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A Clinical Index for Disease Activity in Cats with Chronic Enteropathy

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Abstract

Background: There is a need for a clinically useful, quantitative index for measurement of disease activity in cats with chronic enteropathy (CE).

Objective: To develop a numerical activity index that is of practical value to clinicians treating CE in cats.

Animals: Eighty-two cats with CE.

Methods: Retrospective case review of 59 cats diagnosed with inflammatory bowel disease (IBD). Prospective validation study of 23 cats having either IBD or food-responsive enteropathy (FRE). Multivariate regression analysis was used to identify which combination of clinical and laboratory variables were best associated with intestinal inflammation of IBD. This combination of variables was expressed in a score that was used as an activity index for the prospective assessment of disease activity and of the effect of treatment in cats with IBD or FRE.

Results: The combination of gastrointestinal signs, endoscopic abnormalities, serum total protein, serum alanine transaminase/alkaline phosphatase activity, and serum phosphorous concentration had the best correlation with histopathologic inflammation and comprise the feline chronic enteropathy activity index (FCEAI). Positive treatment responses in cats with CE were accompanied by significant ($P < .05$) reductions in FCEAI scores after treatment.

Conclusions and Clinical Importance: The FCEAI is a simple numerical measure of inflammatory activity in cats with CE. The scoring index can be reliably used in the initial assessment of disease severity for both IBD and FRE and as a measure of clinical response to treatment for these disorders.

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Key words: Clinical scoring; FCEAI; Feline chronic enteropathy activity index; Food-responsive enteropathy; Inflammatory bowel disease.

The causes of chronic enteropathy (CE) in cats are diverse but principally include idiopathic inflammatory bowel disease (IBD) and food-responsive enteropathy (FRE).[1–7] Both of these disorders are characterized by persistent or recurrent signs of gastrointestinal disease, different pathogenetic mechanisms, and each is diagnosed retrospectively by response to specific treatment.[8] Clinical signs in affected cats are highly variable and severity of disease can differ greatly among cats, depending on the type of enteropathy, localization, and extent of affected regions of the gastrointestinal tract.[1–3] Defining disease activity in cats with CE is of practical relevance to clinicians because it aids determination of initial disease burden and serves to guide assessment of various therapies on inflammatory activity. A suitable and quantifiable index, like those utilized in humans[9–12] and dogs with IBD,[13,14] has not been designed previously for use in cats.

The objective of the present study was to develop a numerical index of the disease activity present in cats with CE. We believed that such a clinical index should contain the following requirements: (1) it should have broad application to the most common forms of feline CE, including IBD and FRE; (2) it should incorporate gastrointestinal signs considered by clinicians to be important indicators of disease activity; (3) it should utilize observations readily available at the time of a cat visit; (4) it should contain objective parameters that are routinely measured during diagnostic evaluation; (5) it should be simple to compute; and (6) it should reflect visit-to-visit changes in disease status because of therapeutic interventions.[9,13]

The development of the feline chronic enteropathy activity index (FCEAI) described herein is based on the need for a useful clinical and research tool for assessment of inflammatory activity in cats with CE. Moreover, the evaluation of the FCEAI in a prospective pilot study demonstrated the potential utility of this scoring index in defining disease activity at diagnosis and in response to medical therapy.

Abbreviations:

CE	chronic enteropathy
FCEAI	feline chronic enteropathy activity index
FRE	food-responsive enteropathy
IBD	inflammatory bowel disease

Materials and Methods

Retrospective Study Criteria for Case Selection

Medical records of the Iowa State University, Veterinary Teaching Hospital (ISU-VTH) were searched to identify all cats with a diagnosis of idiopathic IBD between July 1993 and July 2003. The resultant medical records were reviewed by one of the authors

(J.C.). Cats were included in the study if they satisfied the clinical criteria for idiopathic IBD including: persistent (>3 weeks) gastrointestinal signs; failed responses to dietary (commercial intact protein or hydrolysate elimination diets) or symptomatic (paraciticides, antibiotics, gastrointestinal protectants) therapies alone; thorough diagnostic evaluation with exclusion of other causes for gastroenteritis; and histologic diagnosis of intestinal inflammation.[1,15] All cats had been fed an elimination diet for a minimum of 14 days to rule out adverse food reactions. Additionally, metronidazole or amoxicillin with clavulanic acid had been administered to most cats for 2–3 weeks if they failed to respond to dietary intervention alone.

The minimum diagnostic evaluation performed on each cat included a CBC, serum biochemistry profile, urinalysis, feline trypsin-like immunoreactivity (fTLI), direct (wet mount) and indirect (zinc sulfate flotation) examination of feces for nematode and protozoan parasites, survey abdominal radiographs, and histopathologic review of mucosal biopsy specimens (performed by different service pathologists) obtained via gastroduodenoscopy, colonoscopy, or both. The performance of a particular endoscopic procedure was dictated by the history and predominant clinical signs exhibited by each cat. Endoscopic examination was performed after therapeutic trials. Thus, only cats fulfilling all 4 clinical criteria for IBD were eligible for inclusion in the retrospective study. Exclusion criteria included those cats that had responded positively to either dietary or antimicrobial interventions or that had evidence of other underlying disorders (based on results of diagnostic testing) causing chronic gastroenteritis.

Data Collection

Signalment, salient history (including dietary and antibiotic administration trials), clinical signs, clinicopathologic findings, endoscopic observations, diagnostic imaging results, cytologic, and histopathologic data were recorded. The selection of these variables was based on analysis of previous evidence-based reports of IBD in cats.[1–4] A minimum of 5 biopsy specimens from the stomach, duodenum, and colon or some combination of these organs were reexamined histologically and graded by a single pathologist (M.A.). Intestinal inflammation was defined using recently described World Small Animal Veterinary Association histopathologic guidelines.[15,16] Histopathological severity (mild to severe IBD) was based on alterations in mucosal height, villous morphology, epithelial erosions or ulcers, edema/fibrosis, inflammatory cell infiltration, and intraepithelial lymphocytes. Cats with normal histology, intestinal neoplasia, infectious diseases, or other potential causes for gastroenteritis were excluded. The number of gastrointestinal signs (vomiting, diarrhea, weight loss, anorexia, and lethargy) present in each cat was recorded. Endoscopic lesions of mucosal friability, granularity, erosions or all the three were also noted to be present or absent in IBD cats. Reference values were total white blood cell (WBC): 5.5–19.5 × 10^3/µL; PCV: 30–45%; total protein: 6.1–8.0 g/dL; albumin: 2.1–3.5 g/dL; alanine transaminase (ALT): 20–125 IU/L; serum alkaline phosphatase (ALP): 0–60 IU/L; and phosphorous 4.0–7.6 mg/dL.

Pilot Study

A single center (ISU-VTH) prospective study was performed (2004–2006) and comprised a total of 23 cats referred for diagnostic evaluation of CE. A standard diagnostic examination was performed in each cat and included a CBC, serum biochemistry profile, urinalysis, fecal examinations for parasites, survey abdominal radiographs, abdominal ultrasound, and tests for gastrointestinal function including measurement of serum fTLI concentration, serum feline pancreatic lipase immunoreactivity (fPLI) concentration, and serum folate and cobalamin concentration. Each cat was assigned a baseline (pretreatment) FCEAI score as described in results. All cats were treated initially with an intact protein elimination diet[a,b,c] fed exclusively for at least 14 days. Cats that responded to the elimination diet, as evidenced by improved or completely resolved clinical signs alone, were assigned a diagnosis of FRE and maintained on the elimination diet indefinitely. Those cats that failed to respond to dietary intervention underwent gastrointestinal endoscopy and mucosal biopsy specimens. Histopathologic evaluation was performed by the same pathologist (M.A.) by identical grading criteria. Cats diagnosed with idiopathic IBD were maintained on the elimination diet and were administered prednisolone (2 mg/kg PO per day) for 21 days followed by a tapering dosage over 4–6 weeks. Both FRE and IBD cats were reevaluated and assigned a FCEAI score at the end of the 21-day induction treatment period.

Ethical Considerations

The retrospective and pilot studies were approved by the ISU Institutional Animal Care and Use Committee. All clients gave written or verbal informed consent for enrollment of their pet into the prospective clinical trial.

Data Analysis and Statistics

Multivariate logistic regression was used to determine which of the 13 independent variables identified from the data of the retrospective study best predicted the ordinal histopathological severity of IBD (dependent variable). The potential association between gastrointestinal signs and intestinal inflammation was examined using the variable appetite combined with alterations in attitude/activity, vomiting, diarrhea, or weight loss. The relationship between each of the independent variables and a histologic diagnosis of IBD was then determined and expressed as a P-value.

For the pilot study, the pretreatment scores between IBD and FRE were compared by Wilcoxon's rank-sum tests. A paired sample Wilcoxon's signed-rank test was applied to test the score difference before and after treatment for each of the IBD group and FRE group. Statistical analyses were performed with SAS software. For all analyses, a P-value of <.05 was considered significant.

Results

Retrospective Study

Sixty-six cats were initially diagnosed with idiopathic IBD. Reexamination of biopsy specimens reduced the number of cats with IBD to 60. These reasons included 2 cats diagnosed with well-differentiated alimentary lymphoma, 1 cat diagnosed with epitheliotropic lymphoma, 1 cat diagnosed with a mast cell tumor, and 2 cats that had no histopathologic evidence of intestinal inflammation. An additional cat, suspicious for FIP based on laboratory results, was also excluded from the study. The mean age of the 59 remaining cats with IBD was 7.7 years with a range of 1.3–15 years. Thirty-five (55%) of the diseased cats were spayed females and 24 (45%) were neutered males. A total of 9 breeds were represented with the most common being domestic short hair (49%) followed by domestic long hair (29%), Siamese (7%), and Persian (5%). All other breeds represented <10% of the total population. The independent variables studied in all 59 cats with IBD are shown in Table 1. The means ± standard deviations for variables with approximately bell-shaped distributions were body weight

Table 1. Independent variables used in development of activity index.

Variable	Unit/Code
Attitude/activity	0 = normal; 1 = slight decrease; 2 = moderate decrease; 3 = severe decrease
Appetite	0 = normal; 1 = slight decrease; 2 = moderate decrease; 3 = severe decrease
Vomiting	0 = none; 1 = mild (1 time/wk); 2 = moderate (2–3 times/wk); 3 = severe (> 3 times/wk)
Diarrhea	0 = well-formed feces; 1 = slightly soft feces, fecal blood, mucus, or slightly increased frequency (2–3 times/d); 2 = very soft feces or moderately increased frequency (4–5 times/d); 3 = watery diarrhea or severely increased frequency (> 5 times/d)
Weight loss	0 = none; 1 = mild (<5% loss); 2 = moderate (5–10% loss); 3 = severe (> 10% loss)
Total WBC	Count×10^3/μL
PCV	%
Total protein	g/dL
Albumin	g/dL
ALT	IU/L
ALP	IU/L
Phosphorous	mg/dL
Endoscopic lesions	Granularity, friability, ulcer/crosions

ALT, alanine aminotransferase; ALP, alkaline phosphatase; WBC, white blood cell.

Table 2. Derivation of the FCEAI.

Variable	Assessment	P-Value	Inclusion
GIT signs	No or yes	.088	Yes
Attitude/activity			
Appetite			
Vomiting	Scored 0–3[a]		
Diarrhea			
Weight loss			
Endoscopic lesions	0 = no; 1 = yes	.035	Yes
Total WBC	0 = normal; 1 = increased	.133	No
PCV	0 = normal; 1 = decreased	.176	No
Total protein	0 = normal; 1 = increased	.054	Yes
Albumin	0 = normal; 1 = decreased	.126	No
ALT	0 = normal; 1 = increased	.107	Yes[b]
ALP	0 = normal; 1 = increased	.044	Yes
Phosphorous	0 = normal; 1 = decreased	.085	Yes

ALT, alanine aminotransferase; ALP, alkaline phosphatase; FCEAI, feline chronic enteropathy activity index; WBC, white blood cell.

[a]For codes see Table 1.

[b]Combined with ALP as a single variable.

(4.0 + 1.4 kg); PCV (37 + 6%); total protein (7.0 + 1.2 g/dL); albumin (2.7 + 0.8 g/dL); and phosphorous (3.7 + 1.3 mg/dL), respectively. The medians and ranges for variables with skewed distributions were total WBC (10.4 × 10^3/μL, 5.2–35.4 × 10^3/μL); ALT (61, 10–737 IU/L); and ALP (27, 9–132 IU/L). Fifty of 59 cats (85%) had mucosal lesions of increased friability, granularity, erosions, or all three on gastrointestinal endoscopic examination. Histologically, all cats showed variable infiltration of lymphocytes, plasma cells, and eosinophils into the lamina propria, which was accompanied by mucosal inflammation. The final histopathologic diagnoses were mild IBD (n = 25), moderate IBD (n = 24), and severe IBD (n = 10). Other abnormalities in cats with IBD included hypocobalaminemia (mean serum cobalamin concentration <100 ng/L) in 3/8 cats, which had serum cobalamin concentrations evaluated and radiographic evidence of nonspecific enteritis (eg, fluid distended small intestinal bowel loops) in 15/59 (25%) cats.

Each independent variable in Table 1 was coded in such a way that the anticipated value in a normal cat was 0, and that a value >0 was expected to measure progressively greater activity of CE. As a result of the pilot analysis performed on this large data set, the number of independent variables was reduced from 13 to 9 (Table 2). These other variables were dropped because they were shown to be poorly associated with histopathologic severity of intestinal inflammation and the clinician's subjective impression of disease activity. The remaining 5 independent variables of gastrointestinal signs, endoscopic lesions, serum total protein, serum ALT/ALP,

and serum phosphorus concentrations that best predicted the dependent variable and which met the requirements set forth for the index were chosen as components of the FCEAI (Table 2). The variable ALT was initially dropped from the index but later reinstated and combined with ALP as a single parameter because of the importance attributed to it by previous studies, as well as intuitively by the participating clinicians.[1–4] An example of how to calculate the FCEAI in a cat with IBD is shown in Table 3.

Pilot Study

In order to gain an impression of the clinical utility of the FCEAI in cats with CE, the index was prospectively evaluated in 23 cats having chronic gastrointestinal signs. The baseline characteristics of the 2 groups of cats were broadly similar (Table 4). Both forms of CE had numerous laboratory abnormalities present at the time of diagnosis including hyperproteinemia, hypocobalaminemia, hypophosphatemia, and increased serum activity of liver derived enzymes. Additionally, some cats in both groups (3 cats with IBD and 3 cats with FRE) showed increase in serum fPLI (mean serum fPLI = 8.8 μg/L and 7.6 μg/L in cats with IBD and FRE, respectively). Results of diagnostic imaging showed nonspecific findings of enteritis (ie, fluid-distended small bowel loops, thickened intestinal walls, mesenteric lymphadenopathy) and changes suggestive of pancreatitis (ie, presence of a cranial abdominal mass, pancreatic hypoechogenicity, peripancreatic hyperechoic fat[17]) in 7/23 (30%) and 4/23 (17%) of diseased cats, respectively. Ultrasonographic changes to the morphology of the small intestines were usually diffuse but were most evident in the duodenum and proximal jejunum. Focal wall (duodenal) thickening observed in 3 cats with IBD was consistent with a diagnosis of mixed mucosal inflammation, evidenced by

Table 3. Example of calculation of the FCEAI for a given patient.

	Factor	Subtotal
Gastrointestinal signs		
Attitude/activity	☑ mild ☐ mod ☐ sev	= 1
Appetite	☐ mild ☐ mod ☐ sev	= 0
Vomiting	☐ mild ☑ mod ☐ sev	= 2
Diarrhea	☐ mild ☐ mod ☐ sev	= 0
Weight loss	☐ mild ☑ mod ☐ sev	= 2
Endoscopic lesions	☐ no ☑ yes	= 1
Total protein	☐ normal ☑ increased	= 1
ALT/ALP	☑ normal ☐ increased	= 0
Phosphorous	☐ normal ☑ decreased	= 1
Add subtotal to derive composite FCEAI score ➡		8

mod, moderate; sev, severe.

Table 4. Distribution of some clinicopathologic variables in feline CE.

Variable	FIBD (n = 17)	FRE (n = 6)
Male sex, n (%)	7 (41)	3 (50)
Mean age (years)	10.4	7.7
Disease duration (months)	4.8	6.0
Gastrointestinal signs, n (%)		
Attitude/activity	10 (59)	4 (66)
Appetite	12 (71)	5 (80)
Vomiting	11 (65)	4 (66)
Diarrhea	9 (53)	3 (50)
Weight loss	13 (76)	4 (66)
Laboratory abnormalities, n (%)		
Hyperproteinemia	3 (18)	2 (33)
↑ ALP/ALT	4 (23)	1 (17)
Hypocobalaminemia	3 (18)	1 (17)
↑ fPLI	3 (18)	3 (50)
Hypophosphatemia	8 (47)	2 (33)

FIBD, feline inflammatory bowel disease; FRE, food responsive enteropathy; ALP, alkaline phosphatase; ALT, alanine aminotransferase; fPLI, feline pancreatic lipase immunoreactivity; CE, chronic enteropathy.

lymphocytic, plasmacytic, and eosinophilic infiltrates based on results obtained from fine-needle aspiration cytology. Endoscopic lesions of increased granularity, friability, erosions, or all three to the intestines were seen in 16/17 (94%) of the cats with IBD. A greater number of endoscopic abnormalities were generally associated with increasing severity of clinical disease. Care was taken to obtain multiple mucosal specimens from both the duodenum and jejunum in all cats. Histopathologic lesions in all cats with IBD were characterized by variable degrees of lymphocytic-plasmacytic (LP) mucosal inflammation.

The mean FCEAI score of the FRE group was 6.7 before initiating the elimination dietary trial with a range from 5 to 9, and decreased to 0 after 21 days of treatment ($P = .03$; Fig 1). All cats responded to dietary intervention alone with dramatic resolution of signs within the first 10 days. In cats with IBD, the mean FCEAI score was 8.2 before endoscopic examination (range 4–13) and decreased to 0.4 (range 0–2) after treatment with the elimination diet and oral prednisolone ($P < .001$; Fig 1). No significant difference of pretreatment FCEAI scores was observed between cats with IBD and FRE ($P = .18$). All 17 cats with IBD (100%) achieved full clinical remission, defined as a 75% or greater reduction in posttreatment FCEAI score compared with its corresponding pretreatment value after 3 weeks of induction

medical therapy. Interobserver variation of FCEAI scores performed on the same cat by the 2 clinicians (A.J., J.C.) was very good for both initial and repeat visits (complete agreement between clinicians in 16 and 20 cats), regardless of the form of CE evaluated. There was occasional disagreement of 1 point of cumulative total in scoring among clinicians in a subset of cats with IBD on the initial (pretreatment) visit. However, there was complete agreement among clinicians in the posttreatment FCEAI scores for 9/10 cats with IBD that were evaluated independently by both clinicians during the same visit (data not shown).
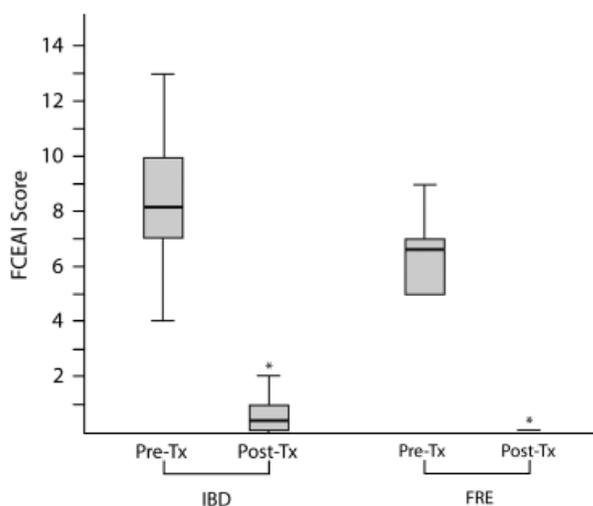
Fig 1. Effect of medical therapy on clinical disease activity in food-responsive and cats with IBD based on FCEAI scores. Box plots show the mean, range, 25 and 75% quartiles for FCEAI scores. *P < .05 compared with pretreatment value. IBD, inflammatory bowel disease; FRE, food-responsive enteropathy; Tx, treatment; FCEAI, feline chronic enteropathy activity index.

Discussion

The present study utilized 2 separate but complementary approaches to develop and assess the FCEAI. First, in a retrospective analysis of 59 cats diagnosed with idiopathic IBD, clinicopathologic and endoscopic variables were evaluated for their potential association with histopathologic lesions of intestinal inflammation. Five independent variables correlated best to histopathologic inflammation and were selected for the final calculation of the FCEAI. We thought it necessary to have a uniform set of parameters that could be temporally assessed and recorded by clinicians at different centers. This would allow data collected at each center to be comparable with those collected at other centers, and for data to be compared when collected at different times. Furthermore, a numerical index was needed whereby the magnitude of the numerical value would be proportional to the degree of disease activity. This index could then serve as the principal measure of response to a therapeutic trial and could also be used to tailor medical therapy for an individual cat's need.

Secondly, validation of the potential utility of the FCEAI was assessed in a prospective clinical trial of 23 cats presented with histories of chronic gastrointestinal disease. Seventeen cats diagnosed with IBD were fed an elimination diet and prescribed prednisolone (2 mg/kg PO q24h) whereas FRE cats were fed an elimination diet alone. The FCEAI score was determined before and during therapeutic intervention (at treatment day 21). Collectively, the data of the present study indicate that the FCEAI is a useful method for assessing clinical disease activity in cats with IBD or FRE at diagnosis. Furthermore, positive treatment responses were accompanied by changes in the FCEAI, suggesting that this clinical scoring system is suitable for monitoring the effect of induction therapy in cats with CE.

The association among clinical signs, laboratory findings, and histopathology of FCE has been reported in relatively few case-based studies. The occurrence of gastrointestinal signs, hyperproteinemia, increased serum ALT activity, endoscopic abnormalities, and severity of histopathologic lesions is reported for 26 cats with IBD.[1] Cats diagnosed with LP) gastroenteritis[2] or LP colitis[3] had anorexia, vomiting, watery diarrhea, and large bowel diarrhea that were accompanied by hypoproteinemia, high serum ALT and ALP activity, endoscopic changes to the intestinal mucosa, and histopathologic inflammation that varied among different anatomic sites in the same cat. Similarly, 60 cats diagnosed with LP enterocolitis had signs of gastrointestinal disease, increased serum activity of ALT and ALP enzymes, hyperproteinemia, and intestinal inflammation of varying severity.[4] Still others have shown a positive correlation among the number of gastrointestinal signs, mucosal proinflammatory cytokine expression, duodenal histopathology, and mucosally associated bacteria in cats with IBD.[18] Additionally, cats with FRE can have concurrent signs of gastrointestinal disease with dermatologic disease; however, only mild histopathologic changes and infrequent biochemical changes were noted in food-sensitive cats.[5,19] The emergent themes of these earlier studies, including the presence of salient gastrointestinal signs, biochemical alterations, endoscopic lesions, and LP mucosal inflammation in cats with CE, formed the framework for determining whether these and other independent variables correlated most closely with intestinal inflammation in design of the FCEAI.

Hypocobalaminemia and increased serum fPLI concentrations occur in some IBD and FRE cats. Low serum cobalamin concentration has been described previously in cats with enteric, hepatic, pancreatic disease, or all three, and has been associated with refractoriness to treatment in cats with CE.[20,21] Relatively few cats with IBD in the retrospective study had cobalamin concentrations assessed that precluded its evaluation as an independent variable in the FCEAI. The reasons for exclusion of this diagnostic test in some cats included the absence of a commercially available, validated assay during the early portion of the retrospective study time frame, case-dependent treatment decisions such as empirical cobalamin supplementation made by different clinicians, and client cost constraints. However, hypocobalaminemia was a more consistent observation in both cats with IBD and FRE of the pilot study. Six of 7 (5 with IBD and 1 with FRE) cats with hypocobalaminemia in this study were successfully treated with weekly cobalamin injections which corrected the cobalamin concentrations into the reference range within 6 weeks after initiating vitamin therapy. One other cat with IBD required intermittent weekly cobalamin injections, along with maintenance glucocorticoid and elimination dietary therapies, beyond this timeframe to maintain clinical remission.

It is also possible that some cats with IBD also had pancreatic inflammation, evidenced by increased serum fPLI concentrations, which would have contributed to onset and progression of gastrointestinal signs. Supporting this contention were the abnormalities in the pancreas and intestines detected on diagnostic imaging in some cats. While cats with IBD might have increased serum fPLI concentrations, this association does not appear to influence clinical outcome based on a recent report.[d] Previous investigations have suggested a potential causal association among small intestinal inflammation, pancreatitis, and hepatic disease such as triaditis in cats with histories of CE.[20,22–24] However, these earlier data were derived from retrospective studies, have focused on distinct subsets of cats, have utilized different indices for diagnosis of organ-specific disease, and have not confirmed a distinct temporal relationship among pancreatic, hepatic, and intestinal inflammation—namely that they occurred simultaneously. Furthermore, alterations in tissue morphology do not always indicate disturbances in organ fuction or the presence of clinically significant inflammation.[25,26] Additional studies are warranted to determine whether cobalamin and fPLI are useful variables in the long-term, overall clinical assessment of cats with CE.

Hypophosphatemia was a relatively common electrolyte abnormality observed in cats with CE at initial presentation. Low serum phosphorus concentrations might be caused by maldistribution (translocation of

phosphate from extracellular to intracellular fluid), increased loss (reduced renal absorption of phosphate), or decreased intake (decreased intestinal absorption of phosphate).[27] The causes for hypophosphatemia in some cats of the present study remain unknown, but might be attributable to malnourishment, malabsorptive disorders, and chronic vomiting or some combination of these etiologies.[28] Serum concentrations of phosphorous normalized in most hypophosphatemic cats (data not shown) after successful treatment for their underlying gastrointestinal disease.

Endoscopic lesions to the small intestinal mucosa were the FCEAI variable most significantly associated with histologic abnormalities. Consistent with earlier reports, endoscopic observations of mucosal friability, granularity, and erosions or some combination of these lesions predominated in most cats with IBD.[1,2] Surprisingly, the presence of endoscopic abnormalities did not appear to influence short-term response to treatment, as all cats with IBD in the pilot study had full clinical remission by treatment day 21. Whether endoscopic severity in cats with IBD is associated with long-term negative outcome, as it has been shown in dogs with IBD, will require additional investigation.[14]

The proposed index incorporates assessment of the dynamic changes in individual variables that best reflect the disease course in cats with CE. This is possible because the FCEAI is composed of a set of clinical and laboratory parameters that permit repeated measures, the exception being endoscopic abnormalities which may not be evaluated in cats with FRE or reevaluated in most cats with IBD that respond favorably to medical therapy. When repeat endoscopy is not possible, omission of this variable is required, which will automatically decrease the posttreatment FCEAI score, assuming that endoscopic lesions were present on the initial examination, by 1 point. The use of only 5 variables in calculation of posttreatment disease severity should be taken into consideration when evaluating the efficacy of medical therapy in these instances. Another advantage and important feature of this index is that it contains a number of objective variables including serum total protein, ALT and ALP activities, and phosphorus concentrations which can be quantified. To systematically assess the usefulness of the FCEAI in cats with CE, we prospectively compared baseline (pretreatment values determined at diagnosis) and posttreatment FCEAIs in 17 cats with IBD and 6 cats with FRE. Both disease groups showed significant reduction in their mean FCEAI scores by 21 days posttreatment which agreed with the clinician's overall assessment of clinical illness. Moreover, the decline in FCEAI scores observed posttreatment in these cats was generally associated with numerical reductions in both clinical and laboratory variables alike, suggesting that the index is suitably weighted by both sets of parameters.

The present study has some potential limitations. We cannot conclusively exclude infection with *Tritrichomonas foetus* as contributing to large bowel diarrhea in some cats. Specific tests such as selective protozoal culture or polymerase chain reaction with species-specific primers for diagnosis of *T. foetus* infection were not performed in the retrospective study as this protozoan was not a recognized pathogen in cats at this time.[29,30] However, we consider it unlikely that infection with *T. foetus* was present because most cats were middle-aged, relatively few cats presented with signs of large bowel disease alone, significant risk factors (ie, multi-cat household or kennel facility) for disease were rarely evident, and at least 1 direct fecal examination for detection of parasitic organisms was performed in all cats.

It is a possibility that some cats were incorrectly diagnosed with IBD versus well-differentiated alimentary lymphoma, especially in the retrospective portion of this study.[31,32] To minimize this potential, we utilized a single experienced veterinary pathologist (M.A.) with expertise in gastrointestinal histopathology to review all endoscopic specimens. Histopathologic examination of duodenal tissues from 3/66 cats in the original IBD retrospective study population resulted in the reclassification of these cats into a final disease category of intestinal lymphoma. It is our approach to first perform routine morphologic and immunophenotypic analysis of histologic tissues followed by assessment of clonality when lymphoma is a differential diagnosis. Molecular clonality determination of feline lymphoma was not performed in any cats of this study to conclusively exclude alimentary lymphoma.[33,34] As discussed by others, procurement of full-thickness biopsy specimen from all segments of the intestine with the collection of extraintestinal samples, especially mesenteric lymph nodes, may be helpful in diagnosing feline intestinal lymphoma.[35,36] Moreover, older cats with ultrasonographic evidence of muscularis propria thickening are more likely to have lymphoma versus IBD.[37] Endoscopic biopsy specimen of the upper small intestine (duodenum, jejunum in some instances) was performed in all cats of the present study and may have missed more distal sites (eg, ileal mucosa) of neoplastic cellular infiltration. Therefore, ileal biopsy specimens should be obtained in cats to increase diagnostic yield whenever gastroduodenoscopy or colonoscopy is performed, especially because smaller diameter feline endoscopes now make endoscopic biopsy specimens of the ileum easier to perform.[15,35,36] This recommendation is supported by our observation that 4 cats in the retrospective or pilot study had concurrent ileoscopy performed which confirmed IBD (n = 2) or lymphoma (n = 2), respectively.

Footnotes

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