5-13-2022

Comparison of abdominal computed tomography to ultrasound in the diagnosis of canine biliary disease manifesting as acute abdominal signs

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A Thesis
Submitted to the Faculty of
Mississippi State University
in Partial Fulfillment of the Requirements
for the Degree of Master of Science
in Veterinary Medical Science
in the Department of Clinical Science

Mississippi State, Mississippi

May 2022

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Date of Degree: May 13, 2022

Institution: Mississippi State University

Major Field: Veterinary Medical Science

Major Professor: Alison M. Lee

Title of Study: Comparison of abdominal computed tomography to ultrasound in the diagnosis of canine biliary disease manifesting as acute abdominal signs

Pages in Study: 98

Candidate for Degree of Master of Science

Biliary diseases are uncommon, potentially fatal causes of acute abdomen in dogs. Little information is present comparing the performance of computed tomography (CT) to ultrasound in identifying canine biliary pathology. Thirty-five client-owned dogs presenting for acute abdomen signs received an abdominal ultrasound and contrast-enhanced abdominal CT. Two authors reviewed the randomized, anonymized CT and ultrasound studies. Twenty-eight dogs had biliary pathology and seven dogs serving as controls had no evidence of biliary disease. The final diagnoses of patients with biliary pathology included cholelithiasis, gallbladder mucoceles, cholangiohepatitis/cholangitis, extrahepatic biliary obstruction, gallbladder wall edema, gallbladder wall mass, and cystic mucosal hyperplasia. Computed tomography was more accurate in identifying cholelithiasis than ultrasound. No statistical difference in the odds to identify other biliary pathology was identified between ultrasound and CT. Findings from this study suggest CT may be used in place of ultrasound in canine patients presenting for acute abdominal signs of biliary origin.

DEDICATION

I would like to dedicate this thesis to my family and friends who have supported me throughout this process. My partner, Eddie, has been my greatest supporter who has been there for me through my entire veterinary education, internship, and residency. I am so thankful to have had him on this journey as he has kept our family thriving. This is as much yours as it is mine.

To my beautiful son, Matthew, your smiles, laughter, and love have kept me grounded these last few years. You are a constant motivation to keep going even when the work was overwhelming. It is an honor to be your mom.

To my parents and sister, thank you for always supporting my dreams and academic career. This has been a long journey and without you all, this would not have been possible.

To my brother, you've always inspired me to be my best, stay positive, and just make it happen. I miss you every day and hope you're proud.

To my elementary school best friend, Dr. Deirdre Mikolajcik, it has been amazing watching you thrive from afar. We started out in 5th grade being the new kids both set out to accomplish great things and make a difference. Look how far we've come.

ACKNOWLEDGEMENTS

A special thank you to my committee members and residency mentors (Drs. Alison Lee, Marc Seitz, and Alyssa Sullivant) for all of your guidance and support throughout this research project and residency. This journey would not have been possible without you.

I would also like to thank my resident mates, fellow house officers, the diagnostic imaging department, and the small animal internal medicine and emergency services. The support you all provided in recruiting case and acquiring studies is greatly appreciated.

Dr. Robert Wills and Kimberly Woodruff, thank you both for the work you performed while running statistics. Without your expertise and guidance, I would have been truly overwhelmed in the data analysis.

To my mentors at Kansas State University (Drs. David Biller, Laura Armbrust, Katherine Tucker-Mohl, Mackenzie Hallman, and Paxton Harness) and Diagnostic Imaging (Drs. Christina Copple and Leila Grant), thank you for the wonderful guidance, leadership, and mentorship you provided during my veterinary training and for the career guidance. You all are a large part of the reason that I was able to obtain and complete a diagnostic imaging residency. Without you none of this would have been possible.

I would like to also thank the ACVR for funding the grant for this project.

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CHAPTER I

INTRODUCTION

Canine Hepatobiliary Anatomy

The biliary system consists of the gallbladder, the cystic duct, the bile duct, hepatic ducts, inter- and intralobular ducts, bile ductules, and hepatic canaliculi.[1] Hepatic lobules are small polygonal functional units of liver parenchyma which are approximately 1 mm in diameter.[2] The hepatic lobules have a single curved sheets of cells in a single layer which enclose numerous liver sinusoids, which are blood filled cavities that allow passive transport of intersinusoidal blood.[2] A single central vein is within the center of the hepatic lobules which is the origination of the hepatic efferent blood flow.[2] The central veins converge to form the intralobular veins which then continue to fuse to form the hepatic veins.[2] The hepatic veins then terminate within the caudal vena cava.[2] The portal vein delivers functional blood from the stomach, intestines, pancreas, and spleen to the liver.[2] Approximately 80% of the blood flow to the liver comes from the portal vein with the other 20% being delivered from the hepatic arteries which contain oxygenated blood from the aorta and celiac artery.[2] The hepatic artery supplies much of the liver framework, including the hepatic capsules, blood vessel walls, intrahepatic biliary duct system, and nerves.[2]

The gallbladder is a saccular organ located within a fossa between the right medial and quadrate lobes of the liver and connects to the bile duct via the cystic duct. The cranial aspect of the gallbladder is a blind ended sac called the fundus or apex.[2] The larger middle portion of the

gallbladder is the body.[2] The caudodorsal aspect of the gallbladder tapers as it courses towards the cystic duct and is called the gallbladder neck.[2] The gallbladder stores and concentrates the bile up to 10 times the initial concentration where it becomes dark brown to greenish brown from the original golden yellow to orange color which is within the hepatic biliary system.[1,2] The gallbladder stores bile where it is concentrated, acidified, and modified between feedings.[1] However, the gallbladder does not have an indispensable function as cholecystectomy is usually well tolerated.[1]

The gallbladder wall structure and layering resemble the intestines as it is embryologically derived from the gastrointestinal tract (Figure 1.1).[1] Mucosa with microvilli and surface epithelium outline the luminal surface which increases the surface area allowing for resorptive and exchange processes.[1] Also like the intestine, the gallbladder wall layers in order from inner to outer: mucosal lamina propria (with a lymphoplasmacytic population, lymphatics, and blood vessels), muscularis layer which aids in the expression of bile, layer of connective tissue, and outermost serosa.[1] Mucus glands within the gallbladder mucosa produce mucin that protects the luminal surface epithelium from the cytolytic effects of bile acids.[1] Mucin production is stimulated by inflammatory cytokines, endotoxins, and prostaglandins.[1] The lymphatic vessels within the lamina propria may be grossly visible during portal hypertension, chronic passive congestion, or hepatobiliary inflammation.[1] Fluid leaked from the gallbladder lymphatic vessels with these disease processes can cause gallbladder wall thickening which can be observed ultrasonograpically.[1]

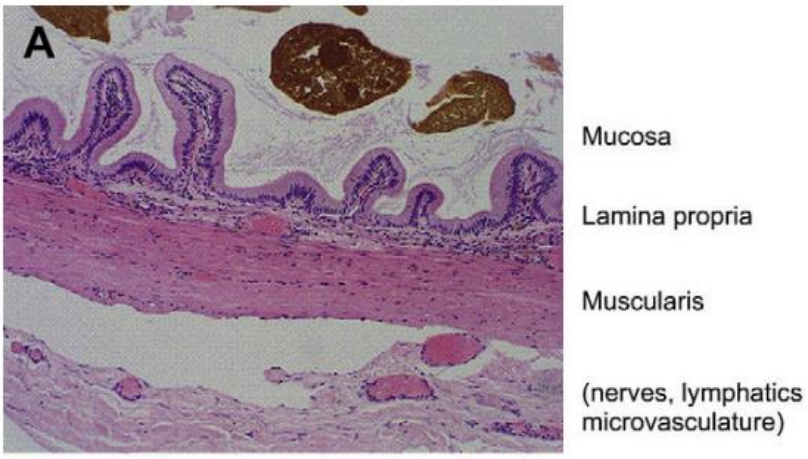

Figure 1.1 Photomicrograph of a normal canine gallbladder. Adapted from Center SA. Diseases of the Gallbladder and Biliary Tree, *Veterinary Clinics of North America - Small Animal Practice*, 2009;39(3):543-598.

The cystic duct extends from the neck of the gallbladder to the junction of the first tributary of the hepatic ducts (Figure 1.2).[2] The bile duct then continues and receives other hepatic ducts.[1,2] The bile duct in a medium sized dog is 5 cm long and 2.5 mm in diameter.[1] The free portion of the bile duct courses through the hepatoduodenal ligament as it extends from the liver to the duodenum.[2] The intramural portion of the bile duct tunnels through the descending duodenal wall to terminate within the duodenum.[2] The intramural portion of the canine bile duct is 1.5–2 cm in length which terminates on a small hillock where the bile duct opens centrally at a small rosette (Figure 1.3).[2] In the dog, the bile duct then continues to terminate within the major duodenal papilla via the bile duct sphincter (sphincter of Oddi) along with the pancreatic duct, the smaller of the two pancreatic ducts.[1,2] Because of the close proximity of the pancreatic duct to the bile duct, pancreatitis is the most common cause of extrahepatic biliary outflow obstruction.[1] Approximately 3 cm distal to the major duodenal papilla, the larger accessory pancreatic duct enters the descending duodenum at the minor

duodenal papilla.[2] The sphincter of Oddi acts as a one-way valve allowing for unidirectional flow of bile from the biliary system into the duodenum and provides protection against duodenal contents travelling retrograde through the biliary tree.[1] There is a double layer of smooth muscle surrounding the intramural portion of the bile duct which allows the activity of the duodenum to control a large portion of bile release in addition to gallbladder wall contraction.[2] There is variability of these muscles in dogs as some have no muscles and some have 3 layers of muscles.[2]

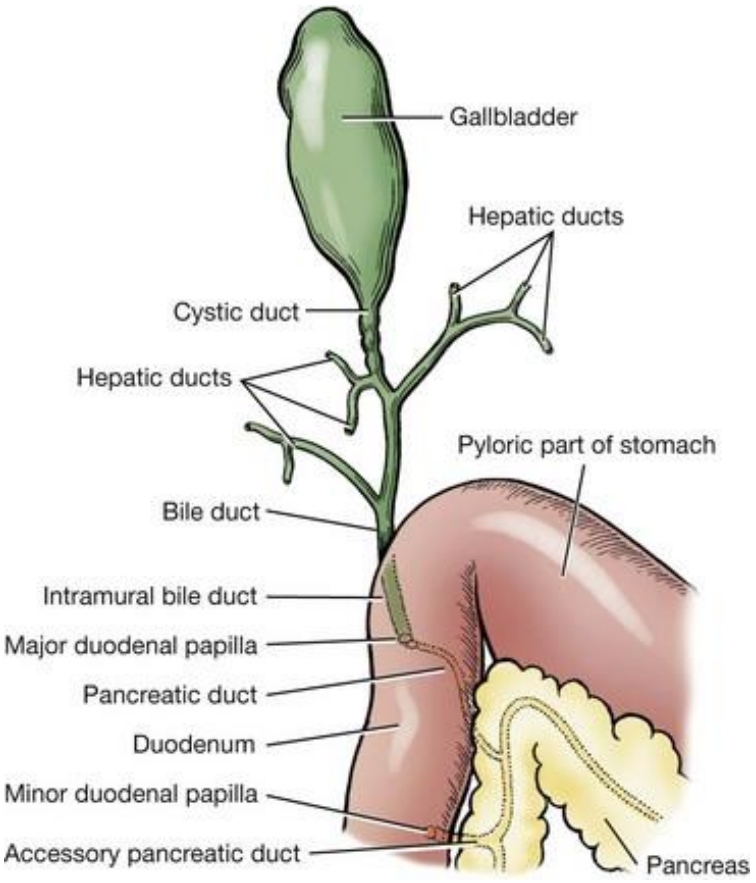

Figure 1.2 Anatomical relationship of the gallbladder, cystic duct, hepatic ducts, bile duct and the major duodenal papilla within the descending duodenum. The pancreatic duct also empties into the descending duodenum at the major duodenum. Adapted from Miller's Anatomy of the Dog, 4th ed. Evans H de LA, Elsevier, 2013.

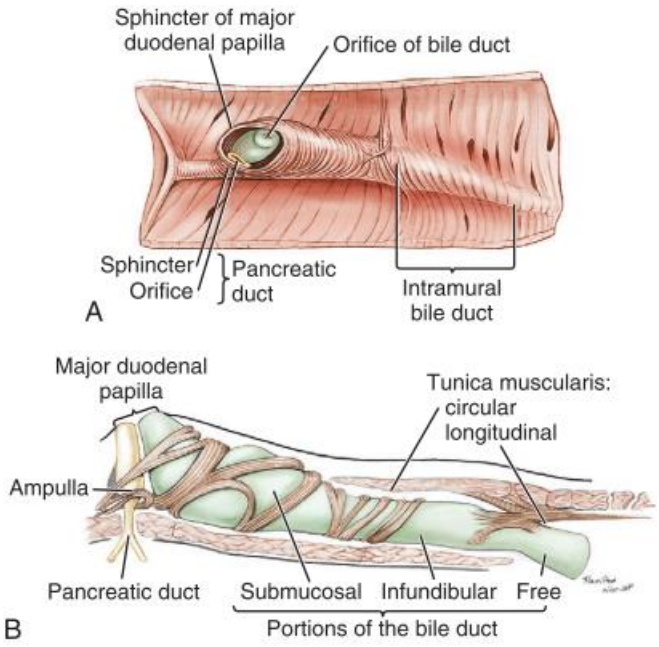

Figure 1.3 A. The major duodenal papilla visualized within the descending duodenum in the dog. The bile duct and pancreatic duct empty separately into the major duodenal papilla in the dog. B. The intramural biliary duct within the duodenal wall with encircling musculature. Adapted from Miller's Anatomy of the Dog, 4th ed. Evans H de LA, Elsevier, 2013.

The vagal nerve innervates the gallbladder and bile duct.[2] The arterial blood supply to the gallbladder and bile duct is provided by the cystic artery which is the left branch of the hepatic artery.[1] Having a single arterial source for perfusion makes the gallbladder and bile duct susceptible to ischemic necrosis following blunt abdominal trauma leading to vascular shearing or from biliary disease.[1] Compromised perfusion and wall necrosis can lead to biliary rupture and bile peritonitis.[1]

Bile is produced by sheets of hepatocytes surrounded by the blood sinuses and is excreted into the bile canaliculi between the cells (Figure 1.4).[2] Hepatocytes have a basolateral membrane which contains microvilli that lines the space of Disse and are bathed in sinusoidal ultrafiltrate.[1] The opposite hepatocyte membrane is the apical-polar (canalicular) membrane which

communicates with the bile canaliculi and contains transporters used to form bile.[1] The bile canaliculi are the site of initial bile formation and are 1 mm in diameter.[1] The hepatic bile is golden yellow to orange in color.[1] The canalicular membranes contain tight junctions that separate bile from sinusoidal blood and ultrafiltrate.[1] Hepatic bile formation is categorized as either bile acid-dependent or independent.[1] The independent mechanism utilizes active transportation of glutathione into the bile canaliculus with modification of the bile in the bile ductal system.[1] Canalicular bile formation is a continuous osmotic process mainly driven by active transporter pumps within the hepatocytes excreting organic solutes including glutathione and bile acids.[1] This active process is then followed by passive excretion of water, electrolytes, and nonelectrolytes (including glucose and amino acids) into the bile.[1]

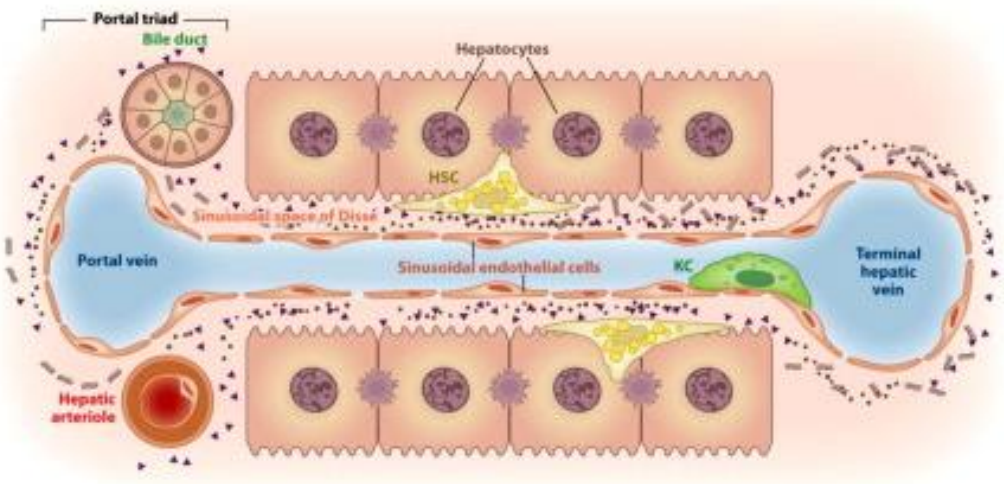

Figure 1.4 Anatomy of the normal hepatic sinusoids, portal triad, and central vein. Hepatocyte basolateral membrane contains microvilli that lines the space of Disse and are bathed in sinusoidal ultrafiltrate. The opposite hepatocyte membrane (apical-polar membrane) communicates with the bile canaliculi and contains transporters used to form bile. The bile then travels to the bile duct and into the biliary system. Adapted from Stellate Cells in Health and Disease, Gandhi CR and Pinzani M, Elsevier Inc, 2015.

Lipid vesicles are also detached from the apical membrane of the bile canaliculus which form micelles.[1] Mixed-micelles are bile salt anions and cations (either sodium or calcium) aggregated with phospholipids, lecithin (also called phosphatidylcholine), and free cholesterol.[1] The bile is maintained isotonic to plasma by the formation of mixed-micelles which also decreases the bile's toxicity to the biliary epithelium.[1]

The salt-independent canalicular bile formation utilizes glutathione, the only endogenous anion known to promote bile under physiologic conditions with the rate of secretion being related to bile flow.[1] Glutathione is strongly osmotic due to its hydrophylic composition, active membrane canalicular exportation, and membrane-affiliated gamma glutamyl transferase hydrolysis.[1] The hyperosmolarity of glutathione causes water and electrolytes to dilute bile through passive osmotic pathways.[1]

The function of bile is to deliver bile acids into the gastrointestinal tract to aid in lipid digestion.[1] Bile acids are amphipathic organic anions synthesized in the liver.[1] Bile acids are primarily conjugated within mixed micelles and circulate efficiently within the enterohepatic circulation.[1] Bilirubin glucuronides are hydrolyzed to unconjugated bilirubin with some being resorbed back into systemic circulation.[1] Normal bile contains less than 2% of bilirubin that is unconjugated.[1]

Bile also functions to transport and ultimately eliminate lipophilic metabolic products and xenobiotics.[1] Xenobiotics are chemical substances that are not created in the patient including plant constituents, medications, food additives, and pollutants.[3] Cholesterol is also a common constituent of bile. High concentrations of cholesterol within bile can increase the risk of developing cholesterol choleliths, which are common in humans.[1] Dogs do not have the same cholesterol bile saturation as humans and therefore do not develop primary cholesterol

choleliths.[1] This is important to consider when using ursodeoxycholate (a medication that helps reduce the cholesterol saturation of bile and causes gradual dissolution of cholesterol-rich choleliths) as a choleretic in dogs when medical management of choleliths is preferred.[1] Since canine choleliths do not have a high cholesterol composition, cholelith dissolution, which is well reported in humans, is unlikely to occur.[1]

The hepatic canalicular bile travels continuously through the bile canaliculi which then connect and continue as the bile ductules (Figure 1.5).[2] The bile ductules then further combine to form the plexiform of intralobular bile ducts which are within the interstitium between the lobules.[2] The intralobular bile ducts converge to form the interlobular bile ducts. The interlobular bile ducts are part of the portal triad which also contains a branch of the hepatic artery and a branch of the portal vein.[2] The interlobular bile ducts then converge to form the intrahepatic bile ducts (Figure 1.6).[2] These ducts course within the hepatic parenchyma centrally towards the bile duct.[2] The intrahepatic interlobular bile ducts become the extrahepatic interlobular bile ducts once they exit the hepatic parenchyma.[2] The extrahepatic bile ducts directly communicate with and terminate within the bile duct. Bile can then enter the gallbladder to be stored or exit the bile duct via the sphincter of Oddi. Bile continuously enters the gallbladder in a low-flow low-pressure system.[1] Hepatic bile secretion and the tonic contraction of the sphincter of Oddi create pressure within the biliary system promoting accumulation of bile within the gallbladder.[1]

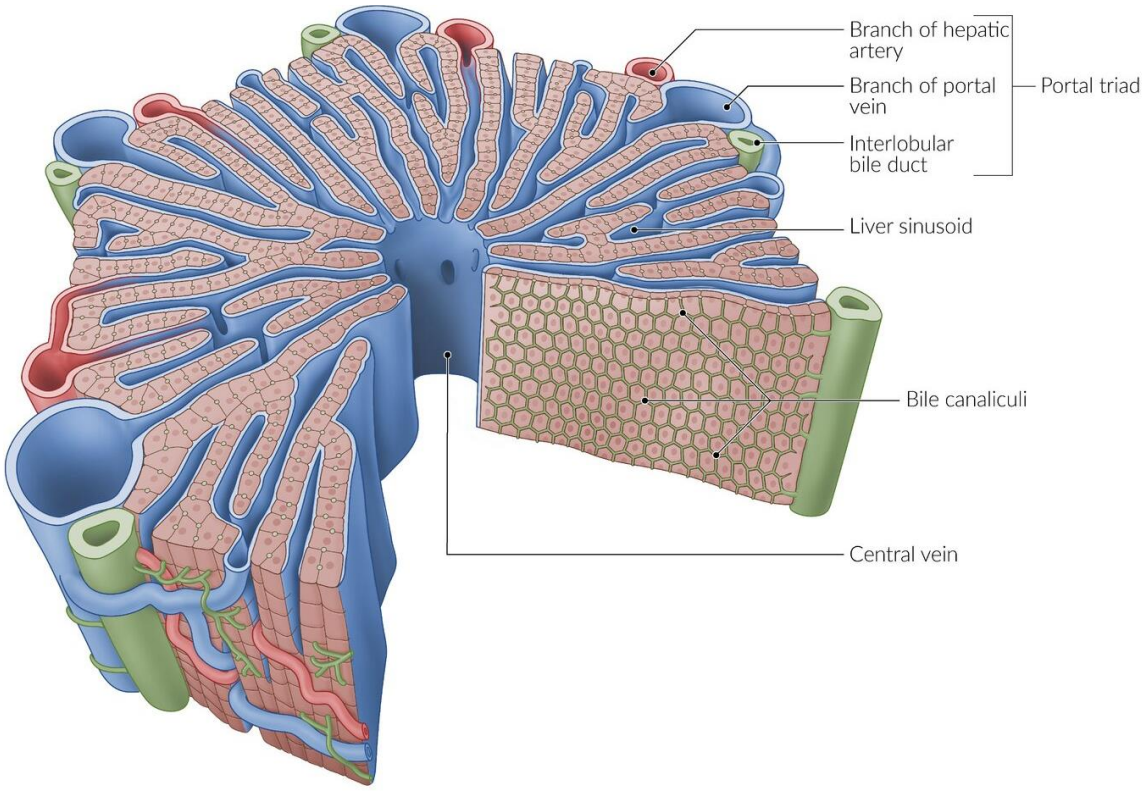

Figure 1.5 Anatomy of the hepatic lobule demonstrating the relationship between hepatocytes, bile canaliculi, portal triad structures (branch of the portal vein, interlobular bile duct, branch of the hepatic artery), and the central vein. Adapted from Amboss.com.

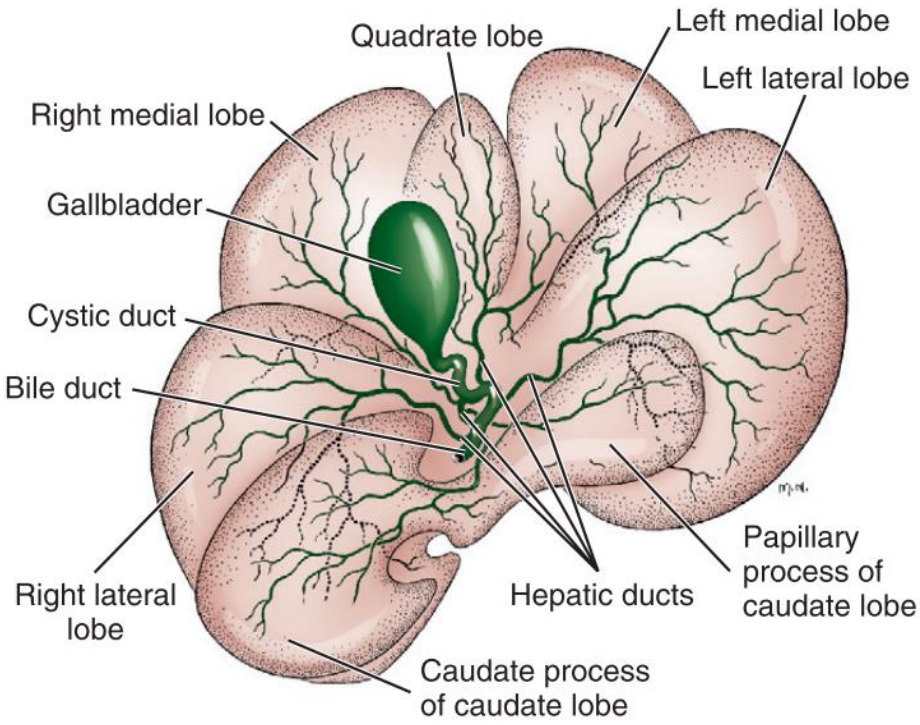

Figure 1.6 Hepatic and biliary anatomy including the gallbladder, hepatic bile ducts, cystic duct, and bile duct. Adapted from Miller's Anatomy of the Dog, 4th ed. Evans H de LA, Elsevier, 2013.

Primary hepatic bile is modified during transportation through the biliary system by secretion and reabsorption of fluid and inorganic electrolytes.[1] Cholangiocytes, epithelial cells that line the biliary tree, uptake bile salts via a sodium dependent transporter as the initial step in the cholehepatic shunt pathway.[1] This pathway allows intrahepatic recycling of bile salts through a periductular capillary plexus which is important for signaling ductular mucin and bicarbonate secretion into bile.[1] The cholehepatic shunt pathway also contributes to the high serum-bile acid concentrations in patients with cholestatic liver disease.[1]

Bile within the gallbladder is acidified by the absorption of sodium cations (Na^+) in exchange for hydrogen cations (H^+) with concurrent passive transfer of potassium cations (K^+)

and calcium (Ca^{2+}) with plasma.[1] Gallbladder biliary sodium bicarbonate (HCO^{3-}) is neutralized by hydrogen cations (H^{+}) with additional excretion via circulatory carbon dioxide (CO^{2}).[1]

Gallbladder motility is controlled by neuroendocrine signals, which coordinate this motility with ingestion of food. [1] Glucagon stimulates canalicular bile formation and ductule bicarbonate secretion.[1] Vagal stimulation, cholecystokinin, and gastrin mildly stimulate hepatic bile production.[1] The presence of free fatty acids and amino acids and gastric distention stimulate parasympathetic vagal stimulation, which in turn releases cholecystokinin and motilin from the duodenum. This triggers gallbladder contraction and relaxation of the sphincter of Oddi. Rhythmic contraction of the sphincter of Oddi regulates periodic duodenal bile release.[1] The relaxation of the sphincter of Oddi is also enhanced by secretin.[1] Secretin also strongly stimulates ductule bile flow which causes an increase in bicarbonate secretion by the gallbladder mucosa producing a mucinous, bicarbonate-rich fluid that mixes with stored bile.[1] Somatostatin strongly inhibits bile secretion within the canalicular and ductular sites.[1] The presence of cholecystokinin also stimulates intestinal peristalsis, which helps to propel the bile salts to the ileum.[1] Within the ileum, the bile salts are recycled back into the enterohepatic circulation via active transportation.[1] With the previously discussed active transporters within the hepatocytes, the enterohepatic circulation is a highly efficient system with approximately 5% of fecal loss per day.[1] Negative feedback from the bile salts returning to the liver then inhibits further cholecystokinin release. Bile salt-dependent bile flow has a potent negative feedback effect at the level of the canaliculus (which is a direct linear relationship), with non-micelle-forming bile salts having the greatest effect.[1] After the completion of meal-initiated gallbladder contraction, the gallbladder relaxes and the sphincter of Oddi tone returns.[1] The flow of bile then returns to the hepatic bile diverting to the relaxed gallbladder for continued storage.[1]

Xenobiotics including erythromycin, glucocorticoids, rifampicin, phenobarbital, oltipraz, and cisplatin can pharmacologically induce the release of motilin as well.[1] Some of the mechanisms of action of these drugs involve modulating bile formation at the canalicular level by inducing transport pump activity via the multidrug resistance-associated protein-2 (MRP-2).[1] The opposite occurs during cholestasis where the MRP-2 activity is down-regulated.[1] Furosemide also has a choleretic effect (increase the volume of bile secretion) by inhibiting active sodium transportation and therefore stimulating bile flow in canine patients but can impose a detrimental effect in dehydrated patients.[4] A canine study also showered ursodeoxycholic acid (UDCA) and dehydrocholic acid induce choleresis as well.[5] Oral UDCA at 50 mg/kg increased bile flow by 70% and increased the concentration of phospholipid, cholesterol, bile acids, and bilirubin in bile within 1 hour of administration.[5] Oral dehydrocholic acid at 50 mg/kg also caused an increase in bile flow (270%) by inducing secretion of electrolytes and water from the bile canaliculi.[5]

Canine Abdominal Imaging

A diagnostic approach in working up canine patients presenting with clinical signs related to biliary pathology includes a complete physical exam, bloodwork including a complete blood count and biochemistry, and diagnostic imaging. Common bloodwork abnormalities include elevated liver enzymes (including alkaline phosphatase [ALP], alanine transaminase [ALT], and gamma-glutamyl transferase [GGT]) and hyperbilirubinemia. If sepsis is present, a neutrophilia with a left shift or a neutropenia may also occur. Diagnostic imaging remains an important tool for patients presenting with acute abdominal pain, as it is often required not only to make a rapid, accurate diagnosis, but also to decide if the patient requires surgical or medical treatment. Traditionally, abdominal ultrasound (US) has been the gold standard in veterinary medicine for

animals presenting for acute abdomen.[6] This is in part due to the ability to eliminate visceral superimposition (a problem in abdominal radiography), to delineate parenchymal detail, and to better discern the presence of free abdominal fluid.[7] In addition, the ultrasonographic features of several conditions resulting in acute abdomen have been well described in dogs, including pancreatitis and gastrointestinal disorders. In fact, US has been shown to improve detection of gastrointestinal foreign bodies when compared to survey radiography.[8] However, US is not without its limitations, which include inter-operator variability and experience level, limited field of view, long study time, potential patient discomfort, and potential lack of visibility of areas of interest due to overlying bowel or free peritoneal gas.[6] In addition, there is poor sensitivity of US to pneumoperitoneum, a critical surgical lesion.[6] Patient size is also a factor when performing US. Previous authors determined that computed tomography (CT) detected a greater number of lesions than US in patients weighing more than 25 kg.[9] In humans, CT is the current gold standard for imaging the acute abdomen, in part due to its relative speed of image acquisition, improved contrast resolution as compared to radiography, and higher spatial resolution than US.[10–12] Many important abdominal structures have been well-described on contrast-enhanced CT in the dog, including the liver, upper and lower urinary tract, spleen, pancreas, gastrointestinal tract, adrenal glands, and hepatic and portal venous system.[6,7] Importantly, however, little information is present in the veterinary literature describing the CT appearance of biliary diseases presenting in dogs with acute abdominal signs. Computed tomography would be an excellent alternative to an abdominal US when a sonographer trained in evaluating the canine biliary tract is not available, especially in an emergency setting, as the biliary tract is difficult to evaluate. Alternatively, CT studies can be performed quickly with sedated patients by personnel with limited training where radiologists can interpret the studies on

or off site and are becoming more common in veterinary hospitals. It is unknown whether CT is as accurate as US to diagnose biliary diseases in these patients.

Canine Biliary Radiography

Abdominal radiographs have limited utility in diagnosis of biliary diseases as there is border effacement of the gallbladder with the liver. Mineral opaque structures within the biliary tree may represent cholestasis or dystrophic mineralization associated with congenital malformations, chronic duct inflammation, or choleliths.[1] Cholecystoliths are mineral opaque stones within the gallbladder and choledocholiths are within the hepatic or cystic ducts or bile duct (Figure 1.7). Choleliths with sufficient calcium bilirubinate will be radiographically visible.[1] A mass effect in the right cranial quadrant of the liver may represent a dilated gallbladder in canine patients with extrahepatic biliary outflow obstruction.[1] Additional consideration for a mass effect within the right cranial abdomen includes pancreatitis, neoplasia, or focal bile peritonitis. Radiographic evidence of abdominal effusion creating poor abdominal serosal and soft tissue opaque whisps over the falciform and/or mesenteric fat may prompt early diagnosis of bile peritonitis.[1]

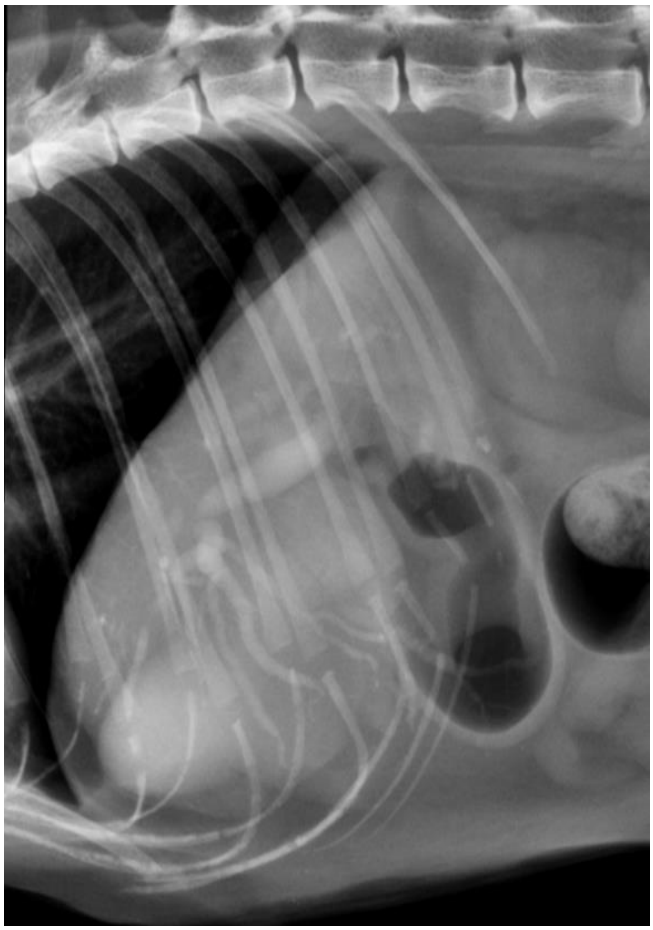

Figure 1.7 A radiograph of a feline patient with mineralization throughout the biliary system including cholecystolithiasis, hepatolithiasis, and choledocholithiasis.

Another biliary pathology able to be identified radiographically is gas within biliary structures or liver. Gas in these locations indicates an emphysematous process such as cholecystitis, choledochitis, hepatic or biliary abscess, necrotic neoplasia, or necrotic granuloma.[1] Gas within the portal vasculature can also originate from emphysematous processes in the intestines or spleen. Identification of gas within the biliary tree warrants percutaneous ultrasound guided aspiration, surgical intervention, and/or antimicrobial therapy.[1]

Cholecystography can also be performed but is now rarely used due to the high availability and better contrast and tomographic resolution of abdominal US and CT (Figure 1.8).

However, radiographic contrast agents have been previously used and described for evaluation of the biliary tree in dogs and cats.[1] Cholecystography can be performed with iodinated contrast administered orally, intravenously, or percutaneously into the gallbladder lumen. Distribution and concentration of contrast agents for evaluating the biliary structures is influenced by variables such as the presence of intraluminal material, hyperbilirubinemia, and bile or hepatic duct occlusion.[1] Cholecystography may identify choleliths, polyps, gallbladder intraluminal masses, or gallbladder sludge, but is not able to confirm bile peritonitis or localize the site of bile leakage.[1]

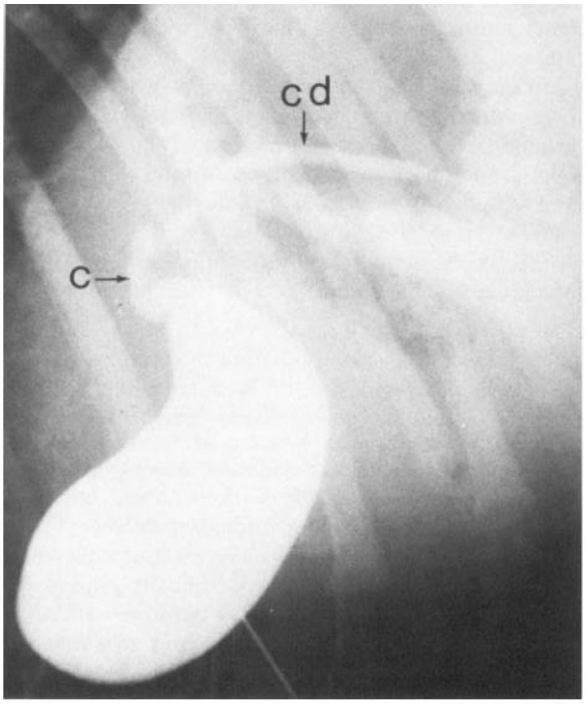

Figure 1.8 Example of percutaneous cholecystogram in a normal dog. c=cystic duct. cd=bile duct. Adapted from Wrigley RH, Reuter RE. Percutaneous Cholecystography in Normal Dogs. *Veterinary Radiology*. 1982;23(6):239-242.

Fluoroscopic percutaneous cholecystography in normal dogs with a Chiba needle has been described where contrast in injected directly into the gallbladder with the guidance of fluoroscopy allowing for reduced risk of bile peritonitis and hemorrhage compared to blind injection.[13] In patients with biliary rupture, ultrasonically guided percutaneous cholecystography allows for presurgical localization of the small gallbladder and the site of leakage.[13] This technique however is minimally used now due to advancements in ultrasonography and cross sectional imaging.[13]

Canine Biliary Ultrasound

Abdominal ultrasound (US) is currently the gold standard method for biliary evaluation in canine patients. Ultrasound can be used to subjectively estimate liver size, identify parenchymal echogenicity changes, identify masses, evaluate for distension and wall thickness of the biliary tree, size and echogenicity of the pancreas and perihepatic lymph nodes, and evaluate for peritoneal effusion and peritonitis/steatitis.[1] The gallbladder is pear-shaped in the longitudinal plane and round in the transverse plane.[14,15] The normal thickness of the gallbladder wall in healthy dogs is 1-2 mm which is a thin hyperechoic line.[1,15] Wall thickness can vary depending on the degree of gallbladder distension.[1] Artifacts such as reverberation and side lobe artifact can cause the appearance of a thickened gallbladder wall (pseudo-thickening). Pseudo-thickening of the gallbladder wall can also occur with peritoneal effusion surrounding the gallbladder as a result of the acoustic interface between fluid and the gallbladder wall.[1] Hyperechoic biliary sediment which is gravity dependent is typical for nonpathologic gallbladder sludge.[1,16,17] Finding gallbladder sludge is common in anorexic or fasted canine patients and may be associated with cholestasis.[18,19] Gallbladders sludge typically is not associated with a distal acoustic shadowing unless there is a mineralized component.[1] The echogenic material in

bile represents conglomerates (1–3 mm) of calcium bilirubinate, cholesterol, and/or lipid droplets suspended in the viscous mucin-rich phase of bile.[1,18,20] The inability to identify the gallbladder may be due to technical difficulties (including overlying gastrointestinal gas, pneumoperitoneum, and body confirmation), gallbladder agenesis, or gallbladder rupture.[1] Ultrasonographically the cystic duct can be traced to the bile duct as it courses to the major duodenal papilla.[1,15] Commonly the bile duct may not be identified in its entirety on US.[1,15] When identified the bile duct normally is less than 3 mm in thickness.[1,15]

The size of the gallbladder fluctuates depending on fasting, feeding, and disease processes including cholestasis, gallbladder mucocele, and biliary outflow obstruction.[1,14] A canine cadaver study revealed the formula for human urinary bladder volume by Hakenberg and others (1983) was most accurate to the actual gallbladder volume and volume was related to the dogs' bodyweight.[14]

$$\text{Volume} = \text{L x W x} \frac{\text{DT} + \text{DL}}{2} \text{ x } 0.625$$

$$\begin{gathered} \text{L} = \text{maximum length} \\ \text{DL} = \text{maximum dorsal to ventral depth in longitudinal section} \\ \text{W} = \text{maximum width} \\ \text{DT} = \text{maximum depth in transverse section} \end{gathered} \quad (1)$$

This study also concluded the two other formulas to calculate volume were also accurate. The first formula uses the principle that the canine gallbladder is ellipse in shape with the equation suggested by Finn-Bodner and others (1993):

$$\text{Volume} = 0.52 \text{ x } (\text{W x DT x L}) \quad (2)$$

The third equation is a formula for volume derived from regression analysis of the linear ultrasonographic measurements:

$$\text{Volume} = -30.2 + 6.08L + 10.6DL \quad (3)$$

Another study evaluated the time-related changes in gallbladder volume determined after an overnight fast and sequentially after administration of a test meal plus or minus low-dose oral erythromycin (motilin stimulus).[21] Gallbladder volume was calculated by use of the same ellipsoid equation:

$$\text{Volume} = L \times W \times DT \times 0.53 \quad (4)$$

Ejection fraction was calculated by:

$$\text{Ejection fraction} = ([\text{gallbladder volume at time 0} - \text{gallbladder volume at specified time point}] / \text{gallbladder volume at time 0}) \times 100 \quad (5)$$

If on initial abdominal US, a gallbladder is of less than or equal to 1 mL/kg body weight and ejection fraction ≥ 25%, there is no need for motility assessment.[21] The study also concluded no treatment or time point was consistently superior as 20 of 22 (91%) dogs achieved gallbladder contraction (maximal ejection fraction ≥ 25%) after ingestion of at least 1 treatment. There were also no significant correlations between body weight and maximal ejection fraction for any treatment. Lastly, the study concluded dogs with a gallbladder volume > 1.0 mL/kg and ejection fraction < 25% may require a combined meal and erythromycin protocol.

A more recent study evaluated the use of three-dimensional (3D) US to evaluate gallbladder lumen in canine patients.[22] The study concluded that 3D US was able to accurately estimate the gallbladder volume and fasting gallbladder volumes determined by 3D

ultrasonography were significantly higher than the corresponding volumes determined by two-dimensional (2D) ultrasonography. Also similar to the previous studies, gallbladder volumes were significantly decreased in the postprandial state compared with the fasting state using 3D ultrasonography, but 2D ultrasonography showed no significant difference.

Canine Biliary Computed Tomography

On computed tomography (CT), the normal gallbladder is ovoid to pear-shaped and hypointense to the surrounding liver (Figure 1.9).[23] As with US, the gallbladder size can vary depending on the amount of bile it contains. While the wall of the gallbladder is not commonly identified on unenhanced CT imaging, after the intravenous injection of iodinated contrast, a thin line of enhancement can be seen along the wall, especially the portion that is adjacent to peritoneal fat.[23] Although the bile duct can sometimes be identified ventral to the portal vein, the majority of the biliary system (especially the hepatic biliary ducts) is not consistently seen with this modality.[23] In one report, the bile duct was visible on CT in 68% of normal dogs, although all dogs in this study weighed less than 15 kgs.[24] This study also reported the estimation of gallbladder volume and bile duct diameter with 3D rendering were not significantly different on CT from those of the US. The bile duct diameter in these patients was not over 3 mm at the porta hepatis and 3.5 mm at the duodenal papilla. The normal Hounsfield unit (HU) of bile has been reported to be 34-35.8 HU.[24,25]

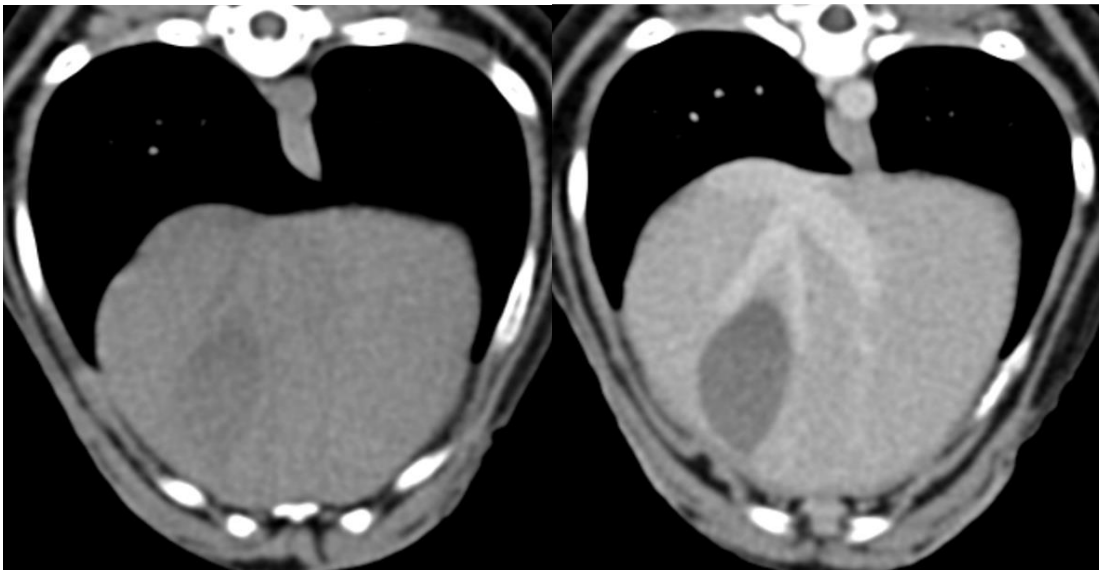

Figure 1.9 Transverse computed tomography soft tissue window images with the left image being precontrast and the right image being a venous postcontrast. The normal gallbladder is ovoid to pear-shaped and hypoattenuating to the surrounding liver (left image). While the wall of the gallbladder is not commonly identified on unenhanced computed tomography imaging, after the injection of contrast, a thin line of enhancement can be seen along the wall, especially the portion that is adjacent to peritoneal fat (right image).

Meglumine iotroxate, brand name Biliscopin, is an iodinated intravenous contrast agent which has increased hepatic metabolism allowing increased deposition of the contrast agent into the hepatobiliary system. This contrast agent has been used for contrast enhanced CT cholangiography for the evaluation of the canine, feline, and human biliary tracts with published pathologies including canine gallbladder mucoceles.[26,27] As biliary opacification requires normal hepatobiliary function, contrast enhancement may be limited in patients with hyperbilirubinemia (due to cholestasis or poor hepatocyte function), hyperproteinemia, or excessively dilated biliary ducts. In these patients, renal excretion is increased. The use of Biliscopin is limited as the gold standard for tomographic evaluation of the biliary system in humans is contrast enhanced magnetic resonance imaging (MRI), and there is no FDA approval of Biliscopin in veterinary

medicine in the United States. This limits the availability of Biliscopin to be used in veterinary medicine.

Canine Biliary Scintigraphy

Biliary scintigraphy is available, but is very expensive, not commonly available, and exposes the patient to ionizing radiation. This modality has been largely replaced by US, CT, and MRI. Radioisotopes can be used for quantitative hepatic perfusion and biliary ejection calculation using synthetic cholecystokinin infusion.[28] Commonly used radioisotopes have short half-lives, including technetium 99mTC and 99mTc-2,6 diisopropylphenylcarbamoylmethyl iminodiacetic acid (DISIDA).[1,28,29]

Canine Biliary Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is not currently commonly used for evaluating the canine biliary tract due to long study acquisition times requiring anesthesia, limited availability of onsite MRI units, motion and respiratory artifacts, and the availability of a few published reports on canine biliary MRI.[30,31] Hepatobiliary MRI most commonly utilizes gadoxetic acid, a hepatocyte-specific contrast agent.[31] Gadoxetic acid (GD-EOB-DTPA) is a paramagnetic, hydrophilic, ionic contrast agent and is utilized as one of the most useful MRI techniques to diagnose liver tumors in humans.[31] This contrast agent accumulates in functioning hepatocytes following the arterial and venous phases (during the hepato-biliary phase) leading to hepatic parenchymal enhancement.[31] Due to the contrast not being taken up by metastatic cells or nonfunctioning hepatocytes, this aids in the diagnosis of liver parenchymal metastases in humans, differentiation of primary hepatic tumors, and diagnosis liver cirrhosis and focal nodular

hyperplasia.[31] A preliminary study found the MR images of proliferative hepatic parenchymal lesions in dogs using gadoxetic acid are similar to those obtained in humans which suggests that the contrast enhancement patterns used in human medicine may be useful in differentiating hepatic parenchymal lesions in dogs.[31]

Magnetic resonance cholangiopancreatography (MRCP) is a newer technique used in humans for the diagnosis of bile duct obstructions which does not require the use of contrast agents or anesthesia.[32,33] Endoscopic retrograde cholangiopancreatography (ERCP, a technique that combines the use of endoscopy and fluoroscopy or radiography to evaluate the biliary and pancreatic ductal system) is still the gold standard for evaluating the biliary and pancreatic systems in humans as therapies can be performed concurrently, but is highly operator dependent, has significant morbidity and mortality, and operators cannot cannulate the bile duct and pancreatic duct in up to 9% of examinations.[32–34] Alternatively, MRCP uses MRI to visualize the biliary and pancreatic hyperintense fluid on T2-weighted images which improves spatial resolution and allows for imaging of the entire pancreaticobiliary tract during a single breath-hold.[32] Although MCRP studies in dogs have not been described, MRCP may be a future imaging modality to diagnose hepatobiliary disease in canine patients.[30]

Hepatobiliary Sampling

Cholecystocentesis is the aspirate sampling of gallbladder bile and can be completed using a percutaneous ultrasound guided method, laparoscopic guidance, or during exploratory abdominal surgery (Figure 1.10).[35–37] Fluoroscopic guided percutaneous cholecystocentesis has also been described but is used much less frequently due to the regular access to US which allows for more accurate sampling and the patient not to be exposed to ionizing radiation.[13] Bile

samples are collected for cytologic evaluation and bacterial culture. A percutaneous transhepatic approach or a direct fundic approach can be used.[1] An advantage of the transhepatic approach is the adherence of the gallbladder to liver in its fossa limits leakage from the puncture.[1] If a direct fundic approach is utilized, complete emptying of the gallbladder of bile to avoid spillage into the peritoneal space is recommended.[1] A study evaluating the percutaneous US guided cholecystocentesis successfully used no chemical restraint and analgesia in their population of dogs, but clinical patients may need mild sedation and/or local anesthesia to successfully perform.[36] This study also used 22-gauge needles to minimize physical damage and elicitation pain.[36]

Complications of cholecystocentesis include hemorrhage, intraperitoneal bile leakage and subsequent bile peritonitis, hemobilia, and bacteremia.[1] Vasovagal reaction may also occur which can result in ventilatory arrest, severe bradycardia, and death; so, clinicians should be prepared to provide anticholinergics and ventilatory assistance during these procedures.[1] Additionally, blunt pressure on the gallbladder provokes high vagal tone and should therefore be avoided.[1] In a study including three hundred percutaneous US-guided cholecystocentesis procedures performed in 201 dogs and 51 cats, the overall incidence of major complications was 8 of 300 procedures (2.7%).[38] Specifically, bile peritonitis occurred in only 2 of 300 procedures (0.7%).[38] Also identified within this study population, an ultrasonographically abnormal gallbladder was found in 52% of cases and which had a sensitivity of 82%, specificity of 55.7%, and accuracy of 61.5% to predict a positive bile culture.[38] Consistent with other studies, this study found a positive bacterial culture in 21.3% of the samples.[38] When these findings were compared, abnormal ultrasonographic findings were only a fair predictor of a positive bile

culture, but did have an increased association of positive bile culture when there was concurrent increased wall thickness and/or an irregular luminal surface on ultrasound.[38]

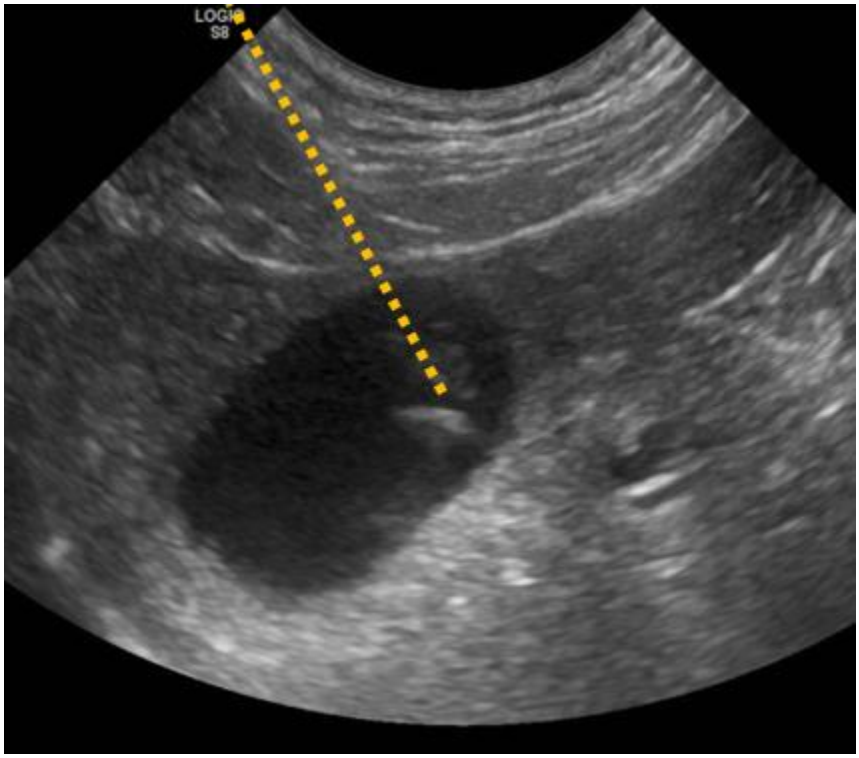

Figure 1.10 Sagittal ultrasonographic image of percutaneous transhepatic cholecystocentesis in a dog. The dashed yellow line outlines the needle within the gallbladder.

Current Limitations in Canine Biliary Imaging

Although there are many reports describing the ultrasonographic features of gallbladder disease in dogs, few reports exist in veterinary literature detailing the CT features of gallbladder disease.[24,25,27,39–41]. Ultrasound findings indicating biliary disease include inspissated, nonmotile, hyperechoic bile organized into a striated or stellate pattern, thickening of the gallbladder wall, pericholecystic echogenic fluid or mesentery, dilation of the hepatic, cystic, or bile ducts, or hyperechoic, distally shadowing structures within the biliary system.[1,39,42] The normal

gallbladder and bile duct appearance and size on CT have recently been reported, with the bile duct measuring less than 3.5 mm in 50 normal dogs weighing less than 15 kgs.[24] The largest and most recent case series described confirmed gallbladder pathology in 34 dogs, which included the first reported CT evaluation of a gallbladder wall hematoma.[41]

Computed tomography is the current gold standard for imaging the acute abdomen in people. As the availability of small animal CT and specialist interpretation increases and the cost of CT decreases, veterinarians will begin using this technology more to image animals presenting with acute abdominal signs. Unfortunately, CT may be limited due to its higher cost, lower availability, required use of general anesthesia or sedation, and use of ionizing radiation as compared to US.

A few reports of other intraabdominal disease processes in dogs have also been published which support CT as being equivalent or superior to abdominal US for evaluating these pathologies. A recent retrospective descriptive study of 13 dogs found CT to have a higher detection rate of canine gastric tumors as compared to ultrasound.[43] Ultrasound identified 69% of gastric tumors while CT identified 92% of gastric tumors, with a low percent agreement of 61.5%.[43] Prior to this, abdominal US and endoscopy had been the imaging modalities of choice for identifying and diagnosing gastric tumors in dogs.[43] This study also found fair agreement in the detection of abnormal lymph nodes on both CT and US with CT identifying more abnormal lymph nodes.[43] Within this patient population, leiomyomas located within the gastric cardia were often missed on ultrasound most likely due to the craniodorsal location within the stomach.[43]

Therefore, there is a critical need to further investigate the CT appearance of conditions resulting in acute abdominal signs, notably those of the biliary system. The purpose of this study

is to describe the CT appearance of various biliary diseases in dogs and to compare the accuracy of CT with abdominal US in the diagnosis of these diseases. This information can be used to aid interpretation and hasten decision making in these critical patients.

Canine Hepatobiliary Disease

Biliary diseases are uncommon but potentially fatal causes of acute abdominal signs in dogs. In dogs, biliary disease can occur secondary to cholelithiasis, gallbladder mucocele, bacterial infection (cholecystitis), neoplasia, and various hepatic diseases. Extrahepatic biliary disease can also result in a secondary biliary disease such as pancreatitis.[1] The underlying pathophysiology of biliary disease is usually attributed to cholestasis, which in turn predisposes the animal to bacterial infection, choliths, and gallbladder mucoceles.[12] With cholestasis, the unabsorbable bile components, including bile salts, phospholipids, and cholesterol, are concentrated and dehydrated by the resorption of water and electrolytes (sodium, chloride, and bicarbonate).[1] This leads to thickening of the bile and formation of inspissated, viscous, dark green/black biliary material.[1] Cocker spaniels and Shetland sheepdogs are reported to be overrepresented breeds presenting for biliary disease, and affected animals tend to be older.[1,39,44] In one study, the median age at time of presentation was 10 years.[39] Unfortunately, clinical signs of biliary disease are generally vague, and these animals often present with nonspecific abdominal signs. In one report of dogs with biliary disease, the most common clinical signs included vomiting, lethargy, anorexia, jaundice, fever, and abdominal pain.[39] Biochemically, canine patients may have elevations in ALP, GGT, and ALT and hyperbilirubinemia.[1,39] Choleresis (enhanced bile flow) also can also cause biliary pathology by producing thin, dilute bile.[1] Choleresis is commonly a therapeutic goal in patients with cholestasis in large bile ducts.[1]

A retrospective, multicenter, case series, descriptive study of 34 dogs is the only descriptive publication which describes confirmed biliary pathology on CT.[41] The final diagnoses were confirmed with cytology, bile culture, surgical findings, and/or histopathology within 1 month of imaging.[41] The most common pathologies were cystic mucosal hyperplasia (44.1%), gallbladder wall edema (26.5%), gallbladder mucocele (23.5%), bactibilia (20.6%), cholecystitis (17.6%), white bile (17.6%), and cholelithiasis (11.8%). The presence of intraluminal nodules, gallbladder wall thickening, hyperattenuating material (35-100 Hounsfield units [HU]), and mineral attenuating material (>100 HU) were the most common abnormalities detected.[41] In this study, the gallbladder wall was best visualized on postcontrast images in 30 of the 32 dogs (94%) that had both precontrast and postcontrast scans available.[41] The median precontrast bile was 37.6 HU (range 9.2-57.3 HU) and the median postcontrast bile was 43.6 HU (range 3.6-57.1 HU).[41] The bile duct was visible in 30 of 34 dogs with the entire duct being able to be traced in 70% of the dogs.[41] No CT findings have been identified as pathognomonic for canine biliary pathology.[41]

Bile Characteristics

Normal HU of bile has been reported to be 34-35.8 HU.[24,25] Hyperattenuating material within the bile ranges from 35-100 HU, and mineral attenuating material is characterized by being >100 HU.[41] Cystic mucosal hyperplasia, gallbladder mucocele, gallbladder wall edema, bactibilia, cholecystitis, and cholelithiasis are pathologies most commonly associated with hyperattenuating material.[41] Hyperattenuating material occurs predominantly in pathologies that cause mucin production such as cystic mucosal hyperplasia and gallbladder mucoceles.[41] It has been hypothesized that this hyperattenuating material may be due to mucinous material as it is in both the gravity dependent portion and suspended locations within the gallbladder lumen.[41]

Similar suspended hyperattenuating luminal contents were noted in dogs with gallbladder mucoceles on CT.[25] Hyperattenuating material less commonly occurred in dogs with gallbladder wall edema, bactibilia, and cholecystitis.[41]

Gallbladder Sludge

Biliary sludge is gravity dependent hyperechoic variably particulate material without acoustic shadowing which may be within the gravity dependent portion (most commonly), suspended, or solid appearing (Figure 1.11).[18] In human patients, biliary sludge is a mixture of cholesterol crystals, bile pigments, and bile salts which are embedded in mucin and often includes particles ≥1 mm (microliths), which likely precede cholecystolith formation.[18] The composition of spontaneous canine gallbladder sludge has not been reported, but lower incidence of canine cholecystoliths compared to humans suggests that canine sludge likely has a different composition or etiology.[18] Support from previous experimental studies indicates canine biliary sludge does not contain substantial amounts of cholesterol.[18,45–47]

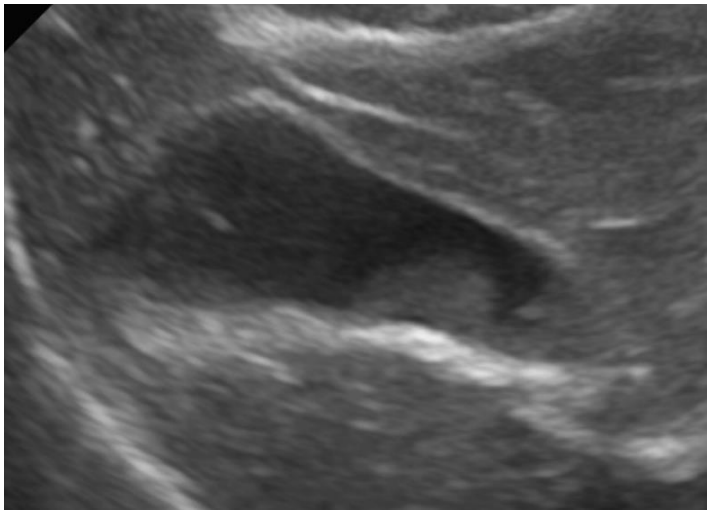

Figure 1.11 A canine patient with gallbladder sludge on ultrasound. This is a longitudinal ultrasonographic image.

A previous study analyzed the components of 43 samples of canine gallbladder contents (21 with biliary sludge and 22 with gallbladder mucoceles) with infrared spectroscopy with 41 of the samples also undergoing bacterial culture.[20] The resultant infrared spectra were compared with that of swine mucin. The contents of 20 (95.2%) biliary sludge and 22 (100%) gallbladder mucocele samples exhibited similar infrared spectra as swine mucin. The study concluded the gallbladder principal components in both biliary sludge and gallbladder mucoceles were mucins, which suggested the possibility that mucins were involved in the pathogenesis of not only gallbladder mucoceles but also biliary sludge.[20] Although biliary sludge and gallbladder mucocele contents exhibited similar infrared spectra, one sample of biliary sludge (4.8%) was determined to be composed of proteins. The rate of bacterial infection of the gallbladder was 10.0% for biliary sludge and 14.3% for gallbladder mucoceles with almost all of the identified bacterial species being intestinal flora. The route of biliary infection in this study was most likely an ascending infection from the duodenum with both biliary sludge and gallbladder mucoceles exhibiting low rates of bacterial infection of the gallbladder.[20] The study suggested it is possible that gallbladder mucoceles and biliary sludge have the same pathophysiology and could represent a continuous disease process.[20] It has been reported that sometimes there is no clear distinction between the findings of severe biliary sludge and gallbladder mucoceles, which makes their differentiation challenging.[20,48]

The clinical implication of canine gallbladder sludge is unclear.[17] Echogenic intraluminal gallbladder material is common and was identified in two-thirds of canine patients undergoing routine abdominal ultrasound examinations.[18] An early study suggested a weak association between the presence of gallbladder sludge and patient age but did not identify a connection to the presence of hepatobiliary disease.[17] This study then concluded that canine

gallbladder sludge should be considered an incidental finding.[17] However, a later study found mobile sludge or precipitate in 24 of 45 dogs with gallbladder disease with 9 of these 24 (37.5%) having gallbladder ruptures.[39] More recently, another study concluded that abnormal gallbladder contents (both sludge and gallbladder mucoceles) in dogs were associated with decreased gallbladder emptying following a meal challenge.[19] This study did not, however, determined if decreased gallbladder contractility was the cause or consequence of the abnormal contents.[18,19] Biliary sludge has been iatrogenically induced in dogs by acute cystic duct ligation and dietary manipulation.[45,46] In both studies, the gallbladder sludge consisted primarily of bilirubinate and mucin with some being complexed with calcium carbonate. Further, in a Shetland sheepdog with a gallbladder mucocele, the gallbladder material had a similar composition to the experimentally induced sludge.[44] However, as this breed has a strong genetic predisposition for defective phoshatidylcholine secretion and subsequent mucocele formation, this finding may not reliably reflect events in other breeds.[18,49]

Canine patients with hyperadrenocorticism and hypothyroidism have been shown to be associated with increased occurrence of gallbladder sludge and gallbladder mucocele formation.[50] This finding suggests a link between or precession of the presence of biliary sludge and the development of a gallbladder mucocele.[18,50] This theory has not been proven, but gallbladder sludge has been reported around or embedded within gallbladder mucoceles.[18,51] In an experimental study, glucocorticoids (oral administration of hydrocortisone 8 mg/kg by mouth twice daily for 3 months) have been shown to alter bile acid profiles in dogs as the bilirubin, cholesterol, and calcium concentrations reversibly decreased during treatment.[47] In a similar separate study, hydrocortisone administration (at 8.5 mg/kg by mouth twice daily for 84 days) caused reversible shifts toward higher concentrations of the more hydrophobic unconjugated bile

acids (chenodeoxycholic acid and deoxycholic acid) and toward lower concentrations of the amphipathic taurine-conjugated bile acids in gallbladder bile.[52] These changes may impact gallbladder epithelial function and mucus production. While gallbladder sludge pathophysiology is not fully understood, it is often treated with a low-fat diet and medications, such as ursodeoxycholic acid and S-adenosylmethionine.[20]

Mineral Attenuating Intraluminal Gallbladder Material

Mineral attenuating material is characterized as any material >100 HU.[25] Mineral attenuation material was the most common CT finding of the most recent study evaluating cases with confirmed various biliary pathologies.[41] Cystic mucosal hyperplasia, gallbladder mucocele, cholelithiasis, white bile, and wall edema were the most common pathologies associated with mineral attenuating material.[41] All of these pathologies except for gallbladder wall edema are associated with cholestasis and/or dysfunction of the gallbladder, which may alter the gallbladder resorption of bile salts, mucin, and electrolytes that promote cholecystolithiasis formation.[41] This study suggested that dogs with gallbladder wall edema develop mineral attenuating intraluminal material likely secondary to other concurrent gallbladder pathologies like cholecystitis and gallbladder mucocele, as they commonly occur simultaneously.[41] Both this study and a previous study evaluating canine gallbladder mucocele on CT reported a common central distribution of the intraluminal mineral material in approximately 67% of cases.[25,41] This material identified on CT appears as hyperechoic material which displays distal acoustic shadowing on US. If this material is not sufficiently mineral opaque and dense enough to change the attenuation of the x-ray beam, it will not be identified on radiographs unless a large amount accumulates together.

Cholelithiasis

Cholelithiasis is the presence of mineral structures within the biliary tree including the intrahepatic bile ducts (hepatolithiasis), large hepatic ducts, cystic duct (choledocholithiasis), bile duct, sphincter of Oddi, and gallbladder (cholecystolithiasis). Cholecystolithiasis is the most common type of cholelith and can be commonly identified on routine abdominal US in both dogs and cats as most choleliths in small animals do not cause clinical signs.[1] Both mineral attenuating and radiopaque choleliths are identified with US as hyperechoic structures which display distal acoustic shadowing and twinkle artifact when of sufficient size and density.[1] Many small choleliths do not contain enough mineral for detection on survey radiographs.[1] Choledocholiths within the bile duct or cystic ducts can be challenging to ultrasonographically identify due to adjacent visceral structures, overlying gastrointestinal gas obscuring detection, and because they are not surrounded by anechoic bile.[1] Cholecystoliths are commonly mobile and gravity dependent and can be differentiated from mural lesions by demonstrating this gravitational mobility.[1,18]

The composition of choleliths in dogs differ than those in humas which are primarily derived from cholesterol crystallization.[1] Most canine choleliths contain calcium carbonate and bilirubin pigments, earning the name ‘‘pigment gallstones.’’[1] There are two categories of pigment gallstones: ‘‘black-pigment’’ stones composed primarily of bilirubin polymers and ‘‘brown-pigment’’ stones composed primarily of calcium bilirubinate.[1] Black-pigment stones are formed during prolonged hyperbilirubinemia where bilirubin polymerization occurs after nonenzymatic deconjugation.[1] Brown-pigment stones commonly develop during cholecystitis and cholestasis.[1] In patients with cholecystitis, bilirubin deconjugation by bacterial b-glucuronidase creates unconjugated bilirubin that precipitates as calcium bilirubinate.[1] Biliary

precipitates and pinpoint calculi promote bacterial colonization by providing a surface for bacterial colony adherence which further promotes calcium bilirubinate aggregate formation.[1] Local inflammation and prostaglandins (especially with cholecystitis and hemorrhage) promotes mucin production which accumulates calcium bilirubinate and bilirubin polymers into cholelith aggregates.[1] This process is additionally enhanced by gallbladder dysmotility and cholestasis.[1] Obstruction of the canine cystic duct increases gallbladder mucin production, cholesterol concentration, and formation of pigment sludge.[52] Each of these products favors cholelith precipitation. First mucin-bilirubin complexes form then sludge particles (1–4 mm in diameter) coalesce and precipitate as gravel and choleliths with increased mucin production.[1] Gallbladder distension from any etiology stimulates local mucin production which can cause the cystic duct to occlude by initiating a self-perpetuating cycle involving biliary sludge accumulation and inspissation.[1] Patients with cholelithiasis must be evaluated to determine if the underlying etiology requires interventional therapy.[1]

Obstructive cholelithiasis is characterized by the presences of clinical signs (most commonly vague acute abdominal signs), finding a dilated bile duct on US or CT, and high liver enzyme activity (especially ALP and GGT) and hyperbilirubinemia on a biochemistry.[1] Obstructive cholelithiasis is more common in middle-aged to older dogs with a higher incidence in small breed dogs and one study identifying an increased incidence in Miniature Schnauzers and Miniature Poodles.[1,52] Surgical intervention is commonly required to treat patients with obstructive choledocholithiasis which usually involves cholecystectomy and lavage of the bile duct.[1] Some patients benefit from temporary bile duct stent placement to allow healing of the surgical site, ensure bile drainage into the duodenum, and decrease risk of bile duct stenosis during recovery, but this is not as commonly performed.[1] A more intricate

cholecystoenterostomy should be performed in patients with irresolvable obstructive choledocholithaisis.[1]

Hypoattenuating Intraluminal Gallbladder Material

Lower bile HU (consistent with fluid attenuation) in dogs is consistent with decreased bile density, most commonly identified with bactibilia.[40] The suspected explanation for lower bile HU is that gallbladder inflammation (as with bactibilia and cholecystitis) alters the gallbladder ability to absorb water and therefore diluting the bile.[41] Cholecystitis can occur from infectious etiologies or extrahepatic biliary outflow obstructions.

Gallbladder Mural Neoplasia

Neoplasia of the gallbladder wall is uncommon in the dog but can be routinely identified on US and CT as focal wall thickening or mass with increased blood flow on color and power Doppler interrogation, strong contrast enhancement, and concave deformation of the gallbladder lumen. Biliary carcinoid tumors have strong arterial contrast enhancement that wash out by the delayed phase (HU arterial 136, HU delayed 71).[40] Adenomas or adenocarcinomas are less common and appear as an irregular and focal wall thickening.[1] Larger pedunculated masses can cause gallbladder outflow obstruction due to cystic duct occlusion.[1] Sessile or polypoid lesions in the gallbladder may be also be identified in dogs with gallbladder cystic mucosal hyperplasia which can appear similar to neoplasia.[1] A single case of canine gallbladder lymphoma (diffuse large B-cell lymphoma) has been reported in a 7-year-old, spayed, female miniature dachshund presented for progressive anorexia and icterus (Figure 1.12).[53]

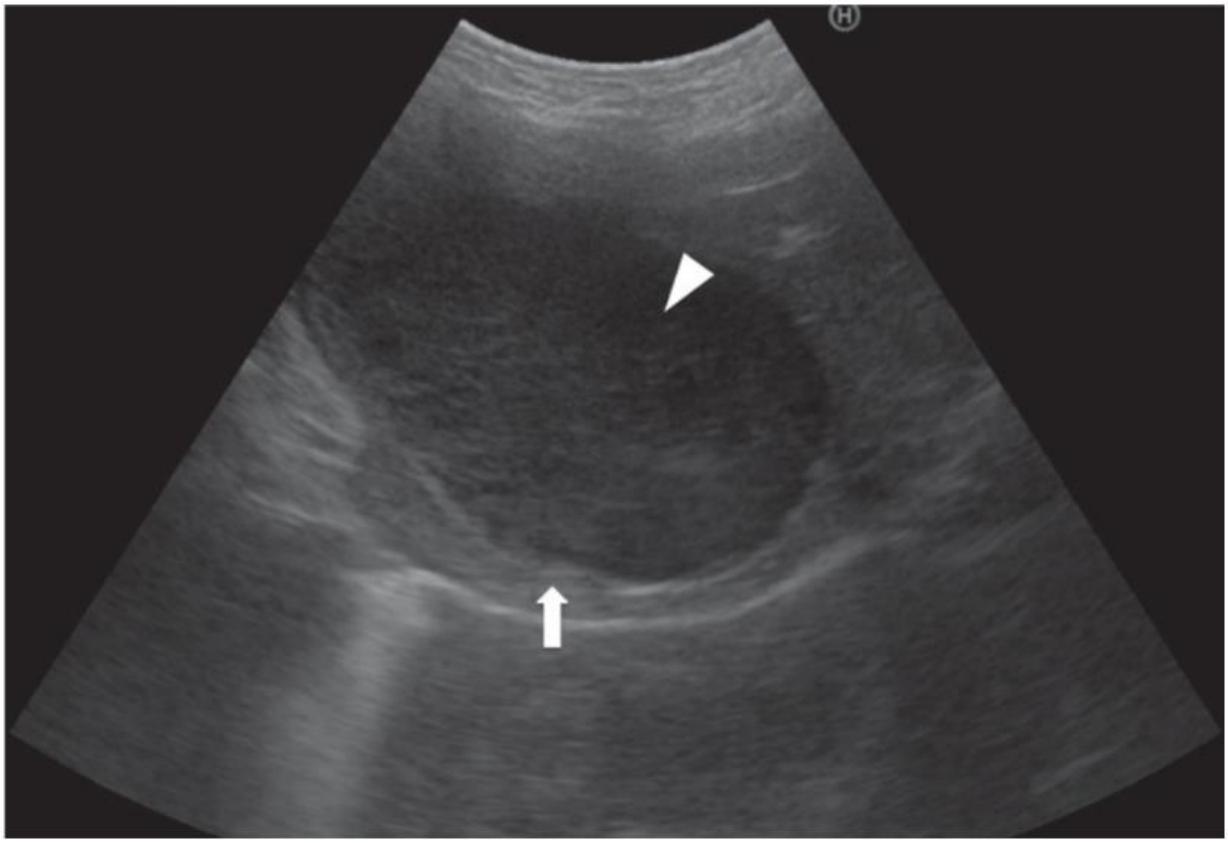

Figure 1.12 Ultrasonography of a canine patient with confirmed lymphoma. White arrow shows the hyperechoic thickened gallbladder wall and the white arrowhead outlines the hyperechoic gallbladder sludge. Adapted from Nagata N, Shibata S, Sakai H, et al. Gallbladder lymphoma in a miniature dachshund. *Journal of Veterinary Medical Science*. 2015;77(1).

Cystic Mucosal Hyperplasia

Cystic mucosal hyperplasia (CMH) appears as polypoid or sessile mural thickening with mucosal margin undulation on US and CT and can also have a nodular CT appearance.[1] Cystic mucosal hyperplasia is commonly present in dogs with gallbladder mucoceles.[1,40] Some dogs with bactibilia have gallbladder wall nodules likely due to underlying cholecystitis.[40] Histopathologically, CMH gallbladder mucosa has many cystic sessile or polypoid hyperplastic

lesions that accumulate mucin within cystic structures and between polypoid villi (Figure 1.13).[1] Commonly there is no evidence of inflammation, and the serosal surface remains intact.[1]

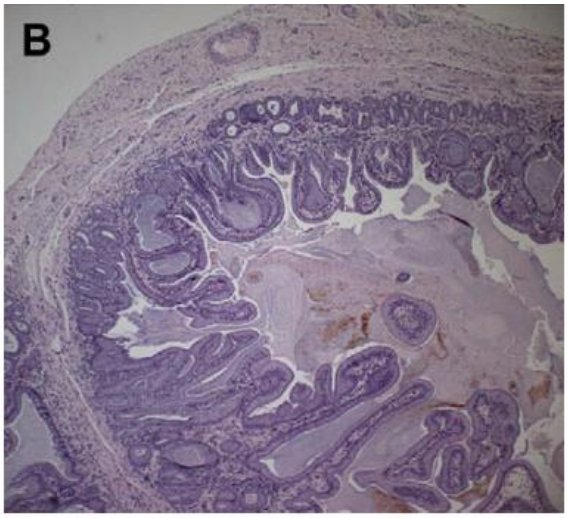

Figure 1.13 Pictomicrograph of a canine gallbladder with a gallbladder mucocele and cystic mucosal hyperplasia. The mucosal wall is thickened and undulating with entrapped mucus. Adapted from Center SA. Diseases of the Gallbladder and Biliary Tree, *Veterinary Clinics of North America - Small Animal Practice*, 2009;39(3):543-598.

White Bile

White bile is the name of bile without bilirubin pigments, therefore causing the bile to be colorless.[54] Bile or cystic duct obstruction as with cholelithiasis and chronic extrahepatic bile duct obstruction due to pancreatitis or a mass effect can produce a white bile syndrome when bile containing pigment is separated from bile in the large ducts.[1]

Cholecystitis

Cholecystitis is defined as inflammation within the gallbladder. The inflammation may be from nonsuppurative or suppurative processes and can be associated with infectious

etiologies, systemic disease, neoplasia, blunt abdominal trauma, or gallbladder obstruction by occlusion of the cystic duct.[1] The presence of cholecystitis can modify bile composition and alter bile flow by increasing ductular secretions of bicarbonate and mucin.[1] In a normal biliary tree, majority of the bile acids are conjugated while in patients with bactibilia or decreased bile pH from local inflammation can result in bile acid deconjugation.[1] Unconjugated bile acids are cytotoxic, alter permeability of vascular structures, and induce further tissue inflammation likely contributing to epithelial edema in patients with septic cholecystitis and choledochitis.[1] Patients with cholecystitis commonly have symmetric or asymmetric thickening of the gallbladder wall which can be identified on US and CT.[1] One patient with cholecystitis and bactibilia has been reported to have strongly arterial enhancing nodules in the gallbladder similar to those of neoplasia (especially carcinoid tumors).[40]

Cystic and bile duct occlusion causes biliary tree inflammation secondary to cholestasis which then can be perpetuated by mechanical irritants such as choleliths.[1] Also with cystic duct occlusion, the gallbladder volume decreases due to occluded inflow of bile, the wall thickens, and white bile forms.[1] Gallbladder dilation occurs with more distal biliary outflow obstruction within the bile duct due to increased backflow into the gallbladder. If gallbladder distention is severe, wall ischemia can occur with subsequent necrotizing cholecystitis and increased risk of gallbladder rupture.[1] Acute septic cholecystitis can also occur with bactiblia.[1]

Symmetric or asymmetric gallbladder wall thickening, dilated bile, cystic, and/or hepatic ducts, double-layered gallbladder wall, hypoechoic gallbladder wall, hyperechoic gallbladder material, and choleliths are common findings with cholangitis identified on US or CT evaluation.1,36,40 Diffuse hyperechogenicity of the gallbladder wall on US may also be observed with gallbladder wall mineralization secondary to chronic cholecystitis.[1] Abdominal

radiography may show decreased cranial abdominal serosal detail consistent with focal peritonitis.[1] A sentinel loop (a single loop of gas dilated small intestine) may implicate a focal ileus on radiographs.[1] Occasionally the gallbladder wall may become mineral opaque due to dystrophic mineralization secondary to chronic inflammation.[1]

Clinical signs of acute cholecystitis include abdominal pain, fever, vomiting, lethargy, ileus, and jaundice.[1] A complete blood count can include a leukocytosis with or without toxic neutrophils and a left shift.[1] Hyperbilirubinemia may be present and is associated with jaundice depending on chronicity, involvement of extrahepatic biliary structures, presence or extent of biliary tree occlusion, or bile peritonitis.[1] Biochemistry findings include elevated liver enzyme activity (ALT) with moderate to marked cholestatic enzymes (ALP, GGT) elevation.

Necrotizing Cholecystitis

Necrotizing cholecystitis involves ischemia and devitalization of the gallbladder wall secondary to sever and/or chronic cholecystitis.[1] Necrotizing cholecystitis often appears as an asymmetric focal trilamination, discontinuation, or thickening of the gallbladder wall on US or CT and often has concurrent adjacent small volume of peritoneal effusion and hyperechoic fat (omental adhesions, chemical peritonitis, and/or gallbladder rupture and bile peritonitis).[1] Gallbladder rupture and bile peritonitis requires prompt surgical intervention, most commonly a cholecystectomy with potential biliary diversion.[1] A common cause of necrotizing cholecystitis is interrupted perfusion from the cystic artery by thromboembolism, a shearing tear delivered from blunt abdominal trauma, bacterial infection, cystic duct obstruction (choleliths, neoplasia), mature gallbladder mucocele causing wall ischemia, or extension of adjacent hepatic inflammatory processes or neoplasia.[1,40]

Emphysematous Cholecystitis and Choledochitis

Emphysematous cholecystitis and choledochitis is gas within the wall or lumen of the gallbladder or segments of the biliary tree.[55] In dogs this has been associated with diabetes mellitus, acute cholecystitis with or without cholecystolithiasis, obstructive cholecystolithiasis, traumatic or thrombotic ischemia, mature gallbladder mucocele formation, neoplasia, incompetent sphincter of Oddi, and occlusion of the cystic artery.[55,56] Emphysematous cholecystitis is rare and can be caused by gas producing bacteria, most commonly *Clostridium perfringes* and *Escherichia coli*.[56] *Clostridium perfringes* has been identified as the cause of acute abdominal signs in a dog with subacute severe necrotizing emphysematous cholecystitis.[56] Emphysematous cholecystitis is a life-threatening condition which can be fatal without early treatment with possible need for surgical intervention (most commonly cholecystectomy) due to the high risk for gallbladder rupture and sepsis with concurrent antimicrobial therapy based on culture and sensitivity of bile and affected biliary tissues.[1,56]

Emphysematous cholecystitis can be diagnosed radiographically as a spherical to ovoid shaped gas opaque structure in the region of the gallbladder which may have fluid-gas interface on horizontal beam projections.[56] Other differential diagnoses for gas filled structures with this appearance include hepatic or perihepatic abscess, liver lobe torsion and entrapment, biliary-enteric fistula, duodenal gas, incomplete sphincter of Oddi, and gallbladder lipomatosis.[56] A case report of a dog with a gas filled gallbladder on radiographs had a possible infarcted gallbladder wall neoplasm (most likely round cell in origin) with a concurrent *Clostridium perfringens* detected on bacteriologic culture.[55]

Ultrasonographic findings of emphysematous cholecystitis include those described with cholecystitis in addition to reverberation or ringdown artifact of the mural or intraluminal

gallbladder gas.[56] This appearance may be difficult to differentiate from intramural mineralization when a small volume of gas is present.[56] When gas is within the lumen or wall of the gallbladder, complete evaluation of the gallbladder and deeper structures is markedly limited on abdominal US due to the reverberation artifact which inhibits the value of this modality. Computed tomography helps bridge this gap as it can allow for direct visualization of the gas location within the hepatobiliary system where gas bubbles can commonly be seen in linear configurations.[56,57]

Parasitic Biliary Infections

Infection with liver flukes (trematodes of the Opisthorchiidae family) in endemic regions can cause acute and chronic cholangitis in cats and occasionally in dogs.[1,58] Liver fluke life cycles require two intermediate hosts, a fresh water snail and a secondary host (such as a fish, reptile, or amphibian) in which metacercaria encyst.[1] The dog or cat tertiary host ingests the flukes by eating the secondary host.[1] Young flukes develop in the small intestines and migrate into the bile tree where they mature within 8-12 weeks.[1] Embryonated eggs pass from bile back into the duodenum and may be detected on fecal exams as early as 12 weeks after infection.[1] Fecal examination may fail to detect eggs due to sporadic passage, variable morphology, small egg size, and development of bile duct obstruction that precludes passage of eggs into bile and feces.[1] Cholecystocentesis can also occasionally identify fluke eggs in bile.[1]

Patients may be asymptomatic with some having progressive clinical signs including weight loss, anorexia, vomiting, diarrhea, jaundice, hepatomegaly, abdominal distention, and death in severely affected patients.[1] Some symptomatic feline patients resolve clinical signs within 24 weeks after infection without treatment.[1] Additional bloodwork abnormalities from those commonly found with cholangitis may include an eosinophilia between 3-14 weeks after

infestation which may persist.[1] Patients with severe chronic cholangitis can develop biliary fibrosis.[1] The hepatic parenchyma usually remains normal and regional lymphadenopathy can develop.[1]

Treatment for liver flukes includes antiparasitic therapy such as praziquantel (20 mg/kg subcutaneously every 24 hours for 3–5 days) when infection is suspected.[1] Fluke eggs may continue to pass in feces for up to 2 months after successful treatment.[1]

Gallbladder Wall Edema

Gallbladder wall edema is the accumulation of fluid within the gallbladder wall causing subsequent wall thickening. A double-rim sign may reflect gallbladder wall edema associated with anaphylaxis, passive congestion due to right sided congestive heart failure or cardiac tamponade due to pericardial effusion, portal hypertension, severe hypoalbuminemia, cholecystitis, sepsis, biliary outflow obstruction, dexmedetomidine administration, blood transfusions, and immune mediated hemolytic anemia.[1,59–61] Gallbladder wall edema can also occur with previously discussed pathologies such as infectious etiologies (bactibilia or systemic infections), systemic inflammatory etiologies, or focal inflammatory etiologies such as hepatitis, pancreatitis, peritonitis, and peritoneal metastatic neoplasia (such as carcinomatosis).

Gallbladder Mucocele

A gallbladder mucocele is an accumulation of green-black, tenacious, and immobile bile and mucus which causes gallbladder distension, cystic mucosal hyperplasia, cholangitis, and biliary outflow obstruction if the material extends into the cystic, hepatic, and bile ducts.[62] The presence of a large gallbladder filled with hyperechoic nongravitationally dependent material (an immobile stellate, radial, or kiwi fruit appearance) and a hypoechoic ‘‘rim sign’’ are consistent

with a gallbladder mucocele on US (Figure 1.14).[1,18,20,41,63,64] Canine gallbladder mucoceles on computed tomography have been reported to have a common central distribution of the intraluminal mineral material in approximately 67% of cases with gallbladder wall distension (Figure 1.15).[25,41] This pattern demonstrates the dense central gallbladder conglomerate comprised of thick sludge with mucin that is tightly adhered to the gallbladder mucosa (hypoechoic rim sign).[1,41] Some gallbladder mucoceles have a mixed echogenic, mosaic-like appearance on US.41 So while there is a variety of ultrasonographic appearances to gallbladder mucoceles, the key to diagnosis is that the luminal contents are not gravitationally dependent and the gallbladder is distended.[41,65,66] Consideration for a gallbladder mucocele is warranted when sequential US examinations fail to identify a reduction in gallbladder size or content after feeding.[1] Additionally, the hepatic parenchyma is often hyperechoic because of coexistent vacuolar hepatopathy or hypoechoic if acute hepatitis is present.[41,43,64] Progressive gallbladder distention may lead to necrotizing cholecystitis.

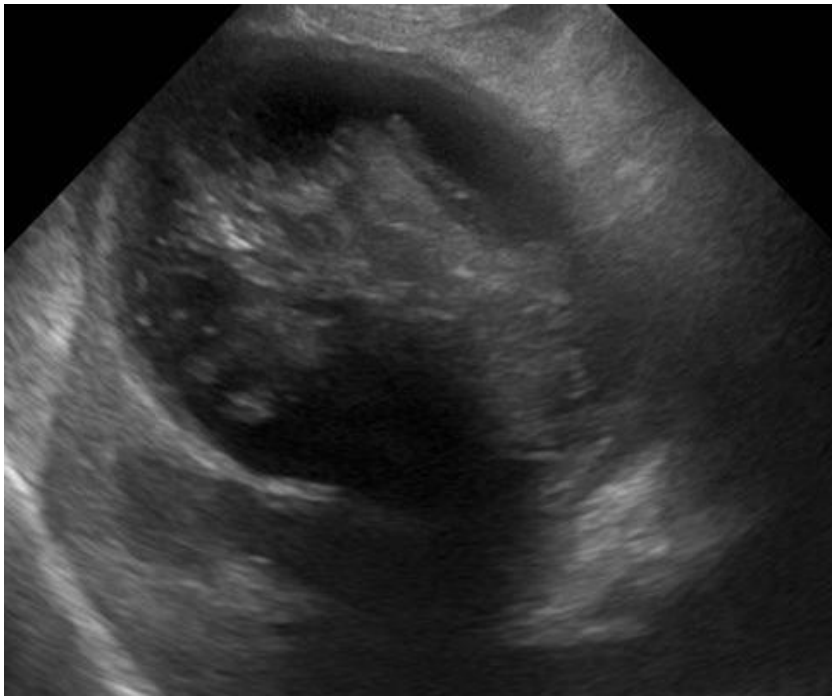

Figure 1.14 Canine gallbladder mucocele on ultrasound, in sagittal view. The gallbladder is markedly dilated with suspended hyperechoic material. The gallbladder wall is thickened and hypoechoic. The surrounding mesentery is hyperechoic consistent with surrounding peritonitis and steatitis.

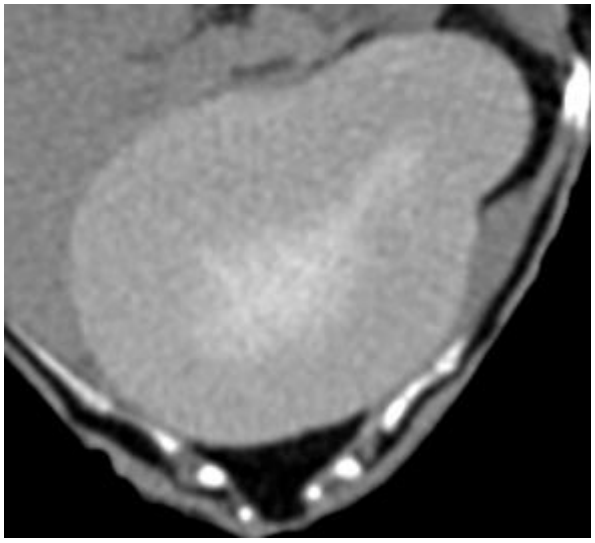

Figure 1.15 Canine gallbladder mucocele on computed tomography (precontrast computed tomography image in a soft tissue window). Gallbladder mucoceles typically cause gallbladder wall dilation and central mineral attenuating material.

Mucins are important in the development of gallbladder mucoceles. Mucins are a type of polysaccharides secreted by mucosal epithelial cells of the gallbladder, stomach, intestines and other organs and act as surfactants and protect the mucosal epithelium by preventing enzymatic self-digestion.[20] The bile is concentrated and dehydrated through the actions of the Na^+/K^+ and Cl^-/HCO^3 pumps of gallbladder epithelial cells and/or aquaporins, channels that transport water.[20] These transport channels normally manipulate the composition of gallbladder bile for production of the final bile product, but in disease states abnormal functioning of bile moisture absorption mechanisms might be involved in the pathophysiology of gallbladder mucoceles.[20]

The specific etiology of gallbladder mucocele development in dogs remains unknown, but a continuous transition from echogenic gallbladder sludge to the stellate and kiwi fruit like pattern has been proposed.[66] Echogenic bile first occupies the gallbladder lumen, then the formed central gallbladder conglomerate adheres to the gallbladder wall margin (stellate pattern), and then fine striations increase with a decrease in residual echogenic sludge in the center of the gallbladder (kiwi fruit like pattern).[66] Decreased gallbladder motility (which can be secondary to geriatric age or steroidal influence) can cause luminal cholestasis and enhanced absorption, promoting formation of biliary sludge and, in theory, gallbladder mucoceles.[1] In an ultrasonographic study with 43 dogs, 23% had immobile echogenic bile, 30% had an incomplete stellate pattern, 12% had the typical stellate pattern, 26% had a kiwi like pattern and stellate combination, 9% had a kiwi like pattern with residual central echogenic bile, and no patients had a kiwi like pattern.[66] The stellate pattern overall was the most common regardless of clinical signs.[66]

Progressive expansion of a gallbladder mucocele can cause gallbladder ischemic necrosis, bile peritonitis, and opportunistic infection.[1] In patients with a gallbladder mucocele

with gallbladder wall rupture, pericholecystic fat will be hyperechoic, the gallbladder may be surrounded by a rim of anechoic fluid creating a hypoechoic "halo", and the gallbladder wall may be hyperemic, thickened, or discuontinuous.[41,64,67] A larger volume of peritoneal effusion is also possible and suggests gallbladder rupture.[1] The diagnostic utility of US for detecting gallbladder rupture in dogs with biliary mucoceles is overall good (especially when combined with other findings including localized echogenic peritoneal fluid, echogenic reaction in the gallbladder fossa, and echogenic diffuse peritoneal fluid) but not very specific.[1,37] The most common pattern in dogs with gallbladder rupture was the incomplete stellate pattern in the study with 43 dogs with gallbladder ruptures due to mucoceles.[66] This study also found no significant correlations between ultrasonographic patterns of gallbladder mucoceles and clinical disease status or gallbladder rupture.[66] However, unfortunately dogs with gallbladder rupture at the time of surgery are 2.7 times more likely to die than dogs without gallbladder rupture.[65] Rarely, a ruptured gallbladder will release a well-organized mucocele into the peritoneal cavity where it may cause pain and peritoneal effusion that can be identified on US.[1,68,69]

Aerobic bacteria have been cultured from bile or gallbladder wall, with a number of enteric organisms identified including *Escherichia coli*, *Enterobacter* spp, *Enterococcus* spp, *Staphylococcus* spp, *Micrococcus* spp, and *Streptococcus* spp.[1]

Approximately 23% of dogs with gallbladder mucoceles do not show clinical signs.[41,64,66] An increased incidence of gallbladder mucoceles has been identified in many dog breeds including Shetland Sheepdogs, American Cocker Spaniels, Chihuahua, Pomeranian, Miniature Schnauzers, Boston Terriers, and possibly Affenpinschers.[43,62,70] Previously identified factors predisposing to canine patients to gallbladder mucocele formation include middle to geriatric age, hyperlipidemia/hypercholesterolemia (idiopathic, pancreatitis, nephrotic syndrome, or

endocrinopathies including hyperadrenocorticism and hypothyroidism), gallbladder dysmotility, neonicotinoids (a class of insecticides chemically related to nicotine), increased serum leptin, and cystic mucosal hyperplasia that adheres to mucinous debris and compromises mechanical gallbladder emptying.[1,71,72] Shetland Sheepdogs and Miniature Schnauzers have a breed predisposition for hyperlipidemia/hypercholesterolemia which may explain their higher incidence of gallbladder mucocele. Overall, these conditions may alter the composition of bile and mucin or effect gallbladder motility (with it likely being many mechanisms working cooperatively concurrently) in gallbladder mucocele formation with both genetic and epigenetic factors affecting each predisposed breed.[19,62]

Various genetic and metabolic factors have been identified to affect gallbladder mucocele formation in dogs. An insertion mutation in the ABCB4 gene has been identified in Shetland sheepdogs with a recent study showing 14/15 affected dogs had gallbladder mucoceles, but not 20/21 unaffected individuals.[48] The ABCB4 gene mutation impairs secretion of a protective phospholipid across the canalicular membrane that protects the gallbladder epithelium to the irritant properties of bile.[48] A later study did not find the ABCB4 gene mutation to be linked to gallbladder mucocele formation in this breed.[73] This mutation may or may not explain the predisposition of this breed to gallbladder mucocele formation.[48]

In another retrospective study of 78 dogs diagnosed with gallbladder mucoceles, the odds of gallbladder mucocele formation in dogs with hyperadrenocorticism were 29 times that of dogs without hyperadrenocorticism.[49] Also in this population, a weaker positive association was identified for hypothyroidism as these patients had a threefold increased risk.[49]

The bloodwork abnormalities in canine patients with gallbladder mucocele are similar to patients with other biliary diseases or may be normal. A previous study showed 11 of 43 dogs

(five symptomatic and six asymptomatic dogs) had normal leukocyte counts and normal concentrations of ALT and total bilirubin.[66] The number of leukocytes and serum concentrations of ALT and total bilirubin were also significantly higher in symptomatic dogs than asymptomatic dogs, but symptomatic dogs did not all have hyperbilirubinemia.[66] Hepatitis with or without cholangitis has been described in patients with gallbladder mucoceles, and liver biopsies are recommended during cholecystectomy.[47]

In order to avert gallbladder mucocele maturation and gallbladder wall ischemic necrosis, as these patients have a higher chance of death, elective cholecystectomies at early stages of gallbladder disease can be performed.[47] Surgical candidates for the elective procedure include subclinical gallbladder mucocele or non-gravity dependent biliary sludge with concurrent gallbladder dysmotility.[47]

Bile Peritonitis

Bile peritonitis is caused by bile exiting the biliary tract into the peritoneal space causing marked inflammation in the abdomen. Abdominal pain with peritoneal effusion containing a disproportionately high bilirubin concentration is consistent with a ruptured biliary tree as with cholecystitis, choledochitis, neoplasia, gallbladder mucocele, or blunt abdominal trauma.[1] These patients require emergency surgical intervention to resolve the biliary leakage site and decontaminate the peritoneal space. In febrile animals with suspected biliary disease, early performance of cytology and cultures of blood, urine, and hepatic or bile aspirates can expedite identification of involved organisms and appropriate treatment whether surgical or medical.[1]

Extrahepatic Biliary Duct Obstruction

Extrahepatic biliary duct obstruction (EHBDO) is a disease process that causes occlusion of the biliary outflow tract through the bile duct which is most commonly from severe pancreatitis and obstructive choledocholithiasis. After acute complete obstruction, dilation of the bile duct and cystic duct are evident within 24 hours.[52,74] Distention of intrahepatic bile ducts occurs within 5 to 7 days after with concurrent hepatomegaly.[52,74] Dilated hepatic ducts are differentiated ultrasonographically from portal and hepatic veins by their irregular branching patterns, tortuosity, and absence of blood flow on Doppler interrogation.[52] Bile duct diameter is variable and specific numerical diameter cutoffs cannot be used to determine the chronicity of obstruction.[1] However, severe duct dilation develops after 4 to 6 weeks of complete EHBDO.[74] Obstruction of hepatic duct(s) within a single liver lobe can be difficult to ultrasound due to the previously discussed limitations of hepatobiliary US examination. Affected animals are not hyperbilirubinemic but do have increased liver enzyme activity.[1] Once distended by chronic obstructive pathologies (greater than 6 weeks), intra- and extrahepatic bile ducts may remain dilated compromising dynamic postprandial assessments and may lead to biliary cirrhosis, portal hypertension, and acquired portosystemic shunts.[1,12,52] If the obstruction resolves within the first several weeks, periductal fibrosis and bile duct distention may completely resolve.[1]

During EHBDO, opportunistic bacterial colonization of the biliary tract may occur from enteric or hematogenously spread agents from the hepato-biliary-enteric bacterial circulation.[1] Antimicrobial treatment of biliary sepsis alone is ineffective because of inadequate antibiotic penetration to the biliary tract and inability to mechanically clear bacterial organisms due to the obstruction.[1] These patients may require surgical biliary decompression. Some patients with EHBDO are intermittently anorexic while others are polyphagic, consistent with fat maldigestion

secondary to the absence of duodenal bile acid delivery.[1] Extrahepatic biliary duct obstruction diagnosis can be diagnosed with abdominal US, CT, and/or exploratory laparotomy.

Severe pancreatitis is the most common cause of EHBDO in dogs and causes obstruction of the bile duct at the level of the duodenal papilla from periductal fibrosis and duct stricture due to severe inflammation.[1] In most dogs with EHBDO secondary to severe acute pancreatitis, obstruction resolves spontaneously as the pancreatitis resolves, and surgical intervention not required.[1] However, if EHBDO persists beyond 14 days due to pancreatitis, temporary or permanent decompression (including stent placement) of the biliary tract may be needed.[1] Canine patients who do require surgical intervention (as with obstructive choledocholithiasis or biliary sludge), a duodenotomy, cholecystostomy, and/or choledochotomy may be necessary for passage of a flexible catheter into the bile duct to verify the site of obstruction and to allow removal of inspissated biliary sludge or choleliths.[1] A previous study of dogs undergoing extrahepatic biliary surgery in dogs with pancreatitis reported a 50% mortality in dogs and prolonged hospitalization length.[75] Thus, the high complication rates of surgery in concurrent pancreatic disease in dogs with EHBDO likely reflects the underlying diseases and their effects on the animal (septic bile peritonitis, higher serum creatinine, prolonged partial thromboplastin time [PTT], and lower postoperative mean arterial pressure) rather than complications of surgery.[75]

A recent retrospective study evaluated 46 dogs with pancreatitis associated bile duct obstruction (PABDO) to see if presumed markers of disease severity are predictors of survival.[76] Thirty-three of 42 (79%) the dogs with PABDO survived. Two of the 4 dogs that underwent percutaneous or surgical decompression of the gallbladder died. This study found that the median bile duct dilatation at the time of ultrasonographic diagnosis of PABDO and peak

bilirubin were not different between survivors and nonsurvivors. The study also concluded dogs with PABDO often have a prolonged course of illness and improve clinically despite biochemical evidence (hyperbilirubinemia) of progression of EHBDO.

Choledochal stenting has been extensively used in humans to presurgically decompress EHBDO, presurgical stabilization, and manage obstructive biliary disease because of malignant processes.[1] Limited publications of dogs with EHBDO managed with choledochal stenting have been reported.[77,78] Stents can be placed during surgical exploration or retrograde endoscopically via the major duodenal papilla.[77,78] Complications of stent placement include stent obstruction with bile concretions, duct stricture formation due to granulation or fibrous tissue deposition (promoted by stent mechanical trauma), and intralumenal interference with bile drainage that promoted cholangitis.[1]

Biliary Congenital Abnormalities

Congenital abnormalities of the gallbladder are rare and include gallbladder agenesis, biliary atresia, and bilobed gallbladder. Gallbladder agenesis is defined as the absence of growth of the gallbladder in utero which is a nonclinical abnormality as the hepatic bile can transit through the remaining biliary tract normally.[1] Biliary atresia is a congenital anomaly where a portion of the bile duct, cystic duct, or hepatic ducts are malformed and stenotic which leads to jaundice and progressive hepatopathy in young animals.[1] A bilobed gallbladder is an uncommon incidental finding in cats.

Fibropolycystic Liver Diseases

Fibropolycystic liver diseases have been identified in many species and often involve the biliary structures and renal tubules.[1] Abnormal embryonic ductal plate development at various

stages forms cystic lesions involving intrahepatic or extrahepatic bile ducts.[1] Embryologically, the ductal plate is comprised of a cylindric tube of cells surrounding portal vein branches.[1] Biliary ducts form through remodel and partial involution of the ductal plates.[1] Ductal malformations form as ductal plate components are unevenly remodeled.[1] The different types of malformations are determined by the time and stage of development at which the embryogenesis and remodeling are disturbed (large ducts versus small ducts, intrahepatic versus extrahepatic).[1]

CHAPTER II

STUDY

Study Objectives

This study was performed with the following objectives:

1) To describe the CT appearance of various biliary diseases in dogs presenting for acute abdominal signs.

2) To compare the accuracy of CT with that of abdominal US in the diagnosis of biliary disease in dogs presenting with acute abdominal signs.

Hypotheses

The hypotheses were that CT will allow for detection of various biliary diseases in the dog, including bile duct enlargement, choleliths, and mucocele formation, with similar accuracy to US, and that US would be superior to CT for investigation of the bile ducts and the diagnosis of cholecystitis due to the small size of these structures in the dog.

Preliminary Studies

Contrast-enhanced abdominal CT is performed frequently at the Mississippi State University College of Veterinary Medicine Animal Health Center, and standard protocols have been developed, which are described in the methods section. In addition, abdominal CT has been performed on animals presenting for acute abdominal signs. Although abdominal US is more

commonly performed in canine patients presenting with acute abdominal signs, in cases in which CT has been performed in these animals, rapid and accurate diagnoses have been made.

Materials and Methods

Study population

This study was a prospective, observational study completed following institutional IACUC approval. The study population consisted of client-owned dogs presenting to the small animal care services with acute abdominal signs suspected to be related to the biliary tract whose diagnostic plan included an abdominal US. Inclusion criteria included patients presenting for any signs of acute abdominal disease potentially referable to the biliary tract, including vomiting, lethargy, anorexia, jaundice, abdominal pain, or fever. Exclusion criteria included dogs with a previous cholecystectomy and patients unable to be sedated. Dogs were enrolled following informed owner consent. Animals enrolled in the study with signs of acute abdominal pain and with no evidence of biliary disease on US, cytology, and histopathology served as negative controls for the comparison of the performance of CT and US. Considering US as the gold standard for diagnosing biliary disease in dogs, sample size calculations using McNemar's test of two dependent groups were performed for detecting biliary disease using available statistical software (G*Power v 3.1.92, Heinrich Heine, Universität Düsseldorf) and determined a total of 60 dogs were required for adequate statistical power to compare the two modalities. Thirty of these dogs would be those diagnosed with biliary disease and 30 of these dogs presenting for acute abdomen with no evidence of biliary disease would serve as negative controls.

Imaging and measurements

Dogs received an abdominal US examination by a board-certified radiologist or by a diagnostic imaging resident under supervision of a board-certified radiologist either immediately prior to or following the CT examination, using a GE LOGIQ S8 ultrasound machine (General Electric, Boston, MA) with a C3-10-D Broad Spectrum microconvex transducer (6-10 MHz) or a 11L-D linear transducer (9-12 MHz), depending on body size (General Electric, Boston, MA). Briefly, the dogs were placed in dorsal or in left lateral recumbency, depending on body size. The hair was locally clipped, and coupling gel was applied to provide adequate probe contact. An US was performed according to the preferences of the sonographer and included both still images and cine clips of the liver, gallbladder, bile duct, and pancreas.

Dogs were sedated as needed, using protocols chosen by the attending clinicians on each case. The sedation protocol was recorded. The animals then underwent a dual-phase abdominal CT examination using a Toshiba Aquilion 16-slice multi-detector scanner (Toshiba Corp, Toshiba American Medical Systems, INC., Tustin, CA). Dogs were positioned in ventral recumbency, and the field of view included the cranial aspect of the diaphragm cranially and the acetabula caudally. The following protocols were used: 16 x 0.5 or 16 x 1.5 mm collimation, 100-120 kVp, 80-200 mAs, a helical pitch of 1.5, and a field of view large enough to encompass the abdomen. All protocols were based on patient size and determined by the principal investigators or a board-certified radiologist overseeing radiology residents, interns, and certified technicians. A precontrast series was acquired. Immediately following this acquisition, all animals were administered a bolus of ioversol (Optiray 320, Guerbet, Princeton, JN) or iohexol (Omnipaque 240, GE Healthcare, Marlborough, MA) at 704 mg/kg body weight for ioversol and 527 mg/kg body weight for iohexol via an intravenous catheter followed by a saline flush, some

with the assistance of a power injector. Early hepatic (10-30 seconds) and late venous (90-120 seconds) post-contrast series were then acquired. All images were acquired using a soft tissue algorithm with variable slice thickness ranging from 1 mm to 3 mm, based on patient size. Transverse, sagittal, and dorsal reconstructions were created based on volume acquisitions in all phases.

Following imaging, all CT and US images and clips were sent to a picture archiving and communication system (PACS) and displayed using a digital imaging and communications in medicine viewer (eUnity, Client Outlook Inc, Ontario, Canada). The radiologist and a radiology resident were blinded to the results of the US and reviewed randomized, anonymized CT images and US images and cine clips. Specifically, the evaluators recorded the following on CT: gallbladder wall thickness, HU of the bile, presence or absence of hyperattenuating material within the gallbladder lumen (and whether or not it is gravity dependent), ability to identify the bile duct and intrahepatic bile ducts, and, if applicable, size of the bile duct and intrahepatic bile ducts. The following US findings were recorded: gallbladder wall thickness, presence or absence of hyperechoic material within the gallbladder lumen, ability to identify the bile duct and intrahepatic bile ducts, and, if applicable, size of the bile duct and intrahepatic bile ducts. The CT and US appearance of the liver and pancreas and a final CT and US diagnosis were also recorded. The observers' measurements were averaged. Any discrepancies were discussed until a consensus was made.

Patients were considered to be positive for biliary pathology on CT or US for any of the following criteria: thickened gallbladder wall, dilated bile duct or intrahepatic bile ducts, cholelithiasis, and findings previously described to be consistent with a gallbladder mucocele. The presence of gallbladder sludge on US was not considered as positive for biliary pathology.

While it has been linked to decreased gallbladder emptying, there has not been a strong correlation to clinical signs as an isolated finding in dogs. Final clinical diagnoses were positive for biliary pathology by pathology identified by US, cytology, and/or histopathology. Mineral attenuating structures identified on CT were also considered to be positive for pathology as it has been previously acknowledged to be more sensitive that US in the detection of mineral attenuating structures.[23] The final clinical diagnoses were used to compare the positive or negative diagnoses of CT and US.

Statistical Methods

Agreement between each modality and final clinical diagnosis for the outcomes of gallbladder wall mass, gallbladder mucocele, gallbladder wall edema, cholelith, cholangitis, hepatitis, pancreatitis, pancreatic edema, and cystic mucosal hyperplasia and agreement between the two modalities for the previously listed outcomes as well as wall thickness, bile HU, bile duct identification, bile duct size, hepatic duct identification, hepatic size, liver, and pancreas were assessed by intraclass correlation coefficients (ICC)[79] using PROC MIXED in SAS for Windows v. 9.4 (SAS Institute, Inc., Cary, NC). Models for each pairwise comparison were fitted with the outcome as the dependent variable and method of diagnosis (US vs CT, US vs final clinical diagnosis, or CT vs final clinical diagnosis) as the fixed effect with dog identity included as a random effect[80]. The association between true pathology diagnosis and diagnosis by each modality (US or CT) were assessed by separate logistic regression models using PROC LOGISTIC in SAS for Windows v9.4 with true pathology as the dependent variable. Where necessitated by scarcity of data, analysis of penalized maximum likelihood estimates using the firth option was used. An alpha level of 0.05 was selected a priori. Although no standard values for acceptable agreement using ICC have been established,[81] suggested that ICC values less than

0.5, values between 0.5 and 0.75, values between 0.75 and 0.9, and values greater than 0.9 indicated poor, moderate, good, and excellent agreement. All statistical analyses were performed by a board-certified epidemiologist with extensive experience in statistical analyses.

Study results

Study population results

The age of the population ranged from 2 to 20 years old with a mean of 9.1 years old and median of 10 years old. The weight of the population ranged from 2.6 to 50 kg with a mean of 12.4 kg and median of 7.2 kg. The breeds of the included dogs were as follows: 5 Yorkshire terriers, 4 mixed breed dogs, 3 Labrador retrievers, 2 chihuahuas, 2 miniature poodles, 2 miniature schnauzers, 2 standard poodles, and 1 of each the following American pit bull, beagle, boxer, Cairn terrier, Chinese crested, dachshund, English bulldog, Jack Russell terrier, maltepoo, Maltese, rat terrier, Shetland sheepdog, Shih tzu, Welsh corgi, and West Highland terrier.

Anorexia was the most common clinical sign (24 of 35 patients). Vomiting (21 of 35 patients) and lethargy (20 of 35 patients) were the next most common clinical signs. The least common clinical signs were jaundice (4 of 35 patients), abdominal pain (2 of 35 patients), and fever (1 of 35 patients). Twenty-six of the 35 patients with clinical signs had at least 2 or more clinical signs.

Imaging results

Thirty-five patients were enrolled in the study with 28 having biliary pathology and seven having no evidence of biliary disease serving as controls. The final clinical diagnoses of patients with biliary pathology included cholelithiasis (n=7), gallbladder mucoceles (n=6), cholangiohepatitis/cholangitis (n=6), extrahepatic biliary obstruction (n=5), gallbladder wall

edema (n=2), gallbladder wall mass (n=1, malignant carcinoid), and cystic mucosal hyperplasia (n=1). The gallbladder mucoceles also had cholangiohepatitis with many also having cystic mucosal hyperplasia. One of the gallbladder mucoceles had confirmed gallbladder wall rupture with one other case having a possible ruptured at surgery. The five extrahepatic biliary duct obstructions were due to pancreatitis (n=2) and choledocholithiasis (n=3). Three cases (bacterial cholangitis, cholecystitis, and cystic mucosal hyperplasia) also had mineralized gallbladder sludge and/or pinpoint choleliths on the CT studies. The final diagnoses in the control patients included pancreatitis (n=2), neoplasia involving the liver (n=2, metastatic oral melanoma and lymphoma), hepatitis (n=1), acute hemorrhagic gastroenteritis (n=1), and presumed Fanconi syndrome (n=1). The summary of the patients' signalment, final positive or negative diagnosis for biliary pathology, and described final clinical diagnosis and cytology and histopathology results are summarized in Table 1.

Table 2.1 Summary of the patient's signalment (age, sex, breed, weight), true pathology diagnosis of positive or negative for biliary pathology, and described final clinical diagnosis with cytology and histopathology diagnoses when available. For sex, FI=female intact, FS = female spayed, MI=male intact, and MN=male neutered.

Age (years)	Sex	Breed	Weight (kg)	True Pathology	Described Final Clinical Diagnosis and Cytology/Histopathology Results
10	FS	Miniature Poodle	10.6	Positive	Gallbladder mucocele confirmed by surgery and histopathology. Liver histopathology - cholangiohepatitis
8	FS	Miniature Schnauzer	8.6	Positive	Copper storage disease on liver biopsy. Cholelith
4	MN	American Pit Bull	33.5	Positive	Presumed anaphylaxis
9	FS	Shetland Sheepdog	6.1	Positive	Gallbladder mucocele on surgery and histopathology. Liver histopathology - chronic active hepatitis
9	FS	Miniature Schnauzer	6	Positive	Pancreatitis. Cholangiohepatitis. Probable delayed plasma transfusion reaction
20	MN	Mixed bree dog	6.3	Positive	Gallbladder mucocele confirmed by surgery and histopathology. Liver histopathology - cholestatic hepatic portal fibrosis and mild suppurative cholangiohepatitis
12	FS	Rat Terrier	8.8	Positive	Gallbladder mucocele confirmed by surgery and histopathology.

Table 2.1 (continued)

4	FS	Yorkshire Terrier	7.2	Negative	Pancreatitis
14	MN	Standard Poodle	20	Negative	Oral melanoma metastasis to liver
10	FS	English Bulldog	17.1	Positive	Gallbladder mass malignant carcionoid on histopathology
10	MN	Miniature Poodle	4.2	Positive	Pancreatitis causing extrahepatic biliary duct obstruction
10	FS	Welsh Corgi	17.4	Negative	Histopathology - stage IV multicentric T cell lymphoma of liver
12	FS	Chinese Crested	4	Positive	Histopathology - severe cholangiohepatitis (lymphoplasmacytic and suppurative) and severe acute hepatocellular necrosis. Concern for toxin then severe chronic pancreatitis
6	FS	Maltese	5.7	Positive	Pancreatitis. Cholelithiasis. Liver cytology - cholestasis and suspect mild mixed inflammation with neutrophilic predominance
8	MN	Cairn Terrier	8.5	Positive	Liver histopathology - moderate to severe chronic cholangiohepatitis that is likely due to an ascending biliary tree infection with chronic cholestasis
10	MI	Chihuahua	3.4	Positive	Cholelith. Pancreatitis. Liver cytology - cholestasis
12	FS	Beagle	6.7	Positive	Ruptured gallbladder mucocele at surgery. Necropsy concluded systemic inflammatory response syndrome secondary to necrosuppurative cholecystitis
5	FI	Labrador Retriever	44.5	Positive	Cholelith. Chronic hepatitis. Liver cytology - significant cholestasis and mild to moderate hepatocellular vacuolization
9	FS	Mixed breed dog	2.6	Positive	Cholecystolithiasis. Obstructive choledocholithiasis.
9	FS	Mixed breed dog	18.2	Positive	Cholecystolith. Gastritis. Hyperadrenocorticism. Liver cytology - mild lipid accumulation
4	FS	Shih Tzu	5.8	Negative	Presumptive Fanconi Syndrome
7	FI	Boxer	23.8	Negative	Liver histopathology - vacuolar hepatopathy (steroid hepatopathy), diffuse, chronic, severe with mild cholestasis. Small intestines histopathology - proliferative enteritis.
10	MN	Standard Poodle	23.9	Positive	Bacterial cholangitis. Mineralized gallbladder sludge and pinpoint choleliths. Bile cytology - significant bactibilia with E. coli growth. Liver cytology - no significant hepatocellular atypia
3	FI	Jack Russell Terrier	5.6	Negative	Gastroenteritis. Possible pancreatitis
11	FS	Labrador Retriever	23.3	Positive	Severe pancreatitis with secondary extrahepatic biliary obstruction. Bile cytology - normal with no growth on culture. Liver cytology - cholestasis
10	FS	Yorkshire Terrier	7.2	Positive	Pancreatitis. Gastritis. Colitis. Mineralized gallbladder sludge/pinpoint cholecystolithiasis
9	MN	Yorkshire Terrier	4.9	Positive	Cholecystitis. Cholelithiasis. Pancreatitis. Normal bile cytology with no growth on culture. Liver cytology - compatible with lymphoma and evidence of cholestasis.
12	FS	Yorkshire Terrier	3.6	Positive	Obstruction secondary to choledocholith and cholecystolithiasis. Surgery confirmed. Gallbladder culture - moderate growth of possible hemolytic Escherichia coli. Pancreatitis
4	FS	Yorkshire Terrier	3.4	Negative	Acute hemorrhagic gastroenteritis
11	FS	Maltepoo	4.7	Positive	Obstruction secondary to choledocholith and cholecystolithiasis. Cholecystitis. Liver cytology - probable mild mixed inflammation and modest amounts of cholestasis. Bile culture - heavy growth of Enterobacter cloacae. Bile cytology - significant bactibilia

Table 2.1 (continued)

14	MN	Chihuahua	5.6	Positive	Cystic mucosal hyperplasia, mineralized gallbladder sludge/pinpoint cholecystoliths. Right external iliac artery thrombus. Bile cytology: normal. Bile culture: Growth of Bacillus sp
2	FS	Mixed bree dog	15.2	Positive	Protein-losing enteropathy. Cholangitis vs gallbladder wall edema. Pancreatic edema. Stomach histopathology - eosinophilic, lymphoplasmacytic gastritis with fibrosis, mild, chronic-active. Duodenum histopathology - eosinophilic, lymphoplasmacytic duodenitis with lacteal dilation, mild to moderate, chronic-active
12	FS	Dachshund	5.6	Positive	Mineralized gallbladder sludge or pinpoint choleliths. Concern for primary liver pathology. Liver cytology - minimal evidence of active chronic hemorrhage, mild hepatic lipidosis, probable mild mixed inflammation
5	MI	Labrador Retriever	50	Positive	Severe acute pancreatitis. Focal choledochitis
12	MN	West Highland Terrier	10.3	Positive	Gallbladder mucocele with possible rupture. Pancreatitis

Statistical evaluation was performed to evaluate agreements between both modalities (US and CT) compared to the final clinical diagnoses (Table 2.2).

Table 2.2 Summary of positive and negative final diagnoses determined on true pathology, ultrasound, and computed tomography.

	US	CT	TRUE
Total positive	22	29	28
Total negative	13	6	7

There was a significant association between the final US positive or negative diagnosis for biliary pathology and the final clinical diagnosis (p=0.0116) via analysis of paralyzed maximum likelihood estimates and a chi-square (Figure 2.1). The odds of the final clinical diagnosis being positive when the US diagnosis was positive is 51.9 times greater than when the US diagnosis was negative. This was a 95% Wald confidence limits of 2.421->999.999. The overall calculated accuracy of the ultrasonographic final diagnoses compared to the true pathology was 82.9% (29/35 of patients). There were six false negative cases due to

cholelithiasis which were identified on CT. When the six false negative diagnoses for cholelithiasis were removed, US agreed with the remaining 29 final clinical diagnoses with other biliary pathologies (discussed more below).

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	14.4794	1	0.0001
Score	14.4478	1	0.0001
Wald	6.3765	1	0.0116

Analysis of Penalized Maximum Likelihood Estimates

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept		1	-0.1431	0.5561	0.0663	0.7969
USPathology	Positive	1	3.9498	1.5642	6.3765	0.0116

Odds Ratio Estimates

Effect	Point Estimate	95% Wald Confidence Limits	
USPathology Positive vs Negative	51.925	2.421	>999.999

Figure 2.1 Statistical evaluation of the final positive or negative ultrasonographic diagnosis compared to the true diagnosis for biliary pathology in this group of canine patients.

There was a significant association between the final CT positive and negative diagnosis and the final clinical diagnosis for biliary pathology (p=0.0022) via analysis of paralyzed maximum likelihood estimates and a chi-square (Figure 2.2). The odds of the final clinical diagnosis being positive when final CT diagnosis was positive is 247.0 times greater than when CT final diagnosis was negative. The overall calculated accuracy of the CT final diagnosis

compared to the true pathology was 97.1% (34/35 of patients). One false positive case had identified a dilated bile duct on the CT study (bile duct measured 5 mm in diameter) while the biliary tract was normal on US.

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	23.1203	1	<.0001
Score	29.5132	1	<.0001
Wald	9.3721	1	0.0022

Analysis of Penalized Maximum Likelihood Estimates

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept		1	-2.5649	1.5851	2.6182	0.1056
CTPathology	Positive	1	5.5093	1.7996	9.3721	0.0022

Odds Ratio Estimates

Effect	Point Estimate	95% Wald Confidence Limits	
CTPathology Positive vs Negative	246.982	7.258	>999.999

Figure 2.2 Statistical evaluation of the final positive or negative computed tomographic diagnosis compared to the true diagnosis for biliary pathology in this group of canine patients.

Both US and CT successfully identified the one gallbladder wall mass (malignant carcinoid) with 100% agreement in all cases (Figure 2.3).

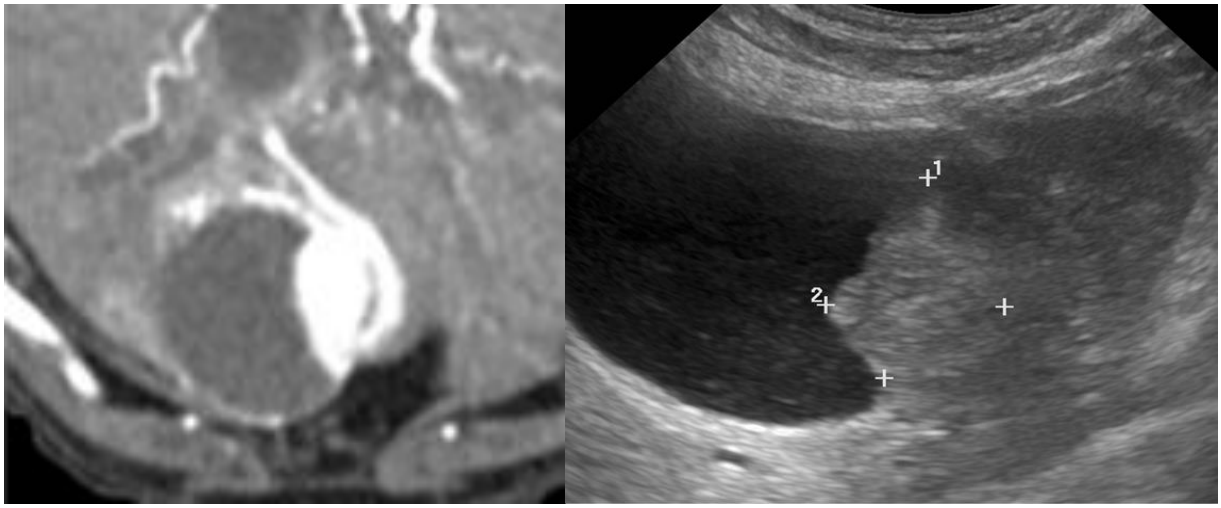

Figure 2.3 Canine malignant gallbladder carcinoid on CT and US. Left image: Strong homogenous arterial contrast enhancing gallbladder wall mass on CT (transverse soft tissue window). Right image: Same gallbladder wall mass on US (longitudinal view) which displayed a large amount of blood flow on color Doppler interrogation.

Ultrasound and CT performed equally to identify all of the gallbladder mucoceles as there were no discordant pairs and the ICC equaled 1.0000 (Figure 2.4). Both US and CT successfully identified the six gallbladder mucoceles with 100% agreement in all cases. All gallbladders had similar imaging appearances as previously described.

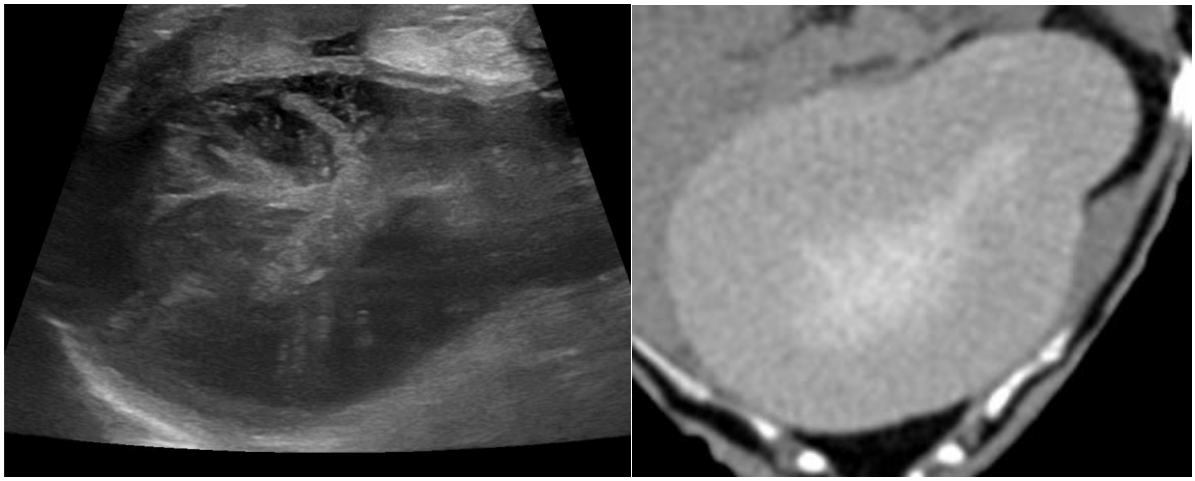

Figure 2.4 Canine gallbladder mucocele on US and CT. Left image: Classic appearance of a canine gallbladder mucocele with central stellate hyperechoic intraluminal material, gallbladder dilation, thickened and hypoechoic gallbladder wall, small volume surrounding peritoneal free fluid, and hyperechoic mesentery consistent with peritonitis. Right image: Same gallbladder mucocele on CT (noncontrast enhanced transverse soft tissue window) with severe gallbladder dilation and central hyperattenuating material.

There was no significant difference with moderate agreement between the proportions that were positive and negative on US and CT in the identification of the gallbladder wall edema as the McNemar's test P-value was 0.2500 and ICC was 0.55556. Both US and CT successfully identified the two gallbladder wall edema cases. Additionally, CT had three false positives for gallbladder wall edema. There was no significant difference with moderate agreement between the proportions that were positive and negative on CT identifying gallbladder wall edema as the McNemar's test P-value was 0.2500 and ICC was 0.66340.

There was no significant difference with good agreement between the proportions that were positive and negative on US and CT in the identification of the cholangitis as the McNemar's test P-value was 0.2500 and ICC was 0.82796. Both US and CT successfully identified the 21 cholangitis cases with US agreeing with all of the final clinical diagnoses of the

cases with and without cholangitis. Many of these cases had concurrent pathologies such as a gallbladder mucocele or cholelithiasis. There was no significant difference with good agreement between the proportions that were positive and negative on CT identifying cholangitis as the McNemar's test P-value was 0.2500 and ICC was 0.84368.

There was statistical significance with poor agreement in the identification of cholelithiasis between US and CT as the McNemar's test P-value was 0.0039 and ICC was 0.47297. Ultrasound only successfully identified five of the 13 cases with cholelithiasis resulting in eight false negatives (Figure 2.5). This was statistically significant as the McNemar's test P-value was 0.0078 and ICC was 0.70431. Computed tomography identified all the cases of cholelithiasis with one additional false positive (a case with a confirmed gallbladder mucocele). There was no significant difference with excellent agreement between the proportions that were positive and negative on CT identifying cholecystolithiasis as the McNemar's test P-value was 1.0000 and ICC was 0.96129. This showed CT agreed with the cholelithiasis final diagnosis more than US.

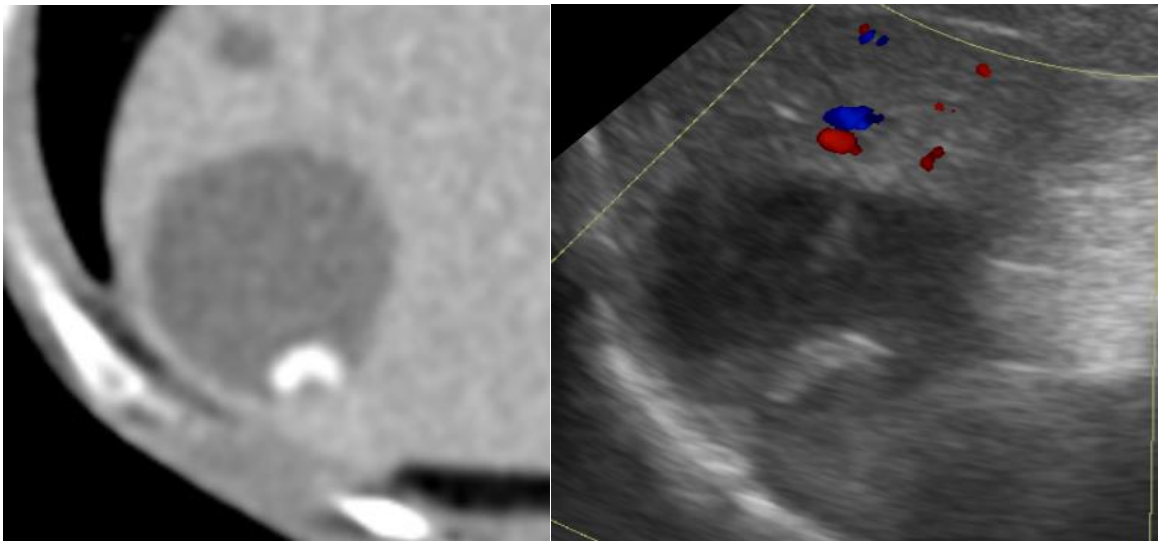

Figure 2.5 Canine cholelithiasis on CT and US. Left image: Mineral attenuating structure in the gravity dependent portion of the gallbladder on CT consistent with a cholecystolith (contrast enhanced transverse soft tissue window image). Right image: Same structure on US with color Doppler interrogation in the sagittal plane. This structure is hyperechoic and has a similar shape to the structure on CT but does not display distal acoustic shadowing or twinkle artifact so was dismissed as inspissated gallbladder sludge.

There was no significant difference with poor agreement between the proportions that were positive and negative on US and CT in the identification of hepatitis as the McNemar's test P-value was 0.5488 and ICC was 0.21667. There was no significant difference with poor agreement between the proportions that were positive and negative on US and CT in the classification of the liver as being normal or abnormal as the McNemar's test P-value was 0.2266 and ICC was 0.39189. Not all cases had liver cytologic and/or histopathologic.

Ultrasound identified eight of the 16 confirmed hepatitis cases with three false positives and eight false negatives. There were 16 cases determined to be normal on US that were also normal on the final hepatic diagnosis. There was no significant difference with moderate

agreement between the proportions that were positive and negative on US identifying hepatitis as the McNemar's test P-value was 0.2266 and ICC was 0.59151.

Computed tomography identified five of the 16 confirmed hepatitis cases with three false positives and 11 false negatives. There were 16 cases determined to be normal on CT that were also normal on the final hepatic diagnosis. There was no significant difference with poor agreement between the proportions that were positive and negative on CT identifying hepatitis as the McNemar's test P-value was 0.0574 and ICC was 0.48794.

There was no significant difference with poor agreement between the proportions that were positive and negative on US and CT in the identification of pancreatitis as the McNemar's test P-value was 0.2891 and ICC was 0.46341. No pancreatic cytologic and/or or histopathologic diagnoses were obtained, and these were the clinical final diagnoses due to ultrasonographic appearance, blood work abnormalities, and clinical exam findings. There was no significant difference with poor agreement between the proportions that were positive and negative on US and CT in the classification of the pancreas as being normal or abnormal as the McNemar's test P-value was 0.1797 and ICC was 0.45076.

Ultrasound identified seven of the 15 confirmed pancreatitis cases with one false positive and eight false negatives. There were 19 cases determined to be normal on US that were also normal on the final pancreatic diagnosis. There was a significant difference with moderate agreement between the proportions that were positive and negative on US identifying pancreatitis as the McNemar's test P-value was 0.0391 and ICC was 0.67773.

Computed tomography identified 11 of the 15 confirmed pancreatitis cases with one false positive and four false negatives. There were 19 cases determined to be normal on CT that were also normal on the final pancreatitis diagnosis. There was no significant difference with good

agreement between the proportions that were positive and negative on CT identifying pancreatitis as the McNemar's test P-value was 0.3750 and ICC was 0.81291.

There was no significant difference with moderate agreement between the proportions that were positive and negative on US and CT in the identification of pancreatic edema as the McNemar's test P-value was 0.5000 and ICC was 0.65263. Ultrasound identified two of the three confirmed pancreatic edema cases with no false positives and one false negative. There was no significant difference with good agreement between the proportions that were positive and negative on US identifying pancreatic edema as the McNemar's test P-value was 1.0000 and ICC was 0.86996.

Computed tomography identified three of the three confirmed pancreatic edema cases with one false positive and no false negatives. There was no significant difference with good agreement between the proportions that were positive and negative on CT identifying pancreatic edema as the McNemar's test P-value was 1.0000 and ICC was 0.89385.

There was no significant difference with poor agreement between the proportions that were positive and negative on US and CT in the identification of cystic mucosal hyperplasia as the McNemar's test P-value was 0.0625 and ICC was 0.42748. Subjectively cystic mucosal hyperplasia was easier to identify on US as it was easier to differentiate between the intraluminal bile and the cystic wall thickening where on CT the wall thickening and the bile were similar in attenuating and confluent (Figures 2.6 and 2.7). Adjacent material of a different attenuation such as mineralized intraluminal material was necessary to identify the cystic mucosal hyperplasia on CT to outline the undulating and thickened mucosa (Figure 2.7). The periphery of the gallbladder wall did enhance as a thin rim.

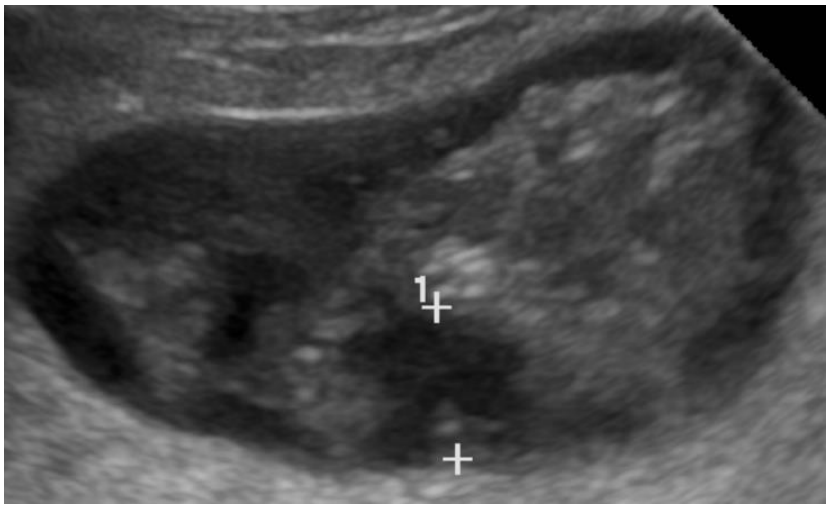

Figure 2.6 Cystic mucosal hypertrophy identified on US (sagittal view). There is multifocal hypoechoic thickening of the gallbladder wall.

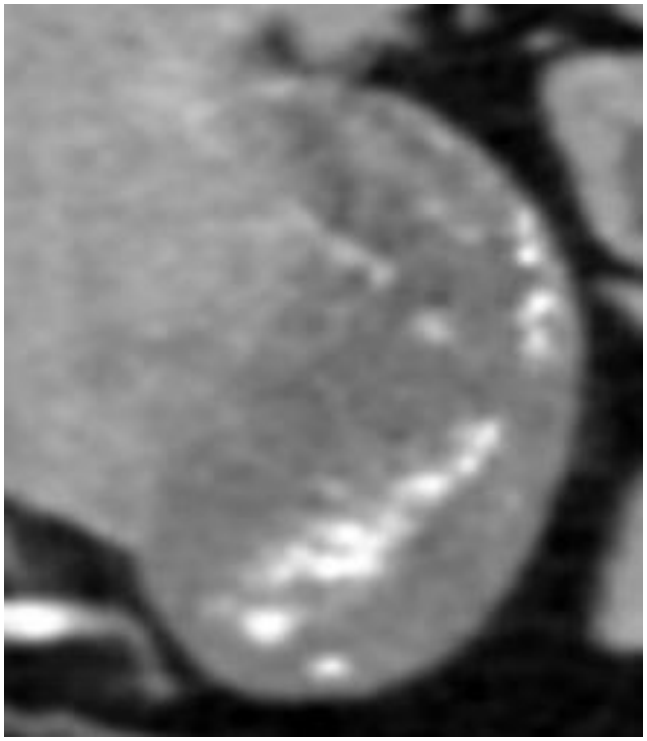

Figure 2.7 Canine patient with confirmed cystic mucosal hyperplasia and cholecystolithiasis on CT (venous contrast enhanced soft tissue window in a sagittal reconstruction). The mineralized intraluminal material outlines the undulating gallbladder mucosal margin which is consistent with cystic mucosal hypertrophy.

There was moderate agreement between US and CT in the measurement of gallbladder wall thickness as the convergence criteria was met and the ICC was 0.53775. Eighteen cases had a gallbladder wall that was thickened (>2 mm) on at least one of the modalities (summarized in Table 3). Eleven of these cases measured thickened on both CT and US, and seven cases measured thickened on only one of the modalities. The box and whiskers plot (Figure 2.8) shows the difference in millimeters (mm) between the measured thickness of the gallbladder wall on US and CT. The average difference was 1.46 mm. The median difference was 0.7 mm. The minimum difference was 0 mm, and the maximum difference was 8.7 mm.

Table 2.3 Gallbladder (GB) wall thickness measured on ultrasound (US) and computed tomography (CT) with the difference in millimeters (mm). Agreement was determined as yes (Y) or no (N) if both modalities agreed that the gallbladder wall was enlarged (greater than 2 mm in thickness). N/A = not applicable.

US GB Wall Thickness (mm)	CT GB Wall Thickness (mm)	Difference (mm)	Agreed if enlarged
3.6	2.2	1.4	Y
0.7	2	1.3	N/A
12.4	11	1.4	Y
11.1	2.4	8.7	Y
2.7	1.7	1	N
8.9	2	6.9	N
4.5	9.2	4.7	Y
1.5	2	0.5	N/A
1	1.6	0.6	N/A
1.2	1.5	0.3	N/A
1.6	1.2	0.4	N/A
1.9	2.1	0.2	N
3.9	2.1	1.8	Y
1.3	1.5	0.2	N/A
2.8	4.5	1.7	Y
1.6	1.2	0.4	N/A
6.7	2.9	3.8	Y
1.8	1.8	0	N/A

Table 2.3 (continued)

1.2	1.9	0.7	N/A
0.9	1.5	0.6	N/A
1.2	1.1	0.1	N/A
0.9	1.4	0.5	N/A
3.4	3.1	0.3	Y
1.2	2.1	0.9	N/A
1.3	1.9	0.6	N/A
0.7	1.5	0.8	N/A
3.5	3.5	0	Y
1.2	2.4	1.2	N
0.8	1.5	0.7	N/A
2.3	1.6	0.7	N
8.4	3	5.4	Y
3.1	2.4	0.7	Y
1.5	1.4	0.1	N/A
1.1	2.8	1.7	N
2.7	1.9	0.8	N

Average difference:	1.46
Median difference:	0.7
Minimum difference:	0
Maximum difference:	8.7

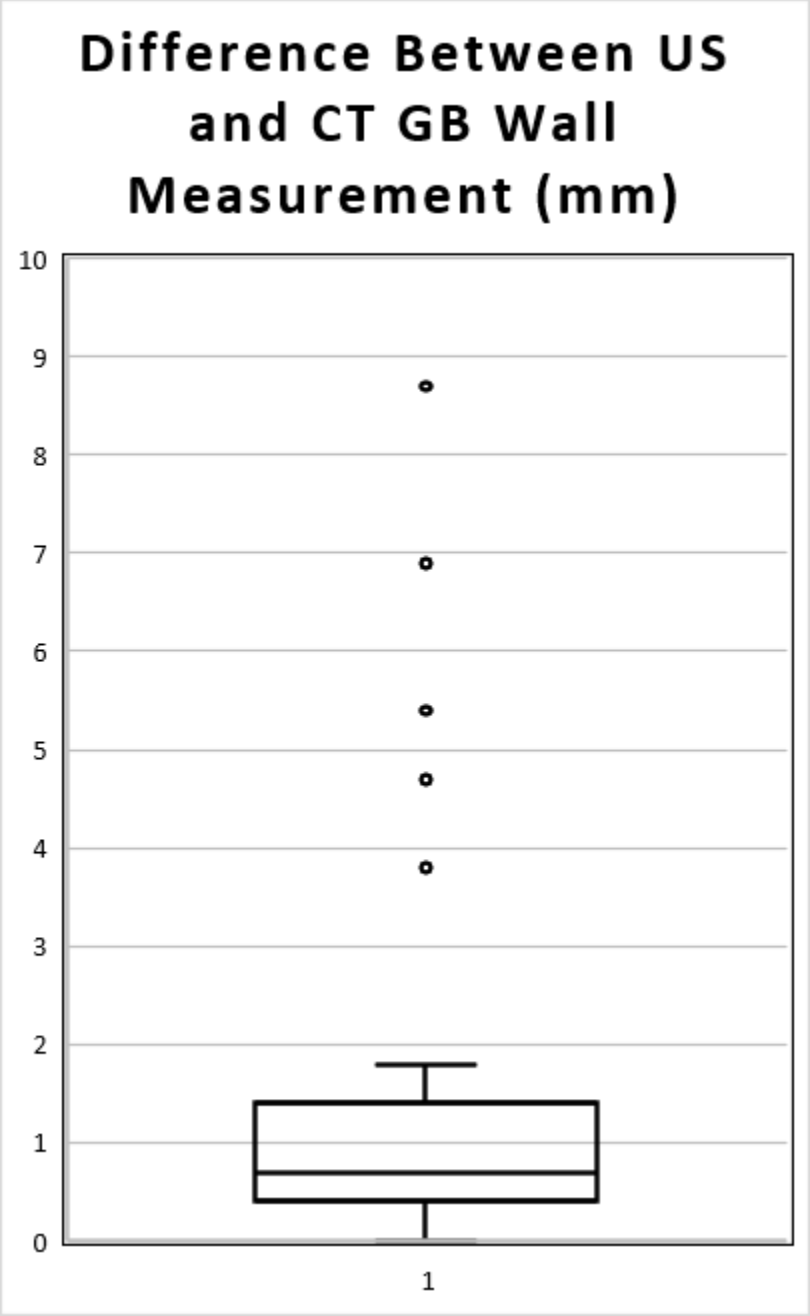

Figure 2.8 Box and whiskers plot of the difference in millimeters (mm) between the measured thickness of the gallbladder wall on US and CT.

The bile duct was identified in all CT studies. The bile duct was identified in 18 of 35 patients on US. Nine of these 18 bile ducts that were identified on US were normal in size. The

bile ducts that were unidentified on US and were identified on CT (17 patients), only four of these bile ducts were dilated on the CT studies, ranging from 3.5-9.9 mm in diameter. Sixteen cases had a bile duct that was enlarged (>3 mm) on at least one of the modalities (Table 2.4). Nine of these cases measured thickened on both CT and US, and seven cases measured thickened on only CT. The box and whiskers plot (Figure 2.9) shows the difference in millimeters (mm) between the measured bile duct thickness on US and CT of the bile ducts that were measured on both modalities. The average difference was 1.88 mm. The median difference was 0.7 mm. The minimum difference was 0 mm, and the maximum difference was 13.6 mm. There was poor agreement between US and CT in the measurement of bile duct size when it was identified as the convergence criteria was met and the ICC was 0.43153.

Table 2.4 Bile duct (BD) thickness measured on ultrasound (US) and computed tomography (CT) with the difference in millimeters (mm). Agreement was determined as yes (Y) or no (N) if both modalities agreed that the bile duct was enlarged (greater than 3 mm in thickness). N/A = not applicable.

US BD Thickness (mm)	CT BD Thickness (mm)	Difference (mm)	Agreed if enlarged
Not seen	2.8	N/A	N/A
2.2	2.6	0.4	N/A
Not seen	2.1	N/A	N/A
7.3	9	1.7	Y
1.2	3.4	2.2	N
6.3	5.6	0.7	Y
2.1	2.8	0.7	N/A
Not seen	2.1	N/A	N/A
1.1	3.7	2.6	N
6.6	12.1	5.5	Y
6.9	5.8	1.1	Y
Not seen	2.9	N/A	N/A
Not seen	1.8	N/A	N/A
Not seen	4.7	N/A	N
Not seen	3.5	N/A	N
Not seen	1.7	N/A	N/A
6.7	6.8	0.1	Y
Not seen	2.9	N/A	N/A
4.3	6.5	2.2	Y
Not seen	1.7	N/A	N/A
2.2	1.7	0.5	N/A
Not seen	1.8	N/A	N/A
Not seen	9.9	N/A	N
Not seen	1.7	N/A	N/A
2.4	16	13.6	N
1.7	1.7	0	N/A
1.3	1.7	0.4	N/A
8.3	8.3	0	Y
Not seen	1.9	N/A	N/A
4.2	5.7	1.5	Y
2.5	2	0.5	N/A
Not seen	1.8	N/A	N/A
Not seen	2.3	N/A	N/A
6.6	6.7	0.1	Y
Not seen	4.5	N/A	N

Table 2.3 (continued)

Average difference:	1.88
Median difference:	0.7
Minimum difference:	0
Maximum difference:	13.6

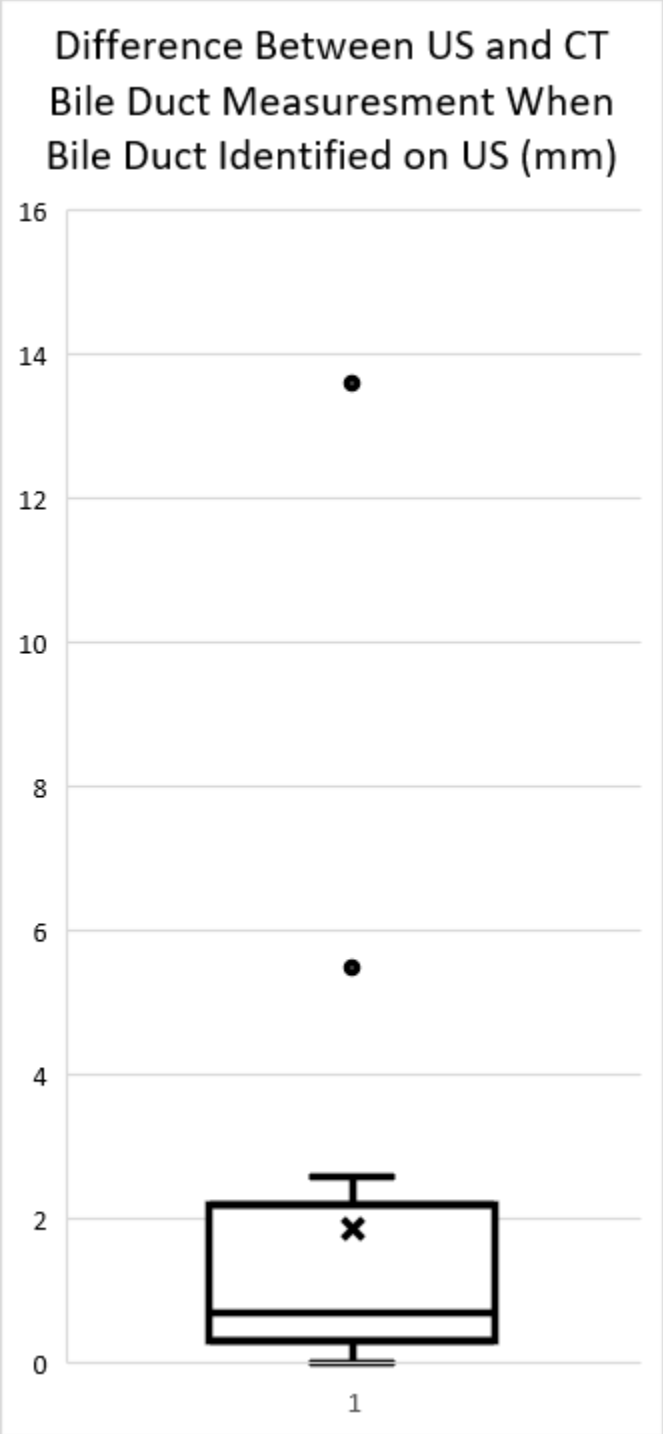

Figure 2.9 Box and whiskers plot of the difference in millimeters (mm) between the measured thickness of the bile duct on US and CT. These are the calculated differences between the bile ducts that were identified on both modalities.

The hepatic bile ducts were identified on five of the US studies. The hepatic bile ducts were identified on 20 of the CT studies. There was no agreement between US and CT in the measurement of hepatic bile duct size when it was identified as the convergence criteria was met and the ICC was 0.

Hypoattenuating bile was identified in 11 cases with a range of 10-29 HU. The final clinical diagnoses of these cases included cholangitis (n=5), extrahepatic biliary duct obstruction (n=4), gallbladder wall mass (n=1, carcinoid), and a case with cholelithiasis, pancreatitis, cholestasis.

CHAPTER III

DISCUSSION

Discussion

This study aimed to compare the performance of contrast-enhanced dual phase abdominal CT to abdominal US when diagnosing biliary disease in dogs presenting with acute abdominal signs.

The data supported the first hypothesis that CT would allow for detection of various canine biliary diseases with similar accuracy to US. The data did not support the second hypothesis that US would be superior to CT for investigation of the bile ducts and the diagnosis of cholecystitis due to the small size of these structures in the dog. The study found that CT identified all bile ducts while US did not. There also was no agreement of the hepatic bile duct identification between the 2 modalities which does not support US having better identification of these structures.

There is a significant association between the final US and CT positive or negative diagnosis for biliary pathology and the final clinical diagnosis via analysis of paralyzed maximum likelihood estimates and a chi-square (US had P-value= 0.0116 and CT had P-value= 0.0022). Computed tomography had a higher odds ratio of the final clinical diagnosis being positive when the CT diagnosis is positive (247.0 times greater than when the CT diagnosis is negative) versus US which was 51.9 times greater than when the US diagnosis is negative. The 95% Wald confidence limits for each modality were 2.421->999.999 (towards infinity). This is

an unusual value for the upper limit of the confidence interval (trending towards infinity) and is due to the low numbers of negative results (n=7). This suggests there is not a good estimate of the odds ratio but since there is a significant association, and the odds ratio is greater than 1.

Overall, there was no statistical difference between US and CT to identify the gallbladder mucoceles, gallbladder wall mass, gallbladder wall edema, cholangitis, pancreatic edema, and cystic mucosal hyperplasia.

Subjectively cystic mucosal hyperplasia was easier to identify on US as it was easier to differentiate between the intraluminal bile and the cystic wall thickening where CT it appeared as homogenous with the intraluminal bile. Adjacent material with a different attenuation (such as mineral) was necessary to identify the cystic mucosal hyperplasia on CT as the wall did not diffusely contrast enhanced because of the wall thickening is more fluid attenuating.

Cholelithiasis was the most common biliary pathology in this patient group which is similar to previous publications.[40] Cholelithiasis was the only pathology with statistical difference between US and CT to identify. This is not an unexpected finding as CT is known to be better at identifying mineral structures, especially small ones.[23] There may also be a bias towards CT having better identification of choleliths since it was used as the gold standard in this study to identify mineral structures. Abdominal radiographs were also obtained for each study prior to ultrasound. Of the six false negative US cases for cholelithiasis identification, only one of the cases had a faintly mineralized structure within the region of the gallbladder on the corresponding radiographs. Radiography could have been used as a confirmatory test, but due to the small structure size and/or amorphous mineralized gallbladder sludge, majority of these structures did not cause enough change in the x-ray beam attenuation to be identified.

Possible causes for decreased US identification of cholelithiasis include small structure size, decreased viewability from overlying gas or mineral structures, and lack of US artifacts suggesting mineral composition such as distal acoustic shadowing and twinkle artifact. Additional consideration for the decreased ability of US to identify small choleliths is the use of spatial compounding. Spatial compounding is an ultrasonographic technique and setting that obtains ultrasonographic information from several different angles of interrogation and combines them to produce a single image. This reduces speckle artifact and distal acoustic shadowing which improves interrogation of structures deep to distally shadowing structures and betters delineated margins.[83] The compromise to reducing distal acoustic shadowing with spatial compounding is smaller mineral structures may not display enough shadowing to be identified as mineral leading to false negative cases and decreased sensitivity. This was identified in a canine study comparing conventional ultrasonography to spatial compound imaging evaluating canine nephrolithiasis as distal acoustic shadowing artifacts were present in 43% of spatial compound imaging mode and 86% of conventional imaging mode.[84] This may be a focus of interest for future projects where spatial compounding is turned off during examination of the biliary tract for a brief period to evaluate for these small structures.

There was moderate agreement between US and CT for gallbladder wall thickness. Over half of the cases had a difference between the measurements <1 mm. The cases with >1 mm difference would be clinically significant as normal is <2 mm in thickness. A possible cause for the >1 mm difference between modalities includes CT being unable to differentiate between cystic mucosal hyperplasia and intraluminal fluid. Another possible cause may be changes in pathology between studies. Most patients received both studies within 1 hour of each other, but a couple of patients were dehydrated upon presentation, and it was deemed not safe for the patients

to receive intravenous contrast. Patients who are dehydrated are at a high risk of acute kidney failure after intravenous iodinated contrast administration. These patients received intravenous fluid therapy overnight and the contrast enhanced CT study was performed the following morning. All studies were performed within 24 hours. It is possible these there was a change in pathology (progression or improvement) over this time period within these couple of patients. If the underlying etiology was due to inflammation (such as pancreatitis or cholangiohepatitis) supportive care may have allowed the biliary pathology to improve due to the decreased inflammation. In cases where extrahepatic biliary outflow obstruction was present, pathology may have progressed as the obstruction persisted. Also, intravenous fluid therapy may have led to a positive fluid balance leading to gallbladder wall edema from increased hydrostatic pressure or cholecystitis. However, due to the few cases this occurred in, it likely did not affect the overall average differences. A third possible cause is volume averaging which may artificially increase or decrease the measurement of the gallbladder wall thickness. Volume averaging is an artifact that occurs when tissues of widely different attenuation (such as mineral and soft tissue) are included in the same computed tomographic voxel producing a beam attenuation proportional to the average value of the tissues. Volume averaging has been shown to cause more severe deviations in measurements of items or tissues with high contrast differences such as bone, air, and soft tissue.[85] Further, measurements are most accurate on CT in the axial plane as volume averaging causes progressive inaccuracy of measurements in sagittal and dorsal reconstructions.[85] Volume averaging would likely increase the gallbladder wall thickness which was adjacent to the surrounding hepatic parenchyma as it would cause an increase in the attenuation of the affected voxels leading to a thicker wall appearance as the attenuations of each tissue are similar. The opposite would likely occur for the gallbladder wall thickness when

surrounded by peritoneal fat as there is a high contrast difference between the soft tissue and fat attenuation which would lead to artificially small gallbladder wall. Similar findings have been found in other regions of the body where there is high contrast difference between adjacent tissue types such as loss of visualization of osseous nasal turbinates due to surrounding fluid (high contrast difference of the thin osseous nasal turbinates and surrounding fluid) and appearance of tympanic bulla wall thickening with surrounding fluid (high contrast difference of the relatively thicker tympanic bulla wall and fluid).[86,87] This has also been confirmed with aluminum phantoms surrounded by water and gas where the phantom thickness was artificially enlarged when surrounded by fluid than when surrounded by gas.[87] This phenomenon is worsened with soft tissue algorithms and reconstructions.[87]

There was also poor agreement between US and CT for bile duct thickness. Computed tomography identified the bile ducts in all studies. The bile ducts not identified on US were both normal in size and enlarged. There are numerous potential causes for the difference in measurement between the two modalities. Computed tomography has better evaluation of the porta hepatis due to lack of overlying structures as compared to US which may allow for a more thorough evaluation of the bile duct along its course. There are additional US artifacts which can also limit the ability for US to evaluate the bile duct which include the distal acoustic shadowing from overlying gastrointestinal gas or mineral structures such cholelithiasis and dystrophic mineralization. Ultrasound is also limited by depth penetration and body confirmation which includes overlying ribs and stomach. Additionally, volume averaging on CT can also cause variation in measurements for the bile duct thickness similar to the gallbladder wall thickness measurement. The last possible cause for the difference between modality measurements is the potential time difference between studies with changes in pathology over that time window.

There was no agreement between US and CT in the measurement of hepatic bile duct size when the duct was identified. Hepatic ducts were the least identified biliary structure. Hepatic ducts dilate with chronic biliary duct obstruction of at least 5-7 days duration. A possible cause for differences in identifying the ducts and their measurements between the two modalities is the difficulty distinguishing hepatic ducts from vessels on US. Commonly color or power Doppler is required to differentiate the hepatic bile ducts from the hepatic vasculature. With severe hepatic duct dilation, the hepatic ducts may also become tortuous which can help differentiate hepatic bile ducts from the portal vasculature. Also, if the hepatic bile ducts are normal in size, they may be too small to identify. Lastly, volume averaging on CT likely also contributes to this difference as these are small structures which can be averaged to the surrounding hepatic parenchyma.

Patients with hypoattenuating bile had diagnoses consistent with previously reported pathologies including cholangitis, extrahepatic biliary outflow obstruction, and gallbladder wall mass. Hypoattenuating bile is caused by any pathology which decreases the ability of the gallbladder to absorb fluid to further concentrate the bile. This therefore leads to increased fluid attenuation of the bile.

Although beyond the initial investigative purpose of this project, the comparison of US and CT diagnosis of hepatitis was evaluated as the hepatic system is intimately related to the biliary system. There was poor agreement of US and CT to the final clinical diagnosis of hepatitis with many false positives and negatives. This is not an unexpected finding as hepatitis is difficult to diagnose on each modality. A previous study found 64% of sonographically normal livers had histologic abnormalities.[88] A liver with acute hepatitis on US appears enlarged and hypoechoic. A liver with chronic hepatitis with cirrhosis and fibrosis appears small and lobulated with hyperechoic striations on US. Acute hepatitis on CT also appears enlarged with

increased arterial contrast enhancement with hypervascular inflammation. There may also be regions of decreased contrast enhancement in areas of necrosis. Computed tomographic appearance of chronic hepatitis is a small and lobulated liver with noncontrast enhancing striations consistent with cirrhosis and fibrosis. The liver may also be normal one either modality and cytology or histopathology is requited for definitive diagnosis. False positives of hepatitis were also common in this group of canine patients. Not all of the included cases had liver cytologic and/or histopathologic diagnoses which is a limiting factor in confirming if the diagnostic imaging diagnosis of hepatitis was correct.

There was no significant difference with poor agreement between the proportions that were positive and negative on US and CT in the identification of the pancreatitis. There was a significant difference with moderate agreement between the proportions that were positive and negative on US identifying pancreatitis. This is consistent with previous literature with one study determining a sensitivity 68% of US to identify acute pancreatitis.[89,90] No pancreatic cytologic and/or histopathologic diagnoses were obtained which may lead to false negative or false positive pancreatitis diagnoses as these cases were determined to be positive for pathology if there were changes present on US, blood work changes consistent with pancreatitis (most commonly elevated canine lipase [SNAP cPLI] or specific canine pancreatic lipase [Spec cPL/cPLI]), or physical exam findings in correlation with the clinical history. Canine lipase has a lower specificity (50-78%) and a relatively high sensitivity (74-100%) for pancreatitis but can result in many false positives.[90] The manufacturer states that a positive SNAP test (IDEXX Laboratories, Inc) must be confirmed by measuring Spec cPL because the SNAP test is abnormal for dogs in the equivocal zone of 200 to 400 μg/L.[90] Ultrasound can help with this diagnosis as a previous study of 157 dogs found when only one of pancreatic enlargement, altered pancreatic

echogenicity or hyperechoic mesentery was identified, the sensitivity was high at 89% but specificity was low at 43% for diagnosing pancreatitis.[91] When all three changes were identified, the sensitivity and specificity were 43% and 92%, respectively.

The ultrasonographic appearance of acute pancreatitis includes changes such as pancreatic thickening, hypoechoic pancreas, pancreatic edema, hyperechoic peripancreatic mesentery, and peritoneal effusion. The pancreas may also have hypoechoic nodules in regions of necrosis or abscessation. Focal functional small intestinal ileus and gastritis can occur due to local inflammation. Severe pancreatitis can also cause extrahepatic biliary duct obstruction with additional findings consistent with previously described changes. The ultrasonographic appearance of chronic pancreatitis in dogs includes pancreatic thickening, heterogeneous hyperechogenicity, and less peripancreatic hyperechoic mesentery due to decreased active peripancreatic peritonitis. The pancreas again can appear normal in cases with acute or chronic pancreatitis.

There was no significant difference with good agreement between the proportions that were positive and negative on CT in identifying pancreatitis. This is not unexpected as a pancreas with acute and chronic pancreatitis can appear normal on CT. Canine acute pancreatitis changes included pancreatic thickening, increased contrast enhancement with hypervascularization, hypoattenuating postcontrast if necrotizing, pancreatic edema, and ill-defined borders. There may also be increased contrast enhancement of peripancreatic mesentery and peritoneal effusion due to surrounding peritonitis and steatitis. Noncontrast enhancing nodules may be present in regions of focal necrosis or abscessation. Lastly, similar to the ultrasonographic changes, concurrent focal functional small intestinal ileus, gastritis, and extrahepatic biliary duct obstruction may also be present. The CT changes consistent with

chronic pancreatitis include pancreatic thickened and heterogeneous hypoattenuation due to lipid replacement and fibrosis.

In conclusion, CT was more accurate at identifying cholelithiasis than US. No statistical difference was identified in the odds to identify other biliary pathology between US and CT in these canine patients presenting for acute abdominal signs.

The clinical implications of this research can help determine if a clinician should use US or CT when working up a canine patient presenting for acute abdominal signs that are suspected to be of biliary origin. Ultrasound can be a great first diagnostic imaging modality for these patients as it shows great parenchymal detail, has increased sensitivity for finding small volume peritoneal effusion, and has no significant difference in the ability to detect pathology in canine patients <25 kg.[9] Ultrasound is less expensive than CT and may be able to obtain more information in patients who are dehydrated and cannot receive intravenous contrast due to the risk of acute kidney failure. However, US is very limited by the sonographer's comfort level and skill in being able to evaluate intraabdominal structures, especially the hepatobiliary tract due to location and limitations of beam penetration to these deep structures. Numerous studies comparing CT to US for various abdominal pathologies has shown CT having no significant difference or improved identification of intraabdominal pathology including canine gastric neoplasia, canine surgical cases presenting for acute abdominal signs, and canine patients >25 kgs. [6,9,43] The results of this study were consistent with this conclusion in addition to CT having increased identification of mineral attenuating structures. Additional benefit to CT is increased tomographic evaluation of deeper anatomical structures and limited training required for study acquisition. Computed tomography studies can be sent to a remote radiologist for interpretation which allows for a better global view of the pathology than US studies submitted for review by a

sonographer not comfortable in biliary evaluation. This benefit of CT is often worth the tradeoff of exposure to ionizing radiation as the medical management or surgical intervention can be pursued sooner. There is low risk for adverse events in the medical use of radiation for this type of CT study in dogs.

With the findings of this study, it would be very reasonable for a hospital to continue using US as the gold standard for imaging in canine patients (especially those <25 kg) presenting for acute abdominal signs with concerns for biliary pathology when a clinician, sonographer, or radiologist comfortable in imaging the biliary system is available. In facilities where CT is available, when a sonographer is unavailable, or when there is a high concern for cholelithiasis, CT is likely a better first choice for an imaging modality.

Limitations

The main limitation of this study is the limited sample population and under powering of this study, which may have resulted in a Type II error. A type II error occurs when one fails to reject the null hypothesis that is actually false producing a false negative. As in this study, the type II error may cause the false impression that CT is equivalent to US to identify biliary pathology in these dogs. Our sample size is smaller than expected due to the COVID pandemic and subsequent hospital shutdowns and decreased patient numbers. The acquired sample size was only 35 of the originally calculated 60 from the power calculation (28 positive and 7 negative). A larger sample size would help to confirm these findings.

An additional limitation is the lack of standardization of sedation protocols. Different protocols may have an effect on the CT or US appearance of the gallbladder wall or duct size. The majority of the patients received dexmedetomidine as part of their sedation protocol. A recent publication revealed dexmedetomidine used in canine patients causes gallbladder wall

edema in 24% of systemically healthy client-owned dogs (n=79).[59] While the use of dexmedetomidine may have caused gallbladder wall edema, it was not a common finding in this population of dogs and was likely clinically insignificant. The two patients with the primary finding being gallbladder wall edema had pathologies consistent with formation of gallbladder wall edema which included anaphylaxis and protein losing enteropathy with concurrent pancreatic edema.

An additional limitation is the lack of histopathology in all patients and within all regions of the biliary tract. Lack of histopathological diagnosis in all imaged regions may have revealed no true pathology in regions which appeared abnormal on the imaging modalities or confirmed pathology in false negative cases. This may be particularly relevant in the patient within this study where the bile duct was dilated on the CT study but not on US. Sampling all regions of interest in these patients is not ethical and thus was not performed.

A fourth limitation was that it was difficult for the 2 examiners (a board-certified radiologist and a radiology resident) to be truly blinded to all studies due to small size of the service. The studies were anonymized and randomized to limit this, but certain cases may have been memorable, such as the single gallbladder wall mass.

Future Studies

Future work from this project can stem in two directions. In one direction, future work stemming from this project can include a more detailed description of various biliary diseases in larger numbers of animals. This can include gallbladder mucoceles (both intact and ruptured), biliary neoplasia, cholelithiasis, and cholecystitis. In addition, future work can explore the CT appearance of biliary disease in feline patients. In the other direction, future work comparing the performance of CT to US in acute abdominal canine patients for other diseases, including

splenic, hepatic, gastrointestinal, pancreatic, and urogenital diseases, can be investigated. The ultimate goal is to determine if CT is as accurate or more accurate in diagnosing these pathologies in canine patients compared to abdominal US. If so, this could allow for patients to be diagnosed and treated more quickly and would allow for personnel without extensive US experience to obtain a diagnosis quickly and accurately. These factors would clearly benefit these patients greatly, especially when treatments or surgery can be initiated more quickly (in some cases, hours earlier). Magnetic resonance imaging can also be explored to replace CT as the primary way for tomographic evaluation of the biliary system in canine patients in nonemergent cases as it is being used in human medicine.

Synopsis

This study did not detect a difference in the ability of contrast-enhanced dual phase abdominal CT and US to identify biliary pathology in patients presenting for acute abdominal signs. This study also found that CT was better at identifying cholelithiasis than US. These findings suggest CT may be able to be used in place of US if a clinician confident in US is unavailable which may hasten decision making (whether surgical or medical) in canine patients presenting for acute abdominal signs of biliary origin, especially those with cholelithiasis.

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