LABORATORY INVESTIGATION

Pilot Study of the Safety and Efficacy of Gallbladder Cryoablation in a Porcine Model: Midterm Results

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ABSTRACT

Purpose: To investigate the midterm safety and efficacy of computed tomography (CT)–guided percutaneous gallbladder cryoablation in swine.

Materials and Methods: Three swine underwent gallbladder cryoablation. Cryoprobes were positioned percutaneously at the gallbladder margins or within the gallbladder lumen under CT guidance. Two freeze/thaw cycles were performed. One animal was euthanized on postprocedure day 4 as a result of hematemesis unrelated to the ablation. The other 2 animals were euthanized at postprocedure days 30 and 48, respectively. The gallbladder and bile ducts were resected and examined microscopically.

Results: Gallbladder cryoablation was completed with freeze/thaw cycle durations of 7.5–10 minutes (mean, 9.4 min ± 1.3) and ablation margins of 5.8–11.5 mm (mean, 7.8 mm ± 1.9). No nontarget ablation was observed. Laboratory values at postprocedure day 4 and the time of euthanasia were within normal limits. Two of 3 animals thrived and exhibited appropriate activity and weight gain. Contrast-enhanced CT immediately before euthanasia demonstrated delayed linear enhancement of the gallbladder wall. Gross inspection at autopsy revealed fibrotic-appearing gallbladders. Cholecystography revealed no communication to the biliary tree. Histologic examination demonstrated complete gallbladder wall fibrosis. Autopsy of the animal euthanized on day 4 revealed a gastric mucosal ulcer distant from the ablation site with no gastric serosal injury.

Conclusions: Gallbladder cryoablation is a promising alternative to surgical cholecystectomy, with complete transmural gallbladder wall fibrosis and cystic duct occlusion seen at 30 and 48 days in swine. Further studies are required to establish procedural safety and long-term efficacy.

Perioperative complication rates associated with cholecystectomy in elderly patients may be as high as 31%, necessitating percutaneous drainage in cases of acute cholecystitis (1,2). Percutaneous cholecystostomy is not a definitive treatment for acute calculous cholecystitis, with reported 1- and 3-year recurrence rates of 35% and 46% following cholecystostomy tube removal (3). Many patients are left with "tubes for life," with frequent required tube exchanges taking up valuable patient time and hospital resources.

Multiple attempts have been made in the past to fulfill the need for a definitive, minimally invasive gallbladder treatment. Recently, Lee et al (4) used n-butyl cyanoacrylate and coils to occlude the cystic duct and acetic acid for mucosal ablation of the gallbladder in 5 canines. Complete mucosal ablation was not achieved, with remnant or regenerated mucosa identified in the gallbladder neck (4). To our awareness, reproducible complete mucosal ablation has yet to be reliably achieved.

It has been postulated that mucosal regeneration occurs from mucosal deposits within Rokitansky–Aschoff sinuses, into which the ablative solution does not pass (4). Residual mucosa may place patients at risk for recurrent gallstone disease or mucocele formation (4). Definitive treatment requires complete and permanent mucosal ablation and occlusion of the cystic duct.

Cryoablation is a thermal ablation technique that induces cell death by exposure to low temperatures and has been successfully applied in the oncologic setting. Readily visible

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ablation margins on computed tomography (CT) and ovoid ice-ball morphology make it well suited for applications in anatomically challenging locations. Previous work has demonstrated the technical feasibility of CT-guided gallbladder cryoablation (5), with transmural gallbladder ablation seen at 5 hours following the procedure. The purpose of the present study was to establish the midterm safety and efficacy of gallbladder cryoablation in swine as a possible alternative to cholecystectomy.

MATERIALS AND METHODS

The study protocol was approved by the institutional animal care and use committee. Farm pigs (n = 3; 40–54 kg) fasted for at least 8 hours before the procedure. Following induction with intramuscular acepromazine 0.5 mg/kg and ketamine 25 mg/kg, subjects were anesthetized with 2%–5% isoflurane (Piramal Critical Care, Bethlehem, Pennsylvania) and mechanically ventilated throughout the procedure. Antibiotic therapy with intravenous cefazolin 22 mg/kg was administered 1 hour before the procedure. After the procedure, animals were treated with a 5-day course of oral trimethoprim/sulfamethoxazole (15 mg/kg twice daily).

Percutaneous Cholecystostomy

The gallbladder was identified by using a MicroMAXX ultrasound (US) system (SonoSite, Bothell, Washington). A 10-F multipurpose drainage catheter (Cook, Bloomington, Indiana) was advanced into the gallbladder percutaneously via a transperitoneal approach under US guidance. Cholecystography was performed with 50 mL iohexol (GE Healthcare Little Chalfont, United Kingdom) to identify the cystic and common bile ducts. The gallbladder contents were then aspirated.

Contrast-Enhanced CT

A contrast-enhanced CT scan of the abdomen was performed (64-slice LightSpeed; GE Healthcare) for anatomic delineation and procedural planning with the use of 100 mL iohexol administered intravenously via a power injector at 5 mL/s. Helical acquisitions at 0.625 mm were reconstructed at 1.25-mm intervals in the axial plane during the arterial and portal-venous phases. Contrast-enhanced CT of the abdomen was performed by using the same technique immediately after the procedure and before euthanasia, with 15-minute delayed images acquired during the latter.

Cryoablation

The Endocare Cryocare cryoablation system (Endocare, Irvine, California) was used. Four PCS-24 cryoprobes (Endocare) were used in 2 experiments, and one 8-mm cryoprobe was used in 1 experiment. Two different technical approaches were chosen to explore any potential safety advantages and differences in technical difficulty with 4 small-diameter punctures or 1 large-diameter puncture.

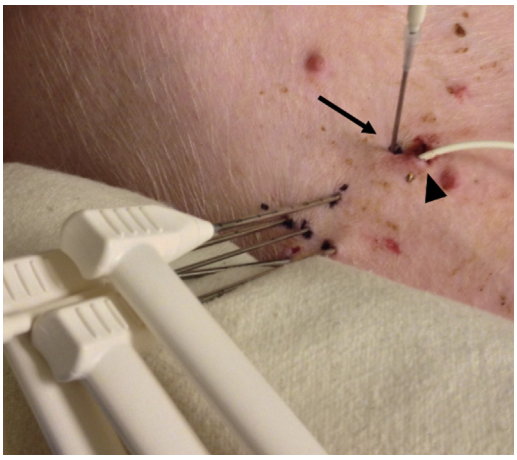

Figure 1. Procedural photograph demonstrates lateral subcostal approach for PCS-24 cryoprobe placement. Note the thermocouple (arrow) and cholecystostomy tube (arrowhead) in place.

PCS-24 cryoprobes were positioned percutaneously at the gallbladder margins under CT guidance by using a lateral subcostal approach (Fig 1). The 8-mm cryoprobe was inserted centrally within the gallbladder lumen through a 24-F introducer sheath, which had been advanced into the gallbladder lumen following CT-guided percutaneous access and serial dilation. Two freeze/thaw cycles were performed with noncontrast CT scanning at 2-minute intervals to assess the extent of ice-ball formation. Freeze cycle duration was varied to achieve 5-mm ice-ball coverage beyond all gallbladder margins and avoid nontarget ablation. Vital signs were recorded throughout the procedure. The cryoprobes and cholecystostomy tube were removed after the second freeze cycle.

Follow-up

Complete blood count and liver function tests were performed at baseline, postprocedure day 4, and the time of euthanasia. Daily assessment of activity level, behavior, food and fluid intake, and weight was performed by the veterinary staff. Intramuscular buprenorphine 0.1 mg/kg, twice daily for 2 days, was used for postprocedure analgesia. Animals were euthanized via intravenous injection of potassium chloride at 4, 30, and 48 days following completion of the procedure, respectively. Cholecystography was performed at autopsy by direct puncture of the gallbladder with a 19-gauge single-wall needle and injection of 20 mL iohexol under fluoroscopic observation. The gallbladder and surrounding liver tissue were resected en bloc and fixed in formalin for sectioning at 3-mm intervals. Histologic examination was performed by a member of the team experienced in swine histopathology (M.S.) following hematoxylin and eosin or Masson trichrome staining. The entirety of the gallbladder (ie, fundus to neck) was examined to exclude the presence of incomplete ablation or mucosal regeneration.