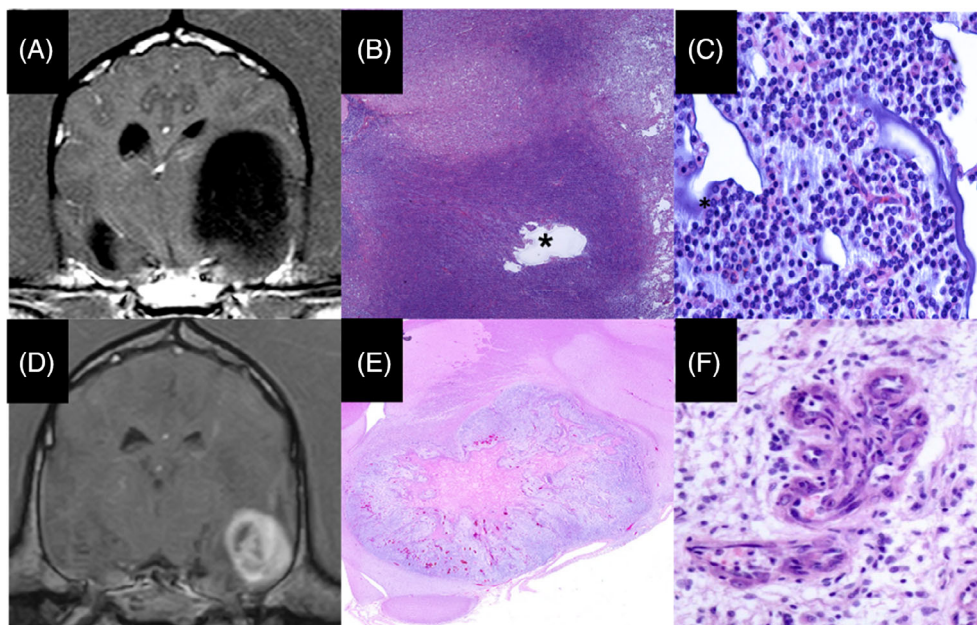
FIGURE 1 Transverse postcontrast T1-weighted magnetic resonance image of a homogeneous, nonenhancing canine low-grade oligodendroglioma (OG) (A) with corresponding histology (B and C) and of a strongly ring-enhancing high-grade OG (D) with corresponding histology (E and F). (A) shows the lack of contrast enhancement (CE) in low-grade OG. In histology, low magnification of the same low-grade OG (B) shows a dense population of neoplastic cells infiltrating the neuropil and the subarachnoid space. Necrosis is absent, while a mucinous lake (asterisk) is present in the center of the mass. High magnification shows layers of densely packed cells with scant cytoplasm and hyperchromatic nuclei, embedded in abundant mucinous background and supported by delicate "chicken wire" capillaries. Note the absence of necrosis and microvascular proliferation. Marked peripheral ring of CE visible in a high-grade OG (D) and correlated with central necrosis (E) and presence of peripheral microvascular proliferation with hypertrophic glomeruloid capillaries (F) in histology

TABLE 1 Percentages and counts (in brackets) of the evaluated MRI features in 32 dogs with histologically confirmed OG

	Grade	
	OG	OG
MRI features	II (n = 8)	III (n = 24)
Origin		
Intraaxial (27)	87.5% (7)	83.3% (2)
Extraaxial (5)	12.5% (1)	16.7% (4)
Localization		
Cerebrum (28)	100.0% (8)	83.3% (20)
Diencephalon (1)	.0% (0)	4.2% (1)
Caudate nucleus (1)	.0% (0)	4.2% (1)
Brainstem (1)	.0% (0)	4.2% (1)
Ventricle (1)	.0% (0)	4.2% (1)
Affected cerebral lobes[a]		
Frontal lobe (16)	25.0% (2)	58.3% (14)
Piriform lobe (12)	62.5% (5)	29.2% (7)
Temporal lobe (8)	62.5% (5)	12.5% (3)
Parietal lobe (1)	12.5% (1)	.0% (0)
Border definition		
Well-defined (24)	50.0% (4)	83.3% (20)
Ill-defined (8)	50.0% (4)	16.7% (4)
Margins		
Smooth (28)	87.5% (7)	87.5% (21)
Irregular (4)	12.5% (1)	12.5% (3)
Shape		
Ovoid (27)	75.0% (6)	87.5% (21)
Amorphous (5)	25.0% (2)	12.5% (3)
Lateralization		
Right (18)	50.0% (4)	58.3% (14)
Left (11)	37.5% (3)	33.3% (8)
Midline (3)	12.5% (1)	8.3% (2)
Signal		
Homogeneous (9)	75.0% (6)	12.5% (3)
Heterogeneous (23)	25.0% (2)	87.5% (21)
T2w intensity		
Hyperintense (32)	100.0% (8)	100.0% (24)
T1w intensity		
Hypointense (32)	100.0% (8)	100.0% (24)
FLAIR intensity		
Hyperintense (26)	87.5 (7)	79.2% (19)
Hyperintense in the periphery (6)	12.5% (1)	20.8% (5)
GRE signal voids[b]		
Yes (16)	12.5% (1)	88.2% (15)
No (9)	87.5% (7)	11.8% (2)
Restricted diffusion (ADC, DWI)	.0% (0)	.0% (0)
Contrast enhancement		
Degree of CE		
None (3)	37.5% (3)	.0% (0)
Mild (5)	62.5% (5)	.0% (0)

TABLE 1 (Continued)

	Grade	
	OG	OG
MRI features	II (n = 8)	III (n = 24)
Moderate-to-marked (24)	.0% (0)	100.0% (24)
CE pattern		
Ring (18)	.0% (0)	75.0% (18)
Complete (16)	.0% (0)	66.7% (16)
Partial (2)	.0% (0)	8.3% (2)
Peripheral (13)	.0% (0)	54.2% (13)
Central (5)	.0% (0)	20.8% (5)
Focal (4)	50.0% (4)	.0% (0)
Nonuniform (7)	12.5% (1)	25.0% (6)
Intratumoral cystic structures		
None (10)	50.0% (5)	20.8% (5)
Single cyst (6)	12.5% (1)	20.8% (5)
Multiple ITFs (16)	25.0% (2)	58.3% (14)
Areas of necrosis (25)	37.5% (3)	91.7% (22)
Peritumoral edema		
None (6)	25.0% (2)	16.7% (4)
Mild (14)	37.5% (3)	45.8% (11)
Moderate (8)	25.0% (2)	25.0% (6)
Marked (4)	12.5% (1)	12.5% (3)
Contact with the ventricles[a]		
Yes (26)	75.0% (6)	83.3% (20)
No (6)	25.0% (2)	16.7% (4)
Ventricular distortion (29)	87.5% (7)	91.7% (22)
Ventricular invasion (6)	12.5% (1)	20.8% (5)
Meningeal contact[a]		
None (3)	12.5% (1)	8.3% (2)
Small (17)	25.0% (2)	62.5% (15)
Broad (12)	62.5% (5)	29.2% (7)
Precontrast signs of meningeal infiltration (3)	12.5% (1)	8.3% (2)
"Dural tail" sign (13)	50.0% (4)	37.5% (9)
Elevated ICP (18)	50.0% (4)	58.3% (14)
Other features[a]		
Distant ependymal enhancement (2)	.0% (0)	8.33% (2)
Distant meningeal enhancement (8)	25.0% (2)	25.0% (6)
Syringohydromyelia (10)	25.0% (2)	33.3% (8)
Hydrocephalus internus (19)	75.0% (6)	54.2% (13)
Adjacent bone changes (4)	.0% (0)	16.7% (4)

Abbreviations: ADC, apparent diffusion coefficient; CE, contrast enhancement; DWI, diffusion-weighted imaging; FLAIR, fluid attenuated inversion recovery; GRE, gradient-recalled echo; ICP, intracranial pressure; ITF, intratumoral fluid accumulation; MRI, magnetic resonance imaging; OG, oligodendroglioma.
[a]More than one possible criterion for a single case.
[b]GRE images were only available in 25 dogs.

retriever (n = 2). One dog of each of the following breeds also was included: Border terrier, Continental bulldog, Artois Hound, German

TABLE 2 Associations of MRI criteria with OG grade, P-values of Fisher exact tests

MRI criteria	Grade		
	OG II (n = 8)	OG III (n = 24)	P value
Signal			
Heterogeneity	25.0% (2)	87.5% (21)	.002
GRE signal voids[a]	12.5% (1)	88.2% (15)	.037
CE			
None	37.5% (3)	.0% (0)	.002
Moderate-to-strong CE	20.0% (1)	100.0% (24)	.000
Ring pattern	.0% (0)	75.0% (18)	.000
Cystic structures	37.5% (3)	79.2% (19)	.042
Areas of necrosis	37.5% (3)	91.7% (22)	.005

Abbreviations: CE, contrast enhancement; GRE, gradient-recalled echo; MRI, magnetic resonance imaging; OG, oligodendroglioma.
[a]GRE images were only available in 25 dogs.

FIGURE 2 Transverse T2-weighted (A), fluid attenuated inversion recovery (FLAIR) (B), precontrast T1-weighted (C), and postcontrast T1-weighted (D) magnetic resonance images of a high-grade canine oligodendroglioma. A well-defined, smoothly marginated, ovoid, intraaxial mass is visible in the left frontal lobe, surrounded by moderate perilesional edema (arrow). The mass has heterogeneous T2-weighted (A) and FLAIR (B) signal intensity with a central cystic structure, and presents a marked, complete, peripheral ring of contrast enhancement (D).
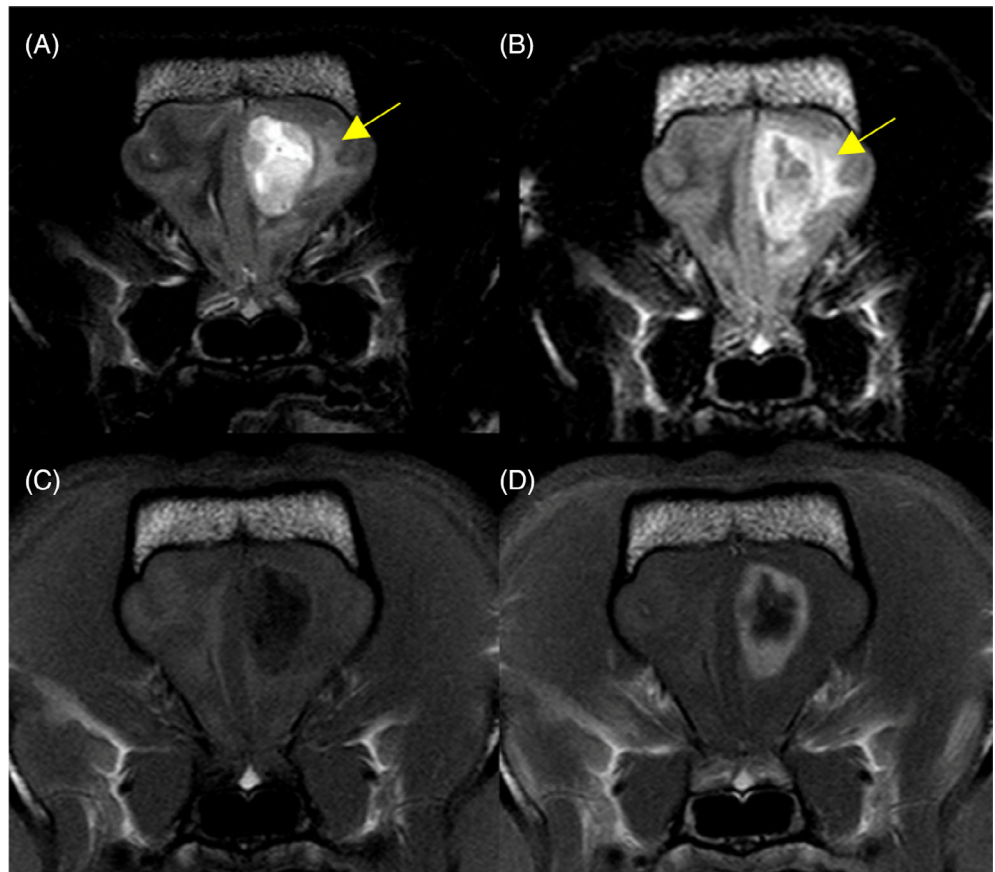
Shepherd dog, Bernese Mountain dog, Beauceron, Bolonka Zwetna, Bichon, Irish Water Spaniel, Pomeranian, Doberman Pinscher, Jack Russell Terrier, and mixed breed dog.

3.2 | Neuropathology

Among the 32 OGs that comprised our study population sample, 24/32 (75%) were OGs III and 8/32 (25%) were OGs II. The histological diagnosis was based on necropsy in 30/32 (93.8%) dogs, including 3 with concurrent necropsy brain biopsy, and on antemortem brain biopsy in 2/32 (6.5%) dogs. The mean time between MRI and necropsy was 0.5 days (range, 0-7). Both were performed on the same day in 26/30 cases, and they were 1, 3, 4 and 7 days apart, respectively, in the remaining 4 dogs. Microvascular proliferation was visible in all OGs III (100%), which meant that no other histological feature was required for discrimination between low- and high-grade OG in our sample.[14] All examined areas of moderate-to-marked CE on

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MRI matched areas where microvascular proliferation was found on histology (Figure 1).

3.3 | MRI features evaluation

All MRI studies were performed at the division of clinical radiology, Department of Clinical Veterinary Medicine, Vetsuisse Faculty, University of Bern, Bern, Switzerland, with a low-field MRI scanner in 7 dogs (Hitachi Airis II 0.3T, Hitachi Medical Systems, Düsseldorf, Germany), and 2 high-field MRI scanners (Philips Panorama HFO 1T, Philips Medical Systems, Nederland B.V., Best, the Netherlands and Philips Intera 1.5T, Philips Medical Systems, Nederland B.V., Best, the Netherlands) in 24 and 1 dog, respectively. All MRI studies but 1 included at least T2w fast spin echo (T2w FSE), FLAIR, and T1w spin echo sequences before and after IV administration of 0.5 mL/kg of gadoteric acid (Clariscan, 0.5 mmol/mL, GE Healthcare AG, Opfikon, Switzerland). In 1 case, no precontrast T1w sequence was available. A GRE sequence (T2*w) was available in 25/32 dogs. Diffusion-weighted imaging using a b-value of 800 s/mm^2 and ADC mapping were available in 17/32 dogs. The evaluated MRI features are presented in Tables 1. The most common MRI features were well-defined (28/32), ovoid (27/32), smoothly marginated (28/32), intraaxial (27/32) masses. The most common location was the cerebrum (28/32), and the most affected cerebral lobes were the frontal (16/30) and piriform (12/30) lobes. Most OGs were in close contact with the ventricles (26/32) and the meninges (29/32). Contrast enhancement was visible in 29/32 dogs and was assessed as moderate-to-marked in 24/29 and mild in 5/29. A ring pattern of enhancement was present in 18/29 dogs. In the b800 diffusion-weighted images, tumors were hypointense (9/17), hypointense with a hyperintense periphery (4/17), hyperintense (3/17), or isointense (1/17) relative to gray matter. All tumors (17/17) had high ADC values relative to normal gray matter.

3.4 | Association between MRI features and OG grade

All OGs III showed moderate-to-marked CE. All OGs without CE were OG II. All OGs with a ring enhancing pattern were OG III (Figure 2). Moderate-to-marked CE and a ring enhancing pattern were not seen in OG II cases (Figure 3). Tumor heterogeneity, and presence of areas of necrosis, GRE signal voids, and cystic structures were associated with OG grade (Fisher's exact tests, $P < .05$; Table 2). Tumor heterogeneity (OR, 21.00; 95% confidence interval [CI], 2.82-156.12; $P < .01$), and presence of areas of necrosis (OR, 18.33; 95% CI, 2.39-140.39; $P = .03$), GRE signal voids (OR, 11.67; 95% CI, 1.22-110.95; $P < .01$), and cystic structures (OR, 6.33; 95% CI, 1.11-36.00; $P = .04$) were more likely to be present in OG III cases. None of the other imaging features was associated with grade.

4 | DISCUSSION

Our study supports the use of MRI to help differentiate between low- and high-grade OG in dogs. In our sample, all high-grade OGs had moderate-to-marked CE. A ring pattern of CE was seen in most dogs with OG III (75%), whereas it was not observed in dogs with OG II, suggesting this CE pattern is very specific for high-grade OG in dogs. This finding is in accordance with previous studies in dogs suggesting that CE is an important means of classifying gliomas according to
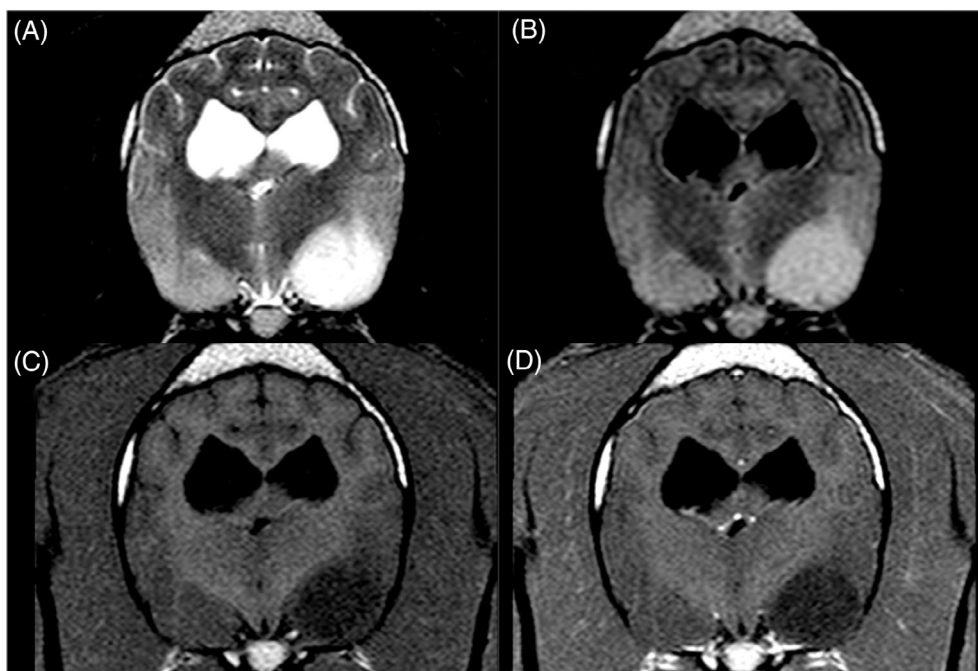

FIGURE 3 Transverse T2-weighted (A), fluid attenuated inversion recovery (FLAIR) (B), precontrast T1-weighted (C), and postcontrast T1-weighted (D) magnetic resonance images of a low-grade canine oligodendroglioma. A well-defined, smoothly marginated, ovoid, intraaxial mass is visible in the left piriform lobe. The mass (A-D) has a homogeneous T2-weighted (A) and FLAIR (B) signal intensity and presents no contrast enhancement (D).

grade.[3,6,7] All high-grade OGs of our sample featured microvascular proliferation and are considered to have an incomplete blood-brain-barrier.[22] Based on the revised classification system,[14] the presence of microvascular proliferation is sufficient for an OG to be considered high-grade. The comparison of MRI with histology showed that areas of moderate-to-marked CE on MRI matched well with areas of microvascular proliferation. Therefore, our results support the hypothesis that moderate-to-marked CE could be an indicator of microvascular proliferation, thus indicating high-grade OG.

In contrast to OG III, OG II showed either no or mild CE. All OGs without CE were low grade OGs. This finding is in accordance with previous studies in which none to mild CE was associated with grade II gliomas.[3,6] In 5/8 OG II (80%), mild CE was seen but no microvascular proliferation was detected on histology. The mild enhancement might be a consequence of leakage or extravasation of contrast medium from adjacent vasculature which is another reported mechanism of CE on MRI.[23]

In addition to the severity and pattern of CE, our study identified other MRI features associated with OG III: precontrast tumor signal heterogeneity, presence of GRE signal voids, cystic structures, and areas of necrosis. These features previously have been described in gliomas, and association with high-grade glioma has been suggested but not confirmed.[3,6]

In humans, quantitative ADC values have high accuracy in separating high- from low-grade glioma.[24] In this species, ADC values <1.07 provide sensitivity and specificity of 79.7% and 60.0%, respectively, in determining high-grade gliomas.[25] This situation has not been established in veterinary medicine.[26] In our study, high- and low-grade OGs had similar diffusion characteristics, with none of the tumors showing restricted diffusion.

Our study focused specifically on MRI features of a group of histologically-confirmed OGs in dogs. In addition to describing their MRI characteristics, we identified specific imaging features in high-grade and low-grade OGs, respectively, that were not be identified in previous studies that did not separate OG from astrocytoma.[3,5-8] Although MRI has a reported sensitivity of 84.4% and specificity of 93.7% for diagnosing glioma in dogs,[27,28] distinction between glioma and other intracranial diseases or between OG and astrocytoma is challenging. Some MRI features identified in the OGs of our study however may be used to differentiate them from other lesions. For example, a caudal location in the occipital lobes, a hypointense signal on T2w and contralateral lesions were associated with granuloma over glioma.[29] Similarly, a homogeneous T1w/T2w signal intensity, a peripheral T2w/T2*w hypointense halo, and an even ring of CE were associated with ring-enhancing abscesses rather than gliomas.[30] The MRI characteristics of the OGs included in our study corroborate the findings applicable to gliomas. Regarding distinction between glioma and cerebrovascular accident, the signal intensity on diffusion-weighted sequences was the most important criterion. Contrary to cerebrovascular accidents, gliomas always featured unrestricted diffusion.[31] In all OGs with diffusion-weighted sequences included in our study, diffusion was not restricted and this finding emphasizes the importance of diffusion-weighted sequences in routine screening of intracranial lesions. A presumptive diagnosis of glioma therefore may be reached considering these key features in association with the animal's signalment. Distinguishing between OG and astrocytoma based on MRI remains challenging because of overlapping imaging characteristics.[7,27,28] Imaging features associated with astrocytoma were the presence of moderate to extensive peri-tumoral edema, lack of ventricular distortion, and isointense or hyperintense T1w signal intensity, whereas OG was in contact with the brain surface.[6] This last criterion also was identified in most of the dogs from our sample of confirmed OGs, of which 90.6% (29/32) featured contact with the meninges. Nonetheless, our results should not be extrapolated to astrocytomas because they may behave differently than OGs. Similar specific studies focusing on confirmed astrocytomas also should be conducted to test these hypotheses.

Recently, MRI features such as poor margin definition, irregular margin, presence of drop metastases, and T2w heterogeneity have been identified as risk factors for shorter survival in dogs with histopathological diagnosis of glioma, and drop metastases were exclusively present in high-grade OG.[7] In our sample, poorly defined and irregular margins as well as suspicion for metastases were more common in high-grade OG, but only tumor signal heterogeneity was significantly associated with high-grade OG.

The search for ante-mortem criteria for tumor grade prediction has been motivated mostly by the assumption that tumor grade would correlate with prognosis and response to treatment, as it does in human medicine where low-grade OG are associated with a better response to treatment.[9] In dogs, an association between the grade of glioma and its prognosis has been suggested but remains unproven, and treatment routinely is carried out without knowledge of glioma type or grade.[32-34]

To improve treatment options and provide adequate prognosis, we believe the grade of the tumor should be known antemortem, which can be determined by brain biopsy. Brain biopsy can be performed in combination with knowledge of the MRI findings, targeting regions of CE which we believe are most critical for establishment of the tumor grade. In our experience, the information provided by the present study also could be used in conjunction with brain biopsy when the latter provides the type but not the grade of glioma.

One limitation of our study is the relatively low number of OG II (n = 8) resulting in uneven ratio of high-to-low grade OG (24/8). This factor should be considered when conclusions are drawn from the statistical analysis. However, this uneven ratio reflects our hospital population and the relative frequency reported in previous studies.[1,3,6,7] Other limitations are the limited number of cases with available diffusion-weighted images, distortion from the diffusion images obtained using the 1T magnet unit, and lack of quantitative analysis of the ADC values. Future studies investigating the usefulness of DWI in predicting the grade of glioma should focus more on quantitative evaluation.

Our results support the idea of targeting areas of CE when performing stereotactic brain biopsy in cases of presumed glioma on MRI. The results emphasize MRI as a surrogate complementary to histology performed on brain biopsy samples to increase the diagnostic

value for grading of OG.[17] Prospective studies testing treatment response and survival time on 2 groups obtained based on the presumptive diagnosis of high- or low-grade OG should be considered.

5 | CONCLUSION

Based on our results, we conclude that contrast enhanced MRI is a useful noninvasive tool for ante-mortem prediction of the grade of OG in dogs, with moderate-to-marked CE or a CE ring pattern being strongly indicative of OG III. Additional features indicative of high-grade OGs are the presence of intratumoral cystic structures, GRE signal voids, and areas of necrosis. Although our study does not allow for drawing conclusions of grade if the type of glioma is not confirmed, the obtained information may be useful in the future to establish prognostic studies in dogs with intracranial glioma. Additional similar studies focusing on intracranial astrocytoma in dogs should be considered to identify differences and similarities concerning MRI-based grading of astrocytoma.

CONFLICT OF INTEREST DECLARATION
Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION
Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION
Authors declare no IACUC or other approval was needed.

HUMAN ETHICS APPROVAL DECLARATION
Authors declare human ethics approval was not needed for this study.

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