

Correlation between Ultrasonographic Imaging of the Gallbladder and Gallbladder Content in Eleven Cholecystectomised Dogs and their Prognoses

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ABSTRACT. A comparison was performed between preoperative ultrasonographic and macroscopic findings for gallbladders and their contents in eleven dogs that were found to have any content in the gallbladder and then underwent cholecystectomy. In addition, correlation was considered between prognosis and age, hematologic analysis, serum biochemical analysis and ultrasonographic findings. Ultrasonographic findings of the gallbladder were classified into 3 patterns: 1) hyperechoic content filling the entire gallbladder and precipitated immobile content, 2) a somewhat thinner hypoechoic area in the exterior layer with a less distinctive border adjacent to the internal hyperechoic area than pattern 3 with moth-eaten or mosaic-form hypoechoic portions scattered within the internal hyperechoic area and 3) a thick hypoechoic area in the exterior layer with a distinctive border adjacent to a prominent internal hyperechoic area. The macroscopic findings of the contents mainly consisted of biliary sludge and concentrated bile in pattern 1, a softer mucous mass in pattern 2 and an elastic mucous mass in pattern 3. Pattern 2 seemed to be in the stage before the kiwi fruit-like pattern that characterizes gallbladder mucocele, suggesting disorder of the gallbladder and bile excretion as well as onset of cholangiohepatitis associated with such disorders. In regard to association with prognosis, the mean ages were 11.8 ± 1.5 years in death cases and 8.4 ± 2.8 years in surviving cases, while the total WBC counts were $46,600 \pm 11,912 /\mu\text{L}$ in the death cases and $18,266 \pm 9,411 /\mu\text{L}$ in the surviving cases, showing significant differences ($p < 0.05$) in age and total white blood cell count between the two groups.

KEY WORDS: canine, gallbladder mucocele, gallbladder sludge, prognosis, ultrasonographic imaging.

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In clinical practice for small animals, hepatobiliary diseases are increasingly being diagnosed with the prevalence of blood chemistry, radiology and ultrasound [1, 3, 4, 8, 10–12, 14, 16]. Occasions in which cases are encountered with suspected gallbladder mucocele (GM) based on ultrasound findings have also been increasing [1, 3, 12, 14, 16]. In recent years, there has been a trend for early cholecystectomy to be considered preferable for treatment of cases with GM [1, 3, 12, 14]. Besso *et al.* [3] reported the changes in gallbladder ultrasound findings in GM. In clinical cases, however, differentiation of biliary sludge deposition associated with cholecystitis from GM may be sometimes difficult based on ultrasound findings. In addition, the timing of cholecystectomy tends to be determined late because of unknown details in rate of GM progression [14]. This study reports some findings that were obtained from comparative examination between gallbladder ultrasound findings and macroscopic findings of gallbladder content in cases with a history of cholecystectomy and consideration of the dogs' prognoses.

MATERIALS AND METHODS

The dogs used in this study: A total of 11 dogs were used

in the present study (No. 1–11). Nine of the dogs had been diagnosed as having a disorder in bile excretion with content retained in the gallbladder based on blood chemistry and abdominal ultrasound and had undergone cholecystectomy; one subacute dog had jaundice due to disorder in bile excretion with content retained in the gallbladder and had undergone cholecystectomy; and one dog had undergone preventive cholecystectomy due to retention of a massive amount of deposits in the gallbladder for a year. The dog breeds were 4 Shetland sheepdogs, 2 Pomeranians, a Maltese, a Beagle, an American Cocker spaniel, a Shiba and a Labrador retriever. Six dogs were male, and 5 were female, including 1 neutered female. The ages of the dogs were 3 to 14 years old, and their body weights were 3.6 to 16.2 kg. Their medical histories included: mitral regurgitation in 2 dogs (No. 1, 2), pemphigus foliaceus in 1 dog (No. 3), obesity in 1 dog (No. 4) and hypothyroidism in 2 dogs (No. 8 and 10). No. 10 was received hormone replacement therapy for 6 months before surgery (Table 1).

Gallbladder ultrasound findings and macroscopic findings for the gallbladder and its contents during surgery were compared in these 11 dogs to examine the correlation between them. Additionally, changes in ultrasound findings for the gallbladder contents were examined over 6–11.5 months in 2 dogs (No. 2 and 10) that had a preoperative gallbladder ultrasound. Histopathological examination was performed on the dissected gallbladders of 8 dogs (No. 1, 3–5,

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Table 1. Profiles of the eleven dogs that underwent cholecystectomy

No.	Breeds	Sex	Age	B.W.	Medical histories
1	Maltese	♂	12Y	3.3	Mitral regurgitation
2	Pomeranian	♀	14Y	4.0	Mitral regurgitation
3	Shetland sheepdog	♂	12Y	9.2	Pemphigus foliaceus
4	Beagle	♀ (sterilized)	9Y	16.2	Obesity (BCS:5)
5	A. Cocker spaniel	♀	3Y	8.8	
6	Shiba	♀	10Y	11.6	
7	Shetland sheepdog	♀	8Y	9.4	
8	Shetland sheepdog	♂	10Y	6.6	Hypothyroidism
9	Labrador retriever	♂	11Y2M	33.5	
10	Shetland sheepdog	♂	9Y6M	9.9	Hypothyroidism*
11	Pomeranian	♂	10Y7M	3.6	

*: Receiving Hormone replacement therapy.

7 and 9–11), and bacterial culture was performed on the gallbladder contents of 8 dogs (No. 1–3, 5, 7 and 9–11).

Abdominal ultrasound examination: Ultrasound examination of the gallbladder was performed using an ultrasound scanner (Hitachi EUB-6500, 5–9 MHz convex array probe EUP-C532) by holding the dog in a standing or supine position to observe the whole gallbladder from the posterior ventral rib or caudal right seventh intercostals, where the gallbladder can be observed in order to evaluate thickening (> 3–3.5 mm) [1, 3] and presence or absence of perforation of the gallbladder wall. If any sludge was found in the gallbladder, it was evaluated by observing the gallbladder from various angles as much as possible. These dogs were also examined to determine whether the sludge would move in the gallbladder due to gravity or changing their positions from a right/left lateral position to a standing and supine positions in turn.

Macroscopic observation on the gallbladder and its contents: Direct macroscopic observation was performed for tension degree, presence or absence of rupture, necrosis and perforation of the gallbladder wall, color/hardness of the deposits and proportion of mucus and presence or absence of calculus/crystalline particles in the sludge.

Histopathological examination of the gallbladder and liver: The gallbladders were dissected from 8 of the 11 dogs (No. 1, 3–5, 7 and 9–11) and histopathologically examined. Sphenoidal liver biopsy was also performed in 6 of the 8 dogs (No. 4, 5, 7 and 9–11). Hematoxylin-eosin staining (H-E staining) and Alcian blue/PAS double staining were performed for the gallbladder, and HE and silver staining were performed for the liver.

Association with prognosis: In each case, blood tests were performed immediately before surgery to obtain measurements for a substantial number of cases in both groups, including the total white blood cell count (WBC), packed cell volume (PCV), serum alanine aminotransferase (ALT), serum alkaline phosphatase (ALP), total bilirubin (T-bil), total cholesterol (T-Cho) and blood ammonia (NH₃), in order to examine the association with age, ultrasound findings and prognosis.

RESULTS

Preoperative gallbladder ultrasound findings: None of the 11 cases showed thickening of the gallbladder wall of 3 mm or more. Discontinuity of the gallbladder wall and/or echo-free space in the exterior portion of the gallbladder was found in 2 dogs (No. 2 and 3). The gallbladder content was immobile in 10 of the 11 dogs (No. 1–10). The content filled the entire gallbladder lumen in 9 of the 11 cases (No. 1–8, 10). Hyperechoic and immobile content precipitated onto the bottom of the gallbladder in one dog (No. 9). The content had a hypoechoic exterior layer in 8 of the 11 cases (No. 1–3, 5–8, 10). The hypoechoic area of the exterior layer was at least 10 mm thick in 2 dogs (No. 1 and 6), 4 to 8 mm thick in 2 dogs (No. 2 and 5) and 1 to 3 mm thick in 4 dogs (No. 3, 7, 8 and 10). The echo pattern of the interior hyperechoic area was uneven with somewhat fine sporadic moth-eaten hypoechoic portions in 5 of the 8 dogs (No. 2, 4, 6, 7 and 10), and coarse mosaic-form hypoechoic portions were scattered within the interior hyperechoic area in 2 of the 8 dogs (No. 3 and 5). The central hyperechoic area had an oval form in No. 1 and a star shape form in No. 6, and the border between the central hyperechoic area and the surrounding hypoechoic area was distinctive in these dogs. Dogs No. 2, 3 and 5 had somewhat blurred borders between the central hyperechoic area and the hypoechoic area, with a thinner hypoechoic exterior layer than that of dogs No. 1 and 6 (Table 2).

Macroscopic findings for the gallbladder and its contents: The gallbladder was dilated in all cases, and the gallbladder wall was tense due to the inner pressure. Necrosis in the gallbladder wall was macroscopically observed in No. 2 and No. 3. Perforation was found in the necrosis area in No. 3. One dog (No. 1) had gallbladder contents consisting of a hard and elastic mucous mass in an egg-form molded by the gallbladder, and 5 dogs (No. 2, 3, 5, 6 and 8) had somewhat softer mucous masses. The contents of the above 6 dogs were macroscopically diagnosed as gallbladder mucocele. The contents from 2 dogs (No. 4 and 10), mainly consisting of mucous, were soft and easily broken when extracted, with a dark green color as a whole. The gallblad-

Table 2. Ultrasound imaging of the gallbladder wall and content before surgery and macroscopic findings for the content

No.	Ultrasound findings				Macroscopic findings		U/S pattern
	Gallbladder wall		Gallbladder content (before surgery)		Gallbladder Content		
Thickening	Discontinuity	Thickness of hypoechoic portion	Shape of hyperechoic portion	Pattern within hyperechoic portion			
1	-	-	≥10 mm	Oval with distinctive border	Virtually even	Elastic mucus mass	3
2	-	+	4-8 mm	Irregular with somewhat blurred border	Sporadic hypoechoic portions 2-3 mm in size	Somewhat soft mucus mass	2
3	-	+	2-3 mm	Irregular with somewhat blurred border	Coarse sporadic hypoechoic portion	Somewhat soft mucus mass	2
4	-	-	1-2 mm	Filled the entire gallbladder	Sporadic hypoechoic portions 2-4 mm in size	Black-green tar-like content	2
5	-	-	4-5 mm	Irregular with somewhat blurred border	Coarse sporadic hypoechoic portion	Somewhat soft mucus mass	2
6	-	-	≥10 mm	Starform with distinctive border	Sporadic hypoechoic portions 2-3 mm in size	Somewhat soft mucus mass	3
7	-	-	1-2 mm	Virtually evenly filled	Sporadic hypoechoic portions 2-3 mm in size	Black-green viscous crystalline material	1
8	-	-	2-3 mm	Layered structure		Somewhat soft mucus mass	2
9	-	-	0 mm	Precipitated onto the bottom of the gallbladder	—	Immobile biliary sludge with viscous concentrated bile	1
10	-	-	1-2 mm	Filled the entire gallbladder	Sporadic hypoechoic portions 2-4 mm in size	Tar-like soft mucus mass	2
11	-	-	*	*	*	Biliary sludge	*

U/S pattern : Ultrasound patterns in gallbladder content (Fig. 3).

* : Mobile content.

der content of dog No. 7 consisted of mainly viscous material comprised of irregular black-green crystalline particles, ranging from fine to coarse particles in size. Dog No. 9 had viscous biliary sludge precipitated and immobilized onto the bottom of the gallbladder, and the dog No. 11 had concentrated bile with slight flow ability. The gallbladder sludge from both dogs No. 9 and 11 contained small amounts of black-green particles with a particle size ranging from fine to 0.5-3.0 mm (Table 2).

Histopathological finding for the gallbladder and liver: Findings of chronic cholecystitis were obtained for the gallbladder in all 8 dogs (No. 1, 3-5, 7 and 9-11) histopathologically examined. Hyperplasia of the gallbladder mucosa and/or increased mucous production were found in 4 cases (No. 1, 2, 3 and 5). Necrosis in the gallbladder mucus was found in the dog No. 5. Dog No. 7 had a hemorrhage spreading from the lamina propria to the mucous muscular layer. Atrophy and flattening of the gallbladder mucosa was found in dogs No. 9 and 10. Lymphocytic and plasmacytic inflammatory cells infiltration was found around the liver portal vein in all cases examined (No. 4, 5, 7 and 9-11).

Microbiological findings for gallbladder content: Bacterial culture was performed for 8 dogs. Aerobic culture was performed for 3 dogs (No. 1, 2 and 7). For 5 dogs (No. 3, 5, 9 to 11), both aerobic and anaerobic cultures were performed. *Streptococcus pyogenes* were isolated from dog No. 7, although the results from the remaining 7 dogs were all negative.

Changes in gallbladder ultrasound findings in two dogs: Changes in the preoperative ultrasound findings for the gallbladder were observed at 11.5 months in dog No. 2 and at 6

months in dog No. 10. In dog No. 2, hyperechoic contents were found with a somewhat blurred border in the gallbladder 11.5 months before surgery (Fig. 1-a), and a similar finding was made a month later. Ultrasound imaging after 5 months revealed a more distinctive border between the interior hyperechoic area and hypoechoic area around it (Fig. 1-b). In dog No. 10, on the other hand, the ultrasound examination performed 6 months before the operation revealed that somewhat hyperechoic and immobile content was precipitated onto the bottom of the gallbladder by gravity, and a hypoechoic area was found in the cervix of the gallbladder. The surface of the portion of the content adjacent to the basal part of the gallbladder mucosa was uneven (Fig. 2-a). In dog No. 10, the proportion of the somewhat hyperechoic content gradually increased afterward, although a hypoechoic area along with the gallbladder mucosa, characteristic of GM, was not formed (2-b).

Five dogs, No. 1 to 3, 6 and 9, died within a week after cholecystectomy. The remaining 6 dogs made good progress for 6 months or more after surgery. Perioperative clinical findings, hematology and blood chemistry results from the dead cases suggested that the most significant factor for cause of death was liver dysfunction [14]. In regard to the association of prognosis with each measurement of WBC, PCV, ALT, ALP, T-bil, T-Cho and NH₃, age and ultrasound findings, the mean age of death cases (11.8 ± 1.5 years) was significantly higher than that of surviving cases (8.4 ± 2.8 years; p<0.05, Mann Whitney U-test). Between prognosis and WBC, death cases had a significantly higher mean WBC (46,600 ± 11,912/μL) than the survival cases (18,266 ± 9,411/μL) (p<0.05, Mann-Whitney U-test). No

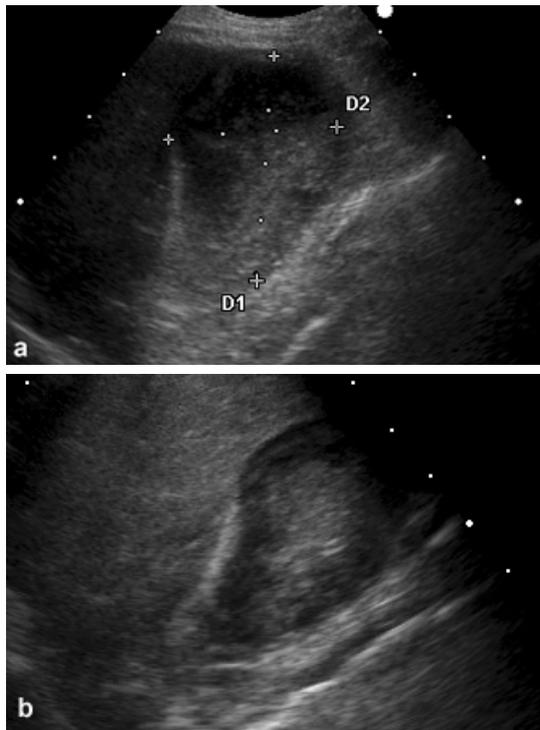


Fig. 1. Changes in ultrasound imaging of the gallbladder in case No. 2 (1-a, 11.5 months before surgery; 1-b, immediately before surgery).

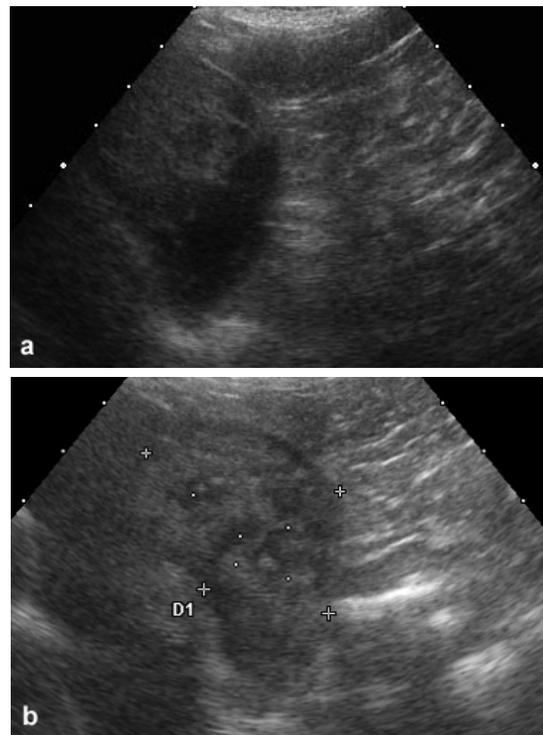


Fig. 2. Changes in ultrasound imaging of the gallbladder in case No. 10 (2-a, 6 months before surgery; 2-b, immediately before surgery).

association was found between blood test measurements such as PCV, ALT, ALP or T-bil and prognosis. The three patterns of ultrasound findings had no association with blood test findings or prognosis in this study (Table 3).

DISCUSSION

Crews *et al.* [5] classified ultrasound findings in the gallbladder into three groups, GM (21 dogs), gallbladder mobile sludge (19 dogs) and gallbladder mobile precipitate (5 dogs), in a retrospective study report on 45 dogs with gallbladder disease and/or gallbladder rupture. The report

of Crews *et al.* included no comparison between ultrasonographic findings for gallbladder content and visual findings, and all dogs with immobile biliary content were classified into GM within the 45 dogs. The preoperative ultrasound findings for the gallbladder sludge from the eleven dogs in this study were roughly divided into 3 patterns. Pattern 1 had hyperechoic content filling the entire gallbladder (No. 7) or immobile content precipitated onto the bottom of the gallbladder (No. 9). Pattern 2 (No. 2–5, 8 and 10) had a somewhat thinner hypoechoic area in the exterior with a less distinctive border adjacent to the interior hyperechoic area than that of pattern 3, and moth-eaten/mosaic-form hypo-

Table 3. Hematology and blood chemistry findings vs. patterns in gallbladder ultrasound findings and prognosis in the 11 cases

		Case No.										
		1	2	3	4	5	6	7	8	9	10	11
WBC	/ μ L	54400	49000	60100	10500	31900	30400	13900	25500	39100	7300	20500
PCV	%	42	44	47	57	48	45.9	43	42.5	40	45	38
ALT	U/L	>1000	>1000	141	>1000	1735	2331	478.4	14	1023	<10	>1000
ALP	U/L	2577	>2000	409	>1500	>4000	12543	695.6	ND	310	62	>3500
T-bil	mg/dl	2.9	5.2	18	17.2	9.3	2.8	1.4	3.6	23	ND	3.6
T-Cho	mg/dl	ND	ND	ND	>400	400	>400	ND	367	281	390	ND
NH3	μ mol/L	90	87	90	ND	16	103	ND	ND	ND	11	43
Ultrasound pattern		3	2	2	2	2	3	1	2	1	2	*
Prognosis		†	†	†	Good	Good	†	Good	Good	†	Good	Good

*: Mobile content.

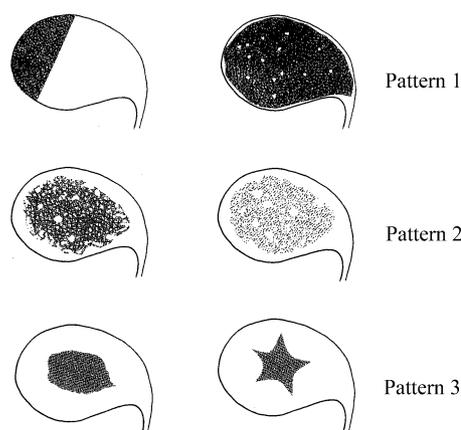


Fig. 3. Ultrasound patterns of the gallbladder content. Pattern 1, pattern 2 and pattern 3.

echoic portions were scattered within the interior hyperechoic area. Pattern 3 (No. 1, 6) had a thick hypoechoic area in the exterior layer with a distinctive border adjacent to the interior hyperechoic area (Fig. 3). Based on comparison of the ultrasound findings and macroscopic findings of the content during surgery between these three patterns, the gallbladder content in pattern 1 mainly consisted of biliary sludge and concentrated bile. The gallbladder content in pattern 2 was a somewhat softer mucus mass. The moth-eaten portions within the hyperechoic area corresponded to viscous concentrated bile, and the mosaic-like hypoechoic portions corresponded to the more mucus portion than the surroundings. In pattern 2, the more distinctive and broader the hypoechoic area in the exterior layer was, the higher the proportion of mucus was. Pattern 3 was one of the typical ultrasound findings that have been considered as being typical for GM [3]. The macroscopic findings of the gallbladder content included a mucous mass molded by the gallbladder. The exterior portion mainly consisted of mucus and corresponded to the hypoechoic area, and the interior black-green portion, with a fine sand-like texture, corresponded to the hyperechoic area. Therefore, as correlation was found between the ultrasound findings and the macroscopic findings for the gallbladder content, it seemed possible to predict whether the gallbladder content is a mature and hardened mucus mass, soft mucus mass or mainly biliary sludge.

In this study, 9 of the 11 dogs (No. 1 to 8 and 10) had content completely filling the gallbladder. Three of these dogs (No. 4, 7 and 10) did not have a semi-solid mucous mass but instead had a tar-like (No. 4 and 10) or crystalline (No. 7) blackish green content. These 3 dogs had echo pattern 1 (No. 7) or 2 (No. 4 and 10), and their low echo portions adjacent to the gallbladder mucosa were as thin as 1 to 2 mm. It seemed that the content could be inferred more properly by evaluating the thickness of the low echo portion adjacent to the inner wall of the gallbladder as well as the content pattern.

Four (No. 1–3 and 6) of the five dogs showed obvious characteristics of GM in both the ultrasound findings and the macroscopic findings during surgery. Three (No. 1, 3 and 6) of these cases had been brought to the hospital for GM symptoms for the first time. In regard to GM, as obvious clinical symptoms are rarely manifested until the disease is advanced, it seems that owners are less likely to become aware of abnormalities in their dogs [1, 12, 14, 16].

In dog No. 2, an old Pomeranian in which gallbladder ultrasound findings were followed for 11.5 months, the need for surgical therapy, possible onset of acute symptoms due to GM and risks at the time of onset were repeatedly explained to the owner. However, onset of jaundice and worsening of general condition forced emergency surgery, and what is worse, the prognosis was poor. In dog No. 10, which received hormone replacement therapy for hypothyroidism, on the other hand, a preventive cholecystectomy was performed, and the progress after surgery has been good for at least two years; the dog is now 12 years old.

Based on the fact that the three patterns of ultrasound findings had no association with blood test results and prognosis in the cases in this study, content completely filling the gallbladder seems to increase the risk of gallbladder necrosis, regardless of whether the gallbladder content is mucous or biliary sludge. Up to now, however, there have been little or no reports on the speed of deposition within the gallbladder or time period required to fill it up. Biliary sludge is apt to appear frequently in dogs with hypothyroidism, hyperadrenocorticism, diabetes mellitus or hyperlipidemia. It is assumed that biliary excretion disorder in the gallbladder may be associated with deposit of biliary sludge in diabetes or hypothyroidism [1, 2, 6, 7, 9, 13, 15], although whether this is directly related to the mechanism of increased mucus production or not is unknown [1].

Besso *et al.* [3] presented a diagram of changes in GM ultrasound findings stating that the pattern of hyperechoic bile changes to a stellate pattern and then a kiwi fruit-like pattern. Applying the diagram of Besso *et al.* to the cases in the present study, the three patterns seemed to correspond to a change from a pattern of hyperechoic bile to a stellate pattern or kiwi fruit-like pattern. In particular, pattern 2 seemed to be in the stage before the kiwi fruit-like pattern and stellate combination. Four of the cases (No. 2, 3, 5 and 6) suggested that liver dysfunction due to cholecystitis and/or disorder in bile excretion may also occur before the change of GM to a semi-solid form by maturation in the gallbladder.

Cholecystectomy or surgery to assure accessibility in the bile duct by duodenotomy is not a necessarily difficult technique in actual clinical practice for small animals. The perioperative mortality rate, however, in cases with GM is as high as 20 to 50%, although there is some variation between reporters [3, 12, 14, 16]. Aged dogs or dogs that already have advanced liver dysfunction tend to have a higher postoperative mortality rate [14]. More proper prediction of postoperative progress is as important as determining whether surgery is needed when an animal is diagnosed as

having GM or gallbladder disease by gallbladder ultrasound examination. Both Pike *et al.* [12] and Aguirre *et al.* [1], reported that the results of blood tests showed that the total white blood cell count was increased in death cases compared with surviving cases, possibly reflecting disease severity, degree of tissue damage, biliary peritonitis and secretion of intrinsic cortisol, according to their reports. Furthermore, Pike *et al.* [12] stated that dogs with gallbladder rupture have high a WBC, ALP and T-bil [11]. Crews *et al.* [5] reported no difference in blood chemistry and hematology findings, except for higher blood lymphocyte counts, in surviving dogs compared with dead dogs. In the present study, the mean age and WBC count in the death cases were significantly higher than in the surviving cases. Therefore, it seemed that age and WBC count may need to be focused on as predictive factors for prognosis.

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