Comparison of clinical, endoscopic, and histologic features between dogs with chronic gastritis with and without lymphofollicular hyperplasia

Mathieu R. Faucher DVM

Vincent Biourge DVM, PhD

Alexander J. German BVSc, PhD

Valérie Freiche DVM, PhD

From the Department of Internal Medicine, Clinique Vétérinaire Alliance, 33300 Bordeaux, France (Faucher); Royal Canin Research Center, 30470 Aimargues, France (Biourge); Institute of Ageing and Chronic Disease and Institute of Veterinary Science, University of Liverpool, Neston CH64 7TE, England (German); and Department of Internal Medicine, Université de Paris-Est, École Nationale Vétérinaire d'Alfort, 94704 Maisons-Alfort, France (Freiche).

Address correspondence to Dr. Faucher (m.faucher@veterinaire-alliance.fr).

OBJECTIVE

To compare clinical, endoscopic, and histopathologic features between dogs with chronic gastritis (CG) with and without lymphofollicular hyperplasia (LFH).

ANIMALS

64 and 56 dogs with CG with (cases) and without (controls) LFH, respectively.

PROCEDURES

The medical record database of a referral clinic was searched to identify dogs that underwent endoscopic examination of the upper portion of the gastrointestinal tract and were subsequently determined to have CG with or without LFH between October 2006 and February 2011. Signalment and clinical, endoscopic, and histologic findings were compared between cases and controls. Logistic regression was used to identify factors associated with CG with LFH.

RESULTS

Compared with controls, cases were significantly younger and more likely to be of a brachycephalic phenotype. The proportions of dogs with a poor body condition or diarrhea were significantly lower and the proportions of dogs with inspiratory dyspnea, exercise intolerance, or hyperemia and discoloration of the gastric mucosa were significantly higher for the case group, compared with the control group. Inspiratory dyspnea, gastric mucosal hyperemia, and gastritis severity were positively associated, whereas poor body condition was negatively associated, with CG with LFH on multivariable logistic regression.

CONCLUSIONS AND CLINICAL RELEVANCE

The strong positive association between inspiratory dyspnea and CG with LFH suggested that the condition may be a consequence of an increase in negative intrathoracic pressure rather than a distinct clinical entity. Prospective studies are warranted to elucidate the mechanism by which inspiratory dyspnea contributes to the development of CG with LFH. (*J Am Vet Med Assoc* 2020;256:906–913)

Chronic gastritis is a commonly diagnosed condition in dogs evaluated for signs of chronic gastrointestinal disease.[1] After proper anamnestic, clinical, biological, and ultrasonographic evaluations have been conducted, diagnosis of CG is dependent on endoscopic examination of the upper portion of the gastrointestinal tract (upper gastrointestinal tract) and histologic evaluation of gastric biopsy specimens. Histologic findings are used to subclassify CG on the basis of the predominant cell infiltrate (ie, lymphocytic, plasmacytic, neutrophilic, eosinophilic, or granulomatous) and to determine whether there is concomitant LFH.[1] Architectural abnormalities (eg, atrophy, hypertrophy, fibrosis, edema, and ulceration) and the extent of inflammation help to better characterize gastritis. When foreign bodies, parasites, and systemic disease have been eliminated as the cause of gastritis, the inciting etiology is often deemed to be a reaction to dietary or bacterial antigens or occult parasitism. Gastritis is further characterized as diet responsive, antibiotic responsive, steroid responsive, or parasitic on the basis of the patient's response to treatment.[1]

Chronic gastritis with LFH is defined as the presence of a follicle-like aggregation of lymphoid cells in the lamina propria of the gastric wall.[2] The current veterinary literature contains little information regarding the histologic pattern of CG with LFH. In 1 study,[3] histologic findings of endoscopically obtained gastric biopsy specimens for 501 dogs were reported;

ABBREVIATIONS

BAOS	Brachycephalic airway obstructive syndrome
CG	Chronic gastritis
CI	Confidence interval
GHLO	Gastric *Helicobacter*-like organism
LFH	Lymphofollicular hyperplasia
WSAVA	World Small Animal Veterinary Association

482 of those dogs were examined because of vomiting, but CG with LFH was diagnosed in only 3. In another study[4] of 73 brachycephalic dogs, CG was diagnosed in 50 of 51 dogs for which gastric biopsy specimens were available for review, and concomitant follicular proliferation was identified in 19. Other reports of follicular gastritis in dogs and cats are typically associated with infections caused by *Helicobacter* spp.[5] The purpose of the study reported here was to compare the clinical, endoscopic, and histologic features of dogs with CG with and without LFH.

Materials and Methods

Animals

The study had a retrospective case-control design. The medical record database of Clinique Vétérinaire Alliance, a private small animal referral clinic in Bordeaux, France, was searched to identify records of dogs that underwent endoscopic examination of the upper gastrointestinal tract with collection and histologic evaluation of gastric biopsy specimens between October 2006 and February 2011. Dogs were eligible for study inclusion if the endoscopic report and histologic report for gastric biopsy specimens were available for review. Dogs were classified as cases or controls on the basis of histologic findings. Cases were defined as dogs with CG with histologic evidence of LFH, and controls were defined as dogs with CG without histologic evidence of LFH. Dogs with a histologic diagnosis of gastric neoplasia were excluded from the study. All dogs were examined and underwent endoscopic evaluation of the upper gastrointestinal tract as part of a routine diagnostic workup with the owners' consent.

Medical records review

For each study-eligible dog, information extracted from the medical record included age, breed, sex and neuter status, and body weight at the time of the endoscopic examination and clinical signs associated with the gastrointestinal tract (eg, vomiting, regurgitation, ptyalism, and diarrhea). Body condition score was not routinely recorded; therefore, dogs that were described as being underweight or in poor condition were classified as having a poor body condition, and all other dogs were classified as not having a poor body condition. Information regarding clinical signs associated with the respiratory tract and BAOS (eg, inspiratory dyspnea, exercise intolerance, and syncope) was also extracted from the record of each dog, as were other pertinent clinical examination findings and CBC and serum biochemical results when available.

Endoscopic examination

For each dog, food but not water was withheld for at least 12 hours before the endoscopic procedure. Each dog was premedicated with either acepromazine maleate (0.05 mg/kg [0.023 mg/lb], IV) or diazepam (0.2 mg/kg [0.09 mg/lb], IV). Anesthesia was induced with sodium thiopental (10 mg/kg [4.5 mg/lb], IV) or propofol (4 mg/kg [1.8 mg/lb], IV) and maintained with isoflurane in oxygen following orotracheal intubation. Brachycephalic dogs also received glycopyrrolate (0.005 mg/kg [0.002 mg/lb]), IV) and maropitant citrate (1 mg/kg [0.45 mg/lb], SC) immediately before the procedure.

All endoscopic examinations were performed by the same investigator (VF). Each dog was positioned in left lateral recumbency. A flexible endoscope[a] with an insertion tube (external diameter, 8.6 mm) was used for the procedure. Reusable biopsy forceps[b] (external diameter, 2.3 mm) were used to obtain at least 6 gastric biopsy specimens from different parts (fundus, body, and antrum) of the stomach. Reports of endoscopic findings (endoscopic reports) and associated endoscopic images were retrospectively reviewed by the investigator (VF) who performed each examination. Because the endoscopic reports were not originally written in accordance with WSAVA standardized gastrointestinal endoscopy reporting guidelines,[6] information regarding the extent of the following criteria was extracted from the reports and graded on a scale from 0 (absent or clinically normal) to 3 (severely affected or abnormal): hyperemia, edema, mucosal discoloration, erosions or ulcerations, gastric contents, and pyloric abnormalities. Macroscopic CG with LFH was defined as the presence of multiple small punctiform areas on the mucosal surface of a specific area of or the entire stomach[7] and was determined on the basis of evaluation of endoscopic images.

All gastric biopsy specimens were fixed in neutral-buffered formalin and submitted to the Laboratoire d'Anatomie Pathologique Vétérinaire du Sud-Ouest in Toulouse, France, for histologic evaluation soon after collection. At the laboratory, specimens were processed for histologic evaluation in a routine manner (ie, embedded in paraffin, cut into 4-µm-thick sections, and stained with H&E stain) and evaluated by veterinary pathologists who were certified by the European College of Veterinary Pathologists. Histologic findings were reported in accordance with criteria established by the 2008 WSAVA Gastrointestinal Standardization Group.[2] Those findings were reviewed jointly by 2 investigators (MRF and VF) for the study reported here. The presence of fibrosis and classification of the inflammatory infiltrate as follicular or nonfollicular were recorded. The presence of spiral bacteria consistent with GHLOs and extent of inflammation were graded on a scale of 0 (absent) to 3 (severe).

Statistical analysis

Descriptive statistics were generated for both cases (dogs with CG with LFH) and controls (dogs with CG without LFH). The Mann-Whitney test was used to compare age and weight between cases and controls. Brachycephalic phenotype, clinical signs of interest (poor body condition, vomiting, regurgitation, diarrhea, exercise intolerance, ptyalism, inspira-

tory dyspnea, and syncope), and histologic evidence of fibrosis were assessed as dichotomous variables (present or absent). The remaining histologic variables of interest (extent of gastritis and GHLOs) and endoscopic variables of interest (hyperemia, edema, mucosal discoloration, erosions or ulcerations, gastric contents, and pyloric abnormalities) were assessed as categorical variables on a 4-point subjective scale where 0 = absent, 1 = mild, 2 = moderate, and 3 = severe. For each dichotomous and categorical variable, the frequency distribution was compared between cases and controls by means of a χ^2 test or Fisher exact test when the count was < 5 in 1 or more cells or the Cochrane-Armitage trend test (for ordered variables with > 2 categories). All analyses were 2-sided, and values of $P < 0.05$ were considered significant.

Logistic regression was used to identify factors associated with CG with LFH. Explanatory variables in the logistic regression models were as described for comparisons between cases and controls with some minor adjustments. Sex (male or female) and neuter status (neutered or sexually intact) were assessed as 2 separate variables. Data for variables that were assessed on a 4-point scale were collapsed into 3 categories to ensure balance among groups. Briefly, data for the 2 grade categories with the smallest numbers of animals were combined. Thus, data for grades 2 (moderate) and 3 (severe) were combined for all variables except gastritis severity, for which data for grades 0 (absent) and 1 (mild) were combined. Univariable models were assessed initially, and variables with a value of $P < 0.1$ were eligible for inclusion in a multivariable model. Multivariable models also included all possible 2-way interaction terms between all eligible explanatory variables. The multivariable models were built by use of a combination of backward and forward stepwise elimination, with the least significant variable eliminated after each step. Only variables that did not make the model unstable and had a value of $P < 0.05$ were retained in the final multivariable model.

Two multivariable logistic regression models were initially created. One model included explanatory variables for factors associated with only patient signalment and clinical signs, and the other model included explanatory variables associated with only endoscopic and histologic factors. A third multivariable logistic regression model was subsequently created that assessed all explanatory variables. Results of all logistic regression models were reported as the ORs and associated 95% CIs and *P* values. All analyses were performed with statistical software programs.[c,d]

Results

Dogs

The case (dogs with CG with LFH) and control (dogs with CG without LFH) groups included 64 and 56 dogs, respectively. Dogs in the case group had a median age of 3 years (range, 0.3 to 13.9 years) and a median body weight of 12 kg (26.4 lb; range, 3 to 69 kg [6.6 to 151.8 lb]). There were 32 (50%) sexually intact males, 3 (5%) neutered males, 14 (22%) sexually intact females, and 15 (23%) neutered females. Breeds most commonly represented in the case group included French Bulldog (n = 16), Miniature Poodle (5), Cavalier King Charles Spaniel (4), and Boxer, English Bulldog, Golden Retriever, Jack Russell Terrier, and West Highland White Terrier (3 each). Additionally, there were 2 dogs of each of 4 breeds and 1 dog of each of 16 breeds.

Dogs in the control group had a median age of 6.2 years (range, 0.3 to 14.5 years) and a median body weight of 14 kg (30.8 lb; range, 2 to 46 kg [4.4 to 101.2 lb]). There were 29 (52%) sexually intact males, 4 (7%) neutered males, 11 (20%) sexually intact females, and 12 (21%) neutered females. Breeds most commonly represented in the control group included Yorkshire Terrier (n = 8), Miniature Poodle (4), and French Bulldog, Lhasa Apso, and Shih Tzu (3 each). Additionally, there were 2 dogs of each of 5 breeds and 1 dog of each of 25 breeds. The sex distribution ($P = 0.640$) and median body weight ($P = 0.911$) did not differ significantly between the case and control groups. However, the median age for the case group was significantly ($P < 0.001$) younger than that for the control group, and the proportion of brachycephalic dogs was significantly ($P = 0.010$) greater in the case group (28/64 [44%]) than in the control group (12/56 [21%]).

Clinical signs

Clinicals signs were assessed as present or absent, and the prevalence of each clinical sign in each group of dogs was summarized **(Table 1)**. The proportions of dogs with vomiting ($P = 0.093$), regurgitation ($P = 0.131$), ptyalism ($P = 0.404$), and syncope ($P = 0.924$) did not differ significantly between the case and control groups. The proportions of dogs with a poor body condition ($P = 0.006$) or diarrhea ($P = 0.008$) were significantly lower, whereas the proportion of dogs with inspiratory dyspnea ($P < 0.001$) or exercise

Table 1—Prevalence of select clinical signs for dogs with CG with LFH (cases; n = 64) and dogs with CG without LFH (controls; 56).

Clinical sign	Cases	Controls	*P* value*
Poor body condition	3 (5)	12 (21)	0.006
Vomiting	50 (78)	36 (64)	0.093
Regurgitation	19 (30)	10 (18)	0.131
Diarrhea	14 (22)	25 (45)	0.008
Exercise intolerance	14 (22)	2 (4)	0.003
Ptyalism	6 (9)	3 (5)	0.404
Inspiratory dyspnea	22 (34)	2 (4)	< 0.001
Syncope	1 (2)	1 (2)	0.924

Values represent the number (%) of dogs unless otherwise indicated. Data were obtained from a retrospective review of medical records of dogs that underwent an endoscopic examination of the upper portion of the gastrointestinal tract at a small animal referral practice between October 2006 and February 2011.

*For χ^2 or Fisher exact test (performed when the expected number of dogs in at least 1 cell was < 5), values of $P < 0.05$ were considered significant.

intolerance ($P = 0.003$) were significantly greater for the case group, compared with control group.

Endoscopic and histologic findings

All endoscopic variables could be assessed for only 61 of the 64 cases and 53 of 56 controls. Histologic variables could be assessed for only 63 of 64 cases and 55 of 56 controls. For those cases where it was not possible to assess all variables (endoscopic or histologic), only a short summary was available in the medical file; this was sufficient to assign them to an appropriate group (case or control) but not to assess the effect of all variables. Frequency distributions for endoscopic and histologic findings were summarized **(Table 2)**. Hyperemia ($P < 0.001$) and discoloration ($P < 0.001$) were more severe and gastric contents were more often absent ($P = 0.008$) in cases than in controls. However, the frequency distributions for edema ($P = 0.256$), erosions or ulcerations ($P = 0.836$), and pyloric abnormalities ($P = 0.942$) did not differ between cases and controls. Forty-seven of the 64 (73%) cases and 6 of the 56 (11%) controls met our definition of macroscopic CG with LFH (presence of multiple small punctiform areas scattered on the mucosal surface of a specific area of or the entire stomach; **Figure 1**).

The prevalence of fibrosis did not differ significantly ($P = 0.525$) between cases and controls. However, cases had more severe histologic evidence of gastritis ($P < 0.001$) and were more likely to have GHLOs present ($P = 0.044$) than were controls.

Factors associated with CG with LFH

Following univariable analyses, clinical factors eligible for inclusion in the multivariable logistic regression model included age, brachycephalic phenotype, poor body condition, vomiting, diarrhea, exercise intolerance, and inspiratory dyspnea. The final multivariable

Table 2—Frequency distributions for select endoscopic and histologic findings for the dogs of Table 1.

Variable	Category	Cases	Controls	*P* value*
Endoscopic findings				
Hyperemia	Absent	5 (8)	17 (32)	< 0.001
	Mild	26 (43)	29 (55)	
	Moderate	25 (41)	7 (13)	
	Severe	5 (8)	0 (0)	
Edema	Absent	30 (49)	19 (36)	0.256
	Mild	20 (33)	23 (43)	
	Moderate	4 (7)	10 (19)	
	Severe	7 (11)	1 (2)	
Discoloration	Absent	7 (11)	19 (36)	< 0.001
	Mild	24 (39)	26 (49)	
	Moderate	27 (44)	8 (15)	
	Severe	3 (5)	0 (0)	
Erosions or ulcerations	Absent	57 (93)	49 (92)	0.836
	Mild	2 (3)	2 (4)	
	Moderate	1 (2)	2 (4)	
	Severe	1 (2)	0 (0)	
Gastric contents	Absent	53 (87)	35 (66)	0.008
	Mild	4 (7)	10 (19)	
	Moderate	2 (3)	5 (9)	
	Severe	2 (3)	3 (6)	
Pyloric abnormalities	Absent	48 (79)	42 (79)	0.942
	Mild	7 (11)	7 (13)	
	Moderate	3 (5)	3 (6)	
	Severe	3 (5)	1 (2)	
Histologic findings				
Gastritis severity	Absent	0 (0)	0 (0)	< 0.001
	Mild	8 (13)	28 (51)	
	Moderate	31 (49)	21 (38)	
	Severe	24 (38)	6 (11)	
GHLO	Absent	36 (57)	36 (65)	0.044
	Mild	8 (13)	13 (24)	
	Moderate	8 (13)	3 (5)	
	Severe	11 (17)	3 (5)	
Fibrosis	Absent	14 (22)	15 (27)	0.525
	Present	49 (78)	40 (73)	

Endoscopic variables could be assessed for only 61 of the 64 cases and 53 of 56 controls. Histologic variables could be assessed for only 63 of 64 cases and 55 of 56 controls. All variables were subjectively assessed on a scale of 0 (absent) to 3 (severe) except fibrosis, which was assessed as present or absent on the basis of information extracted from the original reports and images of endoscopic and histologic findings.

*Cochrane-Armitage trend test was used for ordered variables with > 2 categories.

See Table 1 for remainder of key.

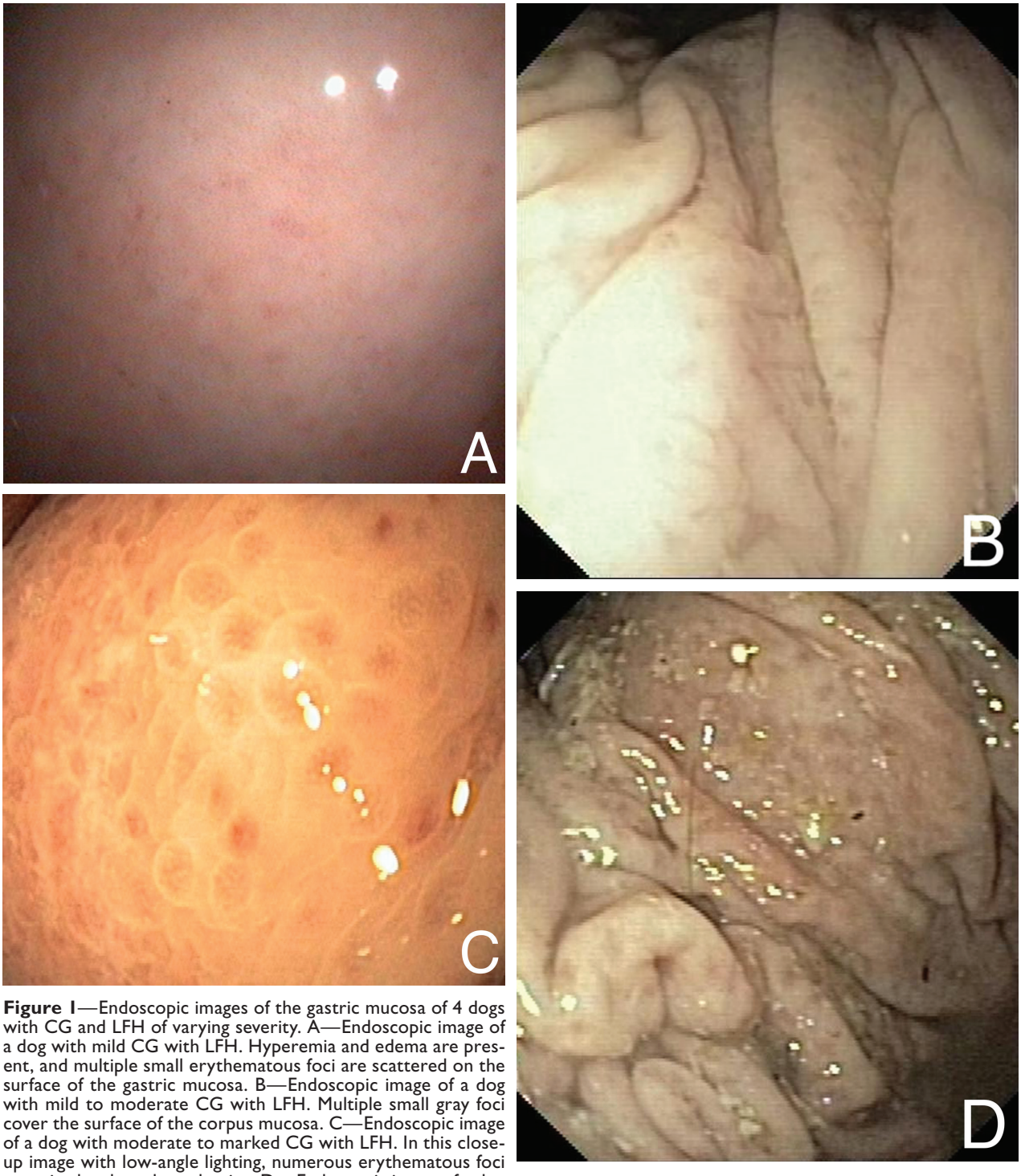

Figure 1—Endoscopic images of the gastric mucosa of 4 dogs with CG and LFH of varying severity. A—Endoscopic image of a dog with mild CG with LFH. Hyperemia and edema are present, and multiple small erythematous foci are scattered on the surface of the gastric mucosa. B—Endoscopic image of a dog with mild to moderate CG with LFH. Multiple small gray foci cover the surface of the corpus mucosa. C—Endoscopic image of a dog with moderate to marked CG with LFH. In this close-up image with low-angle lighting, numerous erythematous foci are raised and partly coalescing. D—Endoscopic image of a dog with marked CG with LFH. The gray foci are larger than those in panel C and cover a large portion of the gastric corpus mucosal surface.

model for clinical factors associated with CG with LFH included poor body condition and inspiratory dyspnea. The odds of CG with LFH was negatively associated with poor body condition (OR, 0.21; 95% CI, 0.05 to 0.87; $P = 0.032$) and positively associated with inspiratory dyspnea (OR, 13.48; 95% CI, 2.94 to 61.73; $P < 0.001$).

Endoscopic and histologic variables eligible for inclusion in the multivariable logistic regression model included hyperemia, discoloration, gastric contents, gastritis severity, and presence of GHLOs. The final multivariable model for endoscopic and histologic variables associated with CG with LFH included hyperemia and gastritis severity. The odds of CG with LFH was positively associated with both variables **(Table 3)**. When the multivariable logistic regression analysis included endoscopic and histolog-

Table 3—Final multivariable logistic regression model for identification of endoscopic and histologic variables associated with CG with LFH for the dogs of Table 1.

Variable	Category	OR (95% CI)	*P* value
Hyperemia	Absent	Referent	—
	Mild	2.92 (0.87–9.75)	0.082
	Moderate-severe	9.30 (2.31–37.50)	0.002
Gastritis severity	Absent-mild	Referent	—
	Moderate	4.97 (1.73–14.32)	0.003
	Severe	10.62 (2.76–40.94)	< 0.001

— = Not applicable.

Table 4—Final multivariable logistic regression model for identification of clinical, endoscopic, and histologic variables associated with CG with LFH for the dogs of Table 1.

Variable	Category	OR (95% CI)	*P* value
Poor body condition	Present	0.08 (0.01–0.59)	0.014
Inspiratory dyspnea	Present	68.56 (5.63–837.00)	< 0.001
Hyperemia	Absent	Referent	—
	Mild	7.15 (1.19–42.84)	0.031
	Moderate-severe	15.48 (2.31–103.88)	0.005
Gastritis severity	Absent-mild	Referent	—
	Moderate	4.77 (1.29–17.71)	0.019
	Severe	20.53 (3.91–107.71)	< 0.001

— = Not applicable.

ic variables as well as clinical factors, the final model included poor body condition, inspiratory dyspnea, hyperemia, and gastritis severity **(Table 4)**.

Discussion

The present study was the first to describe and compare the clinical, endoscopic, and histologic features between dogs with CG with LFH (cases) and dogs with CG without LFH (controls). Findings were based on a retrospective review of the medical records of dogs that underwent endoscopic examination of the upper gastrointestinal tract at a referral clinic over a 53-month period.

Results of the present study indicated that cases were significantly younger and more likely to have a brachycephalic phenotype and inspiratory dyspnea, compared with controls. The apparent predisposition of young dogs to CG with LFH might have been associated with the overrepresentation of brachycephalic dogs in the case group relative to the control group. Brachycephalic dogs are often evaluated for BAOS, and if endoscopy of the upper gastrointestinal tract is indicated, it is performed at the time of corrective surgery for BAOS. Although brachycephalic phenotype was positively associated with the odds of CG with LFH on univariable logistic regression, it was not retained in either of the final multivariable models that assessed clinical factors, which suggested that it was not as strongly associated with CG with LFH as other factors such as inspiratory dyspnea. There was a very strong positive association between inspiratory dyspnea and the odds of CG with LFH. This suggested that the respiratory consequences of BAOS might be more important to the development of CG with LFH than simply a brachycephalic phenotype. Further research is necessary to validate that supposition. Specifically, endoscopic and histologic findings for a larger population of nonbrachycephalic dogs with CG with LFH than that evaluated in the present study need to be evaluated.

Clinical signs associated with the gastrointestinal tract (eg, ptyalism, regurgitation, and vomiting) have been reported in dogs with BAOS,[4,8–10] but the mechanistic link between BAOS and those clinical signs has yet to be elucidated. A direct causal relationship is suggested by the fact that gastrointestinal signs often improve following surgical correction of the BAOS.[8,9] Brachycephalic dogs are predisposed to excessive esophageal length, hiatal hernia, gastroesophageal reflux, gastritis, and pyloric mucosal hyperplasia and stenosis. For dogs with BAOS, it is possible that an increase in negative intrathoracic pressure may promote gastroesophageal reflux and hiatal hernia. However, it is unclear how that might contribute to the development of CG with LFH, and further research is warranted.

Vomiting is the hallmark of CG; therefore, it was not surprising that it was the most frequent clinical sign recorded for dogs in both the case and control groups. We were somewhat surprised that cases appeared to be less likely than controls to have diarrhea or be in poor body condition and that poor body condition was significantly and negatively associated with the odds of CG with LFH in the 2 multivariable regression models in which it was evaluated. Interestingly,

body weight was not significantly associated with the odds of CG with LFH. The apparently disparate findings for poor body condition and body weight were likely a function of interbreed differences in body conformation or muscle condition (neither of which were evaluated in the present study). Because diarrhea and poor body condition are generally considered to be more specific for intestinal disease than gastric disease, it is possible that CG with LFH is unlikely to be associated with inflammation in the intestinal tract. However, in a study[4] of gastrointestinal tract lesions in brachycephalic dogs, histologic evidence of CG with LFH was detected in 19 of 50 (38%) dogs, of which most also had evidence of duodenitis. Small intestinal biopsy specimens were not obtained for most dogs of the present study, so we could not evaluate the relationship between the presence of small intestinal inflammation and CG with LFH. A possible explanation for the negative association between poor body condition and the odds of CG with LFH was that some cases were overweight. Similar to inspiratory dyspnea, obesity might exacerbate gastroesophageal reflux in dogs. Obesity is positively associated with gastroesophageal reflux in humans[11] and adversely affects respiratory function in dogs.[12] Unfortunately, for the dogs of the present study, body condition score was not routinely recorded, and the information provided in the medical record was generally insufficient for retrospective assignment of a body condition score. Additional studies are necessary to better elucidate the relationship between body condition and CG with LFH.

Macroscopically, CG with LFH is defined as the presence of multiple small gray-to-red punctiform areas on the gastric mucosa.[7] However, macroscopic examination of the gastrointestinal mucosa is an unreliable predictor of microscopic gastrointestinal abnormalities in both human and veterinary medicine.[13–16] In the present study, macroscopic CG with LFH was identified in 47 of 64 (73%) cases and 6 of 56 (11%) controls. The inconsistent agreement between macroscopic and microscopic (ie, histologic) CG with LFH might have been caused by the acquisition of biopsy specimens from areas devoid of lymphoid nodules or the lack of lymphoid nodules that were large enough for visual identification during endoscopic examination. Nevertheless, the macroscopic definition of CG with LFH used for the present study likely contributed to the case group having a significantly greater prevalence of gastric mucosal hyperemia and discoloration than the control group.

In human patients with CG, histologic identification of lymphoid follicles within the gastric mucosa is characteristic of *Helicobacter pylori* infection.[17,18] In dogs, there is currently no evidence that *Helicobacter* spp induce CG, and *Helicobacter* spp are generally considered commensal organisms capable of antigenic stimulation. Some dogs may develop gastritis owing to a loss of tolerance to *Helicobacter* spp rather than any intrinsic pathogenic properties of those bacteria. Follicular hyperplasia has been reported in dogs with GHLO infections, but the specificity of that criterium is not well characterized.[19] However, investigators of another study[20] found no correlation between the density of *Helicobacter* spp and number of lymphoid aggregates observed in gastric lesions of dogs. In the present study, cases were more likely to have GHLOs present in gastric biopsy specimens than were controls; however, the presence of GHLOs was not significantly associated with the odds of CG with LFH in the final multivariable logistic regression model.

The present study had some limitations. Perhaps the most notable limitation was its retrospective design. Study data were derived from the contemporaneous notes recorded into the medical records of study subjects by the clinician who managed each patient, and the endoscopic reports had to be retrospectively transcribed in accordance with WSAVA standardized criteria for this study. Additionally, although all gastric biopsy specimens were processed by the same laboratory, they were histologically evaluated by multiple pathologists, and interobserver variation in the histologic interpretation of the biopsy specimens may have affected our findings.[21] Finally, despite the many statistically significant associations identified between CG with LFH and various clinical, endoscopic, and histologic factors, association does not equate to causality. It is possible some of the significant associations identified were the result of other unmeasured variables. The findings of the present study need to be validated by prospective studies.

Results of the present study indicated that there was a strong positive association between inspiratory dyspnea and CG with LFH. That finding suggested that CG with LFH may be a consequence of an increase in negative intrathoracic pressure rather than a distinct clinical entity. Prospective studies are warranted to validate the results of this study and elucidate the mechanism by which inspiratory dyspnea contributes to the development of CG with LFH.

Acknowledgments

No third-party funding or support was received in connection with this study or the writing or publication of the manuscript. Dr. German is an employee of the University of Liverpool, but his position is financially supported by Royal Canin, which is owned by Mars Petcare. Dr. German has also received financial remuneration from Mars Petcare for providing educational material, speaking at conferences, and consulting; however, all such remuneration was for projects unrelated to the work reported in this manuscript. Dr. Bourge is an employee of Royal Canin.

The authors thank Dr. Virginie De Almeida for assistance with data collection and Dr. Frédérique Degorces-Rubiales for the histologic review of gastric biopsy specimens.

Footnotes

a. Video endoscope GIF 160, Olympus, Rungis, France.
b. Reusable biopsy forceps, Optomed, Les Ulis, France.
c. StatsDirect, version 3.0.171, StatsDirect Ltd, Birkenhead, England.
d. JMP, version 14.0, SAS Institute Inc, Cary, NC.

References

1. Simpson KW. Inflammation. In: Washabau RJ, Day MJ, eds. *Canine and feline gastroenterology.* St Louis: Saunders, 2013;616–619.

2. Day MJ, Bilzer T, Mansell J, et al. Histopathological standards for the diagnosis of gastrointestinal inflammation in endoscopic biopsy samples from the dog and cat: a report from the World Small Animal Veterinary Association Gastrointestinal Standardization Group. *J Comp Pathol* 2008;138(suppl 1):S1–S43.
3. van der Gaag I. The histological appearance of peroral gastric biopsies in clinically healthy and vomiting dogs. *Can J Vet Res* 1988;52:67–74.
4. Poncet CM, Dupré GP, Freiche VG, et al. Prevalence of gastrointestinal tract lesions in 73 brachycephalic dogs with upper respiratory syndrome. *J Small Anim Pract* 2005;46:273–279.
5. Simpson K, Neiger R, DeNovo R, et al. The relationship of *Helicobacter* spp. infection to gastric disease in dogs and cats. *J Vet Intern Med* 2000;14:223–227.
6. Washabau RJ, Day MJ, Willard MD, et al. Endoscopic, biopsy, and histopathologic guidelines for the evaluation of gastrointestinal inflammation in companion animals. *J Vet Intern Med* 2010;24:10–26.
7. Simpson KW. Diseases of the stomach. In: Ettinger SJ, Feldman EC, Côté E, eds. *Textbook of veterinary internal medicine.* 8th ed. St Louis: Elsevier, 2017;1495–1515.
8. Poncet CM, Dupré GP, Freiche VG, et al. Long-term results of upper respiratory syndrome surgery and gastrointestinal tract medical treatment in 51 brachycephalic dogs. *J Small Anim Pract* 2006;47:137–142.
9. Kaye BM, Rutherford L, Perridge DJ, et al. Relationship between brachycephalic airway syndrome and gastrointestinal signs in three breeds of dog. *J Small Anim Pract* 2018;59:670–673.
10. Reeve EJ, Sutton D, Friend EJ, et al. Documenting the prevalence of hiatal hernia and oesophageal abnormalities in brachycephalic dogs using fluoroscopy. *J Small Anim Pract* 2017;58:703–708.
11. El-Serag H. The association between obesity and GERD: a review of the epidemiological evidence. *Dig Dis Sci* 2008;53:2307–2312.
12. Mosing M, German AJ, Holden SL, et al. Oxygenation and ventilation characteristics in obese sedated dogs before and after weight loss: a clinical trial. *Vet J* 2013;198:367–371.
13. Çolakoğlu EÇ, Börkü K, Haydardedeoğlu AE, et al. Correlation between endoscopic and histopathological findings in dogs with chronic gastritis. *J Vet Res* 2017;61:351–355.
14. Elta GH, Appelman HD, Behler EM, et al. A study of the correlation between endoscopic and histological diagnoses in gastroduodenitis. *Am J Gastroenterol* 1987;82:749–753.
15. Levy N, Stermer E, Boss JM. Accuracy of endoscopy in the diagnosis of inflamed gastric and duodenal mucosa. *Isr J Med Sci* 1985;21:564–568.
16. Marchesi MC, Timpano CC, Busechian S, et al. The concordance between endoscopic and histological diagnosis in 114 dogs affected by gastric disease. *Vet Ital* 2017;53:309–313.
17. Genta RM, Hamner HW. The significance of lymphoid follicles in the interpretation of gastric biopsy specimens. *Arch Pathol Lab Med* 1994;118:740–743.
18. Rosh JR, Kurfist LA, Benkov KJ, et al. *Helicobacter pylori* and gastric lymphonodular hyperplasia in children. *Am J Gastroenterol* 1992;87:135–139.
19. Simpson KW, McDonough PL, Strauss-Ayali D, et al. *Helicobacter felis* infection in dogs: effect on gastric structure and function. *Vet Pathol* 1999;36:237–248.
20. Suárez-Esquivel M, Alfaro-Alarcón A, Guzmán-Verri C, et al. Analysis of the association between density of *Helicobacter* spp and gastric lesions in dogs. *Am J Vet Res* 2017;78:1414–1420.
21. Willard MD, Jergens AE, Duncan RB, et al. Interobserver variation among histopathologic evaluations of intestinal tissues from dogs and cats. *J Am Vet Med Assoc* 2002;220:1177–1182.