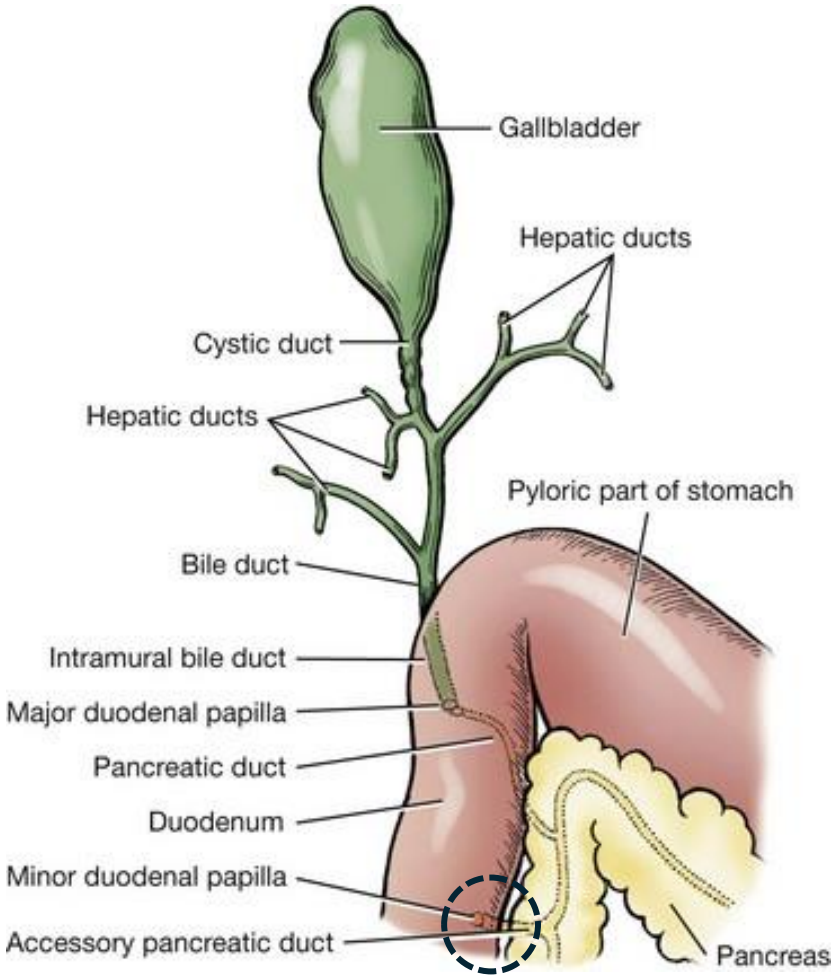
Gallbladder mucocele

BIEN 진료수의사 김 별

- Biliary system
- 담낭점액종이란?
- GBM의 진단
- 치료- 내과적 접근
- 치료- 수술
- 예후

Anatomy



담낭 -> 담즙의 저장 및 농축

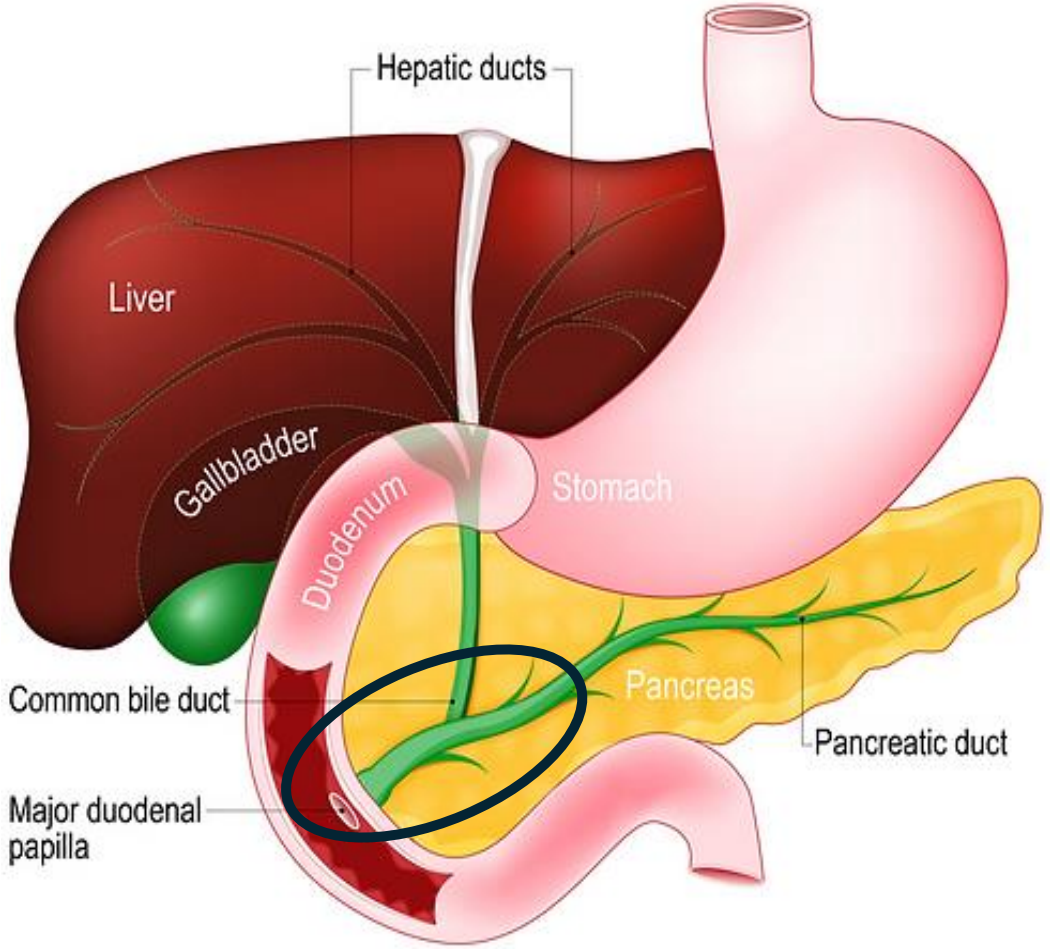
담즙

- 지방의 소화, 흡수, 산의 중화
- Cholesterol, lecithin, phospholipid, bile salt, conjugated bilirubin, electrolytes, and water.
- Hepatocytes -> bile canaliculi-> intralobular ducts-> interlobular duct -> lobar ducts-> intrahepatic bile ducts-> hepatic duct -> common hepatic duct -> cystic duct -> GB
- GB -> cystic duct -> CBD -> Oddi sphincter -> duodenum

Anatomy

Cat ?

- CBD가 십이지장으로 들어가기 전에 major pancreatic duct와 융합
- Increased risk of ascending infection of the pancreas



Anatomy

- GB wall: (개) 2-3mm 이하, (고양이) 1mm 이하
- CBD diameter: 최대 (개) 3-3.5mm, (고양이) 4mm

The common bile duct was considered normal (<4 mm), mildly dilated (5–6 mm) and moderately dilated (>7 mm)

- GB motility
  - Parasympathetic
  - CCK
  - Motilin
  - Oddi sphincter

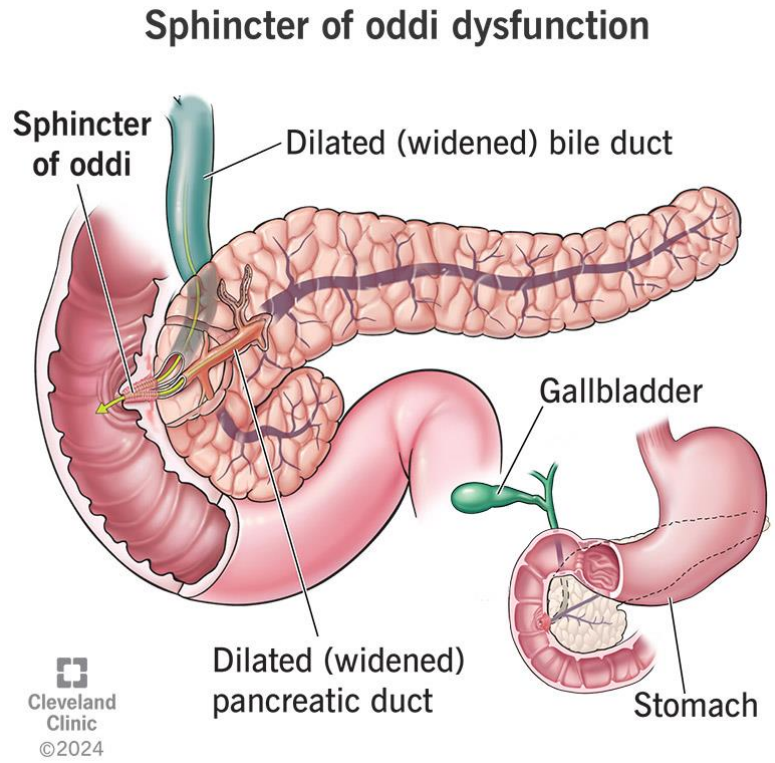
dysmotility →

GBM

Cholelith formation

…

- A healthy dog's gallbladder volume is typically around 1.2 mL/kg after a period of fasting.
- The median gallbladder volume for dogs is 0.6 mL/kg after 12 hours without food



GBM?

- Gallbladder mucocele
- Accumulation of bile-laden mucus within the gall bladder
- Most common reason for biliary surgery in dogs

- 담낭 내 슬러지는 정상 담낭에서도 쌓일 수 있으므로 반드시 임상적 의의 X
- GBM에서는 저에코성 점액이 담낭벽 내측경계에 축적, 에코성의 담즙은 담낭 중심부에 위치 -> 자세변경에도 이동X
- gallbladder epithelial mucus hypersecretion and hypokinesia
- Result in cholestasis and affect gallbladder wall integrity.
- can result in emergent clinical disease associated with extrahepatic bile duct obstruction, cholecystitis (sterile or infectious), biliary rupture, and systemic inflammatory response syndrome

GBM – Etiology

- Etiology -> unclear
- Breed: Shetland sheepdog, cocker spaniels, miniature schnauzer, beagles, poodle
- Age: 10yr (3~17yr)
- gallbladder dysmotility, decreased bile flow or stasis, and altered bile composition
- a multifactorial pathogenesis with both genetic and metabolic influences.
- affected dogs have a high incidence of concurrent endocrinopathies and hyperlipidemia
  - Hyperadrenocorticism
  - Hypothyroidism ···
- Drugs (E.g. exogenous steroid)

- 고양이의 GBM?

-> 내분비질환은 비교적 드물기 때문에 선천성 담도(12%)이상으로 인한 담즙정체가 주요 발생기전으로 생각됨

GBM – Clinical features

- Slow progression -> variable clinical signs
- 임상증상 없이 초음파상 발견되는 경우가 흔함
- acute abdominal pain (due to EHBO, pancreatitis, bile peritonitis)
- 구토, 식욕부진, 복통, 기력저하 등이 일반적으로 나타날 수 있음
- Fever -> septic cholecystitis, bile peritonitis와 관련성
- Icterus
- 수술 전 임상증상 median time: 4-5days

- A total of 17.6% (211/1194) of dogs did not exhibit clinical signs at the time of cholecystectomy.
- Eighty-two percent (982/1194) of dogs with GBM demonstrated at least one clinical sign attributable to biliary tract disease,
- vomiting 80.0% (786/982), lethargy 46.7% (458/982), anorexia 46.2% (454/982), diarrhea 18.3% (180/982), painful abdomen 16.7% (164/982), hyporexia 11.2% (110/982), and jaundice 9.8% (96/982).

Table 1. Prevalence of Common Clinical Signs, Physical Examination Findings, and Biochemical Abnormalities in 48 Reported Cases of Canine Gallbladder Mucoceles[2–4,6,7]

Clinical Signs	Incidence
None	23%
Vomiting	70%
Anorexia	65%
Lethargy	65%
Polyuria/polydipsia	27%
Diarrhea	12.5%
Physical Examination	
Abdominal pain	60%
Icterus	46%
Fever (>102.7°F [39.3°C])	22%

Clinical signs (where reported)	166	-
Vomiting	115	69.30
Lethargy	73	44.00
Anorexia	70	42.20
Abdominal pain/discomfort	32	19.30
Icterus	27	16.30
PU/PD	13	7.80
Symptomatic vs. asymptomatic (where reported)	122	-
Symptomatic	87	71.30
Asymptomatic	35	28.70

Diagnosis – Clinical pathology

- 일반적인 임상병리학적 소견으로 다른 간담도계 질환과의 구별 불가
- Hypercholesterolemia, hyperbilirubinemia가 일반적
- **담즙정체성 효소>>>간세포성 효소 증가** (기저질환에 따라 다양하지만)

Clinicopathologic findings (where reported)	-	-
Increased ALP	108/110	98.20
Increased ALT	90/103	87.40
Increased GGT	78/91	85.70
Increased total bilirubin	79/95	83.20
Increased AST	28/45	62.20
Increased cholesterol	15/27	55.60
Increased lipase	4/12	33.30
Increased amylase	13/44	29.50
Leucocytosis	23/49	46.90
Bacterial culture	-	-
Number of cultures performed	111	-
Number of positive cultures	15	13.50

- 간세포성/leakage enzyme

- 간외 담즙정체에서 시작되어 간내 독성 축적 -> 간세포 손상으로 효소 누출.
- ALT는 2~10배 정도 증가, AST는 소폭 증가

- 담관/담즙정체성 표지자 enzyme

담즙정체 질병에 대한 specificity는 제한적

- ALP는 담관폐색 8시간 후부터 증가하여 2-4일 후 15배까지 증가, 1-2주 후에는 100배 이상 증가
- GGT는 담즙정체에 반응하여 증가

-> GGT와 ALP 함께 측정할 때 진단적 가치 증가 (개에서 비교적 ALP는 민감도, GGT는 특이도 높음)

Diagnosis – Clinical pathology

- Septic/ bile peritonitis -> leukocytosis (neutrophilia), left shift

- Bilirubin
- post-hepatic jaundice (tbil > 2-3mg/dL)
- Hyperbilirubinemia: 스테로이드성 ALP 증가와 원발 담즙정체의 구분에 도움

- Coagulation test
- 담도폐색에 의한 vit K deficiency (지용성 비타민 흡수 저하)
- coagulation factors II, VII, IX, X are vit K dependent -> prolonged PT

Diagnosis – Clinical pathology

Journal of Veterinary Internal Medicine Open Access

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Evaluation of coagulation parameters in dogs with gallbladder mucoceles

Michelle Pavlick [1], Armelle DeLaforcade [1], Dominique G Penninck [1], Cynthia R L Webster [1,✉]

Author information · Article notes · Copyright and License information

PMCID: PMC8295708 PMID: 34196054

TABLE 6.

Summary of coagulation parameters in 23 dogs with gallbladder mucoceles

Coagulation parameters associated with thrombotic tendencies		Coagulation parameters associated with bleeding tendencies	
Increased TEG *G*/MA	(83%, 19/23)	Prolonged aPTT	(41%, 9/22)
Increased fibrinogen	(41%, 9/22)	Decreased vWF activity	(24%, 5/21)
Increased D-dimers	(40%, 6/15)	Prolonged PT	(14%, 3/22)
Thrombocytosis	(39%, 9/23)	Increased LY60	(17%, 4/23)
Decreased AT activity	(17%, 4/23)	Prolonged TEG *K*	(4.3%, 2/23)
Increased factor VIII activity	(13%, 2/23)	Increased PC activity	(4.3%, 1/23)
Decreased PC activity	(4.3%, 1/23)	Decreased fibrinogen	(4.5%, 1/22)

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Abbreviations: aPTT, activated partial thromboplastin time; AT, antithrombin; MA, maximum amplitude; PC, protein C; PT, prothrombin time; TEG, thromboelastography; vWF, von Willebrand's factor.

- dogs with GBM are predisposed to thrombotic complications.
- A recent large multicenter retrospective study of dogs undergoing cholecystectomy found that 14/179 (7.8%) of dogs died from documented thrombotic events.
- If dogs with GBM are hypercoagulable before surgery as our study would suggest, this hypercoagulable state may be potentiated by surgical cholecystectomy.-> perioperative use of anticoagulants or antiplatelet drugs.

Diagnosis – US

- GBM의 표준 검사방법
- 초음파상 패턴에 따라 6가지 type으로 구분

- Gravitational dependency / independency
- CBD diameter, patency
- GB wall thickness, integrity
- Abdominal fluid, hypoechoic change of pericholecystic fat-> GB rupture, or peritonitis susp.
- US for detecting GB rupture: sensitivity 86%, specificity 100%

- 초음파상 소견이 반드시 질병의 severity와 일치하지 않는다

GBM type

초음파상 특징으로 6 types 분류

(I) organized echogenic debris occupying >30% of lumen

(II) combination of organized echogenic debris with partial stellate strands adhered to the gallbladder wall

(III) stellate pattern

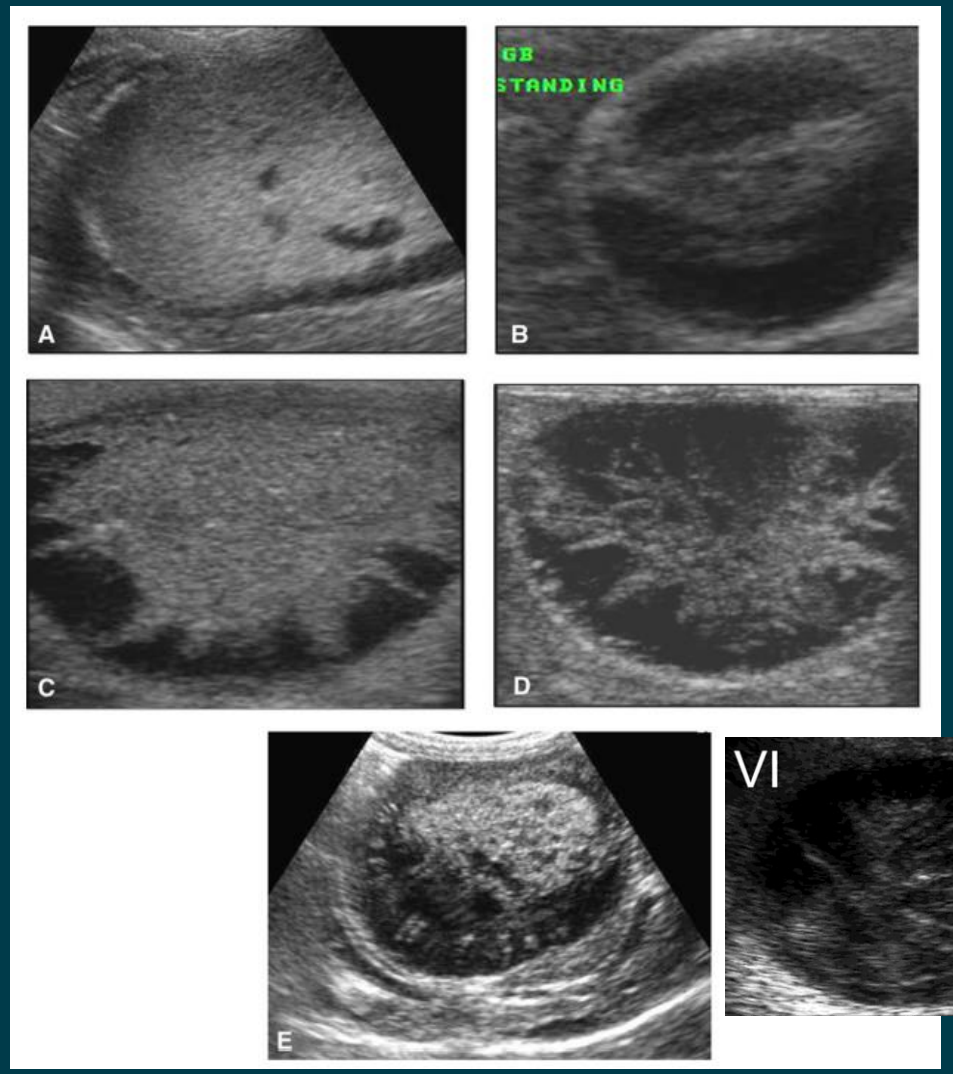
(IV) combination of stellate and kiwi pattern

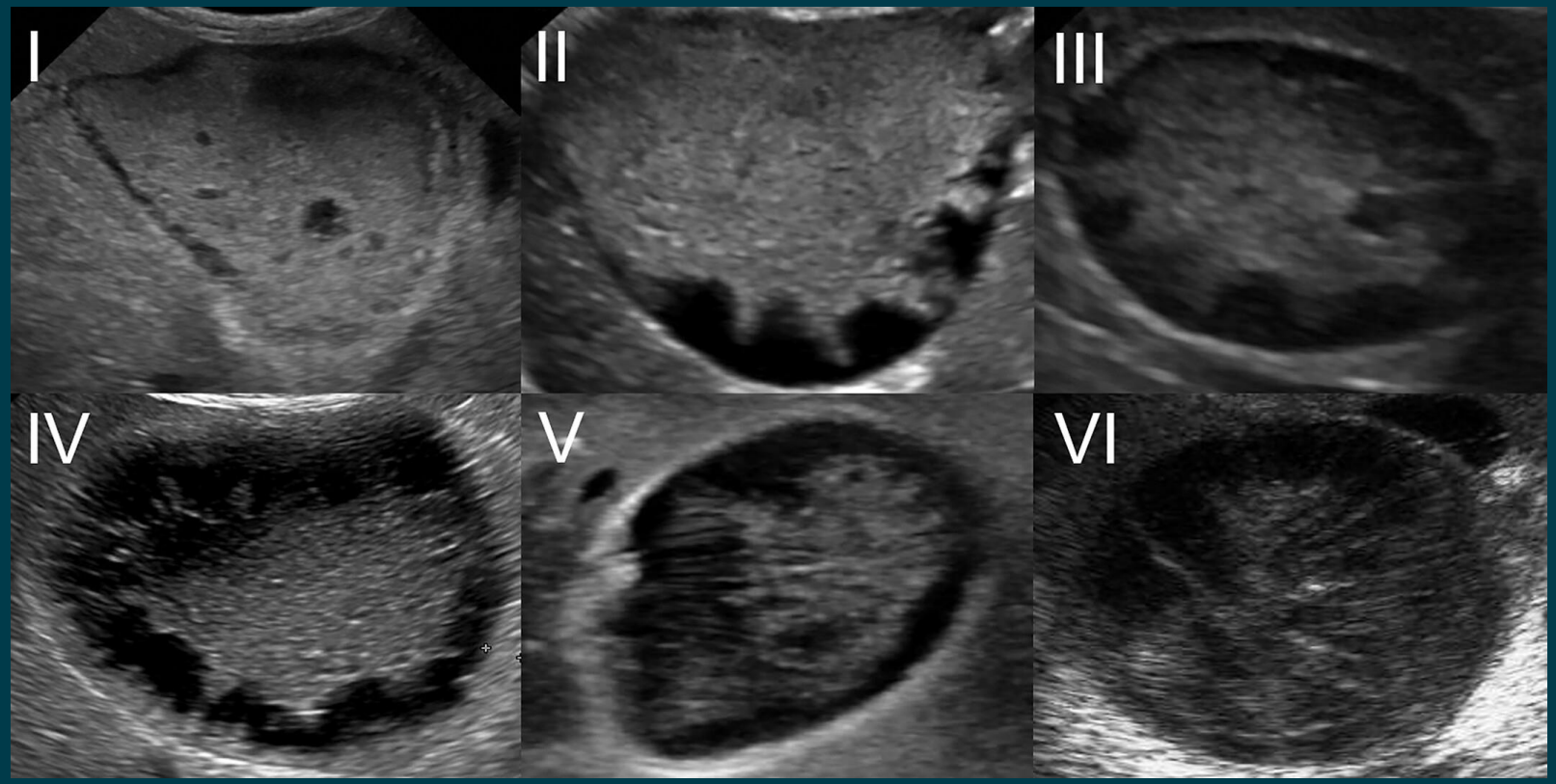
(V) kiwi pattern with echogenic debris

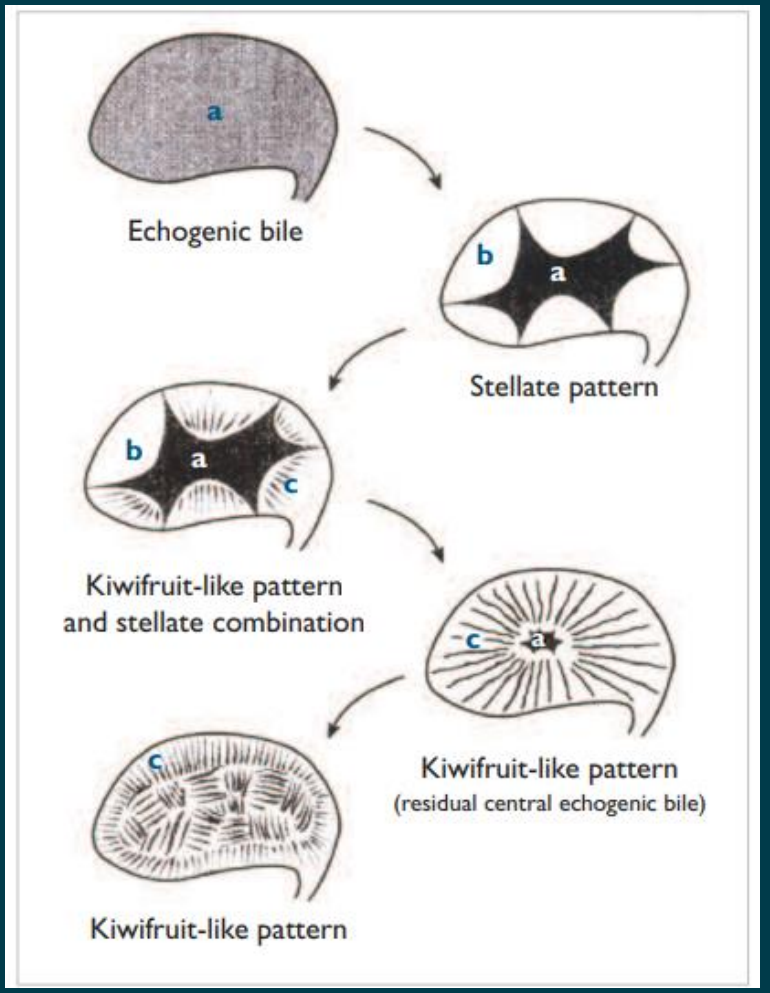
(VI) kiwi pattern

COMPARISON BETWEEN ULTRASONOGRAPHIC AND CLINICAL FINDINGS IN 43 DOGS WITH GALLBLADDER MUCOCELES

JIHYE CHOI, AHYOUNG KIM, SEOYEON KEH, JUYEON OH, HYUNWOOK KIM, JUNGHEE YOON




I
II
III
IV
V
VI


a
Echogenic bile
b
a
Stellate pattern
b
a
c
Kiwifruit-like pattern
and stellate combination
c
a
Kiwifruit-like pattern
(residual central echogenic bile)
c
Kiwifruit-like pattern

GBM type

COMPARISON BETWEEN ULTRASONOGRAPHIC AND CLINICAL FINDINGS IN 43 DOGS WITH GALLBLADDER MUCOCELES

JIHYE CHOI, AHYOUNG KIM, SEOYEON KEH, JUYEON OH, HYUNWOOK KIM, JUNGHEE YOON

- The clinical significance of gallbladder mucocele could not be predicted using ultrasonographic bile patterns because the stellate pattern including types 2 and 3 was the most common in dogs regardless of clinical signs.
- Type 2 was statistically more common in dogs that ruptured their gallbladder compared with those with an intact gallbladder, although this bile pattern was not a pathognomonic sign for gallbladder rupture.
- Based on the lack of correlation between gallbladder wall thickness and gallbladder mucocele, the thickening of gallbladder wall may not be a predictor of mucosal hyperplasia.
- Findings indicated that ultrasonographic patterns of gallbladder mucoceles alone may not be valid bases for treatment decisions in dogs. However, findings supported the recommendation of cholecystectomy for dogs showing clinical signs of hepatobiliary disease, elevated total bilirubin concentration, and the type 2 ultrasound pattern of gallbladder mucocele.

TABLE 4. Ultrasonographic Features of Gallbladder Mucocele in Symptomatic vs. Asymptomatic Dogs

	Symptomatic dogs ($n = 24$)	Asymptomatic dogs ($n = 19$)	Dogs with gallbladder rupture ($n = 11$)
Ultrasonographic pattern			
Type 1	7 (29%)	3 (16%)	2 (18%)
Type 2	8 (33%)	5 (26%)	7 (77%)
Type 3	1 (4%)	4 (21%)	0
Type 4	6 (25%)	5 (26%)	2 (18%)
Type 5	2 (8%)	2 (11%)	0
Type 6	0	0	0
Thickening of gallbladder wall†	4	1	1
Extrahepatic bile duct dilation‡	6	3	2
Discontinuation of gallbladder wall	6	0	5
Pericholecystic mesenteric swelling	13	2	10
Peritoneal effusion	12	0	9

†Thickening of gallbladder wall >3 mm.
‡Extrahepatic bile duct dilation >4 mm.

GBM type + prognostic factor

Journal of Veterinary Internal Medicine Open Access

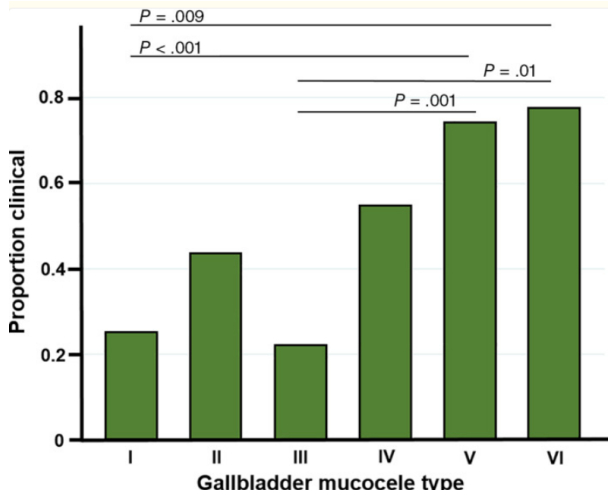
J Vet Intern Med. 2022 Feb 15;36(2):565–575. doi: 10.1111/jvim.16384

Ultrasonographic patterns, clinical findings, and prognostic variables in dogs from Asia with gallbladder mucocele

Jared A Jaffey [1,✉], Rachael Kreisler [2], Kate Shumway [3], Yan-Jane Lee [4,5], Chung-Hui Lin [4,5], Lawren L Durocher-

- to determine if ultrasonographic GBM type was associated with several relevant clinical variables.
- The most common GBM types ->type II (55/185, 30%), type IV (44, 23.7%), and type I (32, 17.3%; Figure 2). Fifty-five percent (118/216) of dogs had clinical signs. Eighty-four percent (99/118) of those dogs had ≥1 biliary tract clinical sign directly related to GBM, and those most commonly reported included vomiting 72% (71/99), anorexia 60% (59/99), and lethargy 33% (33/99).
- Cholecystectomy was performed in 39.4% (85/216) of dogs with 84% (71/85) and 16% (14/85) of them being clinical or subclinical, respectively. Eighty-nine percent (76/85) of dogs that had a cholecystectomy performed had a pre-operative GBM type designation. -> type II (30%; 23/76), type IV (27%; 21/76), type V (20%; 15/76), type III (9%; 7/76), type I (7%; 5/76), and type VI (7%; 5/76).

- Dogs with GBM type V as compared to I and III, and dogs with type VI compared to I and III were more likely to exhibit signs of biliary tract disease (Figure 3).
- There was no significant difference in age, weight, or fold change in total bilirubin between GBM types.



Treatment – medical management

- Ursodeoxycholic acid (UDCA): choleretic and hepatoprotectant at 10- 15 mg/kg/day PO

  담관 완전폐색 시 choleretic drugs 사용은 폐색 유발 위험성 (~20mg/kg/day, high dose 30mg/kg/day?)

- S-adenosylmethionine (SAMe): precursor of cysteine that is essential in the production of the antioxidant glutathione, and therefore is hepatoprotectant at 18- 40 mg/kg PO once daily
- Antibiotics: 4-8wks 유지 <- C&S or empirical

- empirical antibiotics: 2nd cephaolsporine, ampicillin (22mg/kg q8h), AMC (12.5mg/kg q12h)

- low-fat diet: animals with dyslipidaemias
- Concurrent endocrinopathies must be treated appropriately.
- Monitoring: 6-8주, 또는 2-4개월 간격

Treatment – surgery

- Preoperative management
  - hemodynamic resuscitation: IV fluid
  - empirical antibiotics
  - coagulation deficiency -> vit K supplementation (0.1-0.2mg/kg q12h)
    (0.5-1.5 mg/kg q12h for 3 doses, 24-48 hours prior to surgery)
- **Cholecystectomy**: therapeutic gold standard
- With or without CBD flushing -> “patency of CBD”
- Liver biopsy
- Bile sampling -> C&S

: 9-66% 환자에서 세균감염 동반 (E.coli, Enterobacter, Enterococcus, Staphylococcus, Streptococcus…)

- Laparoscopic cholecystectomy

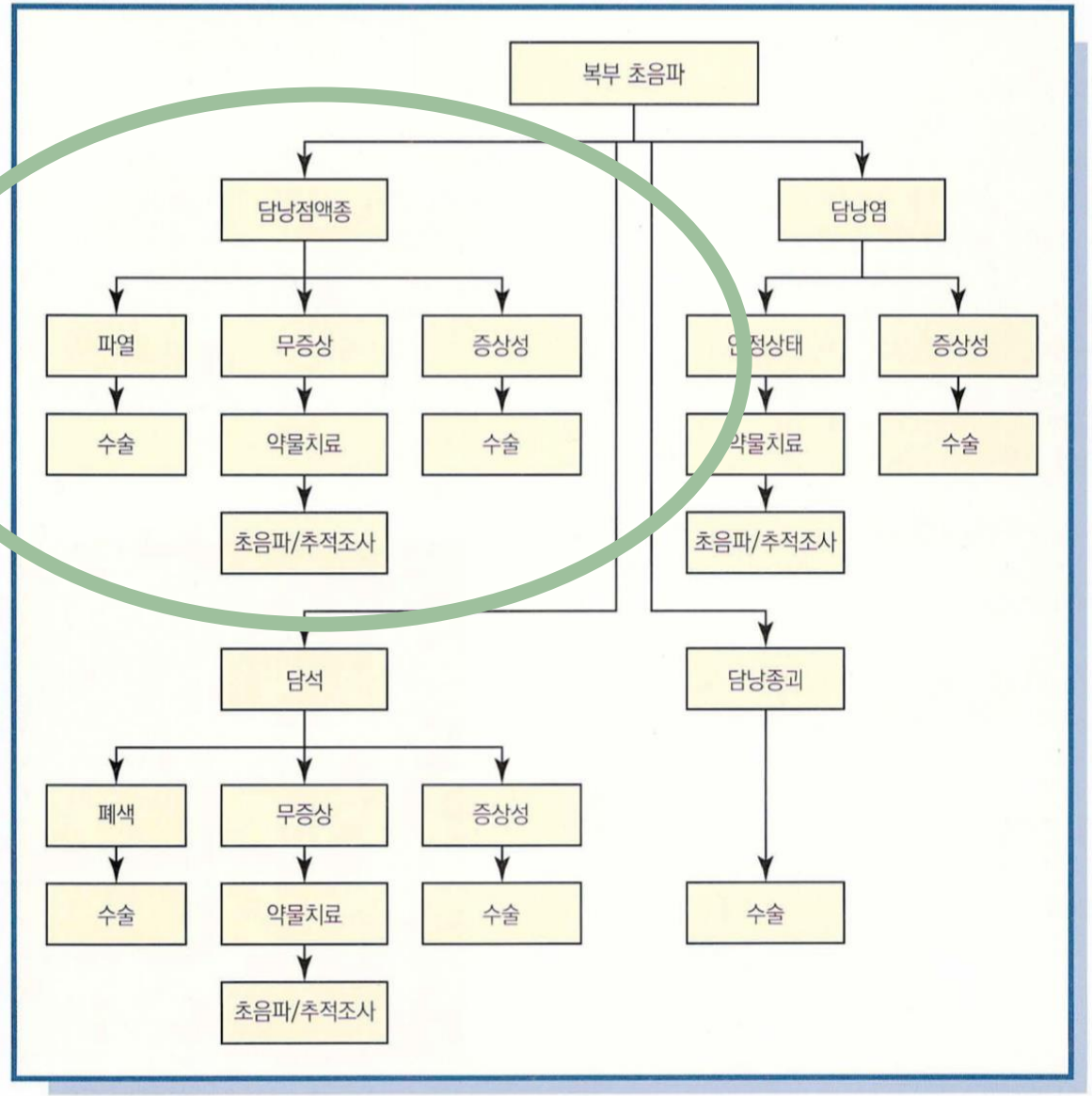


그림 288-2 담낭과 간외 담도계의 질병 알고리즘.

Treatment – decision making ?

Journal of Veterinary Internal Medicine / Volume 33, Issue 5 / p. 2057-2066
STANDARD ARTICLE | Open Access

Long-term survival of dogs treated for gallbladder mucocele by cholecystectomy, medical management, or both

Max Parkanzky, Janet Grimes, Chad Schmiedt, Scott Secrest, Andrew Bugbee

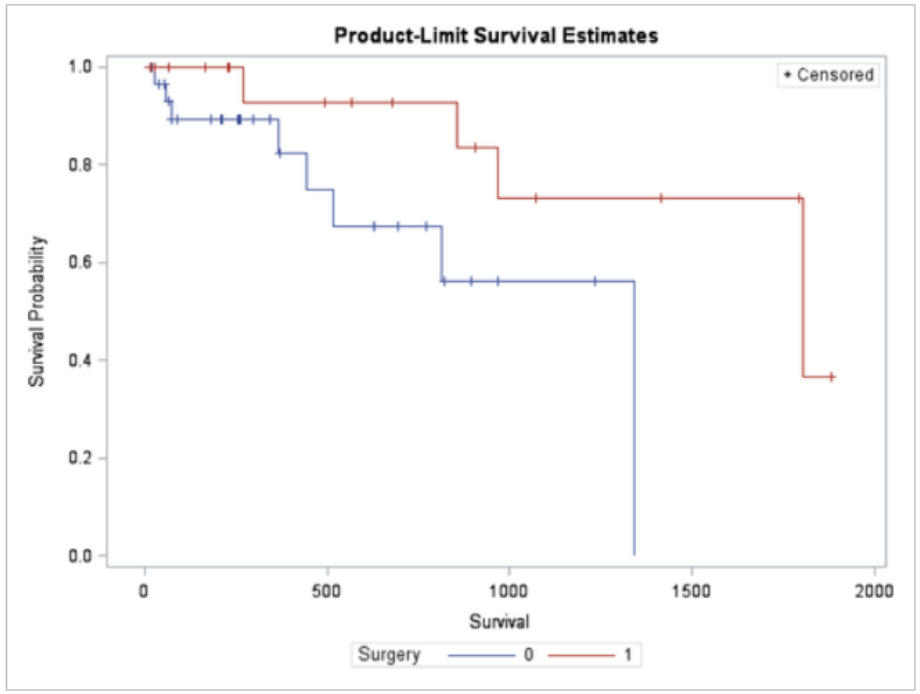


Figure 2

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Survival probability based on the 2-group model starting 14 days postdiagnosis with a gallbladder mucocele (GBM). Dogs initially treated with cholecystectomy (surgery = 1) demonstrate a better long-term survival compared to dogs initially treated medically (surgery = 0); *P* = .04, hazard ratio, 4.13 (1.02-16.82)

Table 4. Ultrasound classification of biliary mucoceles (GBM type)

GBM type	Description	Sx # (%)	Med # (%)	Med-Sx # (%)
1	Immobile echogenic bile	4 (11)	4 (13)	1 (12.5)
2	Incomplete stellate pattern	12 (32)	16 (52)	3 (38)
3	Typical stellate pattern	10 (26)	9 (29)	2 (25)
4	Kiwi-like pattern and stellate combination	4 (11)	2 (6)	1 (12.5)
5	Kiwi-like pattern with residual central echogenic bile	6 (16)	0 (0)	1 (12.5)
6	Kiwi-like pattern	0 (0)	0 (0)	0 (0)
Rupture	Concern for GB rupture in the ultrasound report	18 (47)	3 (10)	2 (25)

Abbreviations: # (%), number of dogs (% within treatment group) with associated GBM type; GB, gallbladder; GBM type, gallbladder mucocele ultrasonographic classification; Med, medically managed group; Med-Sx, medical then surgical group; Sx, surgical treatment group.

Elective vs Non-elective

- Elective: no or mild clinical signs, with no indication of biliary obstruction
- Nonelective: dogs with icterus and questionable patency of the biliary system
- ALT, TBIL, ALB were the only serum biochemical analytes significantly associated with outcome
- Dogs in the nonelective cholecystectomy group had significantly greater serum ALT, ALP, GGT, TBIL; and WBC count and lower serum albumin concentration than dogs in the elective cholecystectomy group
- Neither intraoperative hypotension (P = 0.59) nor duration of hospitalization (P = 0.051) was significantly associated with outcome.
- Dogs in the nonelective group had a significantly (P = 0.02) higher mortality rate (5/25 [20%]) than dogs in the elective group (1/45 [2%]).

AVMA Publications

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Outcome of elective cholecystectomy for the treatment of gallbladder disease in dogs

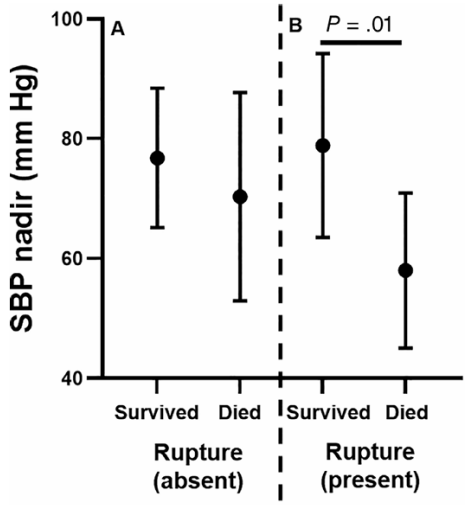
Gabina Youn BVetMed, Michelle J. Waschak DVM, MS, Kevin A. R. Kunkel DVM, and P...

		Survivors		Nonsurvivors		
Analyte	Reference interval	No. of dogs	Value	No. of dogs	Value	*P* value
ALT (U/L)	12–118	64	714.4 ± 931.2	6	1,645.0 ± 1,214.8	0.03
ALP (U/L)	5–131	63	2,360.6 ± 2,618.7	6	3,859.5 ± 2,943.4	0.19
GGT (U/L)	1–12	56	47.8 ± 58.0	6	31.8 ± 20.6	0.19
Total bilirubin (mg/dL)	0.1–0.3	59	2.42 ± 3.97	6	7.57 ± 4.80	0.004
Albumin (g/dL)	2.7–4.4	60	3.34 ± 0.60	6	2.73 ± 0.45	0.02
Calcium (mg/dL)	8.9–11.4	59	10.1 ± 0.97	6	9.73 ± 0.82	0.38
Amylase (U/L)	290–1,125	60	709.2 ± 363.9	5	798.8 ± 392.6	0.61
Lipase (U/L)	77–665	55	525.0 ± 803.0	5	664.6 ± 766.1	0.71
Cholesterol (mg/dL)	92–324	55	415.9 ± 241.5	6	371.8 ± 101.1	0.42
Triglycerides (mg/dL)	29–291	52	282.7 ± 429.2	3	2,428.7 ± 1,091.5	0.08
BUN (mg/dL)	6–31	63	18.9 ± 18.6	5	45.5 ± 48.0	0.23
Creatinine (mg/dL)	0.5–1.6	60	0.88 ± 0.59	6	2.03 ± 1.73	0.17
WBCs (× 10^3 cells/µL)	4.0–15.5	52	12.3 ± 6.1	5	28.2 ± 19.1	0.14
Hct (%)	36–60	51	45.1 ± 7.4	4	46.6 ± 2.6	0.69

	Elective		Nonelective		
Analyte	No. of dogs	Value	No. of dogs	Value	*P* value
ALT (U/L)	45	581.4 ± 852.2	25	1,177.2 ± 1,101.1	0.01
ALP (U/L)	45	1,597.4 ± 980.9	24	4,211.7 ± 2,950.9	< 0.001
GGT (U/L)	40	33.3 ± 48.8	22	68.0 ± 60.1	0.02
Total bilirubin (mg/dL)	40	0.77 ± 1.55	25	6.38 ± 5.01	< 0.001
Albumin (g/dL)	41	3.49 ± 0.52	25	2.95 ± 0.60	< 0.001
Amylase (U/L)	41	692.5 ± 288.8	24	755.7 ± 467.3	0.55
Lipase (U/L)	39	612.6 ± 932.6	21	395.6 ± 422.3	0.22
Cholesterol (mg/dL)	38	413.9 ± 257.7	23	407.5 ± 180.9	0.92
Triglycerides (mg/dL)	38	356.3 ± 547.4	17	505.5 ± 925.2	0.54
BUN (mg/dL)	43	22.81 ± 21.29	25	18.60 ± 26.68	0.48
Creatinine (mg/dL)	43	0.99 ± 0.66	23	0.98 ± 1.05	0.95
WBCs (× 10^3 cells/µL)	36	11.16 ± 6.06	21	18.05 ± 11.38	0.02
Hct (%)	35	45.78 ± 6.90	20	44.12 ± 7.76	0.42

Prognosis

- Long-term prognosis: variable
- Septic/ bile peritonitis: high mortality
- Perioperative mortality 22-40% -> 이 기간에 생존한 환자의 장기생존률은 매우 양호



- Complications of surgery
  - bile peritonitis, sepsis, DIC and surgical-site dehiscence

- Poor prognosis
  - concurrent pancreatitis
  - Elevation of the serum lactate concentration post-operatively
  - post-operative hypotension

- END -

감사합니다!