Objective—To describe techniques for endoscopic retrograde cholangiography (ERC) and endoscopic retrograde biliary stenting of the common bile duct (CBD) for minimally invasive treatment of extrahepatic bile duct obstruction (EHBDO) in dogs.

Design—Experimental study and clinical report.

Animals—7 healthy research dogs and 2 canine patients.

Procedures—ERC and endoscopic retrograde biliary stenting were performed in healthy purpose-bred research dogs and client-owned dogs with a diagnosis of EHBDO that underwent an attempted biliary stent procedure. Research dogs were euthanized after completion of the procedure and underwent necropsy. With dogs under general anesthesia, the pylorus was cannulated with a side-view duodenoscope, and the duodenum was entered. The major duodenal papilla (MDP) and minor duodenal papilla were then identified, and the MDP was cannulated. Endoscopic retrograde cholangiography and endoscopic retrograde biliary stenting were attempted with the aid of endoscopy and fluoroscopy in all dogs. Procedure time, outcome for duodenal and MDP cannulation, and success of stent placement were recorded.

Results—Endoscopic retrograde cholangiography was successfully performed in 5 of 7 research dogs and in 1 of 2 patients. Biliary stenting was achieved in 4 of 7 research dogs and 1 of 2 patients, with a polyurethane (n = 4) or self-expanding metallic stent (1). One patient had a mass such that visualization of the MDP was impossible and no attempt at biliary cannulation could be made. After placement, stent patency was documented by means of contrast cholangiography and visualization of biliary drainage into the duodenum intra-operatively. No major complications occurred during or after the procedure in any patient. Follow-up information 685 days after stent placement in 1 patient provided evidence of biliary patency on serial repeated ultrasonography and no evidence of complications.

Conclusions and Clinical Relevance—ERC and endoscopic retrograde biliary stenting were successfully performed in a small group of healthy dogs and 1 patient with EHBDO, but were technically challenging procedures. Further investigation of this minimally invasive technique for the treatment of EHBDO in dogs is necessary before this may be considered a viable alternative to current treatment methods. (J Am Vet Med Assoc 2015;246:436–446)
evaluation, and localize gallstones to facilitate removal. Additionally, with this technique, bile duct obstructions can be definitively diagnosed and treated via therapeutic interventions including sphincterotomy or retrograde endoscopic biliary stenting. In human patients, ERCP is now considered the optimal minimally invasive treatment modality for diagnosis of many biliary and exocrine pancreatic tract diseases in adults. Diagnostic and therapeutic ERCP has more recently been described in children and has been found to be highly effective when performed with correct equipment and by appropriately trained operators. The most common cause of biliary obstruction in human patients is cholelithiasis, followed by pancreatitis, pancreatitis-associated biliary strictures, pancreatic or biliary neoplasia, and CBD strictures. Endoscopic retrograde sphincterotomy with biliary stenting is considered the treatment of choice for many of these conditions. Traditional reported treatment for EHBD in veterinary small animal patients involves laparotomy with surgical manipulation of the CBD and pancreatic duct via choledochotomy, diversion procedures such as cholecystoenterostomy, or surgical stent placement across the MDP. Surgical biliary diversion techniques in dogs and cats have been associated with a 25% to 73% and 50% to 75% mortality rate, respectively. When a traditional open surgical approach was used for the placement of biliary stents, the mortality rate has been reported to be 30.7% in dogs and 28% in cats, respectively. Prolonged anesthesia times (median, 3.5 hours; range, 2.4 to 6.75 hours) and manipulation of the pancreatic and biliary system in unstable patients may contribute to the high morbidity and mortality rates reported with traditional rerouting surgery or open surgical stent placement. In human patients, similar risks and complications of traditional open surgeries in debilitated patients have led to the use of interventional radiology-guided procedures (eg, placement of cholecystostomy tubes and percutaneous biliary stenting) and interventional endoscopy techniques (eg, ERCP and biliary stenting) in an effort to minimize procedure-related complications. Frequently, biliary stenting is recommended as a bridge to more invasive biliary surgery once the patient is stabilized. The use of cholecystostomy tubes or decompressive cholecystocentesis are other minimally invasive options for temporary biliary decompensation, although these procedures do not allow drainage of bile salts into the gastrointestinal tract. Endotoxemia and bacterial translocation may occur because the lack of luminal bile salts may promote increased intestinal permeability and intestinal bacterial overgrowth, which can overwhelm the hepatic reticuloendothelial system. This typically requires enteric bile salt replacement of the drained bile via a feeding tube until patency is reestablished. These procedures often help stabilize the patient, which can facilitate a more definitive permanent decompressive procedure at a later time.

In 1974, Falkenstein et al reported performing ERCP in healthy dogs for physician training and research purposes and indicated that success in achieving CBD cannulation improved with experience. In 2005, Spillmann et al first reported successfully performing diagnostic ERCP in 7 clinically normal research dogs and 30 canine patients with vague gastrointestinal signs. To our knowledge, endoscopic biliary stenting has not been reported in the veterinary literature to date. The objective of the study reported here was to describe our initial experience with ERC and endoscopic retrograde biliary stenting of the CBD for minimally invasive treatment of EHBD in dogs. The feasibility of the technique was evaluated in healthy research dogs, followed by treatment of 2 patients with EHBD.

Materials and Methods

Case selection—Data were collected from a group of healthy purpose-bred research dogs and from client-owned dogs with a diagnosis of EHBD that underwent an attempted biliary stent procedure by the authors. The study was approved by the Institutional Animal Care and Use Committees of the Matthew J. Ryan Veterinary Hospital of the University of Pennsylvania and of the Animal Medical Center, New York.

Research dogs—Healthy research dogs (n = 7) were selected from a colony of purpose-bred Beagle or mixed-breed dogs with ectodermal dysplasia being euthanized as an endpoint in studies unrelated to the present study. Each dog was otherwise healthy on the basis of results of a physical examination, CBC, and serum biochemical analysis performed on the day of the procedure. After ERC and biliary stenting was complete, dogs were euthanized while anesthetized by IV administration of propofol at 1 mg/kg (0.45 mg/lb), followed by a solution of pentobarbital sodium (390 mg/mL) and phenytoin sodium at a dose of 8.5 mg/kg (3.9 mg/lb), IV. A necropsy was performed including a thorough gross examination of the gastrointestinal, pancreatic, and extrahepatic biliary tracts.

Clinical cases—Endoscopic retrograde cholangiography and endoscopic biliary stenting were attempted as treatment for 2 patients with EHBD evaluated at the Animal Medical Center. Client informed consent was obtained prior to considering this treatment modality. Patients were selected on the basis of consideration of appropriate patient size and the absence of gall bladder disease or other indications for open surgical or laparoscopic exploration.

Medical record review—For clinical cases, information regarding history, signalment, clinical signs, diagnostic imaging results (abdominal ultrasonography and abdominal radiography), laboratory test results (CBC, serum biochemical profile, coagulation profile, canine pancreatitis lipase immunoreactivity, thromboelastography, and urinalysis), preoperative medical treatment, procedure time, procedure details, duration of hospitalization, complications, and short- (<1 month) and long-term (>1 month) outcomes was recorded.

Procedure—At least 1 physician (a board-certified gastroenterologist; MK, MS, or HG) assisted with each procedure reported in this study. Each had extensive experience in performing ERCP in human patients and comparative knowledge of complicated biliary anatomy.
Dogs were placed under general anesthesia with a standard liver dysfunction protocol for our hospital consisting of methadone (0.3 mg/kg [0.14 mg/lb], IM) and glycopyrrolate (0.01 mg/kg [0.0045 mg/lb], IM) as premedication; maropitant (1 mg/kg, SC) as an anti-nausea medication, and propofol (6 mg/kg [2.7 mg/lb] IV) for induction. Inhalation anesthesia was maintained with isoflurane in oxygen after endotracheal intubation. Patients were administered perioperative antimicrobials (cefotixin, 30 mg/kg [13.6 mg/lb], IV, once, then 20 mg/kg [9.1 mg/lb], IV q 2 h). A mouth gag was placed for routine gastrointestinal endoscopy. With the duodenoscope (11.3 mm), the gastric lumen was entered, the pylorus was cannulated, and the duodenum was entered. The MDP and minor duodenal papilla were then identified (Figures 1 and 2). The MDP was cannulated with a sphincterotome catheter (Figures 1 and 2). This required gentle manipulation of the endoscope and control of the working channel lever to direct the catheter into the orifice, as well as manipulation of the cutting wire of the sphincterotome to direct the catheter. A guide wire was then advanced through the lumen of the sphincterotome catheter and up the CBD with fluoroscopic guidance to confirm appropriate catheter placement. After the catheter was positioned in the lumen, a 1:1 mixture of saline (0.9% NaCl) solution and iodinated contrast material was injected slowly through the catheter to identify the CBD (Figures 1–3). Approximately 1 to 3 mL was infused in the event the catheter was in the pancreatic duct to avoid overdistension. Once CBD cannulation was confirmed, an additional 5 to 10 mL of contrast solution was infused and a guide wire was advanced through the sphincterotome and into the CBD, by means of fluoroscopic and endoscopic guidance. The guide wire was then advanced to the cystic duct. Next, the catheter was advanced over the guide wire and into the CBD for a sphincterotomy, when necessary. This was typically performed when the CBD opening at the MDP was too small to accept the appropriate size stent or stent delivery system (5F to 7F polyurethane stent or 10F SEMS delivery system). When required, a sphincterotomy was performed with monopolar cautery in the blend mode at 15 to 18 W. Once the guide wire was beyond the obstruction and within the cystic duct or proximal CBD, the sphincterotome catheter and endoscope diameter were used to measure the length of CBD that would be stented. The sphincterotome catheter was then removed over the wire with endoscopic and fluoroscopic guidance. Finally, the appropriately sized biliary stent was advanced over the guide wire through the working channel of the endoscope and advanced into the CBD to traverse the opening at the MDP. Once the stent was in place and bile began to drain, the guide wire was removed. In the research dogs, after euthanasia, the plastic stents
were removed with an endoscopic-guided grasping instrument with both fluoroscopic and endoscopic guidance.

Procedure details were recorded for each dog including the following: success of duodenoscopic cannulation of the pylorus, success in identifying the MDP, success in identifying the minor duodenal papilla, success in MDP cannulation with a sphincterotome catheter, the need for sphincterotomy, success in guide wire advancement up the CBD, success in biliary stent placement, and the type and size of biliary stent placed. Any complications noted during or after the procedure were also recorded.

Following ERC and biliary stenting, patients received standard treatment for pancreatitis and EHBDO, including analgesia (buprenorphine, 0.02 mg/kg [0.01 mg/lb], IV, q 4 to 6 h), liver disease supportive medications such as UDCA (10 mg/kg [4.5 mg/lb], q 24 h), antimicrobial treatment including enrofloxacin (10 mg/kg, q 24 h) and metronidazole (7.5 mg/kg [3.4 mg/lb], IV, q 12 h), and IV fluid therapy (3.75 mL/kg/h [1.875 mL/lb/h]). Immediately after stent placement, a canine pancreatitis lipase immunoreactivity test and canine liver panel were performed and amylase and lipase activities were obtained; these tests were repeated 24, 48, and 72 hours after the procedure.

Follow-up—For patients, follow-up information was obtained via scheduled reevaluations (1 week, 2 weeks, and 1, 3, 6, 9, 12, and 18 months after the procedure) including results of physical examination, laboratory tests (CBC, serum biochemical analyses), and diagnostic imaging (abdominal ultrasonography, abdominal radiography). Additionally, owners were contacted at the time of writing to evaluate their overall satisfaction with the procedure and outcome.

Results

Research animals—Endoscopic retrograde cholangiopancreatography was attempted in 7 research dogs. The dogs consisted of 5 female and 2 sexually intact male dogs that weighed a median of 18.6 kg (40.9 lb; range, 11.1 to 27.1 kg [24.4 to 59.6 lb]), with a median age of 36 months (range, 25 to 60 months).

The pylorus was cannulated with the side-view duodenoscope successfully in 6 of 7 research dogs. The MDP and minor duodenal papilla were identified in 5 of 7 and 6 of 7 dogs, respectively (Table 1). Balloon dilation (12 mm) of the pylorus was attempted in 2 dogs in which the side-view duodenoscope could not be advanced passively through the pylorus; this was successful in 1 dog. Advancing the endoscope over a guide wire did not aid in passage of the side-view duodenoscope. Air (in place of water) was used to manually inflate the balloon to help maintain compliance. Endoscopic retrograde cholangiography was successful in 5 of 7 dogs. In 1 dog, inadvertent submucosal injection of contrast at the MDP precluded cannulation, and in a second dog, we were unable to pass the duodenoscope through the pylorus.

In the research dogs, ERC was successful in 5 of 7 dogs and biliary stenting in 4 of 7 (Table 1). A 5F (n = 3) or 7F (1) polyurethane stent was used in the research dogs (Figure 1). Contrast was initially injected into the submucosal tissue of the duodenum at the MDP in 2 dogs. This was of no clinical consequence in one dog, but made cannulation and stent placement impossible in the other.

The median procedure time was 90 minutes (range, 24 to 180 minutes). All polyurethane stents were easily removed endoscopically with a grasping instrument.
upon completion of the study. On postmortem examination, there were no signs of gastrointestinal or CBD perforation at the site of the sphincterotomy or cannulation, and no complications were apparent from pyloric balloon dilation.

**Clinical Cases**

**Case 1**—An 11.5-year-old 33-kg (72.6 lb) spayed female Weimeraner was evaluated for signs of EHBDO. On physical examination, the dog was lethargic and markedly icteric with no evidence of abdominal discomfort on deep palpation. Two weeks prior to initial examination, a diagnosis of pancreatitis had been made by the referring veterinarian on the basis of a history of vomiting, inappetence, and signs of abdominal discomfort, with supportive findings on abdominal ultrasonography (ie, hypoechogenic pancreas, hyperechoic pancreatic adipose tissue, and a mild peripancreatic abdominal effusion). At that time, liver enzyme activity was mildly increased (ALP, 525 U/L [reference range, 0 to 140 U/L]; ALT, 355 U/L [reference range, 0 to 120 U/L]) as was total bilirubin concentration (1.8 µg/dL; reference range, 0.1 to 0.5 µg/dL). During the subsequent 2 weeks prior to referral, the clinical signs of pancreatitis resolved but biochemical and ultrasonographic evidence of EHBDO developed. Results obtained on the day of the procedure at the Animal Medical Center were as follows: ALP activity, 2,947 U/L (reference range, 10 to 150 U/L); ALT activity, 704 U/L (reference range, 5 to 107 U/L); γ-glutamyltransferase activity, 90 U/L (reference range, 0 to 14 U/L); cholesterol concentration, 603 mg/dL (reference range, 112 to 328 mg/dL); and total bilirubin concentration, 26.7 mg/dL (reference range, 0 to 0.4 mg/dL). An abdominal ultrasound examination performed the morning of the ERCP procedure revealed a CBD diameter of 1.3 cm (reference range, <0.3 mm), consistent with a diagnosis of EHBDO. Additionally, prior to the procedure, the canine pancreatitis lipase immunoreactivity was 36 µg/L (reference range, <200 µg/L), and results of a coagulation profile and thromboelastography were within reference limits. As an incidental finding, thoracic radiographs showed a widened cranial mediastinum and echocardiography revealed a 2×3-cm heart base mass. For 5 days prior to referral, the dog had been treated with ampicillin (22 mg/kg [10 mg/lb], IV, q 8 h), enrofloxacin (10 mg/kg, IV, q 24 h), metronidazole (7.5 mg/kg, IV, q 12 h), famotidine (0.5 mg/kg [0.23 mg/lb], IV, q 24 h), dolasetron (0.5 mg/kg, IV, q 24 h), and UCDA (13.6 mg/kg [6.2 mg/lb], PO, q 24 h).

The dog was placed under general anesthesia with the standard liver dysfunction protocol as described and positioned in left lateral recumbency. The pylorus was cannulated with the side-view duodenoscope, and the MDP and minor duodenal papilla were successfully identified. Endoscopic retrograde pancreatography was initially performed via cannulation of the minor duodenal papilla prior to identifying the MDP. This resulted in contrast filling the accessory pancreatic duct, at which time the catheter and endoscope were

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**Table 1**—Technical success of ERC and endoscopic retrograde biliary stenting of the CBD in 7 healthy research dogs and 2 patients with EHBDO.

<table>
<thead>
<tr>
<th>Group</th>
<th>Successfully cannulate pylorus</th>
<th>Successfully perform ERC</th>
<th>Successfully perform ERP</th>
<th>Successfully place stent</th>
<th>Procedural complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n = 2)</td>
<td>2/2</td>
<td>1/1</td>
<td>2/2</td>
<td>1/1</td>
<td>0/1</td>
</tr>
<tr>
<td>Research dogs (n = 7)</td>
<td>6/6</td>
<td>5/6</td>
<td>6/6</td>
<td>4/6</td>
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Research dogs consisted of 5 female and 2 sexually intact male dogs selected from a colony of purpose-bred Beagles or mixed-breed dogs with ectodermal dysplasia being euthanized as an end point to studies unrelated to the present study. Dogs weighed a median of 18.6 kg (40.9 lb), range, 11.1 to 27.1 kg (24.4 to 59.8 lb), with a median age of 36 months (range, 25 to 60 months). The patients were an 11.5-year-old spayed female Weimeraner with EHBDO and a history of pancreatitis and a 7-year-old spayed female mastiff with EHBDO because of granulomatous eosinophilic duodenitis. Stents included an SEMS® (diameter, 8 mm; length, 60 mm) in 1 dog, a 5F stent® in 3 dogs, and a 7F stent® in 1 dog. Procedural complications included submucosal edema from contrast agent injection that prevented cannulation of the pylorus, which was possible with 12-mm balloon dilation (research dog); submucosal edema from contrast injection that prevented cannulation of the pylorus (research dog); and inability to cannulate the pylorus with the endoscope because of small patient size (research dog). Additionally, case 2 had a mass present such that visualization of the MDP was impossible and no attempt at biliary cannulation could be made.
withdrawn orally and the MDP was identified and cannulated. Endoscopic retrograde cholangiography identified a CBD stricture (Figure 2). Biliary stenting was performed with an 8 × 60-mm SEMS. The procedure time (as measured from the time the endoscopy commenced to when it was finished) was 24 minutes. An 18F esophagostomy tube was placed prior to recovery in the event the patient developed clinical evidence of pancreatitis and enteral supplementation was needed. Recovery from the procedure was uneventful.

On recovery, treatment included analgesia (buprenorphine, 0.02 mg/kg, IV, q 4 to 6 h), UDCA (10 mg/kg, PO, q 24 h), enrofloxacin (10 mg/kg, PO, q 24 h), metronidazole (7.5 mg/kg, IV, q 12 h), and IV fluid therapy (3.75 mg/kg/h). Abdominal ultrasonography was performed 18 hours after stent placement and indicated decompression of the CBD proximal to the stent and a normal-sized gall bladder (3 × 3.5 cm). There was no clinical evidence of pancreatitis. The patient was discharged 48 hours following placement of the biliary stent.

This patient had increased canine pancreatic lipase immunoreactivity (753 µg/L) evident immediately after the stent placement procedure. This test was performed to assess whether the ERP had resulted in any biochemical evidence of pancreatitis. After 24 hours, this value had decreased to 462 µg/dL, and at 48 hours, it was within reference range at 56 µg/L. There were no clinical signs or physical examination findings that suggested pancreatitis at any time after the procedure. The total bilirubin concentration decreased from 26.7 mg/dL before the procedure to 23.1 mg/dL 3 days after the procedure. In the absence of jaundice on physical examination, the patient was discharged 4 days after the previous procedure.

Abdominal ultrasound examinations 2, 4, 8, 12, and 18 months after the procedure showed resolution of the pancreatitis. Sediment was variably present within the gall bladder or stent lumen, but there were no new or progressive changes evident within the liver or biliary tract. Liver enzyme activity increased slightly at 8 months (ALP, 231 U/L; ALT, 130 U/L), but the bilirubin concentration remained within reference range throughout the 18 months of follow-up after the procedure. After the stent placement procedure, the dog was treated continually with UDCA (12 mg/kg [5.5 mg/lb], PO, q 24 h). At the time of last follow-up (685 days [22.5 months] after the procedure), the patient was clinically normal, and abdominal ultrasonographic examination indicated biliary patency. The heart base tumor was echogenically larger but of no apparent clinical consequence.

Case 2—A 7-year-old spayed female Mastiff that weighed 59 kg (129.8 lb) was referred for evaluation of EHBDO. On physical examination, the dog was lethargic and icteric and had muscle wasting, with a body condition score of 3 on a scale of 1 to 9 and no evidence of abdominal discomfort on palpation. The dog had a 1-year history of intermittent vomiting, poor appetite, and weight loss, but results of a CBC and serum biochemical analysis had been within reference ranges 2 months prior to evaluation for ERCP. One month prior to initial examination at the Animal Medical Center, the dog was evaluated by the referring veterinarian for an acute episode of vomiting and results for liver enzyme activity were found to be markedly abnormal (ALP, 1,278 U/L; ALT, 2,810 U/L), with a total bilirubin concentration of 3.1 mg/dL. Abdominal ultrasonography at that time revealed distension of the gall bladder and CBD, with a possible mass effect at the level of the MDP. The pancreas was ultrasonographically normal, and canine pancreatitis lipase immunoreactivity was also within reference range (36 µg/L). A diagnosis of EHBDO was suspected, but the following day, total bilirubin concentration had decreased to 1.8 mg/dL and medical treatment with antimicrobials (amoxicillin and metronidazole) and UDCA was pursued. The initial improvement continued for 1 week, but then increases in liver enzyme activity recurred over the following 3 weeks prior to referral for evaluation of EHBDO. The ALP activity increased from 590 to 3,485 U/L, ALT activity from 679 to 2,434 U/L, and total bilirubin concentration from 0.8 to 11.1 mg/dL. Results of a coagulation profile and thromboelastography were within reference range during examination at the Animal Medical Center, prior to ERCP. Repeated abdominal ultrasonography at that time revealed persistent distension of the biliary tract, but the mass was no longer identified. The patient was being treated with amoxicillin (13.5 mg/kg [6.1 mg/lb], PO, q 12 h), UDCA (10.2 mg/kg [4.6 mg/lb], PO, q 24 h), and metronidazole (8.5 mg/kg [3.9 mg/lb], PO, q 12 h).

The dog was placed under general anesthesia with oxymorphone (0.1 mg/kg [0.045 mg/lb], IM) and gly-
coppyrollate (0.01 mg/kg, IM) as premedicants, administration of maropitant (1 mg/kg, PO) to prevent signs of nausea, and propofol (6 mg/kg, IV) for induction. Anesthesia was maintained by means of inhalation anesthesia with isoflurane in oxygen. The pylorus was successfully cannulated with the side-view duodenoscope, and the minor duodenal papilla was successfully identified. However, a large mass was present in the area of the MDP such that the MDP could not be visualized or cannulated. After 80 minutes of attempted endoscopic identification, a laparotomy was performed. The owner declined traditional retrograde surgery via a cholecystoenterostomy, and surgical placement of a biliary stent was not possible because of the presence of a large mass at the MDP. Several biopsy samples were obtained for subsequent histologic examination. The biliary system was decompressed and diverted by use of a prototype subcutaneous choledochal bypass device in which a 10F locking-loop cholecystostomy tube was connected subcutaneously through a shunting port to a multifenestrated 10F catheter that was inserted into the distal portion of the duodenum for internal diversion. This device was then successfully flushed with contrast solution to confirm patency of the diversion system under fluoroscopic guidance. This novel device was used to decompress the biliary system pending the results of examination of the biopsy samples.

Histologic examination of biopsy samples of the mass showed severe transmural erosinophilic and plasmacytic enteritis and fibrosis with deep ulceration. Bilirubin concentration decreased within 24 hours after biliary diversion from 11.1 to 4.5 mg/dL. However, 2 days later, bilirubin concentration increased to 6.0 mg/dL, and an abdominal radiograph showed a kink in the tubing of the cholecystostomy catheter. This was resolved via a small subcutaneous incision with the patient under general anesthesia by means of a protocol similar to that previously described. The dog then commenced steroid treatment (prednisone, 0.34 mg/kg/d [0.15 mg/lb], PO) as a result of the histopathologic findings. Over the following 2 weeks, the bilirubin concentration returned to reference limits but the dog had a deterioration of underlying hind limb weakness related to previous orthopedic and neurologic disease and died suddenly 1 month later during an episode of acute respiratory distress. The owners declined a postmortem examination.

Discussion

The results of the present study supported the premise that ERCP and biliary stent placement are possible in a small group of healthy research dogs and selected canine patients with EHBDO. This procedure may be considered as a potential treatment for EHBDO for veterinary patients and may be more successful as clinician experience increases with proper training and availability of specialized equipment. Although surgically assisted choledochal stenting is not a new concept in veterinary medicine,16,17,35–38 it has only been reported as an adjunct to surgical biliary decompression, requiring laparotomy, enterotomy, biliary and pancreatic manipulation, and prolonged surgery times.16,17 In a 2006 study reporting the use of surgically placed stents in 13 dogs, the surgery times (median, 3.5 hours; range, 2.45 to 6.75 hours) and mortality rate (31% to 50%) were still high, with outcome dependent on the etiology of the obstruction.16 With more experience, decreased anesthesia times and reduced morbidity rate with ERCP, compared with results for traditional surgery, would be expected in veterinary patients, as has occurred for human patients. This is the first technical description of the use of endoscopic biliary stents in a small group of dogs. As found with human patients, success is dependent on operator experience and MDP visibility.5,35 With the availability of smaller duodenoscopes designed for pediatric human patients, we anticipate achieving greater success with ERCP and biliary stenting in appropriately selected small animal patients, making these procedures a more viable treatment option for these patients.

In the present study, the major difficulty encountered with ERC was cannulation of the pylorus with the side-view endoscope. In this series, the failure of cannulation (29 dogs) was due to the large diameter of the endoscope (11.3 mm). Dilation with a balloon catheter improved the success in one of the dogs. The use of a smaller duodenoscope (7.5 mm), which was not available for this study but which has been subsequently used to successfully treat several veterinary patients in our practice, may improve overall success rates in the future. Further investigation of balloon dilation of the pylorus in dogs and cats combined with the use of the larger duodenoscope is needed. Once the duodenum was entered, the next limiting factor was obtaining successful visualization of the MDP and having enough working space to angle the endoscope to catheterize the MDP to the CBD. We suggest that successful visualization of the MDP in patients may be challenging when a tumor or other duodenal lesion is present in this region.

Once the CBD is catheterized, the need for a sphincterotomy at the MDP prior to stent placement, is controversial. In human patients, this can be associated with higher risks of complications (2% to 20%),5,6,7,32,36,37 including hemorrhage, perforation of the duodenal or CBD wall, pancreatitis, and reflux of gastrointestinal contents into the CBD. The benefits of sphincterotomy typically include easier stent cannulation, the ability to remove large choledoliths, and opening of the ampulla when stenosis is present.5,6,7,36

Pancreatitis is the most common complication of ERCP in human patients (1% to 20%).5,7,36–38 A study evaluating pancreatic enzyme activity after ERP (not ERC) in clinically normal dogs found no clinical signs of pancreatitis and no associated complications. In that study,39 there was a transient increase in the serum amylase and lipase activities and canine pancreatitis lipase immunoreactivity measured in blood samples obtained 10 minutes after ERP, with these values returning to baseline by day 2, similar to that seen in 1 patient of the present study. In our clinical experience, transient elevations of pancreatic enzyme activity may also occur in human patients without symptoms of pancreatitis. Another experimental study40 was performed in clinically normal dogs with aggressive interventions, including pancreatic acinarization, pancreatic duct sphincter-
otomy, and pancreatic duct stenting in an attempt to induce pancreatitis during ERP, not ERC. None of these procedures would be performed in the clinical setting in a patient with EHBDO during ERP for decompression of the CBD. The goal of that study was to induce pancreatic reflux and create a model for ERCP-induced pancreatitis, which would be mild and self-limiting. It was found in that same study that the dogs in which a pancreatic stent was placed had less pancreatic inflammation and necrosis, compared with those dogs without stents. Additionally, for dogs in this experimental study in which clinical pancreatitis was created via aggressive ERP methods, it was difficult to induce clinical signs of the disease, although common to cause temporogressive ERP methods, it was difficult to induce clinical study in which clinical pancreatitis was created via aggressive ERP methods, it was difficult to induce clinical signs of the disease, although common to cause temporary biochemical changes suggestive of pancreatitis. In that study, excessive amounts of contrast were injected into the pancreatic duct (> 20 mL), compared with the volume indicated for ERP in patients (1 to 3 mL), in addition to balloon occlusion, sphincterotomy, infusion of UDCA, or a combination of these procedures, in an attempt to create edema, cytotoxicosis, and pancreatic inflammation. Additionally, considering the CBD and a small branch of the pancreatic duct in dogs typically have separate openings into the duodenum at the MDP and the major branch of the accessory pancreatic duct is at the minor duodenal papilla, which was the duct being cannulated during ERP in that pancreatitis model, not during ERC for treatment of EHBDO, the risk for the induction of clinical pancreatitis by ERC should be far less in canine EHBDO patients. In 1 patient described in the present report, biochemical, but not clinical, evidence of pancreatitis was present after ERCP even though this patient also underwent ERP. Typically, we suggest that ERP would not be necessary in dogs with EHBDO if the MDP is initially identified. The primary identification of the minor duodenal papilla, rather than the MDP (case 1), was likely due to inexperience. In this patient, the MDP was only 1.5 cm from the pylorus and was initially passed upon entry to the duodenum.

In the patient of this report (case 1) that successfully underwent stenting, a noncovered SEMS was used, which is not retrievable. In human patients being treated for benign disease such as pancreatitis-induced EHBDO or a benign stricture of the CBD, a temporary stent would be considered as either single (eg, for pancreatitis) or multiple (eg, for stricture) plastic stents or a covered SEMS (also for stricture) that could be removed after a few months. The reason a stent may need to be removed over time is because of the risk of ascending cholangitis. The surviving patient of this report did not have clinical evidence of ascending cholangitis at the time of last follow-up (685 days).

Because there are fewer complications with therapeutic ERCP for EHBDO decompression, compared with traditional surgeries in human patients, we suggest that this treatment modality holds great promise for small animal veterinary patients. It must be emphasized that the most common reason for EHBDO in adult humans is obstructive cholelithiasis, followed by tumors, strictures, and obstructive pancreatitis. Dogs, on the other hand, most commonly develop obstruction because of obstructive pancreatitis and associated ascending cholangitis. Cholelithiasis is rarely a primary cause. Stone removal in human patients during ERCP is one of the more common therapeutic interventions requiring sphincterotomy, stenting, and lithotripsy and therefore is the most common cause of complications. Simple stenting for relief of a biliary obstruction associated with inflammation or strictures is often considered less technically demanding. Additionally, because of the separate ducts in the dog and the need for temporary biliary diversion during an episode of pancreatitis, compared with the needs in human patients, we suggest that this procedure is even more promising in this species.

A study in clinically normal dogs was performed by comparing surgical biliary diversion, after a biliary obstruction was manually created, with surgically assisted biliary stenting, with or without secondary surgical diversion. This study indicated that surgical biliary diversion induced more severe hepatic cholangitis histopathologic lesions, which were not seen with biliary endoprosthesis. Both procedures were associated with bacterial contamination and thickening of the CBD wall, but the dogs with biliary stents maintained adequate patency.

Because of the high mortality rates reported for surgical treatment of EHBDO (up to 75%) in veterinary patients, these data further support the need for this type of preliminary investigation in an effort to find new treatment modalities that may decrease overall morbidity and mortality rates. The cause for such high mortality rates with traditional surgery is not clear but is postulated to be associated with the systemic disease process, resulting in sepsis, impaired reticuloendothelial function, and surgical risks in such patients. Traditional open surgery may require excessive pancreatic manipulation and prolonged anesthesia times in very debilitated patients and may have a high risk of dehiscence and abdominal contamination associated with the enterotomy incision. With endoscopic biliary stents, some of these risks may be averted because of minimal pancreatic manipulation endoscopically, lack of the need for laparotomy and intestinal surgery, and the relative speed of the procedure performed by trained personnel. Additionally, data from human patients suggest that urgent endoscopic decompression, prior to considering more aggressive surgical revisions, in the case of obstructive biliary jaundice may provide a means for stabilization and reduced morbidity and mortality rates.

Choosing the type and size of biliary stent is important and varies for each type of biliary obstruction. Biliary stents come in various shapes, sizes, and materials. They are considered either temporary (typically a plastic polyurethane or covered self-expanding metallic material) or permanent (metallic partially covered or uncovered). The type of stent placed is dependent on the condition being treated, desire for removal, and need for long-term patency. For temporary biliary obstruction relief, such as for patients with obstructive pancreatitis, polyurethane plastic stents are most commonly used and easy to remove after the resolution of disease. These stents have been found to maintain patency for between 3 and 6 months typically, which is
the time needed for resolution of the underlying disease in human patients. Stent size is usually selected on the basis of the diameter of the CBD, which is estimated from the cholangiogram. In smaller dogs, we consider a 5F or 7F stent an appropriate size to prevent CBD wall trauma. The size of the stent in the dogs of the present report was chosen on the basis of case of catheter insertion into the CBD. If the 5F catheter was easy to advance, then a 7F stent was chosen. If it was tight during advancement, then a 5F stent was chosen. In cases of biliary obstruction secondary to biliary strictures or neoplasia, permanent metallic stents are often chosen to try to avoid the risk of occlusion and stent migration. These stents should be sized to fit the lumen of the CBD and should not be undersized like a plastic biliary stent.

One patient (11.5-year-old spayed female Weiner) described in the present report had a benign biliary stricture secondary to acute pancreatitis. Benign strictures are commonly reported in human patients associated with chronic pancreatitis, anastomotic lesions after liver transplantation, inflammatory diseases, and biliary stone disease. Endoscopic treatment is preferred over surgical intervention in such patients, with the most common treatment involving biliary stent placement (1 or multiple plastic stents, covered or partially covered SEMSs, or uncovered SEMSs). When a stent is needed beyond a 3-month period, plastic stent patency is considered a drawback and SEMSs are considered superior to reduce the number of stent exchanges required. Bare, uncovered SEMSs are integrated into the biliary mucosal tissue, decreasing the risk of stent migration, and cannot be removed. These stents can result in mucosal hyperplasia and tissue ingrowth through the open interstices of the mesh. Bare SEMSs are most commonly used for malignant obstructions or in cases when stent removal is not desired and the risk of migration is high. Covered stents have a polymeric sheath over the mesh, which acts as a physical barrier to prevent tissue ingrowth (tumor or stricture), but do not incorporate into the mucosal tissue; these covered stents have a much higher migration risk and a higher risk of maintaining an infected biofilm on the surface.

In the patient of this report that underwent stenting (case 1), an uncovered SEMS was chosen because of advanced age (11.5 years), benign permanent condition, and the owner's desire to avoid the risk of stent migration. At the 18-month follow-up, there was no evidence of any negative effects from this stent choice (ie, occlusion, migration, or ascending cholangitis), with the patient being clinically normal.

One concern with short- or long-term biliary stenting is the risk of ascending cholangitis. This has been reported to be less of an issue than that seen with permanent biliary diversion surgeries in dogs. For this reason, after biliary stenting, unlike in human patients, we typically treat our canine patients with a 2- to 4-week course of antimicrobials, as in the present report, and follow carefully with serial liver enzyme evaluations and repeated abdominal ultrasonography. Additionally, to help maintain thin biliary secretions, patients may be maintained on UDCA. Ursodeoxycholic acid is widely used for the treatment of choledochal liver disease in both human and veterinary patients. There are many mechanisms of action of UDCA, including protection of injured cholangiocytes against the toxic effects of bile acids, stimulation of biliary secretions, inhibition of hepatocyte apoptosis, and decreased biliary cholesterol saturation. In the case of biliary sediment, UDCA is intended to reduce cholesterol absorption in the bile, thereby reducing the cholesterol component in bile sediment or stones, which can result in stone dissolution. Additionally, UDCA has been found to increase the synthesis of transporters in the canalicular membrane of hepatocytes, which enhances bile flow while making the bile acid composition less hydrophobic and less cytotoxic within hepatocytes and possibly decreasing the viscosity of bile. Because of these properties and the presence of biliary sediment in the bile of one of the patients in the present report, we elected long-term treatment with UDCA.

There are many limitations to the present study. The first is that there were only a small number of healthy research dogs in which biliary stents were placed. Because this was an experimental study to evaluate technique, safety, and short-term efficacy, this was deemed appropriate. Additionally, this technique was then performed in only 2 patients, 1 (case 1) that had a CBD stricture, warranting placement of a permanent metallic stent and the second (case 2) that had a mass which prevented visualization of the MDP, such that no attempt at biliary cannulation could be made. For the first patient, the permanent metallic stent was different than the temporary polyurethane stents used in the 7 research dogs; however, it merits reporting because of the clinical need for treatment in this dog and the successful outcome. Because this was a clinical case, we felt it was appropriate to use this type of stent in this patient. Additionally, this decision was made on the basis of the recommendations of the highly experienced physician gastroenterologists involved in the procedure, who felt that an uncovered SEMS was the best choice for this patient. An additional limitation is that all of the procedures described were performed by a team of experienced board-certified subspecialist veterinarian and physician interventionalists. As such, procedural success with these techniques would be more likely. We suggest that outcomes may not be as good in a traditional veterinary hospital environment, when the procedures are performed by individuals and clinical teams with less experience. These are technically difficult endoscopic procedures. However, as has occurred in human medicine, outcomes would be expected to improve over time when clinicians elect to participate in specific and ongoing training. Furthermore, attention to appropriate patient selection and assurance of an adequately trained clinical team is imperative when considering this procedure because if ERCP is unsuccessful, prolonged anesthesia time may compromise an already unstable patient because of the need to convert to traditional open surgery. We advise that ERCP should also be reserved for treatment of dogs with EHBDO secondary to pancreatitis, strictures, tumors, or chololithiasis and not for treatment of patients with concurrent biliary mucoceles or pancreatic or hepatic abscesses, which require surgical debridement.
or cholecystectomy. Finally, if concurrent hepatic or gastrointestinal biopsy is required, ultrasound- or endoscopic-guided biopsy can be considered.

Endoscopic retrograde cholangiography and concurrent endoscopic retrograde biliary stenting were possible in some dogs of the present study, but were technically challenging to perform. Further investigation of ERC and endoscopic retrograde biliary stenting in canine patients is needed with collection of short- and long-term outcome data before this procedure can be generally recommended; however, initial results were promising.

References


From this month’s AJVR

Evaluation of a ferret-specific formula for determining body surface area to improve chemotherapeutic dosing

Krista L. Jones et al

**Objective**—To use CT-derived measurements to create a ferret-specific formula for body surface area (BSA) to improve chemotherapeutic dosing.

**Animals**—25 adult ferrets (19 live and 6 cadavers).

**Procedures**—Live subjects were weighed, and body measurements were obtained by each of 3 observers while ferrets were awake and anesthetized. Computed tomography was performed, and a 3-D surface model was constructed with open-source imaging software, from which BSA was estimated. The CT-derived values were compared with BSA calculated on the basis of the traditional tape method for 6 cadavers. To further validate CT analysis software, 11 geometric shapes were scanned and their CT-derived values compared with those calculated directly via geometric formulas. Agreement between methods of surface area estimation was assessed with linear regression. Ferret-specific formulas for BSA were determined with nonlinear regression models.

**Results**—Repeatability among the 3 observers was good for all measurements, but some measurements differed significantly between awake and anesthetized ferrets. Excellent agreement was found between measured versus CT-derived surface area of shapes, traditional tape versus CT-derived BSA of ferret cadavers, and CT-derived BSA of cadavers with and without monitoring equipment. All surface area formulas performed relatively similarly.

**Conclusions and Clinical Relevance**—CT-derived BSA measurements of ferrets obtained via open-source imaging software were reliable. On the basis of study results, the recommended formula for BSA in ferrets would be 9.94 X (body weight)²/3; however, this represented a relatively minor difference from the feline-derived formula currently used by most practitioners and would result in little practical change in drug doses. (Am J Vet Res 2015;76:142–148)