Received: 1 March 2024 | Accepted: 31 July 2024

DOI: 10.1111/jvim.17168

STANDARD ARTICLE

Journal of Veterinary Internal Medicine Open Access

ACVIM American College of Veterinary Internal Medicine

Video capsule endoscopy findings in dogs with chronic enteropathy and in healthy dogs

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Funding information
Skogsborg's Research Foundation, Grant/Award Number: 25173801; Carenet, Grant/Award Number: 2020.4.1-4652; Sveland's Research Foundation, Grant/Award Number: 25172801; Thure F och Karin Forsbergs Stiftelse, Grant/Award Number: 2020-01

Abstract

Background: Video capsule endoscopy is a noninvasive technique for evaluation of the gastrointestinal tract.

Objective: To investigate the safety of using the video capsule ALICAM in dogs with chronic enteropathy (CE) >10 kg, and to compare macroscopic gastrointestinal morphology between CE dogs and healthy controls (HC).

Animals: Fifteen CE dogs and 15 similarly breed, age and body weight matched HC.

Methods: All dogs underwent a clinical work up including blood analyses, fecal samples, abdominal ultrasonographic examination, and blood pressure measurement. The dogs were withheld from food for 16 hours before and 8 hours after they PO received an ALICAM. All recordings were quality assessed, and blindly evaluated by 2 trained observers.

Results: The median age of CE dogs and HC was 3.3 (interquartile range [IQR] 2.5-5.9) years and 4.7 (IQR 3.3-5.6) years, respectively. The median body weight in the CE dogs and HC was 25.9 (IQR 20.6-30.9) kg, and 29 (IQR 16.2-30.5) kg, respectively. Complete recordings of the gastrointestinal tract were obtained from all dogs without complications. No significant differences were found between groups regarding number of abnormalities such as irregular mucosa, erythema, nonbleeding erosions, bleeding erosions, and dilated lacteals, as well as severity and extent of the abnormalities.

Conclusions and Clinical Importance: The use of ALICAM for evaluation of the gastrointestinal tract in CE dogs and HC seems safe and feasible regarding gastrointestinal transit and macroscopic morphology assessment in dogs >10 kg. Abnormalities were found in similar proportions in CE dogs and HC.

Abbreviations: ARE, antibiotic-responsive enteropathy; BCS, body condition score; CCECAI, canine chronic enteropathy clinical activity index; CE, chronic enteropathy; DSI, distal small intestine; FRE, food-responsive enteropathy; HC, healthy control; IRE, immunosuppressant-responsive enteropathy; MSI, middle small intestine; NRE, nonresponsive enteropathy; PLE, protein losing enteropathy; PSI, proximal small intestine; VCE, video capsule endoscopy.

KEYWORDS
ALICAM, canine, gastrointestinal disease, small intestine

1 | INTRODUCTION

Chronic enteropathy (CE) in dogs is characterized by persistent (>3 weeks) or recurring signs of gastrointestinal disease, such as vomiting, diarrhea, hyporexia, and weight loss.[1,2] The diagnosis of CE is made by exclusion of other medical conditions, such as endocrine, hepatic, pancreatic and renal disease, endoparasites, or other infections.[2-4] Chronic enteropathy is, depending on treatment response, classified as food-responsive (FRE), immunosuppressant-responsive (IRE), nonresponsive (NRE), and possibly antibiotic-responsive (ARE).[1,2,5,6] Traditional bidirectional gastrointestinal endoscopy is used in some cases for macroscopic evaluation, and for acquirement of biopsies to confirm the presence of gastrointestinal inflammation.[4,7] The advantage of bidirectional gastrointestinal endoscopy is that it provides the opportunity to obtain gastrointestinal mucosal biopsies from the stomach, duodenum, upper jejunum, colon, cecum and ileum for histological evaluation, but disadvantages are that it requires general anesthesia and does not allow evaluation of the entire jejunum.[7]

Video capsule endoscopy (VCE) is a noninvasive endoscopic technique to macroscopically evaluate the entire gastrointestinal tract, as opposed to traditional gastrointestinal endoscopy. Video capsule endoscopy has been used in human medicine for more than a decade, but has not been widely used in animals.[8] In human medicine, there are a number of indications for VCE, such as inflammatory bowel disease, suspected gastrointestinal bleeding, and small bowel tumors.[9] Capsule retention is the most feared complication of VCE, and is defined as the presence of the video capsule in the gastrointestinal tract for a minimum of 2 weeks. Crohn's disease is a risk factor for incomplete examinations in human medicine.[10] In studies of VCE in dogs, it has mainly been used for evaluation of the treatment response to antiparasiticides,[11-13] and to detect bleeding lesions in the gastrointestinal tract of dogs with suspected gastrointestinal bleeding.[14-18] A veterinary specific endoscopic capsule (ALICAM, Infiniti Medical LLC, Redwood City, California) was used to evaluate quality of visualization of the gastrointestinal mucosa, complications, and risk factors for incomplete studies in dogs with overt or questionable gastrointestinal bleeding. The study showed that VCE using the ALICAM video capsule was a safe procedure that can be used to diagnose a variety of bleeding lesions throughout the entire gastrointestinal tract of dogs.[17] To the authors' knowledge, there are no previous studies where VCE has been used to assess dogs with CE, and further evaluation of the veterinary specific video capsule ALICAM is warranted to understand the advantages and limitations of this relatively new diagnostic method.

The aim of the study was to investigate the safety of using the video capsule ALICAM in dogs >10 kg with CE, and to compare macroscopic gastrointestinal morphology between CE dogs and healthy controls (HCs).

2 | MATERIALS AND METHODS

2.1 | Dogs

In this prospective study, 15 dogs with CE and 15 HC dogs were recruited at 2 Swedish animal hospitals: the University Animal Hospital at the Swedish University of Agricultural Sciences (SLU), Uppsala, and AniCura Albano Animal Hospital, Stockholm, from June 2021 to July 2022. The study protocol was approved by the ethical committee of the Swedish Board of Agriculture, and informed owner consent was acquired from all owners before enrollment in the study. Privately owned or university research and teaching colony dogs with CE, that were older than 1 year with a body weight between 10 and 70 kg, were recruited. All dogs had undergone at least 1 elimination diet trial for at least 4 weeks and did not improve clinically. Dogs with CE that were treated with proton pump inhibitors, sucralfate, maropitant, cobalamin, or folic acid supplementation could be included in the study. The exclusion criteria were CE dogs that had responded well to a food trial and were considered food-responsive, hypoadrenocorticism, pancreatitis, a mass like lesion in the gastrointestinal tract detected with abdominal ultrasonography, intestinal parasites, and signs of other organ related systemic disease. Dogs were also excluded if they had been treated with steroid or prokinetic therapy within 6 months before inclusion in the study.

Healthy privately owned or university research and teaching colony dogs that were age, and weight matched as accurately as possible with the CE dogs, were included. An age difference of maximum ±3 years between the CE dog and their matched HC dog was allowed. The CE dogs were as closely as possible matched with HC dogs of the same breed, or with dogs from a closely related breed. Exclusion criteria for HC dogs included history of gastrointestinal disease, allergic- or immunologic disease, abnormal findings at abdominal ultrasonography, intestinal parasites, significant abnormalities in CBC or blood biochemistry, or if they received any medication besides prophylactic treatment. One year after the VCE, the owners of all HC dogs and the caretaker of the university research and teaching colony HC dogs, were contacted to confirm that the dogs had not developed any clinical signs of gastrointestinal disease.

2.2 | Diagnostic procedures

All included dogs underwent a physical examination, blood analyses, fecal flotation, blood pressure measurement and standard abdominal ultrasonography, within 2 weeks before the VCE. Dogs were also classified using the canine chronic enteropathy clinical activity index (CCECAI).[19] All diagnostic procedures were performed at the University Animal Hospital, SLU. Blood analyses included CBC, biochemistry, resting cortisol, cobalamin, folic acid, serum trypsin-like immunoreactivity,

pancreatic lipase immunoreactivity, serum total thyroxine, and canine thyroid stimulating hormone. An ACTH-stimulation test was performed if resting cortisol was below the reference interval of the laboratory (<30 nmol/L).[20] All blood samples were analyzed at the accredited laboratory at the University Animal Hospital, Uppsala, and fecal samples were analyzed at the accredited laboratory at the Swedish Veterinary Agency, Uppsala. All dogs were dewormed with fenbendazole 50 mg/kg q 24 hours PO for 5 days, after fecal sampling.

The blood pressure measurements were performed with high definition oscillometry, HDO (S + B medVet Babenhausen, Germany) as described elsewhere,[21] at the University Animal Hospital, SLU, by the examining veterinarian (J.Ho.). Only the dog and its owner were present in the room during blood pressure measurements. All dogs were withheld from food for a minimum of 12 hours before ultrasonographic examination and the abdominal ultrasonographies were performed by a board-certified specialist in veterinary diagnostic imaging (J.I.). The ultrasonographies were performed with the dogs in dorsal recumbency, with linear L11 and microconvex C3-10 transducers (GE Medical LOGIQ E9 Ultrasound Imaging System). Small dogs were examined only with the L11 linear transducer, and larger dogs were additionally examined with the microconvex transducer when lower frequencies were required to evaluate the entire abdominal cavity. The abdomen and gastrointestinal tract were overall evaluated as normal or abnormal, and any abnormalities were recorded. Images were stored in a picture archive and communication system (PACS, GE centricity RA 600 v 8.0; General Electric Medical Systems) using the DICOM file format and reviewed at a dedicated workstation.

2.3 | Video capsule endoscopy procedures

Any treatment with sucralfate or proton pump inhibitors was terminated at least 48 hours before administration of the video capsule. The dogs were withheld from food for 16 hours before the veterinary specific video capsule ALICAM (Infiniti Medical LLC, Redwood City, California) was administered PO by a veterinarian (J.Ho.) at the animal hospital. They were also withheld from food for 8 hours after administration, after which they were allowed to eat their normal diet. All dogs were kept in their home environment while the video capsule was transported through the gastrointestinal tract. The owners were instructed to look for the excretion of the ALICAM, and to document the time of excretion, as well as to report any newly noted clinical signs or potential adverse effects. The device was collected by the owner after excretion and handed in at the University Animal Hospital to the examiner (Johanna Holmberg). If the video capsule had not been excreted within 72 hours after administration, a radiographic examination was performed to detect the location of the ALICAM.

2.4 | Image and data analysis

The video images and data were masked and analyzed individually by 2 board-certified internists (A.D. and J.S.) that are trained and experienced in reading ALICAM video capsule images. The recordings were subjectively assessed regarding quality of visualization of the gastrointestinal mucosa, macroscopic gastrointestinal morphology and capsular transit time. Assessment of the quality of visualization was based on a protocol from human medicine.[22] It was graded as score 1, < 25% of the mucosa visible per frame (poor visualization), score 2, 25% to 50% of the mucosa visible per frame (limited visualization), score 3, >50% to 75% of the mucosa visible per frame (adequate visualization), and score 4, >75% of the mucosa visible per frame (good visualization). Each part of the gastrointestinal tract (esophagus, stomach, small intestine and colon) was evaluated separately and the following criteria were assessed: mucosal color (normal, erythematous, pale, other), mucosal surface (normal, irregular, edematous, other), extruding lesions (nonbleeding, bleeding), protruding lesions (nonbleeding, bleeding), flat lesions (red spot, other), and angioectasia. In the small intestine, the villi were further evaluated regarding villi shape (normal, edematous, atrophic, hypertrophic), villi color (normal, red, white). Macroscopic gastrointestinal abnormalities were described based on modified criteria from the Lewis inflammatory score and the Saurin score.[23] Both of these scoring systems are widely used in VCE in human medicine, where the Lewis inflammatory score is used to classify villous edema, ulcerations and stenosis, and the Saurin score is used to classify lesions based on the potential of clinically significant bleeding.[23] In the present study, we used modified criteria from the Lewis score for description of villous appearance and ulcerations, and modified criteria from the Saurin score to describe extruding, protruding and flat lesions. On the basis of modified criteria from these scoring systems, all mucosal abnormalities of the present study were classified according to level of severity (0: normal, 1: mild, 2: moderate, 3: severe), distribution (1: localized, 2: patchy, 3: diffuse), and longitudinal extent (1: <10% length of segment, 2: 10%-50% length of segment, 3: >50% length of segment). Erosions were classified according to number of lesions (1: single, 2:2-7, 3: ≥8), percentage of the frame occupied by the largest lesion (1: <25%, 2: 25%-50%, 3: >50%), longitudinal extent describing the length of the segment (1: <10%, 2: 10%-50%, 3: >50%), bleeding potential (0: no potential of bleeding, 1: low/uncertain potential of bleeding, 2: high potential of bleeding, 3: actively bleeding). Based on the Lewis inflammatory score system, the small intestine was divided into proximal small intestine (PSI), middle small intestine (MSI), and distal small intestine (DSI), when describing the macroscopic appearance of the small intestine.[23] The establishment of these three tertiles is based on the transit time from the duodenum to the cecum.[23] After individual evaluation of all dogs' recordings, the 2 readers compared their results and came to a consensus agreement regarding the macroscopic findings that they initially had assessed differently.

2.5 | Statistical analyses

Descriptive statistical calculations were performed in JMP Pro (v16.0, Cary NC). Proportions, medians, interquartile ranges (IQRs), and ranges are reported. Differences in transit time were tested by

Wilcoxon rank-sum test. The macroscopic findings were compared between CE dogs and HC, to investigate any potential differences in macroscopic gastrointestinal morphology and capsular transit time between groups. Comparisons between categorical data were performed by either the Chi-2 or Fischer's exact 2-tailed tests. Subanalyses were performed with pairwise comparisons if the overall *P*-value was <.05, and 1 or both variables included >2 groups by the Fischer's exact test with Bonferroni correction for multiple comparisons. Statistical significance was set at $P < .05$.

3 | RESULTS

3.1 | Dogs

Fifteen CE and 15 HC dogs were included, and dog characteristics for each group are described in Table S1. The breeds represented were German shepherd dog (n = 6), Labrador retriever (n = 6), Rottweiler (n = 4), Beagle (n = 4), Boxer (n = 4), Nova Scotia duck tolling retriever (n = 2), Samoyed (n = 2), American Staffordshire terrier (n = 1), and Staffordshire bull terrier (n = 1). The study population comprised of 7 males and 8 females in the CE group, and 6 males and 9 females in the HC group. There were 13 privately owned CE dogs and 13 privately owned HC dogs. Two CE dogs and 2 matched HC dogs were university research and teaching colony beagle dogs. The median age of CE dogs was 3.3 (IQR 2.5-5.9) years and the median age of HC dogs was 4.7 (IQR 3.3-5.6) years. The median body weight of CE dogs and HC dogs was 25.9 (IQR 20.6-30.9) kg, and 29.0 (IQR 16.2-30.5) kg, respectively. In CE dogs, vomiting and diarrhea were reported in 67% (10/15) and 60% (9/15), and hyporexia and weight loss was reported in 80% (12/15) and 53% (8/15). The difference between the median CCECAI in CE dogs (6; range, 4-16) and HC dogs (0; range, 0-1) was significant ($P < .05$). According to the CCECAI score, CE dogs were classified as having mild (n = 4), moderate (n = 9), severe (n = 1), and very severe (n = 1) gastrointestinal disease. In the HC group, 7 dogs received a score of 1 on the CCECAI score, because of feces frequency of 2 times per day. None of the HC dogs had developed signs of gastrointestinal disease within a year after the ALICAM administration.

3.2 | Laboratory and abdominal ultrasonography results

Of the CE dogs, 27% (4/15) had hypoalbuminemia and 20% (3/15) had hypocobalaminemia. In the CE dogs, levels above the reference range of C-reactive protein (1/15, 7%), alanine aminotransferase (1/15, 7%), and alkaline phosphatase (1/15, 7%) were reported. All other blood sample results were within reference ranges. Ultrasonographic abnormalities were detected in 40% (6/15) of the CE dogs, where 33% (5/15) dogs had hyperechoic striations in the small intestinal mucosa. One CE dog also had mild peritoneal effusion and delayed gastric emptying with retained content in the stomach, and 1 CE dog had an extra moderately thickened hypoechoic layer in the wall of the ileum that is normally not visible. All HC dogs had blood test results within reference values, and abdominal ultrasonographies without abnormalities. All dogs of both groups had blood pressure measurements within the normal reference range (<140 mm Hg).[21]

3.3 | Video capsule endoscopy results

Of 30 ALICAM capsules, 28 video capsules were successfully retrieved through defecation. In 1 CE dog and 1 HC dog, the initial video capsules were not found by the owners, despite thorough instructions on how to look for them. The dogs had not vomited since administration, and at the radiographic examination performed 72 hours after oral administration, video capsules were not detected in the gastrointestinal tract. The capsules were most certainly excreted in the feces without the owners noticing it. These 2 dogs received an additional ALICAM PO, both of which were excreted without any complications, and complete recordings were obtained. There was no case of capsule retention, and complete recordings were obtained from all dogs. There was no statistically significant difference between CE dogs and HC dogs in median gastric capsular transit time (CE: 75.9, IQR 22.7-110, HC: 49.6, 25.1-97.8 minutes; $P = .46$) and median small intestinal capsular transit time (CE: 108, IQR 90.0-126.65, HC: 122.9, IQR 90.5-168.1 minutes; $P = .34$).

The assessment scores of visualizations for all dogs are presented in Table 1. For 90% of the macroscopic gastrointestinal normal and abnormal findings, the examiners had made the same assessment. For 10% of the findings, they had initially made different assessments, but came to a consensus agreement. Normal mucosal surface was detected in >50% of the longitudinal extent of the stomach (CE: 14/15, HC: 10/15), PSI (CE: 14/15, HC: 15/15), MSI (CE: 13/15, HC: 15/15), and DSI (CE: 15/15, HC: 14/15). Normal mucosal color was detected in >50% of the longitudinal extent of the stomach (CE: 14/15, HC: 15/15), PSI (CE: 15/15, HC: 15/15), MSI (CE: 15/15, HC: 15/15), and DSI (CE: 15/15, HC: 15/15). Results regarding gastrointestinal mucosal abnormal findings, and location of abnormalities, are presented in Figures 1–3. There were no statistically significant differences between groups regarding presence, extent or level of severity regarding erythema, irregular mucosa, edematous mucosa, red spots, nonbleeding and bleeding erosions, or angioectasia. Regarding villi appearance in the small intestine, there were no statistically significant differences between the groups in the presence, extent or level of severity of white villi (dilated lacteals), hyperemic villi, hypertrophic villi, or edematous villi. Detailed information regarding summarized results of the VCE readings in all dogs are presented in Tables S2–S8. Examples of macroscopic abnormalities are shown in Figure 4.

4 | DISCUSSION

This prospective study showed that VCE with ALICAM is a safe and feasible method regarding gastrointestinal mucosal visualization

Quality of visualization 1-4/4	Total number of dogs (n = 30)	CE (n = 15)	HC (n = 15)
Stomach			
1	9	4	5
2	7	6	1
3	5	2	3
4	9	3	6
Proximal small intestine			
1	0	0	0
2	1	0	1
3	12	6	6
4	17	9	8
Middle small intestine			
1	0	0	0
2	0	0	0
3	8	3	5
4	22	12	10
Distal small intestine			
1	0	0	0
2	5	3	2
3	10	4	6
4	15	8	7
Colon			
1	16	9	7
2	12	5	7
3	2	1	1
4	0	0	0

TABLE 1 Scores of visualization quality of the gastrointestinal mucosae in all dogs (n = 30) as well as in the CE group (n = 15) and HC group (n = 15).

Note: Score 0: Impossible to visualize the mucosa, 1: Mucosa is visible in <25% of the frame, 2: Mucosa is visible in 25% to 50% of the frame, 3: Mucosa is visible in >50% to 75% of the frame, 4: Mucosa is visible in >75% of the frame. There was no significant difference in quality of visualization between the dogs with CE and HC. In both groups, the quality of visualization in the small intestinal segments was significantly better than the visualization in the stomach and colon, and the quality of visualization was significantly better in the stomach compared to the colon ($P < .05$).
Abbreviations: CE, chronic enteropathy dogs; HC, healthy control dogs.

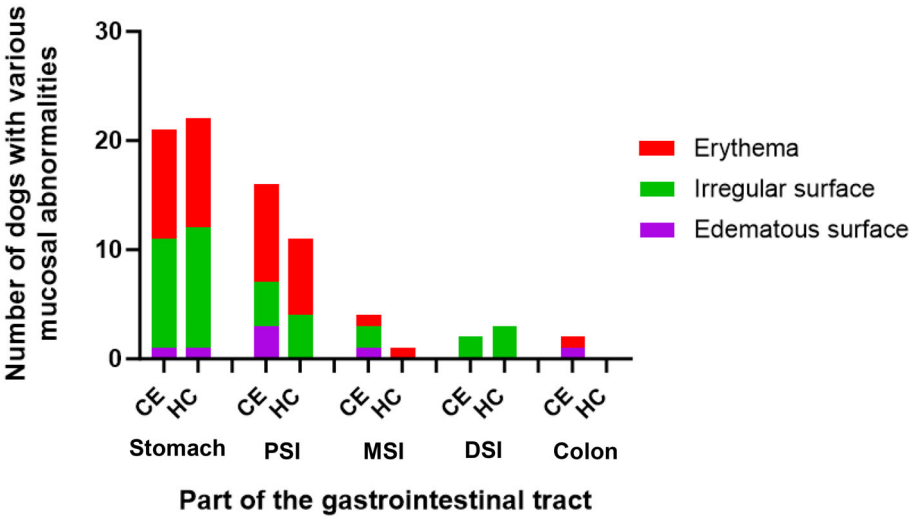

FIGURE 1 Mucosal abnormalities in the gastrointestinal tract in dogs with CE (n = 15) and HC (n = 15). Multiple macroscopic abnormalities could be present in the same dog. CE, chronic enteropathy dogs; DSI, distal small intestine; HC, healthy control dogs; MSI, middle small intestine; PSI, proximal small intestine.

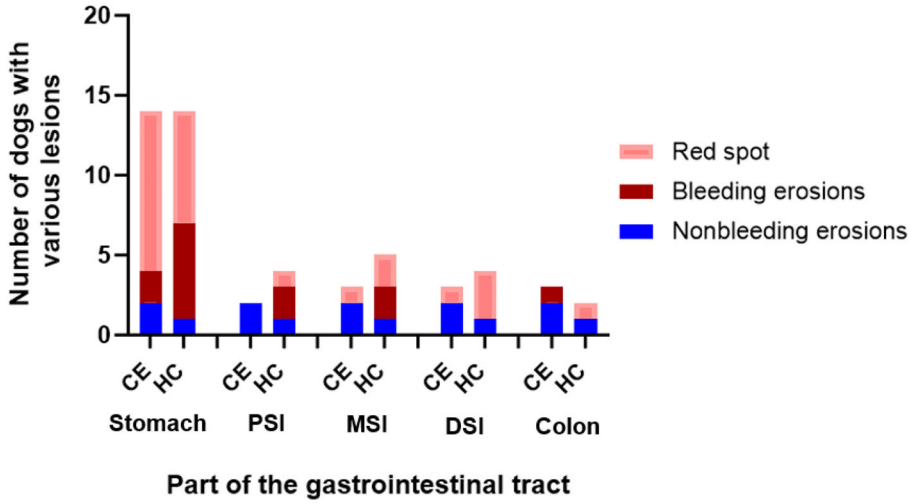

FIGURE 2 Mucosal lesions in the gastrointestinal tract in dogs with CE (n = 15) and HC (n = 15). Multiple mucosal lesions could be present in the same dog. CE, chronic enteropathy dogs; DSI, distal small intestine; HC, healthy control dogs; MSI, middle small intestine; PSI, proximal small intestine.

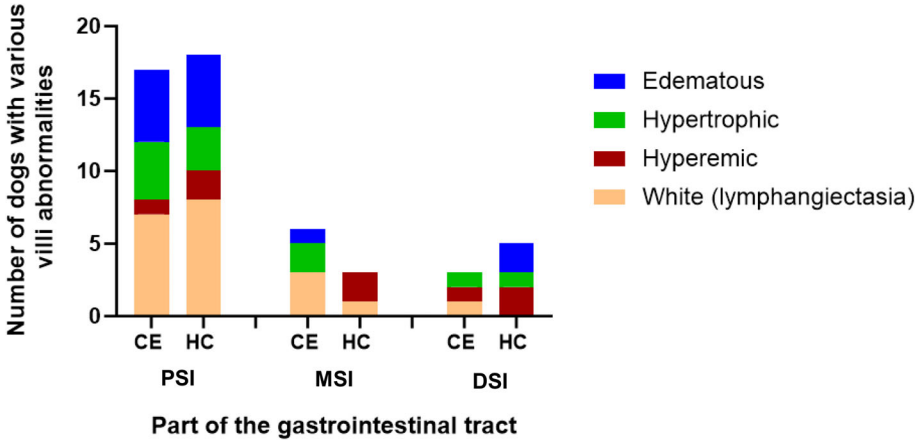

FIGURE 3 Villi abnormalities in the proximal, middle and distal small intestine in dogs with CE (n = 15) and HC (n = 15). Multiple villi abnormalities could be present in the same dog. CE, chronic enteropathy dogs; DSI, distal small intestine; HC, healthy control dogs; MSI, middle small intestine; PSI, proximal small intestine.

and transit time estimation of video capsules, in dogs >10 kg, with and without CE. Video capsules passed the entire gastrointestinal tract within the recording time of the ALICAM, and complete studies were obtained from all dogs. There was no statistically significant difference between the groups regarding number of macroscopic gastrointestinal abnormalities, severity or extent of the abnormalities, which was an unexpected finding.

No statistically significant differences between the groups were identified regarding erythematous mucosa, irregular mucosal surface, edematous mucosa, red spots, nonbleeding and bleeding erosions, abnormal villi appearance, or angioectasia. In human medicine, VCE is used to evaluate patients with inflammatory bowel disease, and mucosal features that can be seen include erythema, loss of villi, villous edema, and ulcerations.[24] However, a challenge in human medicine is that VCE findings suggestive of inflammatory bowel disease are rather nonspecific.[25] Detection of lesions is based on the assumption that the mucosa in the normal individual is intact, and it suggests that the presence of even small erosions indicate disease.[26] In a human study performed on 40 healthy volunteers, it was shown that 19% had ulcers and 41% had erosions, and it was concluded that the healthy people in the study had similar lesions to the lesions seen in people with obscure gastrointestinal bleeding.[27] In another human study, VCE was performed in 413 healthy volunteers. Mucosal erosions and petechiae were detected in the small intestine of 13.7% of the individuals, and the lesions ranged from 1 to 20 lesions per individual.[28] Furthermore, it has been shown that lesions in the small intestine were found in 10% of human patients with arthritis that were not treated with NSAID.[29] Thus, it could potentially be difficult, in dogs as well, to know which macroscopic abnormalities that are clinically significant, and which findings that could occur in healthy dogs without gastrointestinal disease. Because neither traditional bidirectional endoscopy nor VCE are commonly performed in healthy dogs, information about the macroscopic gastrointestinal appearance is scarce in healthy dogs, and it is possible that healthy dogs can have more macroscopic abnormalities than we are aware of. Conclusions regarding the clinical importance of macroscopic mucosal abnormalities and lesions in dogs with CE, or dogs with suspected gastrointestinal bleeding, should therefore be drawn with caution.

In the present study, dilated lacteals in the proximal small intestine were detected in a similar number of CE dogs (47%, 7/15) and HC dogs (53%, 8/15), with comparable severity and extent. In a dog that has been withheld from food, dilated lacteals indicate intestinal

lymphangiectasia, but the definitive diagnosis is made by histological assessment in a dog with gastrointestinal clinical signs and hypoalbuminemia.[30] In dogs, intestinal lymphangiectasia can occur secondary to for example chronic inflammatory enteropathy, and it also seems to be a genetic susceptibility in some breeds like the Yorkshire terrier, Norwegian lundehund, Rottweiler, and Soft-coated wheaten terrier.[30-34] It is an unexpected result that a similar number of HC and CE dogs had dilated lacteals in the present study, as it has most often been associated with clinical gastrointestinal disease.[32,33] However, none of the HC dogs had developed clinical signs of gastrointestinal disease when contacted a year after their ALICAM administration, which implies that the identified dilated lacteals are probably not a result of progressive occult disease. Possibly, it could rather represent a degree of normal variation. It is also possible that there would have been a larger difference between the CE and HC dogs regarding presence, severity and extent of dilated lacteals, if a higher number of CE dogs with severe gastrointestinal disease according to the CCECAI score, would have been included. In human medicine, presence of lymphangiectasia has been described in healthy individuals.[35] A prospective study of 134 asymptomatic individuals that underwent upper gastrointestinal endoscopy as part of a routine health examination, showed that 11.2% of total cases were suspected of having duodenal lymphangiectasia based on the macroscopic appearance at the endoscopy, and it was histologically confirmed in 8.9% of total cases.[35] In the present study, the proportion of HC with dilated lacteals was larger than the proportion of healthy individuals with lymphangiectasia in the human study. However, there was a smaller study population in the present study, and the lymphangiectasia was not histologically confirmed. In a previous study, where ALICAM was used to assess the effect of fat loading on the gastrointestinal villi appearance in healthy dogs, VCE examination before the fat loading revealed that mucosal changes were absent or mild in all 4 dogs in the control group.[36] The sample size was limited and details regarding what the mild changes represented were not presented, which makes it difficult to compare the results of the current study to the previous study. To the authors' knowledge, there are no other studies that have described the presence of dilated lacteals in healthy dogs that has been withheld from food, and further studies are required to investigate if this is a consistent finding.

The gold standard for diagnosis of inflammatory bowel disease in humans, and of chronic inflammatory enteropathy in dogs, is traditional bidirectional gastrointestinal endoscopy where gastrointestinal biopsies are obtained for histological examination.[2,6,24] A limitation of VCE is the inability to obtain gastrointestinal biopsies, and it is possible that the CE dogs in the present study had more histological abnormalities than the HC dogs. However, histopathology is also a method associated with limitations, and previous studies have failed to show an association between histology and the presence and severity of clinical signs.[37-39] Another potential explanation for the abnormal findings in the HC dogs in the present study is that they could suffer from occult disease. However, as mentioned before, none of the HC dogs enrolled in the study had developed clinical signs of gastrointestinal disease a year after their VCE, and they were still clinically healthy according to the owners. Because similar macroscopic findings were found in CE dogs and HC dogs, with comparable severity and extent, the utility of using VCE for the detection of inflammatory lesions can be questioned. However, VCE seems to be an efficient method of detecting gastrointestinal ulcerations, as shown in previous studies.[14-18]

One of the advantages with VCE compared to traditional bidirectional gastrointestinal endoscopy is the ability to evaluate the entire small intestine. In the present study, some of the mucosal abnormalities were found in the MSI, meaning that these abnormal findings would not have been discovered with traditional gastrointestinal endoscopy. Another advantage of VCE compared to traditional gastrointestinal endoscopy is that it is noninvasive and does not require anesthesia, which is favorable in dogs where anesthesia might be contraindicated, and to avoid potential complications such as regurgitation and aspiration pneumonia.[40,41]

In the present study, there was no case of capsule retention, and complete examinations were obtained in both dogs with CE and HC dogs. This is a positive result as the rate of incomplete recordings in human medicine have been reported to be 20% to 30%.[10,42,43] In a previous study where ALICAM was used in dogs with gastrointestinal bleeding, it was reported that incomplete studies was the most common complication which occurred in 39% of the dogs, especially after oral administration compared to endoscopic deployment in the duodenum.[17] That same study showed that CE was a risk factor for capsular retention,[17] and in human medicine, Crohn's disease is also a known risk factor for incomplete examinations.[10] The video capsules were administered PO to all dogs in the present study and none of them were retained in the stomach, supporting that oral administration of the video capsule seem to be feasible also in dogs with CE >10 kg body weight. However, most of the dogs were classified with moderate gastrointestinal disease according to the CCECAI score, and it is possible that there would have been more cases of capsule retention if more CE dogs with severe gastrointestinal disease had been included. In 1 of the CE dogs, there was a suspicion of delayed gastric emptying at the ultrasonographic examination, but the dog had a complete VCE examination. Prokinetic treatment before VCE has been described as a possible intervention when there is a suspicion of decreased transit time.[44] However, human studies have reported conflicting results regarding the use of prokinetic therapy to decrease the risk of incomplete VCE.[44-47]

The minimum body weight allowed for inclusion in the present study was 10 kg, which is in agreement with a previous study that investigated a wireless motility capsule in dogs.[48] According to the manufacturer of the ALICAM, the video capsule has been tested in dogs with a body weight of 4.3 kg.[49] Nevertheless, the minimum body weight in the present study was set with a safety margin, but in future studies, dogs with a body weight <10 kg could possibly also be included.

Studies from human medicine have shown that the detection rate and interobserver agreement using VCE are low to moderate between readers,[50,51] and it is therefore beneficial to have more than 1 observer of the VCE examinations. In the present study, the initial agreement of the 2 blinded observers was 90%, which is quite high. To the authors' knowledge, there are to this date no studies available regarding interobserver variations in VCE in dogs, and this is something that could be considered for future studies.

5 | LIMITATIONS

In the present study, all dogs were withheld from food for 16 hours before- and 8 hours after the ALICAM administration, to improve the quality of the images. This time period is recommended by the manufacturer,[52] and is comparable to a previous prospective study of VCE in dogs.[17] However, in 53% (16/30) of all dogs, the quality of visualization in the colon was classified as poor. A limitation of VCE is that the diagnostic yield can be decreased by limited visibility of the gastrointestinal mucosa, and bowel preparation is something that could be considered for future studies. In human medicine, bowel preparation in addition to fasting before the VCE is recommended, but there is lack of sufficient evidence to support a specific preparation protocol.[22,53,54] The VCE was not compared with traditional bidirectional endoscopy in the present study, and it is difficult to know if more macroscopic findings would have been detected if inflation of the stomach and colon would have been possible. Another limitation is the use of white light only which might lead to missing structural

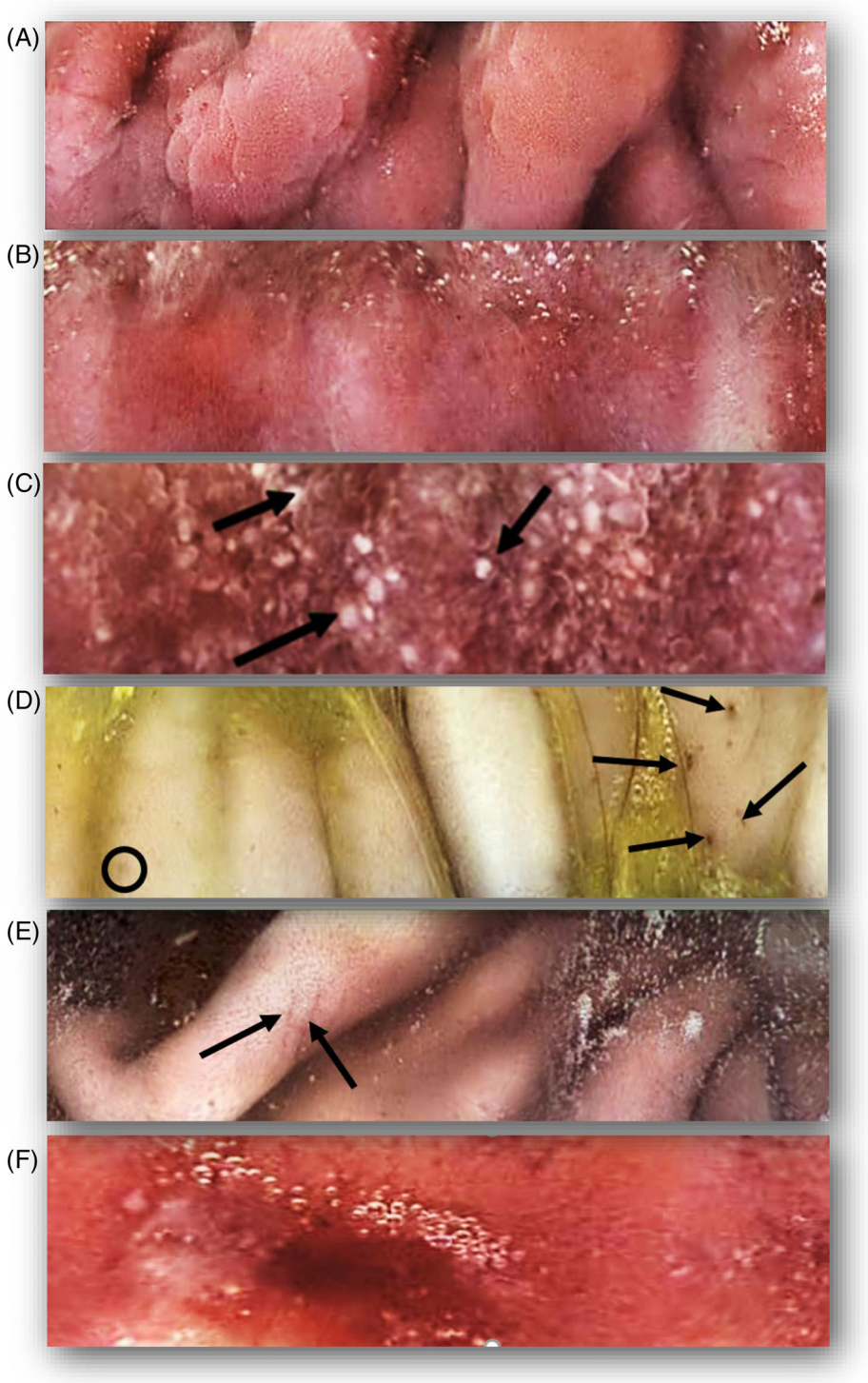

FIGURE 4 Video capsule images of (A) irregular gastric mucosa in a HC dog; (B) erythema of the small intestinal mucosa in a CE dog; (C) dilated lacteals in the small intestine in a HC dog; (D) nonbleeding gastric erosions in a CE dog; (E) nonbleeding gastric erosions in a CE dog; (F) bleeding small intestinal erosion in a HC dog. CE, chronic enteropathy dog; HC, healthy control dog.

lesions, in contrast to advanced endoscopic techniques such as narrow band imaging.[55] The HC dogs were matched with the CE dogs as accurately as possible during the study period, but there is still a slight variation in breed, sex, age and body weight between the CE dogs and HC dogs, which could possibly have affected the result. An ACTH-stimulation test was performed if resting cortisol was below the reference of the laboratory at the University Animal Hospital, SLU (<30 nmol/L). This cutoff is lower compared to the typical cutoff of 55 nmol/L used for ruling out hypoadrenocorticism.[56] However, a previous study has shown that a cutoff value of 28 nmol/L had a sensitivity of 98.2% and a specificity of 91.5% for the diagnosis of hypoadrenocorticism in dogs.[20] No prior sample size power calculation was performed, and the sample size was constrained by finances and expense of the video capsules. The study groups were therefore limited in numbers, which could have impacted the results. The majority of the dogs in the present study were classified with moderate gastrointestinal disease according to the CCECAI score. Future studies should include more CE dogs with severe gastrointestinal disease.

6 | CONCLUSIONS

In conclusion, this prospective study showed that VCE with ALICAM is a safe and feasible method regarding gastrointestinal capsular transit of video capsules in dogs with CE and HC dogs >10 kg, and none of the video capsules were retained in the stomach. There was no significant difference between CE and HC dogs regarding number, severity and extent of macroscopic gastrointestinal abnormalities, and future studies are required to further evaluate these findings. Regardless if dogs undergo VCE or conventional gastrointestinal endoscopy, an individual variation in macroscopic mucosal appearance can lead to the diagnosis of gastrointestinal disease, without necessarily being linked to the gastrointestinal signs. Information about the macroscopic gastrointestinal appearance is scarce in healthy dogs, and it is possible that healthy dogs can have more macroscopic abnormalities than previously thought.

ACKNOWLEDGMENT

This study received funding from Carenet, Jan Skogsborg's, Thure F and Karin Forsberg's, and Sveland's Research Foundation, Sweden.

CONFLICT OF INTEREST DECLARATION

Jenny Stiller has been a consultant for Infiniti medical since December 2021. Alice Defarges was a consultant for Infiniti Medical during the enrolment of the study. No other authors declare a 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

Approved by the ethical committee of the Swedish Board of Agriculture: Dnr. 5.8.18-00042/2021.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Holmberg J, Ljungvall I, Pelander L, et al. Video capsule endoscopy findings in dogs with chronic enteropathy and in healthy dogs. *J Vet Intern Med*. 2024;38(5):2454-2463. doi:10.1111/jvim.17168