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Prognostic value of small intestinal dilatation in dogs with protein-losing enteropathy

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ABSTRACT. To date, little is known about the prognostic significance of ultrasonographic findings in dogs with protein-losing enteropathy (PLE). The aim of this retrospective study was to examine the prognostic value of ultrasonographic findings in dogs with PLE. A total of 26 dogs with PLE were included: 20 dogs with chronic enteropathy and 6 dogs with gastrointestinal lymphoma. The presence of small intestinal dilatation was associated with shorter survival time in dogs with PLE (P=0.003). The presence of hyperechoic intestinal mucosal striations was associated with longer survival time in dogs with PLE (P=0.0085). The results of the current study indicate that the presence of small intestinal dilatation might be associated with poor prognosis in dogs with PLE.

KEY WORDS: canine, intestinal dilatation, prognosis, protein-losing enteropathy, ultrasound

Protein-losing enteropathy (PLE) in dogs is characterized by hypoalbuminemia due to excessive loss of plasma proteins through the gastrointestinal mucosa. PLE in dogs has three major causes: chronic enteropathy (CE), primary intestinal lymphangiectasia (IL), and gastrointestinal lymphoma (GIL) [4, 6]. Dogs with PLE secondary to CE or primary IL have a variable prognosis since, like dogs with GIL, some dogs with PLE secondary to CE or primary IL show a poor response to treatment and prognosis despite intense immunosuppressive and nutritional treatment [6].

Although little information on survival and prognostic factors in canine PLE is available, several prognostic factors, such as hypoalbuminemia [1, 3] and hypovitaminosis D [2, 20] in dogs with PLE secondary to CE, have been reported in previous studies. In addition, the severity of clinical signs, clonal rearrangement of lymphocyte antigen receptor genes, histopathological diagnosis, and response to initial treatments have been reported to predict the prognosis of canine PLE associated with CE, IL, and GIL [12].

Ultrasonography (US) is an important tool for screening the gastrointestinal tract of dogs with chronic gastrointestinal signs, such as vomiting and diarrhea. Several studies have reported the diagnostic value of US findings of the small intestine for the diagnosis of chronic inflammatory intestinal diseases in dogs with and without PLE. A previous study reported that hyperechoic mucosal striations had a sensitivity of 75% and a specificity of 96% for the diagnosis of PLE in dogs [8, 19]. Another study reported that intestinal wall thickness was not sufficiently specific or sensitive for the diagnosis of inflammatory bowel disease in dogs [16].

Little is known about the prognostic significance of B-mode US findings of the small intestine in dogs with PLE. In our previous study, we compared the clinical findings of dogs with food-responsive PLE (FR-PLE) with those of dogs with immunosuppressant-responsive PLE (IR-PLE) or nonresponsive PLE (NR-PLE) secondary to CE [11]. We found that the survival time of dogs with FR-PLE was significantly longer than that of dogs with IR/NR-PLE and that US findings of the small intestine, such as hyperechoic intestinal mucosal striations and loss of intestinal layering, were not useful for differentiating FR-PLE from IR/NE-PLE [11]. In this study, dogs with GIL were excluded from the analysis because dogs with GIL were not thought to be candidates for ultralow-fat diet (ULFD) intervention [11]. Thus, the prognostic significance of B-mode US findings in dogs with PLE secondary to GIL is not known.

It is sometimes difficult to use US to detect abnormalities of the small intestine in dogs with PLE, even in GIL dogs. The authors occasionally encounter US findings of fluid-distended small intestine without any other abnormalities in dogs with PLE secondary to CE or GIL. US findings of generalized fluid distension and atonic small intestine were reported in puppies with parvovirus

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infection and are thought to be attributed to the functional ileus secondary to viral enteritis [18]. In addition, US changes, including fluid-distended atonic small intestine, in puppies with parvoviral infection appeared to correlate with the clinical condition of the patients [18].

Thus, the purpose of this study was to examine the prognostic value of several B-mode ultrasonographic findings of the small intestine, including fluid-distended atonic small intestine, in dogs with PLE, including GIL cases.

The medical records of all dogs that underwent upper gastroduodenoscopy with or without lower gastrointestinal endoscopy from 1 September 2012 to 30 April 2017 at the Hokkaido University Veterinary Teaching Hospital and were diagnosed with PLE secondary to CE, primary IL or GIL were reviewed. In all cases, informed consent for the use of clinical data was obtained from the owner. Inclusion criteria for the dogs with PLE were hypoalbuminemia (<2.6 g/dl); histological evidence of gastrointestinal tract diseases known to be associated with PLE (e.g., lymphocytic-plasmacytic enteritis, primary IL and GIL) in endoscopic biopsy specimens; and the absence of other causes of hypoalbuminemia based on physical examination, complete blood count, serum biochemistry, fecal examination, urinalysis, radiography, and abdominal ultrasonography. Dogs with small-cell and large-cell GILs diagnosed by endoscopic biopsy specimens were included in this study. However, dogs with GIL that was diagnosed as large-cell lymphoma by cytological examination of fine-needle aspiration specimens of the thickened intestinal wall (>10 mm) with complete loss of layering or moderately to markedly enlarged regional lymph nodes (>10 mm) were excluded. Dogs with concurrent disorders were also excluded from the study.

All dogs were fasted for 12 hr before sonographic examination. The hair on the ventral abdomen was clipped, alcohol and coupling gel were applied, and examinations were performed in dorsal recumbency without sedation. For all the examinations, a Aplio 500 US system (Canon Medial Systems Corp., Ootawara, Japan) or a HI VISION Preirus (Hitachi Aloka Medical Ltd., Tokyo, Japan) were used. A 12 MHz linear array transducer (PLT-1204BT, Canon Medial Systems Corp.) or 12 MHz linear array transducer (EUP-L75, Hitachi Aloka Medical Ltd.) was used to examine the gastric fundus and antrum, duodenum, jejunum, ileum, colon, and abdominal lymph nodes in all but one dog. In one Labrador retriever, a 7.5 MHz convex array transducer (EUP-C532, Hitachi Aloka Medical Ltd.) was used to examine the gastrointestinal tract and abdominal lymph nodes. In addition to examining the sonographic appearance of the small intestine, the liver, spleen, pancreas, kidneys, and urinary bladder were also examined. All US studies were performed by two of the authors (H.O. and M.T.) with more than 10 years of experience in abdominal US examination.

For histopathological examination, mucosal biopsy specimens were obtained from the stomach, proximal duodenum, and distal duodenum in all dogs and from the ileum in 5 dogs (2 dogs with CE and 3 dogs with GIL) by endoscopy under general anesthesia using VQ-8143B or VQ-5112B flexible video endoscope (AVS, Tokyo, Japan) according to the dog's body weight. Multiple mucosal biopsies (6–8) were collected for histopathological diagnosis using VQ-143Q-B53 or VH-142-B52 biopsy forceps (AVS) according to the dog's body weight. Ileal tissue collection was performed by attending clinicians on the basis of the clinical signs. During endoscopy, at least 6 mucosal samples were collected from each previously noted segment of the gastrointestinal tract. Histopathological examination was conducted by an American College of Veterinary Pathologist board-certified pathologist (Y.K.) using a scoring system based on the World Small Animal Veterinary Association (WSAVA) guidelines [5]. Polymerase chain reaction for antigen receptor gene rearrangement (PARR) was performed on a case-by-case basis based on clinical findings and histopathological analysis. Immunohistochemistry was not performed in any cases in this study.

The following information was collected from the medical records: breed, age, weight, sex, clinical signs, plasma albumin concentration, date of intestinal endoscopy, treatments, date of death, and cause of death. The severity of clinical signs was evaluated using two previously described activity indexes, namely, the canine inflammatory bowel disease activity index (CIBDAI) and the canine chronic enteropathy clinical activity index (CCECAI) [1, 9]. Follow-up information was collected up to May 2017 from the medical records or communication with the referring hospitals. Dogs were divided into 2 groups based on survival at the end of the study: survivors and nonsurvivors.

In this study, US findings of intestinal dilatation were defined as multisegmental (more than two bowel segments affected) fluid distension, atonic duodenum, jejunum, or ileum in which more than 40% of the diameter of the intestinal tract was filled with fluid. The thickness of the duodenal and jejunal walls was measured from both the long and short axes, and the means of these measurements were used for calculations. Ultrasonographic images of the duodenum, jejunum and ileum (small intestine) were retrospectively but not blindly evaluated by one of the authors (H.O.) using still images, and the following findings were extracted: the presence of hyperechoic intestinal mucosal striations, defined as multiple clear intramucosal hyperechoic lines [19]; the presence of small intestinal corrugation, defined as an undulating or rippled bowel wall [10]; the presence of small intestinal dilatation, defined as multisegmental fluid-filled small intestine [18]; complete loss of wall layering, defined as indistinguishable intestinal layers, the most reliable predictor of an intestinal tumor [15]; and the thickness of the duodenal and jejunal wall. Figure 1A–C shows the appearance of small intestinal dilatation, hyperechoic intestinal mucosal striations, and small intestinal corrugation.

Data distribution was analyzed by using the Shapiro-Wilk test. Baseline variables from survivors and nonsurvivors were compared using Fisher's exact test for categorical variables and Student's *t*-test or the Mann-Whitney *U* test for continuous variables. To compare differences in survival time from the day of endoscopic examination depending on the presence or absence of ultrasonographic findings, Kaplan-Meier analysis and log-rank tests were performed. We conducted univariate Cox proportional hazard analysis for each ultrasonographic variable that was a potential prognostic factor in dogs with PLE. All statistical analyses were performed using JMP 14 software (SAS Institute Inc., Cary, NC, USA). Statistical significance was defined at $P<0.05$.

Twenty-six dogs with PLE were included in this study. On the basis of the histological evaluation, 20 dogs were diagnosed

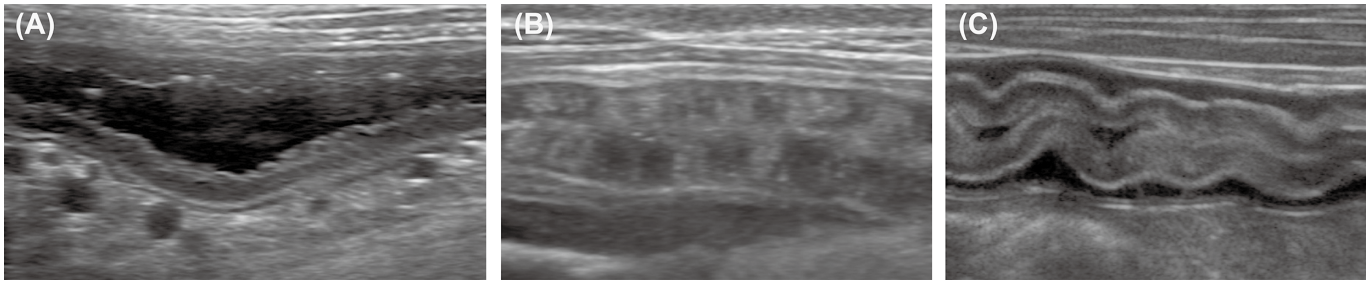

Fig. 1. A, Longitudinal image of a dilated jejunal segment in a dog with small-cell lymphoma. B, Longitudinal image of hyperechoic intestinal mucosal striations in the jejunal segment in a dog with lymphocytic-plasmacytic enteritis with intestinal lymphangiectasia. C, Longitudinal image of a corrugated jejunal segment in a dog with lymphocytic-plasmacytic enteritis.

with CE (3 with lymphocytic-plasmacytic enteritis and 17 with lymphocytic-plasmacytic enteritis with IL), 2 dogs were diagnosed with small-cell lymphoma, and 4 dogs were diagnosed with large-cell lymphoma. None of the dogs with PLE that fulfilled the inclusion criteria and had appropriate still images of the small intestine were diagnosed with primary IL during the study period. The mean age and median body weight of the dogs with CE were 8.6 years (standard deviation, SD=± 2.3 years) and 4.8 kg (range, 2.2 to 11.5 kg), respectively. The 20 dogs with CE consisted of 12 females (8 spayed females and 4 intact females) and 8 males (6 castrated males and 2 intact males). The breeds of the dogs with CE were as follows: 6 Miniature dachshunds; 3 Boston terriers; 3 Yorkshire terriers; 2 Welsh corgis; and one each of Miniature schnauzer, Italian greyhound, Chihuahua, Cavalier King Charles spaniel, Papillon, and Japanese spitz. Among these 20 dogs, 4 dogs had decreased appetite, 3 dogs experienced vomiting, and 15 dogs had soft feces or diarrhea (soft feces in 2 dogs and diarrhea in 13 dogs) at the first visit. Four dogs had none of the clinical signs listed in CIBDAI and showed only hypoalbuminemia with or without ascites (CCECAI was 3, 3, 4, and 1 in these 4 dogs). Twelve dogs had ascites. The median CIBDAI score and CCECAI score of 20 dogs with CE were 4 (range, 0–17) and 6.5 (range, 1–18), respectively. The median WSAVA score of 20 dogs with CE was 4 (range, 1–8). The mean age and median body weight of the dogs with GIL were 9.8 years (SD=± 1.7 years) and 7.1 kg (range 4.1 to 23.2 kg), respectively. Among these dogs were 1 spayed female and 5 males (3 castrated males and 2 intact males). The dog breeds were as follows: 2 Miniature dachshunds and one each of Jack Russell terrier, French bulldog, Shiba Inu, and Labrador retriever. Among these 6 dogs, 6 dogs had decreased appetite, 3 dogs experienced vomiting, and 6 dogs had soft feces or diarrhea (soft feces in 1 dog and diarrhea in 5 dogs) at the first visit. One dog had ascites. The median CIBDAI score and CCECAI score of 6 dogs with GIL were 11.5 (range, 9–15) and 12 (range, 9–16), respectively.

PARR was performed in 10 dogs (4 with CE and 6 with GIL). One dog with CE and 1 dog with GIL were negative, whereas 1 dog with CE showed clonal rearrangements of lymphocyte antigen receptor genes for B-cells, and 2 dogs with CE and 5 dogs with GIL showed clonal rearrangement of lymphocyte antigen receptor genes for T-cells.

All dogs were treated according to disease and clinical status. Dogs with CE were treated with a combination of prednisolone (0.5 to 2.0 mg/kg/day) (15/20), antibiotics (3/20), cyclosporine (5–10 mg/kg/day) (2/20), chlorambucil (2 mg/m^2/day) (2/20), an ULFD (18/20), a low-fat dry diet (12/20), and a hydrolyzed dry diet (1/20). Among 20 dogs with CE, 15 dogs were considered to have FR-PLE and 5 dogs were considered to have IR/NR-PLE based on the response to ULFD as previously reported [11]. Dogs with small-cell lymphoma were treated with prednisolone (2 mg/kg/day) (2/2) and chlorambucil (2 mg/m^2/day) (2/2). Dogs with large-cell lymphoma were treated with prednisolone (4/4) and multidrug chemotherapy consisting of L-asparaginase, doxorubicin, vincristine, and cyclophosphamide (3/4).

Four dogs with CE and 6 dogs with GIL, all of which were thought to have displayed progression of CE or GIL, died during the study period (nonsurvivors). No dogs were euthanized. Sixteen dogs remained alive at the end of the study period (survivors). The overall median follow-up time was 131 days (range, 14 to 1,416 days).

Signalment and plasma albumin concentrations were compared between the survivor and nonsurvivor groups (Table 1). The nonsurvivor group was significantly older (mean age, 10.2 versus 8.3 years old; P<0.039) and had higher CIBDAI scores (mean score, 12.2 versus 3.2; P<0.0001) and CCECAI scores (mean score, 13.5 versus 5.3; P<0.0001) than the survivor group. Plasma albumin concentrations were significantly lower in the survivor group than in the nonsurvivor group (mean, 1.6 versus 2.0 g/dl; P<0.04).

Among the 26 dogs with PLE, small intestinal dilatation was found in 2 dogs with CE and 2 dogs with GIL. US images of intestinal dilatation in these four dogs are shown in Fig. 2. In addition, signalment, plasma albumin concentrations, presence of ascites, histological diagnosis, and survival time of these four dogs are shown in Table 2. Hyperechoic intestinal mucosal striations were found in 15 dogs with CE and 1 dog with GIL. Small intestinal corrugation was found in 4 dogs with CE and 3 dogs with GIL. US findings in the survivor and nonsurvivor groups were compared (Table 1). Small intestinal dilatation was found in 0 of 16 dogs (0%) in the survivor group and 4 of 10 dogs (40%) in the nonsurvivor group (P=0.014). Hyperechoic intestinal mucosal striations were found in 13 of 16 dogs (81%) in the survivor group and 3 of 10 dogs (30%) in the nonsurvivor group (P=0.015). Small intestinal corrugation was found in 3 of 16 dogs (19%) in the survivor group and 4 of 10 dogs (40%) in the nonsurvivor group (P=0.37). The duodenal wall thickness did not differ between the survivor group (median, 4.3 mm; range, 3.4–5.6 mm) and

Table 1. Baseline signalment, plasma albumin concentration, and ultrasonographic findings for survivor and nonsurvivor in dogs with protein-losing enteropathy

Variable	Survivor	n	Nonsurvivor	n	*P* value
Mean age, years (SD)	8.3 (± 2.2)	16	10.2 (± 1.8)	10	0.039 (T)
Median weight, kg (range)	4.5 (1.9–11.5)	16	5.6 (2.5–23.2)	10	0.13 (M)
Female, number (%)	10 (62.5)	16	3 (30)	10	0.23 (F)
Mean CIBDAI (SD)	3.2 (± 2.8)	16	12.2 (± 2.9)	10	<0.0001 (T)
Mean CCECAI (SD)	5.3 (± 3.1)	16	13.5 (± 3.2)	10	<0.0001 (T)
Mean ALB, g/dl (SD)	1.6 (± 0.46)	16	2.0 (± 0.44)	10	0.04 (T)
Intestinal dilatation, number (%)	0 (0)	16	4 (40)	10	0.014 (F)
Hyperechoic intestinal mucosal striations, number (%)	13 (81.3)	16	3 (30)	10	0.015 (F)
Intestinal corrugation, number (%)	3 (18.8)	16	4 (40)	10	0.37 (F)
Duodenal wall thickness, mm (range)	4.3 (3.4–5.6)	16	4.3 (3.0–5.0)	9	0.51 (M)
Jejunal wall thickness, mm (range)	3.6 (3.1–4.6)	16	3.5 (2.9–5.7)	10	0.28 (M)

ALB, plasma albumin concentration; CCECAI, canine chronic enteropathy clinical activity index; CIBDAI, canine inflammatory bowel disease activity index; F, Fisher's exact test; M, Mann-Whitney *U* test; SD, Standard deviation; T, Student *t* test.

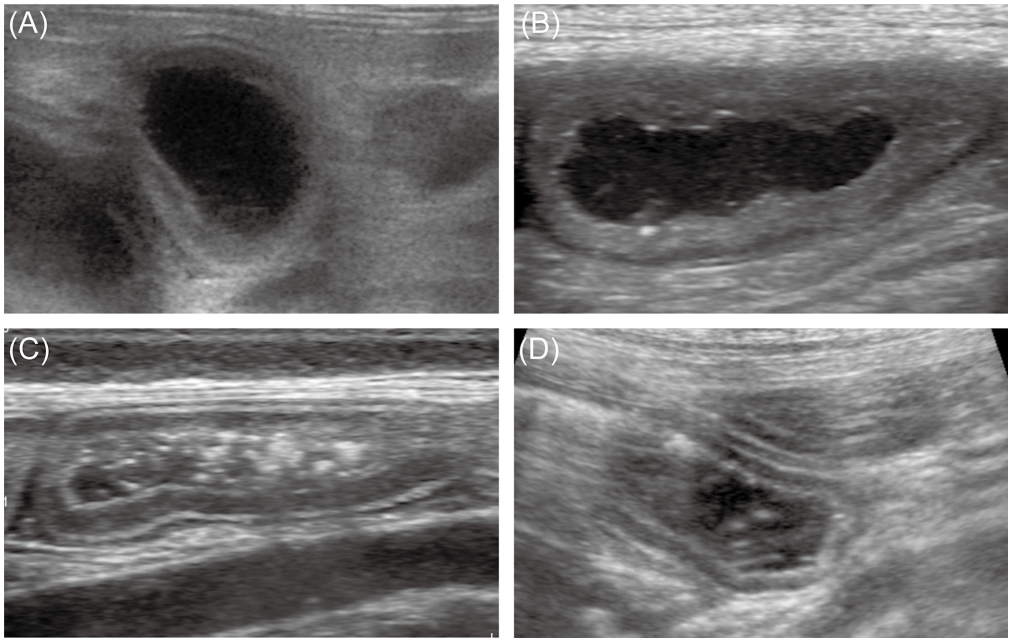

Fig. 2. Ultrasonographic images of the small intestine in four dogs with intestinal dilatation. A, Axial image of the ileum of a dog with lymphocytic-plasmacytic enteritis. B, Longitudinal image of the jejunum of a dog with lymphocytic-plasmacytic enteritis. C, Longitudinal image of the jejunum of a dog with small-cell lymphoma. D, Longitudinal image of the jejunum of a dog with large-cell lymphoma. Sixty-seven percent (A), fifty-seven percent (B), forty-seven percent (C), and fifty-six percent (D) of the diameter of the intestinal tract filled with fluid, respectively.

Table 2. Baseline signalment, plasma albumin concentration, presence of ascites, histological diagnosis, and survival time of four dogs with intestinal dilatation

Dog breed	Age (year)	Sex	CIBDAI score	CCECAI score	ALB (g/dl)	Ascites	Histological diagnosis	Survival time (day)
Cavalier King Charles Spaniel	9	Female	11	14	1.2	+	LPE with IL	16
Miniature Dachshund	9	Male	14	17	1.4	−	LPE with IL	18
Miniature Dachshund	9	Spayed female	9	9	2.3	−	Small-cell lymphoma	81
Shiba Inu	7	Male	9	9	2.4	−	Large-cell lymphoma	150

ALB, plasma albumin concentration; CCECAI, canine chronic enteropathy clinical activity index; CIBDAI, canine inflammatory bowel disease activity index; IL, intestinal lymphangiectasia; LPE, lymphocytic-plasmacytic enteritis.

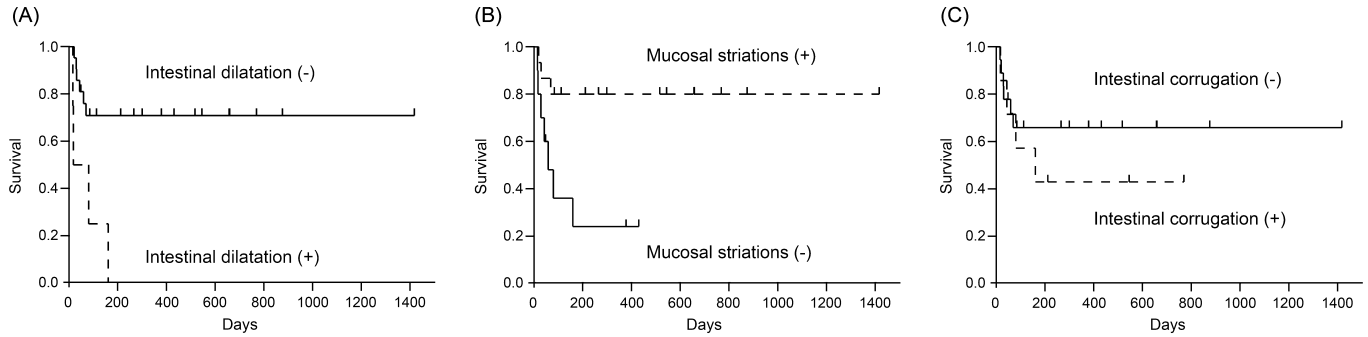

Fig. 3. A, Kaplan-Meier survival curves showing survival in dogs with (dashed line) and without (solid line) small intestinal dilatation. B, Kaplan-Meier survival curves showing survival in dogs with (dashed line) and without (solid line) hyperechoic intestinal mucosal striations. C, Kaplan-Meier survival curves showing survival in dogs with (dashed line) and without (solid line) small intestinal corrugation.

Table 3 Results of univariate Cox proportional hazard analysis for the ultrasonographic findings of the small intestine in dogs with protein-losing enteropathy

Ultrasonographic findings	*P*	Hazard ratio	95% confidence interval
Small intestinal dilatation	0.017	5.50	1.41–19.60
Hyperechoic intestinal mucosal striation	0.012	0.19	0.04–0.70

the nonsurvivor group (median, 4.3 mm; range, 3.0–5.0 mm) (*P*=0.51). A still image of the duodenum could not be obtained from one GIL dog. In addition, the jejunal wall thickness did not differ between the survivor group (median, 3.6 mm; range, 3.1–4.6 mm) and the nonsurvivor group (median, 3.5 mm; range, 2.9–5.7 mm) (*P*=0.28).

Figure 3 shows the Kaplan-Meier curves for dogs with PLE according to the presence or absence of small intestinal sonographic changes. The presence of small intestinal dilatation was associated with shorter survival time in dogs with PLE (*P*=0.003) (Fig. 3A). The presence of hyperechoic intestinal mucosal striations was associated with longer survival time in dogs with PLE (*P*=0.0085) (Fig. 3B). The presence of small intestinal corrugation was not associated with survival time (*P*=0.43) (Fig. 3C).

Univariate Cox proportional hazard analysis was performed to examine the prognostic value of ultrasonographic findings for shortened survival time in dogs with PLE. The results are shown in Table 3. The hazard ratios for the presence of small intestinal dilatation and hyperechoic intestinal mucosal striations were 5.50 (95% confidence interval (95% CI), 1.41–19.6) and 0.19 (95% CI, 0.04–0.70), respectively.

In addition, US findings of the small intestine in dogs with CE were compared between 15 dogs with FR-PLE and 5 dogs with IR/NR-PLE. There was no significant difference in the presence of small intestinal dilatation, hyperechoic intestinal mucosal striations, or small intestinal corrugation in dogs with FR-PLE and IR/NR-PLE. Small intestinal dilatation was found in 0 of 15 dogs (0%) with FR-PLE and 2 of 5 dogs (40%) with IR/NR-PLE (*P*=0.053). Hyperechoic intestinal mucosal striations were found in 13 of 15 dogs (87%) with FR-PLE and 2 of 5 dogs (40%) with IR/NR-PLE (*P*=0.073). Small intestinal corrugation was found in 3 of 15 dogs (20%) with FR-PLE and 1 of 5 dogs (20%) with IR/NR-PLE (*P*=1.0).

The current study demonstrated that multisegmental small intestinal dilatation was associated with poor prognosis in dogs with PLE secondary to CE and GIL. In contrast, the presence of hyperechoic intestinal mucosal striations was associated with longer survival time. This is the first study demonstrating the prognostic value of B-mode ultrasonographic findings of the small intestine in dogs with PLE secondary to CE and GIL.

In a previous study, generalized fluid distension and atonia were observed in the duodenum (37/40) and jejunum (38/40) of dogs with parvoviral enteritis [18]. A pattern of fluid distension within the small intestine is thought to be attributed to functional ileus secondary to severe intestinal mucosal damage, such as extensive epithelial necrosis with villus atrophy and disruption of the lamina propria. Other studies also reported that generalized reduction or absence of peristalsis with dilated intestinal segments may indicate paralytic ileus and can be associated with severe pancreatitis, inflammatory bowel disease, neoplasia, and severe systemic disease [7, 14]. In the current study, small intestinal dilatation was observed in PLE dogs in only the nonsurvivor group (4/10) and not the survivor group (0/16). Thus, the results of the current study indicated that the presence of multisegmental small intestinal dilatation might be a prognostic factor in dogs with PLE secondary to CE and GIL. Extensive small intestinal mucosal disruption secondary to severe enteritis in 2 dogs with CE or the infiltration of lymphoma cells in 2 dogs with GIL might be the cause of the small intestinal dilatation in 4 PLE dogs in the nonsurvivor group in the current study. Histological severity of the small intestine in 20 CE dogs was evaluated by the WSAVA guidelines, and the median WSAVA score was 4 (range, 1–8). The WSAVA scores of 2 CE dogs with intestinal dilatation were 8 and 4, respectively. Because of the small number of CE dogs with intestinal dilatation, it was difficult to elucidate the association between the histological severity of the small intestine and the presence of the US findings of intestinal dilatation. In addition, there are no established histological criteria for scoring the severity of the intestinal mucosal

damage of endoscopic biopsy specimens in dogs with GIL. Further study with a larger number of cases is necessary to examine the association between the histological severity of the small intestine and the presence of the US findings of intestinal dilatation especially in dogs with PLE secondary to CE.

Our previous study reported that CCECAI was significantly lower and survival times were significantly longer in dogs with FR-PLE than in dogs with IR/NE-PLE [11]. The use of a fat-restrictive diet, especially a homemade ULFD, improved the plasma albumin levels and the prognosis of dogs with FR-PLE secondary to CE or IL [11, 13, 17]. As mentioned previously, hyperechoic mucosal striations are thought to be a sensitive and specific US finding for the diagnosis of PLE and are associated with lacteal dilation [8, 19]. Thus, the presence of hyperechoic intestinal mucosal striations might be associated with a favorable prognosis in dogs with PLE secondary to CE or IL. However, the detection rate of hyperechoic intestinal mucosal striations was not different between dogs with FR-PLE and dogs with IR/NE-PLE in our previous study. In contrast, the current study demonstrated that the presence of hyperechoic intestinal mucosal striations was associated with a favorable prognosis in dogs with PLE. The major reason for the differences between the current study and our previous study could be that the current study included dogs with PLE secondary to GIL. In fact, hyperechoic intestinal mucosal striations were found in only 1 dog with GIL. In addition, the current study also demonstrated that there was no significant difference in the presence of hyperechoic intestinal mucosal striations between dogs with FR-PLE and dogs with IR/NR-PLE.

Small intestinal corrugation was not associated with survival time in the dogs with PLE examined in this study. Duodenal and jejunal corrugation has been observed in not only lymphocytic-plasmacytic enteritis but also hemorrhagic enteritis, neoplasia, peritonitis, and most commonly pancreatitis [10] and is thought to be a nonspecific ultrasonographic finding for the diagnosis of intestinal disorders in dogs. The results of the current study also indicated that small intestinal corrugation is not a useful prognostic indicator of PLE secondary to CE and GIL in dogs.

Intestinal wall thickness was reported to differ between dogs with inflammatory intestinal diseases and dogs with intestinal tumors [15]. However, intestinal wall thickness has not been found to be sufficiently specific or sensitive for the diagnosis of inflammatory bowel disease in dogs [16]. In the current study, we compared the duodenal and jejunal wall thickness of dogs with PLE in the survivor and nonsurvivor groups and found no significant differences between groups. The results of the current study indicated that intestinal wall thickness might not be useful for predicting survival time in dogs with PLE, except for dogs with marked wall thickening (thickness greater than 1 cm) [15].

In the current study, we used not only dogs with CE but also dogs with GIL for survival analysis. As a result, six out of 10 nonsurvivor dogs were GIL cases. In addition, two out of 4 dogs with intestinal dilatation were GIL dogs. On the other hand, only one out of 6 dogs (17%) with GIL showed hyperechoic intestinal mucosal striations. The inclusion of dogs with GIL is thought to have a large influence on the results of survival analysis of dogs with PLE because GIL, especially large-cell GIL, is known to be associated with poor prognosis. Thus, the results of the current study should be interpreted with caution.

Our study had several limitations. First, the current study included only a small number of dogs, especially a small number of PLE dogs with small intestinal dilatation. Thus, the sensitivity and specificity of ultrasonographic findings for the prediction of prognosis in dogs with PLE could not be determined. Second, follow-up US examinations were not performed on four dogs with intestinal dilatation; thus, it is not known whether intestinal dilatation can improve after treatment of underlying disorders. Third, in the current study we used not only PLE dogs with CE but also PLE dogs with GIL. In future studies, it will be necessary to examine the prognostic values of ultrasonographic findings separately in PLE dogs with CE, small-cell GIL, and large-cell GIL with a larger number of cases. Fourth, because of the retrospective nature of the current study, we could not completely standardize the image acquisition technique used during abdominal ultrasonography. We used two types of ultrasound equipment and two sonographers to perform US examinations. Fifth, evaluation of ultrasonographic images was not performed blindly. Thus, possible bias in the interpretation of ultrasonographic findings cannot be excluded. Sixth, except for wall thickness, we did not separately evaluate the ultrasonographic findings of the duodenum and jejunum. Thus, in future studies, we need to collect ultrasonographic findings from the duodenum and jejunum separately. Finally, hypoalbuminemia secondary to liver dysfunction was not completely excluded among 21 dogs because fasting total bile acid was measured in only 5 of 26 dogs with PLE.

In conclusion, the results of the current study indicate that the presence of small intestinal dilatation might be associated with poor prognosis in dogs with PLE secondary to CE and GIL.

CONFLICT OF INTEREST. The authors declare no conflicts of interest.

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