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Development and validation of an endoscopic activity score for canine inflammatory bowel disease

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ABSTRACT

The aim of this study was to develop and prospectively validate a simple endoscopic score of disease activity for dogs with inflammatory bowel disease (IBD). Archived endoscopic still images and video recordings of gastric, duodenal, and colonic endoscopic examinations were displayed to novice and experienced endoscopists for assessment of inflammatory activity using established descriptions. The mucosal appearances evaluated were normal tissue, erosions, friability, increased granularity, lymphangiectasia (duodenum), and mass (colon). Fleiss and Cohen's Kappa statistics were used to estimate the inter-observer agreement of the index.

For duodenal assessment, there were statistically significant ($P < 0.05$) differences in inter-observer agreement, with experienced endoscopists performing better than novice endoscopists in the accurate identification of mucosal appearance of the duodenum. In contrast, there was no significant difference between novice and experienced endoscopists in their interpretation of gastric ($P = 0.10$) and colonic ($P = 1.0$) mucosal appearances. Validation studies using endoscopic video clips to assess the same endoscopic parameters by quantitative (lesion number and severity) and qualitative (presence of mucosal lesions) methods showed moderate-to-substantial agreement between experienced endoscopists. Based on the observations that the quantitative and qualitative scores of mucosal appearances are virtually identical, and that qualitative assessment was performed more quickly and objectively than quantitative assessment, we propose a simple endoscopic activity score based on qualitative criteria alone in dogs with inflammatory bowel disease.

Introduction

The pathogenesis of canine inflammatory bowel disease (IBD) probably involves interplay between the mucosal immune system and the intestinal microbiota, similar to human IBD (i.e. Crohn's disease, CD, and ulcerative colitis, UC; Allenspach, 2011; Sartor, 2006; Xavier and Podolsky, 2007). Diagnostic tests including dietary trials, routine hematology, parasitic and bacteriologic fecal analyses, radiographic imaging, and histopathologic examination of intestinal biopsy specimens serve to eliminate other causes of chronic enteropathy. Gastrointestinal (GI) endoscopy is a useful and relatively non-invasive technique to diagnose IBD. It allows direct visualization of the mucosa for the acquisition of targeted biopsies to evaluate the severity and extent of intestinal inflammation (Roth et al., 1990; Zoran, 2001).

Determination of an inflammatory state is critical for defining disease activity and for tailoring IBD therapy. Endoscopic measures of mucosal inflammation in human IBD have been in use for over 40 years; however, no standardized model has been established (Truelove and Witts, 1955; Powell-Tuck et al., 1978; Seo et al., 1992; Lichtiger et al., 1994; Walmsley et al., 1998). Most indices for CD and UC are based on observations of mucosal erythema, increased granularity, vascular pattern, spontaneous bleeding, and mucosal damage (mucus, fibrin, exudates, erosions and ulcer), using simple scoring systems to define inflammatory activity. To date, no similar validated endoscopic score exists in veterinary medicine, and there is only limited trial data (Allenspach et al., 2007; Garcia-Sancho et al., 2007) evaluating the duodenal appearance of canine IBD, despite the suitability of the dog as a spontaneous animal model for intestinal inflammation (Jergens and Simpson, 2012). We recently reported that the inter-observer agreement for duodenal

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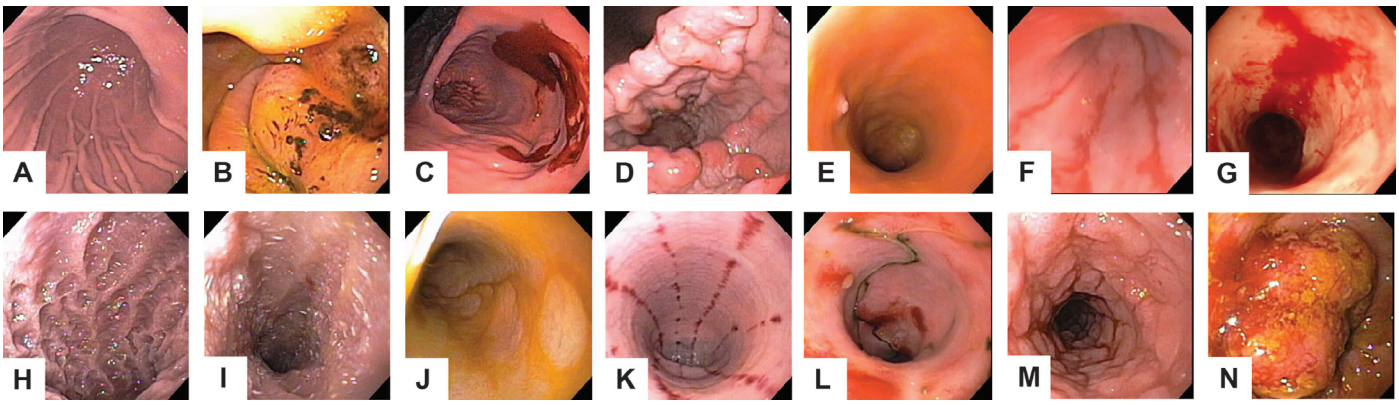

Fig. 1. Representative still images used in the development phase of the endoscopic study. (A) normal stomach; (B) gastric erosions; (C) gastric friability; (D) gastric granularity; (E) normal duodenum; (F) duodenal erosions; (G) duodenal friability; (H) duodenal granularity; (I) duodenal lymphatic dilatation; (J) normal colon; (K) colonic erosions; (L) colonic friability; (M) colonic granularity; (N) colonic mass.

endoscopic assessment of canine IBD differed among trainee and experienced endoscopists on the basis of operator experience (Slovak et al., 2014). The aim of the present study was to develop and validate an endoscopic disease activity score for the mucosal appearance of the stomach, duodenum and colon of dogs with IBD.

Materials and methods

Study design

The study was comprised of four parts. In the first part (development phase), the most relevant duodenal endoscopic variables (still images) in dogs with IBD were selected and scored for inter-observer agreement between novice and experienced endoscopists. For the second part of the development phase, an activity score based on endoscopic variables (still images) affecting the gastric and colonic mucosa was designed and assessed for inter-observer agreement among novice and experienced endoscopists. In the third part (the validation phase), representative video clips of approximately 5 min duration of gastroenteroscopic and/or colonoscopic examinations were assessed simultaneously but scored independently by two experienced endoscopists using the endoscopic criteria derived from the development phase. In the fourth phase, a simplified score was proposed based on the validation test results of endoscopic activity observed in the stomach, duodenum, and colon of dogs with IBD.

Endoscopic examinations

The details of the initial duodenal examination tests are described elsewhere (Slovak et al., 2014). In brief, the duodenal endoscopic mucosal appearance obtained from 25 dogs diagnosed with IBD at a single study center was assessed for inter-observer agreement. For the development phase of the study, 27 dogs diagnosed with IBD from 2002 to 2012 underwent gastroscopic examination, and 23 dogs with IBD from 2002 to 2011 undergoing colonoscopy were evaluated at the same study center. Endoscopic mucosal lesions were assessed for inter-observer agreement. Archived endoscopic still images from individual GI procedures were retrieved from a computerized database and reviewed. A total of 30 gastric, 35 duodenal and 30 colonic still images were selected for operator evaluation. A canine IBD activity index (CIBDAI) score as described by Jergens et al. (2003) was assigned retrospectively during the development phase of the study.

For each dog in the validation phase, a CIBDAI score was prospectively assigned and a video recording of the entire gastroduodenoscopic procedure ($n = 23$) and colonoscopic procedure (using 10 of the same dogs) was performed. Approximately 5 min of representative endoscopic video recording, including the insertion phase of obtaining mucosal biopsies of each organ(s), was evaluated. Two gastroenterologists (JES, AEJ), experienced in the examination of small and large intestinal mucosa in dogs with chronic enteropathies, then reviewed these clips and independently scored the presence/absence and severity of endoscopic mucosal abnormalities using criteria derived from the development phase of the study.

Endoscopic data collection and interpretation

Endoscopic procedures were performed using a commercial video endoscope (Olympus GIF-160, Olympus Optical) with still images and video recordings of GI mucosa captured by the endoscopist. The file size of the downloaded images was approximately 100 kb, with a pixel array of 640 × 480 and 24-bit color. These still images were then arranged in a presentation for testing purposes (Microsoft Office PowerPoint, Mac 2011 14.3.9). The images were assessed by three experienced and five novice endoscopists for inflammatory activity. Experienced endoscopists were defined as individuals with advanced clinical training (rotating internship and residency trained in small animal internal medicine) and active and consistent operator participation in a minimum of 50 GI endoscopy procedures (primary clinician/case responsibility) over the preceding 24 months. These operators were experienced and familiar with mucosal lesions as identified using GI endoscopy. Neither JES nor AEJ were included in this experienced operator group. Novice endoscopists had minimal endoscopic training, lacked consistent endoscopic operator experience, and had participated in less than five procedures over the same 24-month period.

Images were randomized using a web-based randomization program[1] and assessed independently by each endoscopist for mucosal appearance as originally determined by JES and AEJ. Neither the clinical data nor the date on which the image was taken was made known to the endoscopists. The endoscopic parameters evaluated for the stomach included: granularity ($n = 6$), friability ($n = 6$), erosions ($n = 8$), hyperemia ($n = 3$), normal pre-biopsy mucosa ($n = 3$), and normal post-biopsy mucosa ($n = 4$). Parameters for the small intestine included: granularity ($n = 6$), friability ($n = 6$), erosions ($n = 7$), lymphatic dilation ($n = 5$), hyperemia ($n = 5$), normal pre-biopsy mucosa ($n = 4$), and normal post-biopsy mucosa ($n = 2$). For the colon, the following parameters were evaluated: granularity ($n = 7$), friability ($n = 6$), erosions ($n = 7$), mass ($n = 2$), normal pre-biopsy mucosa ($n = 5$), and normal post-biopsy mucosa ($n = 3$; Fig. 1). Written definitions of each endoscopic parameter were made available to all endoscopists prior to still image testing (Table 1). If an individual image was interpreted as having more than one mucosal abnormality, the endoscopist was asked to identify the predominant lesion.

For the validation phase, the results of the archived image assessment were validated using video clips on a test sample of dogs with IBD. These dogs were different from those used in the development phase. Five-minute video streams most representative of an endoscopic procedure were evaluated by a pair of experienced endoscopists (JES and AEJ) using both quantitative (i.e. 0–2 scoring based on the presence/extent of abnormal mucosal appearance) and qualitative (i.e. scoring based only on the presence of abnormal mucosal appearances) indices of endoscopic activity. For all dogs with IBD, the insertion phase (with mucosal biopsy) of the endoscopic procedure was used to produce video clips for scoring. This concept was important, since endoscopic disease activity assessment during insertion vs. withdrawal could likely affect interpretation of friability but not erosions, enhanced granularity, lymphatic dilatation or mass lesions (Samuel et al., 2013).

Table 1
List of mucosal appearances evaluated endoscopically (development phase).

Appearance	Definition
Normal mucosa	No macroscopic lesions to mucosal surface
Friability	Bleeding on contact with endoscope or biopsy forceps
Granularity	Alteration in the texture of the mucosa
Erosion	Superficial linear mucosal defect(s) with hemorrhage
Hyperemia	Gradations of mucosal redness (pale to red)
Lymphatic dilatation	Multifocal to diffuse white foci within the mucosa
Mass	Abnormal growth of tissue projecting into lumen

[1] See: http://www.randomizer.org (accessed 24 December 2014).