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Feasibility, complications, and quality of visualization using video capsule endoscopy in 40 dogs with overt or questionable gastrointestinal bleeding

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Abstract

Background: Prospective studies describing video capsule endoscopy (VCE), its feasibility, and complications in dogs are limited.

Objective: To assess VCE, quality of visualization, complications, and risk factors for incomplete studies in dogs with overt or questionable gastrointestinal bleeding (GIB).

Animals: Forty dogs with overt or questionable GIB.

Methods: Prospective, multicenter, interventional study. From August 2017 to March 2020, dogs were examined by VCE (ALICAM) because of overt or questionable GIB. Reported outcomes included diagnostic results of VCE study, quality of visualization, and complications. Risk factors for incomplete studies were evaluated using logistic regression.

Results: In total, 40 dogs (13 overt, 27 questionable GIB) were included. The capsules were administered PO in 29 and endoscopically in 11 dogs (6 duodenum, 5 stomach). One capsule was not retrieved. In 24 of 39 recordings, bleeding lesions were identified (10 overt GIB, 14 questionable GIB). Overall, the quality of visualization was poor to limited in the stomach and colon, and adequate to good in the small intestine. The most common complication was an incomplete study in 15/39 studies, particularly after oral administration (13/28). Risk factors for incomplete study after oral administration included administration of simethicone or opioids, chronic enteropathy, and capsule gastric transit time >6 hours.

Conclusions and Clinical Importance: Video capsule endoscopy can be used to diagnose a variety of lesions causing bleeding in the gastrointestinal tract of dogs with questionable GIB. Incomplete studies are the most common complications in dogs after oral administration of capsules.

KEYWORDS
anemia, canine, gastroenterology, hemorrhage, simethicone

Abbreviations: BCS, body condition score; CGTT, capsule gastric transit time; CI, confidence interval; GI, gastrointestinal; GIB, gastrointestinal bleeding; INF, infinity; MOVEH, Mississauga Oakville Veterinary Emergency Hospital; n, sample size; NG, nasogastric; OR, odds ratio; OVC-HSC, Ontario Veterinary College Health Sciences Centre; PEG, polyethylene glycol; VCE, video capsule endoscopy; VEC, Veterinary Emergency Clinic Toronto.

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1 | INTRODUCTION

Video capsule endoscopy (VCE) provides a noninvasive endoscopic imaging technique for the evaluation of the gastrointestinal (GI) tract. It has been increasingly used for 2 decades in humans.[1] The main advantage of VCE over traditional bidirectional endoscopy is the visualization of the entire small intestine. In humans, VCE is superior in diagnosing obscure GI bleeding (GIB) (ie, GIB without a lesion identified after upper and lower conventional endoscopy) compared to other modalities, such as double-balloon endoscopy.[2-4] Therefore, 1 of the main indications of VCE administration is recurrent or persistent obscure GIB as well as unexplained iron deficiency anemia.[5,6] European and North American VCE guidelines addressing indications, bowel preparation, reporting, and training are available and support the optimal use of VCE in human gastroenterology.[5,6] Incomplete studies defined as failure to reach the cecum within recording time are the most common complications in people.[7] Other complications reported include capsule retention, aspiration of the capsule into the airways, and technical complications, such as failure to activate the capsule.[8-10]

In contrast to human medicine, VCE is not widely used in animals. The initial reports in dogs and pigs were conducted as experimental studies before human use.[11-13] More recently, there are several studies mostly in the form of retrospective case reports and case series of dogs[14-21] and horses.[22] Video capsule endoscopy is mainly used to detect bleeding lesions in dogs with overt GIB and suspected occult GIB,[19-21] and for evaluation of treatment response to GI antiparasiticides.[15-17] Thus far, incomplete studies and vomiting of the capsule are the only reported complications in dogs.[14,15,17-19,21] Based on a prospective study about feasibility and diagnostic ability of VCE (Endo Capsule, Olympus America Inc, Center Valley, Pennsylvania) in 8 dogs, it can be used to detect gastric and small intestinal bleeding mucosal lesions.[19] The conclusions from this study are limited by the small number of dogs (2 control dogs, 8 dogs with GIB). Additionally, other aspects of VCE, such as quality of visualization and possible risk factors for incomplete studies, were not examined. Larger prospective studies in dogs with overt and occult GIB evaluating feasibility, quality of visualization, and complications are lacking, and further investigations of a veterinary specific capsule endoscope (ALICAM, Infiniti Medical LLC, Redwood City, California) are warranted. This information is crucial for veterinarians in order to understand the advantages and limitations of this relatively new diagnostic procedure.

In this study, we aimed to assess the feasibility, quality of visualization, and complications of VCE in dogs with overt or questionable GIB. We hypothesized that VCE is a safe procedure that can detect bleeding lesions in the entire GI tract and that similar to people, incomplete studies, where the capsule does not reach the colon during recording time, will be the most common complication. As a secondary objective, we sought to identify possible demographic and clinical risk factors for incomplete studies.

2 | MATERIALS AND METHODS

2.1 | Dogs

This was a prospective multicenter study performed in dogs presented with overt or questionable GIB to 1 of the following veterinary referral hospitals: Ontario Veterinary College Health Sciences Centre (OVC-HSC, University of Guelph, Guelph, Canada), Mississauga Oakville Veterinary Emergency Hospital (MOVEH, Oakville, Canada), and Veterinary Emergency Clinic Toronto (VEC, Toronto, Canada). Dogs were enrolled from August 2017 to March 2020. Dogs were included if they presented with overt GIB defined as hematemesis, melena, or hematochezia. Moreover, dogs were included if GIB was considered 1 of the differential diagnoses based on the presence of acute GI-related clinical signs (eg, anorexia, vomiting) with concurrent ulcerogenic risk factors (ie, ongoing or recent treatment with nonsteroidal anti-inflammatory drugs [NSAIDs] or corticosteroids, chronic enteropathy, pancreatitis, historical GI ulceration)[23-25] or findings on bloodwork consistent with occult GIB (ie, unexplained anemia or microcytosis).[26,27] Chronic enteropathy was defined as the presence of GI-related clinical signs for at least 3 weeks and was diagnosed after exclusion of extra-GI and infectious diseases via routine bloodwork, fecal examination, and abdominal ultrasound. Dogs with chronic enteropathy either responded positively to a diet change, or had GI endoscopy performed revealing an inflammatory enteropathy, or both. Unexplained anemia was defined as a decrease in hematocrit or hemoglobin without evidence of hemolysis, a bone marrow disease affecting several cell lines or an evident cause for blood loss. The study protocol was approved by the University of Guelph Animal Care Committee. Owner consent was obtained for each dog before enrollment into the study. Costs of VCE were partially covered by the study. Dogs with a body weight of <4.5 kg,[28] coagulopathy, suspected partial or complete GI obstruction, and GI perforation were excluded from study enrollment. Each dog had a thorough diagnostic workup performed which included at least hematology, serum biochemistry, and abdominal ultrasound.

2.2 | Video capsule endoscopy procedures

All dogs received an ALICAM capsule. Dogs were fasted for 12 to 24 hours before, and for 8 hours after capsule administration. Only in dogs with recently resolving anorexia were shorter fasting times of 8 to 12 hours permitted in order to minimize the overall peri-VCE fasting time to avoid any possible detriment to the dog's recovery. Bowel preparation was not standardized and was performed at the discretion of the attending clinicians and included both oral or nasogastric (NG) tube and rectal treatments. Rectal protocols included 20 to 40 mL/kg warm water enemas for awake dogs, and for anesthetized dogs rectal delivery of warm water until clear liquid was drained. Polyethylene glycol (PEG, 40-60 mL/kg) was given PO or via NG tube 12 to 24 hours before capsule administration. Simethicone (25-200 mg per dog) was administered once PO, 30 minutes before

capsule administration as recommended in humans.[29] Metoclopramide was administered as needed either as part of the treatment of the underlying disease (using it as an antiemetic or prokinetic) or as a prokinetic for possible improved VCE study completion in dogs which had previous signs of delayed gastric emptying and an ongoing chronic disease that could predispose them to recurrent GI dysmotility, such as diabetes mellitus.

The capsule was administered PO or endoscopically. Endoscopic deployment was performed if GI endoscopy was part of the diagnostic workup or if oral administration was not possible because of dysphagia or the dog's temperament. The goal of the endoscopic deployment was placement of the capsule directly into the duodenum. If this was not possible, the capsule was placed into the stomach. Early during the enrollment period, an endoscopic basket (Falcon rotatable retrieval basket, STERIS, Mentor, Ohio) was used for deployment. However, because of difficulties of passing the basket through the pylorus with the capsule oriented perpendicularly to the scope, a capsule endoscope delivery device (AdvanCE capsule endoscope delivery device, STERIS) was used after December 2018. The dogs were discharged home into the care of their owners after capsule administration or continued to be hospitalized if required for their ongoing care. Owners and hospital staff were instructed to check for capsule excretion and to document the time of retrieval. The capsules were returned to the OVC-HSC where the images were downloaded and subsequently analyzed by a board-certified internist (A. M. Defarges) who was trained and experienced in reading VCE examinations.

2.3 | Outcome measures

Data reported included bowel preparation, capsule transit time from administration to collection, recording time from capsule activation to termination of image acquisition, diagnostic results of VCE study, diagnostic yield for overt GI bleeders, quality of visualization, and complications. Bleeding lesions were categorized as actively and recently bleeding erosions or ulcers, bleeding GI masses, angioectasia, and bleeding of unknown origin. Bleeding lesions caused by endoscopic biopsies were not reported. Any other abnormalities that were considered clinically significant were also recorded. Diagnostic yield was defined as the proportion of dogs in which a GIB source was identified using VCE out of the total number of overt GI bleeders who received VCE. The quality of visualization was scored by 1 examiner (A. M. Defarges) for the stomach, small intestine (proximal, middle, and distal thirds), and colon separately. The score was adapted from human medicine, and scored as follows based on the percentage of mucosa visualized: score 1, ≤25% (poor visualization); score 2, 25% to 49% (limited visualization), score 3, 50% to 74% (adequate visualization), and score 4, ≥75% (good visualization).[30] Clinical adverse events or complications as observed by the owner or clinicians during administration or passing of the capsule were documented. Incomplete studies were defined as failure to reach the colon within recording time. Capsule retention was defined according to its use in human gastroenterology as the presence of the capsule in the GI tract for a minimum of 2 weeks.[7,9]

2.4 | Statistical analyses

Categorical variables were presented as frequencies, percentages, or both. Numerical data were tested for normality using Shapiro-Wilk test and inspection of QQ plots. All numerical data were non-normally distributed and were expressed as median and range.

To identify risk factors for incomplete studies of capsules administered PO, univariable logistic regression was performed. We examined the assumption of linearity by including a quadratic term for each laboratory parameter. Dogs who received VCE via endoscopic deployment were excluded from analysis because none of the dogs that had endoscopic deployment of the capsule into the duodenum had an incomplete study. Sex, weight, age, body condition score (BCS, out of 9), administration of PEG, simethicone, or metoclopramide, rectal enema, hospitalization, recent sedation (butorphanol, dexmedetomidine, ketamine; within 24 hours of capsule administration) and opioid use (butorphanol, buprenorphine, fentanyl, hydromorphone, tramadol; within 24 hours of capsule administration), presence of overt versus questionable GIB, concurrent chronic enteropathy, and capsule gastric transit time (CGTT) >6 hours were used as independent variables. Odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were reported for all variables. Ordinary logistic regression was performed unless estimates were approaching positive infinity or zero in which case, exact logistic regression was performed and median unbiased estimates of the ORs were reported. Goodness-of-fit was assessed via Hosmer-Lemeshow test where continuous independent variables were included in the model (ie, binary data). Scatter plots of residuals and predicted values of logistic regression models were used to identify outliers.

Commercial statistical software packages (MedCalc Statistical Software 18.11.6, MedCalc Software bvba, Ostend, Belgium; STATA 15, Stata Corp, College Station, Texas) were used for all statistical analyses. Significance level α was set .05.

3 | RESULTS

3.1 | Dogs

Forty client-owned dogs were enrolled. Thirty-six dogs were enrolled at OVC-HSC, 3 dogs at MOVEH, and 1 dog at VEC. The median age of dogs was 8 years (range, 4 months to 15 years) and the median weight was 23.3 kg (6.8-51.6 kg). Median BCS was 5 (2-8). Twenty-one (53%) dogs were female (18 spayed, 45%; 3 intact, 8%), and 19 (47.5%) dogs were male (17 neutered, 43%; 2 intact, 5%). A total of 24 breeds were represented, with dogs of mixed breed (8 dogs, 20%) and Golden Retriever (7 dogs, 18%) being the most common. Data for the 40 dogs is summarized in Table S1.

Thirteen (33%) dogs presented with overt GIB (6 melena, 4 hematochezia, 2 melena and hematochezia, 1 hematemesis and melena).

TABLE 1 Overview of bowel preparation in 40 dogs before video capsule endoscopy administration

	PEG and simethicone	PEG	Simethicone	No PEG or simethicone
Rectal enema	9	2	5	15
No rectal enema	6	2	0	1

Notes: PEG was administered PO or via nasogastric tube. Simethicone was given PO 30 minutes before capsule administration. Each cell contains the number of dogs.
Abbreviation: PEG, polyethylene glycol.

TABLE 2 Summary of the administration and recovery of video capsule endoscopies from 40 client-owned dogs

	Total, n (%)	Overt GIB, n (%)	Questionable GIB, n (%)
Total number, n	40	13	27
Administration			
Oral administration	29 (73%)	7 (54%)	22 (82%)
Endoscopic deployment	11 (28%)	6 (46%)	5 (19%)
Deployment into stomach	5 (13%)	3 (23%)	2 (7%)
Deployment into duodenum	6 (15%)	3 (23%)	3 (11%)
Recovery of capsule			
Fecal excretion	36 (90%)	12 (92%)	25 (93%)
Expulsion via spontaneous vomitus	1 (3%)	—	1 (4%)
Recovery during necropsy	2 (5%)	1 (8%)	1 (4%)
Lost capsule	1 (3%)	—	1 (3%)

Notes: Forty dogs received VCE (13 dogs with overt gastrointestinal bleeding, 27 dogs with questionable gastrointestinal bleeding). One capsule was not collected after excretion and the data were lost. Each cell contains the number (percentage) of capsules.
Abbreviations: GIB, gastrointestinal bleeding; n, number of dogs.

Twenty-seven (68%) dogs were included for questionable GIB based on GI-related clinical signs in combination with unexplained anemia (13, 33%), administration of NSAIDs (5, 13%), administration of prednisone, unexplained microcytosis, history of gastric ulcer, and historical chronic enteropathy with concurrent pancreatitis (1 each, 3% each), or administration of prednisone in combination with unexplained anemia (5, 13%).

In 26 (65%) dogs, VCE was performed as a first-line endoscopic test before conventional GI endoscopy. Of these, conventional GI endoscopy was performed after VCE as a result of its findings in 4 dogs. Three (8%) dogs had previous conventional GI endoscopy performed in which 2 dogs had no source of bleeding identified (conventional endoscopy performed 5 and 9 months earlier), and 1 dog had colonic angioectasia diagnosed by previous GI endoscopy and VCE that had been performed 2 years before. In 11 (28%) dogs, VCE was placed endoscopically directly after negative GI endoscopy (upper, lower, or both).

3.2 | Video capsule endoscopy procedures

Thirty-eight (95%) dogs were fasted for 12 to 24 hours before VCE administration. In 2 (5%) dogs, a shorter fasting time of 8 hours was chosen to decrease the overall fasting time as these dogs' anorexia was just resolving. The majority of dogs (31 dogs, 78%) received rectal enemas, 20 (50%) dogs received oral simethicone, and 19 (48%) received PEG (Table 1). One dog did not receive bowel preparation except for fasting. Ten (25%) dogs received metoclopramide (0.3-0.5 mg/kg every 8 hours PO/SC; 2 mg/kg/day CRI IV) at the time of capsule administration.

Twenty-nine (73%) dogs received VCE via oral administration, and 11 (28%) via endoscopic deployment (Table 2). In 10 dogs, GI endoscopy was performed as part of the diagnostic workup; in 1, oral administration was not possible because of the dog's temperament. Six capsules were successfully placed into the duodenum endoscopically using a delivery device. In the remaining 5 dogs, the pylorus could not be passed after duodenal endoscopic biopsies were obtained, and the capsule was deployed into the stomach (in 4 dogs using an endoscopic basket, in 1 dog using an endoscopic delivery device).

Of 40 capsules, 39 (98%) were retrieved; 1 capsule was not collected after excretion. Recovery by defecation was successful in 36 (90%) dogs, and 1 (3%) capsule was vomited (Table 2). Of the 37 studies in which the capsule was spontaneously excreted, transit time from administration to excretion or expulsion of the capsule was available in 35 (95%) dogs and ranged from 2.5 hours to 8 days (median 30.5 hours). Median recording time from capsule activation to termination of image acquisition was available in 39 capsules and was 15 hours and 58 minutes (range, 8 hours and 42 minutes to 22 hours and 18 minutes).

Two (5%) capsules were retrieved from the stomach on postmortem examination. One dog was euthanized 6 days after administration of the VCE (before spontaneous excretion) because of worsening anemia. Another dog died unexpectedly at home approximately 12 hours

TABLE 3 VCE findings of 39 available studies in dogs with and without GI bleeding and their respective locations

	Total, n (%)	Overt GIB, n (%)	Questionable GIB, n (%)
Total number, n	39	13	26
Actively or recently bleeding lesion(s)	24 (62%)	10 (77%)	14 (54%)
Erosion(s) and/or ulcer(s)	19 (49%)	7 (54%)	12 (46%)
Gastric mass	1 (3%)	—	1 (4%)
Angioectasia/suspected angioectasia	3 (8%)	2 (15%)	1 (4%)
Bleeding of unknown origin	1 (3%)	1 (8%)	—
Location of bleeding site			
Stomach	20 (39%)	6 (46%)	14 (54%)
Proximal third small intestine	3 (8%)	2 (15%)	1 (4%)
Middle third small intestine	2 (5%)	2 (15%)	—
Distal third small intestine	2 (5%)	2 (15%)	—
Colon	3 (8%)	1 (8%)	2 (8%)
Clinically significant non-bleeding lesions			
Non-bleeding erosion(s)	8 (21%)	3 (23%)	5 (19%)
Dilated intestinal lacteals	2 (5%)	—	2 (8%)
Erythematous mucosa	2 (5%)	—	2 (8%)
Focal, irregular, hypertrophic intestinal mucosa	1 (3%)	1 (4%)	
Location of non-bleeding lesions			
Stomach	3 (8%)	—	3 (12%)
Proximal third small intestine	3 (8%)	1 (8%)	2 (8%)
Middle third small intestine	3 (8%)	—	3 (12%)
Distal third small intestine	5 (13%)	2 (15%)	3 (12%)
Colon	4 (10%)	1 (8%)	3 (12%)

Notes: Video capsules of 39 dogs were available for analysis (13 dogs with overt gastrointestinal bleeding, 26 dogs with questionable gastrointestinal bleeding). Each cell contains the number (percentage) of studies.
Abbreviations: GI, gastrointestinal; GIB, gastrointestinal bleeding; n, number of dogs.

after capsule administration. No cause of death was identified on postmortem examination. In both cases, the capsule was located in the stomach and GI perforation was not identified.

3.3 | Gastrointestinal findings

Of the 39 capsules available for analysis, 15 (39%) studies were incomplete only revealing images of esophagus and stomach. All sites of GIB and GI abnormalities identified on VCE are reported in Table 3. In 24 (62%) capsules, bleeding lesions of the GI tract were identified. Examples of bleeding GI lesions noted via VCE are provided (Figure 1 A-D). In dogs with overt GIB (13), 10 (77%) VCE examinations showed actively or recently bleeding lesions. Although 3 dogs with overt GIB did not have a source of bleeding identified, 2 of these 3 nondiagnostic studies were incomplete examinations because of temporary gastric retention and only 1 of these studies was negative despite passage of the capsule through the GI tract. In the latter study, the capsule was placed endoscopically into the duodenum. During conventional upper GI endoscopy, at VCE placement, no bleeding lesions were identified, and VCE did not reveal any lesions. Visibility in the colon was poor because of insufficient preparation. However, from a clinical perspective, this dog had melena and hematemesis so a lesion in the upper GI tract was suspected. In dogs with questionable GIB (26), bleeding lesions were identified in 14 of 26 (54%) studies.

Capsule endoscopy also identified nonbleeding GI abnormalities and their sites within the GI tract (Table 3). In 2 dogs, dilated lacteals were identified in the small intestine (Figure 1E) and lymphangiectasia was histologically confirmed via traditional endoscopic biopsies.

3.4 | Quality of visualization

The quality of visualization throughout the GI tract is provided (Table 4). The median scores for stomach, proximal, middle, distal small intestine, and colon were 2, 4, 4, 3, and 1, respectively. The quality of visualization of the gastric and colonic mucosa was limited because of the presence of food, debris, feces, or bubbles.

3.5 | Complications

The most frequent complication was incomplete recording of the GI tract. Of the 39 capsules available for analysis, 15 (39%) studies

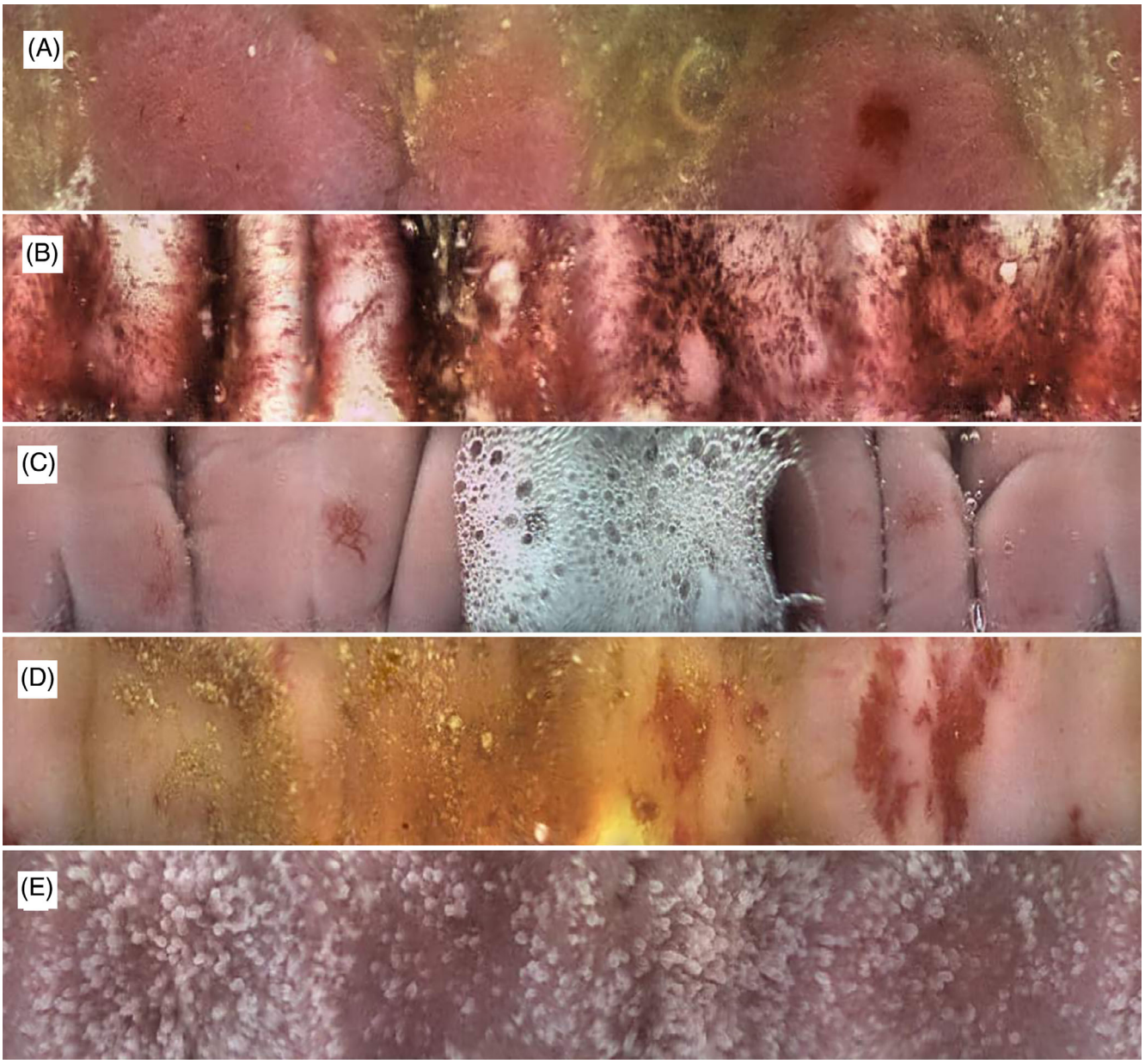

FIGURE 1 Video capsule endoscopy images of bleeding (A-D) and nonbleeding (E) lesions. A, Gastric ulcer. B, Multiple punctate gastric erosions/ulcers with mainly hematin. C, Gastric angioectasia. D, Colonic angioectasia. E, Dilated lacteals in mid third small intestine

(4 overt GIB, 10%; 11 questionable GIB, 28%) were incomplete. All capsules of incomplete studies remained within the stomach during the entire recording time. Thirteen of 28 (46%) capsules (3 overt GIB, 11%; 10 questionable GIB, 36%) which were given PO resulted in incomplete studies. Two (1 overt, 1 questionable GIB) of 5 capsules deployed endoscopically into the stomach resulted in incomplete studies. All capsules that were placed directly into the duodenum revealed images of the remainder of the GI tract.

All 29 dogs that received the capsule PO swallowed it without complication. When deployed endoscopically, difficulties passing the capsule through the pylorus were encountered in all 4 dogs where an endoscopic basket was used and in 1 of 7 dogs using the endoscopic capsule delivery device. In the latter, the pylorus could not be passed because of persistent pylorospasm (after endoscopic duodenal biopsies were obtained) despite the delivery device allowing longitudinal alignment of the capsule.

One dog, a 9-year-old female spayed Miniature Schnauzer (6.8 kg), vomited the capsule 66 hours after administration. Another dog, a 10-year-old female spayed mixed breed dog (22.8 kg), was reported to be restless and uncomfortable at home within 6 hours after capsule administration. Both dogs had received pre-procedural bowel preparation with PEG PO (24 hours before), simethicone (30 minutes before), and metoclopramide at the time of capsule administration. On reevaluation of the mixed breed dog, physical examination revealed borborygmi. Abdominal radiographs showed a gas-filled cecum and colon; the capsule remained within the stomach. The clinical signs resolved within 24 hours without any further intervention and before spontaneous excretion of the capsule. Video

TABLE 4 Scores of visualization quality of the GI mucosae assessed by video capsule endoscopy in client-owned dogs

	Total, n (%)	Overt GIB, n (%)	Questionable GIB, n (%)
Stomach (n = 33)			
1	15 (46%)	6 (60%)	9 (39%)
2	10 (30%)	4 (40%)	6 (26%)
3	5 (15%)	—	5 (22%)
4	3 (9%)	—	3 (13%)
Proximal third small intestine (n = 24)			
1	2 (8%)	1 (11%)	1 (7%)
2	2 (8%)	—	2 (13%)
3	4 (17%)	2 (22%)	2 (13%
4	16 (67%)	6 (67%)	10 (67%)
Middle third small intestine (n = 24)			
1	1 (4%)	1 (11%)	—
2	5 (21%)	2 (22%)	3 (20%)
3	4 (17%)	1 (11%)	3 (20%)
4	14 (58%)	5 (56%)	9 (60%)
Distal third small intestine (n = 24)			
1	5 (21%)	4 (44%)	1 (7%)
2	3 (13%)	1 (11%)	2 (13%)
3	10 (42%)	2 (22%)	8 (53%)
4	6 (25%)	2 (22%)	4 (27%)
Colon (n = 24)			
1	14 (58%)	6 (67%)	8 (53%)
2	7 (29%)	2 (22%)	5 (33%)
3	2 (8%)	1 (11%)	1 (7%)
4	1 (4%)	—	1 (7%)

Notes: The score was based on the percentage of mucosa visualized: score 1, ≤25% (poor visualization); score 2, 25% to 49% (limited visualization); score 3, 50% to 74% (adequate visualization); and score 4, ≥75% (good visualization). The quality of visualization of the stomach was scored in 33 dogs (excluding 6 dogs in whom capsule was deployed directly into duodenum), and of small intestine and colon in 24 dogs (excluding 15 dogs with incomplete examinations). Each cell contains the number (percentage) of studies.
Abbreviations: GIB, gastrointestinal bleeding; n, number of examinations.

capsule endoscopy revealed multifocal punctate bleeding gastric erosions/ulcers. As mentioned previously, 1 dog was euthanized and another 1 died before spontaneous excretion of the capsule. In both cases, euthanasia/death was concluded to be unrelated to administration of the capsule.

One capsule was not collected after excretion and the data were lost. Abdominal radiographs ruled out GI retention of the capsule.

3.6 | Risk factors for incomplete study

Results of univariable logistic regression analysis for all investigated possible risk factors for incomplete examinations of VCE that were administered PO are shown in Table 5. Dogs in whom the capsule was deployed endoscopically were excluded from this analysis. The risk of incomplete study was highest if CGTT >6 hours. Other significant risk factors for incomplete study were chronic enteropathy, administration of simethicone before capsule administration, and recent administration of opioids within 24 hours of capsule administration.

4 | DISCUSSION

Based on our results, VCE is a safe and easy procedure. It can be used to diagnose a variety of bleeding lesions throughout the entire GI tract of dogs. However, diagnostic yield can be decreased by poor visibility of the GI mucosa and incomplete studies. The latter occurred in 13 of 28 (46%) of capsules administered PO.

In human gastroenterology, VCE is recommended in patients with overt GIB (excluding hematemesis) after negative esophagogastroduodenoscopy and colonoscopy.[5,6] In our study, VCE was frequently used as a first-line diagnostic over conventional endoscopy because of owner preference to avoid general anesthesia. Moreover, because of study funding, VCE was less expensive for owners than traditional GI endoscopy which might have led to a bias towards performing VCE as a first diagnostic step. Our results are therefore not directly comparable to those of human VCE studies.

Our diagnostic yield in dogs with overt GIB was 77%. Because dogs with questionable GIB might not actually have had GI hemorrhage given that the inclusion criteria for this group were less restrictive and anemia or microcytosis were possible but not required criteria, we could not assess the diagnostic yield of VCE in this group. In human patients with obscure overt GIB (ie, unknown origin of overt bleeding after traditional GI scoping), the reported diagnostic yield of VCE ranges from 50% to 72%.[5] Given that in our study the inclusion criteria for dogs receiving VCE were less restrictive (ie, dogs without obscure GIB) and that VCE was frequently performed as a first line endoscopic technique, our results are not comparable to those of human reports. In comparison to other studies in dogs, our diagnostic yields were lower. In a prospective study, bleeding lesions were identified in all 8 dogs, 6 with overt GIB and 2 with occult GIB. In a retrospective study, GI erosions or ulcers were noted in 14 of 16 dogs with microcytosis or overt GIB. Possible reasons for variability in diagnostic yield include differences in frequencies of incomplete studies and visibility of the GI mucosa. Incomplete studies were also reported in the previously mentioned studies, but it did not decrease the diagnostic yield as gastric lesions were visualized in these dogs.[19,21] Visibility of the GI mucosa was not assessed in these studies, therefore its influence on diagnostic yield cannot be evaluated.[19,21] Different types of capsules could have also impacted diagnostic yield. In a previous study in dogs, an axial-viewing capsule was used,[19] whereas in this and a study from 2019, a lateral-viewing device was used.[19,21] However, in people, image quality and diagnostic yield of lateral- and axial-viewing capsules are comparable for relevant bleeding lesions.[31,32]

To improve diagnostic yield and image quality, most dogs were fasted for 12 to 24 hours before VCE examinations. Some dogs also

TABLE 5 Univariable logistic regression analysis of risk factors for incomplete studies after oral administration of video capsules in 28 client-owned dogs

Parameter	Dogs, n	Incomplete studies, n (%)	OR	95% CI	*P* value
Body weight	28	13	0.95	0.88-1.02	.17
Age	28	13	0.95	0.78-1.15	.58
BCS	28	13	0.98	0.57-1.66	.93
Sex			0.30	0.06-1.42	.13
Male	13	4 (31%)			
Female (referent)	15	9 (60%)			
Administration PEG			2.92	0.57-15.05	.2
Yes	18	10 (56%)			
No (referent)	10	3 (30%)			
Administration simethicone			10.50	1.07-102.48	.04
Yes	20	12 (60%)			
No (referent)	8	1 (13%)			
Administration metoclopramide			1.78	0.32-10.01	.51
Yes	7	4 (57%)			
No (referent)	21	9 (43%)			
Rectal enema			2.22	0.43-11.60	.34
Yes	19	10 (53%)			
No (referent)	9	3 (33%)			
Hospitalization			1.02	0.23-4.53	.98
Yes	15	7 (47%)			
No (referent)	13	6 (46%)			
Recent Sedation			4.40	0.89-21.78	.07
Yes	12	8 (62%)			
No (referent)	16	5 (39%)			
Opioids			9.17	1.64-51.43	.01
Yes	14	10 (77%)			
No (referent)	14	3 (23%)			
Presence of overt GIB			0.83	0.15-4.63	.83
Yes	7	3 (43%)			
No (referent)	21	10 (48%)			
Chronic enteropathy			10.75[a]	1.29-+INF	.01
Yes	5	5 (100%)			
No (referent)	23	8 (35%)			
CGTT			50.51[a]	6.38-+INF	<.0001
>6 hours	16	13 (81%)			
<6 hours (referent)	12				

Notes: Thirteen of 28 video capsule endoscopy studies (46.4%) were incomplete, that is, did not reach the colon during recording time. In all cases, the capsule remained within the stomach during recording time. Of the 10 dogs who received metoclopramide, 7 dogs received it as part of the treatment of the underlying disease, either via parenteral administration during hospitalization for several days (5 dogs, duration of metoclopramide administration: 3-9 days) or as long-term PO administration at home before and after VCE administration (2 dogs). In 3 dogs, metoclopramide was prescribed to facilitate VCE movement as these dogs had a history of GI dysmotility and had a chronic condition (chronic enteropathy, 1 dog; chronic intermittent GIB, 1 dog; diabetes mellitus, 1 dog) that could have predisposed them to delayed gastric emptying. In these dogs, metoclopramide was given for 2 days (the day of and 1 day after VCE administration). Sedatives and opioids were administered within 24 hours before capsule administration. Sedatives included dexmedetomidine (2-5 μg/kg IV bolus), butorphanol (0.2-0.4 mg/kg IV bolus), hydromorphone (0.05 mg/kg IV bolus), and ketamine (0.1-0.6 mg/kg/hr IV continues rate infusion). Opioids included buprenorphine (0.01-0.02 mg/kg IV every 8 hours), butorphanol (0.2-0.4 mg/kg IV once), hydromorphone (0.025-0.05 mg/kg every 6-8 hours), fentanyl (2-6 μg/kg/hr IV continuous rate infusion), and tramadol (2 mg/kg PO every 12 hours). Ordinary logistic regression was performed for all independent variables except for chronic enteropathy and CGTT for which exact logistic regression was used. For each continuous variable, there was no evidence of lack of model fit and no outliers were identified. Assumption of linearity was met for each variable. The referent category is defined as the category of comparison for the other category.

Abbreviations: BCS, body condition score; CGTT, capsule gastric transit time; CI, confidence interval; GI, gastrointestinal; GIB, gastrointestinal bleeding; +INF, positive infinity; n, number; OR, odds ratio; PEG; polyethylene glycol.

[a]Odds ratios represent the median unbiased estimate based on exact logistic regression.

received PEG, simethicone, or rectal enemas. Nonetheless, in most dogs a visibility score of 1 or 2 was attributed to the gastric and colonic mucosa which indicates that <50% of the mucosa was visible. Current guidelines for VCE in human patients recommend a 12 to 24 hours pre-VCE fasting time as well as bowel preparation, but there is insufficient evidence to recommend a specific type of preparation.[5,33,34] Similar to people, there are no standardized preparation protocols in dogs. Pre-VCE fasting time in other studies in dogs ranged from 12 to 48 hours.[15-20] One study reported enhanced image quality when dogs were administered PO PEG instead of physiologic saline.[18] Given that bowel preparation was not standardized in our study, conclusions regarding the optimal preparation cannot be drawn.

As previously noted, incomplete VCE examination was the most common complication. It was encountered in 39% of all cases and in 47% of capsules administered PO. This is consistent with other reports in humans and dogs.[8,19,21] Reported risks for incomplete studies in people range from 20% to 30%.[7,8,35-38] Reported incidences of incomplete studies for PO administered VCE capsules in dogs with GIB are 13% (2 of 16 dogs)[21] and 38% (3 of 8 dogs).[19] In studies assessing VCE in dogs with intestinal parasitism, 17% (3 of 18 dogs) of VCE studies were incomplete.[15,17] The differences in incomplete study rates in reports in dogs might be because of differences in health status of the dogs (eg, hospitalized versus ambulant, acute versus chronic disease), size of dogs, capsule endoscopes (eg, size, battery life), and preparation protocol (eg, fasting time).

The administration of simethicone before VCE examination was identified as a risk factor for incomplete studies. Simethicone was administered in these dogs in order to improve visualization as shown in human patients.[39] Simethicone is a surfactant that reduces surface tension causing gas bubbles in the GI tract to coalesce, disperse, and promotes the expulsion of intestinal air. Its empirical use is thought to be safe in dogs, but studies regarding its utility and adverse effects have not been published.[40] In people, administration of simethicone has been shown to improve visualization of the mucosa without affecting completion rate or diagnostic yield.[29] The antifoaming agent was given PO 30 minutes before oral capsule administration in 20 dogs; this has not been reported in previous VCE studies in dogs.[19-21] As it promotes expulsion of gas, this might have caused abdominal discomfort in some dogs and could have affected GI motility. However, as the protocol for bowel preparation was not standardized and given the heterogenicity of our dogs, randomized and blinded clinical trials assessing the effect of simethicone on GI motility and in dogs receiving VCE are required. Until such information is available, our results should be interpreted with caution.

Additional risk factors for incomplete examinations included chronic enteropathy and recent administration of opioids within 24 hours of capsule administration. Crohn's disease is a known risk factor for incomplete examination in people.[7] Primary GI disease, such as inflammatory bowel disease, can cause GI dysmotility.[41,42] Similarly, we suspect that administration of opioids caused decreased GI motility and possibly ileus resulting in incomplete studies.[43]

The most significant risk factor for an incomplete study was a capsule gastric emptying time (CGTT) >6 hours. In people, a CGTT of >45 minutes is a reported risk factor for incomplete study with an OR of 3.1 (95% CI, 1.70-5.70, $P < .001$).[38] Although VCE has not been validated yet as a tool for evaluation of GI transit in dogs, wireless motility capsules have been validated in dogs to assess solid phase transit times.[44,45] In most dogs, the capsule did not exit the stomach with the initial meal.[45] Therefore the authors concluded, that the CGTT cannot be correlated with gastric emptying of normal ingesta. Nonetheless, this risk factor might be helpful in the future as possible interventions to promote passage of the capsule could be implemented in dogs in whom the capsule still resides inside the stomach after 6 hours.

Several tactics to decrease risk of incomplete studies have been evaluated in people. Studies assessing the effect of prokinetics, such as metoclopramide and erythromycin, on completion rates have had contradictory results.[46-49] Therefore, in the North American guidelines for the use of VCE, it was concluded that there is only low quality evidence for efficacy of prokinetics to improve study completion in people.[5] Similarly, administration of metoclopramide in healthy dogs and in 3 dogs with GIB did not improve the completion rate.[14,19] Administration of metoclopramide in our study was not associated with the odds to completing VCE. However, given the heterogeneity of both the duration and mode of administration of metoclopramide as well as the overall small number of dogs receiving metoclopramide, this finding should be interpreted with caution. Randomized clinical trials are needed to assess the efficacy of prokinetics in VCE studies in dogs.

Endoscopic deployment of the capsule into the duodenum might increase completion rates of VCE. Studies in people have shown differing results with decreased incidence of incomplete studies in some reports,[50,51] and no effect in others.[52] These conflicting results could be because of differences in indications when endoscopic placement was performed. In our study, all 6 capsules that were deployed endoscopically into the duodenum resulted in a complete examination. Duodenal VCE placement was performed after nondiagnostic conventional GI endoscopy, and complete GI studies were achieved despite these dogs being afflicted by other potential risk factors for incomplete studies (such a chronic enteropathy). Further studies are required to assess completion rates of endoscopic deployment in dogs with known risk factors of incomplete examination.

Other possible complications recorded were rare reports of vomiting of a gastric retained capsule and abdominal discomfort during the first 24 hours after VCE administration. In both cases, it is unclear if the capsule was the cause of these clinical signs. The dog who vomited the capsule 66 hours after its administration was the smallest dog (6.8 kg). It is possible that the capsule was too big to pass through the dog's pylorus. However, successful passage of the ALICAM was reported in a dog of 6.9 kg.[21] Vomiting of the capsule was also noted in 2 large breed dogs in another study.[19] To our knowledge, abdominal discomfort after capsule administration has not been reported in people or dogs. It is possible that this was caused by medications used for preparation (eg, PEG, simethicone) rather than the capsule itself. The capsule was lost in 1 dog because of failure of retrieval from feces despite clear instructions to all owners and hospital staff about the necessity to return the capsule. Although this has

not been reported in other studies in dogs,[20,21] it has been documented in people.[31]

This prospective study had several limitations. First, bowel preparation was not standardized. Therefore, conclusions regarding advantages, disadvantages, and the effect of certain protocols cannot be drawn. Additionally, 2 dogs only had an 8-hour fast before VCE administration. This could have negatively affected the visualization of the gastric mucosa. However, in these dogs it was elected to shorten the fasting time as they were just recovering from a period of anorexia. Second, the study did not compare the diagnostic accuracy of VCE to other endoscopic techniques. Hence, the frequency of missed lesions because of the inability to insufflate the stomach or because of the coverage of the mucosa by food or feces could not be assessed. Third, the VCE studies were only read by 1 examiner. In human medicine, interobserver agreement can be low to moderate, depending on the lesions.[53-55] However, agreement for actively bleeding lesions was reported to be high.[53,55] To our knowledge, studies assessing interobserver agreement in dogs are lacking. Ideally 2 experienced examiners would have evaluated the VCE studies but based on a limited number of experienced examiners available worldwide, this was not feasible.

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CONFLICT OF INTEREST DECLARATION

Alice M. Defarges has been an employee of Infiniti Medical since March 1st, 2020 but did not work for this company during enrollment of dogs.

OFF-LABEL ANTIMICROBIAL DECLARATION

Some dogs in this study received metronidazole, tylosin, ampicillin, cefazolin, and cefoxitin as part of their treatment for either GI disease (metronidazole and tylosin) or extra-GI disease (ampicillin, cefazolin, and cefoxitin). These drugs are not licensed for use in dogs in Canada and were chosen as they are considered safe and their use in these dogs was deemed indicated.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

The study was approved by the University of Guelph Animal Care Committee, and owner consent was obtained before blood collection and administration of video capsule endoscopy.

HUMAN ETHICS APPROVAL DECLARATION

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

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SUPPORTING INFORMATION

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

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